Optimising the Outcome of Lower Limb Arthroplasty

By

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Abstract
This study was an exploration of numerous factors that influence patient outcome following hip and knee arthroplasty surgery. Total hip and knee arthroplasty are two of the most commonly performed orthopaedic procedures to relieve pain and improve joint function the most commonly indication being osteoarthritis. Surprisingly, understanding which patients will achieve optimal benefit is important but remains difficult and controversial. This is confounded by an increasing active and ageing population, with high inherent expectations. Furthermore, young patients present for hip and knee replacement surgery hoping to restore their quality of life, which typically includes physically demanding activities.

Advances in bioengineering technology have driven prosthesis development but universal economic constraints in healthcare services dictate that further developments will be governed by their cost-effectiveness. It is with this background that necessitates every facet of patient care being evaluated to optimise outcome.

The narrative of this study reflects the patient clinical pathway:
- Pre-operative care and optimization
- Intraoperative interventions
  - Biomechanical prosthesis stability
  - Pharmaceutical adjuncts
  - Infection eradication
- Post-operative complications
- Analysis of patient outcomes

This study incorporates 24 peer-reviewed journal articles published since 2006 representing a portion of my entire research portfolio. The published work spans my surgical career to date from junior doctor, Masters student, higher surgical trainee, clinical fellow, consultant surgeon and senior clinical lecturer. The data and development related to these articles originates from a spectrum of clinical and academic institutions, namely local district general hospital, UK teaching hospital, specialist orthopaedic hospitals and world renowned academic centres.

The conclusions drawn from this study highlight only some of the facets of the patient clinical pathway and demonstrate the need for ongoing research into this topic.
Acknowledgments

I am forever indebted to Katie, my wonderful wife, and our boys Harry and Charlie. They are what it is all about.

I want to thank my mum and dad; to whom I owe so much, in so many ways.

I wish to thank David Ricketts & Matt Solan as friends, colleagues and mentors. Their continued professional support has been crucial to both my academic and clinical career. I am very grateful for their ongoing help and guidance.

I would like to acknowledge the huge contribution Mr Tom Roper has made, and continues to make, to research I continue to be involved with at Brighton & Sussex Medical School. He has helped provide the article metrics that are included in the appendices of this study. My eyes are now open to the skill and experience of clinical librarians, and also to ‘altmetrics’.

Research is impossible without collaboration and teamwork. I am indebted to all the co-authors that have helped me with the various projects that are incorporated in this study. I have made many friends in the process.
Dedication

This work is dedicated to a great friend, colleague, co-author and mentor.

He is missed by many.

Neil Bradley

Declaration

I declare that whilst studying for the degree of Doctor of Philosophy by Publication by the University of Portsmouth I have not been registered for any other award at another university. The work undertaken for this degree has not been submitted elsewhere for any other award. The work contained within this submission is my own work and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due acknowledgement has been made in the text.

Benedict Aristotle Rogers

October 2017
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Preface

Hip and knee replacement surgery is increasing common in an aging population and this thesis is divided into chapters that analyse separate aspects of care at each step on the patient pathway, namely: pre-operative care, intra-operative care, post-operative complication and assessment of surgical outcomes. This thesis does not, and cannot, afford a complete discourse surgical care.

The thesis provides a narrative that combines 24 published peer reviewed articles that I have authored or co-authored over ten years. The table in subsequent pages sets out the complete collection of articles, including title, study design and size, along with futures areas of research.

In the appendices of this thesis, all articles are included in their full text format in addition to their citation metrics and as such this body of published work on Optimising the Outcome of Lower Limb Arthroplasty contributes to knowledge in this field.
## Published Articles

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Chapter 1 - Introduction

Knee and hip replacement surgery are frequently performed and highly successful for pain relief and functional improvement in people with advanced arthritis. The most common indication for the procedure is osteoarthritis (1). The goals of hip and knee replacement surgery include pain relief, functional improvement and satisfaction (2). Such surgeries are now increasingly considered for patients younger than 55 years, making improved decision making about whether a patient should undergo the procedure and subsequent optimisation of outcomes important (3). This thesis cites, in the addition to others, twenty-four scientific peer-reviewed papers that I have authored that consider pre-operative (4–8), intra-operative (9–17) and post-operative (18–27) factors that influence patient outcomes. The full text manuscripts of these twenty-four papers are included in the appendices.

There are significant clinical and fiscal implications of sub-optimal outcomes and complication associated with these operations. This impacts on the patient, clinicians, hospital resources and wider society especially in the UK with an aging demographic with increasing expectations. As such the demand for hip and knee replacement surgery has been predicted to increase, in conjunction with patient expectations (28,29). In addition to an ageing population there is a well-documented increase in co-morbidities, with obesity being highlighted as of particular concern by the recent report of the UK Chief Medical Officer, which has received wide media coverage (30,31).

Patients undergoing lower limb joint replacement surgery transition through a common clinical pathway from pre-operative status, the hospital admission and surgical procedure, the post-operative clinical outcome with the concurrent risk of complications. This clinical timeline provides the framework for this dissertation, considering the optimisation of various aspects of each phase of the patient pathway.

Numerous factors influence the clinical outcomes, some of which are not fully understood and this thesis is not an exhaustive discourse, rather an examination of a selection of some key factors. However, the optimisation of these common operations will undoubtedly afford benefits for patients and carers, hospitals, clinicians and the wider society.

Pre-operative care commences with the appropriate and timely referral from primary care and novel models have now evolved (8). The pre-emptive identification and treatment of anaemia in patients awaiting hip replacement is a simple but effective way of optimising one
common peri-operative problem (6). With an ageing demographic, patients with multiple co-morbidities and a high surgical risk is common and delivering safe surgical care of this cohort is increasingly important (4,5).

Specific surgical technique planning is required for all surgical procedures, but particularly in complex cases. Developmental dysplasia of the hip (DDH) presents as hip in-congruence secondary to low or high dislocation (32). Pathological changes include flattening or inversion of the labrum and capsular structures (limbus) in association with hypoplasia of the capital femoral ossific nucleus and abnormal acetabular development with a high inclination and reduced femoral head coverage. When considering a total hip replacement for DDH, these anatomical features require specific surgical techniques and implants that highlights the need for optimal pre-operative planning. This is expanded upon with a current concepts review that I was the lead author for (7).

Three facets of intra-operative optimisation are evaluated in this thesis. Firstly, methods to achieve biomechanical stability of the knee and hip prostheses, using a variety of techniques including structural allograft and porous metal implants (16,13,10,17). Secondly, techniques used to optimise the eradication of periarticular infection, including antibiotic elution from cements spacers in both the hip (15) and the knee (14,33). Finally, the use of pharmaceutical adjunct to minimise post-operative complications and enhance recovery are reviewed, considering both the use of tranexamic acid in hip hemiarthroplasty surgery (11) and high volume multimodal wound infiltration in total knee arthroplasty (9).

There are two serious post-operative complications that have been focused upon, namely venous thromboembolism (VTE) and heparin-induced thrombocytopenia. Various overall aspects of VTE following orthopaedic surgery are reviewed (24) in addition to an analysis of whether adequate VTE prophylaxis is being achieved (21). A more detailed study of patient compliance with oral factor Xa inhibitor (Rivaroxaban), a modern therapeutic adjunct, following hip and knee replacements is included (18). Finally, a recent systemic review analyses the use of aspirin for VTE prophylaxis in the context of modern surgical practice (27).

Heparin-induced thrombocytopenia is a potentially fatal complication following the use of low molecular weight heparins are commonly used after lower limb arthroplasty surgery. This was evaluated as an initial overview (25) and subsequently as an audit and international review (23).
The evaluation of surgical outcomes remains a topic of much ongoing research. This thesis includes two aspects of the measure of surgical outcomes. Firstly, outcomes that are non-patient reported including the radiological methods of patellar height measurement after knee replacements (26,34) and the outcome of total hip replacement for hip fracture in octogenarians by dislocation rate, 30-day and one year mortality, revision surgery and periprosthetic fracture (19). Secondly, the use of patient reported outcome measures to assess healthcare quality in general (20) and then a specific analysis of patient satisfaction following THA and its association with pre-operative Western Ontario and McMaster score (22).
Chapter 2 - Pre-Operative Optimisation

The increasing incidence of lower limb degenerative joint pathology and the increasing demand for surgical intervention has led to initiatives in the UK to streamline the initial patient referral and avoid unnecessary hospital out-patient appointments. The NHS Plan formalised the concept of General Practitioners with Special Interests with the aim of providing ‘over one million out-patient appointments in the community rather than hospital’ (35,36). The evidence base for the effectiveness for triaging patients for surgical procedures by non-surgeons remains unclear as highlighted in a prospective study I conducted (8). We demonstrated that time delays, patient confusion regarding professional roles and diagnostic indecision are significant problems for patients subsequently referred to hospital orthopaedic clinics, risking sub-optimal patient care and medicolegal implications.

It is estimated that high-risk surgical patients account for nearly 10% of the total inpatient surgical caseload, whilst account for 80% of deaths after any surgical procedure. The hospital mortality for these patients is 10-15% and is clearly influenced by the efficacy of perioperative care. The difficulties of perioperative management of high risk surgical patients was highlighted by the National Confidential Enquiry into Patient Outcome & Death (NCEPOD) report ‘Knowing the risk – A review of perioperative care of surgical patients’ in December 2011 (37). In response to this, we published a review of the relevance, management principles and key recommendations that came about as a consequence of the 2011 NCEPOD report (4). In particular, with the high caseload of such patients and the widespread implementation of protocol-driven clinical care, we highlighted the need for intensive care clinicians and surgeons to provide a combined care approach. The limitations of the NCEPOD reports were also highlighted.

To date, there is no agreement amongst anaesthetists, surgeons or researchers as to the definition of a ‘high risk’ surgical patient. The NCEPOD have used a clinical anaesthetic assessment with no defined parameters to determine whether a case is considered high or low risk. The Royal College of Surgeons of England published a report on ‘Perioperative care of the higher risk general surgical patient’, within which a pre-operative estimated mortality rate of greater than or equal to 5% to define high surgical risk (38).
Using a predictive model, Bhattacharyya et al. identified five critical risk factors for acute postoperative mortality after orthopaedic surgery (39):

- Chronic renal failure
- Congestive heart failure
- Chronic obstructive pulmonary disease
- Hip fracture
- Age greater than 70 years

In a subsequent paper, I outline the key areas for reducing mortality in high risk surgical patients (5). These areas include:

- Identification of high risk patients (as highlight above)
- Pre-operative assessment, triage and preparation
- Consent and informed patient mortality risk
- Improved intra-operative care
- Improved post-operative resource use

Several detailed reports provide evidence-based guidelines for the perioperative care of high risk surgical patients:

1. Royal College of Surgeons of England/Department of Health 2011
   *The higher risk general surgical patient: Towards improved care for a Forgotten Group* (38)

2. The Association of Anaesthetists of Great Britain and Ireland
   *Recommendations for standards of monitoring during anaesthesia and recovery* (40)

3. National Institute of for Health & Clinical Excellence
   *Acutely ill patients in hospital. Recognition of and response to acute illness in adults in hospital (CG50)* (41)

Pre-operative optimisation of anaemia is one facet of reducing perioperative mortality I investigated with a prospective study of 322 patients undergoing total hip replacement. This study highlighted the benefit of quantifying serum haemoglobin levels early to afford prompt, effective and cheap treatment prior to surgery (6).
Thorough pre-operative planning optimises surgical procedures and the importance of this was highlighted in the Current Concepts Review paper I was the lead author on concerning total hip arthroplasty for adult hip dysplasia (7).
Chapter 3 - Intra-operative optimisation

There are numerous facets of intra-operative clinical and surgical care that can be optimised. This thesis will consider three aspects: structural stability of prostheses, pharmaceutical adjuncts and local antibiotic delivery.

3.1 Structural stability

3.1.1 Hip

Implant stability in hip replacements may be anatomically sub-divided into femoral and acetabular component stability. As the need for total hip replacements increases, the incidence of extensive bone loss will increase as a consequence of massive osteolysis, stress shielding and multiple revisions (42–45).

3.1.1.1 Femoral stability

Proximal femoral bone stock deficiency resulting from massive osteolysis, stress shielding, and multiple revisions provides a major challenge for revision hip arthroplasty and is likely to account for a significant future caseload. Various surgical techniques have been advocated for treatment of proximal femoral bone loss including impaction allografting techniques, distal press-fit fixation and massive endoprosthetic reconstruction (megaprostheses) (46–52).

A series of articles co-authored by myself have examined the use of allograft to reconstruct massive proximal femoral bone loss (13,17,12). This series of articles incorporates a systematic review (12), a meta-analysis (13) and the use in developmental dysplasia of the hip (17).

The systematic review had three principal aims:

i) to document variations in the surgical techniques used,

ii) to assess the clinical outcome of allograft prosthesis composites (APC) for massive proximal femoral bone loss,

iii) to quantify complication rates in relation to the surgical technique used.

Sixteen studies reported on outcomes of proximal femoral composite allograft used to reconstruct major bone defects (see Table 1). All studies were retrospective case series and provided level IV evidence. All studies were published within the last fifteen years. The total number of allograft reconstructions reported in all the studies was 498.
Four studies described the complete resection of the proximal femur as the approach employed; however, the trans-trochanteric approach was the most common reported. The management of the proximal host femur varied. In 9 studies the proximal host femur was fully resected, with 5 studies using the split host proximal femur as an onlay graft after the allograft prosthesis composite had been inserted. Two studies did not detail this aspect of the surgical technique. Four studies reported the use of cortical strut allografts to reinforce the allograft-host junction, with one study reporting use in every case (12) (see Table 1).

<table>
<thead>
<tr>
<th>Study</th>
<th>n=</th>
<th>Primary Diagnosis</th>
<th>Mean follow up (yrs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>30</td>
<td>Aseptic</td>
<td>2</td>
</tr>
<tr>
<td>2</td>
<td>21</td>
<td>Tumour</td>
<td>6</td>
</tr>
<tr>
<td>3</td>
<td>55</td>
<td>Tumour, Aseptic, Septic revision</td>
<td>8.8</td>
</tr>
<tr>
<td>4</td>
<td>14</td>
<td>Tumour</td>
<td>10</td>
</tr>
<tr>
<td>5</td>
<td>15</td>
<td>Aseptic failure</td>
<td>2</td>
</tr>
<tr>
<td>6</td>
<td>50</td>
<td>Septic, Aseptic</td>
<td>16.2</td>
</tr>
<tr>
<td>7</td>
<td>44</td>
<td>Aseptic failure</td>
<td>7.1</td>
</tr>
<tr>
<td>8</td>
<td>72</td>
<td>Aseptic</td>
<td>12</td>
</tr>
<tr>
<td>9</td>
<td>15</td>
<td>Aseptic, Septic loosening</td>
<td>4.2</td>
</tr>
<tr>
<td>10</td>
<td>73</td>
<td>Tumour</td>
<td>6.7</td>
</tr>
<tr>
<td>11</td>
<td>32</td>
<td>Tumour</td>
<td>5.6</td>
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<tr>
<td>12</td>
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<td>Tumour</td>
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<tr>
<td>13</td>
<td>20</td>
<td>Tumour</td>
<td>6.3</td>
</tr>
<tr>
<td>14</td>
<td>25</td>
<td>Aseptic, Septic loosening</td>
<td>4.5</td>
</tr>
<tr>
<td>15</td>
<td>37</td>
<td>Tumour</td>
<td>7.5</td>
</tr>
<tr>
<td>16</td>
<td>15</td>
<td>Aseptic, Septic loosening</td>
<td>7.6</td>
</tr>
</tbody>
</table>

Table 1.
List of papers articles incorporated in a systematic review (12), a meta-analysis (13) regarding the use of proximal femoral allografts.
The success rate was defined as the reported survivorship of the allograft prosthesis composites. The total cohort included 498 patients with a mean follow up of 8.1 years (range 2 to 16 years). The pooled success rate was 81% (95% CI, 77%–86%). This suggests that this technique is valid and durable when performed by suitable trained and experienced surgeons, in institutions with the facilities to support such complex surgery. The infection rate ranged from 0% to over 21%, with a pooled mean of 8%. The two studies with a reported infection rate of over 20% had only 14 and 15 patients, respectively (46,67). Conversely, the four studies reporting the lowest infection rates (0 to 4%) had a mean patient cohort of 40 patients (53–55,58). Dislocation is a significant postoperative complication, however five out of the sixteen studies did not report the incidence of dislocation (46,62,63,65,66). For the eleven studies that did report dislocation rate the mean was 12.8% with a range 0% to 40%. The mean reported dislocation rate in studies that used a technique of splitting the host proximal femur to use as an onlay graft was 9.8%, compared to 14.9% in studies that resected the entire proximal femur.

From the surgical approaches detailed in these studies, the risk of dislocation may be minimized by:

i) preservation of the host posterior capsular structures if possible,
ii) good biomechanical reconstruction of length, version and offset of the prosthesis-allograft construct,
iii) maintaining the bone-soft tissue attachment to the host femur, to provide both mechanical stability and to act as a vascularised graft.

The systematic review concluded that, whilst a range of surgical techniques have been described, the following a key points:

i) high caseload is associated with a lower infection rate,
ii) uncemented distal fixation is associated with a reduced the risk of aseptic loosening or fracture,
iii) if available, using the host femur as an onlay graft enhances hip stability whilst acting as a vascularised graft.

A subsequent paper reported a meta-analysis of the proximal femoral allograft (13). The reported success rates ranged from 66% to 95%. The fixed effect and random effects pooled estimates of success were both 81%. The 95% CI was slightly wider for the random effects analysis (0.77-0.86) compared with that of the fixed effect (0.78-0.86). There was no significant data heterogeneity within the pooled success rate analysis (P = 0.0635).
The quantifiable reported structural failures of PFA reconstructions included fracture and aseptic loosening. The range of reported structural failures was from 0% to 55%.

The pooled estimated of structural failure rate was 15% with both fixed (95% CI, 0.12-0.18) and random (95% CI, 0.10-0.19) effects model analysis. There was a significant level of data heterogeneity regarding pooled failure as an outcome (P = 0.0171), principally the result of a single outlying study.

The reported infection rates ranged from 0% to 20%. The fixed and random effect pooled estimates of infection were 8% (95% CI, 0.06-0.11) and there was no significant data heterogeneity (P = 0.6892) regarding infection as an outcome.

The data relating to structural failure of PFA reconstructions have the highest degree (I²) and magnitude (τ²) of heterogeneity and are the only outcome with statistically significant heterogeneity (P < 0.05). Due to confounding factors, the three commonly reported outcomes were not amenable to meta-analysis; non-union, revision surgery of the PFA, and dislocation.

The implications of the systematic review and meta-analysis on proximal femoral allograft are that logistic and ethical issues make it unlikely that future studies on this surgical technique will provide level III evidence or higher.

Furthermore, although qualitative heterogeneity may exist between the studies, all the studies were conducted at academic orthopaedic units and had been accepted by international peer-reviewed orthopaedic journals. Thus, although continued follow-up and critical analysis of this technique should be encouraged, this systematic review and meta-analysis support the use of PFAs for the reconstruction of massive femoral bone loss.

Developmental dysplasia of the hip is a specific patient cohort where proximal femoral bone loss may present a significant challenge and this was evaluated in a co-authored 2012 JBJS (Br) paper (17). The outcome of 28 patients (30 hips) with developmental dysplasia of the hip who underwent revision total hip replacement in the presence of a deficient proximal femur, which was reconstructed with an allograft prosthetic composite, was evaluated. The mean number of previous total hip replacements was three (1 to 8) and the mean age at primary total hip replacement and at the index reconstruction was 41 years (18 to 61) and 58.1 years
(32 to 72), respectively. The indication for revision surgery included mechanical loosening in 24 hips, infection in three and peri-prosthetic fracture in three. Six patients required removal and replacement of the allograft prosthetic composite, five for mechanical loosening and one for infection. The survivorship at 10, 15 and 20 years was 93% (95% confidence interval (CI) 91 to 100), 75.5% (95% CI 60 to 95) and 75.5% (95% CI 60 to 95), respectively, with 25, eight, and four patients at risk, respectively. Additionally, two junctional non-unions between the allograft and host femur required bone grafting and plating.

This study, in conjunction with the systematic review and meta-analysis of proximal femoral allograft composites, demonstrates that allograft prosthetic composite affords a good long-term outcome in the management of proximal femoral bone loss in revision total hip replacement in patients with or without developmental dysplasia of the hip, while preserving distal femoral host bone.

3.1.1.2 Acetabular stability

Massive acetabular bone loss provides a further challenge for the reconstructive surgeon. Periprosthetic pelvic discontinuity exists when there is loss of structural bone between the superior and inferior aspects of the pelvis, resulting from bone loss or fracture through the acetabulum. I co-authored a paper detailing the management of both acute and chronic cases of pelvic discontinuity (16).

This two-centre international study identified 71 cases of pelvic discontinuity that were classified into acute, less than 12 weeks from primary surgery, or chronic, greater than 12 weeks from primary surgery. All cases were treated at academic tertiary referral units, and all surgeries were performed by senior surgeons. There were 9 acute cases and 62 chronic cases. Of the acute cases, over half were the results of iatrogenic acetabular fractures during the insertion of uncemented acetabular cups.

Diagnosis of pelvic discontinuity was made using the criteria described by Berry (68):

i) a visible transverse pelvic fracture on anteroposterior pelvic or Judet radiographs,

ii) medial offset of the inferior part of the pelvis in relation to the superior part of the pelvis as seen by a break in the ilioischial line,

iii) rotation of the hemipelvis as indicated by asymmetry of the obturator ring on the true anteroposterior pelvic radiograph.
In addition, the senior operating surgeon confirmed the definitive diagnosis of pelvic discontinuity once the entire acetabulum was directly visualized intraoperatively. For chronic cases, porous tantalum components afford bone ingrowth to be achieved with a low percentage of bleeding. A large porous tantalum revision shell provides *distraction* that stabilizes the pelvic discontinuity while forming a bridging construct between the ilium and the ischium. A revision shell used in this manner is usually too vertical and retroverted to safely accommodate an acetabular liner. In addition, because of the inherent instability of pelvic discontinuity, additional protection is required to allow bone ingrowth, and this is achieved with a cup-cage reconstruction. By supplementing the construct with an ilioischial cage, a polyethylene liner can, thus, be cemented at the correct inclination and version, independent of the position and version of the acetabular shell.

Regarding the acute cases, the results demonstrate that acute periprosthetic pelvic discontinuity can be successfully treated with *compression* of the posterior column, principally using a plate supplementing a trabecular metal acetabular revision shell. This clinical evidence suggests that cases of acute periprosthetic pelvic discontinuity possess bone healing potential if compression is achieved, assuming normal bone metabolism, in particular no concurrent infective or neoplastic conditions.

Both the results of both the acute and chronic pelvic discontinuity series highlight the clinical application of porous metal. The work of Bobyn and others has highlighted the beneficial biomechanical properties of porous tantalum metal, including high porosity, high coefficient of friction, and a Young modulus similar to bone (69). These properties have made this biomaterial increasingly popular in revision hip arthroplasty (70–75). The use of porous tantalum in the reconstruction of pelvic discontinuity is attractive because bone ingrowth can be achieved with less than 50% of bleeding host bone contact.

3.1.2 Knee

Similarly, loss of bone stock around the knee can lead to structural instability. Previous infections, tumour, and trauma can all result in bone loss that makes a standard primary total knee arthroplasty impossible without restoration of bone stock. More commonly, bone loss in revision knee arthroplasty is a frequent problem and may occur for any of the aforementioned reasons, osteolysis, periprosthetic fracture, or iatrogenic when components are being removed from host bone. The extent of bone loss will determine whether it may be dealt with by simple autogenous bone grafting, cement, metal augments, porous metal supplementation, or
allograft of various sizes. Large uncontained defects of the knee may be treated with use of a large or massive allograft in conjunction with the total knee.

I co-authored a clinical case series and literature review of structural allograft for treating this such bone loss published as both a book chapter (76) and journal article (10). The primary indications for using structural allografts in the setting of knee arthroplasty are:

i) large uncontained defects that are outside the range of metal augments or thicker polyethylene inserts,

ii) patients that are active and require bone-stock restoration for potential future operations,

iii) patients who are physically well enough to tolerate both the surgical procedure and rehabilitation required for successful outcomes.

A relative contraindication is a patient actively smoking, and cessation programs must be implemented prior to surgery. Lastly, presence of active infection is an absolute contraindication for allograft in the arthroplasty patient.

The review paper highlights the preoperative planning and preparation including the consideration of segmental allografts or allograft-prosthetic composites. Allograft-prosthetic composites being considered for bone defects that are uncontained, often circumferential and involving > 25 mm of femur or > 45 mm of the tibia. A critical principle is avoiding cementing the stems to the host bone. Conversely the allograft side of the stem and implant-allograft interface must be cemented to provide stability to construct. No cement should be present between the allograft-host bone junction as it would potentially interfere with graft incorporation.

The review summarises the outcome data to date.

In one of the earliest papers, Stockley et al. reported 20 knees that had undergone a combination of structural allograft and morselized allograft with 85% survivorship at 4.2 years (77). The lowest reported survivorship is that from Ghazavi et al. with only 67% survivorship at 5 years in their 30 patients (78).

A recent publication by Richards et al. compared cohorts with severe bone loss of bone around total knee arthroplasty using femoral allograft compared with metal augments (79).
Despite the presence of more significant bone loss in the allograft group, these had better clinical outcome scores than the control cohort. This strengthens the argument for allograft use in patients with severe bone loss.

Backstein et al. have one of the largest cohorts to date with 61 patients. The survival rate at 5.4 years was 85.2% (80). Of note in this series, the infection rate was 6.5% (4/61); however, a high union rate of 98.4% (60/61) was seen radiographically.

Structural allograft is a viable method for restoring peri-genicular bone stock. These complex procedures should be performed by surgeons with expertise in revision arthroplasty and with access to a dedicated bone bank. Allograft reconstruction is not indicated in the low demand or elderly patients who would benefit from implantation of an endoprosthesis, which allows rapid mobilization and recovery. Rather, the optimal allograft candidate is a young, higher demand and relatively healthy patient who is likely to require further revisions and can adhere to the rehabilitation protocol. The restoration of bone stock is a key component in choosing allograft in the reconstruction (10,76).

3.2 Therapeutic adjuncts

3.2.1 Tranexamic acid

Minimising blood loss and improving post-operative pain and function can both be enhanced by the use of various chemotherapeutic agents. Tranexamic acid (TXA) is an anti-fibrinolytic agent that binds with plasminogen to competitively block lysine binding sites. This prevents plasminogen interaction with fibrin, thus inhibiting plasmin induced fibrinolysis and clot breakdown. The use of TXA has been advocated in both elective and trauma surgery. However, a thorough literature search showed limited studies investigating the specific use of TXA for hip hemiarthroplasty surgery, despite this patient cohort being particularly susceptible to the effects of blood loss (81–83).

The aim of our study was to evaluate the effect of TXA use on postoperative transfusion rates and haemoglobin (Hb) levels following hemiarthroplasty surgery for hip fractures (11). This was a retrospective cohort study conducted for consecutive hip hemiarthroplasties for fractures between June 2013 and October 2014 comparing patients with or without prophylactic TXA before incision. During the study, 305 hemiarthroplasties were performed with 271 cases eligible. TXA was given in 84 (31%) cases, and both patient groups were matched for known confounding factors. Patients given TXA had a lower transfusion rate.
(6% versus 19%. \( P = 0.005 \)) and less blood loss (Hb drop > 20 g/L) on day 1 post-surgery (26% versus 42%; \( P = 0.014 \)). One transfusion was prevented with every 8 patients given prophylactic TXA. There were no differences in the 30 and 90-day mortality rates with TXA use.

The study demonstrated that TXA is cost-effective, reduces the need for blood transfusions and is safe for all patients undergoing hip hemiarthroplasty for fractures.

3.2.2 Wound infiltration

High volume multimodal wound infiltration is now considered an aspect of enhanced recovery regimes for hip and knee replacement surgery with a variety of therapeutic mixtures advocated.

There are potential benefits of infiltrating high volumes of local anaesthetics around the soft tissues of replaced hip and knee joints. The risk of systemic toxicity is minimized with diluted local anaesthetic solution, affording a high volume to be used. One of the principal advantages is that analgesia agents are administered intraoperatively by the surgeon, thereby minimizing the need for additional invasive procedures.

I co-authored a systematic review, limited to randomised controlled studies, to evaluate if such wound infiltration during knee replacements results in reduced pain and opiates requirement, with early rehabilitation and discharge (9).

Although better pain relief in the immediate postoperative period with wound infiltration is gained after TKA, there is no definite evidence that this leads to a reduction in opiate consumption, the achievement of early milestones, or a reduction in hospital stay. The roles of individual agents in achieving pain relief and the use of percutaneous wound catheter for postoperative doses are also unclear. There are few reports of complications, including falls and delayed mobilization, when femoral nerve blocks are used. Wound infiltration analgesia should be used at the preference of the surgeon and anaesthetist provided regular review of their practice is undertaken to identify any untoward side effects. Further randomized trials with sufficient sample size comparing each outcome, including pain scores, opiate consumption, and length of hospital stay, should be undertaken.

3.3 Infection control
3.3.1 Knee

Periprosthetic joint infection frequently necessitates a two-stage revision, in the knee frequently using articulating antibiotic cement spacers. The chemotherapeutic benefit of cyclical loading of cement spacers was investigated in a basic science study led (14).

The effects of articulation, specifically cyclical fatigue loading, on the elution of antibiotics from polymethylmethacrylate cement knee spacers has not been clearly defined. The maintenance of joint movement is an advantage in maintaining the condition of the soft tissues, but the question arises as to whether the articulation per se influences the biology and pharmacokinetics of antibiotic elution. Tobramycin has a broad antimicrobial action with minimal effect on polymethylmethacrylate strength, while vancomycin is effective against methicillin-resistant Staphylococcus aureus and Staph. epidermidis with similarly low adverse biomechanical effects on polymethylmethacrylate (84–86). Our in vitro study considered the differential effect of static or dynamic loading on the elution of vancomycin and tobramycin with a null hypothesis proposing that the cyclical loading of cement spacers has no significant effect on elution.

The results provide evidence that, in addition to the benefit to the soft tissues claimed for articulating spacers, the dynamic loading of cement knee spacers per se affords a biological advantage by significantly enhancing antibiotic elution. The precise mechanism of antibiotic release from bone cement is uncertain. It is generally thought that it is directly released from the surface of the bone cement in the initial phase, and then subsequently released from a network of cracks and voids (87–90). Absorption of water to bone cement is thought to have a role in controlling the slow phase of antibiotic release (88–90). Our study suggests that cyclical dynamic loading enhances this process, probably by a mechanism of cyclical changes in the microstructure of the bone cement.

Further related work has been published by other authors to evaluate whether the indentation of bone cement spacers with a MacDonald dissector increased the elution of antibiotic in vitro (91). Using an ‘area under the curve’ analysis, gentamicin elution was seen to be increased with cement indentation. Colleagues and I submitted a letter of reply to this article, raising methodological concerns regarding the buffering solution used, the effect of cyclical loading amplitude and the mechanical effect of multiple indentations on the biomechanical properties of the construct (33).
3.3.2 Hip

I subsequently co-authored a study evaluating a novel surgical technique for achieving the same cyclical loading of cement spacers in the hip (15). Using cement augmentation of the acetabulum in revision hip arthroplasty for infection, this technique afforded enhanced mechanical stability in addition to improved antibiotic elution.

In summary, following thorough debridement, a cement acetabular shelf is formed utilising cancellous screws inserted into the supra-acetabular rim; upon which antibiotic loaded bone cement/ polymethylmethacrylate is allowed to set. This construct affords improved acetabular coverage and hence improved hip stability, whilst articulation with a standard femoral cement spacer provides the potential benefit of increased antibiotic local elution.

In this small published case series, fifteen infected hip protheses underwent removal, cement acetabular augmentation and insertion of a femoral cement spacer. Eleven hips had successful infection eradication and subsequently underwent a second stage revision procedure a mean duration of 15 weeks (range 9–48 weeks) after the first stage.

No dislocations or fractures of the cement spacers were observed. In addition, no cases of antibiotic-associated renal toxicity have occurred, although this technique should be used with caution in patients with significant renal impairment. Second-stage reconstruction was considered only when there was clinical and serological evidence of infection eradication.
Chapter 4 - Minimising post-operative complications

4.1 Venous thromboembolism

In a series of six published papers I have evaluated various aspects of venous thromboembolism (VTE), including deep vein thrombosis (DVT) and pulmonary embolism (PE), some of the commonest complications following hip and knee replacement surgery, and how this can be minimised (24,21,18,27,25,23).

Current estimates suggest that if no measures are taken following hip or knee replacement surgery, the incidence of fatal PE is approximately 0.4%; equating to over 5,000 fatalities a year for the 1.5 million surgical procedures. I published a review of thromboprophylaxis in orthopaedic surgery in 2010 highlighting that numerous guidelines and evidence have been published, though none to date incorporate newer treatment modalities such as oral factor Xa inhibitors (24). The individual patient VTE risk reflects combined patient and surgery specific factors (see Box 1 below).

Box 1: Surgical risk factors for VTE

- Lower limb surgery higher risk than upper limb
- Degree of soft tissue/bone dissection
- Joint or limb position during surgery
- Positioning of retractors during surgery
- Length of surgery
- Amount of blood loss

Historically there was undoubtedly clear evidence for the need for VTE prophylaxis because the incidence of VTE events after THR approached 50% in patients in whom no preventive measures were taken (92). Contemporary surgical procedures and postoperative regimens have drastically changed over the last three decades, and the incidence of untreated VTE is now likely to be substantially lower.

The review highlighted that VTE prophylaxis is multi-factorial and both the clinician and patient should be aware of this. However, the plethora of published guidelines on this subject is a cause of potential confusion and there are several factors that cause resistance to their
implementation, including a lack of awareness, perceived conflicting evidence, practicality, the low overall incidence and bias.

Education of the clinician and patient is vital because not only is the incidence of VTE greatest after the patient has usually been discharged, but also patient; compliance with the general measures will help reduce risk. With the likelihood of numerous future publications on this topic, the clinician should endeavour to remain up to date with the best available contemporary evidence to guide clinical practice.

Studies investigating the incidence of postoperative VTE demonstrate that the mean time to thromboembolism is greater than previously estimated. Two large meta-analyses advocate VTE prophylaxis be continued for up to 4 weeks following total hip arthroplasty surgery (THA) (93,94). Concern now exists that the length of treatment varies depending upon the prophylaxis used.

Two commonly used pharmaceutical options for VTE prophylaxis in the UK are low molecular weight heparin (LMWH) and oral Factor Xa inhibitors (e.g. rivaroxaban). I published a two-part study to assess, using a local audit and international survey, the duration of VTE prophylaxis currently achieved with LMWH and to examine whether this may be improved with the use of rivaroxaban, an oral Factor Xa inhibitor (21).

The survey demonstrated that four out of 39 (10.2%) units that routinely prescribe LMWH do so for at least 4 weeks following surgery. The audit demonstrated that rivaroxaban afforded a superior mean duration of postoperative VTE prophylaxis (35 days versus 5.4 days; P < 0.05) and superior patient satisfaction. There was no difference in the incidence of bleeding, wound infection or thrombotic complications.

Therefore, patients are exposed to an increased VTE risk following hip replacement surgery due to the inadequate prescription of LMWH. This is poor clinical practice, contrary to current evidence-based guidelines and has potential medicolegal implications. However, rivaroxaban affords a superior patient compliance compared with subcutaneous LMWH, thus ensuring that patients receive VTE prophylaxis for the current recommended period of time.

This study was then supported and superseded by a larger study (n = 3,145) on patient–reported compliance with rivaroxaban following hip and knee arthroplasty (18) whereby patients completed an anonymous self-administered questionnaire six weeks after surgery.
Postoperatively 2947 (94%, 2947/3145) received rivaroxaban. Two thousand eight hundred and twenty-four patients (96%, 2824/2947) completed all in-hospital doses. Seven per cent (203/2824) of patients did not attend the 6-week follow-up. Two thousand one hundred sixty-three (83%, 2163/2621) completed all prescribed doses, 98 (4%, 98/2621) were non-compliant and 360 (14%, 360/2621) had incomplete data. Gender, age, body mass index and preoperative haemoglobin all correlated with non-compliance ($P > 0.05$). Type and side of surgery did not correlate with compliance. Patient-reported non-compliance for rivaroxaban is 4% which compares favourably to other VTE prophylaxis modalities.

4.2 Heparin induced thrombocytopenia

Heparin induced thrombocytopenia (HIT) is associated with thrombosis, independent of heparin type, dose or route of administration and is one of the most important immuno-haematological problems in clinical medicine. With the increased use of low molecular weight heparin (LMWH) for venous thromboembolism prophylaxis following hip and knee arthroplasty surgery, orthopaedic clinicians need to be aware of HIT and its management. We published a review article highlighting the incidence, required monitoring, treatment and lack of insight about HIT (25).

In summary, the use of a simple monitoring protocol can facilitate the prevention of HIT, based upon guidelines from the British Society of Haematology (95).

- All patients who receive heparin (of any form) should have a platelet count on day one of commencing treatment.
- All patients receiving LMWH should have platelet counts every 2-4 days from day 4 – 14 whilst on treatment
- If the platelet count drops by 50% or below normal lab limits, HIT should be considered and heparin stopped and haematological consultation obtained.

This review article was subsequently followed by an local audit and international survey of HIT following surgery (23). An initial patient survey demonstrated that only 2 out of 48 at-risk patients (4%) had a full blood count performed more than four days after commencing LMWH. Following the dissemination and implementation of the above guidelines, a second survey demonstrated a significant improvement ($P < 0.05$), with 23 out of 40 (57.5%) at-risk patients having a full blood count performed more than four days after commencing LMWH.
The secondary survey demonstrated a significant improvement ($P < 0.05$) in the monitoring of HIT compared with the primary survey (57.5% compared to 4%).

This audit demonstrated that the risk of HIT, a potential fatal complication of LWMH use, can be substantially reduced by the simple clinical audit. In addition, a subsequent telephone survey highlighted a low awareness of both the condition of heparin-induced thrombocytopenia and the BSH guidelines and no units routinely monitored for HIT.
Chapter 5 – Clinical outcomes

Evaluating the overall outcomes remains a topic of much ongoing research and debate. Numerous methods are employed and overall may be categorised into two groups:

- Non-patient reported outcome measures (non-PROMS)
- Patient reported outcome measures (PROMs)

5.1 Non-patient reported outcomes measures

I have evaluated and published objective non-PROMs data for total hip replacement surgery for fractures in octogenarians (96). The purpose of this study was to establish the safety profile, survival and short-term results for patients of 80 years and over who received THA for fracture according to United Kingdom National Guidelines (97). Functional outcome scores such as the Oxford/Harris Hip Scores were not performed.

Over a two-year period, 354 patients aged over 80 years were admitted with a displaced intracapsular hip fracture. Using defined clinical guidelines, 38 patients underwent THA with a median age of 84 years, mean follow-up of 20 months. There were no dislocations or periprosthetic fractures and patient survival was 97% at 30 days and 87% at one year. There was one revision for deep infection.

The management of hip fracture in elderly patients is an increasingly important aspect of orthopaedic care worldwide. This study shows that THA is a safe and efficient use of resources when performed in selected patients over 80 years old. This represents a significant caseload for orthopaedic services within the United Kingdom and is likely to increase in the future. In the UK projections estimate that the incidence will rise from 70,000 patient events per year in the UK to 101,000 by 2020 (98,99). The potential cost of treating all fragility fractures in this patient population is £2.2 billion per year (100). Several randomised studies have supported the use of arthroplasty over internal fixation of displaced intracapsular fractures (101,102).

This study demonstrates that THA in suitably selected octogenarians can produce excellent short term results without a high risk of complication. However, evidence regarding the long-term cost-effectiveness and patient related outcomes of these patients will require a much larger patient cohort. An increasingly active elderly population now expects optimal functional capability following a fracture of the femoral neck. This study demonstrates that
total hip arthroplasty for selected octogenarians afford a low complication rate with the
majority of patients returning to independent living.

In a separate study the measurement of patella height, key to effective knee function
following total knee replacement, was evaluated (26). In particular, the relative
reproducibility and accuracy of four ratios used to measure patellar height, namely the
Blackburne-Peel, Caton-Deschamps, Insall-Salvati and modified Insall-Salvati, before and
after total knee arthroplasty. The radiographic study analysed 720 measurements per each of
two independent observers. It demonstrated that the theoretical advantage of using the Insall-
Salvati and modified Insall-Salvati ratios in measuring true patellar height after total knee
arthroplasty needs to be balanced against their significant inter-observer variability and
inferior reliability when compared with other ratios.

Whilst numerous methods exist for measuring a patella height, both clinicians and academics
should be aware of their inherent limitations. This is something that can be extrapolated to
numerous clinical measurements.

5.2 Patient reported outcome measures

Patient-reported outcome measures are standardized, validated questionnaires that are
completed by patients to measure their own functional status and general health. They were
originally designed for use in clinical trials (103). Since 2009, wider use of patient-reported
outcome measures within the NHS has been proposed to augment mortality data from
Hospital Episode Statistics, which are considered an insufficient measure of quality.

Specific examples of the processes and outcomes that may be quantified with patient-reported
outcome measures data

Processes
1. Communication: improved communication between patient and health-care provider
2. Concordance: agreement between patient and health-care provider about problems
and solutions
3. Provider behaviours: changes in health-care providers’ diagnosis and treatment of
patient conditions
Outcomes

1. Patient satisfaction: patient-reported satisfaction with the consultation, treatment or care overall
2. Health status: patients’ health and wellbeing as indicated by clinical measures or patient reports
3. Resource use: patients’ subsequent use of health and other services.

Furthermore, controversies exist regarding the widespread implementation, data collection and interpretation of PROMs within the UK and internationally (104). I published a review article that considered some of the relevant issues inherent in collecting and analysing patient-reported outcome measures data (20).

In a further study, for which I was the lead author, standard PROMs for total hip replacement were evaluated in relation to patient satisfaction (22). The rationale for this study was that the routine collection of patient-reported outcome measures (PROMs) has been introduced in several countries, not only to quantify success but also as a possible means of defining a threshold for surgery (104).

Prospective data for a cohort of patients undergoing total hip replacement from two large academic centres were collected, and pre-operative and one-year post-operative WOMAC scores and a 25-point satisfaction questionnaire were obtained for 446 patients. Satisfaction scores were dichotomised into either improvement or deterioration.

Satisfaction was compared using receiver operating characteristic (ROC) analysis against pre-operative, post-operative and δ WOMAC scores. The results demonstrated that pre-operative WOMAC score does not predict the post-operative WOMAC score or patient satisfaction after THA. The results imply that WOMAC scores can therefore not be used to prioritise patient care.

Expanding the use of PROMs to prioritise patients for surgery remains controversial and currently lacks a substantial base of evidence. A recent study based in the United Kingdom which prospectively analysed a cohort of 1,523 total knee arthroplasties (TKAs) and 1,784 THAs demonstrated that the pre-operative Oxford hip and knee scores did not predict post-operative patient satisfaction and should not be used to prioritise care (104). Thus, both WOMAC and Oxford hip and knee scores are unsuitable for predicting outcomes and satisfaction, and therefore should not be used to prioritise patient care.
Whilst the use of PROMs is valued for its transparency with the aim to improve the quality of surgical care, their use is not without difficulty. Further large studies are required to refine and quantify the use of PROMs in all aspects of lower limb arthroplasty surgery.
Chapter 6 - Conclusions

This thesis highlights multi-faceted nature required to optimise the outcomes of hip and knee replacement surgery, which are increasingly common surgical procedures. The collection of 24 published peer reviewed articles I have co-authored represents only a small fraction of the possible interventions and evaluations. In addition, numerous innovations are likely to be developed in this field in the coming years and this study highlights the need for each to be rigorously evaluated.

Furthermore, understanding the complex interaction between the human, prosthetic, physiological and pharmaceutical factors that influence patient outcome, some of which have been evaluated in this study, remains not fully understood. These interactional factors are inherent in the complexity of patient care in its entirety, not only in orthopaedic surgery. As such, the understanding multifactorial systems is relevant to the wider field of medicine.

It remains clear that further research is required in every aspect of surgical care along the patient pathway for lower limb arthroplasty. As modern western societies have an increasingly populous and ageing demographic, global fiscal constraints will dictate a close evaluation of all aspects of care to optimise clinical outcomes of lower limb arthroplasty. Clinicians, scientists and academics must continue to question and evaluate all interventions, with the aim of delivering surgery that is both safe and of the highest quality.
Chapter 7 - Future Work

This thesis brings into relief several aspects that warrant further investigation and would afford a positive impact on the knowledge base and clinical care. The following are further research questions I wish to pursue.

1. *What is the effect of physiotherapist-lead clinics on lower limb arthroplasty operation rates?*
   
   A retrospective case study may provide sufficient clarity to afford a significant differential operation rates & time-to-surgery for two patient cohorts, namely those referred directly to secondary care and those referred via a physiotherapy-lead clinic. The study would follow on from the retrospective case-series analysis of Multi-professional triage teams (MPTT) (Rogers, Kabir & Bradley 2008) and be augmented with a cost-benefit analysis. The rationale for such a study is the continuing changes in the access to secondary care lack clinical or financial evidence. The results of such a retrospective case study could form part a service improvement audit cycle, thereby leading to a prospective study directly comparing physiotherapy-lead clinics with traditional surgeon-lead clinics.

2. *What is the cost-utility outcome of an expanded pre-operative screening protocol for elective orthopaedic surgery?*
   
   Pre-operative screening forms a critical stage in the patient pathway for elective orthopaedic surgery and there is the potential for further reductions in clinical risk with concurrent cost saving. The optimal amount of pre-operative health screening to maximise clinical and cost benefit is not defined. Furthermore, it is probable that a non-linear correlation exists between increasing financial cost (of healthcare screening) and clinical benefit. Defining this correlation will have potential significant clinical and economic benefits. A retrospective case series study may afford sufficient data to allow regression analysis to highlight the cost-utility of the individual components of pre-operative assessment. However, retrospective studies may have insufficient statistical power, but afford data for power analysis to plan prospective studies.

3. *How surgical risk is defined in lower limb arthroplasty patients?*
   
   The reviews included within this thesis highlight the need for a formal systematic review, considering the current published evidence, which defines high perioperative
risk for lower limb arthroplasty. Currently no specific definition exists for high risk
directly validated for hip and knee surgery. In addition, there are no existing
registered relevant protocols published on PROSPERO – International prospective
register of systematic review¹.
To conduct a systematic review on surgical risk for lower limb arthroplasty, search
terms must be adjusted to incorporate elective and trauma surgery, with publication
date date limits to ensure relevance to modern surgical practice.

4. **How do we stratify risk for hip fracture patients proceeding to total hip arthroplasty?**
   Based upon the data & information used from the systematic review of surgical risk
   (see point 2 above) I would aim to develop a validated risk scoring system for patients
   who have sustained hip fractures and are proceeding to joint replacement surgery.
   The data points for such a scoring system are likely to incorporate assessments of
   numerous physiological, pathological and social parameters. Considering the ongoing
   healthcare fiscal constraints, a scoring system will need to incorporate a cost analysis
element. To my knowledge, no pathology-specific scoring systems currently involve
clinical and economic components, which could be viewed a significant omission
considering the projected burden of hip fractures.

5. **What is the comparative cost of cemented versus uncemented hip replacements?**
   This research question will necessitate the design and development of a randomised
   clinical trial to identify the current and projected costs of the two main types of hip
   replacements. A full health economic analysis of the entire patient pathway would be
   required and the study could utilise mandatory data, such as the UK National Joint
   Registry. Such a randomised cost-based study, combining clinical and dedicated
   fiscal outcomes, could provide a template for the analysis of other facets of surgical
care.

6. **What is the comparative venous thromboembolic event (VTE) risk following lower
   limb arthroplasty. A prospective multi-centre clinical study of aspirin versus low
   molecular weight heparin and oral antithrombotic agents.**

¹ Centre for Reviews and Dissemination, University of York, UK.
https://www.crd.york.ac.uk/PROSPERO
This continues to be an important clinical question with proponents for and against the use of aspirin for VTE thromboprophylaxis following hip and knee replacements. The studies presented in this thesis highlight a clear rationale for Level 1 evidence on this topic. I aim to instigate such a study with the involvement and collaboration of numerous key stakeholders, including the National Institute for Clinical Excellence (NICE), British Hip Society (BHS)/British Association for Surgeon of the Knee (BASK), British Orthopaedic Association (BOA), British Haematological Society, and Royal College of General Practice (RCGP). An initial expression of interest and support from all stakeholders will be essential, followed by an agreement of methodology. This study will require non-pharma funding and will involve high recruitment numbers to meet statistical significance. In addition, a practical design to compare aspirin against NICE–approved anticoagulation will be needed to facilitate recruitment. The primary outcome measures would include the rate of clinical detected, and imaging confirmed, venous thromboembolic event at three weeks after knee replacement and four weeks after hip replacements. These periods being the NICE-recommended duration of chemoprophylaxis following lower limb arthroplasty. The patient cohorts will need to be matched for pre-operative thromboembolic risk using approved and validated scoring systems currently in clinical use.

7. Why does vancomycin elution from bone cement not increase with weight bearing articulation?

The basic science publications presented in this thesis demonstrate the differential elution characteristics of tobramycin and vancomycin from bone cement under weight-bearing articulation ex-vivo. Our understanding of the interaction between antibiotics, bone cement (polymethyl methacrylate) and loading is incomplete. Furthermore, the clinical implication of this is unclear. A translational clinical study comparing the clinical outcomes of 1st stage revision total knee replacements using articulating bone cement spacers with either tobramycin and vancomycin should be conducted. Such a prospective clinic study should be undertaken in a small number of tertiary centres that undertake a high volume of such cases. In addition, and with the appropriate consent and ethical approval it would be feasible to conduct a double-blinded study.
8. *How do we define patient satisfaction after lower limb arthroplasty?*

This thesis has demonstrated that numerous validated Patient Reported Outcomes Measure (PROMs), including Oxford Hip Score (OHS) & Western Ontario McMaster scores (WOMAC), do not correlate with patient satisfaction after lower limb arthroplasty. If patient satisfaction is deemed a key outcome measure, then it must be incorporated, or correlated, to a specific PROM. I am currently undertaking a systematic literature review to evaluate whether any such measures currently exist.

Furthermore, there are increasing reports that inappropriate criteria, such as pre-operative Oxford Hip Score and Body Mass Index, are now used to ration the access to healthcare, despite a clear lack of scientific evidence. This highlights the need to critically review whether these scoring systems are being implemented correctly and if there is a role for an amended or update PROM that more readily reflects patient satisfaction.
References

References in **bold** contribute to body of published work submitted in evidence for the award of PhD by publication.


36. Improvement, Expansion and Reform; the next 3 years. Priorities Plan Framework 2003-2006, Department of Health (UK), 2002


60. Lee SH, Ahn YJ, Chung SJ, Kim BK, Hwang JH. The use of allograft prosthesis


### Additional Published work in trauma and orthopaedics

<table>
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</tr>
</tbody>
</table>
Scientific Publications


48. Rogers BA, Thornton-Bott P, Cannon SR, Briggs TWR. Interobserver variation in the


Book chapters

1. Rogers BA, Garbedian S, Kauhinad R, Safir OA, Gross AE

2. Rogers BA
   Lower limb – pelvis, hip, femur, and tibia
   In Trompeter A Elliot D, editors Trauma for the FRCS (Tr + Orth).
   Oxford: Oxford University Press; 2015

3. Rogers BA, Garbedian S, Kauhinad R, Safir OA, Gross AE
   Developmental Dysplasia of the Adult Hip
   Mazon, Diaz, Fairen & Suarez, editors In Displasia de Cadera del Adulto. 2nd Edition,
   Madrid: Ínecot; 2011.

4. Kauhinad R, Rogers BA, Garbedian S, Safir OA, Gross AE
   Structural Allograft for Bone Loss in the Knee – Arthroplasty Options
   In Prof G Bentley editor. European Textbook of Surgical Orthopaedics and Traumatology
   London: Springer-Verlag; 2014

5. Rogers BA
   Hand Examination. In Rapid Orthopaedic Diagnosis,
   Editor Seyed Behrooz Mostofi
   London: Springer-Verlag; 2008
Published letters

1. Benedict A Rogers & NJ Little
   Surgical site infection with methicillin-resistant Staphylococcus aureus after primary total hip replacement
   J Bone Joint Surg Br., Nov 2008; 90-B: 1537

2. Benedict A Rogers & S Rang
   Intra-Articular Block Compared with Conscious Sedation for Closed Reduction of Ankle Fracture-Dislocation

3. Benedict A. Rogers & S Rang
   Femoral Nerve Block for Diaphyseal and Distal Femoral Fractures in the Emergency Department

4. Benedict A. Rogers
   Patella Alta: Association with Patellofemoral Alignment and Changes in Contact Area During Weight-Bearing

5. Benedict A. Rogers & DM Ricketts
   Can Vitamin C Prevent Complex Regional Pain Syndrome in Patients with Wrist Fractures?

6. S Phillips & BA Rogers
   Rivaroxaban for thromboembolism prophylaxis after orthopaedic surgery
   Anaesthesia Oct 2010;(65)10:1043-1044

   Medium- and long-term results of high tibial osteotomy using Garches external fixator and gait analysis for dynamic correction in varus osteoarthritis of the knee
   http://www.bjj.boneandjoint.org.uk/content/98-B/5/601
   14th June 2016

8. SS. Folkard, A Ray, DM Ricketts, BA Rogers
   Arthroscopic fixation of an avulsion fracture of the tibia involving the posterior cruciate ligament
   http://www.bjj.boneandjoint.org.uk/content/97-B/9/1220.abstract/reply#jbjsbr_el_9838
   11th Nov 2015
9. A Ray, DM Ricketts, BA Rogers
A combination of subscapularis tendon transfer and small-head hemiarthroplasty for cuff tear arthropathy: a pilot study
www.bjj.boneandjoint.org.uk/content/97B/8/1090.abstract/reply#jbjsbr_el_9843
13 October 2015

10. DG Wilson, E Lindisfarne, MA Khan, DM Ricketts and BA Rogers
The influence of age, gender and treatment with steroids on the incidence of osteonecrosis of the femoral head during the management of severe acute respiratory syndrome
www.bjj.boneandjoint.org.uk/content/96B/2/259.abstract/reply#jbjsbr_el_7171
31 March 2014

11. E. Lindisfarne, E. Dawe, M. Chowdhry, BA Rogers, P. Stott, D. Ricketts
Metal ions in MoP: what is the clinical significance?
www.bjj.boneandjoint.org.uk/content/96B/1/43.abstract/reply#jbjsbr_el_7681
3 March 2014

12. DA Butt, M Gajewar, I Roushdi, BA Rogers and DM Ricketts
Treatment of non-traumatic rotator cuff tears: a randomised controlled trial with one-year clinical results
www.bjj.boneandjoint.org.uk/content/96B/1/75.abstract/reply#jbjsbr_el_7018
21 Feb 2014

13. KS Marenah, S Bellringer, D Butt, EJ Dawe, BA Rogers & DM Ricketts
Corail uncemented hemiarthroplasty with a Cathcart head for intracapsular hip fractures
www.bjj.boneandjoint.org.uk/content/95B/11/1538.abstract/reply#jbjsbr_el_6927
17 Dec 2013

14. NP Chotai, DGG Wilson, EJ Dawe, BA Rogers & DM Ricketts
Internal fixation of intracapsular fractures of the hip using a dynamic locking plate. Does the TFN represent a true advance in treatment?
www.bjj.boneandjoint.org.uk/content/95B/10/1402/reply#jbjsbr_el_6920
18 Dec 2013

15. Page PRJ, Rogers BA and Ricketts DM.
Response to Karantana et al. “Surgical Treatment of Distal Radial Fractures with a Volar Locking Plate Vs Conventional Percutaneous Methods: A Randomized Controlled Trial”.
http://jbjs.org/article.aspx?articleid=1740609
Oct 2013
16. WKM Kieffer, D Yeoh, S Yousaf, BA Rogers, Ricketts DM
Improvement in quality of life after arthroscopic capsular release for contracture of the shoulder.
www.bjj.boneandjoint.org.uk/content/95B/7/942/reply#jbjsbr_el_6648
Sept 2013

17. EA Lindisfarne, K Gallagher, PFD Bowles, D Yeoh, S Butler, BA Rogers, DM Ricketts
Primary total hip replacement with a Furlong fully hydroxyapatite-coated titanium alloy femoral component
www.bjj.boneandjoint.org.uk/content/95B/4/467.abstract/reply#jbjsbr_el_6458
11th July 2013

18. SV Voon, WKM Kieffer, EA Lindisfarne, BA Rogers, DM Ricketts
Severe open tibial fractures in combat trauma: management and preliminary outcomes
www.bjj.boneandjoint.org.uk/content/95B/1/101/reply#jbjsbr_el_6371
25th April 2013

19. EA Lindisfarne, K Gallagher, S Yousaf, BA Rogers, DM Ricketts
Unilateral lower limb loss following combat injury
www.bjj.boneandjoint.org.uk/content/95B/2/224/reply#jbjsbr_el_6365
24 April 2013

20. Benedict A Rogers & AD Carrothers
In vitro phenotypic modulation of chondrocytes from knees of patients with osteochondritis dissecans
http://web.jbjs.org.uk/cgi/eletters/94-B/1/62#5818,
13 Jan 2012

Longer term management of self-harm: summary of NICE guidance
http://www.bmj.com/node/544684?tab=responses,
12 December 2011

22. Benedict A Rogers & NJ Little
Measurement of Patellar Height
http://web.jbjs.org.uk/cgi/eletters,
September 2010

23. Benedict A Rogers
Joint distraction and movement for repair of articular cartilage
http://web.jbjs.org.uk/cgi/eletters/92-B/7/1033#5246,
30 June 2010
24. K Brogan & BA Rogers
Is There a Head Size Cut-Off Below Which a Resurfacing Procedure Should Not Be Done?
www.ejbjs.org/cgi/eletters/92/3/30#11670,
9 June 2010

25. Benedict A Rogers
Thrombosis Prevention after Total Hip Arthroplasty
www.ejbjs.org:80/cgi/eletters/92/3/527#11621,
29 April 2010

26. Benedict A Rogers & K Brogan
Cemented versus uncemented hemiarthroplasty
www.jbjs.org.uk/cgi/eletters/92-B,
1 Feb 2010

27. Benedict A Rogers & K Brogan
Prophylaxis of Venous Thromboembolism
www.jbjs.org.uk/cgi/eletters/92-B,
2 Feb 2010

28. Benedict A Rogers
The subacromial injection of tenoxicam or methylprednisolone
www.jbjs.org.uk/cgi/eletters/92-B/1/77#2927,
8 Jan 2010

29. Benedict A Rogers, P Panose, S Vig
Comparison of the Clinical Results of Three Posterior Cruciate Ligament
Reconstruction Techniques
www.ejbjs.org/cgi/eletters/91/11/2543#11325,
Nov 2009

30. Benedict A Rogers, P Panose, S Vig
Comparison of AO Type-B and Type-C Volar Shearing Fractures of the Distal Part of
the Radius
www.ejbjs.org/cgi/eletters/91/11/2605#11327,
Nov 2009

31. Benedict A Rogers
The effect of obesity on the mid-term survival and clinical outcome of cementless THR
www.jbjs.org.uk/cgi/eletters/91-B/10/1296#2740,
11 Oct 2009
32. Benedict A Rogers, NJ Little & C Emeagi  
Unstable Distal Radial Fracture Treatment  
www.ejbjournal.org/cgi/eletters/91/  
Aug 2009  

33. Benedict A Rogers & C Emeagi  
Suture-Button Fixation of Isolated Lisfranc Injuries  
www.ejbjournal.org/cgi/eletters/91/5/1143#10755,  
2 June 2009  

34. Benedict A Rogers  
ACL reconstruction in patients over 50 years  
www.jbjs.org.uk/cgi/eletters/90-B/11/1446#2261,  
17 Dec 2008  

35. Benedict A Rogers  
Comparing the Holland nail with the dynamic hip screw  
www.jbjs.org.uk/cgi/eletters/90-B/8/1073#2055,  
6 Aug 2008  

36. Benedict A Rogers  
Is it joint line and/or patella height that matters?  
www.jbjs.org.uk/cgi/eletters/90-B/7/879#2015, 1 Jul 2008  

37. Benedict A. Rogers & J Phadnis  
Malunited distal radius fractures  
www.jbjs.org.uk/cgi/eletters/90-B/5/629#1980, 30 June 2008  

38. Benedict A Rogers  
Super-surgery fears  
The Daily Telegraph, 5th June 2008  

39. Benedict A Rogers  
Gene and Protein Expression in Human Osteoarthritic Cartilage Explants  
www.ejbjournal.org/cgi/eletters/90/4/833#8967, 13 May 2008  

40. Benedict A. Rogers, NJ Little, J Phadnis  
Obesity in total hip replacement  
www.jbjs.org.uk/cgi/eletters/90-B/4/424#1880,  
24 Apr 2008
41. Benedict A. Rogers  
The GP Revolution  
The Independent on Sunday, p56  
26 April 2008

42. Benedict A Rogers  
Acute Patellar Dislocation in Children and Adolescents  
www.ejbjs.org/cgi/eletters/90/3/463#7828,  
6 Mar 2008

43. Benedict A Rogers, M Dhamdhere & NJ Little  
Confounding factors in the valid assessment of patients undergoing knee surgery  
www.ejbjs.org/cgi/eletters/90/2/264#7780,  
23 Feb 2008

44. Benedict A Rogers & S Rang  
Femoral Nerve Block for Diaphyseal and Distal Femoral Fractures in the Emergency Department  
www.ejbjs.org/cgi/eletters/89/12/2599#6655,  
9 Jan 2008

45. Nick J Little, K Dalzell, BA Rogers  
Anterograde intramedullary nail of diaphyseal humeral fractures can cause shoulder pain  
www jbjs org/uk/cgi/eletters/90-B/1/61#1781,  
14 Feb 2008

46. Benedict A Rogers & C Roslee  
Venous Thromboembolism in Patients with Primary Bone or Soft-Tissue Sarcomas  
www.ejbjs.org/cgi/eletters/89/11/2433#5306,  
15 Oct 2007

47. Benedict A Rogers & C Roslee  
Revision anterior cruciate ligament (ACL) reconstruction  
www jbjs org/uk/cgi/eletters/89-B/8/1051#1615,  
29 Sep 2007

48. Benedict A Rogers & C Roslee  
Articular cartilage restoration in load-bearing osteochondral defects  
www jbjs org/uk/cgi/eletters/89-B/8/1099#1612,  
29 Sep 2007
49. Benedict A Rogers & DM Ricketts
   Hip fracture management
   www.bmj.com/cgi/eletters/335/7619/563,
   27 Sep 2007

50. Benedict A Rogers
   Chondrocyte apoptosis in the regenerated articular cartilage
   www.jbjs.org.uk/cgi/eletters/89-B/7/977#1570,
   29 Aug 2007

51. Benedict A Rogers
   Insufficient duration of venous thromboembolism prophylaxis after total hip or knee replacement
   www.jbjs.org.uk/cgi/eletters/89-B/6/799#1483,
   12 Jul 2007

52. Benedict A Rogers
   Assessment and management of chronic patellofemoral instability
   www.jbjs.org.uk/cgi/eletters/89-B/6/709#1474,
   10 Jul 2007

53. Benedict A Rogers
   Healing of full-thickness defects of the articular cartilage in rabbits
   www.jbjs.org.uk/cgi/eletters/89-B/5/693#1419,
   23 Jun 2007

54. Benedict A Rogers
   Genetic modification of chondrocytes with insulin-like growth factor-1
   www.jbjs.org.uk/cgi/eletters/89-B/5/672#1425,
   23 Jun 2007

55. Benedict A Rogers & N J Little
   Comparison of topical fibrin spray and tranexamic acid on blood loss after total knee replacement
   www.jbjs.org.uk/cgi/eletters/89-B/3/306#1327,
   25 Apr 2007

56. Benedict A Rogers & DM Ricketts
   Metal ion levels in a triathlete with a metal-on-metal resurfacing arthroplasty of the hip
   www.jbjs.org.uk/cgi/eletters/89-B/4/538#1381,
   26 May 2007
57.  Nick J Little, BA Rogers & A Khaleel  
    Biomechanical reconstruction of the hip  
    www.jbjs.org.uk/cgi/eletters/88-B/6/721#1324,  
    25 Apr 2007

58.  Benedict A Rogers & D Johnstone  
    UK hospitals can improve the efficiency of red cell use.  
    www.bmj.com/cgi/eletters/328/7445/934,  
    25 April 2004
Published abstracts

1. BA Rogers, R Pearce, R Walker, M Bircher
   The Incidence and Outcome of Neural Injuries Following Pelvic and Acetabular Fractures

2. BA Rogers, F Middleton, N Spearwood-Porter, S Kinch, N Bradley,
   A Roques, A Taylor, M Browne
   Does cyclical loading Affect Antibiotic Elution and Strength of Articulating Cement Knee Spacers?
   Proceedings of AAOS Annual Meeting, Vol 12 (2011); 527

3. BA Rogers, R Pearce, R Walker, M Bircher
   The Incidence and Outcome of Neural Injuries Following Pelvic and Acetabular Fractures
   South Thames Orthopaedic Proceedings, March 2010, 8; 47

4. BA Rogers, NJ Little
   Intra- and Inter-Observer Variation in the Measurement of Patellar Height after Total Knee Replacement Using Digital Radiography
   Event Proceedings of Institute of Mechanical Engineers, May 2009, 203-205

5. BA Rogers, A. Cowie, C. Alcock, and J. Rosson
   Identification and Treatment of Anaemia In Patients Awaiting Hip Replacement

6. BA Rogers, C Murphy, SR Cannon, TWR Briggs
   Topographical Glycosaminoglycan Variation In Human Articular Cartilage

7. BA Rogers, L Unitt, SR Cannon, TWR Briggs
   Pre-operative knee function predicts the sequential improvement in clinical & functional outcomes following total knee arthroplasty

8. BA Rogers, R Carrington, J Skinner, G Bentley, TWR Briggs
   The Sequential Improvement in Clinical Outcome Following Autologous Chondrocyte Implantation – a 7-year follow up.

9. BA Rogers, AS Cowie, C Alcock, and JW Rosson
   Identification and Treatment of Anaemia In Patients Awaiting Hip Replacement

10. BA Rogers, C Kabir, N Bradley
An Audit of Orthopaedic Referrals Via Multi Professional Triage Teams
British Journal of Surgery (July 2007) 94, 156-157

11. BA Rogers, C Kabir, C Coates
Pre-operative delay predicts post-operative stay in trauma surgery
European Journal of Trauma, April 2006, 32(1): 128

12. BA Rogers, N Little, J Pringle, SR Cannon
Adamantinoma – a new histological variant

13. BA Rogers, DJ Johnstone
Audit on the Efficient use of Crossmatched Blood in Elective Total Hip and Total Knee Replacement
The Surgeon 3(3); Jun 2005: S55

14. BA Rogers, J Pleat & MPH Tyler
Operation Notes: an audit of the Royal College of Surgeons of England guidelines.
The Surgeon 3(3); Jun 2005: S50

15. BA Rogers, TWR Briggs
The Effectiveness of Specialist Orthopaedic Hospitals in the UK
The Surgeon 3(3); Jun 2005: S35

16. BA Rogers, N Little, D Back, TWR Briggs
Long Term Functional Outcome in Kinemax and Press Fit Condylar Total Knee Arthroplasty – A Thirteen Year Review.
The Surgeon 3(3); Jun 2005: S95

17. BA Rogers, NJ Little, D Back, TWR Briggs
Anterior Knee Pain Following Kinemax and PFC Total Knee Arthroplasty.
The Surgeon 3(3); Jun 2005: S28

18. BA Rogers, L Unitt, SR Cannon, TWR Briggs
The sequential outcome improvement following Kinemax total knee replacement - a prospective, multi-centre study
The Surgeon 3(3); Jun 2005: S55
Appendix 1

Rogers BA, Kabir C, Bradley N.
An audit of orthopaedic referrals via Multi-Professional Triage Teams.

**Contribution by BA Rogers.**

Data collection
Data analysis
Manuscript writing & editing

**Citation Metrics**

- Web of Science: 6
- Google Scholar: 13
- Altmetrics: 0
  - Tweets:
  - Facebook:
  - Mendeley readers:
An audit of orthopaedic referrals via Multi-Professional Triage Teams

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ABSTRACT

INTRODUCTION: Multi-Professional Triage Teams (MPTTs) were created to reduce the caseload of hospital orthopaedic clinics and this prospective study evaluated referrals made to a district general hospital orthopaedic department from a lower limb MPTT clinic.

PATIENTS AND METHODS: Over 9 months, 277 referrals to a lower limb hospital orthopaedic clinic were assessed. The temporal delay to hospital clinic review between patients seen at the MPTT clinic and those referred directly by their general practitioner (GP) was analysed using an ANOVA test. A qualitative assessment of diagnoses given to patients reviewed at the MPTT clinic was performed.

RESULTS: The 132 patients initially reviewed at the MPTT clinic and subsequently referred to a hospital consultant waited significantly longer (140 days compared to 62 days by direct GP referral; \( P < 0.05 \)) to see an orthopaedic consultant. Over three-quarters of this patient cohort incorrectly identified the healthcare professional conducting their consultation at the MPTT clinic. One-third of cases (31%) had no diagnosis made and 22% were assessed as having an incorrect diagnosis.

CONCLUSIONS: Time delays, patient confusion regarding professional roles and diagnostic indecision are significant problems for patients referred to hospital orthopaedic clinics from MPTT clinics. This risks sub-optimal patient care and may lead to future medicolegal implications.

KEYWORDS

General Practitioner with Special Interest (GPwSI) – Referral – Outcome – Multi-Professional Triage Team (MPTT)

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The NHS Plan formalised the concept of General Practitioners with Special Interests (GPwSI), proposing that by 2006 ‘at least 1 million more out-patient appointments will take place in the community rather than hospital’.1,2 This extended role was also introduced for other healthcare professionals including physiotherapists, nurses and podiatrists. Within the field of musculoskeletal medicine, the extended role for GPwSIs and physiotherapists were combined to create Multi-Professional Triage Teams (MPTTs). These clinics were developed within the primary care setting and aimed to reduce the quantity, but improve the quality, of referrals made to hospital-based orthopaedic care.

The development of GPwSI clinics, such as the MPTT clinic, has gained considerable momentum through policy rhetoric rather than a substantive evidence base for their introduction. To our knowledge, no published studies have assessed the temporal delays and perception of patients reviewed and subsequently referred by an MPTT clinic. This prospective study evaluated consecutive referrals made to a district general hospital orthopaedic department from a lower limb MPTT clinic over a 9-month period.

Patients and Methods

Patients initially consulting their GP were allowed to choose being referred to the MPTT clinic, staffed by GPwSIs and physiotherapists, or referral directly to a hospital clinic. Patients assessed at the MPTT clinic were either investigated and referred for physiotherapy or referred on to an orthopaedic consultant for a further opinion.

Over 9 months, a survey was performed of 277 consecutive patients referred to a lower limb orthopaedic clinic at a district general hospital. None of the patients referred to


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hospital clinics were triaged by either the senior author or other clinicians. A proforma (Fig. 1) was completed for 132 patients referred via the MPTT clinic and 145 patients referred directly from their GP (Fig. 2). For every patient initially reviewed at the MPTT clinic, it was recorded whether a diagnosis was made and if it was correct, as assessed by the senior author.

Comparative statistical analysis of the temporal differences between the two groups was performed using an ANOVA (SPSS v.11.5; SPSS Inc., Chicago, IL, USA)

Results
A total of 191 patients were seen in the MPTT clinic with 152 (69.1%) referred on to the hospital lower limb orthopaedic clinic. Over half of the patients referred on were assessed by a general practitioner with a special interest (76 out of 132), the remainder were reviewed by a specialist physiotherapist (Fig. 2). During the study period, a total of 277 new referrals were seen in the hospital clinic.

Figure 3 demonstrates the temporal delays for patients referred directly to a hospital orthopaedic clinic or patients initially assessed at an MPTT clinic. Patients were seen in the MPTT clinic a mean of 52.6 days (range, 19–155 days) following their GP referral and subsequently seen in the orthopaedic clinic 88.4 days (range, 18–255 days) later. This delay was significantly longer ($P < 0.05$) than the mean 62.4 days (range, 17–176 days) identified for patients referred directly by their GP to the hospital orthopaedic clinic.

Figure 4 shows which healthcare professional each of the 132 patients assessed at the MPTT clinic thought they had seen. Over one-third of these patients reported they had previously seen an ‘orthopaedic consultant’ at the MPTT clinic when they had in fact been seen by a physiotherapist or GPwSI. Overall, 84% of this cohort of patients incorrectly identified the healthcare professional conducting their consultation at the MPTT clinic.

Figure 5 shows the proportion of patients seen at the MPTT clinic that had the correct diagnosis, no diagnosis or the incorrect diagnosis made. The diagnosis made by the MPTT clinic agreed with that made by the orthopaedic consultant in 47% of cases. One-third of cases (31%) referred from the MPTT clinic had no diagnosis made and 22% were assessed as having an incorrect diagnosis.

Discussion
The introduction of GPwSIs and clinics such as the MPTT clinic was born out of the laudable goal of improving patient

![Figure 1](image1.png)

**Figure 1** Patient proforma for survey.

![Figure 2](image2.png)

**Figure 2** Flow chart detailing the number of patients referred to a hospital orthopaedic clinic directly or via an MPTT clinic. Patients referred via an MPTT clinic were assessed by either a GP with a special interest (GPwSI) or a specialist physiotherapist.

![Figure 3](image3.png)

**Figure 3** Referral time to hospital orthopaedic clinic. Comparison of delay from initial GP referral to hospital orthopaedic clinic review for patients seen either via an MPTT clinic or referred direct. $P < 0.05^*$

*ANOVA statistical analysis.
services as well as a broader shift in care toward the primary care sector.\textsuperscript{2,5} Few studies have considered the effects of this significant change, the majority being produced from researchers in a primary care setting analysing short-term general health measures.\textsuperscript{6} Baker et al.\textsuperscript{3} showed that short-term health outcomes, quantified using the SF-36 health survey, are similar for patients assessed at a GPwSI clinic as those referred directly to hospital clinics. That study, conducted entirely from a primary care perspective, made no assessment of the temporal delays involved or the diagnoses made.

In this study, patients seen by the MPTT clinic and subsequently referred to hospital had to wait significantly longer to see an orthopaedic consultant (140 days versus 62 days; \textit{P} < 0.05) than those patients referred directly to a hospital clinic by their GP.

The diagnostic accuracy of the lower limb MPTT clinic assessed in this study (Fig. 5) is subjective and, therefore, potentially open to bias. With 22\% of cases referred from the MPTT clinic deemed to have an incorrect diagnosis and one-third with no diagnosis, this may represent the case-load complexity inherent in lower limb musculoskeletal medicine or evidence of the learning curve of the MPTT clinicians. However, many patients seen in the MPTT clinic had the same diagnosis made by both the initial referring GP and the hospital consultant, suggesting the GPwSI clinic was a superfluous tier of care for this patient cohort.

It is unlikely that these results would be replicated within the setting of an upper limb MPTT clinic. Several common upper limb conditions (\textit{e.g.} carpal tunnel syndrome and tennis elbow) are amenable to rapid diagnosis and initial treatment in a GPwSI-led clinic, prior to referral to a hospital consultant.

Furthermore, in this study, patients reviewed and referred via a MPTT clinic were generally unsure of the healthcare professional that had previously assessed them (Fig. 4). The resulting uncertainty can lead to mixed messages, heightened patient concerns and unrealistic expectations.

The delay to secondary care, the patient confusion regarding professional roles and the diagnostic indecision may not only have a detrimental effect on the standard of patient care, but may well have future medicolegal implications. Further, the benefits of the recent reduction in waiting list times to less than 6 months is not achieved for patients referred to the MPTT clinic and who subsequently require surgery due to the inherent delay.

Examples of avoidable delays include long-standing degenerative changes in the knee being over investigated when joint replacement was more appropriate and a symptomatic and undiagnosed lateral discoid meniscus.

There is variation in the organisation of GPwSI-led clinics, some running concurrently with consultant clinics affording the opportunity for a more consensual professional opinion and mutual education. Pearce et al.\textsuperscript{4} showed that, although an extended role for physiotherapists is generally acceptable to patients, 81\% of cases required consultant input and 76\% of dissatisfied patients had not seen a consultant. Currently, no competency framework exists for GPs with a special interest in musculoskeletal medicine and no on-going appraisal of patient outcomes.\textsuperscript{7}
Conclusions
No comprehensive evidential support exists detailing the clinical outcome of patients seen at GPwSI-led clinics, such as a MPTT clinic. This study highlights concerns regarding patients referred on for a consultant opinion; however, the outcome of patients seen in these clinics and not referred to an orthopaedic consultant is unknown. In view of the data presented, this may be of concern and should necessitate further evaluation and audit.

References
Appendix 2

DeBarr P, Kieffer WKM, Oliver T, Gallagher K, Rogers BA.
High-risk patients and perioperative practice.

Contribution by BA Rogers.
Concept
Manuscript writing & editing

Citation Metrics
Web of Science: 0
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High-risk patients and perioperative practice

In an ageing population, the number of patients at high surgical risk is increasing. There are a number of identified risk factors for inpatient mortality following surgical procedures. Within the National Health Service, high-risk elective patients are usually assessed and identified prior to surgery. However, the subsequent management of these patients is frequently compromised from a lack of intensive treatment unit or high dependency unit beds, with surgeons and anaesthetists faced with the decision as to whether or not to proceed with the planned surgery. Often, the surgery is undertaken without the suitable resources available due to the pressure to achieve targets and avoid surgical cancellations.

In order to maintain and improve standards of medical and surgical care it is important to review the management of patients, by undertaking confidential surveys and research, and by maintaining and improving the quality of patient care and publishing their results. The number of high-risk patients is high and is likely to significantly increase in coming years. Improving the mortality in this patient cohort should be considered a priority in the UK and other countries.

**Identified issue**
A substantial subset of surgical patients are deemed high surgical risk. In December 2011, the National Confidential Enquiry into Patient Outcome and Death (NCEPOD) published a report entitled ‘Knowing the risk – A review of the peri-operative care of surgical patients’. This report highlighted the process of care for patients aged 16 years and over, who underwent inpatient surgery (both elective and emergency), and their outcome at 30 days. It reported a worryingly high mortality rate in ‘high-risk’ surgical patients, when compared with other healthcare systems such as the USA.

**Relevance**
With an ageing population, the caseload of high-risk surgical patients is likely to increase significantly in coming years with a significant impact on the resources of intensive care and high dependency units. The findings of the 2011 NCEPOD report have substantial implications for clinical practice.

There are a number of identified risk factors for inpatient mortality following surgical procedures. Using a predictive model, Bhattacharyya et al. identified five critical risk factors for postoperative mortality: chronic renal failure, congestive heart failure, chronic obstructive pulmonary disease, hip fracture and an age of greater than 70 years. The mortality rate was 0.25% for patients with no critical risk factors, demonstrating a linear increase with additional critical risk factors. Up to 39% of general surgical patients have preoperative anaemia, defined according to WHO criteria: Hb < 12.0 g/dl for females and Hb < 13.0 g/dl for males, which has been associated with an increased perioperative morbidity and mortality. However, the role of preoperative anaemia as a single predictive factor of poor outcome in elective surgery remains controversial. Mantella et al. reported in 2011 that existing comorbidities, rather than preoperative anaemia, were independently associated with major morbidity and mortality.

High-risk surgical patients are frequently older with a greater risk of impaired nutritional status, and screening tools aim to identify poor nutritional reserve. Greene et al. reported a five-time increase in postoperative wound complications among patients with decreased nutritional status, identified by a lymphocyte count of <1500 cells/mm, and a sevenfold increase when preoperative albumin was <3.5 g/dl.

Nasal colonisation with *Staphylococcus aureus* (MSSA), especially with methicillin-resistant *S. aureus* (MRSA), has also been shown to be a risk factor for surgical site infections. *Staphylococcus* nasal colonisation among orthopaedic patients was shown to be 18% for MSSA and 2.17% for MRSA. Institutionalised and nursing home patients are at an increased risk for positive nasal colonisation by *S. aureus*. Among other risk factors for positive colonisation are haemodialysis, immunodeficiency and increased age.

Within the National Health Service (NHS), high-risk elective patients are usually assessed and identified prior to surgery. However, the subsequent management of these patients is frequently compromised from a lack of intensive treatment unit or high dependency unit beds, with surgeons and anaesthetists faced with the decision as to whether or not to proceed with the planned surgery. Not uncommonly, and out of misguided kindness to the patient and relatives, the surgery is undertaken without the suitable resources available due to the pressure to attain targets and avoid surgical cancellations. In the majority of cases no adverse outcomes occur; however, the lack of resources is one of the principal reasons the figures highlighted in the recent NCEPOD report are so bad.

**NCEPOD**
The purpose of the NCEPOD is to assist in maintaining and improving standards of medical and surgical care by reviewing the management of patients, by undertaking confidential surveys and research, and by maintaining and improving the quality of patient care and publishing their results. The 2011 report documented an overall mortality at 30 days of 1.6%; with the mortality in the ‘high-risk’ group being 6.2% compared with 0.4% in their low-risk group. Overall, the NCEPOD rated the care of ‘high-risk’ surgical patients as ‘good’ in only 48%. In order to address this disparity, and improve clinical care, they made a number of principle recommendations (see Table 1).

This is the latest report highlighting the worse than expected management of such patients in the United Kingdom (UK). The 2007 NCEPOD report ‘Trauma: who cares?’ identified deficiencies in both organisation and clinical care leading to almost 60% of patients receiving a standard of care below that of good practice.
Table 1. Principle recommendations; NCEPOD ‘Knowing the risk – a review of the perioperative care of surgical patients’

1. There is a need to introduce a UK wide system that allows rapid and easy identification of patients who are at high risk of postoperative mortality and morbidity. (Departments of Health in England, Wales & Northern Ireland)
2. All elective high-risk patients should be seen and fully investigated in pre-assessment clinics. Arrangements should be in place to ensure more urgent surgical patients have the same robust work-up. (Clinical Directors and Consultants)
3. An assessment of mortality risk should be made explicit to the patient and recorded clearly on the consent form and in the medical record. (Consultants)
4. The postoperative care of the high-risk surgical patient needs to be improved. Each Trust must make provision for sufficient critical care beds or pathways of care to provide appropriate support in the postoperative period. (Medical Directors)
5. To aid planning for provision of facilities for high-risk patients, each Trust should analyse the volume of work considered to be high risk and quantify the critical care requirements of this cohort. This assessment and plan should be reported to the Trust Board on an annual basis. (Medical Directors)

Table 2. Generic principles of enhanced recovery pathways

Preoperative
- Thorough preoperative intervention to optimise health and medical condition
- Management of patient expectation through preoperative education and counselling
- Organisation of discharge arrangements

Intraoperative
- Atraumatic and minimally invasive surgical techniques
- Shortened surgical times
- Optimised anaesthesia – usually regional anaesthetic techniques with light sedation
- Promotion of normovolaemia, normothermia and prevention of hypoxia

Postoperative
- Early physiotherapy intervention and promotion of ambulation
- Regular and effective analgesia with avoidance of opiates where possible
- Rapid introduction of normal hydration and feeding
- Promotion of a ‘wellness’ model of care – catheter, drains and drips are removed as soon as possible, and independence with washing, dressing and socialisation is promoted

Discharge
- Patients are discharged home
- Criteria-based discharge protocol managed by the multidisciplinary team
- Patients have clear instructions on how to progress rehabilitation independently

To date there is no concordance among anaesthetists, surgeons or researchers as to the definition of a ‘high-risk’ surgical patient. The NCEPOD utilised an anaesthetist-led clinical assessment, with no prescribed parameters, to ascertain whether each case was deemed high or low risk. In 2011 the Royal College of Surgeons of England and Department of Health reported on the ‘Peri-operative care of the higher risk general surgical patient’. They used a preoperative estimated mortality rate of greater than or equal to 5% to define the ‘high-risk’ surgical patient. Campling et al. published the 30-day mortality following any operation to be between 0.7% and 1.7%, and considered a ‘high-risk’ patient to be when their risk of death was greater than or equal to twice that of the general population or if they had an absolute risk of death to be greater than or equal to 5%. The challenge that faces surgeons and anaesthetists is to try and identify these patients and try to reduce their mortality risk.

IMPROVEMENTS IN THE CARE OF THE ‘HIGH-RISK’ SURGICAL PATIENT

The NCEPOD report identified four areas for improvement in the care of the ‘high-risk’ surgical patients:

1. Identification of the ‘high-risk’ group
2. Improved preoperative assessment, triage and preparation
3. Improved intraoperative care
4. Improved use of postoperative resources.

The difficulty in identifying this ‘high-risk’ surgical group has been highlighted. It has been estimated that a significant surgical caseload, between 5% and 10%, can be considered in this category, while anaesthetists involved in the NCEPOD study identified 20% of the surgical patients as ‘high risk’. Despite numerous definitions, scoring systems and investigations to identify ‘high-risk’ patients in the literature, none has been accepted as the definitive method or definition.

In contrast to the NCEPOD report, where 20% of elective ‘high-risk’ surgical patients were not seen in a preoperative assessment clinic, the vast majority of elective orthopaedic patients undergo a preoperative assessment, usually in conjunction with anaesthetic input. The NCEPOD reported a higher 30-day mortality in ‘high-risk’ patients not seen in a preoperative assessment clinic. There has been a recent proposal for a role of Primary Care to include identifying fitness for surgery. In addition to the optimisation of medical comorbidities, including volaemic and nutritional status, there has been interest in optimising physiological reserve with the use of exercise regimens. This is also an ideal setting to confirm the suitability for proceeding with surgical intervention. Considering that a frank discussion of the risks, including mortality risk, is integral to ‘informed consent’ it is notable that the NCEPOD found only 7% of patients had any mention of mortality on their written consent forms.

It is well documented that fluid optimisation and intraoperative monitoring of cardiac output improve outcome in ‘high-risk’ patients. Despite this, cardiac monitoring was rarely used in these patients and inadequate intraoperative monitoring was associated with a threefold increase in mortality in the NCEPOD study. Patients who suffered intraoperative complications had a 30-day mortality of 13.2% compared with 5.7% in those without.

In many other countries, patients who undergo major surgery routinely receive a higher level of postoperative care than is delivered in the UK to NHS patients. This may in part be due to the overall health resources allocated to critical care but is also related to relative inefficiency in that a high number of critical care units operate with fewer than six beds. The NCEPOD determined that only 20% of surgical patients categorised as ‘high risk’ were managed postoperatively in a critical care facility; the vast majority were returned to ward care. Almost half of the ‘high-risk’ patients who died never went to a critical care facility. For those ‘high-risk’ patients not discharged from surgery to a higher level of care, only 74% had records of being monitored by an early warning scoring system, or ‘track and trigger’ system, to detect deterioration in physiological status. A substantial increase in the number of critical care beds is unlikely in the current fiscal climate, and therefore the challenge is to ensure patients receive the appropriate level of postoperative care required to optimise outcomes.

Enhanced recovery pathways (ERPs) are becoming increasingly common, with the aim of improving outcomes, speeding up recovery and reducing complications, adverse events and general morbidity. An ERP focuses on optimis-
ing each aspect of the patient’s journey and promotes the patient as an active participant in their recovery and rehabilitation post-surgery (see Table 2). Successful pathways are delivered by multidisciplinary teams and the improvements to the quality of care are largely thought to be due to the increased organisation of the care that is delivered. 19

**DISCUSSION**

Unfortunately the recent NCEPOD report is further evidence of the difficulties in the management of ‘high-risk’ surgical patients.1 With the high caseload of such patients and the widespread implementation of protocol-driven clinical care, intensive care physicians and surgeons must ensure a high-quality service to this patient cohort.

The recent NCEPOD recommendations may be insufficient, as the data only describe the clinical care for the most seriously ill patients within the NHS. In a healthcare system with no residual surplus capacity or funding, the trauma patient with often life-threatening injuries undergoes surgery frequently with suboptimal postoperative care resources.

The definition of quality and the ability to measure of quality-related outcome measures remains controversial. Numerous studies have highlighted the difficulties in interpreting patient-reported outcome measures (PROMS). 20–30 While the debate exists regarding the widespread use of PROMS, the NHS must not ignore the most longstanding and definitive outcome measure available, namely mortality. Intensive care physicians and surgeons are managing a higher number of high-risk patients and adequate resources should be available; a situation not currently occurring based on the evidence of the NCEPOD report. 1 The longer term clinicians, with a duty of care, must ensure adequate resources and facilities are available for such patients. The NCEPOD report clearly demonstrates that currently avoidable deaths are regularly occurring. 1

In conclusion, the caseload of high-risk patients is substantial and is likely to significantly increase in coming years. Improving the mortality in this patient cohort should be substantial and is likely to significantly increase in coming years.

**REFERENCES**

1. Knowing the risk. A review of the peri-operative care of surgical patients. London: National Confidential Enquiry into Perioperative Deaths, 2011. [Author: Please provide the author(s) and publisher details for reference 12. Please check editor name]


11. Trauma who cares? London: National Confidential Enquiry into Perioperative Deaths, 2007. [Author: Please provide author name(s) for reference 11]


Appendix 3

Rogers BA, Cowie A, Alcock C, Rosson J.
Identification and treatment of anaemia in patients awaiting hip replacement.

Contribution by BA Rogers.
Data collection
Manuscript writing & editing

Citation Metrics

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Identification and treatment of anaemia in patients awaiting hip replacement

BA ROGERS, A COWIE, C ALCOCK, JW ROSSON

Department of Trauma and Orthopaedics, The Royal Surrey County Hospital, Guildford, Surrey, UK

ABSTRACT

INTRODUCTION The correction of anaemia prior to total hip arthroplasty reduces surgical risk, hospital stay and cost. This study considers the benefits of implementing a protocol of identifying and treating pre-operative anaemia whilst the patient is on the waiting list for surgery.

PATIENTS AND METHODS From a prospective series of 322 patients undergoing elective total hip arthroplasty (THA), patients identified as anaemic (haemoglobin (Hb) < 12 g/dl) when initially placed upon the waiting list were appropriately investigated and treated. Pre- and postoperative Hb levels, need for transfusion, and length of hospital stay were collated for the entire patient cohort.

RESULTS Of the cohort, 8.8% of patients were anaemic when initially placed upon the waiting list for THA and had a higher transfusion rate (23% versus 3%; \( P < 0.05 \)) and longer hospital stay (7.5 days versus 6.6 days; \( P < 0.05 \)). Over 40% of these patients responded to investigation and treatment whilst on the waiting list, showing a significant improvement in Hb level (10.1 g/dl to 12.7 g/dl) and improved transfusion rate.

CONCLUSIONS Quantifying the haemoglobin level of patients when initially placed on the waiting list helps highlight those at risk of requiring a postoperative blood transfusion. Further, the early identification of anaemia allows for the utilisation of the waiting-list time to investigate and treat these patients. For patients who respond to treatment, there is a significant reduction in the need for blood transfusion with its inherent hazards.

KEYWORDS

Total hip arthroplasty – Anaemia

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Total hip arthroplasty (THA) is a common orthopaedic procedure and pre-operative anaemia increases the incidence of intra-operative and postoperative morbidity and mortality for this procedure.\(^1\)\(^-\)\(^4\) The clinical presentation of anaemia is variable and thus the clinician needs to rely upon haematological indices.

UK Government targets dictate a maximum waiting-list time of 18 weeks for THA surgery within the NHS.\(^1\) It has previously been proposed that identifying patients at risk of peri-operative anaemia, by carrying out a full blood count upon referral by their general practitioner (GP), allows for appropriate investigation and treatment before surgery.\(^5\) However, current practice often involves anaemia being identified as part of the routine assessment shortly before surgery, leading to possible delays and cancellations whilst investigation and treatment is instigated.

The correction of anaemia prior to THA surgery reduces surgical risk, hospital stay and cost.\(^1\)\(^-\)\(^4\) The use of oral iron therapy has been extensively reviewed since it is a frequently employed treatment. Although shown to reduce the incidence of anaemia prior to joint replacement surgery,\(^7\) the clinical value of its use following surgery has recently been questioned.\(^8\) No consensus exists as to the most beneficial way of treating anaemia with oral iron therapy, as there are significant gastrointestinal side effects.\(^7\)

Homologous blood transfusion has numerous inherent risks and complications including infection, incompatibility, immunosuppression\(^9\)-\(^11\) and, specifically, is associated with a higher rate of infection following THA surgery.\(^12\)-\(^15\) Thus, it is beneficial to reduce the blood transfusion rate and correction of pre-operative anaemia has been demonstrated to be one method of achieving this.\(^3\)

This study considers the benefits of implementing a protocol of early identification and treatment of pre-operative anaemia whilst the patient is on the waiting list for surgery. Specifically, we aimed to answer the following questions:
1. What percentage of patients were anaemic when initially placed upon the waiting list?
2. What percentage of patients responded to investigation and treatment of anaemia whilst on the waiting list?
3. Did this approach reduce the transfusion rate?

**Patients and Methods**

We prospectively analysed 522 patients undergoing elective primary THA over a 5-year period; of these, 181 were female and 141 were male with an average age of 67 years (range, 31–90 years). Osteoarthritis (primary or secondary) and osteonecrosis were the principal indications for surgery. No patients had rheumatoid arthritis.

A full blood count (FBC) was performed on each patient when initially placed on the waiting list. Patients anaemic at this point in time (Hb ≤ 12 g/dl) were investigated and treated accordingly. All patients were subsequently assessed within a nurse-lead pre-operative assessment clinic, including a further FBC. The mean waiting list time was 24.5 weeks.

A variety of prostheses were used depending upon the clinical indication. A drain was routinely used for the first 24 h after surgery and the patient mobilised as soon as possible. Pharmacological thrombo-embolic prophylaxis was provided using either daily aspirin (75 mg) or warfarin/low molecular weight heparin for high-risk patients – the dose being titrated to INR and continued for a period of 6 weeks following surgery. No mechanical thrombo-embolic prophylaxis was employed.

The following parameters were measured:
1. Patient demographics
2. Haemoglobin (Hb)
   - When initially put on waiting list (W/L Hb)
   - Pre-operative assessment clinic
   - Following operation (day 1)
3. Patient requiring blood transfused?
4. Length of hospital stay

The entire patient cohort was subdivided depending on the haemoglobin levels when initially placed on the waiting list (W/L Hb) and at the pre-assessment clinic. Patients with an Hb ≤ 12 g/dl when placed on the waiting list were further subdivided into: (i) patients in whom anaemia improved prior to surgery, *i.e.* pre-operative Hb > 12 g/dl – ‘responders’; and (ii) patients in whom anaemia failed to improve, *i.e.* pre-operative Hb < 12 g/dl – ‘non-responders’.

Chi-square (for group comparisons) and unpaired *t*-test (for continuous variable comparison) analyses was performed with statistical significance considered to be *P* < 0.05. The statistical package used was SPSS for Windows v.10.1.0.

**Results**

From the initial patient cohort of 522 patients, 26 (8.8%) were found to be anaemic (Hb < 12 g/dl) when initially placed upon the waiting list. Following investigation and treatment, 11 of these patients responded to treatment and were found to have an Hb > 12 g/dl prior to surgery (Fig. 1). A total of 16 patients (4.9%) were anaemic (Hb < 12 g/dl) at the pre-operative assessment, 10 patients fewer than the 26 initially found to be anaemic.

The demographic profile of these separate patient subgroups demonstrate an even gender distribution for patients with an Hb > 12 g/dl when initially placed upon the waiting list, but a statistically significant female predominance (*P* = 0.02) in patients with an Hb < 12 g/dl (Table 1).

Of the 26 patients found to be anaemic when initially placed upon the waiting list, four underwent oesophagogastroduodenoscopy (OGD) that was unremarkable and one patient was diagnosed with thyrotoxicosis. Additional

<table>
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<th>Table 1</th>
<th>Demographic patient profiles for each of the subgroups in the study, including responders and non-responders</th>
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<tr>
<td></td>
<td>Male</td>
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<tr>
<td>Waiting list (Hb &gt; 12 g/dl)</td>
<td>139 (47%)</td>
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<tr>
<td>Waiting list (Hb &lt; 12 g/dl)</td>
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<td>Responders</td>
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treatment entailed cessation of non-steroidal anti-inflammatory drugs (NSAIDs) and concurrent oral iron therapy.

Anaemic patients who responded to investigation and treatment prior to surgery (‘responders’) showed a significant improvement in haemoglobin level (10.1 g/dl to 12.7 g/dl; \( P = 0.02 \); Fig. 2).

There was no statistical difference (\( P = 0.85 \)) in the length of hospital stay between anaemic patients who responded to treatment and non-anaemic patients, but a significant difference between the responding and non-responding groups (\( P = 0.04 \)). Correspondingly, responders and non-anaemic patients were of similar age whilst the non-responders were significantly older (\( P = 0.0024 \); Table 2). The transfusion rate for responders was significantly lower than non-responders (1 out of 11 patients compared to 5 out of 15 patients; \( P < 0.05 \)).

Discussion

The identification and correction of anaemia prior to THA surgery is important and deserves attention.\(^1\)\(^,\)\(^3\)\(^,\)\(^4\)\(^,\)\(^15\) Blood transfusion is associated with a prolonged hospital stay\(^2\)\(^,\)\(^12\) and increased peri-operative risks\(^1\)\(^11\) including infection.\(^8\)\(^,\)\(^15\).

In our series, 26 out of 522 patients (8.8%) were anaemic when initially placed upon the waiting list for THA. This compares favourably to previous studies,\(^3\) possibly reflecting the high socio-economic profile of the hospital catchment area. These patients were predominantly female (24 out of 26 patients) and 10 years older than the non-anaemic group, highlighting the need to carefully assess this patient group prior to elective THA surgery.

Over 40% of anaemic patients responded to investigation and treatment whilst on the waiting list. These patients were characteristically younger than the non-responding group and were discharged at a similar time to the non-anaemic group. Whilst one patient in this group was diagnosed with thyrotoxicosis, all other patients were prescribed oral iron therapy with concurrent cessation of NSAIDs.

Anaemic patients who responded to treatment whilst on the waiting list showed a significant improvement (\( P = 0.02 \)) in haemoglobin level (10.1 g/dl to 12.7 g/dl). They were less likely to require transfusion than patients who failed to respond to treatment. The length of hospital stay and overall transfusion rate (5%) in this study compares favourably with other studies.\(^3\)\(^,\)\(^15\)

Our results indicate that the additional cost of performing a full blood count (approximately £1 per test) when the patient is initially placed upon the waiting list is outweighed by the advantages of early identification of anaemia in patients awaiting primary THA surgery. Estimation of haemoglobin level at this stage highlights those at risk of requiring a blood transfusion and allows the waiting-list time to be utilised to instigate appropriate investigate and treatment.

Conclusions

This study demonstrates the benefits of the early identification, investigation and treatment of pre-operative anaemia for patients undergoing elective total hip arthroplasty.

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Length of hospital stay and patient age for non-anaemic patients, responders and non-responders</th>
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<td>Length of stay (days)</td>
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<tr>
<td>Non-anaemic</td>
<td>6.6</td>
</tr>
</tbody>
</table>

References

4. Day M. Orthopaedic departments will have more difficulty meeting 18 week waiting target. BMJ 2007; 335: 64.
5. Andrews CM, Lane DW, Bradley JG. Iron pre-load for major joint replacement.
Appendix 4

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Reducing mortality for high risk surgical patients in the UK.

**Contribution by BA Rogers.**

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Reducing mortality for high risk surgical patients in the UK

by BA Rogers, AD Carrothers and Chris Jones

Over 40 million surgical procedures are performed per annum in the USA and Europe, including several million patients who are considered to be high risk (Bennett-Guerrero et al 2003). Overall, the risk of death or major complications after surgery in the general surgical patient population is low, with a post-operative mortality rate of less than 1% during the same hospital admission (Niskanen et al 2001).

Concerns have existed regarding the surgical outcomes of high-risk patient in the UK compared to similar sized hospitals and populations in North America (see Figure 1) (Peachem et al 2002, Bennett-Guerrero et al 2003). However, in December 2011 the National Confidential Enquiry into Patient Outcome and Death (NCEPOD) published a report ‘Knowing the Risk: A review of the perioperative care of surgical patients’ (NCEPOD 2011). The report highlighted that nearly 80% of postoperative deaths occurred in ‘high risk’ surgical patients. An expert panel considered that less than 50% of high-risk patients received good quality care.

This review considers some of the important issues and recommendations highlighted in the report.

The 2011 NCEPOD report

It is estimated that high-risk surgical patients make up approximately 10% of the inpatient surgical workload, whilst accounting for 80% of deaths after a surgical procedure. The hospital mortality rate for this cohort is approximately 10-15% and the figure is undoubtedly affected by the provision of perioperative care (Pearse et al 2006).

The recent NCEPOD report suggested that improvements are necessary in the care of high-risk surgical patients. The evidence for this is that the reported 30 day mortality of this group is almost 7%, which represents over 75% of all postoperative deaths (NCEPOD 2011).

The data collection by NCEPOD showed substantial methodological improvement compared with previous reports which attracted criticism. In particular, it was a prospective study that provided denominator data. This method was preferable to considering perioperative deaths in isolation which would lead to a degree of selection bias and therefore difficulties in extrapolating recommendations. In addition, the use of peer review of medical notes by an expert panel of advisors ensured qualitative data in support of the quantitative evidence.

Enhancing perioperative care can be split into the separate stages of a patient’s care pathway, namely:

Identification of high-risk groups

There are frequently difficulties in identifying what constitutes ‘high-risk’. The report highlighted that 20% of surgical cases faced was deemed high risk and that 79% of deaths occurred in this group. Further, half of the high-risk patients were undergoing elective procedures; therefore the urgency of the surgery is a poor predictor. A substantial number of high-risk patients were ASA grade 1 - 2. There was a lack of consensus as to what defined high perioperative risk.

Pre-operative assessment, triage and preparation

The report highlighted that nearly 20% of elective high-risk patients failed to be seen in a pre-assessment clinic. These had a significantly higher 30-day mortality than patients who were seen in a pre-assessment clinic. Pre-operative weight loss can lead to increased post-operative morbidity and mortality and therefore an assessment of nutritional status is beneficial (Heys & Gardener 1999). Systematic preoperative assessment can identify patients at high risk of cardiac complications and can guide the application of appropriate risk reduction strategies (Bekker et al 2011).

The optimisation of oxygen delivery to tissue prior to major surgery has been shown to be a significant and cost effective improvement in perioperative care (Boyd et al 1993, Wilson et al 1999). It has been shown to be especially important for elderly patients (Hamel et al 2005, Tingle 2010).

Consent

In only 7% of cases was there any documentation of the risk of death. This was concerning particularly as the GMC requires doctors to have a clear discussion with patients regarding surgical risks (GMC 2006, RCS 2008).
Detailed clinical guidelines for the monitoring of high risk and acutely ill patients have been published by NICE (2007)

**Figure 1** Risk-adjusted mortality rates for US (n = 1056) and UK (n = 1539) cohorts based on the multivariate logistic regression model. The relationship between the risk of death predicted by the Portsmouth Physiological and Operative Severity Score for the enurmeration of Mortality and morbidity (P-POSSUM) and the risk-adjusted mortality rates in each of these cohorts based on the multivariate logistic regression model is shown. Reprinted from Bennett-Guerrero et al 2003

**Improved intra-operative care**

In those patients considered to have inadequate fluid management, the 30-day mortality rate was nearly five times that of patients receiving adequate fluid therapy (20.5% v 4.7%). Arterial lines, central lines and cardiac output monitoring were only used in 27%, 14% and 5% respectively, for high-risk patients.

Cardiac monitoring was rarely used, though good evidence exists for its benefits, and suboptimal intra-operative monitoring correlated with a three-fold increase in mortality. For example, intraoperative monitoring, using continuous 12-lead ECG assessment and transesophageal echocardiography, may identify treatable myocardial ischemia and arrhythmias in a timely manner (Bakker et al 2011).

**Improved postoperative resource use**

Of the patients who died, over 50% were never admitted to critical care departments and 48% of the high-risk patients who died never went to critical care.

Detailed clinical guidelines for the monitoring of high risk and acutely ill patients have been published by NICE (2007). Though beyond the remit of this review, the NCEPOD report clearly demonstrates that the guidelines developed by NICE are not being fully implemented.

There is a substantial evidence base for the importance of physiological monitoring. A multicentre, prospective, observational study found that the majority (60%) of primary events (deaths, cardiac arrests and unplanned ICU admissions) were preceded by documented abnormal physiology, the most common being hypotension and a fall in Glasgow coma scale (Kause et al 2004).

- A national system must allow the rapid and easy identification of patients at high risk of postoperative mortality and morbidity.
- The decision to operate on high-risk patients should be made at a consultant level jointly between surgeon and clinical care clinicians.
- All elective and more urgent high-risk surgical patients should be seen and fully investigated in pre-assessment clinics. Arrangements should exist to ensure urgent surgical patients have the same robust work up.
- The consent form should clearly state the mortality risk.
- Improved intra-operative monitoring for high risk patients.
- The postoperative care of the high-risk surgical patient needs to be improved. Each hospital must provide sufficient critical care beds in the postoperative period.
- The annual caseload of high-risk surgical patients and their critical care requirements should be quantified and reported to hospital trust board.

**Box 1 Principle recommendations**

Reprinted from: NCEPOD 2011 ‘Knowing the risk: A review of the perioperative care of surgical patients’

Another study found that mortality increased with the number of physiological abnormalities (p<0.001), being 0.7% with no abnormalities, 4.4% with one, 9.2% with two and 21.3% with three or more (Goldhill 2005, Goldhill et al 2005).

**Recommendations**

The need for improved care of high-risk surgical patients has been clearly demonstrated. Previously published data from the Intensive Care National Audit & Research Centre, collating the outcomes of over 4 million surgical procedures, highlighted deficiencies in the use of critical care resources for high risk surgical patients (Pears et al 2006).
Reducing mortality for high risk surgical patients in the UK

Continued

The NCEPOD report details significant areas for clinical improvement within the UK (NCEPOD 2011). In addition there are several, recently published, reports that provide evidence-based guidelines for perioperative management of high-risk surgical patients, that are beyond the scope of this editorial.

They include:

It is now the challenge of clinicians, hospital managers and allied healthcare professionals to implement these standards and protocols with continual auditing at both a local and national level.

Based on the findings of the 2011 NCEPOD report some key organisation recommendations are proposed (see Box 1). Each of these recommendations requires a varying amount of resources, both in clinical and financial terms. However, the long term cost benefits of optimal care is likely to far exceed the current expenditure for this patient cohort. The re-structuring of resources, at a local, regional and national, may be essential in order to achieve this.

References
Bakker EJ, Ravensbergen NJ, Poldermans D 2011 Perioperative cardiac evaluation, monitoring, and risk reduction strategies in noncardiac surgery patients. Current Opinions in Critical Care 17 (5) 409-15
Bennett-Guerrero E, Hyun JA, Shariat S et al 2003 Comparison of P-POSSUM risk-adjusted mortality rates after surgery between patients in the USA and the UK British Journal of Surgery 90 (2) 1993-8
Boyd O, Grounds RM, Bennett ED 1993 A randomized clinical trial of the effect of deliberate perioperative increase of oxygen delivery on mortality in high-risk surgical patients Journal of the American Medical Association 270 (22) 2699-707
Feachem RG, Sekhon NK, White KL 2002 Getting more for their dollar: a comparison of the NHS with California’s Kaiser Permanente British Medical Journal 324 (7330) 135-41
General Medical Council 2006 Good medical practice: The duties of a doctor registered with the GMC Available from: www.gmc-uk.org/static/documents/content/GMP_0910.pdf [Accessed April 2012]
Goldhill DR 2005 Preventing surgical deaths: critical care and intensive care outreach services in the postoperative period British Journal of Anaesthesia 95 (1) 88-94
Goldhill DR, McNally F, Mandersloot C, McGinty A 2005 A physiologically-based early warning score for ward patients: the association between score and outcome. Anaesthesia 60 (6) 547-53
Hamel MB, Henderson W, Khuri S 2005 Surgical outcomes for patients aged 80 and older: morbidity and mortality from major noncardiac surgery Journal of the American Geriatric Society 53 (3) 424-9
Hoye SD, Gardner E 1999 Nutrients and the surgical patient: current and potential therapeutic applications to clinical practice Journal of the Royal College of Surgeons of Edinburgh 44 (5) 283-93
National Confidential Enquiry into Perioperative Deaths 2011 Knowing the risk. A review of the perioperative care of surgical patients London, NCEPOD

Niskanen MM, Takala JA 2001 Use of resources and postoperative outcome European Journal of Surg 167 (9) 643-9
Pease RM, Hamilton DA, James P et al 2006 Identification and characterisation of the high-risk surgical population in the United Kingdom Critical Care 10 (3) R81
Tingle J 2010 Report identifies defects in care for elderly surgery patients British Journal of Nursing 19 (22) 1346-7

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Appendix 5

Rogers BA, Garbedian S, Kuchinad RA, Backstein D, Safir O, Gross AE.
Total hip arthroplasty for adult hip dysplasia.

Contribution by BA Rogers.

Concept

Manuscript writing & editing

Citation Metrics

Web Of Science: 13
Google Scholar: 36
Altmetrics: 54
Tweets: 2
Facebook: 0
Mendeley readers: 52
Preoperative planning is essential to define anatomy, clarify the operative approach and exposure, and ensure that suitable implants are available.

Concerns exist regarding the long-term effectiveness and safety of hip resurfacing arthroplasty for the young dysplastic hip.

In light of current evidence, concerns exist regarding the use of metal-on-metal articulations for hip arthroplasty in the young dysplastic hip.

The ideal bearing surface is not known, although the longest data available support the use of metal-on-polyethylene.

Introduction and Etiology
Developmental dysplasia of the hip (DDH) presents as hip incongruence secondary to low or high dislocation. Pathological changes include flattening or inversion of the labrum and capsular structures (limbus) in association with hypoplasia of the capital femoral ossific nucleus and abnormal acetabular development with a high inclination and reduced femoral head coverage. The increasing use of ultrasound has produced earlier diagnosis to allow earlier treatment and a resultant improved prognosis.

The term dysplasia fails to convey the varied underlying pathology, and the term congenital hip disease has been advocated. The term developmental dysplasia of the hip (DDH) is used worldwide and shall be used in this article, although it fails to convey the often congenital etiology of this condition.

Incidence
The incidence of established neonatal hip dislocation in untreated populations is approximately one to two per 1000, and that of neonatal hip instability is between fifteen and twenty per 1000. Thus, a large proportion of cases of neonatal instability resolve in the first few weeks of life without treatment. Substantial geographical and ethnic variations exist, with a high incidence reported in northern Scandinavia.

DDH provides a large caseload for the orthopaedic surgeon. Lloyd-Roberts et al. reported that hip dysplasia was attributable to one-third of cases of osteoarthritis, with relative acetabular retroversion being a common associated factor. Wroblewski noted that an in-turned acetabular labrum was a common feature of hips that had osteoarthritis secondary to dysplasia.

Diagnosis
Adult patients with DDH sequelae typically report groin pain that is exacerbated with physical activity. Young adults may report lateral hip pain, exacerbated by crossing the affected leg over and stretching the hip abductors. Labral tears or chondral pathology may present with locking, catching, or giving way. Painless clicking can result from the iliopsoas tendon snapping over the uncovered anterior aspect of the femoral head.

Hip range of motion is generally preserved unless severe subluxation or secondary osteoarthritis is present. Young adults with hip dysplasia may exhibit increased internal rotation due to...
greater femoral anteversion. Decreased internal rotation of the hip may be a sign of secondary osteoarthritis. The impingement test, with hip flexion, adduction, and internal rotation, is sensitive for detection of labral pathology or impingement of the femoral head-neck junction against the anterior acetabulum. Physical examination of the hip, in particular assessment of extension, abduction, and external rotation, may reveal instability. An accurate measurement of limb lengths with use of clinical examination and radiographs, and a detailed neurovascular examination of the lower extremities, is essential for all patients.

Initial radiographs should include a lateral radiograph of the hip and a standing anteroposterior radiograph of the pelvis for assessment of the Tönnis angle and lateral center-edge angle of Wiberg (Fig. 1-A). A lateral center-edge angle of >25° is considered normal, 20° to 25° is considered borderline normal, and <20° indicates dysplasia and is pathological. The association between DDH and osteoarthritis was confirmed by Murphy et al., who demonstrated that osteoarthritis of the hip developed by the seventh decade of life in all patients who had moderate to severe dysplasia (lateral center-edge angle <15°).

The Tönnis angle measures the inclination of the weight-bearing zone of the acetabulum, (normal, <10°; Fig. 1-B). The ventral center-edge angle is measured in a manner similar to the lateral center-edge angle and should be 20° to 25° or greater on the false-profile view; measurements of <20° suggests deficiency in anterior acetabular coverage of the femoral head.

The role for computed tomography is limited to planning for acetabular re-directional osteotomy. Magnetic resonance imaging is useful for the assessment of symptomatic hips (e.g., hips with disorders such as a labral tear or chondral defect) that show no signs of structural abnormality on radiographs. Hip arthroscopy should be reserved for hips that have minimal radiographic abnormalities but in which intra-articular pathology is suspected.

Classifications
Numerous classification systems have been described for DDH although those described by Hartofilakidis et al. and Crowe et al. are the ones that are most commonly used (Table I).

The classification system of Hartofilakidis et al. describes the anatomical abnormalities in DDH: mild dysplasia (Type A) (Fig. 2-A), low dislocation (Type B) (Fig. 2-B), and high dislocation (Type C) (Fig. 2-C). The classification system of Crowe et al. can be quantified in one of two ways: first, on the extent of proximal migration of the femoral head as compared with the height of the undeformed femoral head (i.e., Type-I hips...
have migrated <50% of the height of the undeformed femoral head; Type-II, 50% to 74%; Type-III, 75% to 100%; and Type-IV, >100%), and second, by dividing the vertical distance between the interteardrop line and the femoral head-neck junction by the vertical distance between the line connecting the ischial tuberosities and the line connecting the iliac crests (Type I, <0.10; Type II, 0.10 to 0.15; Type III, 0.16 to 0.20; and Type IV, >0.20) (Fig. 3).

Both classification systems have been demonstrated to be reliable and reproducible. In a study in which 145 radiographs were assessed by three experienced surgeons working in different units, the range of kappa values for the interobserver error was 0.90 to 0.92 and 0.85 to 0.93 for the classification systems of Crowe et al. and Hartofilakidis et al., respectively. Similar ranges of kappa values were obtained for intraobserver error. However, the need for a whole pelvic radiograph, the variability of the location of the femoral head-neck junction, and the assumption that proximal migration is directly proportional to severity are drawbacks of the classification of Crowe et al. Similarly, when using the classification system of Hartofilakidis et al., although it is difficult to differentiate borderline cases, the system does have the advantage of providing insight into the structural anatomical changes to be encountered at the time of hip surgery.

In summary, these two classification systems assess the hip from different perspectives: Crowe et al. is quantitative and Hartofilakidis et al. is qualitative, and both can be used for clinical or research purposes.

**Treatment Options**

Nonoperative treatment for hip dysplasia includes nonsteroidal anti-inflammatory drugs, which are known to have improved efficacy when combined with other treatments such as physiotherapy, activity modification, and patient education.

**Joint-Preserving Surgery**

While this review focuses on arthroplasty techniques for the dysplastic hip, periacetabular osteotomy and femoral osteotomies may be considered if minimal articular cartilage degeneration has occurred. Realignment of the congruous dysplastic acetabulum with a periacetabular osteotomy can reduce symptoms for some years, even if a degree of osteoarthritis exists. Beneficial outcomes have been reported for patients with Tönnis grade-3 or 4 radiographic osteoarthritis, providing that an improvement in the cartilage-space interval is achieved. However, there is a substantial learning curve for the periacetabular osteotomy surgery and a complication rate of as much as 15%.

Evidence suggests that periacetabular
osteotomy affords a good outcome for patients who are less than thirty years old and have good-to-excellent hip-joint congruency at the time of the operation.

Total hip arthroplasty is possible after a periacetabular osteotomy. Parvizi et al. analyzed forty-one patients with this condition, and their results demonstrated a reduction in pain and good bone stock after implantation of the acetabular component. However, following a periacetabular osteotomy, the acetabulum had a tendency to be retroverted in twenty-three of the forty-one hips.

Arthroplasty

Preoperative Planning

Thorough preoperative planning is essential to clarify the operative technique and surgical approach, assess available bone stock, and determine the position and choice of the femoral and acetabular implants.

Good-quality, calibrated radiographs are needed to size and correctly plan the position of the components, which can be done digitally or with traditional acetate templates. Decisions should be made regarding the approach, type, and length of any proximal femoral osteotomy; the approximate size and type of implants to be used; the need for bone graft (autologous, allograft, or bone substitutes); and the possibility of a wake-up test if substantial limb-lengthening (i.e., >3 cm) is expected.

Operative Approach

A trochanteric osteotomy or slide provides superior access to the hip joint and also the capability to restore abductor biomechanics by advancing the trochanter distally. Copious irrigation minimizes the risk of thermal necrosis during a proximal femoral osteotomy. At our institution, reduction of the trochanteric osteotomy is achieved with use of cerclage wires and the placement of autologous bone graft, especially distally. Excessive soft-tissue dissection from osseous fragments is avoided to minimize the risk of osteonecrosis.

Use of a modification of the trochanteric slide, so as to maintain the integrity of the external rotators and the posterior capsule, will reduce the risk of dislocation while preserving the continuity of the vastus lateralis muscle with the osteotomized trochanter and the hip abductors. If performed carefully, a trochanteric slide can be repeated on a previously osteotomized greater trochanter with good results. The posterior approach is also commonly used and provides good exposure in less severely dysplastic hips; in addition, with careful repair of the short external rotator muscles, the risk of dislocation should be similar to a transgluteal or trochanteric slide approach.

If a subtrochanteric shortening derotational osteotomy is required, the use of a trochanteric osteotomy may compromise the fixation of the proximal sleeve of the femoral component. Furthermore, the subtrochanteric derotational osteotomy allows correction of the posterior position of the greater trochanter at the time of the insertion of the femoral component, further stabilizing the subtrochanteric osteotomy.

An excellent exposure was described after using the Smith-Petersen approach for severely dysplastic hips, but that approach...
was associated with a high reported rate of femoral nerve palsy\textsuperscript{44}. The iliofemoral approach provides excellent extensive exposure, although a large-muscle dissection is required with no benefit demonstrated over other approaches\textsuperscript{45}.

A large iliocrest muscle release to lower the hip center has been described\textsuperscript{46}. However, it is not clear how much soft-tissue release is required before the trial components are inserted, and such a soft-tissue release increases the risk of weakness and instability.

### Acetabular Reconstruction

Acetabular reconstruction is critical. The acetabular cup is ideally placed at the site of the true acetabulum; however, a high— but not lateral—position may be acceptable\textsuperscript{47-52}.

A high hip center utilizes live host bone, thus reducing the requirement for bone graft, and is technically easier than determining the level of the true acetabulum. However, there are several disadvantages of a cup positioned in the ilium, including a persisting limp and high dislocation rate\textsuperscript{44,51}. Excessive shear stresses and a high rate of component loosening are seen in hips that have a high hip center\textsuperscript{51}. The main predictors of loosening are a lack of lateral osseous support, the degree of preoperative dislocation, and the height of the acetabular component relative to the true acetabulum\textsuperscript{49}. If there is adequate bone stock on the anterior and posterior aspects of the acetabular component, 75% to 80% coverage of the acetabular cup is adequate\textsuperscript{53,54}.

In a recent study of fifty-three cementless cups inserted in dysplastic hips, with a minimum follow-up of ten years, the polyethylene wear rate was significantly greater when the cup was positioned in >45° of inclination (p = 0.045) or if the cup was placed lateral to the acetabular teardrop by >25 mm (p = 0.001)\textsuperscript{55}. In addition, aseptic loosening of the femoral component was significantly greater when the cup was placed >25 mm superior to the teardrop (p = 0.049).

An acetabular component should ideally achieve 75% to 80% bone coverage, and a suboptimal small cup size is frequently required due to the relative lack of available bone to stabilize a high-center cup. The small cup size results in a reduced femoral head-neck ratio and inferior wear properties. A high hip center does not allow for anatomical limb lengthening, and further revision surgery is difficult due to the lack of bone stock. A combination of a suboptimal head-neck ratio, the high shear stresses, and the limited limb-lengthening

![Fig. 2-B shows low dislocation (Type B); the false acetabulum is continuous with the true acetabulum.](image)

![Fig. 2-C shows high dislocation (Type C); the false acetabulum is noncontinuous with the true acetabulum.](image)
correction results in a high dislocation rate, as the lesser trochanter may impinge on the ischium.

The intraoperative identification of the true acetabulum can be difficult due to the abnormal anatomy. The confluence of the ischium and the pubis identifies the true level, and the surgical exposure should be adequate to visualize these landmarks. The fovea should be cleared of residual soft tissue to evaluate acetabular depth, and intraoperative radiographs may be used to confirm acetabular height and depth.

Achieving optimal medialization of the cup can be difficult while avoiding overreaming, producing a reduction in bone stock, and risking medial migration of the cup, loss of position, and fatigue fractures of the acetabulum. If the correct anatomical height of the true acetabulum has been identified, the degree of medialization can be determined after initial reaming by drilling and measuring the depth of a small hole in the floor of the acetabulum. Reaming should continue to approximately 3 to 4 mm from the inner cortex, thus leaving sufficient bone stock for future revision surgery. A trial cup should be used to ensure coverage of at least 70% and, if this is not achieved, then bone-grafting should be considered.

Cementless acetabular components afford bone ingrowth and enhance longevity by resisting tensile and shear stresses at the host-prosthesis interface. Modern acetabular components, with porous metal backing, have shown enhanced ingrowth and may reduce the amount of host-bone coverage that is necessary.

**Restoration of Bone Stock**

Anterolateral acetabular bone deficiency poses an important problem in total hip arthroplasty for dysplasia. Several surgical options exist, including a high hip center, placement of the acetabular component in a medialized or protruded position, or structural bone-grafting to the superolateral aspect of the acetabulum (also known as a shelf graft).

**Shelf Graft**

A shelf graft provides osteoconductive lateral support with the potential for enhanced bone stock for revision surgery. This technique provides reliable early clinical results with encouraging long-term results.

The operative technique has been described. Femoral head autograft (or rarely allograft) can be used to construct a shelf graft. Residual cartilage is reamed away to expose subchondral bone. The graft is placed at, or just within, the superior edge of the acetabulum (Figs. 4-A and 4-B) and initially secured with 3.2-mm drill bits placed in an oblique-to-vertical direction through the
Bone-Cement Augmentation and Reinforcement Rings

Encouraging early results have been reported with bone cement that was used to fill superior acetabular defects \cite{x, y, z}. Gill et al. reported on two series of reconstructions in which reinforcement rings or cages were used \cite{a}. In the initial series, a Müller reinforcement ring (also known as a roof ring) was used in eighty-seven consecutive patients with severe dysplasia, more than forty of whom received a morselized autologous femoral-head graft. The authors advocated restoration of the anatomical hip center with use of an acetabular roof reinforcement ring; bone graft was used medially and superiorly to augment bone stock. Gill et al. recommended that bone cement should not replace bone stock, as the authors believed that it contributed to aseptic loosening \cite{b}.

Subsequently, Gill et al., in a series of thirty-three hips (two of which were revised as a result of aseptic loosening), reported on the use of a Ganz ring and used an inferior hook position in the obturator foramen to provide further stability \cite{c}.

In summary, for patients with DDH, it is preferable to place the cup at the level of the true acetabulum, at an appropriate inclination, rather than in the superior, lateral, and vertical position of the false acetabulum. Structural bone graft, bone cement augmentation, and reinforcement rings are possible options when a large portion of the acetabular component remains uncovered.

Femoral Reconstruction

A small femoral intramedullary canal, femoral hypoplasia, marked femoral anteversion, a posterior position of the greater trochanter, and previous osteotomies are possible problems during femoral component insertion \cite{d}. If the hip center is lowered, a femoral shortening osteotomy may be necessary to avoid excessive tension on neurovascular structures, in particular the

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**TABLE I Principal Classification Systems of Hip Dysplasia**

<table>
<thead>
<tr>
<th>Classification</th>
<th>Type</th>
<th>Description</th>
<th>Acetabular Anatomy During Surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crowe et al. \cite{22}</td>
<td>I</td>
<td>Proximal displacement &lt;0.10 of pelvic height or less than 50% subluxation</td>
<td>Segmental deficiency of the superior wall</td>
</tr>
<tr>
<td></td>
<td>II</td>
<td>Displacement of 0.10 to 0.15 or subluxation 50% to 74%</td>
<td>Secondary shallowness due to fossa-covering osteophyte</td>
</tr>
<tr>
<td></td>
<td>III</td>
<td>Displacement of 0.16 to 0.20 or subluxation 75% to 100%</td>
<td>Anterior and posterior segmental deficiency</td>
</tr>
<tr>
<td>Hartofilakidis et al. \cite{4, 5, 21}</td>
<td>IV</td>
<td>Displacement &gt;0.20 or subluxation &gt;100%</td>
<td>Narrow opening and inadequate depth of the true acetabulum</td>
</tr>
<tr>
<td>Dysplasia (Type A)</td>
<td></td>
<td>The femoral head is contained within the original acetabulum despite the</td>
<td>Segmental deficiency of the entire acetabulum with narrow opening</td>
</tr>
<tr>
<td></td>
<td></td>
<td>degree of subluxation</td>
<td>Inadequate depth</td>
</tr>
<tr>
<td>Low dislocation</td>
<td></td>
<td>The femoral head articulates with a false acetabulum, which partially</td>
<td>Excessive antversion</td>
</tr>
<tr>
<td>(Type B)</td>
<td></td>
<td>covers the true acetabulum to a varying degree</td>
<td>Abnormal distribution of bone</td>
</tr>
<tr>
<td>High dislocation</td>
<td></td>
<td>The femoral head is completely out of the true acetabulum and migrated</td>
<td></td>
</tr>
<tr>
<td>(Type C)</td>
<td></td>
<td>superiorly and posteriorly to a varying degree</td>
<td></td>
</tr>
</tbody>
</table>

---

*Note: The table content was extracted and presented in a structured format to improve readability.*
sciatic nerve. Careful femoral canal preparation minimizes the risk of cortical perforation with a guidewire, as does the use of intraoperative radiographs, which ensures the accurate passage of the intramedullary guidewire.

For mild dysplasia, a small-size conventional femoral component can be considered. For severe dysplasia, a straight and narrow stem with limited medial curvature is beneficial, since there is frequently little remaining calcar following the femoral neck osteotomy. A derotational femoral osteotomy may be required for femoral anteversion of $>40^\circ$, and a custom or modular implant allowing version adjustment of the femoral neck will be needed. Modern, small, straight taper-stemmed implants can be rotated to neutralize femoral anteversion and mitigate the need for a derotational femoral osteotomy.

The importance of femoral component modularity was highlighted by Silber and Engh, who reported that sixteen of nineteen patients required modular components due to variation in femoral size and shape and the loss of the metaphyseal flare.

When a subtrochanteric osteotomy is performed, cementless components are commonly used to avoid cement leakage and resultant nonunion at the osteotomy site. However, Charity et al. reported good results from their series of fifteen patients with severe dysplasia who underwent subtrochanteric osteotomy and subsequent insertion of a polished, smooth, cemented femoral component.

**Femoral Osteotomy**

When the hip center is reconstructed at the level of the true acetabulum, lengthening the lower limb by $>4$ cm carries the risk of sciatic nerve palsy. A number of intraoperative methods of measuring limb length have been described; however, to date, none have been demonstrated to be superior. The amount of femoral shortening that will be required can be determined intraoperatively and compared with the preoperative determination of limb lengths through the use of templates and radiographs.

Proximal or subtrochanteric osteotomies have been described for femoral shortening. Subtrochanteric osteotomies performed with transverse, step, oblique, or double-chevron cuts allow for both angular and rotational correction in addition to shortening, and the results of several clinical studies support their use.

In summary, anatomical variations may be encountered when preparing for femoral-component insertion in patients...
with hip dysplasia. The modularity of modern revision components is greatly beneficial; however, a femoral osteotomy may be required and thorough preoperative planning will aid decision-making regarding femoral reconstruction.

Resurfacing Arthroplasty
The third generation of hip resurfacing arthroplasty implants have a cemented femoral component and a press-fit acetabular component\textsuperscript{89}. The advantages of this technique include the conservation of the femoral neck, minimal wear, and a reduced risk of dislocation due to the large diameter of both components\textsuperscript{90-93}. Such advantages would be of benefit to the young patient with DDH. However, concerns exist regarding the failure rates of first and second-generation implants\textsuperscript{94,95}, the rate of femoral neck fracture\textsuperscript{96}, metal hypersensitivity, and increased serum levels of metal ions\textsuperscript{97-100}.

Few studies specifically address metal-on-metal hip resurfacing arthroplasty for DDH patients who have arthritic changes. Early techniques and hip-resurfacing implants were associated with high rates of femoral neck fractures and femoral-side loosening for mild dysplasia\textsuperscript{101}. Amstutz et al. addressed previous failures of hip resurfacing in patients with mild dysplasia by using new techniques for femoral component fixation and meticulous bone preparation and demonstrated that the short-term results for mildly dysplastic hips are similar to the survivorship of hip resurfacing arthroplasty in nondysplastic hips\textsuperscript{102}. Furthermore, the acetabular components in the series of Amstutz et al. remained well fixed at follow-up times of two to eleven years. However, long-term studies of resurfacing for DDH are needed to address specific patient selection criteria, long-term complications and survivorship, and metal ion release.

In consideration of the use of hip resurfacing arthroplasty in general, a recent systematic review of the literature showed that none of the hip-resurfacing arthroplasty implants met full ten-year benchmark implant survival and only thirteen studies demonstrated satisfactory three-year survival\textsuperscript{103}. This study concludes that, until longer-term data are available, concerns remain regarding the effectiveness and safety of hip resurfacing arthroplasty. While the most common mode of failure was aseptic loosening, there is large variation in the rate of femoral neck fracture, the principal cause of which is not fully understood. In addition, a meta-analysis of forty-six studies comparing hip resurfacing arthroplasty with total hip arthroplasty and published in 2010 concluded that, although the functional outcomes associated with hip resurfacing arthroplasty are better or the same as those associated with total hip arthroplasty, there is an increased risk of heterotopic ossification and aseptic loosening after hip resurfacing arthroplasty and the revision rate of hip resurfacing arthroplasty is twice that of total hip arthroplasty\textsuperscript{104}. 

Fig. 4-B
Metal-on-Metal Arthroplasty
The use of metal-on-metal articulation in both total hip arthroplasty and resurfacing arthroplasty remains controversial, with growing concern regarding the incidence of symptomatic periprosthetic inflammatory reactions. A high inclination angle of the acetabular component risks edge-loading and subsequent increased component wear and an elevated serum metal-ion concentration. This process has also been associated with periprosthetic inflammatory masses.

Recent retrieval analysis suggests that the problems related to high wear rate in metal-on-metal hip resurfacing arthroplasty are likely to be similar for all types of metal-on-metal hip arthroplasty. Edge-loading occurred more often in hip resurfacing arthroplasty due to the retention of the femoral neck, which caused impingement-type edge-loading, particularly when the acetabular component had been implanted with a low inclination and either excessive or insufficient version. However, acetabular version in isolation has not been shown to influence the rate of wear in retrieved metal-on-metal hip resurfacing components.

Considering the recent evidence regarding the safety and effectiveness of metal-on-metal articulations for both hip resurfacing arthroplasty and total hip arthroplasty, metal-on-metal articulations cannot be advocated for the young DDH patient. Indeed, as a result of concerns, in April 2010 the United Kingdom Medicines and Healthcare Products Regulatory Agency issued a medical device alert regarding the safety of all types of metal-on-metal hips.

Outcomes and Complications
The complication rate associated with arthroplasty surgery is higher in patients with hip dysplasia than it is in patients who have osteoarthritis, and this difference cannot be accounted for by the younger age at which dysplastic patients present for arthroplasty.

The rate of sciatic nerve palsy following total hip arthroplasty in patients with dysplastic hips has been reported as being higher by ten times or more as compared with the rate seen in patients with nondysplastic hips. Garvin et al. suggested that 2 cm is the safe limit of limb-lengthening. Edwards et al. proposed that the risk of sciatic nerve palsy is greatly increased with lengthening of >4 cm. Suggested precautions include the use of electromyographic monitoring and the use of a wake-up test similar to that used in scoliosis surgery. It is suggested that if limb-lengthening occurs, the sciatic nerve should be exposed and palpated intraoperatively with the knee in flexion and extension to assess the degree of tension. If there is any suggestion of too much tension in the nerve, then a wake-up test should be performed. This test involves reducing the level of anesthesia to allow the patient, while on the operating table, to respond to command—specifically, ankle dorsiflexion to confirm sciatic-nerve motor function. This procedure needs to be fully explained to the patient prior to surgery and patient consent must be obtained, and the anesthetist must also be aware of the potential need to perform this test. Furthermore, if limb-lengthening is done, the ipsilateral knee should be kept flexed immediately following surgery to reduce tension on the sciatic nerve.

The highest rates of hip dislocation have been reported following arthroplasty for dysplasia. It is thought that the risk of dislocation may result from trochanteric nonunion (so-called trochanteric escape) or the impingement of the femoral component on the anterior acetabular column with the hip in flexion and internal rotation. The risk of impingement is greatest with a high hip center and a medialized cup and can be partially resolved by using a femoral component with an increased offset.

The femoral deformities inherent in patients with severe hip dysplasia increase the risk of intraoperative femoral fracture. Thus, as highlighted before, much care must be taken when preparing the femoral canal so as to avoid cortical perforation, and the use of a guidewire to ensure intramedullary position is highly recommended. If a cortical perforation is identified intraoperatively, the femoral component used must then bypass the perforation by at least two cortical diameters and the use of a cortical onlay allograft should also be considered.

Obesity is an increasingly common coexisting problem for young adult patients who present for joint replacement. Recent data support hip arthroplasty in the presence of morbid obesity because the postoperative outcome was not affected and thus the withholding of surgery on the basis of body mass index was considered unjustified. However, this study and others have also reported that obesity is a risk factor for prosthetic infection.

There is a higher infection rate reported for total hip arthroplasty performed for dysplasia as compared with total hip arthroplasty performed for osteoarthritis. The cause is probably multifactorial, including the complexity and duration of the operations, the large exposure and extensive dissection, soft-tissue stripping, and the frequent use of bone graft.

Summary
The anatomical features of hip dysplasia necessitate thorough preoperative planning to ensure that the most appropriate implants, surgical approach, and bone-restoration techniques are used. Currently, long-term clinical data support the use of a metal-on-polyethylene bearing; however, clinicians and patients alike should be aware of the increased complication rate that has been associated with total hip arthroplasty when performed for the treatment of adult hip dysplasia.


Appendix 6

Rogers BA, Sternheim A, Backstein D, Safir O, Gross AE. Proximal femoral allograft for major segmental femoral bone loss: a systematic literature review.

Contribution by BA Rogers.

Concept

Manuscript writing & editing

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Facebook:
Mendeley readers:
Review Article

Proximal Femoral Allograft for Major Segmental Femoral Bone Loss: A Systematic Literature Review

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As the indications for total hip arthroplasty increase, the prevalence of extensive proximal femoral bone loss will increase as a consequence of massive osteolysis, stress shielding and multiple revisions [1–5]. Proximal femoral bone stock deficiency provides a major challenge for revision hip arthroplasty and is likely to account for a significant future caseload [6]. Various surgical techniques have been advocated included impaction allografting, distal press-fit fixation and massive endoprosthetic reconstruction. This review article provides a systematic review of the current literature to assess the outcome of revision hip arthroplasty using allograft to reconstruct massive proximal femoral bone loss.

1. Introduction

As the need for total hip arthroplasty increases, the incidence of extensive proximal femoral bone loss will increase as a consequence of massive osteolysis, stress shielding and multiple revisions [1–5]. Proximal femoral bone stock deficiency provides a major challenge for revision hip arthroplasty and is likely to account for a significant future caseload [6].

Various surgical techniques have been advocated included impaction allografting techniques [7, 8], distal press-fit fixation [9, 10], and massive endoprosthetic reconstruction [11–13]. Individual studies have reported a 58% to 84% survivorship of massive endoprosthetic reconstruction (or megaprostheses) with average followup ranging from 5 to 10 years [11–13]. A recent retrospective review of 403 proximal femoral replacements (endoprosthetic reconstructions) from five institutions reported a 10- and 15-year survival rate of 75%, with mechanical causes being the commonest mode of failure [14].

A proximal femoral allograft reconstruction requires the use of a prosthesis bridging the host-allograft junction and obtaining fixation in the distal femur. The enhancement of future bone stock is an important advantage purported to this method of reconstruction that has been utilized in proximal femoral bone loss secondary to tumors and aseptic osteolysis. Differences in the morphology of the host-allograft junction, the use of cement, and the method of attachment of the host abductor musculature have all been described.

The three principal aims of this systematic review were as follows:

1) to document variations in the surgical techniques used,
2) to assess the clinical outcome of allograft prosthesis composites (APC) for massive proximal femoral bone loss,
3) to quantify complication rates in relation to the surgical technique used.

2. Methods

A comprehensive search of the MEDLINE, EMBASE, and the National Institutes of Health online database PubMed from the earliest records to the time of review (January 2011) was performed. The following Medical Subject Headings (MeSH) terms were used: “allograft,” “composite graft” in the manuscript title, and “proximal femoral” in the manuscript abstract. The keywords were used as both text words and Medical Search Headings (MeSH terms).
Two authors (B. A. Rogers, A. Sternheim) independently applied the search strategy to the different databases and reviewed the selected references. Titles, abstracts and papers were reviewed independently.

The following inclusion criteria were used:

1. studies retrieved by the database search using the Medical Subject Headings detailed above,
2. studies specifically reporting outcomes relating to proximal femur composite.

The following exclusion criteria were used:

1. non-English language,
2. case reports,
3. review articles,
4. not relating to human surgery,
5. patients with advanced oncological pathology,
6. followup less than 2 years.

Where more than one publication existed relating to the outcomes of same cohort of patients from the same institution, the most recent publication only was used.

Full-text manuscripts were obtained and reviewed for the studies identified using the above criteria. The method of review followed the authoritative methodology described by Mohit [15].

Allograft-prosthetic composite (APC) is a technique used to restore bone stock and mechanical stability to the proximal femur (see Figures 1(a)–1(d), and 2). The studies analyzed in this literature review consider a single technique, APC, rather than a single diagnosis; this technique has been utilized for oncological and nononcological surgery.

Eight studies report on APC used in non-oncological conditions (septic or aseptic loosening) and six report on surgeries performed for malignant or nonmalignant proximal femoral pathology. Two studies report on patient cohorts with both indications.

The primary outcome of interest was further revision of the femoral component, and Table 4 shows the reported failure rate and success rate for the allograft prosthetic composite in each study. The success rate was defined as the reported survivorship of the APC.

The total cohort included 498 patients with a mean follow up of 8.1 years (range 2 to 16.2 years). The pooled success rate was 81% (95% CI 77%–86%).

However, the number of cases and length of followup varied substantially between the studies. For example, Roque et al. reported an 82% survivorship rate for 73 allograft prosthesis reconstructions at 6.7 years followup [23], whereas Safir et al. reported 15 year Kaplan-Meier survivorship data on 50 patients of 82% [19].

3. Results

3.1. Studies. Sixteen studies reported on outcomes of proximal femoral composite allograft used to reconstruct major bone defects (see Table 1). All studies were retrospective case series and provide level IV evidence. All studies were published within the last fifteen years. Average followup ranged from 2 to 16.2 years. The total number of allograft reconstructions reported in all the studies was 498. The surgical techniques, clinical outcomes and complications were collated for all these published studies.

3.2. Surgical Techniques. The described surgical techniques varied, as shown in Tables 2 and 3.

Four studies described the complete resection of the proximal femur as the approach employed; however, the transtrochanteric approach was the most common reported.

Regarding the morphology of the osteotomy used at the junction between the proximal allograft and distal host femur, 8 studies reported a transverse femoral osteotomy, 3 that were augmented with plate fixation to enhance stability at the allograft-host junction. The remainder of the studies reported either a step or oblique femoral osteotomy.

The management of the proximal host femur varied. In 9 studies the proximal host femur was fully resected, with 5 studies using the split host proximal femur as an onlay graft after the APC had been inserted. Two studies did not detail this aspect of the surgical technique. Four studies reported the use of cortical strut allografts to reinforce the allograft-host junction [6, 18, 22, 29], with one study reporting use in every case [22].

The techniques used for fixation of the prosthesis to the allograft, and for distal fixation to the host femur is shown in Table 3. There are 14 studies reporting cemented fixation of the prosthesis to the allograft; however, distal fixation varied with 6 uncemented, 4 cemented, 5 studies employed a variety of techniques and one study did not report.

3.3. Clinical Outcomes. The primary outcome of interest was further revision of the femoral component, and Table 4 shows the reported failure rate and success rate for the allograft prosthetic composite in each study. The success rate was defined as the reported survivorship of the APC.

The total cohort included 498 patients with a mean follow up of 8.1 years (range 2 to 16.2 years). The pooled success rate was 81% (95% CI 77%–86%).

However, the number of cases and length of followup varied substantially between the studies. For example, Roque et al. reported an 82% survivorship rate for 73 allograft prosthesis reconstructions at 6.7 years followup [23], whereas Safir et al. reported 15 year Kaplan-Meier survivorship data on 50 patients of 82% [19].

3.4. Complications. Table 4 details the reported major complications. The infection rate ranged from 0% to over 21%, with a pooled mean of 8%. The two studies with a reported infection rate of over 20% had only 14 and 15 patients, respectively [13, 29]. Conversely, the four studies reporting the lowest infection rates (0 to 4%) had a mean patient cohort of 40 patients [6, 16, 17, 20].

Dislocation is a significant postoperative complication, however five out of the sixteen studies did not report the incidence of dislocation [13, 24, 25, 27, 28]. For the eleven studies that did report dislocation rate the mean was 12.8% with a range 0% to 40% [18]. The mean reported dislocation rate in studies that used a technique of splitting the host proximal femur to use as an onlay graft was 9.8%, compared to 14.9% in studies that resected the entire proximal femur.
Failure of the APC, either resulting from aseptic loosening or fracture (Table 4) ranges from 0% to 28%. The mean reported aseptic loosening or fracture rate was 13.7% for studies that used cement for fixation into distal host femur, compared to 9.1% for those studies using uncemented fixation in the distal host femur. However, the difference was not statistically different.

4. Discussion

4.1. Clinical Outcome. Severe proximal femoral bone loss is creating an increasing caseload of complex cases for the reconstructive hip surgeon [6]. The use of allograft prosthesis composite (APC) is one surgical solution used to address this problem and restore mechanical stability to the proximal femur. This analysis reviews the surgical techniques, clinical outcomes and complication, incorporating a total patient cohort of 498 from sixteen studies with a mean follow up of 8.1 years (range 2 to 16.2 years). The pooled success rate was 81% (95% CI 77%–86%), see Table 4, and provides evidence that this technique is valid and durable when performed by suitable trained and experienced surgeons, in institutions with the facilities to support such complex surgery.

4.2. Surgical Approaches and Complications. Surgical technique varied between the studies with regard to surgical approach, storage technique of the allograft bone, fixation techniques of the prosthesis to the proximal allograft, distal host femur and the junction between the allograft and host bone (see Table 2).

Several different surgical approaches were utilized in the reported studies. Four studies all pertain to tumour resection used a direct lateral approach with complete resection of the proximal femur. Trochanteric slide osteotomy was used in two studies both reported on patients who had revision of a failed hip arthroplasty. A transtrochanteric approach was reported by Vastel et al. and led to a high rate of trochanteric nonunion (25/34) with the authors recommending the use of a trochanteric plate to avoid proximal migration of the trochanter [20].
Table 1: Sixteen studies using allograft prosthetic composite in the treatment of proximal femoral bone loss, number of patients per study, primary diagnosis, and mean followup.

<table>
<thead>
<tr>
<th>Study</th>
<th>n</th>
<th>Primary diagnosis</th>
<th>Mean followup (yrs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>30</td>
<td>Aseptic</td>
<td>2</td>
</tr>
<tr>
<td>2</td>
<td>21</td>
<td>Tumor</td>
<td>6</td>
</tr>
<tr>
<td>3</td>
<td>55</td>
<td>Tumor, Aseptic, Septic revision</td>
<td>8.8</td>
</tr>
<tr>
<td>4</td>
<td>14</td>
<td>Tumor</td>
<td>10</td>
</tr>
<tr>
<td>5</td>
<td>15</td>
<td>Aseptic failure</td>
<td>2</td>
</tr>
<tr>
<td>6</td>
<td>50</td>
<td>Septic, aseptic</td>
<td>16.2</td>
</tr>
<tr>
<td>7</td>
<td>44</td>
<td>Aseptic failure</td>
<td>7.1</td>
</tr>
<tr>
<td>8</td>
<td>72</td>
<td>Aseptic</td>
<td>12</td>
</tr>
<tr>
<td>9</td>
<td>15</td>
<td>Aseptic, septic loosening</td>
<td>4.2</td>
</tr>
<tr>
<td>10</td>
<td>73</td>
<td>Tumor</td>
<td>6.7</td>
</tr>
<tr>
<td>11</td>
<td>32</td>
<td>Tumor</td>
<td>5.6</td>
</tr>
<tr>
<td>12</td>
<td>22</td>
<td>Tumor</td>
<td>4.8</td>
</tr>
<tr>
<td>13</td>
<td>20</td>
<td>Tumor</td>
<td>6.3</td>
</tr>
<tr>
<td>14</td>
<td>25</td>
<td>Aseptic, septic loosening</td>
<td>4.5</td>
</tr>
<tr>
<td>15</td>
<td>37</td>
<td>Tumor</td>
<td>7.5</td>
</tr>
<tr>
<td>16</td>
<td>15</td>
<td>Aseptic, septic loosening</td>
<td>7.6</td>
</tr>
</tbody>
</table>

Table 2: Surgical techniques used including approach, the type of femoral osteotomy performed at the host bone-allograft junction, and whether the host proximal femur was resected or split and used as an onlay graft. NR: not reported. Study numbers correlate with Table 1.

<table>
<thead>
<tr>
<th>Study</th>
<th>n</th>
<th>Surgical approach</th>
<th>Femoral osteotomy</th>
<th>Host proximal femur</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>30</td>
<td>Trochanteric slide</td>
<td>Step cut (7) transverse (23)</td>
<td>NR</td>
</tr>
<tr>
<td>2</td>
<td>21</td>
<td>Complete resection</td>
<td>Step cut</td>
<td>Resected</td>
</tr>
<tr>
<td>3</td>
<td>55</td>
<td>NR</td>
<td>Transverse (28), step cut (12)</td>
<td>Resected</td>
</tr>
<tr>
<td>4</td>
<td>14</td>
<td>Complete resection</td>
<td>NR</td>
<td>Resected</td>
</tr>
<tr>
<td>5</td>
<td>15</td>
<td>Posterolateral (9), trochanteric Slide (2)</td>
<td>Oblique</td>
<td>Resected</td>
</tr>
<tr>
<td>6</td>
<td>50</td>
<td>Trochanteric slide</td>
<td>Step cut</td>
<td>Split and onlay</td>
</tr>
<tr>
<td>7</td>
<td>44</td>
<td>Transtrochanteric</td>
<td>Transverse</td>
<td>Split and onlay</td>
</tr>
<tr>
<td>8</td>
<td>72</td>
<td>Hardinge (44), posterior (11), transtrochanteric (17)</td>
<td>Step cut (62), telescoping (10)</td>
<td>Split and onlay</td>
</tr>
<tr>
<td>9</td>
<td>15</td>
<td>Transtrochanteric</td>
<td>Transverse (9), step cut (6)</td>
<td>NR</td>
</tr>
<tr>
<td>10</td>
<td>73</td>
<td>Complete resection</td>
<td>NR</td>
<td>Resected</td>
</tr>
<tr>
<td>11</td>
<td>32</td>
<td>Trochanteric slide (12), resection (20)</td>
<td>Transverse</td>
<td>Resected</td>
</tr>
<tr>
<td>12</td>
<td>22</td>
<td>Complete resection</td>
<td>Transverse</td>
<td>Resected</td>
</tr>
<tr>
<td>13</td>
<td>20</td>
<td>NR</td>
<td>NR</td>
<td>Resected</td>
</tr>
<tr>
<td>14</td>
<td>25</td>
<td>Trochanteric slide</td>
<td>Step cut</td>
<td>Split and onlay</td>
</tr>
<tr>
<td>15</td>
<td>37</td>
<td>Posterolateral (28), transtrochanteric (10)</td>
<td>Transverse</td>
<td>Resected</td>
</tr>
<tr>
<td>16</td>
<td>15</td>
<td>Transtrochanteric</td>
<td>Transverse</td>
<td>Split and onlay</td>
</tr>
</tbody>
</table>

Trochanteric nonunion and abductor strength are also influenced by surgical approach. The trochanteric slide osteotomy aims to maintain the continuum of tissue from the abductors and the greater trochanter to the vastus lateralis. This approach has been reported to have a higher rate of trochanteric union [30]. The trochanteric slide osteotomy has been further modified to maintain the external rotators and thus improve hip stability [30–32]. The junctional osteotomy between the host femur and the proximal allograft was transverse, oblique or step-cut (see Table 2). A step-cut osteotomy may offer more rotational stability while an oblique osteotomy may offer more surface area for bone in-growth compared to a transverse osteotomy. Langlais et al. reported on two cases of loosening with junctional failure that they attributed to a lack of a step-cut osteotomy at the junction [16]. This junction may be further reinforced with strut allografts [6, 18, 22, 29]. Nonunion of the junction between the native femur and the proximal allograft causes macro motion at the junction that is treated with bone grafting, plating, and/or a strut allograft [16]. Host-allograft junctional nonunion may be reduced by augmentation with additional autologous bone graft and supporting it with either a plate or a strut allograft. Several studies highlight the bone union at the host-allograft
Table 3: Table showing methods of implantation of prosthesis into allograft to form the allograft prosthesis composite (APC) and methods for securing APC to distal host femur. NR: not reported. Study numbers correlate with Table 1.

<table>
<thead>
<tr>
<th>Study</th>
<th>Allograft-prosthesis fixation</th>
<th>APC-host bone fixation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Cemented</td>
<td>Uncemented</td>
</tr>
<tr>
<td>2</td>
<td>Cemented</td>
<td>Cemented</td>
</tr>
<tr>
<td>3</td>
<td>Cemented</td>
<td>Cemented</td>
</tr>
<tr>
<td>4</td>
<td>Cemented (16), uncemented (2)</td>
<td>Cemented(14), Uncemented(2), + plating(2)</td>
</tr>
<tr>
<td>5</td>
<td>Uncemented</td>
<td>Uncemented + plating</td>
</tr>
<tr>
<td>6</td>
<td>Cemented</td>
<td>Uncemented</td>
</tr>
<tr>
<td>7</td>
<td>Cemented</td>
<td>Cemented</td>
</tr>
<tr>
<td>8</td>
<td>Cemented</td>
<td>Uncemented (44), cemented (22)</td>
</tr>
<tr>
<td>9</td>
<td>Uncemented</td>
<td>Uncemented (12), cemented (3)</td>
</tr>
<tr>
<td>10</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>11</td>
<td>Cemented</td>
<td>Cemented</td>
</tr>
<tr>
<td>12</td>
<td>Cemented</td>
<td>Uncemented</td>
</tr>
<tr>
<td>13</td>
<td>Cemented</td>
<td>Varied</td>
</tr>
<tr>
<td>14</td>
<td>Cemented</td>
<td>Uncemented</td>
</tr>
<tr>
<td>15</td>
<td>Cemented</td>
<td>Uncemented + plating</td>
</tr>
<tr>
<td>16</td>
<td>Cemented</td>
<td>Uncemented (13), cemented (2), + plating</td>
</tr>
</tbody>
</table>

Table 4: Table showing complications of prosthesis into allograft to form the allograft prosthesis composite (APC) and methods for securing APC to distal host femur. The total cohort included 498 patients with a mean follow up of 8.1 years (range 2 to 16.2 years). The pooled success rate was 81% (95% CI 77%–86%). Success rate: APC not revised. NR: not reported. Study numbers correlate with Table 1.

<table>
<thead>
<tr>
<th>Study</th>
<th>n</th>
<th>Failed constructs</th>
<th>Success rate</th>
<th>Infection</th>
<th>Dislocation</th>
<th>Aseptic loosening or fracture</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>30</td>
<td>3</td>
<td>90%</td>
<td>1 (3.3%)</td>
<td>5 (16.7%)</td>
<td>4 (13.3%)</td>
</tr>
<tr>
<td>2</td>
<td>21</td>
<td>2</td>
<td>82%</td>
<td>0</td>
<td>0</td>
<td>6 (28.6%)</td>
</tr>
<tr>
<td>3</td>
<td>55</td>
<td>6</td>
<td>85%</td>
<td>2 (3.6%)</td>
<td>4 (7.3%)</td>
<td>5 (9.1%)</td>
</tr>
<tr>
<td>4</td>
<td>14</td>
<td>4</td>
<td>78%</td>
<td>3 (21.4%)</td>
<td>NR</td>
<td>1 (7.1%)</td>
</tr>
<tr>
<td>5</td>
<td>15</td>
<td>3</td>
<td>73%</td>
<td>1 (6.7%)</td>
<td>6 (40%)</td>
<td>2 (13.3%)</td>
</tr>
<tr>
<td>6</td>
<td>50</td>
<td>8</td>
<td>84%</td>
<td>2 (4%)</td>
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<td>3 (20%)</td>
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<td>4 (20.7%)</td>
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</tbody>
</table>

junction as a key factor in achieving stability of the composite graft, and thereby lowering the chance of mechanical failure [17, 19, 21, 33].

Cement fixation of the prosthesis to the allograft with cementless fixation to the host femur was used in seven studies (see Table 3) [6, 19, 24, 25, 27–29]. The rationale for cement fixation in the allograft-prosthesis composite is that in-growth and on-growth would not be expected at the allograft prosthesis interface. Only Zmolek and Dorr reported a fully uncemented fixation of the prosthesis and allograft in 11 patients with similar rates of success compared to other studies [18].

Regarding distal fixation to the host femur, an uncemented technique was principally employed in nine studies [6, 18, 19, 22, 24, 25, 27–29], cemented in four studies [13, 16, 17, 20], mixed cemented and uncemented distal fixation in one study [21], and one study did not report whether or cement was used (see Table 3).
For the studies that utilized cementless distal fixation, some employed a press-fit or interference technique whereas others used an oblique or step-cut junctional osteotomy. Safir et al. used an uncemented technique in the distal host femur with a step-cut or oblique osteotomy affording direct loading at the allograft-host femur junction [19]. The authors support the concept that direct loading of the host-allograft junction minimizes allograft resorption. The distal femur being initially reamed to the optimal size, with the proximal femoral allograft also reamed and broached until a good fit was achieved for the long-stem femoral prosthesis. The mismatch in the medullary sizes of the host bone and the allograft resulted in a good press-fit fixation never being achieved between the femoral stem and the distal host femur. Further, the allograft was never over reamed to accommodate a larger femoral component for the host femur. In contrast, Haddad et al. cemented the prosthesis to the distal femur thus stress shielding, the allograft and commented that this may explain the high rate of graft resorption (17%) observed [17].

Overall, cemented fixation in the distal host bone was associated with a higher rate of aseptic loosening or fracture (13.7%) when compared to uncemented distal fixation (9.1%; see Table 4). Whilst the difference was not statistically significant, the benefit of uncemented distal fixation is the reduced risk of junctional nonunion between the host femur and allograft.

The population cohorts, the duration, and complexity of the surgery result in infection rates for APC being greater than that for primary hip arthroplasty (see Table 4). Considering these factors, the pooled 8% infection rate is not unacceptable. The infection rate is, however, related to quantity performed with the lowest infection rates (0 to 4%) being reported in those studies with the greater number of cases [6, 16, 17, 20]. Although observer bias may influence this data, a greater caseload and experience is likely to be beneficial.

The use of native proximal femur with its soft-tissue attachments as an onlay graft around the composite allograft was reported in five studies [19–21, 27, 29]. This vascularised viable bone can promote in-growth into the allograft and preserves the abductor mechanism and short external rotators. These five studies report a lower mean dislocation rate of 9.8%, compared to 14.9% (see Table 4). From the surgical approaches detailed in these studies, the risk of dislocation may be minimized by:

1. Preservation of the host posterior capsular structures if possible,
2. Good biomechanical reconstruction of length, version and offset of the prosthesis-allograft construct,
3. Maintaining the bone-soft tissue attachment to the host femur, to provide both mechanical stability and to act as a vascularised graft.

A constrained acetabular liner may be considered in cases of minimal abductor musculature.

5. Conclusion

The continued followup and analysis of this technique should be encouraged to refine and develop the management of massive proximal femoral bone loss. This review demonstrates that proximal femoral allografts for revision hip arthroplasty in femoral segmental bone loss do provide a durable solution, with current available evidence reporting a survivorship of 80%. Whilst a range of surgical techniques have been described, this study highlights the following:

1. High caseload is associated with a lower infection rate,
2. Uncemented distal fixation is associated with a reduced risk of aseptic loosening or fracture,
3. If available, using the host femur as an onlay graft enhances hip stability whilst acting as a vascularised graft.

References


Appendix 7

Rogers BA, Sternheim A, De Iorio M, Backstein D, Safir O, Gross AE.
Proximal femoral allograft in revision hip surgery with severe femoral bone loss: a systematic review and meta-analysis.

Contribution by BA Rogers.

- Concept
- Data Collection & management
- Manuscript writing & editing

Citation Metrics

- Web Of Science: 8
- Google Scholar: 13
- Altmetrics: 0

  - Tweets:
  - Facebook:
  - Mendeley readers:
Proximal Femoral Allograft in Revision Hip Surgery With Severe Femoral Bone Loss

A Systematic Review and Meta-Analysis

Benedict A. Rogers, MSc, MRCGP, FRCS(orth),* Amir Sternheim, MD, FRCS,* Maria De Iorio, PhD,† David Backstein, MD, MEd, FRCSC,* Oleg Safir, MD, FRCSC,* and Allan E. Gross, MD, FRCSC*

Abstract: This study provides an objective appraisal of available evidence regarding the outcome of proximal femoral allograft for reconstruction of massive proximal femoral bone loss. The primary outcomes were rates of success, structural failure, and infection. A systematic literature review identified 16 studies with a minimum 2-year follow-up. Estimated pooled effect analysis performed with heterogeneity quantified using $I^2$ and $\tau^2$. The total cohort included 498 patients with a mean follow-up of 8.1 years. The pooled success rate was 81%, pooled structural failure rate of 15%, and pooled infection rate of 8%. Significant heterogeneity was observed in structural failure rates ($I^2 = 47.9$, $\tau^2 = 0.29$, $P < .05$). Proximal femoral allografts afford viable reconstruction for massive femoral bone loss when performed by experienced. Keywords: proximal femoral allograft, outcome, meta-analysis, systematic review.

As the need for revision total hip arthroplasty increases, surgeons are increasing, forced to deal with extensive proximal femoral bone loss as a consequence of massive osteolysis, stress shielding, and multiple revisions [1-5]. Proximal femoral bone stock deficiency provides a major challenge for revision hip arthroplasty and is likely to account for a significant future caseload [6].

Various surgical techniques have been advocated for treatment of proximal femoral bone loss including impaction allografting techniques [7,8], distal press-fit fixation [9,10] and massive endoprosthetic reconstruction (megaprostheses) [11-13]. A previous study has reported a 5- to 10-year megaprostheses survivorship of 58% to 84% [14]. A recent retrospective review of 403 proximal femoral arthroplasties (endoprosthetic reconstructions) from 5 institutions reported a 10- and 15-year survival rate of 75%, with mechanical causes being the most common mode of failure [15].

Proximal femoral allograft (PFA) composites combine the use of a long-stem femoral prosthesis and allograft bone. A femoral prosthesis is placed distally within the medullary canal of the host femur, whereas the proximal portion of the stem is positioned and secured within a proximal femur allograft, for example, see Figs 1A to C. The allograft provides initial stability by acting as a strut graft and enhances future bone stock. The potential for enhanced future bone stock may simplify future additional revision surgery and serves as an attachment surface for soft tissues and bone.

There is relatively little published literature describing the outcomes of PFA composites, and all are retrospective case series. The caseload for this surgical technique results from patients with massive femoral bone loss having previously undergone either multiple revision arthroplasty surgery or proximal femoral resection for oncological pathology.

To draw firmer conclusions about overall survival in PFA cases, a meta-analysis of all available data is necessary. Although most studies are retrospective, a meta-analysis is appropriate if strict methodological guidelines are followed [16].

The objective of this systematic review and meta-analysis was to provide an objective appraisal of the
available evidence regarding the outcome of hip arthroplasty surgery using allograft to reconstruct massive proximal femoral bone loss. The primary outcomes of interest were the reported rates of success, structural failure, and infection, whereas the secondary outcomes were the reported rates of major revision surgery to the PFA, dislocation, and nonunion.

Methods

This review was based on the Cochrane methodology for conducting systematic reviews and meta-analysis [17,18].

Study Selection Criteria

Studies reporting the outcome of PFA composites after previous revision hip arthroplasty or proximal femoral resection were identified for this meta-analysis.

A search of the National Library of Medicine (Medline), National Institutes of Health (PubMed), and EMBASE databases from the earliest records to the time of review (February 2011) was performed. The following Medical Subject Headings (MeSH) terms were used: allograft, composite graft in the article title, and proximal femoral in the article abstract.

The keywords were used as both text words and MeSH terms. These were arranged by means of varying combinations of the Boolean operators AND, NOT, and OR, and the results were limited to publications published in English or those that had been translated to English. There were no limitations set on publication date. The PubMed search was then refined to include clinical studies in adult humans. The results were cross-checked with other databases, namely, Google and Google Scholar. The bibliographies of the retrieved trials were examined for additional articles.

The following inclusion criteria were used:

1. studies retrieved by the database search using the MeSH detailed above; and
2. studies specifically reporting outcomes relating to “proximal femur composite” or “allograft prosthesis composite (APC).”

The following exclusion criteria were used:

1. non-English language;
2. case reports;
3. review articles;
4. not relating to human surgery;
5. patients with advanced oncological pathology; and
6. follow-up of less than 2 years.

Thus, studies that reported patients who were lost to follow-up within 2 years of surgery were excluded. For retrospective studies, publications reporting on the same cohort group from the same institution were limited to the most recent publication. Patients who underwent the index resection because of a tumor and later went on to fail because of a local recurrence of the tumor were excluded from outcome analysis.

Article Collection and Analysis

Two authors (BR and AS) independently applied the search strategy to the different databases and reviewed the selected references. Titles, abstracts, and articles were reviewed independently in a sequential and systematic manner (see Fig. 2). A systematic review of each article was performed to assess the methodology, the surgical techniques, and area of bias in accordance with previous published guidelines on literature review [19]. The level of evidence for each article was assessed.
according to the guidelines of the Journal of Bone and Joint Surgery (American Volume) [20]. The extracted data form was then agreed upon. Data were extracted independently by the 2 authors (BR and AS) and were later reviewed jointly to produce the most accurate data. Disagreement was resolved with the senior authors (AEG, DB, and OS).

**Outcome Measures**

Regarding the primary outcomes measures, full statistical meta-analysis, with forest plot graphic representation, was performed for the reported success rate, mechanical failure rate due to fracture or evident loosening of the allograft and/or prosthesis, and the infection rate.

**Major revision surgery** was defined as removal or replacement of the APC due to infection or mechanical failure (loosening or fracture). The rate of major revision surgery was reported without full meta-analysis because it is directly influenced by the other 3 primary outcomes.

Further secondary outcome measures of interest were dislocation rate and the reported nonunion rate, whether surgically revised. Full statistical meta-analysis was not performed with regard the secondary outcome measures.

**Meta-analysis**

Statistical meta-analysis was performed on the selected articles, with forest plots produced for 3 outcomes: pooled success rate, failure rate (combined fracture or loosening), and infection rate. For each of these 3 outcomes, the effect (proportion) was calculated for every individual study and the pooled effect considering all the studies. The meta-analysis was based upon the Freeman-Tukey double arcsine transformation of the frequencies.

Both fixed and random effect model analyses were performed, and the 95% confidence intervals (CIs), stated. With a fixed effect analysis, all of the studies were considered conducted under similar conditions with similar subjects; therefore, the only difference between studies being the power to detect the outcome of interest, whereas the random effect model assumes that there is a different underlying effect for each study. The different effects are combined to estimate an overall effect by taking into account this additional source of variation. Many investigators consider the random effects approach to be a more natural choice than fixed effects, for example, in medical decision-making contexts [21-23].

The heterogeneity associated with the studies incorporated in the meta-analysis was assessed using both the I^2 and r^2 statistics. The I^2 statistic describes the percentage of variation across studies that are due to heterogeneity rather than chance [24,25]. It is a simple expression of inconsistency of the studies' results and depends upon the extent of overlap in CIs across studies. The magnitude of heterogeneity was quantified using a point estimate of the among-study variance of true effects called r^2. P < .05 was deemed significant.

**Publication Bias**

The number of unpublished studies on this surgical technique is unknown, and thus, such a meta-analysis is at risk for publication bias. The overestimated significance of published studies may cause a significant "base rate fallacy" that results from a skewed distribution of effect sizes.

A funnel plot was used to graphically visualize the relationship between sample size and effect size and, therefore, the degree of publication bias. The studies were arranged by sample size on a linear y-axis, and reported success rate or effect size, on a linear x-axis.

**Results**

**Article Selection**

The initial literature search strategy provided 74 possible studies. Subsequent reading of the abstracts led to exclusion of 51 of these studies, and the full-published articles were obtained for the remainder. The articles were assessed, and 2 were excluded for insufficient data pertaining to outcome success and failure, 2 were review articles, and 3 studies were excluded because they originated from institutions that had subsequently published updated studies that were included. Overall, 16 studies met the inclusion criteria and were identified as appropriate for this meta-analysis.
Data Collection

The level of evidence, according to the Journal of Bone and Joint Surgery (American Volume) guidelines, for each article was identified [20]. All articles included in this study had provide level IV evidence.

For each article, the following were quantified: the number of cases, mean follow-up time in years, and the reported success, failure, infection, nonunion, dislocation, and revision rates (see Table 1; available online at www.arthroplastyjournal.org).

The cumulative number of patients treated with a PFA was 498, and the mean duration of follow-up for the included studies was 7.35 years (range, 2-16.2 years). The mean study size was 31 patients (range, 11-73 patients).

Pooled Success Rate

The reported success rates ranged from 66% [26] to 95% [14] (see Table 1; available online at www.arthroplastyjournal.org and Fig. 3). The fixed effect and random effects pooled estimates of success were both 81% (see Fig. 3). The 95% CI was slightly wider for the random effects analysis (0.77-0.86) compared with that of the fixed effect (0.78-0.86).

There was no significant data heterogeneity within the pooled success rate analysis (P = .0635).

Pooled Failure Rate

The quantifiable reported structural failures of PFA reconstructions included fracture and aseptic loosening. The range of reported structural failures was from 0% [14] to 55% [27].

The pooled estimated of structural failure rate was 15% with both fixed (95% CI, 0.12-0.18) and random (95% CI, 0.10-0.19) effects model analysis (see Fig. 4). There was a significant level of data heterogeneity regarding pooled failure as an outcome (P = .0171), principally the result of a single outlying study [27].

Pooled Infection Rate

The reported infection rates ranged from 0% [27] to 20% [28]. The fixed and random effect pooled estimates of infection were 8% (95% CI, 0.06-0.11), see Fig. 5. There was no significant data heterogeneity (P = .6892) regarding infection as an outcome.

Heterogeneity of Outcomes

Table 2 shows the relative heterogeneity of the 3 outcome measures used in the meta-analysis (success, structural failure, and infection). The data relating to structural failure of PFA reconstructions have the highest degree (I^2) and magnitude (τ^2) of heterogeneity and are the only outcome with statistically significant heterogeneity (P < .05).

Publication Bias

The linear scale funnel plot for the selected articles is shown in Fig. 6. The center of the funnel on the x-axis has been defined by the pooled estimate of the success rate, namely, 0.81 (see Fig. 3). Ten studies report a success rate greater than the pooled estimate of success, and 6 reported a lower success rate. There is an even distribution of studies within the funnel plot.

Outcomes Not Amenable to Meta-Analysis

Because of confounding factors, the 3 outcomes commonly reported were not amenable to meta-analysis, namely, nonunion, revision surgery of the PFA, and dislocation. The absolute rates for these outcomes are shown in Table 1; available online at www.arthroplastyjournal.org.

![Fig. 3. Meta-analysis forest plot for success rate after PFA reconstruction. The allocated study number corresponds to those listed in Table 1; available online at www.arthroplastyjournal.org.](image-url)
The nonunion rate ranged from 7% [26] to 77% [29] (mean, 25.25%). The reported dislocation rate ranged from 0% [27,30] to 54.5% [31] (mean, 12.8%). The rate of revision surgery ranged from 5% [14] to 33.9% [26] (mean, 16.8%).

**Discussion**

Severe proximal femoral bone loss is creating an increasing caseload of complex cases for the reconstructive hip surgeon [6]. The use of PFAs is one surgical solution used to address this problem and restores mechanical stability to the proximal femur. The studies analyzed in this literature review and meta-analysis consider a single technique, PFA, rather than a single diagnosis with this technique implemented for both oncological and nononcological orthopedic surgery.

A further subanalysis comparing oncological against nononcological surgery was considered; however, these subgroups were too small to provide adequate statistical power, and furthermore, most studies combined the 2 subgroups of patients and reported the data together. The meta-analysis incorporates a total patient cohort of 498 from 16 studies. With a pooled survivorship rate of more than 80% (see Fig. 3), it provides evidence that this surgical technique is valid and durable when performed by suitable, trained, and experienced surgeons in institutions with the facilities to support such complex surgery.

The large-range structural failures (0% [14] to 55% [27]) secondary to fracture (allograft and/or prosthesis) and aseptic loosening had a pooled estimate of 15% (see Fig. 4). However, a single outlying study [27] significantly influenced this result and caused a significant

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**Fig. 4.** Meta-analysis forest plot for fracture or loosening rate after PFA reconstruction. The allocated study number corresponds to those listed in Table 1; available online at www.arthroplastyjournal.org.

**Fig. 5.** Meta-analysis forest plot for infection rate after PFA reconstruction. The allocated study number corresponds to those listed in Table 1; available online at www.arthroplastyjournal.org.
degree of statistical heterogeneity ($P = .0171$). All the remaining studies reported structural failure rates of less than 30% (see Fig. 4). There were insufficient data regarding allograft resorption to specifically address it as a cause of mechanical failure.

The population cohorts and the duration and complexity of the surgery result in infection rates higher than that for primary hip arthroplasty. However, considering these factors, the pooled 8% infection rate is not unacceptable (see Fig. 5).

Major revision surgery rates for removal or replacement of the PFA were 5% [14] to 33.9% [26] with a mean of 16.8%. The major revision surgery rate closely reflects the reported combined loosening/infection rate, with the nonoperative treatment of some complications accounting for the discrepancy between the 2.

Dislocation is a significant postoperative complication; however, 5 of the 16 studies did not report the incidence of dislocation [13,29,32-34]. For the 11 studies that did report dislocation rate, the mean was 12.8% with a range of 0% [27,30] to 54% [31]. Numerous confounding factors contribute to this complication, including the number of previous surgeries, surgical approach used, alignment and position of the acetabular component, soft tissue tension, and function, none of which could be controlled to allow a valid meta-analysis and pooled estimate.

Two studies did not report the rate of trochanteric nonunion [13,30]. The reported incidence of nonunion varied considerably from 7% [26] to 77% [29] with a mean of 25.25%. However, concerns regarding the exact definition of nonunion used precluded stringent statistical analysis.

The rates of revision surgery for dislocation, trochanteric nonunion, and host-allograft junctional nonunion were reported in only 8 of the 16 studies. Furthermore, where reported, there was insufficient detail regarding such surgery to afford an objective and valid analysis. For example, the rates of liner exchange, bone grafting, and trochanteric takedown were not reported.

The systematic review highlighted some important surgical factors, not amenable to statistical analysis, that influence the success of this technique, surgical approach, allograft preparation and storage, and allograft fixation to host bone.

**Surgical Approach**

Surgical technique varied between the studies with regard to surgical approach, storage technique of the allograft bone, fixation techniques of the prosthesis to the proximal allograft, distal host femur, and the junction between the allograft and host bone.

Trochanteric nonunion and abductor strength are also influenced by surgical approach. The trochanteric slide osteotomy aims to maintain the continuum of tissue from the abductors and the greater trochanter to the vastus lateralis. This approach maintains a higher rate of trochanteric union [35]. When trochanteric nonunion occurs after a trochanteric slide osteotomy, proximal migration of the trochanter is avoided.

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<table>
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<td>Structural failure rate</td>
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<td>.0171</td>
</tr>
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<td>Infection rate</td>
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**Fig. 6.** Funnel plot for the 16 studies used in this meta-analysis using linear scale for reported percentage success rate (x-axis) and linear scale for study sample size (y-axis).
trocchanteric slide osteotomy has been further modified to maintain the external rotators and thus improve hip stability [35-37].

**Allograft Preparation and Storage**

Allograft preparation and storage varied between studies. Nonirradiated fresh allograft, stored just above 0°C, was used in 5 studies to help preserve osteocyte viability [6,27,30,31,38]. However, a further 4 studies used irradiated deep-frozen bone at ~80°C, providing a nonviable structural graft with a lower immunogenic and infection risk [26,33,39,40]. One study reports the use of irradiated and nonirradiated allografts [32], and 2 studies did not report the storage and use of irradiation of the allograft [34,41].

**Allograft Fixation**

Cement fixation of the prosthesis to the allograft with uncemented fixation to the host femur was used in 7 studies [6,28,29,32-34,41]. The rationale for cement fixation in the allograft-prosthesis composite is that ingrowth and on-growth would not be expected at the allograft prosthesis interface. Only Zmolek and Dorr [31] reported a fully uncemented fixation of the prosthesis and allograft in 11 patients with similar rates of success compared with other studies.

Regarding the distal fixation of prosthesis to the host bone, an uncemented technique within distal host bone was principally used in 9 studies [6,28,29,31-34,40,41], and cemented distal fixation was used in 4 studies [13,27,39,42]. One study reported a mixture of cases using both techniques [26]. Two studies did not report whether cement was used [14,30].

Several studies highlight the bone union at the host-allograft junction as a key factor in achieving stability of the composite graft and thereby lowering the chance of mechanical failure [26,41-43]. The junctional osteotomy between the host femur and the proximal allograft was either transverse, oblique, or step cut. A step cut osteotomy may offer more rotational stability, whereas an oblique osteotomy may offer more surface area for bone in-growth compared with a transverse osteotomy.

There are strengths to this meta-analysis that provide a statistical examination of scientific studies. Two independent authors conducted a thorough literature search, and published studies were included regardless of their publication date. This was a contemporary review with 75% of the studies published within the last decade. The cumulative data set (n = 498) is substantially larger than any one study. A potential weakness of a meta-analysis conducted on small sample size studies is the inherent risk of publication bias. However, the funnel plot (see Fig. 6) demonstrates a graphically symmetrical distribution profile of studies, including small studies with results inferior to the pooled estimate of success, which reduces the risk of publication bias.

The limitations of this meta-analysis include the inability of the methods to control the source of any potential bias considering the level IV evidence of all the incorporated studies. The validity of a meta-analysis is influenced by the quality of the constituent studies. In addition, one cannot know how many studies have been performed, and the results are not published.

However, logistic and ethical issues make it unlikely that future studies on this surgical technique will provide level III evidence or higher. Furthermore, although qualitative heterogeneity may exist between the studies, all the studies were conducted at academic orthopedic units and had been accepted by international peer-reviewed orthopedic journals.

In conclusion, although continued follow-up and critical analysis of this technique should be encouraged, this systematic review and meta-analysis support the use of PFAs for the reconstruction of massive femoral bone loss.

**References**


Table 1. Publication List Detailing, Underlying Diagnosis, Number of Cases, Length of Follow-Up, and Success and Complication Rates

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N/R indicates not reported.
Appendix 8


Contribution by BA Rogers.

Data Collection & management

Manuscript writing & editing

Citation Metrics

Web Of Science: 3

Google Scholar: 7

Altmetrics: 0

Tweets:

Facebook:

Mendeley readers:
Segmental proximal femoral bone loss and revision total hip replacement in patients with developmental dysplasia of the hip

The treatment of substantial proximal femoral bone loss in young patients with developmental dysplasia of the hip (DDH) is challenging. We retrospectively analysed the outcome of 28 patients (30 hips) with DDH who underwent revision total hip replacement (THR) in the presence of a deficient proximal femur, which was reconstructed with an allograft prosthetic composite. The mean follow-up was 15 years (8.5 to 25.5). The mean number of previous THRs was three (1 to 8). The mean age at primary THR and at the index reconstruction was 41 years (18 to 61) and 58.1 years (32 to 72), respectively. The indication for revision included mechanical loosening in 24 hips, infection in three and peri-prosthetic fracture in three.

Six patients required removal and replacement of the allograft prosthetic composite, five for mechanical loosening and one for infection. The survivorship at ten, 15 and 20 years was 93% (95% confidence interval (CI) 91 to 100), 75.5% (95% CI 60 to 95) and 75.5% (95% CI 60 to 95), respectively, with 25, eight, and four patients at risk, respectively. Additionally, two junctional nonunions between the allograft and host femur required bone grafting and plating.

An allograft prosthetic composite affords a good long-term outcome in the management of proximal femoral bone loss in revision THR in patients with DDH, while preserving distal host bone.

Developmental dysplasia of the hip (DDH) may be associated with anatomical malformations including a shallow acetabulum, proximal subluxation or dislocation of the hip, excessive anteversion of the femoral neck, a relatively posterior greater trochanter, a narrow femoral canal and abnormal bone quality around the hip. These patients often require total hip replacement (THR) at a young age. Proximal femoral bone loss and early femoral prosthetic loosening may subsequently develop due to the anatomical abnormalities and the high functional demand of these young patients. This may lead to many revision procedures, further proximal femoral loss and an ectatic distal femoral canal. The complication rate following THR is higher in patients with dysplasia than in those with degenerative osteoarthritis; this cannot be fully accounted for by the younger age at which patients with dysplasia present for surgery. These complications include sciatic nerve palsy, with an incidence of between 0.5% and 1%, increasing to 3% to 15% in dysplastic hips, dislocation (5% to 11%), peri-operative femoral fracture, and a higher rate of infection compared with that encountered in the treatment of osteoarthritis. These complications lead to a higher rate of revision at a younger age, which in turn increases the risk of proximal femoral bone loss as a result of mechanical loosening, infection and peri-prosthetic fracture.

Various surgical techniques have been advocated to manage proximal femoral bone loss, including impaction allografting, distal press-fit fixation of a longer stem, massive endoprosthetic reconstruction and the use of an allograft prosthetic composite (APC). Survivorship of between 58% and 84% has been reported for massive endoprosthetic reconstruction with follow-up ranging from five to ten years. The technique of APC reconstruction uses a long stemmed prosthesis that spans the host-allograft bone junction.

The aim of this study was to assess retrospectively the long-term outcome and complications related to revision THR using a proximal femoral APC for the reconstruction of massive proximal femoral bone loss in patients with DDH. The primary outcome of interest was further revision, and the secondary outcomes of interest included other complications such as infection, dislocation and nonunion.
A type 4 defect is a full circumferential bone loss of at least 8 cm in length extending into the diaphysis. Inclusion criteria were previous THR for DDH and a type 4 or 5 bone defect of the proximal femur according to the Gross classification. A type 4 defect is a full circumferential bone loss of > 8 cm in length extending into the diaphysis. A type 5 defect is similar with an associated peri-prosthetic fracture. Both were treated with an APC incorporating a long stemmed prosthesis. A total of 38 patients met the inclusion criteria. Exclusion criteria included patients living abroad, those with < 24 months follow-up and those who had died due to unrelated causes or who had been lost to follow-up within 24 months of surgery. This led to the exclusion of eight patients. The study included four patients who died after ten years of follow-up.

There were a total of 30 hips in 28 patients (25 females, three males) who were followed for a mean of 15 years (8.5 to 25.5). The mean age at primary THR was 41 years (18 to 61). The median number of previous joint replacements on the affected hip prior to the index revision procedure was three (1 to 8). The mean age at the revision with the APC was 58.1 years (32 to 72). The cause for the index revision THR was aseptic loosening of the femoral component in 24 patients, peri-prosthetic fracture in three and infection (second stage revision) in three.

All procedures were performed by the senior surgeon (AEG) through a trochanteric slide approach. The long stem of an APC bridges the host-allograft junction, which is fashioned as a step-cut or oblique osteotomy in order to aid rotational and axial stability of the construct. The prosthesis is cemented proximally in the allograft and uncemented distally in the host bone. The prostheses used were 23 Gross long stem allograft prostheses (DePuy/Johnson & Johnson, Warsaw, Indiana), five Charnley long stem prostheses (DePuy, Leeds, United Kingdom) and two ZMR prostheses (Zimmer, Warsaw, Indiana). Allograft was stored at -70°C after being irradiated with 2.5 Mrad according to the American Association of Tissue Banks accredited tissue bank guidelines. Cultures of the graft were taken before immersion in warm 50% povidone iodine solution. The graft was prepared on a separate sterile surgical table by a second surgical team. The femoral head of the allograft was excised at the base of the lesser trochanter to facilitate insertion of the implant and adjustment of version. Lengthening of the leg was not carried out via the neck cut, but rather by the length of the allograft below the lesser trochanter. A stable graft-host junction is a crucial part of the technique and was achieved with either a step cut or an oblique osteotomy. The greater trochanter of the allograft was excised, allowing attachment of the host trochanter (Fig. 1). Reaming the allograft was then carried out prior to insertion and cementing of the implant. The host canal at the metaphysis was generally larger than the diaphyseal canal of the allograft and therefore a distal press-fit was not achieved. Stability was achieved once union occurred at the graft host junction. Junctional union may be improved with morcellised autograft bone and stability may be enhanced with the addition of strut allografts. The remaining proximal femoral host bone, and its associated soft tissue, was preserved during the extended osteotomy and used as a vascularised onlay graft around the APC.

The post-operative rehabilitation protocol included non-weight-bearing for eight to 12 weeks until there was radiological evidence of union at the graft-host junction. At this time, abductor muscle strengthening exercises were commenced, including active straight leg abduction.

The length of the allograft was measured from the base of the lesser trochanter to the distal end of the graft, excluding the step cut distally and the greater trochanter proximally. The mean length of the 30 allografts was 12.2 cm (6 to 22). Patients were reviewed at six weeks, three months, six months, one year and then annually. Clinical assessment included an evaluation of leg length, wound, range of movement and neurological status. Radiological assessment included an anteroposterior (AP) pelvic view, and an AP and lateral view of the hip and entire femur. Functional outcome was assessed with the original Harris hip score (HHS) before the revision surgery and at final follow-up.

Radiological evaluation focused on 20 patients with a unrevised APC (Figs 2 and 3). The radiographs at final review were assessed by two authors (AS, BAR).
Four patients who had the index surgery in the 1990s and 1980s have since died and radiographs were unavailable. Our institution converted to digital imaging in 2003 and this resulted in loss of the hard-copy radiographs for these four patients, for whom we used the most recent radiological assessment in their notes. We assessed graft union, implant migration and graft resorption. Graft union was assessed at the graft-host interface and was considered to occur when there was evidence of trabecular bridging. We judged clinically relevant implant migration to be present when > 5 mm of migration was evident between radiographs obtained at last follow-up and those obtained previously.22

Graft resorption was classified using the method described by Gross and Hutchinson.25,33 ‘Mild’ resorption involved partial-thickness resorption of < 1 cm in length, ‘moderate’ resorption involved partial-thickness resorption of > 1 cm in length, and ‘severe’ resorption involved full-thickness resorption of any length. This was assessed in all Gruen zones34 excluding zone 1 (trochanteric insertion) and zone 4 (graft-host junction). We expressed inter-observer variability as a percentage of the difference in observations between the two observers for each radiological observation. Our interobserver agreement for graft union and implant migration was 100% (20 of 20), and for graft resorption was 90% (18 of 20), which were the result of discrepancies between ‘mild’ and ‘moderate’ resorption and ‘no’ and ‘mild’ resorption.

The primary outcome was revision surgery for failure of the APC composite. Secondary outcomes were further surgery for bone grafting and plating of the graft-host junction, radiological outcomes, functional outcome (HHS) and post-operative rates of complication, dislocation, fracture and nerve injury.

A total of 11 further revision procedures were undertaken due to acetabular loosening or recurrent dislocation. In all these cases the APC constructs were assessed intraoperatively by the senior author (AEG) and were not deemed to have failed; the acetabular component had failed and these hips were therefore excluded from the primary outcome survivorship analysis.

Statistical analysis. This was performed using SPSS software (SPSS Inc., Chicago, Illinois). The APC survivorship was calculated by the Kaplan-Meier method with 95% confidence intervals (CI) with revision of the APC for loosening as the primary end point. Cox regression analysis was used to determine correlations between failure and APC length and/or number of revision surgeries. The overall outcome was calculated with any additional surgery on the femoral side as the primary endpoint. The HHSs were analysed with a paired t-test. A p-value < 0.05 was taken to be statistically significant.

Results
The APC survival rate was 93% (95% CI 91 to 100) at ten years when 25 patients were at risk, 75.5% (95% CI 60 to 95) at 15 years when eight patients were at risk and 75.5% (95% CI 60 to 95) at 20 years when four patients were at risk. This included six revisions to replace a failed APC. Of these failures, five were due to mechanical loosening that occurred at a mean of ten years (6 to 12.8) and one due to infection. All these patients underwent revision with a new APC (Fig. 4). The failure due to infection occurred 30 months after index surgery. The patient was treated initially with excision arthroplasty and antibiotic therapy. A new APC was undertaken as a second stage procedure eight years later and has since been functioning satisfactorily for 16 years.
Kaplan-Meier analysis for overall survival of the APC including any surgery on the femoral side as an endpoint (Fig. 5) included five patients with mechanical loosening, one infection, two nonunions of the graft-host junction and one peri-prosthetic fracture. This gave a ten-year survival of 83% (95% CI 71 to 98) when 24 patients were at risk. The 15-year survival was 65% (95% CI 48 to 87) when six patients were at risk. Junctional nonunion occurred in two patients and was successfully treated with bone graft and plating at 12 and 86 months after index surgery, respectively. Both patients have long-term uneventful follow-ups of 13 and 24 years, respectively. One patient sustained a peri-prosthetic fracture ten years after the index procedure distal to the APC, which was treated with a plate and strut allograft. The result was satisfactory at eight years post-operatively.

Revision for replacement of the APC did not correlate with the length of the APC (p = 0.22, Cox regression) or with the number of previous THRs (p = 0.81, Cox regression).

Revision of the acetabular component due to dislocation or loosening occurred in 11 patients at a mean of nine years (six months to 23.2 years) from index surgery. These were not considered failures of the APC. Revision of both the acetabular component and the APC occurred in two patients although in both patients several years elapsed between the acetabular and the femoral revisions (6.5 and seven years, respectively).

There were four patients with recurrent dislocation, one at three months, two at six months, and one at 17.6 years. These patients were found to have acetabular loosening and underwent acetabular revision. Nerve injury occurred in one patient who had a post-operative foot drop following lengthening of < 2 cm. The foot drop resolved spontaneously after six months. There were no intra-operative fractures. The mean pre-operative leg-length discrepancy was 3 cm (0 to 7) and 1.5 cm (0 to 7) at one year post-operatively.

The mean pre-operative HSS was 31.93 (4.6 to 49.5), which improved to 71.52 (44.4 to 96.4) at one year post-operatively. At final follow-up it was 67.60 (12.6 to 86.7) (Table I). Both the one-year post-operative and the final follow-up scores were significantly better than the pre-operative scores (t-test, p < 0.001).

Radiological assessment in 20 patients with a successful APC and contemporary radiographs at final follow-up found no evidence of subsidence or nonunion. Mild to moderate allograft resorption was found in four hips. Trochanteric nonunion and migration > 2 cm was observed in four hips.

Discussion
Proximal femoral bone loss in revision THR for DDH is a significant problem. When such bone loss includes the isthmus the option for distal uncemented press-fit fixation is lost. The remaining treatment options include an APC, a cemented endoprosthesis or total femoral replacement. These should be viewed as salvage procedures. The long-term outcomes of APC presented in this study should be viewed in that context.
A search of our institutional database showed that out of 198 revision THRs in DDH patients, in 38 cases (19\%) APCs were used to reconstruct defects in the proximal femur. The young age of these patients makes preservation of the bone stock for the future a significant issue. The technique, with the prosthesis neither cemented nor press-fitted into the distal femur, allows loading of the graft-host bone junction, and a step-cut or oblique osteotomy achieves axial and rotational stability. This load-sharing construct minimises stress shielding and bone resorption of the distal femur. The key to the long-term success of the APC is union at the graft-host bone junction. Failure of an APC begins with failure at this junction. Since the APC is neither cemented nor press-fitted into the distal femur, it may be removed and replaced with a new APC with minimal distal host bone loss when it fails. In all six patients with failure of their APC there was nonunion at the host-graft junction and the existing APC was replaced with a new one.

A potential weakness of this study is its retrospective nature. Given that the study examines patients at long-term follow-up, many of the pre-operative and immediate post-operative radiographs were not available. We relied on the original operative note, the prospectively collected database and the most recent radiographs. A further weakness is that the primary THRs had been performed at different institutions and presented to the senior author (AEG) for revision surgery. There was only written data regarding the native hip.

Several retrospective case series describe the use of APC in revision THR or after proximal femoral resection for oncological disease.\textsuperscript{23-27} We could find no published studies considering femoral bone loss managed with APC in patients with DDH, although our database indicates that 41\% of APCs were performed for DDH (38 of 92 patients).\textsuperscript{28} Cementing an implant into the distal host bone risks unloading the remaining proximal host bone which might result in increased resorption.\textsuperscript{26} In such a scenario, further femoral revision causes additional bone loss when removing cement from the host femur. Endoprosthetic reconstruction is an alternative solution for the management of proximal femoral bone loss. A recent retrospective review of patients who received large endoprostheses after resection of a tumour, from five institutions, reported survival at ten and 15 years of 75\% and 73\%, respectively, from 403 proximal femoral replacements, with mechanical causes being the most common mode of failure.\textsuperscript{35}

In this study of 30 patients, the rate of all further hip surgery at a mean of 15 years was 70\% (21 out of 30): five APC revisions for aseptic loosening, one two-stage revision for infection, one periprosthetic fracture, two junctional nonunions and 11 acetabular component revisions. Nerve injury occurred in only one patient and resolved completely with conservative treatment and there were no intra-operative fractures.

The modified trochanteric slide approach to the hip is advantageous as it maintains a continuum between the abductors and vastus lateralis thus lowering the rate of trochanteric nonunion.\textsuperscript{36,37} However, when trochanteric union fails a trochanteric escape is still possible, as seen in four patients in this study, though none suffered a dislocation. Recurrent surgery to the hip is detrimental to the abductor musculature with most patients having some degree of Trendelenburg lurch.\textsuperscript{38} The trochanteric slide osteotomy also enables optimal exposure of the acetabulum.

The four patients who had recurrent dislocation all had mechanical loosening of the acetabular component, which was revised in isolation.

The overall functional outcome as assessed by the HHS was significantly better at the final follow-up compared with the pre-operative situation (p < 0.001), but the mean overall score (67.6) is still classified as poor (< 70).

We have found excellent long-term survivorship of APCs when used for revision surgery on patients with extensive femoral bone loss who had undergone primary THR for DDH. When the APC fails further revision may be undertaken to another APC without additional loss of host femoral bone stock. Despite excellent survivorship, the authors caution that functional outcomes are not ideal and that the APC should only be considered when diaphyseal fixation is not possible.

**Supplementary material**

A table detailing the mode of failure in nine hips and further procedures required is available with the electronic version of this article on our website www.jbjs.boneandjoint.org.uk

No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article.

**References**


Appendix 9


**Contribution by BA Rogers.**

- Concept
- Data planning and coordination
- Data Collection & management
- Manuscript writing & editing

**Citation Metrics**

- Web Of Science: 15
- Google Scholar: 23
- Altmetrics: 0
  - Tweets:
  - Facebook:
  - Mendeley readers:
The Surgical Techniques and Outcomes for Acetabular Reconstruction in Periprosthetic Pelvic Discontinuity

Benedict A. Rogers, MA, MSc, FRCS(Orth),* Paul M. Whittingham-Jones, FRCS(Orth),† Philip A. Mitchell, FRCS(Orth),‡ Oleg A. Safir, MD, MEd, FRCSC,* Martin D. Bircher, FRCS,‡ and Allan E. Gross, MD, FRCSC*

Abstract: The surgical techniques and outcomes for acetabular reconstruction in periprosthetic pelvic discontinuity cases are reported. The mean time to surgery for 9 patients with acute pelvic discontinuity was 16.3 days, with 8 patients (88%) having posterior column plating and a porous metal acetabular cup. No cases required revision surgery, with a mean follow-up of 34 months (range, 24-67 months). Of the 62 chronic pelvic discontinuity cases, 20 had an ilioischial cage, with a revision rate of 29%. There were 42 cup-cage reconstructions with an 8-year survivorship of 86.3%, with a mean follow-up of 35 months (range, 24-93 months). Stable reconstruction of chronic pelvic discontinuity was achievable by distraction using a cup-cage acetabular reconstruction; however, satisfactory stability of acute pelvic discontinuity was achieved with compression of the posterior column using screw augmentation of the acetabular shell supplemented by posterior column plating. Keywords: pelvic discontinuity, acetabular revision, bone loss, ilioischial cage, cup cage.

Massive acetabular bone loss provides a challenge for the reconstructive surgeon. Periprosthetic pelvic discontinuity describes the loss of structural bone between the superior and inferior aspects of the pelvis, resulting from bone loss or fracture through the acetabulum [1,2]. Although relatively rare at present, the incidence is likely to rise with an aging, active population and an increasing caseload of primary and revision total hip arthroplasty [1,3-6].

Recent improvement in biomaterials such as porous trabecular metal have afforded a superior capacity for bone ingrowth that makes the use of hemispherical uncemented cups feasible for acetabular revision with marked bone loss [7-10]. Unlike the algorithms for management of native acetabular fractures, the treatment of periprosthetic pelvic discontinuity is less well defined [2,8,11-14].

The biology and biomechanical stability differs between acute and chronic pelvic discontinuity, and the reconstructive surgical techniques should differ accordingly. The purpose of this study is to report the surgical techniques, outcomes, and complications of acetabular reconstruction for both acute and chronic pelvic discontinuity treated at 2 tertiary referral orthopedic units.

Methods

Institutional board approval was obtained. This 2-center study identified 71 cases of pelvic discontinuity that were classified into acute, less than 12 weeks from primary surgery, or chronic, greater than 12 weeks from primary surgery. All cases were treated at academic tertiary referral units, and all surgeries were performed by senior surgeons.

The patients’ demographics in both case series are shown in Table 1. In all patients, pelvic discontinuity was based on the radiologic findings and confirmed intraoperatively by the senior author, with the hemipelvis being separated superiorly and inferiorly because of loss of the host bone or fracture through the acetabular columns. Routine radiographic and clinical follow-up was undertaken, and the incidence of complications or revision surgery was obtained.

Acute Case Series

Nine cases of acute pelvic discontinuity secondary were identified, with a mean age of 67.4 years (range, 30-83 years) and a mean follow-up of 34 months (range, 24-67 months). All cases were female. These
cases were managed by senior surgeons at an academic orthopedic department (P.A.M., S.H.B., M.B.), a tertiary referral unit for both pelvic and acetabular trauma and hip reconstruction.

Blunt trauma was the cause of the pelvic discontinuity in 4 cases; iatrogenic trauma during the insertion of uncemented acetabular cups was the cause in the remaining 5 cases. Of the 9 acute cases, most had only 1 previous operation, a primary total hip arthroplasty, on the affected side; whereas a single patient had 2 previous surgeries. All patients with acute pelvic discontinuity had uncemented acetabular components in situ.

The initial diagnosis and referral and preoperative planning used plain radiographs and computed tomography. The criteria described by Berry [15] were used to diagnose pelvic discontinuity including a visible transverse pelvic fracture on anteroposterior pelvic or Judet radiographs, medial offset of the inferior part of the pelvis in relation to the superior part of the pelvis as seen by a break in the ilioischial line, and rotation of the hemipelvis as indicated by asymmetry of the obturator ring on the true anteroposterior pelvic radiograph. However, the senior operating surgeon confirmed the definitive diagnosis of pelvic discontinuity once the entire acetabulum was directly visualized intraoperatively.

A transverse or “T” pattern fracture was seen in most the acute pelvic discontinuity acetabuli. All cases were performed using a posterior or Kocher-Langenbeck approach, and the details of the surgical management of these cases are detailed in Table 2; (available online at www.arthroplastyjournal.org). Acetabular reconstruction used modular trabecular metal acetabular components in all cases. In most cases (8/9), the posterior column was stabilized with a reconstruction plate initially in addition to revising the acetabulum.

### Chronic Case Series

There were 62 cases of chronic pelvic discontinuity, secondary to septic or aseptic periprosthetic bone loss, with a mean age of 67.5 years (range, 27-88 years) and a mean follow-up of 35 months (range, 24-93 months). The reconstructive techniques used for the chronic pelvic discontinuity series include an ilioischial cage or a cup-cage reconstruction [8], performed by or under the direct supervision of one of the senior authors (A.E.G.). Of these 62 cases, 18 (29%) concurrently underwent femoral component revision. The diagnosis was frequently not obvious before surgery, despite the routine use of pelvic computed tomographic scans and Judet view radiographs. Therefore, a high index of suspicion was maintained during surgery, with a pelvic discontinuity specifically checked after initial gentle reaming.

### Operative Technique

A modified trochanteric slide or extended trochanteric osteotomy was performed to obtain an adequate exposure of the acetabular and has previously been described [16-18]. Maintaining the continuity of the vastus lateralis and abductors by using a trochanteric osteotomy affords a good exposure with acceptable rates of limp and nonunion [16-19]. The acetabulum was gently reamed, the degree of acetabular bone loss was assessed, and the diagnosis of pelvic discontinuity was confirmed. The subsequent reconstruction involved either an ilioischial cage (ZCA or Burch-Schneider; Zimmer, Warsaw, Ind) or a cup cage.

The surgical technique for an ilioischial cage reconstruction used by the senior author has previously been described [20]. Morselized bone graft is used in all cases, and 4 cases had additional structural corticocancellous allograft. The appropriate reconstruction cage was chosen based on the size of the bone-grafted acetabulum using acetabular reamers, trial cups, and then a trial reconstruction cage. The inferior flange was either slotted or screwed to the ischium. The superior flange was carefully molded to the lateral acetabular dome of the ilium, with several screws placed through the cage into the dome positioning the flange on the host bone. A polyethylene liner was cemented into the ilioischial cage, ensuring an acetabular orientation of about 45° and 15° to 20° of anteverision.

The surgical technique for a cup cage has also been previously described [8]. The rationale for this construct is that an ilioischial cage provides initial stability to the reconstruction while shielding the trabecular metal cementless acetabular component from mechanical forces until biologic stabilization has taken place, which gives the entire construct its long-term stability. The acetabulum is prepared as described previously, and the defect was sized for a trabecular metal revision shell and a suitable-sized Trabecular Metal Acetabular Revision System cage (Zimmer) to bridge the ilium to the ischium. Morselized bone graft, a mixture of allograft and autograft, is firmly compressed into the acetabulum using spherical compressors. Screw fixation was used to augment the initial press-fit fixation of the acetabular component, and occasionally, this necessitated new drill holes being made through the trabecular metal of the acetabular component. The initial press fit was achieved with no more than 1 to 2 mm of underreaming. It should

### Table 1. Demographics and Follow-Up for Acute And Chronic Pelvic Discontinuity

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be noted that the drilling of new holes through a metal is only approved by the manufacture for the revision acetabular shell component (00-700-56-20; Zimmer). The fixation of the cage was made inferiorly with a slot into the substance of the ischium inferiorly in all patients, thus reducing the risks of screw fracture, cage migration, and sciatic nerve damage [20]. The superior flange of the cage was secured with screws; with care to avoid damaging the extrapelvic (superior gluteal nerve and artery) or intrapelvic (internal iliac and obturator vessels) structures [21-23]. A polyethylene liner was cemented into the cage in the appropriate inclination and version, with cement interdigitating through the holes in the cage to reduce micromotion between the cage and the acetabular component.

The percentage host bone contact to the acetabular shell component was estimated intraoperatively by a method previously reported [24]. In summary, with the trial cup in, each quadrant of the acetabular hemisphere was assessed separately for contact with the host bone, morselized bone graft, or no contact with the bone (uncoverage). Contact with each one of those surfaces was expressed in 20% segments for each quadrant (representing 5% segments for the whole hemisphere). The overall contact was calculated by joining the quadrant scores and was recorded on designated forms.

**Statistical Analysis**

For both the acute and the chronic case series, revision acetabular surgery either for any cause or for failure of the pelvic discontinuity reconstruction (metalwork failure) was used as the primary outcome measure. Where appropriate, Kaplan-Meier survivorship analysis was performed with respect to these outcomes.

**Results**

**Acute**

Six (67%) of the cases used autologous morselized bone graft in addition to the acetabular component. Two patients died of unrelated causes, although at the last follow-up, both hip reconstructions remained intact.

Overall, at the last follow-up, the reconstruction of acute cases had a 100% survivorship, with none of the cases had undergone further revision surgery. There were no reported cases of infection or subsequent dislocation; however, 3 cases had some abductor dysfunction and a limp.

A single case showed radiographic evidence of ischial nonunion but with no associated symptoms, and the patient has not undergone further surgery.

Prereconstruction and postreconstruction radiographs for the reconstruction of acute periprosthetic pelvic discontinuity are shown in Figs. 1 and 2, demonstrating open reduction and internal fixation of the posterior column, revision acetabular cup, and screw supplementation.

**Chronic**

The commonest primary diagnosis for the previous primary total hip arthroplasty in the chronic pelvic discontinuity case series was osteoarthritis (28/62), followed by inflammatory arthropathy (13/62). Four patients had neoplastic bone as the reported primary diagnosis for the previous total hip arthroplasty, including chondrosarcoma and metastatic lung carcinoma, and 2 patients had unspecified neoplastic bone lesions.

**Fig. 1.** Radiograph demonstrating an acute periprosthetic pelvic discontinuity with an uncemented total hip arthroplasty.

**Fig. 2.** Radiograph demonstrating acetabular reconstruction of acute periprosthetic pelvic discontinuity (as shown in Fig. 2) with posterior column plating and a large porous metal acetabular component 28 months after surgery.
The revision rate for the cup-cage reconstructions was 9.5% (4/42 cases), with 2 cases revised for instability and 2 for a failed reconstruction. The revision rate for the ilioischial cage reconstructions was 28.5% (2/7 cases) and 30.7% (4/13 cases) for the ZCA and Burch-Schneider cages, respectively. Of the 6 ilioischial cage reconstructions that required revision, 5 were for failed cages and only 1 for instability.

The incidence of complications and revision rates for different reconstructions, including the mean time to further revision surgery, are shown in Table 3. The reported postoperative complications after the acetabular reconstruction of chronic pelvic discontinuity are detailed in Table 3. Of the 7 reported dislocations, 3 cases required open reduction, during which one had augmentation of polyethylene liner and the other had a constrained liner inserted. The remaining 4 cases of dislocation were managed with a closed reduction. Two cases developed infection, both superficial to the fascia lata, and underwent debridement, washout, and a course of intravenous and then oral antibiotics. Both cases did not require further surgery and at the last follow-up, no infection was clinically evident.

The overall revision rate, at the last follow-up, was 9.5% for cup-cage acetabular reconstruction compared with 28.5% and 30.7%, respectively, for ZCA or Burch-Schneider ilioischial cage reconstruction (see Table 3). The Kaplan-Meier survivorship analysis for the chronic pelvic discontinuity cases managed with cup-cage reconstruction is shown in Figs. 3 and 4. Using any acetabular revision as an end point, the 8-year survivorship was 86.3% (see Fig. 3). However, using revision for a failed pelvic discontinuity reconstruction as an end point, such as metalwork failure and excluding revisions for hip instability, the 8-year survivorship was 93.8% (see Fig. 4).

### Table 3. Complications Associated With the Surgical Management of Chronic Pelvic Discontinuity

<table>
<thead>
<tr>
<th>Complication</th>
<th>Cup Cage (n = 42)</th>
<th>ZCA (n = 7)</th>
<th>Burch-Schneider (n = 13)</th>
<th>Total (n = 62)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dislocations</td>
<td>6</td>
<td>0</td>
<td>1</td>
<td>7</td>
</tr>
<tr>
<td>Infections</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Loose/Failed</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Nerve lesion</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Cup migration*</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Deaths</td>
<td>1</td>
<td>0</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Revisions—instability</td>
<td>2 (4.7%)</td>
<td>0</td>
<td>1 (7.7%)</td>
<td>3 (4.8%)</td>
</tr>
<tr>
<td>Revision—failed cage</td>
<td>2 (4.7%)</td>
<td>2 (28.5%)</td>
<td>3 (23.1%)</td>
<td>7 (11.3%)</td>
</tr>
<tr>
<td>Mean follow-up (mo)</td>
<td>32</td>
<td>34</td>
<td>42</td>
<td>35</td>
</tr>
<tr>
<td>Revision total</td>
<td>4 (9.5%)</td>
<td>2 (28.5%)</td>
<td>4 (30.7%)</td>
<td>10 (16.1%)</td>
</tr>
<tr>
<td>Time to revision (mo)</td>
<td>6.5</td>
<td>16</td>
<td>19</td>
<td>NA</td>
</tr>
</tbody>
</table>

NA indicates not applicable.

* Radiographic cup migration observed, although not revised.
† Mean time from reconstruction to subsequent acetabular revision.

The revision rate for the cup-cage reconstructions was 9.5% (4/42 cases), with 2 cases revised for instability and 2 for a failed reconstruction. The revision rate for the ilioischial cage reconstructions was 28.5% (2/7 cases) and 30.7% (4/13 cases) for the ZCA and Burch-Schneider cages, respectively. Of the 6 ilioischial cage reconstructions that required revision, 5 were for failed cages and only 1 for instability.

The incidence of complications and revision rates for different reconstructions, including the mean time to further revision surgery, are shown in Table 3. The cup sizes used and the amount of contact between the acetabular cup and bleeding host bone after reaming for each of the separate reconstructions used for chronic pelvic discontinuity are shown in Table 4; (available online at www.arthroplastyjournal.org). The overall mode and median cup size was 62-mm outer diameter, with a range of 46 to 80 mm. The mode and median femoral head size used was 32 mm, with a range of 28-40 mm. Eighteen (29%) of the chronic case series had concurrent revision of the femoral component, with 13 of these being modular femoral components (ZMR; Zimmer). For each of the 3 reconstructive methods used, the percentage contact with the host bone was consistently low, with the mean for each method being between 25% and 28% (see Table 4). Of the 62 chronic pelvic discontinuity cases, 5 incorporated structural allograft for the acetabular reconstruction, with 57 having morselized allograft.

The Kaplan-Meier survivorship analysis for the chronic pelvic discontinuity cases managed with cup-cage reconstruction is shown in Figs. 3 and 4. Using any acetabular revision as an end point, the 8-year survivorship was 86.3% (see Fig. 3). However, using revision for a failed pelvic discontinuity reconstruction as an end point, such as metalwork failure and excluding revisions for hip instability, the 8-year survivorship was 93.8% (see Fig. 4).

Fig. 3. Kaplan-Meier survivorship graph for chronic pelvic discontinuity patients treated with cup-cage reconstruction, with any revision as an end point.
Radiographs are presented, demonstrating cup-cage reconstructions for failed ilioischial cage (see Figs. 5 and 6).

**Discussion**

Although the incidence of pelvic discontinuity has been reported at 0.9% of all revision total hip arthroplasties, the caseload is likely to increase with an aging and active population [1,3-5,25]. The inherent instability and lack of bone stock provide a challenge for acetabular revision surgery and risk factors including female sex, older patients, massive bone loss, osteoporosis, and rheumatoid arthritis [1]. Several surgical techniques have been advocated for treatment of periprosthetic pelvic discontinuity (or dissociation), including ilioischial cages [12], plate fixation of structural allografts [26], triflange cups [27]. Steinmann pin fixation [13], acetabular revision with addition pelvic screws [2], acetabular reinforcement rings [28], oblong cups [29], and cup-cage reconstruction [8].

Despite numerous published studies reporting the case series of various treatment options (see Table 5), to date, no clear consensus to treatment has been proposed. In 2005, Sporer et al [30] suggested that the treatment of pelvic discontinuity is dependent on the remaining host bone, the potential for healing of the discontinuity, and the potential for biologic ingrowth of the acetabular components. The aim was to achieve cementless biologic fixation when possible, and an alternative reconstruction when insufficient stability was obtainable. If bone healing potential exists, some authors [31,32] proposed that compression of the posterior column should be achieved, either with a plate or trabecular metal cup acting as an “internal plate.” Plate fixation achieved posterior column compression using the standard biologic principles of fracture fixation. A trabecular metal cup, augmented with acetabular screws above and below the discontinuity, may also afford sufficient biologic stability to afford bone union.

Alternatively, with insufficient host bone healing potential, they suggest that the discontinuity should be bridged and treated in distraction. The initial biomechanical stability of a modular acetabular reconstruction is substantially enhanced with distraction of the pelvic discontinuity compared with compression, particularly in an environment with minimal host bone healing potential. A large-diameter, trabecular metal, revision acetabular component provides the suitable biomechanical properties to both afford a stable initial distraction of a pelvic discontinuity and generate biologic stability by encouraging bone ingrowth [7,9,10,33-35].

However, the report by Sporer et al [30] did not provide supporting clinical evidence and concluded that “the long term clinical results of this treatment remain unknown.” Insufficient bone healing may result from

![Fig. 4. Kaplan-Meier survivorship graph for patients with chronic pelvic discontinuity managed with a cup-cage reconstruction, with revision for a failed pelvic discontinuity reconstruction as an end point.](image)

![Fig. 5. Radiograph demonstrating a periprosthetic pelvic discontinuity secondary to a failed ilioischial cage reconstruction.](image)
either quantitative (osteoporosis or severe osteolysis) or qualitative (infection or neoplastic) bone pathology.

**Chronic Pelvic Discontinuity**

The difficulty in achieving adequate stability with chronic pelvic discontinuity or major column defects was demonstrated in a case series reported by Stiehl et al [26]. Acetabular reconstruction with bulk allograft was supported with anterior and posterior column 3.5-mm AO reconstruction plates. With 10 cases of pelvic discontinuity, 6 required revision surgery, and with a further 7 cases with major column defects, the overall cases series of 17 had a revision rate of 47%. The authors conclude that because of these poor clinical results, this technique could not be recommended.

Several studies have shown that ilioischial rings afford a good clinical outcome for acetabular reconstruction bone defects that do not require bulk allograft or with coexisting pelvic discontinuity [36,37]. However, concerns regarding the high complication of standard ilioischial cages have led the senior author (A.E.G.) to develop the cup-cage technique [8,20]. Goodman et al [20] reported a consecutive series of 61 ilioischial reconstruction rings performed for severe acetabular bone loss, with 10 cases having pelvic discontinuity. Of these 10 cases, 4 needed revision surgery for failure of the ilioischial cage reconstruction, and the outcomes of this previously reported cohort have been incorporated into the data of this study. Figs. 5 and 6 demonstrate such a failed ilioischial cage, revised to a cup-cage acetabular reconstruction. Other studies have reported failure rates of up to 50% for ilioischial cage reconstructions of pelvic discontinuity [38].

The work of Bobyn and others [33] has highlighted the beneficial biomechanical properties of porous tantalum metal, including high porosity, high coefficient of friction, and a Young modulus similar to bone. These properties have made this biomaterial increasingly popular in revision hip arthroplasty [7,9,10,34,35]. The use of porous tantalum in the reconstruction of pelvic discontinuity is attractive because bone ingrowth can be achieved with less than 50% of bleeding host bone contact [8,24]. The results of this study demonstrate a consistently low percentage of contact between the cup and the bleeding acetabular bone for all of the reconstruction techniques used in chronic pelvic discontinuity (see Table 4; available online at www.arthroplastyjournal.org). Therefore, we recommend the use of porous tantalum components in the reconstruction of such cases because of the ability of

![Fig. 6. Radiograph 32 months after a cup-cage reconstruction performed for periprosthetic pelvic discontinuity secondary to a failed ilioischial cage (see Fig. 5).](image)

<p>| Table 5. Literature Review of the Surgical Treatment of Pelvic Discontinuity |
|-----------------------------|------------------|-----------------|------------------|-----------------|-----------------|-----------------|</p>
<table>
<thead>
<tr>
<th>N</th>
<th>Mean Follow-Up</th>
<th>Acute or Chronic</th>
<th>Journal</th>
<th>Year of Publication</th>
<th>Level of Evidence</th>
</tr>
</thead>
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<tr>
<td>Christie et al [27]</td>
<td>39</td>
<td>4.4 y</td>
<td>Chronic</td>
<td>CORR</td>
<td>2001</td>
</tr>
<tr>
<td>Berry et al [1]</td>
<td>27</td>
<td>3 y</td>
<td>Chronic</td>
<td>JBJS (Am)</td>
<td>1999</td>
</tr>
<tr>
<td>Koster et al [29]</td>
<td>4</td>
<td>3.6 y</td>
<td>Chronic</td>
<td>J. Arthroplasty</td>
<td>2006</td>
</tr>
<tr>
<td>Paprosky et al [12]</td>
<td>16</td>
<td>2.6 y</td>
<td>Chronic</td>
<td>CORR</td>
<td>2006</td>
</tr>
<tr>
<td>Bostrom et al [38]</td>
<td>6</td>
<td>30 mo</td>
<td>Chronic</td>
<td>CORR</td>
<td>2006</td>
</tr>
<tr>
<td>Springer et al [14]</td>
<td>7</td>
<td>18 mo</td>
<td>Acute</td>
<td>JBJS (Am)</td>
<td>2005</td>
</tr>
<tr>
<td>Kerboull et al [39]</td>
<td>12</td>
<td>10 y</td>
<td>Chronic</td>
<td>CORR</td>
<td>2000</td>
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<tr>
<td>Peters et al [40]</td>
<td>15</td>
<td>29 mo</td>
<td>Chronic</td>
<td>J Arthroplasty</td>
<td>2004</td>
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<td>Lietman et al [41]</td>
<td>11</td>
<td>5 mo</td>
<td>Chronic</td>
<td>Orthopedics</td>
<td>2001</td>
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<tr>
<td>Kosashvili et al [8]</td>
<td>26</td>
<td>44.6 mo</td>
<td>Chronic</td>
<td>JBJS (Br)</td>
<td>2009</td>
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<tr>
<td>Eggli et al [28]</td>
<td>7</td>
<td>96 mo</td>
<td>Chronic</td>
<td>CORR</td>
<td>2002</td>
</tr>
<tr>
<td>van Haaren et al [42]</td>
<td>6</td>
<td>7 y</td>
<td>Chronic</td>
<td>JBJS (Br)</td>
<td>2007</td>
</tr>
<tr>
<td>Stiehl et al [26]</td>
<td>10</td>
<td>83 mo</td>
<td>Chronic</td>
<td>J Arthroplasty</td>
<td>2000</td>
</tr>
<tr>
<td>Goodman et al [20]</td>
<td>10</td>
<td>3.3 y</td>
<td>Chronic</td>
<td>J Arthroplasty</td>
<td>2004</td>
</tr>
<tr>
<td>This study</td>
<td>71</td>
<td>3 y</td>
<td>Acute (9) and chronic (62)</td>
<td>–</td>
<td>2011</td>
</tr>
</tbody>
</table>

CORR indicates Clinical Orthopedics and Related Research; JBJS Journal of Bone and Joint Surgery; (Br), British Volume; (Am), American Volume.
bone ingrowth to be achieved with a low percentage of bleeding.

A large porous tantalum revision shell provides distraction that stabilizes the pelvic discontinuity while forming a bridging construct between the ilium and the ischium. A revision shell used in this manner is usually too vertical and retroverted to safely accommodate an acetabular liner. In addition, because of the inherent instability of pelvic discontinuity, additional protection is required to allow bone ingrowth, and this is achieved with a cup-cage reconstruction. By supplementing the construct with an ilioischial cage, a polyethylene liner can, thus, be cemented at the correct inclination and version, independent of the position and version of the acetabular shell.

**Acute Pelvic Discontinuity**

The results presented in this study demonstrate that acute periprosthetic pelvic discontinuity can be successfully treated with compression of the posterior column, principally using a plate supplementing a trabecular metal acetabular revision shell. This clinical evidence suggests that cases of acute periprosthetic pelvic discontinuity possess bone healing potential if compression is achieved, assuming normal bone metabolism (ie, no infective or neoplastic conditions). Compression of the posterior column may be provided via an "extra"-acetabular method, specifically a posterior column plate as principally demonstrated in this study. Alternatively, "intra"-acetabular compression can be provided by an uncemented shell augmented with screws above and below a pelvic discontinuity. The results of this study provide medium-term clinical evidence supporting the treatment principles outlined by Sporer et al [30].

Female patients and rheumatoid arthritis are significant risk factors for pelvic discontinuity, and excessive reaming should be avoided to maintain columnar support of the acetabulum [15]. This study, in addition to previous case series, demonstrates that transverse or T-pattern fractures are the commonest associated with acute pelvic discontinuity [14]. The relative stability of these fracture patterns probably differs. Low T-pattern fractures, commonly involving the inferior pubic ramus, are frequently significantly displaced and are likely to be unstable, necessitating open reduction and plate fixation before the insertion of an acetabular component. Currently, no published clinical evidence that quantifies the relative stability of different fracture patterns in acute periprosthetic pelvic discontinuity exists. Because of the massive bone loss seen with chronic pelvic discontinuity, the description of fracture patterns is not applicable, or indeed comparable, to the acute cases.

The contrast in reconstructive techniques used in cases of acute and chronic pelvic discontinuity supports the algorithmic treatment protocol initially proposed by Sporer and Paprosky [10] and Sporer et al [30], whereby the lack of the potential for bone healing in chronic cases dictates that initial stability is achieved with distraction, and biologic cementless fixation subsequently develops. Porous metal components currently provide the best characteristics for this. In comparison, adequate stability is produced in acute cases by compression of the posterior column in conjunction with an uncemented acetabular component.

In conclusion, this study, the largest reported series, demonstrates that stable reconstruction of chronic pelvic discontinuity is achievable with a cup-cage acetabular reconstruction owing to the inherent beneficial biologic and biomechanical properties of porous tantalum metal. This method provides stability by distraction. However, satisfactory stability of acute pelvic discontinuity can be achieved by providing compression using screw augmentation of the acetabular shell and/or posterior column plating.

**References**


Appendix 10

Kuchinad RA, Garbedian S, Rogers BA, Backstein D, Safir O, Gross AE.
The use of structural allograft in primary and revision knee arthroplasty with bone loss.

**Contribution by BA Rogers.**

Data Collection & management

Manuscript writing & editing

**Citation Metrics**

<table>
<thead>
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The Use of Structural Allograft in Primary and Revision Knee Arthroplasty with Bone Loss

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Bone loss around the knee in the setting of total knee arthroplasty remains a difficult and challenging problem for orthopaedic surgeons. There are a number of options for dealing with smaller and contained bone loss; however, massive segmental bone loss has fewer options. Small, contained defects can be treated with cement, morselized autograft/allograft or metal augments. Segmental bone loss cannot be dealt with through simple addition of cement, morselized autograft/allograft or metal augments. For younger or higher demand patients, the use of allograft is a good option as it provides a durable construct with high rates of union while restoring bone stock for future revisions. Older patients, or those who are low demand, may be better candidates for a tumour prosthesis, which provides immediate ability to weight bear and mobilize.

1. Introduction

Dealing with bone loss when performing primary or revision total knee arthroplasty is a challenge for the arthroplasty surgeon. Previous infections, tumour, and trauma can all result in bone loss that makes a standard primary total knee arthroplasty impossible without restoration of bone stock. More commonly, bone loss in revision knee arthroplasty is a frequent problem and may occur for any of the aforementioned reasons, osteolysis, periprosthetic fracture, or iatrogenically when components are being removed from host bone.

Patients with posttraumatic osteoarthritis or deformity requiring knee arthroplasty often have bone loss in the tibia, femur, or both. In this situation, the surgeon must determine the extent of bone loss and whether it may be dealt with by simple autogenous bone grafting, cement, metal augments, porous metal supplementation, or allograft of various sizes. Large uncontained defects of the knee may be treated with use of a large or massive allograft in conjunction with the total knee.

2. Classification

There is no universally accepted classification that is currently used for describing bone loss in knee arthroplasty. Engh developed the Anderson Orthopaedic Research Institute (AORI) classification system that helps to guide treatment for both femoral and tibial sides in revision knee arthroplasty (see Table 1) [1].

Mount Sinai Hospital in Toronto, Canada, has developed a classification system, which simply divides the defects into contained or uncontained categories to be used in the arthroplasty setting (see Table 2) [2–8].

Both classification systems attempt to characterize the defects present and assist the surgeon in developing a treatment algorithm for dealing with bone loss, although the AORI classification is more explicit in detailing various treatment options.

3. Allograft Characteristics

Allograft harvesting should be done according to the criteria of the American Association of Tissue Banks, in sterile...
Table 1: Classification of femoral and tibial bone loss [1].

(a) AORI femoral bone loss classification

<table>
<thead>
<tr>
<th>AORI femur grade</th>
<th>Deficit</th>
<th>MCL/LCL</th>
<th>Bone reconstruction</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1</td>
<td>Intact metaphyseal bone</td>
<td>Intact</td>
<td>Cement or particulate graft</td>
</tr>
<tr>
<td>F2a</td>
<td>Metaphyseal loss single condyle</td>
<td>Intact</td>
<td>Cement or metal augment</td>
</tr>
<tr>
<td>F2b</td>
<td>Metaphyseal loss both condyles</td>
<td>Intact</td>
<td>Cement, metal augment or structural graft</td>
</tr>
<tr>
<td>F3</td>
<td>Deficient metaphysis</td>
<td>Compromised</td>
<td>Structural allograft or segmental replacement</td>
</tr>
</tbody>
</table>

(b) AORI Tibial Bone Loss Classification

<table>
<thead>
<tr>
<th>AORI tibial grade</th>
<th>Deficit</th>
<th>MCL/LCL</th>
<th>Bone reconstruction</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1</td>
<td>Intact metaphyseal bone</td>
<td>Intact</td>
<td>Cement or particulate graft</td>
</tr>
<tr>
<td>T2a</td>
<td>Metaphyseal loss med or lat Plateau</td>
<td>Intact</td>
<td>Cement or metal augment</td>
</tr>
<tr>
<td>T2b</td>
<td>Metaphyseal loss and lat plateau</td>
<td>Intact</td>
<td>Cement, metal augment or structural graft</td>
</tr>
<tr>
<td>T3*</td>
<td>Deficient metaphysis</td>
<td>Compromised</td>
<td>Structural allograft or segmental replacement</td>
</tr>
</tbody>
</table>

* Possible extensor mechanism compromise.

Table 2: Classification of Tibial and Femoral Bone Loss [8].

<table>
<thead>
<tr>
<th>Type</th>
<th>Type of Bone Loss</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>No notable loss of bone stock</td>
<td>There may be erosion of the endosteal bone, but no involvement of the cortex. There has been no migration of the primary component, and bone is largely intact.</td>
</tr>
<tr>
<td>2</td>
<td>Contained loss of bone stock with cortical thinning</td>
<td>The canal is widened, but there is still an intact cortical sleeve.</td>
</tr>
<tr>
<td>3</td>
<td>Uncontained (segmental) loss of bone stock involving &lt;50% of medial and/or lateral condyle</td>
<td>Uncontained bone loss represents less than 50% of medial and/or lateral femoral and/or tibial condyle and is less than 15 mm in depth.</td>
</tr>
<tr>
<td>4</td>
<td>Uncontained (segmental) loss of bone stock &gt;50% of medial and/or lateral condyle</td>
<td>Uncontained bone loss represents more than 50% of medial and/or lateral femoral and/or tibial condyle and is more than 15 mm in depth.</td>
</tr>
</tbody>
</table>

4. Indications

The primary indications for using structural allografts in the setting of arthroplasty are (a) large uncontained defects that are outside the range of metal augments or thicker polyethylene inserts (see Figures 1 and 2), (b) patients that are active and require bone-stock restoration for potential future operations, and (c) patients who are physically well enough to tolerate both the surgical procedure and rehabilitation required for successful outcomes. A relative contraindication is a patient actively smoking, and cessation programs must be implemented prior to surgery. Lastly, presence of active infection is an absolute contraindication for allograft in the arthroplasty patient.

5. Preoperative Preparation and Planning

In the setting of previous infection or posttraumatic defects, active infection must be ruled out. C-reactive Protein, erythrocyte sedimentation rate, and possible knee aspirate should be performed prior to planning any knee arthroplasty procedure especially with use of allografts. Once infection is ruled out, careful planning should include 4 foot standing radiographs of both limbs, standard AP, lateral, and skyline views and, if required, a CT scan. CT scanning can help with determination of whether the defect is contained or uncontained and overall dimensions. As always, these investigations must be combined with a thorough physical exam of the patient, which includes limb alignment, ligamentous stability, and a neurovascular exam.

Preoperative planning incorporates all aspects of the physical exam and investigations but also entails determining surgical approach, dealing with difficult exposure, allograft availability, and arthroplasty component selection. When massive allografts are used, a stemmed implant is required to obtain adequate stability of the component between the host-allograft bone junction. Furthermore, if there is significant ligamentous instability, there should be implants available with higher degrees of constraint.

6. Operative Techniques

Old operative reports detailing prior surgical approaches should be obtained to help the surgeon decide on the optimal conditions and in our institution followed by irradiating the tissue at 25,000 Gy and storage at −70°C [9]. Although some believe that donor allograft does not have to be matched to the recipient’s anatomy, others argue that modifying the allograft weakens it. If the allograft is size matched, application of the graft becomes easier to use in the patient and maintains its inherent strength. Also, allografts that are oversized may make the soft-tissue closure difficult or impossible to perform which is a serious intraoperative complication. To ensure this does not happen, we recommend taking preoperative calibrated radiographs of the allograft and comparing this with the patient’s radiographs [2].

...
Figure 1: AP radiograph showing a knee with severe polyethylene wear and evidence of major bone loss (a). A CT scan showing massive bone loss of the medial and lateral femoral condyles due to osteolysis (b). (reprinted from Backstein et al. [2]).

Figure 2: A radiograph shows uncontained bone loss in the medial femoral condyle secondary to osteolysis (a). A radiograph showing revision TKA with reconstruction of the medial femoral condyle using structural allograft fixed with screws (b).

During the exposure, presence of scar tissue, quadriceps, and patellar tendon contracture and deformity must be adequately dealt with to assist in performing the procedure. Tibial tubercle osteotomy, quadriceps snip, lateral parapatellar arthrotomy, and in situ bony cuts and removal of accessible implants are a few of the adjuncts that can help the surgeon with exposure. It is critical to avoid excessive disruption of the soft-tissue envelope, as wound problems can be a frequent complication of these complex reconstructions [10].

During exposure and debridement, a frozen section should be sent to the pathologist to rule out infection. We typically use a count of less than 5 neutrophils per high power field as a negative result [11]. If infection is suspected or confirmed, the planned surgical procedure is abandoned and a dynamic or static spacer with antibiotic impregnated cement is used until the infection is cleared.

Debridement of nonviable bone and necrotic tissue should also be done during the exposure. The level of debridement should be done to expose healthy bleeding tissue. Implants are removed with microoscillating saws, gigli saws, flexible osteotomes, or through osteotomies. This part of the procedure should be done with care as creating further bone loss increases the complexity of the reconstruction. Furthermore, the quality of the host bone is often osteoporotic and fragile from prior infection, osteolysis, or disuse.

Once exposure is completed, the area of bone loss should be evaluated and classified to determine the type of allograft required for treatment. Ideally, the intraoperative findings should not be unexpected and simply confirm the pathology that was seen in preoperative imaging.
7. Segmental Allografts

Small contained defects less than 10 mm can be treated with morselized autograft, allograft, or cement alone. Uncontained defects that are less than 10–20 mm in size can be treated with metal augments alone; however, larger defects can be dealt with structural allograft or tumour implants [12]. Bone loss of the proximal tibia that involves the entire surface can be treated with metal augments and a thicker polyethylene insert, but the upper limit for this is 45 mm. An alternative option is structural allograft or tumour prosthesis.

If a structural allograft is going to be used, having two surgical teams present is ideal. This decreases the anaesthetic time the patient must endure and is the most efficient use of operating room time. One surgical team should have a sterile back table available to prepare the allograft, while the other team simultaneously does the exposure and bony preparation of the patient.

The major principles of the revision are to determine the level of the joint line that should be measured from the distal femur or proximal fibula. Typically intact host bone is easier to judge where the true joint line should exist. From the medial epicondyle, the joint line is 25–30 mm distal, and, from the tip of the fibula, it is 10–15 mm proximal. Occasionally intraoperative radiographs of the affected and normal knee may be utilized to find the anatomic joint line. Ligamentous structures must also be evaluated to determine whether or not further constraint will be required in the implants. The surgeon must be careful to preserve these attachments during the exposure, debridement, and implant removal.

The goal of the reconstruction should also include balancing the flexion and extension gaps to have a good functional outcome for the patient. Appropriate bone resection and trial implantation position are critical in obtaining this intraoperatively.

The tibial and femoral canals are reamed to have good press fit for trial stems. If needed, offset stems can be used to better align the femoral and tibial trays. Once the trial implants are appropriately positioned, the amount of bone loss should be reevaluated. Irregularly shaped areas of segmental bone loss that is too large for metal augments can be treated with structural allograft. These areas should be made into more geometric defects with the use of precise cutting guides or freehand with an oscillating or reciprocating saw. Once the defects are reshaped, preferably into a square or rectangular shape, they are measured for the height and width. On the back table, the allograft is cut into almost identical size, but slightly larger. We prefer to use bone from the donor that is from the same anatomic region. Osteoporotic allograft bone should be avoided, as this does not have the structural integrity required for support of the implant. If the geometry allows it, a press fit into the defect can be achieved. Certain cases of bone loss caused by infection or osteolysis may result in mixed contained-uncontained defects that can be treated with the press-fit technique. The locations of these areas of bone loss are frequently located at the implant-host interface near the joint line or between medial and lateral columns of the distal femur. In our experience, the addition of supplementary plate fixation does not enhance the allograft stability and may result in a stress riser, due to the additional stiffness, if a plate was placed near the allograft-host bone interface. [Editorial: Meaning extra screw holes through the plate weakens the allograft].

There are certain circumstances when the press-fit of the allograft into a defect is not sufficient and fixation is required. The technique we prefer to employ is to place the allograft into the desired position and place provisional K-wires. We then continue our reaming and preparation of the trial implants with the allograft in situ. Placement of definitive fixation in the form of cancellous screws with washers should be done with the trial stems in place. This must be done to avoid screws blocking the path of the final stemmed implant. The use of a stemmed implant is critical as it shields the allograft from excessive force. Once the allograft is secured we recheck all bony cuts prior to implanting the definitive prosthesis.

8. Allograft-Prosthetic Composites

Massive segmental bone loss of either the femur or tibia cannot be treated with cement, augments, or segmental allograft bone alone and require an allograft-prosthetic component (APC) or tumour prosthesis. These defects are uncontained and are frequently circumferential and involve >25 mm of the femur or >45 mm of the tibia.

After the failed implant is removed and debridement completed, the defects are once again evaluated. If it is decided that a femoral allograft-prosthetic composite is required, the collateral ligaments must be maintained as previously mentioned. Ideally the epicondyle attachments are...
removed with some host bone present for later reattachment to the allograft. Once this is done, an oblique cut is made in the host bone where the prosthetic-composite interface is to be. Alternatively, a step cut may be employed with the longer limb on the host bone side ideally. This may be slightly more challenging to perform and accurately match the host graft interface. Regardless, either an oblique cut or step cut provides good rotational control of the allograft. If this is not feasible, the allograft may be intussuscepted into the host diaphysis if the host canal is patulous. This telescoping of the two interfaces imparts some stability and increases the contact area between the host allograft that may improve the ability of the allograft to incorporate \[2\].

9. Tibial Allograft-Prosthetic Composite

The allograft-prosthetic composite of the tibia is fashioned to size based on careful measurements of the host tibia after a thorough debridement is performed. As always, making the allograft larger and longer than may actually be required is good practice as it is always easier to trim the graft “down to size” if needed. This saves time and avoids unnecessary waste of allograft. As in any stemmed implant, the host canal is reamed to securely fit a stemmed implant with proximal fixation into the host bone of two cortical diameters or a minimum of 5 cm. On the back table, the femoral APC is prepared with the revision cutting guides to make the appropriate bone resections (see Figure 3). The epicondylar attachments of the collaterals are secured to the allograft through transosseous drill-hole tunnels where the collateral ligaments would be in a native distal femur. Sutures are passed through these tunnels and left long to attach the host collaterals once the APC is implanted.

The trial femoral components with their securely fitted stems are implanted into the host diaphysis. The flexion and extension gaps are checked and adjusted as needed. If the extension gap is tight, distal femoral resection of the allograft is performed, and, if the flexion gap is tight, the components are translated anteriorly or downsized. If both flexion and extension gaps are tight, we recommend adjusting cuts on

10. Femoral Allograft-Prosthetic Composite

The epicondylar attachments of the collaterals, which were preserved during exposure, are critical in the securing of the femoral APC. As in the tibia, the femoral canals are reamed to securely fit a stemmed implant with proximal fixation into the host bone of two cortical diameters or a minimum of 5 cm. On the back table, the femoral APC is prepared with the revision cutting guides to make the appropriate bone resections (see Figure 3). The epicondylar attachments of the collaterals are secured to the allograft through transosseous drill-hole tunnels where the collateral ligaments would be in a native distal femur. Sutures are passed through these tunnels and left long to attach the host collaterals once the APC is implanted.

The trial femoral components with their securely fitted stems are implanted into the host diaphysis. The flexion and extension gaps are checked and adjusted as needed. If the extension gap is tight, distal femoral resection of the allograft is performed, and, if the flexion gap is tight, the components are translated anteriorly or downsized. If both flexion and extension gaps are tight, we recommend adjusting cuts on
the femoral side and downsizing rather than taking any more of the native proximal tibia. This will also ensure that overstiffing of the knee does not occur and makes wound closure less difficult.

When it is time to implant the stems of either the femoral or tibial side, a critical principle is to avoid cementing of the stems to the host bone. Conversely the allograft side of the stem and implant-allograft interface must be cemented to provide stability to construct. Meticulous cement technique needs to be utilized to ensure the allograft-implant interface has the requisite stability to allow early motion and rehabilitation (see Figure 4). Thus, a copiously irrigated allograft, which is carefully dried, is requisite prior to cementing. Use of low-dose antibiotic containing cement is acceptable; however, we do not add additional antibiotic to the cement as it weakens it and may potentially result in a poor cement mantle. The cement is allowed to harden the APC, and, once this is done, it is implanted into the host canal through a press fit. Rotational position should be aligned to the previous cautery or marker line as it is impacted. No cement should be present between the allograft-host bone junction as it would potentially interfere with graft incorporation. We emphasize avoidance of cementing stems to the host bone as it can make future revisions extremely difficult.

Once components are implanted, the collaterals are attached using the previously placed heavy suture into the allograft epicondyles. Roughening up the allograft epicondyles and suturing the host epicondylar bony wafer may assist in incorporating the ligaments to the APC. Collaterals are tightened maximally in 90 degrees of knee flexion. Supplemental cerclage wiring of the remaining epicondyle host bone can be done to reinforce the sutures.

At this point, we place morselized autograft at the host-allograft junction and attempt to suture a periosteal or synovial flap around the autograft to secure it. Additional fixation may be required if the step or oblique cuts do not impart adequate stability. We suggest using additional screws rather than a cortical strut, as the strut increases bulk to the construct and may compromise the soft tissues. Similarly, our preference is to avoid plate fixation to the allograft as multiple drill holes weaken the graft and make it susceptible to fracture or accelerated vascularization and resorption. This can be a catastrophic complication.

Overall stability of the knee is rechecked with the implants in situ. It should be anticipated early if a highly constrained implant is required based on physical exam and imaging. It is subtler in determining whether a posterior stabilized polyethylene insert or varus-valgus high-post constrained liner is required. We prefer to use the least constraint possible to avoid transfer of stress to the APC interface.

In general terms, we avoid the highly constrained implants such as a rotating hinge implant, as the force transfer to the APC junction is significant and may lead to early failure.

11. Extensor Mechanism Allograft

During primary or revision arthroplasty the extensor mechanism can be deficient secondary to tubercle avulsion, tendon rupture, proximal tibial bone loss, or erosion of the extensor mechanism from infection. During revision, arthroplasty scarring of the quadriceps and patellar tendon makes the extensor mechanism particularly vulnerable to disruption.

The extensor mechanism allograft is obtained from the bone bank with the complete quadriceps tendon, patellar tendon, and tibial tubercle attached. It is critical to have enough bone at the patellar tendon attachment for distal fit into the host bone.

Once the primary or revision implants are placed, the remnant of the host patella is sheled out of its periosteal sleeve. Distal tubercle is debrided, and a reverse “V” shape osteotomy is made in the area of the native tubercle. This type of osteotomy allows good press fit of the allograft and also resists proximal migration of the allograft tubercle [13].

The allograft is then placed with the host patellar remnant and allograft patella at the same level. This ideally should lie in the femoral trochlear groove of the implant. Once this height is judged, the allograft is marked at the tibial tubercle that should be very close to the native tubercle of the patient. Four small drill holes are made into host tibia for wire passage. The graft is then shaped with a microsagittal saw to fit into the reverse “V” osteotomy site. It is press fit into the recipient site and held with transosseous cerclage wires. Proximally, the allograft quadriceps is then sutured. The allograft quadriceps tendon is attached to the remaining host quadriceps tendon in a running locked fashion with heavy, nonabsorbable suture such as fiber-wire. This is then reinforced with multiple interrupted sutures. At this point, the knee is taken through range of motion to check stability and tracking. Adjustments may still be made at this stage. If tracking and stability are adequate, multiple sutures are placed into the parapatellar tendon region. The knee arthrotomy approach is closed in the usually fashion [14].

12. Soft-Tissue Envelope

Closure of the wound may be challenging, and the most common reason for this is oversized allograft, followed by oversized components. To avoid this problem, careful implant and allograft selection is critical. Tibial tubercle osteotomy is attached with large fragment partially threaded cancellous screws or with transosseous wiring. Quadriceps tendon turn-down or snips are repaired with heavy suture. Closure of the parapatellar arthrotomy is done with heavy suture done in a continuous manner with reinforced interrupted sutures. Deep drains are placed at the preference of the surgeon and subcutaneous and skin layers are closed in the usual fashion. Anticipated wound closure problems should be discussed prior to surgery with your plastics colleagues. If soft-tissue coverage is a problem, rotational flaps and skin-grafting may be necessary [10].

13. Postoperative Care and Rehabilitation

Range of motion is a critical component of recovery, and these should be started as soon as possible provided the
wound coverage is adequate and there are no extensor mechanism issues. If a tibial tubercle osteotomy or quadriceps turnover is performed, we restrict active extension for 6–8 weeks. Restrictions on weightbearing are maintained for 8 weeks followed by progressive increases to full weightbearing once graft incorporation is seen on sequential radiographs. This may take 3–6 months depending on the reconstruction and biology of the patient.

14. Complications

As with all complex reconstructions, preoperative planning is critical in ensuring no untoward intraoperative surprises. We strongly believe that deviating from a carefully thought-out preoperative plan may result in poor outcomes. Critical steps involve allograft and implant sizing and dealing with anticipated wound complications early and aggressively. Furthermore, optimizing the patient’s perioperative health status is crucial, and this must include smoking abstinence.

Despite careful planning, complications still occur. Graft fracture, rapid revascularization, and early resorption lead to weakening of the APC and eventual failure. Another problematic scenario is a periprosthetic fracture that results in further bone loss [15]. Infections are also more prevalent in complex revision surgery. These must be aggressively treated with early debridement, antibiotics, and possible staged revision. As mentioned earlier, wound problems should be treated aggressively with appropriate consultation made to plastic surgery.

Occasionally, the combination of infection and wound problems results in an amputation although this is fortunately a rare occurrence.

15. Results

The use of segmental and structural allografts has been used in both contained and uncontained defects around the knee in arthroplasty for over two decades. The primary data for this comes in the setting of revision knee arthroplasty and has encouraging results. In one of the earliest papers, Stockley et al. reported 20 knees that had undergone a combination of structural allograft and morselized allograft with 85% survivorship at 4.2 years [16]. There were 2 graft fractures and 3 infections in their series. The lowest reported survivorship is that from Ghazavi et al. with only 67% survivorship at 5 years in their 30 patients [17]. However, when looking at the majority of the literature, most authors report 80–93% survivorship of their constructs at 5 years. The survivorship numbers drop off at 10 years with Clatworthy et al. showing a drop of 92% at 5 year to 79% at 10 years [18]. Reference [19] had 46 patients at 10 years with 91% survivorship for femoral head allograft in tibial defects.

A recent publication by Richards et al. compared cohorts with severe bone loss of bone around total knee arthroplasty using femoral allograft compared with metal augments [20]. Despite the presence of more significant bone loss in the allograft group, these had better clinical outcome scores than the control cohort. This strengthens the argument for allograft use in patients with severe bone loss.

Lastly, Backstein et al. have one of the largest cohorts to date with 61 patients. The survival rate at 5.4 years was 85.2% [2]. Of note in this series, the infection rate was 6.5% (4/61); however, a high union rate of 98.4% (60/61) was seen radiographically.

16. Summary

Dealing with bone loss is a significant challenge to arthroplasty surgeons. We believe that structural allograft is a viable method for dealing with this problem with the added benefit of restoring bone stock. These complex procedures should be performed by surgeons with expertise in revision arthroplasty and with access to a dedicated bone bank. Allograft reconstruction is not indicated in the low demand or elderly patients who would benefit from implantation of an endoprosthesis, which allows rapid mobilization and recovery.

The optimal allograft candidate is a young, higher demand and relatively healthy patient that is likely to require further revisions in the future and can adhere to the rehabilitation protocol. The restoration of bone stock is a key component in choosing allograft in the reconstruction. Overall, this method of treatment has good outcomes in the literature despite the complex nature of the procedures.

References


Appendix 11

Lee C, Freeman R, Edmondson M, Rogers BA.
The efficacy of tranexamic acid in hip hemiarthroplasty surgery: an observational cohort study.

Contribution by BA Rogers.
Concept
Data Analysis
Manuscript writing & editing

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Mendeley readers: 22
The efficacy of tranexamic acid in hip hemiarthroplasty surgery: An observational cohort study

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Haemoglobin
Blood loss
Blood transfusion
Orthopaedic
Trauma

A B S T R A C T

Tranexamic acid (TXA) has been shown to reduce perioperative blood loss in elective lower limb arthroplasty surgery. There are potentially even greater physiological benefits in minimising blood loss in hip fracture surgery, however limited evidence exists for TXA use in hemiarthroplasty surgery. This study investigates the effect of TXA use on postoperative transfusion rates and haemoglobin (Hb) levels specifically following hemiarthroplasty surgery for hip fractures.

A retrospective cohort study was conducted for consecutive hip hemiarthroplasties for fractures between June 2013 and October 2014 comparing patients with or without prophylactic TXA before incision.

During the study, 305 hemiarthroplasties were performed with 271 cases eligible. TXA was given in 84 (31%) cases, and both patient groups were matched for known confounding factors. Patients given TXA had a lower transfusion rate (6% vs. 19%; p = 0.005) and less blood loss (Hb drop > 20 g/L) on day 1 post surgery (26% vs. 42%; p = 0.014). One transfusion was prevented with every 8 patients given prophylactic TXA. There were no differences in the 30 and 90-day mortality rates with TXA use.

Tranexamic acid is safe, cost-effective and reduces the need for blood transfusion and should be considered in all patients undergoing hip hemiarthroplasty for fractures.

Introduction

Hip fracture surgery frequently results in a drop in haemoglobin (Hb) and the potential need for blood transfusion [1–3]. For cemented hip hemiarthroplasties, the reported average operative blood loss is approximately 500 ml [4]. Blood loss can result from both the fracture as well as from surgery, and can remain hidden for a period of time after surgery [5,6]. Postoperative anaemia after hip fracture surgery is related to an inferior functional recovery, and a detrimental effect on mortality [1,7].

Allogenic blood transfusions are expensive and have associated risks [8–12]. As a result, numerous methods of blood conservation have been investigated, including preoperative blood donation, perioperative blood salvage, controlled hypotension and the use of pharmacological agents [13–16]. Drugs such as epsilon-aminocaproic acid, Recombinant Human Erythropoietin, and Aprotinin have been shown effective, but routine use are limited by low cost-effectiveness in orthopaedic surgery [17,18].

Tranexamic acid (TXA) is an antifibrinolytic agent that binds with plasminogen to competitively block lysine binding sites. This prevents plasminogen interaction with fibrin, thus inhibiting plasmin induced fibrinolysis and clot breakdown. Tissues injured during surgery release tissue plasminogen activator and activate the fibrinolytic system, during which TXA can exert its effects. The half-life of TXA is approximately 120 min and is renally excreted [19]. The optimal dosage and schedules for TXA administration in hip fracture surgery remain unknown [20–22]. Previous studies have suggested that low-dose regimes (<30 mg/kg, or 1 g) is adequate for most adults [23–25]. Administration of TXA before hyperfibrinolysis was also suggested to be more effective [20,22,26]. 1 g of TXA given intravenously before skin incision should therefore be adequate for most hip hemiarthroplasty procedures.

Over the past decade, there has been growing evidence to demonstrate the blood conservation effects of TXA in a range of surgical procedures [25,27–29]. A thorough literature search (see Appendix A) however shows limited studies investigating the specific use of TXA for hip hemiarthroplasty surgery, despite this patient cohort being particularly susceptible to the effects of blood loss [5,7,16]. The aim of this study is to evaluate the effect of TXA use on postoperative transfusion rates and Hb levels following hemiarthroplasty surgery for hip fractures.
Patients and methods

This retrospective cohort study was conducted between June 2013 and November 2014 in a single centre (Royal Sussex County Hospital, Brighton, UK): a high volume regional Major Trauma Centre (MTC). Inclusion criteria were consecutive patients undergoing hip hemiarthroplasty for fracture. Exclusion criteria included revision surgery, pre-operative transfusion, use of an Austin Moore prosthesis and cases with an incomplete dataset. Fractures were typically operated on within 36 h of presentation using an Exeter Unirx implant (Stryker, MI). Low functional demand patients with significant medical co-morbidities had an uncemented Austin Moore prosthesis.

During the study period no hospital protocol determined the use of TXA in hip fracture surgery, and thus whether patients received prophylactic TXA or not was according to surgeon preference. Patients who received TXA were given a bolus of 1 g intravenously on induction. All patients received routine venous thromboembolism prophylaxis with Tinzaparin 4500 units post-operatively unless contraindicated according to hospital policy. The indication to transfuse was decided on a case-by-case basis, to maintain a postoperative Hb above 80 g/L.

The patient dataset collected included: Age, gender, preoperative residency/mobility, abbreviated mini mental state score (AMTS), American Society of Anaesthesiologists (ASA) grade, anaesthetic type, surgeon grade, Hb levels (preoperative on admission and postoperative day 1 to 3), transfusion requirement, length of stay, mortality and morbidities. The data was collected from Bluespier Theatre Manger (Bluespier International, Droitwich, UK), electronic blood reporting system (WinPath), the National Hip Fracture Database (NHFD), and further correlated with patient notes.

The primary outcome was transfusion within 14 days of surgery. Secondary outcomes were significant Hb drop (defined as >20 g/dL) on post-operative day 1 and day 3 and mortality at 30 and 90 days.

Data was analysed using SPSS version 19. Unless otherwise stated, the Fisher’s exact or Chi square tests were used for categorical data, and T-test for continuous data, with significance set at 5%. Retrospective two-tailed power analysis was done for the primary outcome measure (96.1%). Results are presented as percentages (with numbers in brackets).

Results

In the study period 305 hemiarthroplasties were performed with 271 cases fulfilled the inclusion criteria and were analysed. The patient demographics are summarised in Fig. 1.Eighty-four patients (31%) received prophylactic TXA. There were no significant differences between the TXA vs. no-TXA groups in terms of age, gender, premorbid function, preoperative Hb, anticoagulation use, ASA, anaesthetic type and surgical approach. Table 1 shows the detailed pre-operative comparison between TXA vs. no-TXA cohorts.

The overall transfusion rate was 15% (40 patients). Patients not given TXA were 3 times more likely to require transfusion than patients given TXA (15% vs. 6%; p = 0.005). For every 8 patients given prophylactic TXA, 1 transfusion was prevented, giving a Number Needed to Treat (NNT) of 8 and an absolute risk reduction (ARR) of 12.76%.

The number of cases with significant day 1 Hb drop (>20 g/L) was significantly lower in patients given TXA (26% vs. 42%; p = 0.014). There was no significant difference in mortality between groups at 30 and 90 days (p = 1.00). The postoperative comparisons between the 2 cohorts are detailed in Table 2.

Discussion

TXA is known to be an effective and safe agent for reducing surgical blood loss [19,27,29], though there are limited reports on its use in hip hemiarthroplasty surgery. Hip hemiarthroplasty may result in less blood loss per se than total hip or knee arthroplasty surgery [30], but this patient group is physiologically more susceptible to postoperative anaemia. Such reasons include; older

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**Table 1**

<table>
<thead>
<tr>
<th>Case (TXA, n = 84)</th>
<th>Control (no-TXA, n = 187)</th>
<th>p Value*</th>
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<tbody>
<tr>
<td><strong>Demographics</strong></td>
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<tr>
<td>Age (mean, years)</td>
<td>85.95 ± 7.60</td>
<td>84.66 ± 7.69</td>
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<tr>
<td>Gender</td>
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<tr>
<td>Female</td>
<td>61.9% (52)</td>
<td>71.66% (134)</td>
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<tr>
<td>Male</td>
<td>38.10% (32)</td>
<td>28.34% (53)</td>
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<tr>
<td>Mean pre-op Hb</td>
<td>125.14 ± 14.94</td>
<td>123.33 ± 15.66</td>
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<tr>
<td><strong>Medications</strong></td>
<td></td>
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<tr>
<td>On antplatelet</td>
<td>35.7% (30)</td>
<td>36.36% (68)</td>
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<tr>
<td>Aspirin</td>
<td>26.19% (22)</td>
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<tr>
<td>Clopidogrel</td>
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<td>Consultant</td>
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</tr>
<tr>
<td>Trauma Fellow</td>
<td>22.62% (19)</td>
<td>9.63% (18)</td>
</tr>
<tr>
<td>Specialist Registrar</td>
<td>53.57% (45)</td>
<td>65.78% (123)</td>
</tr>
<tr>
<td>Surgical trainee</td>
<td>2.38% (2)</td>
<td>5.35% (10)</td>
</tr>
</tbody>
</table>

Continuous values expressed as mean ± standard deviation. AMTS—abbreviated mini mental test score.

* Fisher’s exact or Chi square test for categorical data, T-test for continuous data.
age, female gender, lower admission Hb, higher ASA grade, frailty and greater co-existing co-morbidities [2,6,31]. Blood conservation is therefore particularly important in hip fracture patients to prevent complications related to acute postoperative anaemia. TXA is an attractive option for routine clinical use.

This study demonstrates a significant reduction in postoperative transfusion rate and Hb drop with TXA use in hip hemiarthroplasty surgery, with no increase in 30 and 90 day mortality. These results are consistent with previous studies in the literature [25,26,28,29,32,33]. Similar effects of TXA are also demonstrated in randomised control trials (RCT) involving hip fracture surgeries [26,34,35]. Sadeghi and Mehr-Aein [3], and Vijay et al. [35] both reported a significant reduction in transfusion rates with TXA use versus placebo. In the THIF study (TXA in Hip Fracture surgery), Zufferey et al. [26] also reported the same trend with a 30% relative reduction in transfusion rates with TXA use. Summary of the results from these studies is shown in Table 3. The significant heterogeneity between these studies in terms of study population, methodologies and outcome measures should be taken into account on interpretation. In particular, higher blood loss and transfusion requirements in surgeries for extracapsular hip fractures compared to intracapsular hip fractures [6,10,12,36] may lead to variations in the treatment effect of TXA reported.

Although the RCT conducted by Emara et al. [34] showed a reduced transfusion rate with TXA use in hip hemiarthroplasty surgery (5% in TXA versus 35% in placebo group p < 0.05), their study population excluded a significant portion of patients that define the hip fracture population. First, patients with significant cardiorespiratory co-morbidities and preoperative anaemia, which are both prevalent features in the elderly hip fracture population, were excluded from the trial [2,5,31]. In addition, patients recruited into the trial were between 50 and 60 years of age, which is significantly younger than that reported in our study and by the UK National Hip Fracture Database (NHFD), which had an average age of 84 [37]. The pragmatic observational nature of our study therefore has the advantage of capturing real-life practice in an un-preselected population. Our patient demographic in comparison with the NHFD is shown in Table 4, and the similarities suggest that our study population is representative of the hip fracture population seen in everyday practice across the UK.

Despite the wide use of TXA there is concern regarding increased venous thrombosis [3,19,34]. Zufferey et al. [26] reported a 3-fold increase in vascular events (DVT, PE, CVA, MI) at 6 weeks with intravenous TXA use in hip fracture surgery, but this was not statistically significant. A number of meta-analyses find no increase in thromboembolic complications, but were unable to draw conclusions regarding the safety of TXA due to potential bias [25,27,29,32]. In our study, no difference was demonstrated in the incidence of venous thromboembolic (VTE) complications, however not to statistical significance due to low complication rates. Inconsistent symptom reporting in this patient cohort and the lack of routine postoperative VTE investigations could have led to missed VTE events, particularly those that were asymptomatic. We believe mortality is a robust surrogate for clinically significant thromboembolic events in this cohort and we found no difference at either 30 or 90 days post-operatively. A recent population based study by Poeran et al. [33] involving 872,416 patients showed no increase in thromboembolic events.

### Table 2

<table>
<thead>
<tr>
<th>Postoperative outcome comparison of patient groups.</th>
<th>Case (TXA, n=84)</th>
<th>Control (no-TXA, n=187)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RBC transfusion</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Transfusion rate</td>
<td>5.95% (5)</td>
<td>18.72% (35)</td>
<td>0.01</td>
</tr>
<tr>
<td>Avg. units per patient</td>
<td>2.6</td>
<td>2.23</td>
<td>0.43</td>
</tr>
<tr>
<td>Postop Hb (g/L)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Day 1 Hb drop &gt;20 g/L</td>
<td>26.19% (22)</td>
<td>42.25% (79)</td>
<td>0.01</td>
</tr>
<tr>
<td>Day 1 Hb</td>
<td>110.80±16.39 (84)</td>
<td>106.67±14.04 (185)</td>
<td>0.03</td>
</tr>
<tr>
<td>Day 3 Hb</td>
<td>105.73±14.07 (30)</td>
<td>99.04±14.88 (72)</td>
<td>0.04</td>
</tr>
<tr>
<td>Day 1 Hb drop</td>
<td>14.35±10.77 (84)</td>
<td>17.18±10.99 (185)</td>
<td>0.05</td>
</tr>
<tr>
<td>Day 3 Hb drop</td>
<td>20.57±11.68 (30)</td>
<td>25.79±13.14 (72)</td>
<td>0.05</td>
</tr>
<tr>
<td>Mortality</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>30 day</td>
<td>4.76% (4)</td>
<td>4.81% (9)</td>
<td>1.00</td>
</tr>
<tr>
<td>90 day</td>
<td>5.52% (8)</td>
<td>10.16% (19)</td>
<td>1.00</td>
</tr>
<tr>
<td>Thromboembolic event</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Detected DVT/PE</td>
<td>1.19 (1)</td>
<td>2.14 (4)</td>
<td>1.00</td>
</tr>
<tr>
<td>Length of stay</td>
<td>21±15.49</td>
<td>18±18.05</td>
<td>0.26</td>
</tr>
</tbody>
</table>

Continuous values expressed as mean ± standard deviation. DVT—deep vein thrombosis, PE—pulmonary embolism.

& Fishier’s exact or Chi square test for categorical data, T-test for continuous data.

1 2 Cases with postoperative transfusion on day 0 excluded from calculation.

### Table 3

<table>
<thead>
<tr>
<th>Synthesis of results from randomised control trials of TXA use in hip fracture surgery.</th>
<th>TXA regime</th>
<th>Sample size</th>
<th>Blood loss (mL)</th>
<th>Transfusion rate (%)</th>
<th>Transfusion index</th>
<th>No. of hip hemi-arthroplasties</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current study 1 g bolus preop</td>
<td>Case 84</td>
<td>–</td>
<td>6</td>
<td>2.6</td>
<td>84</td>
<td></td>
</tr>
<tr>
<td>Emara et al. [34] 10 mg/kg bolus preop then 5 mg/kg/h infusion</td>
<td>Controls 187</td>
<td>19</td>
<td>35</td>
<td>2.2</td>
<td>187</td>
<td></td>
</tr>
<tr>
<td>Zufferey et al. [26] 15 mg/kg bolus preop and 3 h later</td>
<td>Case 57</td>
<td>975</td>
<td>42</td>
<td>1.0</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Sadeghi and Mehr-Aein [3] 15 mg/kg bolus preop</td>
<td>Case 35</td>
<td>1484</td>
<td>57</td>
<td>1.95</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>Vijay et al. [35] 500 mg bolus preop then 10 mg/kg/h infusion</td>
<td>Controls 45</td>
<td>39</td>
<td>16</td>
<td>–</td>
<td>N/A</td>
<td></td>
</tr>
</tbody>
</table>

* Surgical drain volume.
In fact they reported a significantly lower rate of myocardial infarctions, acute renal failure, PE s and in-hospital mortality with TXA use in joint replacement surgery.

Topical administration of TXA is less well reported than intravenous use. It has been suggested that topical administration may reduce systemic exposure, thereby reducing risk of thromboembolic events. Emara et al. [34] compared intravenous TXA versus topical TXA in a RCT involving 60 hip hemiarthroplasties. Topical TXA were administered by bathing 1.5 g of TXA with 100 mL of saline in the surgical field for 5 min. The authors found that both routes were equally as effective and reported less thrombotic events with topical TXA use.

Routine use of TXA may also provide additional cost–benefits. A single 1 g dose of intravenous TXA costs £1.50 [38]. In contrast, the cost of a unit of packed red cells is £124.85 at our Trust. Adding to this are the cost of blood grouping and cross matching both at £15.97. In our study, 1 transfusion was prevented with every 8 patients given prophylactic TXA (NTN = 8). Extrapolating the data for our trust, it would cost only £271.50 per year to give TXA to every patient undergoing hip hemiarthroplasties; we would in addition save approximately 23 transfusions costing up to £6312.62 per year. Using the arthroplasty data reported by the NHFD 2014, this would equate to an approximate UK–wide cost saving of over £1 million per annum. Cost-effectiveness of TXA has also been shown in a number of studies. [32,33,39,40] Irsson et al. [40] reported a 25% cost reduction with the use of TXA compared with other blood conservation strategies.

Due to the retrospective design of our study, we cannot eliminate selection bias, principally the surgeons’ decision to use TXA, and postoperative transfusion decisions by the attending ward doctors. The rationale for these decisions was not documented in individual cases. Based on anecdotal observation in our unit, patients may be given TXA because of a perceived higher risk of blood loss. However, we could not find a single factor that increased TXA use in a particular patient subgroup. Although we had a significantly larger control group, both patient cohorts were well matched for preoperative HB levels and all other major confounding factors. Retrospective power analysis for the primary outcome measure was 96.1%. We found a greater use of TXA by trauma fellows—possibly a result of increased interest. However, trauma fellows accounted for only 14% of cases performed, and excluding all such cases, did not significantly change the results.

Conclusion

Compiling our findings with the evidence from the most recent literature, the blood conservational effects of TXA is well established and appears to be safe and cost-effective. Blood management is particularly important for hip fracture patients. This study supports the use of tranexamic acid in hemiarthroplasty surgery for hip fractures.


Appendix 12

Banerjee P, Rogers BA.

Contribution by BA Rogers.

Concept
Data Analysis
Manuscript writing & editing

Citation Metrics

Web Of Science: 5
Google Scholar: 9
Altmetrics: 24
Tweets: 2
Facebook: 1
Mendeley readers: 21
Systematic Review of High-volume Multimodal Wound Infiltration in Total Knee Arthroplasty

PURNAJYOTI BANERJEE, DIPORTH, MSc, MRCS(ED); BENEDICT A. ROGERS, MA, FRCS(ORTH)

educational objectives

As a result of reading this article, physicians should be able to:

1. Understand the high-quality evidence regarding the use of multimodal high-volume local wound infiltration in total knee arthroplasty.
2. Understand the contents of the drugs used, intraoperative infiltration techniques, and postoperative placement and use of a wound catheter.
3. Explain the effects of using wound infiltration in immediate postoperative pain relief, early mobilization, and length of hospital stay after total knee arthroplasty.
4. Understand the safety and complications associated with this technique.

ABSTRACT

Pain relief following total knee arthroplasty (TKA) is challenging because early mobilization and rehabilitation are essential for a successful outcome. Postoperative pain can limit recovery, leading to reduced mobility and prolonged hospitalization. There are potential benefits of infiltrating high volumes of local anesthetics around the soft tissues of replaced hip and knee joints. The risk of systemic toxicity is minimized with diluted local anesthetic solution, which also allows a high volume to be used. One of the...
pain relief following total knee arthroplasty (TKA) is challenging because early mobilization and rehabilitation are essential for a successful outcome. Postoperative pain can limit recovery, leading to reduced mobility and prolonged hospitalization. Local anesthetic agents block impulse transmission from some, but not all, peripheral pain receptors following major surgery. In addition, if infiltrated in large quantities, universal local anesthetic sodium channel block may lead to detrimental cardiac and neurologic effects. It has been proposed that the release of inflammatory mediators and proteins secondary to cytolysis induces a stress response in the brain and the spinal cord, stimulating pain, even with a full block of peripheral receptors.

Recent clinical evidence has highlighted the potential benefits of infiltrating high volumes of local anesthetics around the soft tissues of replaced hip and knee joints. The risk of systemic toxicity is minimized with diluted local anesthetic solution, which also allows a high volume to be used. The possible loss of efficacy resulting from this dilution can be compensated with the addition of adjuvant agents such as adrenaline and nonsteroidal anti-inflammatory drugs (NSAIDs). Analgesia may be prolonged up to 48 hours with long-acting local anesthetics and the administration of supplemental doses via a wound catheter at regular intervals.

Local infiltration analgesia uses a systematic infiltration of the periarticular soft tissues with a mixture of ropivacaine (a long-acting local anesthetic with a superior cardiotoxicity profile), ketorolac (an NSAID), and adrenaline (a vasoconstrictor).6,8 In their series of 325 patients undergoing total hip and knee arthroplasty, Kerr and Kohan reported excellent pain control and just one overnight hospital stay in 71% of patients. Due to the simplicity and relative safety of the procedure, it has gained widespread acceptance and use. One of the principal advantages is that analgesia agents are administered intraoperatively by the surgeon and subsequently by the ward staff, thereby minimizing the need for additional invasive procedures. However, some methodological concerns have been expressed regarding the validity of comparing its efficacy with that of other analgesic modalities.

The current systematic review was designed to synthesize the available clinical evidence on the efficacy of high-volume multimodal wound infiltration following TKA, in particular intraoperative administration with and without the supplemental dosage through a suitably placed wound catheter. The aim of this study was to evaluate whether high-volume multimodal wound infiltration reduces pain and opiate intake while enhancing early rehabilitation and discharge when used in patients undergoing TKA.

**Materials and Methods**

A literature search was conducted in June 2012. The databases reviewed included Medline and Embase. The search terms included pain, postoperative, wound infiltration, total knee replacement/arthroplasty, wound catheter, and intra-/extra-articular injection. All studies identified using these search terms were then integrated using the Boolean and, which was subsequently scrutinized manually by the authors to extract the studies that fit the inclusion and exclusion criteria. Studies were limited to randomized trials in English and available through the Internet studying adults between the years 2000 to 2012. Studies published in the past decade were searched to ensure current evidence and the latest perspective on the issue. Furthermore, randomized controlled trials were included to ensure that highest level of evidence. All published articles were identified with the above search strategy. They were first screened using the title and the abstract to extract relevant studies that could be included in a systematic review, which was restricted to patients undergoing TKA. A manual search of the reference lists from selected articles was also performed to further increase the number of publications with relevant data.

**Inclusion Criteria**

Inclusion criteria were the following:

1. Randomized controlled trials reporting results on perioperative wound infiltration in primary unilateral TKA
2. Use of wound catheters
3. Defined research questions
4. Adequately described methodology
5. Use of intermittent injections or continuous infusions
6. Well-defined outcome measures
Exclusion Criteria

Exclusion criteria were the following:

1. Systemic reviews and meta-analyses
2. Nonrandomized trials
3. Studies not published in English
4. Studies published prior to 2000
5. Bilateral TKA with infiltration of both knees
6. Unicompartmental TKA
7. Studies on knee arthroscopic surgery, hip replacements, and nonorthopedic surgical procedures
8. No comparator group
9. Nonrandomized
10. Outcome measures not well defined
11. No validated patient-reported functional outcome scores

Data Extraction

Once the authors identified the studies that appeared to meet the inclusion criteria, they read through the abstracts of the studies to find those that were relevant and fulfilled all of the inclusion criteria. Ideally, at this stage, both authors independently read each article to assess the adequacy of the search results and extract data according to their defined inclusion and exclusion criteria to ensure that the evidence gathered was adequate and relevant. Dissenting opinions regarding a study’s inclusion were resolved with informal discussions between the authors.

The authors included data on pain intensity as measured by the visual analog scale (VAS) from 0 to 10, where 0 represents no pain and 10 represents the worst imaginable pain. Postoperative pain was recorded in hours, opiate consumption in milligrams, and length of hospital stay in days. However, most of these studies suffer from methodological inadequacies and insufficient blinding (Table 3). The assessment of postoperative pain and opiate consumption is not fully described. Furthermore, data are lacking on the consumption and quality of peripheral analgesia or epidural (continuous/intermittent) analgesia techniques used in control groups. Data on the use of comparable systemic analgesia between groups are lacking in some studies. There is no conclusive evidence on the use of wound catheters and postoperative doses of local anesthetics imparting any significant analgesic effects after TKA. However, a similar conclusion cannot be drawn on the use of intra- or extra-articular/intracapsular administration of the drugs. There seems to be a distinct advantage in administering the local anesthetic agents.

RESULTS

A total of 344 studies were found in the Medline database, and 19 were found in Embase. Thus, a total of 363 abstracts were identified that fulfilled the initial search strategy. From these abstracts, 44 studies were considered to be relevant to the study’s design and had all of the inclusion criteria and none of the exclusion criteria described previously. Of these, 18 randomized prospective studies were included in this systematic review, which had the necessary data as outlined previously. All studies identified in Embase were included in Medline except one, which was separately analyzed. These studies are summarized in Tables 1 and 2.

The search suggested that intraoperative wound infiltration with high-volume local anesthetic infiltration provides adequate pain relief for at least the first 6 to 12 hours. However, most of these studies suffer from methodological inadequacies and insufficient blinding (Table 3). The assessment of postoperative pain and opiate consumption is not fully described. Furthermore, data are lacking on the consumption and quality of peripheral analgesia or epidural (continuous/intermittent) analgesia techniques used in control groups. Data on the use of comparable systemic analgesia between groups are lacking in some studies. There is no conclusive evidence on the use of wound catheters and postoperative doses of local anesthetics imparting any significant analgesic effects after TKA. However, a similar conclusion cannot be drawn on the use of intra- or extra-articular/intracapsular administration of the drugs. There seems to be a distinct advantage in administering the local anesthetic agents.

### Table 1

<table>
<thead>
<tr>
<th>Search Results From Medline Database on Wound Infiltration in Total Knee Arthroplasty</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain=469,378</td>
</tr>
<tr>
<td>Postoperative complications (OR)= 5,451,344</td>
</tr>
<tr>
<td>Wound infiltration (OR)=5,179,326</td>
</tr>
<tr>
<td>Knee replacement (OR)=427,335</td>
</tr>
<tr>
<td>Wound catheter (OR)=196,778</td>
</tr>
<tr>
<td>Injection (OR)=5733</td>
</tr>
<tr>
<td>1 and 2 and 3 and 4 and 5 and 6 (AND)=344</td>
</tr>
<tr>
<td>Manual search (AND)=32</td>
</tr>
<tr>
<td>Limits applied=17</td>
</tr>
</tbody>
</table>

*Parentheses contain the Boolean used while expanding each search term.

### Table 2

<table>
<thead>
<tr>
<th>Search Results From Embase on Wound Infiltration in Total Knee Arthroplasty</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain=840,225</td>
</tr>
<tr>
<td>Postoperative complications (OR)= 685,542</td>
</tr>
<tr>
<td>Wound infiltration (OR)=208,384</td>
</tr>
<tr>
<td>Knee replacement (OR)=12,420</td>
</tr>
<tr>
<td>Knee arthroplasty (OR)=23,419</td>
</tr>
<tr>
<td>Wound catheter (OR)=284,755</td>
</tr>
<tr>
<td>Injection (OR)=5625</td>
</tr>
<tr>
<td>1 and 2 and 3 and 4 and 5 and 6 (AND)=19</td>
</tr>
<tr>
<td>Manual search (AND)=19</td>
</tr>
<tr>
<td>Limits applied=1</td>
</tr>
</tbody>
</table>

*Parentheses contain the Boolean used while expanding each search term.

*Limits were randomized trials, adults, 2000-2012, in English, available from the Internet.*
# Table 3

<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Pain Score</th>
<th>Opiate Consumption</th>
<th>Treatment vs Control Length of Stay, d</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Busch et al</td>
<td>Intraoperative wound infiltration vs no injection (n=64)</td>
<td>Reduced VAS immediately and 4 h postop</td>
<td>Reduced at 4, 12, and 24 h postop</td>
<td>Mean, 5.2 vs 5.2</td>
<td>Single-dose wound infiltration vs no injection; no ketorolac and epidural morphine in control group; hinders exact interpretation of short-duration pain relief with wound infiltration; lack of wound catheter may explain relative short-term benefits achieved by treatment group patients.</td>
</tr>
<tr>
<td>Toftdahl et al</td>
<td>Intra- and postop wound infiltration vs continuous femoral nerve block (n=80)</td>
<td>Reduced NRS in treatment group vs femoral block group on postop day 1; similar pain scores on day of operation</td>
<td>Reduced up to end of postop day 1</td>
<td>Median, 5 vs 6</td>
<td>No differences regarding side effects or length of stay seen between groups; small sample size; similar oral analgesia (NSAID/paracetamol/oxycodone) in both groups; femoral blockade group inferior to that reported in the literature; intra-articular bupivacaine (50 mg) and morphine (4 mg) administered with patients and research staff not blinded to patient groups.</td>
</tr>
<tr>
<td>Vendittoli et al</td>
<td>Intra- and postop wound infiltration vs no injection (n=42)</td>
<td>Reduced at 24 and 48 h</td>
<td>Reduced up to 48 h postop</td>
<td>Mean, 4.8 vs 5.2</td>
<td>Not blinded; small sample size; effect predominant within the first 8 h of wound infiltration; similar systemic analgesia (COX-2 inhibitor/acetaminophen) and morphine PCA in both groups; lack of control for ketorolac in no injection group; no effect of 24-h postop administration in catheter.</td>
</tr>
<tr>
<td>Andersen et al</td>
<td>Intraop wound infiltration and postop intra- or extra-articular injection of local anesthetics (n=32)</td>
<td>No difference</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Double-blind placebo-controlled study; small sample size; no difference in pain scores, analgesia between the site of administration.</td>
</tr>
<tr>
<td>Andersen et al</td>
<td>Intraop wound infiltration with postop intracapsular vs intra-articular injection (n=60)</td>
<td>No difference</td>
<td>No difference</td>
<td>Mean, 3.0 vs 2.9</td>
<td>Double-blind study; intraop wound infiltration in both groups; intracapsular vs intra-articular injections 6 and 24 h with no difference.</td>
</tr>
<tr>
<td>Gomez-Cardero et al</td>
<td>Continuous intra-articular 0.2% ropivacaine infusion vs placebo infusion with normal saline (n=50)</td>
<td>Reduced VAS score in first 3 postop d</td>
<td>Reduced opiate consumption for first 3 d in treatment group</td>
<td>Mean, 5.72 vs 7.3</td>
<td>Small sample size; blinding not clear; no NSAID or adrenaline used to enhance analgesic effects, indicating latter may not be needed; despite favorable results, unclear whether effect of pain relief was favorable during rest or motion; continuous infusion can hinder proper rehabilitation in the immediate postop period.</td>
</tr>
<tr>
<td>Andersen et al</td>
<td>Intraop wound infiltration with (treatment group) or without (control group) compression bandage (n=48)</td>
<td>NRS pain score at rest, during flexion, or on straight leg lift was lower for the first 8 h in patients with compression bandage vs noncompression bandage</td>
<td>Not reported</td>
<td>Mean, 2.8 vs 3.3</td>
<td>Compression bandage prolongs intraop analgesic effects after wound infiltration.</td>
</tr>
<tr>
<td>Parvataneni et al</td>
<td>Intraop wound infiltration, not well-defined dose vs femoral nerve block (n=60)</td>
<td>No difference</td>
<td>No data</td>
<td>Mean, 3.2 vs 3.2</td>
<td>Not blinded; variable nonopiod analgesia on request; femoral nerve block not described; pain assessment insufficient.</td>
</tr>
<tr>
<td>Study</td>
<td>Design</td>
<td>Pain Score</td>
<td>Opiate Consumption</td>
<td>Treatment vs Control Length of Stay, d</td>
<td>Comments</td>
</tr>
<tr>
<td>---------------</td>
<td>------------------------------------------------------------------------</td>
<td>------------------------------------------------</td>
<td>--------------------</td>
<td>---------------------------------------</td>
<td>--------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Spreng et al</td>
<td>Intra- and postop wound infiltration vs epidural analgesia, NSAIDs, and opioids in injection group vs systemic analgesia (n=102)</td>
<td>Reduced NSAIDs and opioids in wound infiltration group, which was more effective than systemic analgesia group</td>
<td>Opiate consumption (72 h) was lowest for wound infiltration group (80 vs 101 mg [epidural analgesia group] vs 118 mg [wound infiltration and IV NSAIDs and opioids group]</td>
<td>Median, LIA 3.5 and 4 vs epidural 5.5</td>
<td>Well-designed trial; marginal differences in VAS during knee flexion and opioid consumption between wound infiltration vs wound infiltration and IV NSAIDs and opioids; wound infiltration group only compared with epidural analgesia and not with no-wound infiltration group; controlled epidural analgesia for 48 h not otherwise recommended due to side effects</td>
</tr>
<tr>
<td>Carli et al</td>
<td>Intraop and 24-h wound infiltration vs continuous femoral nerve block (n=40)</td>
<td>Reduced in femoral nerve block group</td>
<td>Reduced morphine PCA consumption in femoral nerve block group</td>
<td>Median, 5 vs 5; no difference</td>
<td>Double-blind; same multimodal nonopioid analgesia; preoperative walking capacity, physical activity, and early total walking time were independent predictors of early recovery; traditional recovery program with low activity limits interpretation on early analgesia and functional recovery</td>
</tr>
<tr>
<td>Essving et al</td>
<td>Intraop wound infiltration vs no injection, followed by 1 top-up dose 21 h postop (n=48)</td>
<td>Postop pain lower at rest in treatment group during the first 27 h and on movement during first 48 h; patient satisfaction higher on days 1 and 7 in same group</td>
<td>Median morphine consumption lower in group A during first 48 h</td>
<td>Median, 3 vs 5</td>
<td>Double-blind placebo-controlled study; good methodology; indicates wound catheter has a beneficial role in prolonging analgesia up to 48 h postop with minimal risk of infection</td>
</tr>
<tr>
<td>Joo et al</td>
<td>Intraop wound infiltration in patients undergoing bilateral TKA with 1 knee infiltrated (treatment arm) and other knee infiltrated with placebo (control arm) in same patient (n=286)</td>
<td>No difference</td>
<td>No difference</td>
<td>Not reported</td>
<td>Poor methodology; same patients used as treatment and control group; lack of favorable outcome explained by patients being subjected to severe pain in placebo-injected knee, which can mask relative pain relief in the injected knee</td>
</tr>
<tr>
<td>Fu et al</td>
<td>Patients undergoing unilateral TKA randomly assigned to receive a multimodal analgesia protocol (comprising oral celecoxib and tramadol preop and postop and intra-articular injection of large doses of morphine, ropivacaine, adrenaline, and betamethasone intraop [trial group] or oral and intra-articular placebo (n=100)</td>
<td>Reduced VAS score at rest and with movement for up to 7 d postop</td>
<td>Reduced significantly in treatment group at 48 h postop</td>
<td>Not reported</td>
<td>Not blinded; no wound catheter used; unclear why effects were applicable after 7 d postop; methodology not robust; betamethasone used, which may have implications not seen in other trials</td>
</tr>
<tr>
<td>Affas et al</td>
<td>Compared local infiltration analgesia and femoral block with regard to analgesia and morphine demand during first 24 h after TKA (n=40)</td>
<td>Better pain relief in first 24 h in treatment group</td>
<td>No difference</td>
<td>Not reported</td>
<td>Not blinded; poor quality of randomization with unequal distribution of osteoarthritis and inflammatory arthritis in each group, although no difference seen, authors advocated wound infiltration because it is inexpensive and easy to use</td>
</tr>
</tbody>
</table>
in the capsule rather than as an intra-
articular injection. The latter seems to make no clinical difference in pain
relief.11,12 This is further supported by
some studies that involved a single
intra-articular injection leading to no
significant pain relief.13-15 However,
one trial with a small sample size
reported significant pain relief after
intra-articular ropivacaine injection
following TKA.16 The assessment of
pain was not clearly defined in this
study and was obtained once in 24
hours with no specification on the pa-
tient's activity. Therefore, the results
of this study should be analyzed with
care.

Other factors may have a posi-
tive effect on wound infiltration with
wound catheters, including infiltrating
the subcutaneous tissues generously
during the intraoperative injection,7
and using a compression
bandage that may prolong the effect
of the local anesthetics.19 Parvataneni
et al20 reported no reduction in post-
operative pain with wound infiltration
combined with multimodal oral anal-
gesia compared with a control group
receiving femoral nerve block. How-
ever, the protocol for local infiltration
was ill defined; therefore, the results
are difficult to interpret. Bianconi
et al21 showed significant pain relief
with local anesthetic infiltration in
total hip and knee arthroplasty patients.
The data on pain relief and length of
hospital stay are variable. Although
many studies reported a positive out-
put, the effects of perioperative lo-
cal wound infiltration are variable. Al-
though some studies that involved a single
intra-articular injection reported no
significant pain relief,13-15 one trial with a small sample size
reported significant pain relief after
intra-articular ropivacaine injection.

The assessment of
pain was not clearly defined in this
study and was obtained once in 24
hours with no specification on the pa-
tient's activity. Therefore, the results
of this study should be analyzed with
care.

Table 3 (cont'd)

<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Pain Score</th>
<th>Opiate Consumption</th>
<th>Treatment vs Control Length of Stay, d</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Andersen et al11</td>
<td>Intra- and postop wound infiltration combined with intra-articular regional anesthesia vs controlled epidural analgesia (n=40)</td>
<td>Lower VAS scores at rest and during knee movement in treatment group</td>
<td>Median cumulated morphine consumption reduced</td>
<td>Median, 4 vs 4</td>
<td>Not blinded; compared wound infiltration with continuous epidural analgesia; both groups had ketorolac; pain assessments not reported in detail and continuous epidural analgesia not as effective as reported in literature; trial stopped prematurely; side effects not reported, with insufficient methodology hindering exact interpretation</td>
</tr>
<tr>
<td>Andersen et al12</td>
<td>Intraop wound infiltration and postop 20 mL/0.5% vs 10 mL/1% ropivacaine intracapsulry (n=48)</td>
<td>No difference</td>
<td>No difference</td>
<td>Median, 3 vs 2.5</td>
<td>Double-blind study; concentration vs volume comparison with similar dose of ropivacaine and similar systemic oral analgesia; no difference between groups and no effect at 6 h, but positive and similar analgesic effect at 24 h postop; intracapsular catheter administration probably necessary for effective analgesia during the early postoperative period</td>
</tr>
<tr>
<td>Dobrydnjov et al19</td>
<td>Intra- vs extra-articular local anesthetics for postop supplementation of wound infiltration analgesia after TKA in patients with rheumatoid arthritis (n=36)</td>
<td>Incidence of high-intensity pain (VAS 7-10) less in intra-articular infusion group</td>
<td>No difference</td>
<td>Not recorded</td>
<td>Double-blind; continuous wound infiltration through wound catheter for 48 h; intra-articular wound catheter may enhance early mobilization after TKA</td>
</tr>
<tr>
<td>Krenzel et al20</td>
<td>Effect of injecting posterior knee capsule with ropivacaine or placebo during TKA (n=66)</td>
<td>Reduced pain score and more straight leg raises at 12 h postop</td>
<td>No difference</td>
<td>Not recorded</td>
<td>Posterior capsular injection did not improve pain or accelerate functional recovery after 12 h in patients also receiving femoral nerve block for pain control after TKA</td>
</tr>
</tbody>
</table>

**Abbreviations:** intraop, intraoperative; IV, intravenous; LIA, local-infiltration anesthesia; NRS, numeric rating score; NSAID, nonsteroidal anti-inflammatory drug; PCA, patient-controlled analgesia; postop, postoperative; preop, preoperative; VAS, visual analog scale.

*All results reported in favor of treatment group (with wound infiltration) unless stated otherwise.
cause most authors did not justify or explain these factors transparently enough to reach a satisfactory conclusion. Another recent well-designed study reported a reduction in opiate requirement and NSAID usage following local wound infiltration after TKA in 3 groups with (a) epidural analgesia or (b) wound infiltration with ropivacaine 150 mg and epinephrine 0.5 mg combined with ketorolac 30 mg and morphine 5 mg given either locally or (c) intravenously. Epidural analgesia was maintained for 48 hours. More importantly, the authors recorded a significant reduction in length of stay in the treatment group (median, 5 vs 3.5 vs 4 days, respectively).

Carli et al. reported significant reduction in pain scores following intraoperative wound infiltration (intraoperatively and 24 hours postoperatively) vs a continuous femoral nerve block and both groups receiving the same multimodal nonopioid analgesia (COX-2 inhibitor and paracetamol) after TKA compared with traditional femoral nerve block. They found no difference in opiate requirement or attainment of early rehabilitation milestones in the treatment group. Both groups had a median length of stay of 5 days. However, the authors did not report the specific role of wound infiltration in length of stay. Patients in both groups were allowed to fully mobilize 3 days postoperatively, which may have affected the length of stay results in this study. Similar results were reported in another study that reported significant reduction in pain and opiate use in the group having wound infiltration, but nausea and vomiting were significantly less frequent in the treatment group, probably secondarily to reduced opiate uptake.

**DISCUSSION**

A systematic review is a powerful tool to assess the efficacy of interventions and of their likelihood to cause harm in a scientific and transparent manner. This estimates the relevance of interventions in a clinical context by gathering evidence from all relevant trials—and more commonly from high-quality randomized controlled studies when available. The systematic review is structured to reduce bias in the collection, appraisal, and interpretation of relevant studies using transparent methodology. This has proven to extract evidence that was not apparent in individual studies. This methodology includes the definition of a clear, often narrow, question to be answered; a structured literature search with well-defined inclusion and exclusion criteria; a quality assessment of retrieved reports; and standardized data handling and analysis.

Poor pain management in the postoperative period can cause several long-term sequel, including chronic pain syndromes, increased postoperative morbidity, and poor quality of life. Novel pain management standard requires adequate postoperative pain management to be a key strategy to avoid any untoward long-time pain-related complication.

The inherent simplicity of the wound catheter technique is that it can easily be placed in situ by the operating surgeon. Furthermore, the postoperative top-up doses can be administered by the nursing staff, avoiding regular specialist medical input. This, combined with the ease of postoperative mobilization by patients, has led to the frequent use of wound catheters.

The current authors’ search has revealed a number of randomized controlled trials examining the efficacy of perioperative local wound infiltration in patients undergoing TKA. This illustrates the interest this approach has evoked among orthopedic surgeons and anesthetists. However, all of these studies have resulted in conflicting evidence. Although most studies were randomized, the sample sizes were often not adequate, allowing them to erroneously accept the null hypothesis (type 2 error). Moreover, the comparator groups were often heterogeneous (eg, femoral block, epidural, etc.), making a logical summation of their results virtually impossible. Some facts that have emerged from one study show that (1) wound infiltration does not cause dangerous levels of ropivacaine in the blood; (2) autologous transfusion is safe when combined with wound infiltration; (3) systemic side effects related to opioids
are probably few in the immediate perioperative period, especially nausea and vomiting; and (4) additional alterations in the technique, like injecting the posterior capsule and using compression bandages, are useful in improving pain management with wound infiltration.\textsuperscript{21}

However, there is no definite evidence on more important aspects, including (1) postoperative pain scores, (2) postoperative opiate consumption, and (3) reduction in length of stay. The literature is highly divided in recommending wound infiltration for achieving these benefits. Furthermore, although most studies have reported no significant complications, one study mentions postoperative infection in the knee.\textsuperscript{26} Hence, no general recommendations can currently be made to support this technique. It is apparent that wound infiltration gives pain relief in the initial 6 to 12 hours postoperatively. However, the role of other drugs, like NSAIDs and adrenaline, has not been clearly evaluated. Few studies have addressed this role.\textsuperscript{23,40} These studies showed some superiority of local infiltration with ketorolac (NSAID) compared with systemic infusion, although it is known that analgesia is obtained by administration of NSAIDs, either locally or systemically, with minor clinical difference in terms of pain relief.\textsuperscript{41} Most studies have not taken into account the effects of the optimized multiple oral analgesics often offered to patients in treatment and comparator groups in the immediate postoperative period. Another study reported a reduction in opiate consumption and better perioperative pain relief leading to a reduction in length of stay with wound infiltration and intra-articular administration of ropivacaine compared with systemic administration of NSAIDs and continuous epidural infusion.\textsuperscript{41} A recent trial reported similar opiate consumption and length of stay with wound infiltration following TKA compared with femoral nerve block.\textsuperscript{39} However, pain with movement of the knee in the immediate postoperative period was significantly lower in the treatment group. This is important because postoperative knee motion is a key rehabilitation step following TKA. The achievement of adequate knee joint movement determines how quickly patients can be safely discharged.

There are no clear beneficial effects of top-up doses with wound infiltration in the postoperative period. Furthermore, this can lead to potential introduction of infection in the joint. Hence, this area needs further research to determine the optimal number and duration of top-up doses that provide patients with the best pain relief without increasing the risk of infection secondary to prolonged catheter placement in the knee joint. The role of other emerging agents may be of interest. Apart from paracetamol and NSAIDs, COX-2 inhibitors, gabapentinoids, and glucocorticoid injections have been tried along with wound infiltration.\textsuperscript{18,42} The role of gabapentin and pregabalin in postoperative pain relief after joint replacement has been reported.\textsuperscript{43} A single high-dose methylprednisolone injection in the joint can provide additional analgesia and reduce opiate intake following TKA.\textsuperscript{38} The evidence favoring these agents is sparse. More randomized controlled trials with sufficient sample sizes need to be undertaken to assess the safety, efficacy, and side effects of these agents.

There is some evidence that when used in conjunction with femoral nerve blocks, a single intraoperative injection can result in significant pain relief in the immediate postoperative period.\textsuperscript{8,24} However, the nerve block technique has its own inherent problems, including nerve damage,\textsuperscript{44} delayed mobilization, and falls due to motor blockade.\textsuperscript{45} Furthermore, when used with wound infiltration, it becomes unclear which technique (nerve block or local anesthetics) actually resulted in pain relief. Thus, wound infiltration should be used in isolation to avoid the potential complications associated with femoral nerve block.\textsuperscript{46} The latter has the advantage of allowing patient mobilization on the day of surgery, resulting in fast-track rehabilitation.\textsuperscript{1}

A limitation of the current review is that the search was confined to Medline and Embase. Although the authors tried to manually search the references to ensure all relevant studies were included, it is possible some may have been missed. Furthermore, the authors did not search other databases, such as Cochrane and CINAHL. The authors did not include grey literature (eg, conference presentations and abstracts) that might contain more evidence regarding this technique. However, it is unlikely that a seriously performed randomized controlled trial is confined to a presentation without being published. The authors made no attempt to statistically compare the results because this was beyond the scope of this article; hence, this article contains some elements of a narrative review. The authors have not assessed cost analyses because that was not a part of their research question.

**CONCLUSION**

This article summarizes the current evidence and the implications of using perioperative wound infiltration analgesia with multimodal high-volume local anesthetic agents combined with additional agents like adrenaline and NSAIDs in patients undergoing TKA. The studies are heterogeneous with different methods and comparators, making valid comparison among the studies difficult. However, almost all of the studies reported better pain relief in the immediate postoperative period with wound infiltration. It is unclear whether this actually leads to a reduction in opiate consumption, the achievement of early milestones, or a reduction in length of hospital stay. The role of individual agents in achieving pain relief and the benefits of using a percutaneous wound catheter is also unclear. No study compares the individual agents with each other; therefore, it is unclear whether NSAIDs or adrenaline are needed in the mixture for wound infiltration. The role
of a wound catheter is also not well established in terms of frequency of administration of bulus doses, continuous infusion, and optimal duration of leaving it in a replaced knee postoperatively. Although few recent reviews have condemned this technique, the evidence is unclear on whether to accept or reject wound infiltration. Currently, wound infiltration analgesia should be used at the preference of the surgeon and anesthetist provided regular review of their practice is undertaken to identify any untoward side effects. Further randomized trials with sufficient sample sizes comparing each outcome, including pain scores, opiate consumption, and length of hospital stay, should be undertaken.

REFERENCES


Appendix 13


Contribution by BA Rogers.

Concept

Manuscript writing & editing

Citation Metrics

Web Of Science: 0
Google Scholar: 2
Altmetrics: 5
Tweets: 1
Facebook: 0
Mendeley readers: 4
Cement Augmentation of the Acetabulum for Revision Total Hip Arthroplasty for Infection

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Abstract

Antibiotic-loaded cement spacers in first-stage revision hip arthroplasty for infection are associated with a high dislocation and fracture rate. This technical note describes a novel surgical technique, utilizing screws and cement, improving acetabular coverage and reducing the risk of mechanical failure.

Fifteen infected hip prostheses underwent removal, cement acetabular augmentation and insertion of a femoral cement spacer. Eleven hips had successful infection eradication and subsequently underwent a second stage revision procedure a mean duration of 15 weeks (9–48) after the first stage. No dislocations or fractures of the cement spacers were observed. This technique affords the potential to reduce the duration of time cement spacers remaining in situ, provides enhanced mechanical stability and improved antibiotic elution through cement-on-cement articulation.

Operative Technique

Patients were placed in the lateral decubitus position with the affected hip up and the administration of antibiotics withheld until biopsy specimens had been obtained. Surgical approach was based on preoperative templating, with 12 cases requiring an extended trochanteric osteotomy and 3 cases using a modified trochanteric slide osteotomy to provide adequate exposure and access for removal of the femoral and acetabular components [1–3].

The surgical exposure included the excision of all the sinus tracks, drainage of all abscesses and the removal of all the in situ components and any potentially infected tissues, including cement. Once the exposure was performed, and the hip dislocated, deep tissue samples from the hip and acetabulum were taken. Ideally, three sets of deep cultures and sensitivity of the infected joint were obtained, including joint fluid, soft tissue and bone.

The in situ femoral components were removed with a combination of flexible osteotomes, use of the extended osteotomy and cortical windows. Care was taken to ensure the removal of any remaining cement, whilst avoiding iatrogenic femoral fracture. Regarding the acetabular component, any iliac screws were removed and the implant was checked for gross loosening. If the component was well fixed, removal was achieved by the use of sequential curved blade styles (Explant Acetabular Cup Removal System, Zimmer Warsaw, IN).

The entire acetabular rim was then visualized along with a small area of the supra-acetabular ilium exposed subperiosteally to avoid damage to the superior gluteal vessels and nerve. Three 3.5-mm unicortical drill holes were made in the juxta-acetabular ilium, approximately 1 cm apart and each 1 cm cephalad to the rim of the superior acetabular, if this region remained intact following debridement of all infected tissue. Three 6.5-mm × 45–50-mm cancellous screws were inserted perpendicular to the surface of the ilium, with approximately 20–25 mm of the screw shaft remained outside the bone (see Fig. 1)

The femoral cement spacer was then prepared on a back table in a standard fashion using a specific mold (StageOne Hip Spacer Mold, Biomet, Warsaw, IN). Preoperative radiographic templates were used to select the most appropriate size femoral component from the four sizes available.

When cured, the femoral cement spacer was inserted with reference to either the greater or lesser trochanter, if still present, to a depth that recreated the physiological limb length. Our protocol was to mix a total of 8 g of antibiotic per 40 g of cement polymer (Surgical Simplex, Limerick, Ireland). Unless otherwise dictated by preoperative cultures and sensitivity of the infected joint fluid, 4 g of both vancomycin and cefazidime per 40 g of cement was used at our institution. Typically three to four bags of cement were used in total per case.

Following reduction of the femoral cement spacer, there was typically a substantial amount of uncoverage, approximately 30–40%, of the cement femoral head. The surface of the ilium along which
the cancellous screws had been inserted was meticulously dried and any remaining soft tissue removed in order to avoid cement debonding. A separate bag of antibiotic loaded cement was then used to form an acetabular augment that was placed around and covering the three ilial screws. The cement acetabular augment was positioned in the posterolateral aspect of the acetabular rim. The surface of the reduced femoral component provided a contour for this augment. Some gentle passive movement of the hip joint while the acetabular cement was setting prevented the acetabular cement bonding to femoral cement component. Closure of the wound was performed in a standard manner for the approach used. Postoperative radiograph of the procedure is shown in Fig. 2.

Postoperative Regime

Patients were mobilized with partial weight bearing, up to 50% of total body weight, from the first postoperative day. Antibiotics were administered via a long intravenous line for a period of least 6 weeks, the choice of antibiotic depending on the sensitivity of the organisms cultured from the deep tissue biopsies. Routine clinical and radiographic follow-up was conducted.

In our institution, no cases of antibiotic-associated renal toxicity have occurred, although this technique should be used with caution in patients with significant renal impairment. Second-stage reconstruction was only considered when there was clinical and serological evidence of infection eradication, consistent with the Musculoskeletal Infection Society [4]. In equivocal cases, an additional hip aspirate was obtained to exclude infection before proceeding with definitive reconstruction.

References

Appendix 14


Contribution by BA Rogers.

Concept

Data collection & analysis

Manuscript writing & editing

Citation Metrics

Web Of Science: 2

Google Scholar: 4

Altmetrics: 0

Tweets:

Facebook:

Mendeley readers:
KNEE: RESEARCH

Does cyclical loading affect the elution of antibiotics from articulating cement knee spacers?

Two-stage revision surgery for infected total knee replacement offers the highest rate of success for the elimination of infection. The use of articulating antibiotic-laden cement spacers during the first stage to eradicate infection also allows protection of the soft tissues against excessive scarring and stiffness. We have investigated the effect of cyclical loading of cement spacers on the elution of antibiotics. Femoral and tibial spacers containing vancomycin at a constant concentration and tobramycin of varying concentrations were studied in vitro. The specimens were immersed and loaded cyclically to 250 N, with a flexion excursion of 45°, for 35 000 cycles. The buffered solution was sampled at set intervals and the antibiotic concentration was established so that the elution could be calculated. Unloaded samples were used as a control group for statistical comparison.

The elution of tobramycin increased proportionately with its concentration in cement and was significantly higher at all sampling times from five minutes to 1680 minutes in loaded components compared with the control group (p = 0.021 and p = 0.003, respectively). A similar trend was observed with elution of vancomycin, but this failed to reach statistical significance at five, 1320 and 1560 minutes (p = 0.0508, p = 0.067 and p = 0.347, respectively). However, cyclically loaded and control components showed an increased elution of vancomycin with increasing tobramycin concentration in the specimens, despite all components having the same vancomycin concentration. The concentration of tobramycin influences both tobramycin and vancomycin elution from bone cement. Cyclical loading of the cement spacers enhanced the elution of vancomycin and tobramycin.

Infection after total knee replacement (TKR) is an infrequent but devastating complication which is difficult to treat. The poor availability of antibiotics at the site of infection, the presence of a biofilm reducing the exposure of bacteria to the antibiotics and the relative immunodeficient zone around an implant are all factors which influence the efficacy of treatment.1-3

There are considerable financial costs and clinical implications from infection including increased morbidity and prolonged or repeated hospital admissions.4,5 Most studies report an incidence of infection of 1% to 2% after primary TKR,6-8 but this may increase to over 4% in patients with rheumatoid arthritis and an incidence of over 12% has been reported in certain groups of patients.9,10 The cost of revision knee surgery as a result of infection is more than twice the cost of an aseptic revision, and several times that of a primary TKR.4,5

Two-stage revision TKR, with the use of antibiotic-impregnated polymethylmethacrylate (PMMA) cement spacers is a widely practised method of managing this problem.11,12 After the removal of the primary prosthesis through thorough debridement, the cement spacer is implanted followed by an extended course of antibiotics. A second-stage procedure is subsequently performed when the patient is considered to be free of infection.13,14 Cement spacers assist in the delivery of antibiotics, maintain limb length and therefore tissue tension, and reduce the formation of soft-tissue contracture or arthrofibrosis, thereby simplifying re-implantation of the new components at the second stage.15-17 Spacers can be articulating or non-articulating (static) and there is debate regarding the benefits of each type.18 The non-articulating type provides a high concentration of antibiotics locally, maintains the joint space and limits the possible risk of introducing the inoculum further into the surrounding tissues by restricting movement of the knee. Several studies have shown their effectiveness.19,20 By contrast, articulating spacers allow joint movement and help to maintain soft-tissue function.21,22 Arthrofibrosis is minimised and function is better than that following the use of...
non-articulating spacers. Several forms of spacer have been described and they can be custom-made during the operation or commercially available as prefabricated components.

The addition of antibiotics to cement, especially in liquid form, adversely affects tensile and compressive strength. Ideal properties of an antibiotic which is mixed with cement include minimal adverse biomechanical effects on PMMA, water solubility; a broad spectrum of antimicrobial action, thermal stability and low allergenicity. As a consequence, there are only a few which fit these criteria. They include tobramycin, vancomycin, gentamicin and cephalosporins. Since gentamicin is commonly a component of the cement used in primary TKR, organisms may acquire gentamicin-resistance.

The release of antibiotics from cement has been studied both in vitro and with in vivo animal models. Static in vitro models have shown a high level of release of local antibiotic from cement which is affected by several factors including the surface area, porosity and the amount, type and number of antibiotics.

However, the effects of articulation, specifically cyclical fatigue loading, on the elution of antibiotics from cement knee spacers has not been clearly defined. The maintenance of joint movement is an advantage in maintaining the condition of the soft tissues, but the question arises as to whether the articulation per se influences the biology and pharmacokinetics of antibiotic elution. Tobramycin has a broad antimicrobial action with minimal effect on PMMA strength, while vancomycin is effective against methicillin-resistant Staphylococcus aureus and Staph. epidermidis with similarly low adverse biomechanical effects on PMMA.

Our in vitro study considered the differential effect of static or dynamic loading on the elution of vancomycin and tobramycin with a null hypothesis proposing that the cyclical loading of cement spacers has no significant effect on elution.

**Patients and Methods**

**Preparation of samples.** All the samples were prepared in an identical manner. Antibiotic-loaded spacers were prepared by the injection of Palacos R (Heraeus Kulzer GmbH, Hanau, Germany) standard radio-opaque cement into Biomet stage-one 70 mm silicone spacer moulds (Biomet Inc., Warsaw, Indiana). The addition of a constant concentration of vancomycin with incremental quantities of tobramycin was investigated (Table I). Vancomycin and tobramycin are two of the most commonly used antimicrobials partly because of their availability in powder form. The dosing schedule used in our study correlated with that of admixtures reported in numerous clinical and in vitro studies. Before the polymerisation of cement, the cement monomer was chilled at -20°C for five minutes in order to extend the working time required to achieve a thorough mix of monomer andcopolymer in the presence of added antibiotics. Vancomycin and tobramycin in their selected amounts and Palacos cement powder were blended for one minute in a small hand orthopaedic cement mixer (DePuy, Blackpool, United Kingdom) before polymerisation. The cement was mixed for one minute prior to being injected in the moulds, according to the manufacturer’s instructions, in air at room temperature (23°C ± 1°C), using a CemVac mixing system (DePuy CMW, Blackpool, United Kingdom). The cement was then injected into the silicone moulds and left to polymerise for a minimum of two hours. After curing, excess material, as a result of the moulding process, was removed from the femoral component taking care not to damage the surface of the condyles. The non-articulating surface of the tibial component was ground to a thickness of 10 mm. Both components were rinsed in distilled water and dried before testing.

**Dynamic testing protocol.** Three sets of spacers were prepared for each of the three concentrations of antibiotics in the cement (Table I). The femoral component was attached to a polymer block conforming to the geometry of the spacer using waterproof silicone sealant (Figs 1 and 2). This was allowed to cure before testing. The femoral and tibial components were placed in the environmental chamber, maintained at 37°C and attached to the actuators as shown in Figure 2 (Instron 8874 servo hydraulic testing machine; Instron, Norwood, Massachusetts). The spacer was immersed in 1 L of phosphate-buffered saline (PBS). The femoral component was aligned relative to the tibial component in 22.5° of flexion. In order to reproduce the maximum tibiofemoral contact force of 2.5 times body-weight at 13% of the gait cycle, the tibial component was then loaded on to the femoral component with a force of 0.1375 kN. Dynamic loading was initiated as per the schedule detailed

**Table I.** Details of the low, medium and high datasets relating the concentration of antibiotic used, the number of spacers used (for the static control group and dynamic testing) and the total number of samples taken per time interval.

<table>
<thead>
<tr>
<th>Mass of vancomycin (g)</th>
<th>Mass of tobramycin (g)</th>
<th>Static spacers</th>
<th>Dynamic spacers</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Number of samples per time interval</td>
<td>Total number of samples per time interval</td>
</tr>
<tr>
<td>Low 1</td>
<td>1.2</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Medium 1</td>
<td>2.4</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>High 1</td>
<td>3.6</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>

* per 40 g of cement powder
in Table II. The femoral component was cycled at a frequency of 1 Hz and an amplitude of 22.5° and the tibial component was loaded at a frequency of 1 Hz with an amplitude 0.1125 kN. The loading cycle (sinusoidal waveform, amplitude of 22.5° (maximum arc of movement of the femoral component), maximum load of 0.25 kN, R = 0.1, frequency (f) = 1 Hz) was selected to represent walking with crutches. The resistance value (R) is a material stiffness test. It expresses a material’s resistance to deformation as a function of the ratio of transmitted lateral pressure to applied vertical pressure. At each interval of the sampling, as indicated in Table II, cyclical loading was paused, the solution agitated to ensure an even distribution of the antibiotics, and three samples (5 ml) of solution collected from separated locations of the environmental chamber and stored at -20°C. The concentration of antibiotics, and hence elution, of these samples was measured by a TDx FLx Immunology Analyser (Abbott Laboratories, Abbott Park, Illinois).

As a control, two spacers for each concentration of antibiotics were prepared. The control samples were immersed in PBS and samples were taken in accordance with the schedule for dynamic testing. Thereafter, samples were taken twice daily, for four weeks. At the end of each day 30 ml of PBS were added to ensure that the sample remained fully immersed in solution.

### Statistical analysis

The data points regarding the concentration of antibiotic, measured using enzyme-linked immunoassay, for each time interval were obtained from a mean of six samples from the two static controls per concentration (three per spacer) and the 12 samples for the dynamic testing from the four dynamic spacers per concentration (three per spacer; Table I).

Non-parametric statistical analysis of variance (ANOVA) was performed to compare the mean elution between the static and dynamic groups. A p-value ≤ 0.05 was considered to be statistically significant.

## Results

### Control group

The elution of both tobramycin and vancomycin, from all three concentrations of the static control samples, is shown graphically in Figure 3. There was a biphasic elution pattern with an initial rapid rate of antibiotic
release which slowed to a steady state from 400 minutes. The interval in the data points after 400 minutes represented the overnight pause in the experiment (see Table II).

In the static control group vancomycin eluted at a higher rate than tobramycin. Furthermore, as the tobramycin concentration was increased in the cement mixture (the low, medium and high data sets), there was a corresponding increase in the release of vancomycin. Dynamic testing: tobramycin elution. The rates of elution of tobramycin from the different concentrations of cement undergoing dynamic testing are shown in Figure 4 with comparison with the corresponding static control group.

Dynamic testing in comparison with the control group increased the elution of tobramycin. The release was dose-related, with an increasing concentration of tobramycin in the cement affording a corresponding increase in its elution. Furthermore, the dose-related elution response was exaggerated by dynamic testing. The mean elution of tobramycin between the static and dynamic groups was examined by ANOVA (Table III). Dynamic cyclical loading was associated with a significantly higher tobramycin elution at all sampling points.

Therefore, with respect to tobramycin elution, we can reject the null hypothesis and state that there is a statistically significant higher elution under dynamic loading compared with static loading.

**Dynamic testing: vancomycin elution.** The rates of elution of vancomycin in the different cement concentrations undergoing dynamic testing in comparison with the corresponding static group are shown in Figure 5.

Similarly to tobramycin, there was a dose-related increase in the elution of vancomycin as the concentration
of tobramycin within the cement was increased. Thus, increasing the concentration of tobramycin in the cement augmented the release of vancomycin during dynamic testing in a dose-related manner.

There was a clear trend of increasing the elution of vancomycin with dynamic testing (Fig. 5) and this increase over the static samples was statistically significant (Table III) with the exception of the sampling time points of five, 1320 and 1560 minutes.

For the elution of vancomycin, the null hypothesis can also be rejected since, overall, higher elution occurred under dynamic loading which was statistically significant.

Discussion

Our results show that there was a biphasic elution of both vancomycin and tobramycin in the static control, with a rapid initial release followed by a plateau in the rate of release after approximately 400 minutes (Fig. 3). Furthermore, the elution of both vancomycin and tobramycin was enhanced by an increasing concentration of tobramycin in the bone cement. This enhancement was more pronounced for the vancomycin elution.

For any concentration of antibiotic cement studied, dynamic loading increased elution compared with the corresponding static control group. Although dynamic loading improved elution per se, its effect on elution was further increased, in a dose-dependent manner, by the presence of tobramycin in the cement.

For tobramycin, a highly statistically significant dose-related increase was observed with dynamic loading compared with the control group (Fig. 5, Table III). Regarding vancomycin, a similar dose-related trend was seen, with statistical significance in all but three time intervals (Fig. 5, Table III). At five minutes, the p-value regarding vancomycin was 0.0508.

Therefore, by adding tobramycin to bone cement, there was enhanced static elution of vancomycin and tobramycin. This enhanced elution was significantly augmented by dynamic loading (Figs 4 and 5, Table III).

The mechanical benefits of maintaining joint movement during a two-stage revision TKR have been well documented.23,24,26 There is debate regarding the use of static or dynamic spacers. Static spacers have the theoretical advantage of reducing the inoculum being introduced into the surrounding soft tissues, which are also free from tension, augmenting antimicrobial action.23,18

However, other reports have indicated a biomechanical advantage of dynamic over static knee spacers.21,24 The biological effect of dynamic cyclical loading per se on cement spacers, specifically differential antibiotic elution, has not previously been clarified since previous investigations have used static in vitro and animal in vivo models. Nevertheless, these previous non-dynamic studies have shown that the antibiotics are released in a biphasic manner in a dose-dependent way39 and that the presence of vancomycin increases the release of tobramycin.40

It is uncertain how the addition of a second antibiotic enhances the release of another antibiotic, although it has been proposed that the second antibiotic increases the porosity of the cement thereby improving the release.40 Evidence elsewhere has shown that the addition of lactose to bone cement increases antibiotic release, as does increasing the surface roughness and surface area.39 This complementary release of antibiotic has been termed by Penner et al180 as passive opportunism. However, at present in vitro testing has not shown the ability of antibiotic bone cement to eradicate completely infection caused by bacteria which adhere to biomaterials.41,42

Antibiotic elution characteristics have been quantified from studies on various mammalian species.17,35,43-47 A common pattern of a peak in the blood concentration after a few hours followed by a gradual reduction in concentration has been found, which was replicated in our study. These animal studies demonstrated that the local tissue concentration of antibiotic was considerably higher than that in the serum, and remained so for several weeks. However, the measured antibiotic concentration within the haematoma reduced within a matter of days.

For staphylococcal species, vancomycin has a minimum inhibitory concentration of 0.25 mg/l to 1.0 mg/l and a minimum bactericidal concentration of 0.25 mg/l, while tobramycin has a minimum inhibitory concentration of 0.12 mg/l to 1.0 mg/l and a minimum bactericidal concentration of 0.1 mg/l to 32.0 mg/l.48,49 It is accepted that a level of at least eight times the minimum inhibitory concentration is required for successful treatment, especially considering the in vitro dilution which occurs with time.50 The antibiotic elutions achieved in our study with dynamic
loading were over ten times the respective minimum inhibitory concentration, 15 mg/l to 50 mg/l for vancomycin and 12 mg/l to 26 mg/l for tobramycin (Figs 4 and 5).

Masri et al.13 using data obtained by joint aspiration before a second-stage revision total hip replacement or TKR have given the clinical guidelines for effective antibiotic concentration. Vancomycin had an inferior release rate if used in isolation, and again the combination of tobramycin with vancomycin gave encouraging results. The release of vancomycin, as assessed by joint aspiration, was found to reduce after four months to levels below the threshold for microbiological activity. However, the addition of tobramycin prolonged its time of beneficial vancomycin. On the strength of these clinical results, they recommended that tobramycin be used in a concentration of 3.6 g per 40 g of bone cement, provided that the articulating spacer did not remain in situ for longer than three to four months. Although providing guidelines, their study was limited by the lack of a control group, confounding patient factors, possible differences in the cement and antibiotic blending techniques and the inclusion of both hips and knees. Our dynamic in vitro study, with a static control group was not compromised by similar methodological limitations. Our results have shown a better elution of tobramycin from bone cement compared with vancomycin for both static and dynamic loading, consistent with the findings of other studies using static in vitro models.40-51

The method of antibiotic mixing with cement was standardised in our study since there is some evidence that cement properties can be altered by the method of blending of vancomycin and tobramycin.12

The addition of antibiotics to bone cement gives inferior mechanical properties, including reduced strength under both tensile and compressive loading.17,28,29 These properties have not been reported for the admixture of tobramycin and vancomycin. Although we have shown in vitro that a mixture of antibiotics under dynamic loading produces enhanced elution, the efficacy of low sustained release of antibiotics in clinical a setting remains unclear. Ideally, there should be an optimal antibiotic concentration at the site of the potential infection at the time of the surgery, and the benefit of continuing for a longer duration is not substantiated.53

In the presence of renal impairment, extended release of either tobramycin (an aminoglycoside) or vancomycin (a glycopeptide) could potentially increase the risk of nephrotoxicity and otoxicity. The peak serum concentrations required for the treatment of infection in other organ systems range from 4 mg/l to 10 mg/l for tobramycin to 30 mg/l to 40 mg/l for vancomycin.34,53 Our results for the elution of tobramycin and vancomycin into a simulated synovial fluid were similar in range. It is unlikely therefore that concentrations would approach nephrotoxic serum levels.

An additional concern is that the widespread use of similar antibiotic mixtures may hasten the emergence of resistant strains. The clinician should always attempt therefore to adjust any antibiotic treatment, whatever the delivery method, in response to known tissue culture and sensitivity.56

The precise mechanism of antibiotic release from bone cement is uncertain. It is generally thought that it is directly released from the surface of the bone cement in the initial phase, and then subsequently released from a network of cracks and voids.39,57-59 Absorption of water to bone cement is thought to have a role in controlling the slow phase of antibiotic release.56-61 Our study suggests that cyclical dynamic loading enhances this process, probably by a mechanism of cyclical changes in the microstructure of the bone cement.

Our results provide evidence that, in addition to the benefit to the soft tissues claimed for articulating spacers, the dynamic loading of cement knee spacers per se affords a biological advantage by significantly enhancing antibiotic elution.

References


Appendix 15

Rogers BA, Phillips S, Foote J, Drabu KJ.
Is there adequate provision of venous thromboembolism prophylaxis following hip arthroplasty? An audit and international survey.

Contribution by BA Rogers.
- Concept
- Data collection & analysis
- Manuscript writing & editing

Citation Metrics
- Web Of Science: 6
- Google Scholar: 11
- Altmetrics: 24
  - Tweets: 1
  - Facebook: 0
- Mendeley readers: 23
Is there adequate provision of venous thromboembolism prophylaxis following hip arthroplasty? An audit and international survey

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ABSTRACT

INTRODUCTION The peak incidence of venous thromboembolism (VTE) occurs 3 weeks following hip arthroplasty surgery and current guidelines proposing VTE prophylaxis continuing for 4 weeks after surgery. This study first compares the duration of treatment and satisfaction between patients prescribed low molecular weight heparin (LMWH) and rivaroxaban, a new oral Factor Xa inhibitor, following elective hip arthroplasty, and second, surveys the duration of LMWH use in other units.

SUBJECTS AND METHODS An international survey detailing the use of LMWH was performed. A prospective audit was performed of 100 hip replacements, with 50 prescribed 40 mg once daily of subcutaneous enoxaparin and subsequently 50 patients prescribed 10 mg once daily of oral rivaroxaban. The duration of treatment, patient satisfaction and complications for both cohorts was quantified and compared against published evidence-based guidelines.

RESULTS The survey demonstrated that four out of 39 (10.2%) units that routinely prescribe LMWH do so for at least 4 weeks following surgery. The audit demonstrated that rivaroxaban afforded a superior mean duration of postoperative VTE prophylaxis (35 days vs 5.4 days; P < 0.05) and superior patient satisfaction. There was no difference in the incidence of bleeding, wound infection or thrombotic complications.

CONCLUSIONS This study demonstrates that patients are exposed to an increased VTE risk following hip replacement surgery due to the inadequate prescription of LMWH. This is poor clinical practice, contrary to current evidence-based guidelines and has potential medicolegal implications. The prescription of rivaroxaban affords a superior patient compliance compared with subcutaneous LMWH, thus ensuring that patients receive VTE prophylaxis for the current recommend period of time.

KEYWORDS

Rivaroxaban – Low molecular weight heparin – Thromboprophylaxis

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Venous thromboembolism (VTE) prophylaxis following orthopaedic surgery remains a controversial topic and the incidence of fatal pulmonary embolism is approximately 0.4% if no measures are taken, equating to over 5000 fatalities a year for the 1.5 million hip and knee replacements performed in Europe.¹⁻³ The 2009 National Confidential Enquiry into Patient Outcome and Death (NCEPOD) report has highlighted that prophylaxis against VTE was less than ideal, with nearly 50% of surgical patients not receiving VTE precautions.⁴ Furthermore, the current President of The Royal College of Surgeons of England has urged surgeons to make the ‘prevention of VTE a clinical priority’.⁵ Recent studies investigating the incidence of postoperative VTE demonstrate that the mean time to thromboembolism is greater than previously estimated. Two large meta-analyses advocate VTE prophylaxis be continued for up to 4 weeks following total hip arthroplasty surgery (THA).⁶,⁷ The Global Orthopaedic Registry recently published that the mean duration to peak incidence of venous thromboembolism following THA to be 21.5 days.⁸ Concern now exists that the length of treatment varies depending upon the prophylaxis used.

Few pharmaceutical options exist for VTE prophylaxis and rivaroxaban (Xarelto®, Bayer), a new once-daily oral
Factor Xa inhibitor, is licensed in the UK for VTE prophylaxis following elective lower limb arthroplasty surgery. Published evidence has demonstrated the efficacy of rivaroxaban to be equal to LMWH. In the UK, LMWH is commonly used following lower limb arthroplasty, supported by the recommendations of the National Institute for Health and Clinical Excellence (NICE) that have been recently been updated to incorporate oral VTE prophylaxis, such as rivaroxaban and dabigatran (Pradaxa®, Boehringer Ingelheim). These guidelines advocate an extended period of VTE prophylaxis of 28–55 days following hip arthroplasty surgery.

The rationale of this two-part study was to assess, using a local audit and international survey, the duration of VTE prophylaxis currently achieved with LMWH and to examine whether this may be improved with the use of rivaroxaban, an oral Factor Xa inhibitor.

### Subjects and Methods

Local departmental approval had been granted for the prescription of rivaroxaban following hip arthroplasty surgery, in conjunction with the discussions with the anaesthetic and pharmacy departments. All surgical procedures were performed or directly supervised by the senior author (KJD).

Verbal and written consent was obtained for all patients and the inclusion criteria were all primary and revision hip arthroplasty surgery in patients with an American Society of Anesthesiologists (ASA) score of 1. The exclusion criteria for this study were; previous anticoagulation therapy, clotting or bleeding abnormalities, significant medical co-morbidities with an ASA score of 2 or more and patient withholding consent.

An initial retrospective survey of 56 consecutive patients who were prescribed 4 weeks of once daily dose of 40 mg of enoxaparin (Clexane®, Sanofi-Aventis), a low molecular weight heparin (LMWH) administered subcutaneously. This was routine practice in our department for all patients following primary or revision hip arthroplasty surgery. For each patient, we documented the duration of prophylaxis received, the incidence of any notable complications and a simple patient satisfaction rating score from 1–5 (most dissatisfied, dissatisfied, ambivalent, satisfied, most satisfied).

Following assessment of the results from the initial survey, and in collaboration with the anaesthetic and pharmacy colleagues, a planned introduction of rivaroxaban was instigated, in accordance with the current evidence for extended VTE prophylaxis, to continue for 55 days following THA surgery.

The prospective portion of this audit commenced immediately following the analysis of the initial survey and there was no other change in patient management. An initial consecutive cohort of 54 patients were prescribed a once daily oral dose of 40 mg rivaroxaban, commenced within 24-h of surgery. Patients received a standard rivaroxaban information sheet prior to surgery and had the opportunity to ask questions when pre-operative consent was obtained.

A local and international survey of 50 English-speaking orthopaedic units regarding current VTE prophylaxis practice following THA surgery was performed by both post and telephone, with a proforma utilised for standardisation. Responses were obtained from 43 units, a response rate of 86%. The local survey included district general and teaching hospitals from all UK regions, with the international survey was limited to large university departments in Australia and Canada.

This was an unsponsored study and we confirm there was no conflict of interest and no financial support has been received in relation to this research. Statistical analysis was carried out using SPSS v11.0.

### Results

There was no statistical difference in the demographics or the numbers of primary and revision hip arthroplasty surgery performed for each cohort, as shown in Table 1.

![Table 1 Patient demographics and associated surgical procedure for low molecular weight heparin (LMWH) and rivaroxaban cohorts](image-url)

<table>
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<th>LMWH group</th>
<th>Rivaroxaban group</th>
<th>P-value</th>
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<td>Total number</td>
<td>56</td>
<td>54*</td>
<td>&gt;&gt; 0.05</td>
</tr>
<tr>
<td>Male</td>
<td>23</td>
<td>26*</td>
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</tr>
<tr>
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<td></td>
</tr>
<tr>
<td>Age (years)</td>
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<td>67 (35–79)*</td>
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</tr>
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<td>45</td>
<td>47*</td>
<td></td>
</tr>
<tr>
<td>Revision THA</td>
<td>11</td>
<td>7*</td>
<td></td>
</tr>
</tbody>
</table>

Statistical tests: *Student’s t-test; #chi-squared test.

The initial retrospective survey of 56 patients prescribed LMWH, the mean duration of treatment of 5.4 days (range, 2–16 days). Further, only 39 out of these 56 patients (69%) received LMWH every day whilst an in-patient. The mean patient satisfaction rating for LMWH was 1.2 out of 5. The secondary survey of 54 patients prescribed rivaroxaban, the mean duration of treatment was 55 days (no variance), with all patients reported taking exactly 55 days. The mean patient satisfaction rating for this patient cohort was 3.5 out of 5, significantly superior (P < 0.05) to LMWH. The comparison of the mean duration of treatment and respective satisfaction ratings for both cohorts is shown in Figures 1.
and 2. There was a statistically significant difference ($P = 0.005$) in the duration of treatment between the two cohorts.

However, there was no statistical difference in the documented associated complications for both cohorts as shown in Table 2. One patient in the LMWH cohort developed a pulmonary embolism 25 days following surgery and was re-admitted under the care of the physicians and was anti-coagulated with warfarin.

The results of the national and international postal and telephone survey regarding the use of LMWH in orthopaedic units for elective hip arthroplasty surgery are shown in Table 3. Overall, of the 45 orthopaedic units surveyed, 39 routinely prescribe LMWH following surgery. However, only four units out of the 39 (10.2%), prescribe LMWH for at least 5 weeks.

### Discussion

The risk of post-discharge symptomatic thrombosis following hip surgery can be reduced by two-thirds if VTE prophylaxis is continued for at least 28 days. The issue now exists as to how VTE prophylaxis can best be provided for 28–55 days following a surgical procedure that routinely requires a hospital stay of less than 7 days?

In light of the evidential support for a 55-day extended period of VTE prophylaxis following hip arthroplasty surgery, the survey results presented in this study, in addition to those of large multicentre arthroplasty registries, highlight that few patients receive LMWH for an adequate duration. The results of a large postal survey of orthopaedic surgeons showed only 42% prescribe an extended duration of VTE prophylaxis beyond discharge, nearly all of which use aspirin. However, the use of aspirin for extended VTE prophylaxis is now questioned since the Pulmonary Embolism Prevention (PEP) study of over 4000 total hip and knee replacements concluded that aspirin provides no benefit over placebo, whilst the 160 mg dosage has an associated significant risk of gastrointestinal bleeding.
Extensive evidence exists supporting the efficacy of LMWH in VTE prophylaxis following lower limb joint arthroplasty; however, logistical and medical concerns exist regarding its use for an extended period of 28–35 days.25,26 Furthermore, heparin-induced thrombocytopenia (HIT) is a known complication of LMWH use and guidelines recommend that all patients should be monitored for this potentially fatal condition.26,27 However, recent evidence shows few patients are monitored for HIT and indeed very few orthopaedic surgeons are aware of the relevant guidelines.26,28 The practicalities of daily subcutaneous injections for up to 55 days can cause difficulties, often necessitating a nurse to administer LMWH to the patient, at considerable financial cost. Therefore, LMWH does provide adequate VTE prophylaxis provided it is correctly administered, for the correct duration and suitable monitoring for HIT is carried out.

Rivaroxaban is a new oral Factor Xa inhibitor that is licensed in the UK for VTE prophylaxis following lower limb arthroplasty.27 Several multicentre studies compare LMWH with rivaroxaban to support its introduction into clinician practice.10,50–52 In summary, rivaroxaban has been demonstrated to be at least as effective as LMWH for VTE prophylaxis. The results of this study demonstrate that it is simple to introduce, and it affords a superior duration of prophylaxis in comparison to LMWH. All the patients in the rivaroxaban cohort received 35 days of treatment. Undoubtedly, the convenience of the oral preparation is the principal factor explaining this, highlighted by the associated superior patient satisfaction. The lack of the requirement for HIT monitoring is a further benefit.

While the documented complications in Table 2 show a higher number of adverse effects in the LMWH cohort, including bleeding, wound infection and one case of pulmonary embolism, the low numbers in this study preclude any statistical judgement from being made.

In addition to rivaroxaban, a direct Factor Xa inhibitor, dabigatran (Pradaxa®, Boehringer Ingelheim) a direct thrombin inhibitor has also been similarly licensed for VTE prophylaxis. Recent studies provide evidence for the efficacy of dabigatran in comparison to LMWH; however, to date, no study has directly compared rivaroxaban with dabigatran.35–37 One area of debate is the bleeding risk profile of these therapeutic agents; however, since the only data available use surrogate comparisons with LMWH, no statistical difference has yet been shown.38 Long-term studies will hopefully provide clarification in the future.

The financial cost of the wide-spread introduction of a new drug must be considered. Using current pricing schedules from the British National Formulary,27 the cost of 4 weeks’ treatment with rivaroxaban (Xarelto® 10 mg once daily oral, Bayer) is £157, compared with £117 for a similar course of enoxaparin (Clexane® 40 mg once daily subcuta-

neous, Sanofi–Aventis). However, if one factors in the costs involved with actually administering enoxaparin, possibly including a district nurse, and correctly monitoring for HIT with regular platelet counts, the difference in cost is likely to be minimal. Furthermore, a UK cost analysis has been incorporated into the technology appraisal guidance by NICE,36 concluding that both rivaroxaban and dabigatran were ‘an appropriate use of NHS resources’.

Conclusions

This study highlights that the duration of VTE prophylaxis following hip arthroplasty surgery currently achieved with LMWH is inadequate in light of the evidence-based guidelines for extended prophylaxis of 35 days. Further, we demonstrate that this inadequate treatment may be improved with the use of rivaroxaban, a new oral Factor Xa inhibitor.

References


Appendix 16


Contribution by BA Rogers.

Data collection & analysis

Manuscript writing & editing

Citation Metrics

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Tweets:

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Mendeley readers:
Patient-Reported Compliance with Thromboprophylaxis Using an Oral Factor Xa Inhibitor (Rivaroxaban) Following Total Hip and Total Knee Arthroplasty

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Rivaroxaban

**A B S T R A C T**

This prospective study examines patient non-compliance (NC) for an oral factor Xa inhibitor (Rivaroxaban) when used as venous thromboembolic (VTE) prophylaxis following lower limb arthroplasty. A total of 3145 patients underwent surgery from May 2010 to December 2011. At 6 weeks patients completed an anonymous self-administered questionnaire. Postoperatively 2947 (94%, 2947/3145) received Rivaroxaban. 2824 (96%, 2824/2947) completed all in-hospital doses. Seven percent (203/2824) of patients did not attend the 6-week follow-up. Two thousand one hundred sixty-three (83%, 2163/2621) completed all prescribed doses, 98 (4%, 98/2621) were NC and 360 (14%, 360/2621) had incomplete data. Gender, age, body mass index and preoperative hemoglobin all correlated with NC (p < 0.05). Patient-reported NC for Rivaroxaban is 4% which compares favorably to other VTE prophylaxis modalities.

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evidence as to the number of "missed VTE prophylaxis doses" that increase the risk of thrombosis or pulmonary embolism.

Newer oral anticoagulants may play an important role in increasing the effectiveness, safety and convenience of VTE prophylaxis, which in turn may decrease VTE NC [34,39]. The aims of this study were to evaluate the rate of compliance to a prescribed course of factor Xa inhibitor (Rivaroxaban, Bayer Schering Pharma AG, Berlin, Germany) following hip and knee arthroplasty, and to examine factors that may be associated with treatment compliance. Although these newer oral thromboembolic agents are now available, the patients' compliance rate is as yet unknown in the orthopedic arthroplasty cohort of patients. This study compares the compliance rate of Rivaroxaban to the established literature compliance rates of other traditional VTE preventative modalities. The NC patients were then compared to the compliant group for age, gender, body mass index, type of surgery, preoperative hemoglobin level and receiving a blood transfusion or any bleeding issues after discharge from hospital to examine for NC patient risk factors.

Materials and Methods

Prospectively collected data of all patients who had undergone total hip and knee arthroplasty from May 3, 2010 to December 14, 2011 at a multi-surgeon, single, tertiary orthopedic center were reviewed. All patients were treated with rivaroxaban following primary and revision total hip and total knee arthroplasty who did not present on long-term anticoagulation or had contraindications to use of the drug: poor renal function, poor liver function, allergy to this medication and cytochromeP3A4 stimulating and inhibiting drugs per drug monograph.

Patients were prescribed a 15-day course of rivaroxaban starting on postoperative day 1 and completed as an outpatient. The current recommendations from the manufacturer are 14 days of treatment starting 6–8 h post-surgery for total knee arthroplasty and 35 days for total hip arthroplasty. We consulted with our local experts on thromboembolism and after review of the literature we felt that there was good evidence for at least 10 days of treatment but limited evidence for longer treatment. With respect to starting 6–8 h of surgery, we wanted to balance effective thromboembolic prophylaxis with effective hemostasis. The new agent, rivaroxaban, had a faster onset to therapeutic anticoagulation than warfarin and we felt that we were not exposing patients to unnecessary risk by starting their thromboembolic prophylaxis the morning after surgery. With respect to the duration of treatment, we argued that the operative times are now shorter, the soft tissue incisions are smaller, the patients are mobilized weight bearing the day after surgery and our institution's average length of stay is 4.4 ± 1.8 days for primary unilateral total knee arthroplasty and 4.5 ± 2.4 days for primary unilateral total hip arthroplasty. Based on these reasons, we felt that most patients are mobile by 15 days following surgery and should be at low risk for thromboembolic events by that time post-surgery.

As standard of care, patients were seen at approximately 6 weeks following surgery at which time they were given a self-administered questionnaire. Patients were asked to answer the following questions:

1) Were you given a prescription for medication (Rivaroxaban) to prevent blood clots when you were discharged from hospital?
2) Did you take that medication daily until it was finished?

Additionally, they were asked whether they had experienced any bleeding issues with the medication or if they had received a blood transfusion since discharge from hospital. Responses were documented as "yes" and "no." Throughout this study we used the World Health Organisation (WHO) definition for anemia: hemoglobin < 130 g/l for males and < 120 g/l for females.

In accordance to the current published literature on VTE modality, non-compliance, for the purpose of this study has been defined as the patient omitting a single dose or more of their discharge postoperative VTE prophylaxis medication. The compliance of patients' prescribed 15-day therapy was then calculated and compared to the published literature compliance rates of other thromboembolic agents. Approval for using the existing database was obtained from the Research Ethics Board at Sunnybrook Health Science Center.

The corporation, Bayer Healthcare, provided funding for this project as an education grant. They provided funding without any conditions. They did not have access to data collection, data entry, data analysis or writing of the manuscript. No prior approval was required by the company prior to submission.

Statistical Analysis

Descriptive statistics [means, standard deviation (SD)] were calculated. Fisher' exact tests and chi-square ($\chi^2$) tests were used to examine the relationship between compliance and patient gender, type of surgery and post-discharge blood transfusion or bleeding issues. Logistic regressions were used to examine the impact of age, BMI, and preoperative hemoglobin (predictor variables) on the binary variable of compliance (response variable).

Results

A total of 3145 patients [1214 (39%) men, 1931 (61%) females, mean age 66 (SD: 11, range 17–94)] underwent lower limb arthroplasty at the Holland Orthopaedic & Arthritic Centre, Sunnybrook Health Sciences Centre (Fig. 1). These were performed by nine fellowship-trained arthroplasty surgeons. Types of surgeries were as follow: 1676 (53%) primary TKA, 1166 (37%) primary THA, 174 (6%) revision TKA, 126 (4%) revision THA, and 3 uni-compartmental TKA (0.1%) during a period of 20 months (Table 2). The average length of stay was 4.4 ± 1.8 days for primary unilateral total knee arthroplasty and 4.5 ± 2.4 days for primary unilateral total hip arthroplasty.

Of 3145 patients, 2947 (94%) were started postoperatively on Rivaroxaban, of which 2824 (96%) completed all in-hospital doses (Fig. 1). Rivaroxaban was discontinued if the surgical team had concerns about hemostasis at the surgical site, non-surgical site bleeding (IV cannula site, femoral nerve block catheter site, hematuria) or if there was a thromboembolic event. In the presence of a proximal DVT or PE the patient was treated with a therapeutic dose of low-molecular-weight heparin and maintained on therapeutic anticoagulation with warfarin for 3–6 months. If there was significant elevation in either the patient's creatinine level or liver function tests, a change to another thromboprophylactic drug was made.
Six-week follow-up was attended by 2621 (93%) of patients. Of 2621 patients, 2163 (83%) reported that they had completed all doses. Of the remaining patients, 98 (4%, 98/2621) reported that they did not complete all doses and 360 (14%, 360/2621) patients had missing data on one of the relevant questions. In the worst-case scenario, when all missing data including those patients who did not attend their 6-week follow-up appointment (203/2824) are considered as NC, the compliance rate is 77% (661/2824).

We further examined the impact of gender, age, BMI, preoperative hemoglobin, and post-discharge bleeding issues and need for blood transfusion on Rivaroxaban NC (Table 3). Women tended to be more NC (68% vs. 32%, \(\chi^2 = 8.61, p = 0.003\)). Type of surgery (THA vs. TKA; primary vs. revision) and side (unilateral vs. bilateral) were not associated with compliance (\(p > 0.05\)). Having a blood transfusion in hospital had a negative impact on completion of all doses of rivaroxaban. Overall 37% of NC had an in-hospital blood transfusion (vs. 16% of NC who did not have a blood transfusion, \(\chi^2 = 26, p < 0.0001\)).

The NC group was more likely to be older (mean age 70 vs. 65 years, Wald \(\chi^2 = 77, p = < 0.0001\)), have a smaller BMI (mean BMI 29 vs. 31, Wald \(\chi^2 = 11.45, p = 0.0007\)) and also have a lower preoperative hemoglobin (mean Hb 138 vs. 141, Wald \(\chi^2 = 19.36, p < 0.0001\)).

In total, 23 patients reported receiving a blood transfusion post-hospital discharge at their 6-week review. Of these 10 (43%) patients were in the NC group (\(\chi^2 = 13.95, p < 0.0001\)). Incidence of bleeding issues reported at 6 weeks was not related to compliance (\(p > 0.05\)).

Seven pulmonary emboli (PE) and 6 deep vein thrombosis (DVT) were reported at 6 weeks postoperatively. Four (4%) of 98 non-compliant patients developed a PE compared to 3 (0.1%) of 2163 patients in the compliant group. This was statistically significant (Fisher’s exact test = 0.01, \(p < 0.0001\)). One (1%) of 98 non-compliant patients developed a DVT compared to 5 (0.2%) of 2163 patients who were in the compliant group. The number of DVTs was not significantly different between groups (Fisher’s exact test = 0.2, \(p = 0.23\)).

Discussion

Outpatient NC to prescribed medications is an ongoing problem, of which much has been published in the literature. Up to 20% of patients fail to collect their prescribed drug and are therefore non-compliant from the start [40]. From those patients who do collect their prescribed medications, rates of compliance have been shown to be related to many factors including the following: the enthusiasm of the prescribing doctor, the disease being treated or primarily prevented (VTE prophylaxis) and the patient’s perception of the importance of the disease [41]. Certainly a more detailed understanding of NC explanatory factors is essential for the development of sophisticated patient compliance programs. In particular, factors such as the detailed recommendations given by general practitioners, the patient–doctor relationship, the patients’ education regarding thrombosis risk and psychological factors describing patients’ behavior and thinking require more detailed investigation [42].

Table 2

<table>
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<th>Sex</th>
<th>1214 (39%) male</th>
<th>1931 (61%) female</th>
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<td>Age (y)</td>
<td>Mean age 66</td>
<td>SD 1</td>
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<tr>
<td>Type of surgery</td>
<td>Primary TKA</td>
<td>Primary THA</td>
</tr>
<tr>
<td></td>
<td>1676 (53%)</td>
<td>1166 (37%)</td>
</tr>
<tr>
<td></td>
<td>Revision TKA</td>
<td>Revision THA</td>
</tr>
<tr>
<td></td>
<td>174 (6%)</td>
<td>126 (4%)</td>
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<tr>
<td></td>
<td>Knee uni-compartmental</td>
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Caron and Roth [43] showed that doctors could not predict their patients’ compliance more accurately than by chance. Specific methods must be used if compliance is to be accurately assessed. Direct questioning is useful in establishing whether a patient is compliant, particularly when an anonymous questionnaire is used. In this manner the patient does not perceive any possible future detrimental effect or treatment bias due to NC. Other objective means of assessing compliance include the following: tablet counting, measuring the concentration of the drug in body fluids, measuring a marker substance added to the drug or measuring the pharmacological effect.

Due to the lack of evidence as to the number of missed VTE prophylaxis modality doses which increase the risk of thrombosis or pulmonary embolism, there is currently no clinically based definition for VTE NC. In concordance to the current published literature on VTE modality NC, we have defined “non-compliance” as the patient omitting a single dose or more of their discharge home postoperative VTE prophylaxis medication.

Evidence exists for an extended period of thromboprophylaxis after hospital discharge following TKA and THA [12,44]. Warwick et al. [18] reported a multicenter study of nearly 15,000 cases, with the mean time to venous thromboembolism of 21.5 days for THA and 9.7 days for TKA. Oral anticoagulants therefore have a significant potential role in an extended period of VTE prophylaxis.

Coumadin is inexpensive and effective if used as recommended with a long history of VTE prophylaxis in North America [7]. In Europe, concerns regarding coumadin’s unpredictable pharmacological profile with an interval to therapeutic effect up to 60 hours, drug and food interactions, varied patient response and the need for frequent laboratory monitoring have resulted in its use being almost completely abandoned [45,46]. New treatment strategies for coumadin including pharmacogenetic dosing and a lower target INR range are currently under investigation [47].

Injectable LMWH remains the dominant form of VTE prophylaxis in Europe. Wilkie and Muller [48] reviewed the literature for those patients who had major orthopedic surgery and been discharged home with LWMH VTE prophylaxis and found an NC rate of 13%–37%, depending on their measurement indicator. This is in keeping with other published NC rates with LMWH [42,49]. Compliance remains a significant issue for LMWH used for VTE prophylaxis following orthopedic surgery.

In a multicenter study of over 8000 patients evaluating the compliance of surgeons with the American College of Chest Physicians (ACCP) guidelines on VTE prophylaxis, Friedman et al. [32] reported that only 47% of THR cases and 61% of TKR cases were compliant with the guidelines. Subset analysis of these cases showed that coumadin had an inferior compliance rate compared to LMWH (33% vs. 63% respectively for THA and 48% vs. 73% respectively for TKA).

Aspirin has been proposed for VTE prophylaxis supported by the evidence reported by the multicenter Pulmonary Embolism Prevention (PEP) collaboration [19]. A comparative study of 4088 patients following THA failed to show a clear benefit to using aspirin as the primary method of VTE prophylaxis [50]. A meta-analysis has shown that the relative rates of VTE, diagnosed by venography, lung scan or angiography, following TKA with aspirin, coumadin and LMWH were 53%, 45% and 29% respectively [26]. In addition, in the published 2012 9th edition American College of Chest Physicians Evidence-Based Clinical Practice Guidelines, one panel member believed strongly that aspirin alone should not be included as an option for prevention of VTE in orthopedic patients [7].

Oral factor Xa inhibitors provide VTE prophylaxis without the potential pharmacologic problems that exist with coumadin, aspirin or LMWH outlined above. In addition, a pilot study of 100 patients suggested that improved compliance was possible with introduction of Rivaroxaban in comparison to LMWH [33].

The results presented in this study demonstrate that when compared with other VTE therapy modalities patients are at least as likely to complete a standardized extended period of thromboprophylaxis regime on an oral factor Xa inhibitor. The direct stated NC rate of prescribed Rivaroxaban was 4% (98/2621). If those patients with missing data (14%, 360/2621) are assumed to be NC then the NC rate increases to 17% (458/2621). If all 203 of 2824 patients lost to their 6-week follow-up are considered NC, then the worse-case NC rate for Rivaroxaban is 23% (661/2824). This compares to the NC for injectable LMWH which has multiple published studies demonstrating NC rates of 5%–40%.

Age, sex and BMI were shown to be significant in terms of non-compliance. Older patients (70 years vs. 65 years), females (68% vs. 32%) and heavier patients (BMI 31 vs. BMI 29) were more likely to not complete their prescribed Rivaroxaban course. This differs from previous studies [30,31], though it is difficult to infer reasons why.

Within the NC group there was a greater incidence of PE (p < 0.0001) postoperatively. There was no difference between the compliant and NC groups in the incidence of reported DVT. Although examining VTE incidence was not the purpose for this study, it is an interesting finding and can only increase the importance of VTE prevention compliance.

Though the results of the study are favorable for compliance of a thromboprophylaxis regime on an oral factor Xa inhibitor, there are limitations to the conclusions. The study was based on a self-reported questionnaire that ultimately depended on patient’s recollection of which medications they took and if they completed the entire course. Previously described methods of tablet counting or pharmacologic analysis were not performed. No rigorous screening for DVT or PE was performed as part of the study protocol therefore their actual prevalence may be understated. However, this study was designed to use medical and surgical relevant end points while capturing clinical experience with this medication. We investigated patients for suspected DVT with Doppler ultrasound while in hospital. Patients with suspected PE were investigated with CT angiogram. The prevalence of DVT and PE may have been higher if routine screening had been in place but we believe that this protocol captured clinically relevant end points, namely symptomatic proximal DVT and clinically relevant PE. In addition we accept that a longer period of thromboprophylaxis (e.g. 35 days for THA) may result in even lower compliance rates, as has been shown in other studies for different drugs.

In conclusion, this study demonstrates that the prescription of Rivaroxaban for VTE prophylaxis for 15 days following lower limb arthroplasty surgery results in excellent compliance compared to the published literature rates for both subcutaneous LMWH and coumadin. Further studies need to be performed in order to fully understand and allow direct comparison of patient compliance for DVT/PE thromboprophylaxis drugs after elective orthopedic arthroplasty surgery.

Acknowledgments

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Orthopaedic and Arthritic Centre, Toronto, for assistance in data collection. In particular the authors would like to acknowledge the work of Deborah Murnaghan RN, Clinical Research Coordinator for this project. She was responsible for collecting the data and assisted in the preparation of the manuscript.

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References

Appendix 17

Wilson DGG, Poole WEC, Chauhan SK, Rogers BA.
Systematic review of aspirin for thromboprophylaxis in modern elective total hip and knee arthroplasty.

Contribution by BA Rogers.
Concept & planning
Manuscript writing & editing

Citation Metrics

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Aims
There is uncertainty regarding the optimal means of thromboprophylaxis following total hip and knee arthroplasty (THA, TKA). This systematic review presents the evidence for acetylsalicylic acid (aspirin) as a thromboprophylactic agent in THA and TKA and compares it with other chemoprophylactic agents.

Materials and Methods
A search of literature published between 2004 and 2014 was performed in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. A total of 13 studies were eligible for inclusion.

Results
Evidence from one good quality randomised controlled trial (RCT) showed no difference in rates of venous thrombo-embolism (VTE) in patients given aspirin or low molecular weight heparin (LMWH) following TKA. There was insufficient evidence from trials with moderate to severe risk of bias being present to suggest aspirin is more or less effective than LMWH, warfarin or dabigatran for the prevention of VTE in TKA or THA. Compared with aspirin, rates of asymptomatic deep vein thrombosis (DVT) in TKA may be reduced with rivaroxaban but insufficient evidence exists to demonstrate an effect on incidence of symptomatic DVT. Compared with aspirin there is evidence of more wound complications following THA and TKA with dabigatran and in TKA with rivaroxaban. Some studies highlighted concerns over bleeding complications and efficacy of aspirin.

Conclusion
The results suggest aspirin may be considered a suitable alternative to other thromboprophylactic agents following THA and TKA. Further investigation is required to fully evaluate the safety and efficacy of aspirin.

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There is considerable uncertainty over the optimal method of venous thromboembolism (VTE) prophylaxis in hip and knee arthroplasty patients, with numerous guidelines in existence worldwide. The American Academy of Orthopaedic Surgeons (AAOS) recommends acetylsalicylic acid (aspirin) as a suitable thromboprophylactic agent and, following criticism of its previous guidance for inadequate balancing of medical risk with bleeding complications, the American College of Chest Physicians (ACCP) has followed suit. The United Kingdom’s National Institute of Health and Care Excellence (NICE) states aspirin’s efficacy in the context of contemporary surgical, anaesthetic and enhanced recovery techniques.

We present a systematic review of the evidence regarding the thromboprophylactic efficacy of aspirin compared with other agents following total hip (THA) and total knee arthroplasty (TKA) using modern surgical and anaesthetic techniques.

Materials and Methods
This study was registered with the International prospective register of systematic reviews (PROSPERO) Centre for Reviews and Dissemination, University of York and conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. A search of NHS Evidence, TRIP, the Cochrane Database of Systematic Reviews, MEDLINE and EMBASE databases was performed using the NHS Evidence Healthcare Databases.
Advanced Search platform. Papers published between 1 January 2004 and 23 September 2015 were included, to increase the likelihood that they described modern arthroplasty and anaesthetic techniques. There were no language restrictions in the initial search but the availability of an English language translation was an inclusion criterion.

We used the Oxford Centre for Evidence-Based Medicine (OCEBM) working group guidance to define levels of evidence with the initial intention of including only level I evidence, later widening this to level III after identifying that too few results were retained to permit meaningful analysis. Analysis for inclusion was performed by two authors (DW and WP), with clarification of peri-operative protocols sought from authors where these were unclear. Any disagreement on level of evidence or inclusion was resolved by consensus or by the senior authors (BR and SC). A PRISMA flowchart is in Figure 1.

Randomised controlled trials (RCT) were assessed for quality using the Cochrane Handbook for Systematic Reviews of Interventions and non-randomised studies using the Cochrane Risk of Bias Assessment Tool for Non-Randomized Studies of Interventions (ACROBAT-NRSI). These tools assess a number of domains including selection, reporting and detection bias and grade the overall risk of bias as low, moderate, severe or unclear. Primary outcomes were any form of venous thromboembolic event and secondary ones were wound complications including oozing and infection. The methods of diagnosis of VTE employed in the relevant study were also noted.

Results

Summary. A total of five studies comparing aspirin with other forms of VTE prophylaxis offered level I evidence and eight studies offered level III evidence from one good quality RCT of 778 patients showed no difference in the rates of VTE in patients given aspirin or low molecular weight heparin (LMWH) following TKA. There was insufficient evidence from trials with moderate to severe risk of bias to suggest aspirin is more or less effective than LMWH, warfarin or dabigatran for the prevention of VTE following TKA or THA. There is evidence, with moderate risk of bias, of increased incidence of wound complications after THA and TKA when dabigatran is used for VTE prophylaxis. Rivaroxaban may reduce the rate of asymptomatic DVT in TKA, but insufficient evidence exists to suggest superiority over aspirin in symptomatic DVT. It may, furthermore, be associated with increased blood loss and wound complications. Significant heterogeneity in thromboprophylactic regimens and assessment made direct comparisons difficult. A summary of trials is included in the supplementary material.

THA. Only one RCT with a moderate risk of bias that examined 121 patients, showed reduced rates of asymptomatic VTE identified on venography with aspirin and pneumatic compression (no DVT) compared with LMWH alone (13 of 17 DVT) in TKA and THA. A total of three further level III studies evaluated THA alone. Out of these, one showed no difference in rates of PE or DVT when comparing LMWH and aspirin in 673 patients, but reported a decreased incidence of wound complications in patients taking aspirin (1% versus 7.9%, p ≤ 0.01). A second involving 123 patients compared dabigatran and aspirin, demonstrating prolonged wound ooze (p = 0.003) and length of stay (p = 0.002) with dabigatran. A comparison of aspirin and warfarin for patients undergoing single-stage bilateral THA showed no difference in the incidence of VTE or wound complications in 644 subjects.

In all, five level III studies examined both THA and TKA together, with only one showing an increased risk of DVT in the TKA subgroup alone.

TKA. A total of four RCTs investigated VTE prophylaxis in TKA alone. The first was good quality with low risk of bias, studying aspirin and LMWH groups in 778 patients. It demonstrated no significant difference between aspirin and LMWH in rates of VTE or wound problems, although a trend (p = 0.091) toward increased wound complications with LMWH was observed. The trial was stopped early due to recruitment difficulties subsequent to the advent of newer oral anticoagulants. The second RCT had an unclear or serious risk of bias and identified no significant difference in the rates of asymptomatic VTE with aspirin and pneumatic compression versus LMWH and pneumatic compression in 274 patients. An increased post-operative drain volume was seen with aspirin (p = 0.03) but was not associated with an increased requirement for transfusion.

The third RCT had a moderate or unclear risk of bias and compared aspirin, LMWH and rivaroxaban in 324 patients. The incidence of asymptomatic DVT was significantly higher in the aspirin group, compared with rivaroxaban (16.4% versus 2.9%, p = 0.014) although there was no significant difference in rates of symptomatic DVT. Wound complications and average hidden blood loss, which represents all peri-operative blood loss and is calculated by the change in pre- and post-operative body red blood cell content as defined by Sehat et al, were both higher with rivaroxaban compared to aspirin (4.9% versus 1.8%, p = 0.014 and 1.7L versus 1.3L, p = 0.04). No statistical difference existed between aspirin and LMWH in any outcome measure.

The fourth RCT pertaining specifically to TKA compared aspirin and LMWH followed by rivaroxaban in 120 patients. It had a severe or unclear risk of bias and demonstrated no statistical difference in rates of asymptomatic DVT, but blood loss was higher in the rivaroxaban group (p ≤ 0.05).

There was one level III study which had a serious risk of bias and compared aspirin with warfarin in THA and TKA in 696 patients. Overall, an increased rate of VTE was seen in the aspirin group. Subgroup analysis revealed this effect was limited to TKA.

Aspirin versus LMWH. A total of four RCTs compared aspirin with LMWH. One good quality RCT with 778 partici-
pants showed aspirin was non-inferior to LMWH ($p \leq 0.001$) for the prevention of VTE in TKA, with a trend towards increased wound complications with LMWH ($p = 0.09$). Another study showed no difference in rates of VTE in TKA in 274 patients, but increased post-operative drain volume with aspirin ($p = 0.03$). The third, examining 121 patients, showed an increased rate of DVT in patients taking LMWH compared with aspirin and pneumatic compression in TKA and THA ($p = 0.002$). Subgroup analysis showed this effect was confined to THA. The final RCT reported no significant differences in rates of DVT or wound complications in 324 TKA patients.

A total of three further level III studies compared aspirin to LMWH in both THA and TKA populations. One examining 1728 patients reported a decreased rate of VTE with aspirin compared with LMWH (0.3% aspirin versus 2.4% LMWH, $p = 0.047$) but this was confounded by the fact that LMWH was given to all patients taking aspirin until discharge, when treatment diverged. This study provided the sole evidence for differing rates of VTE between agents. Another study including 500 patients showed a trend toward decreased rates of VTE with aspirin but failed to reach significance (aspirin 0.2% versus 1.4% LMWH $p = 0.07$). This study also identified a decreased transfusion requirement with aspirin (0.39 units aspirin versus 0.57 units LMWH, $p = 0.001$) although there was no difference in bleeding complications.

A final study showed no difference in rates of VTE with aspirin vs LMWH in 2246 patients with no reporting of wound or bleeding complications. One study on TKA alone with 673 patients reported a decreased rate of wound complications in patients on aspirin (1% versus 7.9%, $p \leq 0.01$).

**Aspirin versus warfarin.** A total of three studies compared aspirin with warfarin. One, with serious risk of bias, demonstrated decreased rates of symptomatic PE and DVT in 696 patients in THA and TKA with no difference in mortality or incidence of bleeding or wound problems. Another study with moderate or unclear risk of bias included 2246 patients and compared aspirin with LMWH (followed by aspirin) or warfarin in THA and TKA. No differences in the incidence of VTE were shown. The final study, also at serious risk of bias, demonstrated no differences in rates of DVT or wound complications between aspirin and warfarin in 644 patients undergoing bilateral THA.

**Aspirin versus novel oral anticoagulants (NOACs).** A total of three studies compared aspirin with dabigatran, all of which carried moderate risk of bias. A paper examining 1728 patients demonstrated a decreased rate of symptomatic VTE, wound complications and length of stay with aspirin compared with dabigatran in TKA and THA. All patients received LMWH whilst in hospital and aspirin or dabigatran as an outpatient. A further paper showed a decrease in time to wound dryness (3.2 versus 6.4 days $p \leq 0.01$) with aspirin in 110 patients undergoing THA and TKA. The final study of 123 patients compared wound discharge and length of stay, demonstrating an increased wound discharge and length of stay in the dabigatran group, compared with the LMWH in hospital and aspirin as an outpatient group in THA.

Rivaroxaban in TKA was evaluated by two RCTs. The first study with 120 patients, showed no difference in asymptomatic DVT rate and no wound complications in either group but higher blood loss with rivaroxaban. The second, examining 324 patients, showed fewer asymptomatic DVTs with rivaroxaban, but no difference in symptomatic DVTs and a significant increase in wound complications and hidden blood loss (as defined above) with rivaroxaban.

**Registry data.** A total of four sets of registry data were identified, including two from the National Joint Registry...
The rate of PE in arthroplasty patients is so low that the sample size required for an RCT would render it impractical. Extended VTE prophylaxis has been shown to reduce rates of both PE and DVT but in absence of a proof of causation of PE by lower limb DVT, the use of asymptomatic DVT as an end point has been questioned. Composite outcomes relating to more common events afford greater statistical efficiency and may provide greater clarity.

Wound complications and infection following THA and TKA are clinically important, with the rate of infection increasing with prolonged wound oozing. Any agent which decreases the risk of prolonged wound discharge may, therefore, reduce infection rates. Prolonged wound oozing has been reported with NOACs, and this review provides evidence that aspirin may confer advantages over NOACs in relation to length of stay, wound oozing and blood loss. While some reports suggest increased rates of wound complications with LMWH the evidence is more equivocal, as is that relating to aspirin versus warfarin. Surgeons should be mindful of bleeding complications with all thromboprophylactic agents, including aspirin.

Compliance and patient satisfaction with oral thromboprophylaxis is better than with injectable LMWH and the use of aspirin for VTE prophylaxis would afford significant financial benefits over LMWH.

This review has some inherent limitations. First, there is a lack of level I evidence and suitably powered trials are clearly required. A total of 3400 patients would afford an adequate non-inferiority trial at 95% power and 5% significance, assuming a baseline symptomatic VTE event rate of 1% and minimally clinically important difference of 1%.

Secondly, significant inter-study heterogeneity exists. There were a variety of dosage regimes, often varying between inpatient and outpatient setting. Studies used different methods of VTE detection and primary endpoints varied between symptomatic and asymptomatic DVT. Post-operative recovery protocols varied, as did the use of mechanical devices. These limitations make direct

<table>
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GA, general anaesthesia; CPM, continuous passive motion; MDT, multidisciplinary.

(NJR) in England and Wales. Both had populations in excess of 100,000 patients and demonstrated no difference in rates of DVT or PE between aspirin and LMWH.25,26 One study of THA patients alone showed increased mortality with the aspirin group (0.65% versus 0.51% p = 0.04),25 and the other an increased rate of return to theatre with aspirin (0.26% versus 0.19% p = 0.01).26 A study of over 17,000 patients from the United States showed no difference in VTE rates between aspirin, warfarin, LMWH or mechanical prophylaxis alone.27 A further United States registry report of almost 100,000 TKAs showed no difference in adjusted outcomes between aspirin and LMWH, but noted the rate of VTE was higher in those taking warfarin.28

Discussion

The quality of early RCTs of aspirin in VTE prophylaxis is poor and current guidance based on them is confounded by the absence of modern peri-operative practice in their protocols. This lends inappropriate weight to the choice of chemical agent, when protection is nowadays conferred by multimodal regimens.6 Mortality rates from VTE following lower limb arthroplasty are low,29,32 with a recent meta-analysis reporting that half of such deaths are the consequence of cardio-pulmonary events,29 half of which in turn were due to PE, irrespective of the thromboprophylactic regimen used.29 Whilst aspirin prophylaxis against VTE may confer an additional cardioprotective effect,33 this is yet to be demonstrated.34 The NJR shows a higher mortality in patients taking aspirin after THA25 but heterogeneity in operative and peri-operative factors make this difficult to interpret.
comparisons difficult and a moderate or severe risk of bias limited the level of significance of the majority of studies. It is probable that all thromboprophylactic agents, in conjunction with modern anaesthesia and early mobilisation, afford adequate effect. Furthermore, the clinical relevance of symptomatic versus asymptomatic VTE remains unquantified, whilst the implications of wound complications is undoubted. Surgeons selecting aspirin should be aware of some reports of increased bleeding, return to the theatre and higher mortality rates in THA reported by the NJR. These concerns are by no means definite and more recent evidence with over 11 000 patients using aspirin as thromboprophylaxis showed no difference in VTE along with a comparable and downward trend in mortality when compared with NJR data. 44

In conclusion, the evidence for aspirin is incomplete, but there is reason to consider it a suitable alternative to other chemoprophylactic agents. Its action may well be enhanced with concomitant use of mechanical prophylaxis. A pragmatic approach to developing thromboprophylactic guidance and to improving the body of evidence for aspirin in the future is needed, as the large numbers required for suitably powered RCTs examining rare outcomes are prohibitive.

Take home message: Aspirin should be considered an appropriate thromboprophylactic agent in THA and TKA.

Supplementary material

A table showing the results of the included studies can be found alongside the paper online at http://www.bj.jboneandjoint.org.uk/

Author contributions:
D. Wilson: Methodology, Study selection and analysis, Writing paper, Editing paper.
W. Poole: Study selection and analysis, Writing paper, Editing paper.
S. Chauhan: Concept, Editing paper, Final revision.
B. Rogers: Concept, Methodology, Writing paper, Editing paper, Final revision.

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References


27. Khattak M, Inacio MCS, Bini SA, Paxton EW. Pulmonary embolism prophylaxis in more than 30,000 total knee arthroplasty patients: is there a best choice? J Arthro-

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Appendix 18

Rogers BA, Little NJ.
Thromboprophylaxis in orthopaedic surgery: a clinical review.

Contribution by BA Rogers.
   Concept & planning
   Manuscript writing & editing

Citation Metrics
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      Facebook:
      Mendeley readers:
Thromboprophylaxis in orthopaedic surgery: a clinical review

by Benedict A Rogers and Nick J Little

Venous thromboembolism (VTE), including deep vein thrombosis (DVT) and pulmonary embolism (PE), is a common cause of cardiovascular mortality and morbidity. Patients undergoing major orthopaedic surgery, including hip and knee arthroplasty, represent a group that is at particularly high risk for VTE, especially patients with risk factors (age >60 years, cancer, prior VTE).

Currently, if no measures are taken, the rate of fatal PE is approximately 0.4%, which equates to over 5,000 fatalities a year for the 1.5 million hip and knee replacements performed in Europe. It is a significant and potentially fatal problem after surgery and, although there are numerous publications/guidelines on reducing its incidence, none includes newer treatment modalities such as oral factor Xa inhibitors.

VTE occurs due to factors that alter the balance of coagulability, venous stasis and venous endothelial damage (Virchow's triad). The prophylactic measures used to reduce incidence act by modifying one or more of these factors. Advances in surgical technique and equipment, such as the increasing use of arthroscopic techniques, have helped reduce the risk of postoperative VTE.

This review provides a synopsis of current therapeutic options and an algorithm for treatment. The risk of VTE needs to be assessed by considering patient and operative risk factors, before deciding on the most appropriate modality to reduce this risk, which may involve physiological, mechanical or pharmaceutical measures.

Assessment of the patient

There are numerous patient factors that are known to increase the risk of VTE (Table 1) (NICE 2007) and, although the relative risk of one or more of these factors is not known, it should alert clinicians with the management and investigations directed appropriately.

Spine injury patients, especially those who have a spinal cord injury, have a high prevalence of DVT, and thromboprophylaxis should be started as soon as possible, taking into account any potential bleeding complications. Evidence to date shows that low-molecular-weight heparin (LMWH) and warfarin are effective in preventing thrombosis.

Assessment of surgery

The VTE risk depends on the surgical procedure, and specific operative risk factors should be considered (Table 2).

Upper limb surgery has a significantly lower VTE risk compared with lower limb surgery, with no evidence to justify the use of pharmaceutical prophylaxis (Willis et al 2009, Randelli et al 2010).

The evidence for the VTE risk in lower limb trauma surgery is more complex. Pharmaceutical VTE prophylaxis is recommended after hip fracture surgery (NICE 2007), but there is little evidence for below-knee trauma or elective surgery (Goel et al 2009).

Special attention should be drawn to hip and knee arthroplasty surgery because of the higher VTE risk. Much research has been published, and evidence suggests that the peak incidence of both venographic and symptomatic thrombosis is at least 10 days after total knee replacement (TKR) and 21 days after total hip replacement (THR) (Planes et al 1996, Warwick et al 2007).

Subsequently, it is advocated that appropriate VTE prophylaxis should continue for at least this period of time.

General measures

Hydration

Haemoconcentration increases blood viscosity and reduces blood flow, especially in the deep veins of the leg in immobile patients, leading to stasis and thus an increased risk of VTE. Although no specific clinical studies have evaluated dehydration in relation to VTE, it is well known that relative dehydration has a detrimental physiological effect. Thus, patients should be well hydrated before, during and especially after surgery.

Leg exercises

Again considering venous stasis as a contributing factor to VTE, patient, specifically limb immobility after orthopaedic surgery increases the risk of DVT about tenfold (Heil et al 2001). In contrast to historical practice, there is no evidence to justify complete bed rest for any condition and every effort should be made to mobilise the relevant limb as soon as possible and ideally to mobilise the whole patient (Allen et al 1999).
There is good evidence to suggest that spinal anaesthesia is beneficial in reducing mortality (Rodgers et al 2000).

### Spinal or general anaesthetic

The type of anaesthetic has been shown to affect the complication rate following surgery. There is good evidence to suggest that spinal anaesthesia is beneficial in reducing mortality (Rodgers et al 2000). The beneficial effect of a spinal anaesthetic is likely to be multifactorial, affecting stasis, coagulability and endothelial integrity, so, if possible and safe, the patient should have a spinal anaesthetic.

### Mechanical measures

These devices reduce venous stasis and include graduated elastic compression stockings (GECs), intermittent pneumatic compression devices and mechanical foot pumps.

#### Graduated elastic compression stockings

There is good meta-analysis evidence for the effectiveness of GECs (Amaragiri 2001). Thigh-length stockings are theoretically superior to knee-length ones, but to date no conclusive evidence supports this (Porteous et al 1989). The use of GECs should be cautioned in patients with severe oedema, neuropathy, deformity, arteriopathy or dermatitis.

#### Calf compression devices

Calf compression devices compress the calf muscles to a pressure of 35–40 mmHg for 10 seconds every minute, which stimulates fibrinolysis. They are usually applied immediately before surgery and frequently replaced by GECs because they can cause discomfort in the conscious patient (Comerota et al 1997).
Thromboprophylaxis in orthopaedic surgery: a clinical review
Continued

Pharmaceutical measures

Determining the true effectiveness of difficult drugs in VTE prophylaxis is difficult due to several factors:

1. Low absolute incidence of symptomatic VTE events and death
2. The use of surrogate outcomes, such as duplex ultrasonography
3. Unclear implication of asymptomatic VTE events
4. The large numbers required to achieve statistical significance.

As a result, several pharmaceutical agents have been proposed for VTE prophylaxis and to date there is controversy as to which is superior.

Aspirin

Aspirin is cheap, readily available and easily administered orally, and has been an antiplatelet function; it has been proposed as an effective modality of VTE prophylaxis. The Antithrombotic Trialists Collaboration reviewed 9,000 randomised patients and showed that aspirin substantially reduced the incidence of both DVT and PE in a wide range of surgical patients (Antithrombotic Trialists’ Collaboration 1994). More recently, a study of over 4,000 patients, prescribed aspirin 150 mg for 6 weeks after total hip and knee replacement surgery, demonstrated a fatal PE rate of 0.07% (Cusick & Beverland 2009).

However, a large multicentre study of over 13,000 patients after hip fracture surgery compared a daily oral dose of 160 mg aspirin against placebo for VTE prophylaxis, and showed no significant difference in death rate and only a 30% risk reduction of symptomatic VTE (Pep 2000). However, there are concerns about bleeding from the surgical site and gastrointestinal tract, with an associated higher transfusion rate. In view of this evidence, the VTE prophylaxis provided by aspirin is not now considered to be significant enough to be justified (Warwick 2004) and it is not licensed in the UK for this indication.

Heparin

Unfractionated heparin

A meta-analysis of 20 studies involving over 7,000 patients showed that LMWH was superior to standard low-dose heparin with respect to DVT and resulted in significantly fewer bleeding complications (Palmer et al 1997).

LMWH

A comprehensive meta-analysis has demonstrated that LMWH is effective in preventing asymptomatic DVT at discharge compared with placebo, dextran, low-dose heparin (LDH) and warfarin (Brookenthal et al 2001). The overall asymptomatic DVT rate was 17% (range 7-33%). The asymptomatic proximal DVT was 7% (range 0-29%); however, the studies were too small to show that LMWH had any effect on fatal PE rate.

Excessive bleeding and heparin-induced thrombocytopenia (HIT) are two issues that the clinician should be aware of when prescribing LMWH.

Bleeding

Increased bleeding has been observed in patients receiving LMWH compared with warfarin (Francis et al 1997). Further, the timing of LMWH administration has a notable effect on the occurrence of major bleeding (Colwell et al 1999) with over three-quarters of patients with a major bleed being administered medication from 0 h to 12 h postoperatively.

Heparin-induced thrombocytopenia

HIT is a known, potentially fatal complication of LMWH use. Recent evidence has highlighted poor monitoring of this condition, especially once a patient has been discharged home (Rogers et al 2009).

Warfarin

Warfarin, via its direct action on the vitamin K-dependent clotting factors, has been shown to reduce asymptomatic DVT incidence compared with controls and once-daily aspirin, but is not as effective as LMWH (Imperiare & Speroff 1994).

However, a specific randomised controlled trial demonstrated that high-dose aspirin (325 mg twice daily) has a greater efficacy in reducing asymptomatic proximal DVT than 10 mg warfarin started the night of surgery and an international normalised ratio (INR) maintained in the region 1.2-1.5 (Lotke et al 1996).

Considering the in-patient stay alone, LMWH is significantly superior to warfarin in preventing symptomatic VTE; however, the benefit is lost after hospitalisation (Colwell et al 1999).

Further, major drawbacks to the use of warfarin are the need for regular monitoring of the prothrombin time and a prevalence of major bleeding of up to 5%.

New oral anticoagulants

Oral direct factor Xa inhibitors

Oral direct factor Xa inhibitors afford an antithrombotic action by combining directly with factor X in the coagulation cascade, without using antithrombin as a mediator. There are two oral direct factor Xa inhibitors currently developed – rivaroxaban and apixaban – with a third – etoxibab – undergoing trials for use in a cardiology setting.

There are four large clinical studies relating to rivaroxaban: for hip replacement the RECORD 1 (Eriksson et al 2008) and RECORD 2 (Kakk et al 2008) studies; and for knee replacement the RECORD 3 (Lassen et al 2008) and RECORD 4 (Turpie et al 2009) studies. The evidence from these large multicentre studies shows the efficacy of rivaroxaban to be at least statistically similar to 40 mg/day LMWH. The results are encouraging, with an oral preparation afforded a higher patient compliance and no monitoring for HIT needed; however, further collaborative clinical evidence is necessary to ensure efficacy.

Recently, apixaban has been compared with LMWH for the prevention of VTE after TKR. Advance 1 (Lassen et al 2009) demonstrated similar outcome measures with enoxaparin and Advance 2 (Lassen et al 2010) demonstrated reduced primary outcome measures (namely VTE, PE and mortality) with apixaban. These are again encouraging but, disappointingly, there are no published trials using apixaban after THR.

Direct thrombin inhibitors

Dabigatran is an oral direct thrombin inhibitor that can be taken once daily. Three large clinical studies compare dabigatran...
with LMWH after THR and TKR, namely the RENOVATE (Eriksson et al 2007), RE-MODEL (Eriksson et al 2007) and REMOBILIZE (Ginsberg et al 2009) studies. The pooled results showed no difference in the prevention of VTE compared with LMWH, and both had similar safety profiles. However, when analysed separately they demonstrated conflicting results, with those from the REMOBILIZE trial suggesting inferior results with dabigatran compared with a twice-daily regimen of LMWH following TKR.

Discussion
Historically there was undoubtedly clear evidence for the need for VTE prophylaxis because the incidence of VTE events after THR approached 50% in patients in whom no preventive measures were taken (Johnson et al 1978). Contemporary surgical procedures and postoperative regimens have drastically changed over the last three decades, and the incidence of untreated VTE is now likely to be substantially lower.

As this review has highlighted, VTE prophylaxis is multi-factorial and both the clinician and patient should be aware of this. However, the plethora of published guidelines on this subject is a cause of potential confusion and there are several factors that cause resistance to their implementation, including a lack of awareness, perceived conflicting evidence, practicality, the low overall incidence and bias. This review does not replace any of the major guidelines currently available (Table 3); rather provision of an outline of the treatment modalities available and a generic algorithm (Figure 1) of the clinical management should be considered.

Education of the clinician and patient is vital because not only is the incidence of VTE greatest after the patient has usually been discharged, but also patient compliance with the general measures (outlined above) will help greatly to reduce risk. With the likelihood of numerous future publications on this topic, the clinician should endeavour to remain up to date with the best available contemporary evidence to guide clinical practice.

Key points
- Venous thromboembolism (VTE) is a potentially fatal complication of orthopaedic surgery.
- The VTE risk varies depending upon patient and surgical factors (see Tables 1 and 2).
- Prevention options include optimising physiology, mechanical and pharmaceutical measures (see Figure 1).
- Various pharmaceutical options now exist, and the specific risks and benefits of any drug need to be considered for individual patients.
- Numerous in-depth guidelines exist on this topic (see Table 3), and the reader should refer to these for a more detailed discourse.

References
Amaragiri 2001 Elastic compression stockings for prevention of deep vein thrombosis (Cochrane Review)
Brookenthal KR, Freedman KB, Lokte PA, Fitzgerald RH, Linner JH 2001 A meta-analysis of thromboembolic prophylaxis in total knee arthroplasty J Arthroplasty 16 (3) 293-300
Cusick LA, Beverland DE 2009 The incidence of fatal pulmonary embolism after primary hip and knee replacement in a consecutive series of 4253 patients J Bone Joint Surg Br 91 (5) 645-8

Table 3 Guidelines
Thromboprophylaxis in orthopaedic surgery: a clinical review

Continued

NICE 2007 Venous thromboembolism: reducing the risk of venous thromboembolism (deep vein thrombosis and pulmonary embolism) in inpatients undergoing surgery. London, NICE.


Heit JA, Silvenstein MD, Mohr DN, Petterson TM, Lohse CM, O’Fallon WM, Melton 3rd LJ 2001 The epidemiology of venous thromboembolism in the community Thromb Haemost 86 (1) 452-63

Imperiale TF, Speroff T 1994 A meta-analysis of methods to prevent venous thromboembolism following total hip replacement JAMA 271 (22) 1780-5


Lotte PA, Palevsky H, Keenan AM, Meranz S, Steinberg NE, Ecker ML, Kelley MA 1996 Aspirin and warfarin for thromboembolic disease after total joint arthroplasty Clin Orthop Relat Res (324) 251-8


Warwick D, Friedman RJ, Agnelli G, Gl-Caray E, Johnson K, FitzGerald G, Turbio FM 2007 Insufficient duration of venous thromboembolism prophylaxis after total hip or knee replacement when compared with the time course of thromboembolic events: findings from the Global Orthopaedic Registry J Bone Joint Surg Br 89 (6) 799-807


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No competing interests declared

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Appendix 19

Rogers BA, Little N, Jones C.
Monitoring and management of heparin-induced thrombocytopenia.

Contribution by BA Rogers.

Concept & planning

Manuscript writing & editing

Citation Metrics

Web Of Science: 2
Google Scholar: 2
Altmetrics: 0

Tweets:

Facebook:

Mendeley readers:
Monitoring and management of heparin-induced thrombocytopenia

Low molecular weight heparins have been used to reduce thromboembolic risk for at least 20 years, but their use is not without risk. This article considers the incidence, monitoring, treatment and lack of insight about heparin-induced thrombocytopenia – a potentially fatal complication of low molecular weight heparin use.

Low molecular weight heparins have been commonly used for over two decades by many medical and surgical specialties. They are at least as effective as other means of thrombosis prevention and are widely used in orthopaedic patients, particularly those undergoing lower limb joint arthroplasty (Leyvraz et al, 1991; Mohr et al, 1993; Wolf, 1994).

Their main advantage is that they can be used without laboratory monitoring and they have less bleeding compared with unfractionated heparin for a given antithrombotic effect (therapeutic index) (Wolf, 1994). Several types of low molecular weight heparin are commonly used including enoxaparin (Clexane, Sanofi-Aventis, Guildford), dalteparin (Fragmin, Pharmacia, Milton Keynes) and tinzaparin (Innohep, Leo Pharmaceuticals, Princes Risborough), with bleeding and thrombocytopenia the most common complications (Joint Formulary Committee, 2006).

Bleeding may occur at various locations: the operative site, epidural space, intrahepatic or retroperitoneal bleeding (Heude and Steinberg, 1999; Shaieb et al, 1999; Stern et al, 2000; Antonelli et al, 2000). Intracerebral haemorrhage following the use of low molecular weight heparin has occurred following neurosurgical and orthopaedic procedures with tragic consequences (Dickinson et al, 1998; Lilikakis et al, 2006).

Heparin-induced thrombocytopenia

Clinical

Heparin-induced thrombocytopenia is one of the most important immunohaematological problems in clinical medicine. It can be associated with thrombosis which is independent of heparin type, dose or route of administration (King and Kelton, 1984; Chong, 1995).

Low molecular weight heparin is associated with two forms of thrombocytopenia. Type I (non-immune mediated) causes a mild thrombocytopenia, typically occurring 1–4 days after starting low molecular weight heparin, with screening tests for heparin-induced thrombocytopenia antibodies negative. No data suggest that type I heparin-induced thrombocytopenia has an increased risk of thrombosis and it is attributable to a direct, reversible, proaggregatory effect of platelets (Antonelli et al, 2000).

Type II heparin-induced thrombocytopenia (immune mediated) typically appears 5 or more days after the start of heparin therapy, but develops more rapidly in patients previously exposed to heparin (Shaieb et al, 1999). It is clinically more important as it can cause life-threatening thromboses. Onset is independent of heparin type, dosage or route of administration and the diagnosis needs both the presence of heparin antibodies and a reduction in platelet count of 50%. Cessation of heparin triggers a rise in the platelet count, usually within 5–7 days, and a delay in the normalization of the platelet count should lead to investigation of other causes of thrombocytopenia.

The estimated incidence of type II heparin-induced thrombocytopenia is between 1% with low molecular weight heparin and 5% with unfractionated heparin. There are variations depending on heparin type (bovine heparins are associated with a higher risk than porcine, so nearly all heparins used in UK are porcine in origin), type of patient (surgical patients are at higher risk than medical patients) and route of administration (intravenous gives a higher risk than subcutaneous).

Thrombosis is the principal risk causing ischaemia and subsequent organ failure to limbs and/or vital organs. It can occur in up to 30% of type II heparin-induced thrombocytopenia – termed the ‘white clot syndrome’ (Chong, 1995). Arterial thromboses secondary to type II heparin-induced thrombocytopenia commonly lead to cerebrovascular accident and myocardial infarction, with venous thromboses causing deep vein thrombosis and pulmonary embolism, and with disseminated intravascular coagulation as a potential devastating consequence. Previous reports have documented a mortality ranging from 15% to 30% (Shaieb et al, 1999; Antonelli et al, 2000). In a small study carried out in the authors’ unit, there was a 8.7% incidence of asymptomatic thrombocytopenia, defined as a platelet count of less than 50% of the preoperative value in patients receiving low molecular weight heparin following lower limb arthroplasty.

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surgery, highlighting the incidence of patients at risk of heparin-induced thrombocytopenia.

**Biology**
Heparin-induced thrombocytopenia results from an antibody-mediated response to heparin triggering a reduction in the platelet count (Burgess et al, 1995; Warkentin, 1999). In heparin-induced thrombocytopenia, heparin causes release of platelet factor 4, a 70-amino acid protein, from alpha granules within the platelets. Heparin binds to platelet factor 4 and then undergoes a conformational change, forming an antigenic complex on the surface of platelets (Figure 1). Patients develop an antibody (IgG) to the heparin–platelet factor 4 antigenic complex that binds to the heparin–platelet factor 4 immune complex on the platelet surface.

The Fc portion of the antibody then activates the platelets by binding to platelet Fc receptors. The reticuloendothelial system subsequently consumes the activated platelets, platelet microaggregates and IgG-coated platelets causing thrombocytopenia. The activation of platelets together with the generation of procoagulant microparticles and the increase in thrombin generation leads to a pro-thrombotic state responsible for the most serious complications of type II heparin-induced thrombocytopenia.

**Guidelines and rationale for monitoring**
The clinical importance of heparin-induced thrombocytopenia is driven by four factors:
1. Heparin use is widespread and on the rise
2. Heparin-induced thrombocytopenia is a devastating prothrombotic disease
3. Heparin-induced thrombocytopenia is a severe, immune-mediated drug reaction that can occur in any patient exposed to heparin
4. Heparin-induced thrombocytopenia presents clinicians with a critical medical dilemma.

In response to this the British Society for Haematology produced evidence-based guidelines for the identification and management of heparin-induced thrombocytopenia (Baglin et al, 2006). These guidelines advocate:

1. All patients who receive heparin (of any sort) should have a platelet count on the day of starting treatment
2. All medical and surgical patients receiving low molecular weight heparin or unfractionated heparin should have platelet counts performed every 2–4 days from days 4–14
3. If platelet count falls by over 50% or below normal lab limits and there are features of heparin-induced thrombocytopenia (Table 1) one must consider it, so stop heparin and inform a haematologist.

**Table 1. Laboratory diagnosis of immune heparin-induced thrombocytopenia**

<table>
<thead>
<tr>
<th>Category</th>
<th>Points (0, 1 or 2 for each category, maximum score = 8)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Timing* of platelet count fall or other sequelae</td>
<td><strong>Thrombosis of other sequelae (e.g. skin lesions)</strong></td>
</tr>
<tr>
<td>&gt;50% fall or platelet nadir 20–100 x 10^9/litre</td>
<td>New thrombosis, skin necrosis, post-heparin bolus acute system reaction</td>
</tr>
<tr>
<td>30–50% fall or platelet nadir 10–19 x 10^9/litre</td>
<td>Progressive or recurrent thrombosis, erythematous skin lesions, suspected thrombosis not yet proven</td>
</tr>
<tr>
<td>Fall &lt; 30% or platelet nadir &lt;10 x 10^9/litre</td>
<td>Platelet count fall too early (without recent heparin exposure)</td>
</tr>
</tbody>
</table>

*From Warkentin and Heddle (2003). Probability score: 6–8 = high, 4–5 = intermediate; 0–3 = low. * First day of immunizing heparin exposure is considered day 0.

**Figure 1. The antibody-mediated response in heparin-induced thrombocytopenia. Adapted from Chong (1995), PF4 = platelet factor 4.**
Diagnosis and treatment

The diagnosis of heparin-induced thrombocytopenia requires awareness and a low threshold for suspecting it. If heparin-induced thrombocytopenia is suspected, based upon the above guidelines, a haematologist should be involved early to plan further management. A fall in platelet count alone does not equate to heparin-induced thrombocytopenia and full evaluation of the clinical scenario is needed to predict the probability of heparin-induced thrombocytopenia. Four principal features point to a diagnosis of heparin-induced thrombocytopenia: the degree of platelet fall, the timing of onset, the presence of thrombus and whether an alternative cause of thrombocytopenia is likely (e.g. sepsis or disseminated intravascular coagulation). These factors have been incorporated in a scoring system (Warkentin and Heddle, 2003) to give a probability of heparin-induced thrombocytopenia (Table 1).

If a high probability of heparin-induced thrombocytopenia is suspected platelet activation assays or immunological assays with platelet factor 4 as the antigen can be used to make the definitive diagnosis. The aggregation of normal platelets in the patient’s plasma with heparin can be detected using a standard platelet aggregometer with a sensitivity of about 85%.

Enzyme-linked immunosorbent assays have a high sensitivity (80–100%) but low specificity for heparin–platelet factor 4, and while some assays detect IgA and IgM, IgG assays have a greater diagnostic sensitivity for heparin-induced thrombocytopenia.

On diagnosing heparin-induced thrombocytopenia the clinician needs to stop heparin and consider the risks and benefits of treatment with an alternative anticoagulant such as lepirudin or danaparoid. Warfarin is not recommended until the platelet count has normalized because in the acute phase it can lead to significant skin necrosis. Platelets should also not be given for prophylaxis as they could contribute to the thrombotic risk.

Lepirudin, a direct, irreversible thrombin inhibitor, reduces the risk of limb amputation, death or new thrombosis if given to achieve an activated partial thromboplastin time ratio of 1.5–2.5. Skin reactions, and hepatic and renal impairment are the common side effects of lepirudin use. Danaparoid is a heparinoid, chemically distinct from heparin, inhibiting factor Xa and thrombin, that in a high dose regimen has a similar efficacy to lepirudin (Farmer et al, 2001). It is monitored by measuring anti-Xa levels, although some consider monitoring is only necessary in patients with severe renal impairment or extremes of body weight (<55 and >90 kg) (Farmer et al, 2001).

Survey and results

In response to a lack of local knowledge regarding this condition, a national survey of 25 district general hospitals, six teaching hospitals and 22 general practice surgeries was conducted regarding the awareness and monitoring of heparin-induced thrombocytopenia (Table 2). This survey assessed a cross section of the medical specialties, in both primary and secondary care. The results highlight a near complete lack of awareness of heparin-induced thrombocytopenia monitoring guidelines and indeed none of the units surveyed routinely monitor the platelet count of patients receiving low molecular weight heparin.

Given how commonly low molecular weight heparin is prescribed, the lack of awareness of a complication of its use is of concern and justifies the need for this condition to be highlighted.

Implications and recommendations

Low molecular weight heparins have been used to reduce thromboembolic risk in both primary care and the hospital setting for at least 20 years (Mohr et al, 1993; Wolf, 1994; Imberti et al, 2006). While providing effective pharmacological thromboprophylaxis, their use in orthopaedic surgery is not without risk (Stern et al, 2000; Bickler et al, 2006; Lillicrap et al, 2006).

A significant improvement in platelet count monitoring for patients at risk of heparin-induced thrombocytopenia can be made by the implementation of a simple protocol and an additional full blood count (approximately £1 per test).

All clinicians should be aware of the common side effects and also the rare adverse reactions that may have serious consequences. Following the publication of case reports showing intracranial haemorrhages as a consequence of heparin-induced thrombocytopenia (Lillicrap et al, 2006) and evidence-based guidelines (Baglin et al, 2006), failure to routine monitor for thrombocytopenia in patients receiving low molecular weight heparins may have medicolegal implications.

Table 2. Survey of the awareness of the guidelines for heparin-induced thrombocytopenia and monitoring for patients receiving low molecular weight heparin

<table>
<thead>
<tr>
<th></th>
<th>Aware of heparin-induced thrombocytopenia guidelines</th>
<th>Monitor platelet count for patients on low molecular weight heparin</th>
</tr>
</thead>
<tbody>
<tr>
<td>UK district general hospitals</td>
<td>4% (1/25)</td>
<td>0% (0/25)</td>
</tr>
<tr>
<td>UK teaching hospitals</td>
<td>17% (1/6)</td>
<td>0% (0/6)</td>
</tr>
<tr>
<td>General practitioners</td>
<td>0% (0/22)</td>
<td>0% (0/22)</td>
</tr>
</tbody>
</table>
Conclusions
Clinicians should be aware of the risk of heparin-induced thrombocytopenia when prescribing heparin, including low molecular weight heparin and unfractionated heparin. The introduction of a simple monitoring protocol will facilitate its prevention. This should include:

- All patients who receive heparin (of any sort) should have a platelet count on day one of starting treatment
- All medical and surgical patients receiving low molecular weight heparin should have platelet counts every 2–4 days from days 4–14 while on treatment.
- If platelet counts drop by 50% or below normal lab limits consider the possibility of heparin-induced thrombocytopenia, stop heparin and inform the haematologist.

If heparin-induced thrombocytopenia is suspected it is essential to withdraw heparin and start an alternative anticoagulant treatment to prevent thromboses. BJHM

Conflict of interest: none.


KEY POINTS
- There is little awareness of heparin-induced thrombocytopenia – a potentially fatal complication of heparin use.
- All patients prescribed heparin should have regular full blood counts to monitor for thrombocytopenia until at least day 14.
- Thrombocytopenia should trigger the cessation of heparin and immediate consultation with a haematologist.

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Appendix 20

Rogers BA, Cowie AS.
The monitoring of heparin induced thrombocytopenia following surgery: an audit and international survey.

Contribution by BA Rogers.

  Concept & planning
  Data Collection
  Manuscript writing & editing

Citation Metrics

  Web Of Science:  8
  Google Scholar:  10
  Altmetrics:      0
  Tweets:
  Facebook:
  Mendeley readers:
RESEARCH & AUDIT

KEYWORDS Heparin induced thrombocytopenia (HIT) / Monitoring / Survey

Provenance and Peer review: Unsolicited contribution; Peer reviewed: Accepted for publication September 2009.

The monitoring of heparin induced thrombocytopenia following surgery: an audit and international survey

by Benedict A Rogers and Andrew S Cowie

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Heparin-induced thrombocytopenia (HIT) is a serious postoperative complication of low-molecular-weight heparin (LWMH) prescribed following surgery and recent evidence based guidelines recommend routine platelet count monitoring for all at-risk patients. With the implementation of these guidelines this clinical study demonstrated a significant improvement (2 - 56% p<0.05) in HIT diagnosis in postoperative patients receiving LWMH. An international survey showed a lack of awareness of heparin-induced thrombocytopenia and its management.

Introduction

Low-molecular-weight heparin (LMWH) is widely used in the prevention of thromboembolism in orthopaedic patients, particularly those undergoing lower limb joint arthroplasty (Leyvraz et al 1991, Mohr et al 1993, Wolf 1994). Several types of LMWH are commonly used including enoxaparin (Clexane®, Rhône-Poulenc Rorer), dalteparin (Fragmin®, Pharmacia) and tinzaparin (Innohep®, LEO), with bleeding and thrombocytopenia having been known complications (BNF 2008). Bleeding may occur at various locations: operative site, epidural, intrahepatic, and retroperitoneal sites, gastrointestinal tract (Antonelli et al 2000, Houde & Steinberg 1999, Shaieb et al 1999, Stern et al 2000). Intracerebral haemorrhage following the use of LMWH has occurred following neurosurgical and orthopaedic procedures, with serious consequences (Dickinson et al 1998, Lillikakis et al 2006).

Heparin-induced thrombocytopenia (HIT) is associated with thrombosis, independent of heparin type, dose or route of administration (Boshkov et al 1993, Chong 1995, King et al 1984). It results from an antibody-mediated response to heparin triggering a reduction in the platelet count (Burgess et al 1995, Gerhard-Herman 2001, Warkentin 1999). The British Society for Haematology (BSH) has produced evidence based guidelines for the identification and management of heparin-induced thrombocytopenia (Baglin et al 2006). In summary the guidelines advocate:

1. All patients require a platelet count on day of starting treatment.
2. Repeat platelet counts should be repeated every 2-4 days from days 4 – 14.

This study audits the implementation and awareness of these guidelines within an orthopaedic unit and compares current practice both in the UK and internationally.

Methods

An audit loop consisting of two sequential surveys detailing the monitoring of at-risk patients was performed before and after the introduction of an evidence based protocol for the monitoring of heparin-induced thrombocytopenia.

Figure 1: Audit loop for monitoring of heparin-induced thrombocytopenia
The initial patient survey demonstrated that only 2 out of 48 at-risk patients (4%) had a FBC performed more than four days after commencing LMWH induced thrombocytopenia - see figure 1. Enoxaparin (Clexane®; Rhône-Poulenc Rorer) was the only LMWH prescribed for patients in this study. Hospital and departmental approval was obtained prior to commencing this audit. Patients who were medically unwell or commenced on warfarin were excluded since their inclusion would not accurately reflect routine HIT monitoring.

The initial 48 patients who received LMWH for longer than 4 days included 35 operative fixations of proximal femoral fractures, one open reduction and internal fixation of a distal femoral fracture, and 12 lower limb joint arthroplasties. The mean average age was 78 years (range 64-93 years), with 29 female and 16 male. The results of the initial survey were compared with the evidence based British Society for Haematology guidelines (Bagin et al 2006) and discussed at a departmental meeting. A protocol recommending a platelet count every 2-4 days in at-risk patients was implemented (see figure 2). A subsequent survey of 53 patients was conducted, with a mean age of 76 years (range 52 - 89 years), with 20 male and 28 female.

A telephone survey questioning awareness of heparin induced thrombocytopenia and the recent BSH guidelines was conducted. Statistical analysis of the results was carried out using a chi-square test with SPSS v12.0 for Windows.

**Results**

The initial patient survey demonstrated that only 2 out of 48 at-risk patients (4%) had a full blood count (FBC) performed more than four days after commencing LMWH - see figure 3.

The second survey demonstrated a significant improvement (p<0.05), with 23 out of 40 (57.5%) at-risk patients having a FBC performed more than four days after commencing LMWH - see figure 4.

The secondary survey demonstrated a significant improvement (p<0.05) in the monitoring of HIT compared with the primary survey (57.5% compared to 4%) - see figure 5.

---

**Guidelines on management of heparin-induced thrombocytopenia**

1. All patients who receive heparin (of any sort) should have a platelet count on day of starting treatment
2. All surgical patients receiving LMWH, platelet counts should be performed every 2-4 days from days 4 - 14
3. If platelet count falls by over 50% or below normal lab limits consider HIT, stop heparin and inform haematologist

**Figure 2: Protocol implemented following initial survey**

**Figure 3: Initial survey of patients receiving LMWH for greater than 4 days**

**Figure 4: Secondary survey, following implementation of BSH guidelines, of patients receiving LMWH for greater than 4 days**

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The monitoring of heparin induced thrombocytopenia following surgery: an audit and international survey

Continued

From the secondary survey, 23 out of 40 patients had platelet count monitoring as outlined by the BSH guidelines. The quantitative change in the platelet count seen in these patients is shown in Figure 6. The postoperative platelet count dropped below 75% of the preoperative level in 13 out of the 23. Two patients demonstrated a reduction of over 50% in the platelet count that responded with the subsequent cessation of LMWH.

A telephone survey of registrars/interns from 46 orthopaedic units (34 district general/community hospitals, 12 teaching hospitals) in 5 countries (England, France, Scotland, Canada and USA) was conducted. There was a low awareness of both the condition of heparin-induced thrombocytopenia and the BSH guidelines and no units routinely monitored for HIT (see Table 1).

Discussion

Low molecular weight heparins have been used to reduce thromboembolic risk in both primary care and the hospital setting for at least twenty years (Clagett et al 1995, Imberti et al 2006, Mohr et al 1993, Wolf 1994). Whilst providing an effective pharmacological thromboprophylaxis, their use in orthopaedic surgery is not without risk (Bickler et al 2006, Lilikakis et al 2006, Stern et al 2000).

This clinical audit demonstrates a significant improvement in platelet count monitoring for patients at risk of heparin-induced thrombocytopenia by the implementation of a simple protocol and an additional full blood count (approximately £1 per test). However, with nearly 50% of at-risk patients still not being monitored, improvements are still needed. The international survey highlights an ongoing lack of awareness regarding heparin-induced thrombocytopenia and the necessary monitoring of platelet counts.

All prescribers of prescription only medications should be aware not only of the common side effects but also of the rare adverse reactions that may have serious consequences. Following the publication of case reports showing intracranial haemorrhages as a consequence of...
heparin-induced thrombocytopenia (Lilikakis et al 2006) and evidence based guidelines (Baglin et al 2006), failure to routinely monitor for thrombocytopenia in patients receiving LMWHs may have medico-legal implications.

The conclusions of this study are:
1. Heparin-induced thrombocytopenia is a rare but potentially life-threatening complication of low molecular weight heparin.
2. Few orthopaedic units are currently aware of the risk of heparin-induced thrombocytopenia when prescribing LMWH.
3. The introduction of a simple monitoring protocol can facilitate its early identification and treatment.

References


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No competing interests declared.

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Appendix 21

Rogers BA, Thornton-Bott P, Cannon SR, Briggs T.
Interobserver variation in the measurement of patellar height after total knee arthroplasty.

Contribution by BA Rogers.

Concept & planning
Data Collection
Manuscript writing & editing

Citation Metrics

Web Of Science: 29
Google Scholar: 48
Altmetrics: 0
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Interobserver variation in the measurement of patellar height after total knee arthroplasty


From the Royal National Orthopaedic Hospital, Stanmore, England

We assessed the reproducibility and accuracy of four ratios used to measure patellar height, namely the Blackburne-Peel, Caton-Deschamps, Insall-Salvati and modified Insall-Salvati, before and after total knee arthroplasty. The patellar height was measured, by means of the four ratios, on the pre- and post-operative lateral radiographs of 44 patients (45 knees) who had undergone total knee arthroplasty. Two independent observers measured the films sequentially, in identical conditions, totalling 720 measurements per observer. Statistical analysis, comparing both observers and ratios, was carried out using the intraclass correlation coefficient.

Before operation there was greater interobserver variation using either the Insall-Salvati or modified Insall-Salvati ratios than when using the Caton-Deschamps or Blackburne-Peel methods. This was because of difficulty in identifying the insertion of the patellar tendon. Before operation, there was a minimal difference in reliability between these methods. After operation the interobserver difference was greatly reduced using both the Caton-Deschamps and Blackburne-Peel methods, which use the prosthetic joint line, compared with the Insall-Salvati and modified Insall-Salvati, which reference from the insertion of the patellar tendon.

The theoretical advantage of using the Insall-Salvati and modified Insall-Salvati ratios in measuring true patellar height after total knee arthroplasty needs to be balanced against their significant interobserver variability and inferior reliability when compared with other ratios.

The patella plays a crucial role in the biomechanics of the knee by extending the lever arm of the extensor mechanism, thus improving the demonstrable strength of quadriceps by between 30% and 50%. The articulation of the patella within the femoral condylar groove creates a joint reaction force which relates both to the degree of knee flexion and contraction of quadriceps. This force in full flexion of the knee when load-bearing can approach five to seven times the body-weight.

The height of the patella alters the joint reaction force for any particular point in the flexion-extension cycle of the knee. A high riding patella, patella alta, may result in chondromalacia patellae, tendinitis of both the patellar and quadriceps tendons, and patellofemoral instability. A low riding patella, patella baja or infera, may be developmental (patella infera syndrome), or because of trauma, neurological disorders, or may occur after surgery on the knee. Limitation of movement, Osgood-Schlatter disease and patellofemoral arthritis may all result from patella baja. Patellofemoral symptoms are responsible for a large percentage of revisions of total knee arthroplasty (TKA).

Because the femoral condylar groove is difficult to define accurately radiologically, several ratios for the measurement of patellar height have been developed which relate the patella to the proximal tibia, namely the Blackburne-Peel, Caton-Deschamps, Insall-Salvati and modified Insall-Salvati methods.

There are few studies on the interobserver variation of the measurement of patellar height. Berg, Mason and Lucas studied 15 patients with three observers and showed that the Blackburne-Peel method was relatively reproducible. Seil et al also showed that this method had the lowest interobserver variability when assessing patellar height, in a study of 21 patients with symptomatic knees. However, Aparicio et al studied lateral radiographs of the knee in 36 children and found that the Caton-Deschamps ratio was more reliable and reproducible than the Blackburne-Peel.
Scuderi, Windsor and Insall\textsuperscript{18} showed differences in the incidence of patella baja after high tibial osteotomy (89\% vs 73\%) depending on whether the Insall-Salvati or Blackburne-Peel ratio was used. After TKA, Koshino et al\textsuperscript{19} found a significant incidence of patella baja when measured using the Insall-Salvati ratio. It has been proposed that neither the Blackburne-Peel nor Caton-Deschamps ratio should be used to diagnose patella baja after TKA since they are altered by the position of the joint line.\textsuperscript{5}

By using these four ratios, we have assessed the reliability and interobserver variability in the measurement of the patellar height for patients who have undergone TKA.

**Patients and Methods**

The lateral radiographs of the knee of 44 patients who had undergone a Kinemax TKA (Stryker, Newbury, United Kingdom) were evaluated. The operations had been performed at our institution, with osteoarthritis or rheumatoid arthritis being the only indications. One patient had undergone bilateral TKA and the radiographs from both procedures, which were performed at different times, were included. Patients who had undergone a high tibial osteotomy, or a revision procedure, were excluded from the study.

Lateral radiographs were taken before and after the operation with the knee in at least 20° of flexion. The patellar height was measured manually by two of the authors (BAR, PT-B) in an independent sequential manner, and under identical conditions. Each examiner was blinded to the patients’ outcome or the conclusions of the other examiner.

Each ratio was derived from two measurements, one below (measurement A) and one above the lower patella (measurement B). Four main methods of measuring patellar
Table I. Individual and overall ratios for the four methods used, before and after total knee arthroplasty

<table>
<thead>
<tr>
<th></th>
<th>Pre-operative*</th>
<th>Post-operative*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CD</td>
<td>BP</td>
</tr>
<tr>
<td>Measurement A</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Interobserver difference</td>
<td>2.73</td>
<td>2.07</td>
</tr>
<tr>
<td>ICC&lt;sup&gt;†&lt;/sup&gt;</td>
<td>0.67</td>
<td>0.54</td>
</tr>
<tr>
<td>95% CI&lt;sup&gt;‡&lt;/sup&gt;</td>
<td>0.52 to 0.74</td>
<td>0.42 to 0.66</td>
</tr>
<tr>
<td>Measurement B</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Interobserver difference</td>
<td>0.67</td>
<td>0.67</td>
</tr>
<tr>
<td>ICC</td>
<td>0.80</td>
<td>0.90</td>
</tr>
<tr>
<td>95% CI&lt;sup&gt;‡&lt;/sup&gt;</td>
<td>0.65 to 0.88</td>
<td>0.65 to 0.88</td>
</tr>
<tr>
<td>Overall</td>
<td></td>
<td></td>
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<tr>
<td>Interobserver difference</td>
<td>0.10</td>
<td>0.08</td>
</tr>
<tr>
<td>ICC</td>
<td>0.53</td>
<td>0.62</td>
</tr>
<tr>
<td>95% CI&lt;sup&gt;‡&lt;/sup&gt;</td>
<td>0.45 to 0.63</td>
<td>0.49 to 0.67</td>
</tr>
</tbody>
</table>

* CD, Caton-Deschamps; BP, Blackburne-Peel; IS, Insall-Salvati; mod IS, modified Insall-Salvati
† ICC, intraclass correlation co-efficient
‡ 95% CI, 95% confidence interval

Results

The mean interobserver variation and intraclass correlation co-efficient, with 95% confidence intervals (CI), before and after TKA for measurements A and B, and the overall ratio for each of the four methods, are shown in Table I. Pre-operatively, there was less interobserver variation and greater reliability with measurement B compared with measurement A for all methods.

The post-operative intraclass correlation co-efficient for measurement A improved relative to its pre-operative value when using the Caton-Deschamps (0.67 to 0.85) and Blackburne-Peel (0.54 to 0.87) ratios, but deteriorated using the Insall-Salvati (0.61 to 0.52) and modified Insall-Salvati (0.66 to 0.53) ratios. There was, therefore, poor reproducibility for measurement A post-operatively using the Insall-Salvati and modified Insall-Salvati ratios. Apart from the Blackburne-Peel ratio, there were small improvements in the post-operative correlation of measurement B. The resulting post-operative intraclass correlation coefficient between ratios showed greater reproducibility using the Caton-Deschamps and Blackburne-Peel methods (0.82 and 0.83) compared with that using the Insall-Salvati and modified Insall-Salvati ratios (0.52 and 0.48).

Overall, there was an improvement in the post-operative ratio compared with pre-operatively when using the Caton-Deschamps (0.53 to 0.82) and Blackburne-Peel (0.62 and 0.83) methods. There were small reductions in the post-operative correlation for both the Insall-Salvati and modified Insall-Salvati ratios.

The results indicate that interobserver variation in the post-operative measurement A is principally responsible for the deterioration of reproducibility of the Insall-Salvati and modified Insall-Salvati ratios. In both these ratios, measurement A represented the length of the deep surface of the patellar tendon. In the original measurements of Insall, he stated that if the patellar tendon could not be adequately visualised, its length could be gauged by using a “clearly defined notch” on the anterior aspect of the proximal tibia.
INTEROBSERVER VARIATION IN THE MEASUREMENT OF PATELLAR HEIGHT AFTER TOTAL KNEE ARTHROPLASTY

There are inaccuracies inherent in determining measurement B with the Blackburne-Peel, Caton-Deschamps and modified Insall-Salvati ratios, since it represents the length of the articular surface of the patella. Before TKA, provided that osteophytes were ignored, this was relatively uncomplicated. However, the articular surface of the patella may not be fully visible after replacement arthroplasty since it may be partially located within the trochlear groove of the femur (Fig. 2) and its length must be estimated.

Discussion

The results from our study indicate that, for patients undergoing TKA, there are significant differences in reliability and interobserver variability in the four main methods used to measure patellar height. These methods rely on the positional relationship between the patella and proximal tibia, while the insertion of the prosthesis alters the accuracy and reproducibility. These differences also vary depending on whether patellar height is measured before or after TKA.

The Blackburne-Peel and Caton-Deschamps ratios both require the precise identification of the proximal joint surface of the tibia for their evaluation. In joints with a significant amount of osteoarthritis or rheumatoid arthritis, visualisation of this surface is difficult and may need to be estimated. However, after TKA the tibial insert provides a precise point of reference, thereby improving the interobserver variability for these methods (Fig. 1). Our study, in order to give an accurate measurement to the new joint surface, compensated for the dishing of the tibial insert in the determination of measurement A for the Blackburne-Peel ratio. A similar compensation is difficult to introduce into the Caton-Deschamps measurement, since unlike the Blackburne-Peel method, it is not made perpendicular to the joint surface.

The application of a particular ratio to the measurement of patellar height in TKA depends on the information required by the clinician. The original description of patella baja was defined before joint replacement surgery and was related to shortening of the patellar tendon, distal positioning of the patella relative to the femoral trochlea and a reduction of the distance between the patella and tibial surface. After TKA, however, the patella may be positioned distal to the femoral condyles and closer to the joint surface of the tibia while the patellar tendon remains a constant length. This has been termed pseudo-patella baja, a reduction in patellar height relative to the joint surface and is related to the thickness of the insert (Fig. 3). It can be due to ‘overstuffing’ of the knee, or as a necessary consequence of soft-tissue release and occurs when the thickness of the tibial tray plus insert is greater than the thickness of tibia removed.

True patella baja necessitates shortening of the patellar tendon, so its measurement requires indices which relate to...
the tibial tuberosity and not to either the tibial plateau or the tibial component of a TKA. The Insall-Salvati and modified Insall-Salvati ratios relate the length of the patella to the length of the patellar tendon and are therefore independent of the joint surface.

The biomechanics of the patellofemoral joint are related to the position of the patella within the trochlear groove and changes to this relationship have been shown to be detrimental. During weight-bearing, the position of the femoral condyles, and hence the trochlear groove, is directly related to the position of the joint line. It is therefore logical to measure the height of the patella from the joint surface, as changes in this height will indicate potential problems. This is especially the case in TKA in which changes in the position of the joint line will not be identified by measuring the length of the patellar tendon.

Despite the theoretical advantages of using the Insall-Salvati and modified Insall-Salvati methods for the assessment of true patellar height, our study highlights their inferior interobserver reproducibility after TKA, mainly related to difficulties in identifying the patellar tendon and tibial landmarks on post-operative radiographs. However, although the Blackburne-Peel and Caton-Deschamps ratios show a greater degree of correlation after TKA, they are affected by the changes in the position of the joint line and do not accurately correlate with true patellar height.

Thus, for the assessment of patellar height in patients undergoing TKA, the clinician should tailor the ratio used to the requirements. Measurement of the true patellar height and identification of true patella baja or alta, necessitate the use of the Insall-Salvati or modified Insall-Salvati ratio. However, these ratios have inferior interobserver correlation and reproducibility; measurements after operation are misleading if the position of the joint line has been altered. The Blackburne-Peel and Caton-Deschamps ratios evaluate patellar height relative to the joint surface and will identify pseudo-patella baja. These methods have superior reliability and interobserver correlation after TKA.

We wish to acknowledge the valuable help and comments of Dr A. Saifuddin (Consultant Radiologist, Royal National Orthopaedic Hospital) in the preparation of this paper. No other benefits have been received or will be received from a commercial party related directly or indirectly to the subject of this article.

References
Appendix 22

Kieffer WKM, Dawe EJC, Lindisfarne EA, Rogers BA, Nicol S, Stott PM.

Contribution by BA Rogers.
Concept & planning
Manuscript writing & editing

Citation Metrics
Web Of Science: 2
Google Scholar: 0
Altmetrics:
Tweets: 2
Facebook: 0
Mendeley readers: 9
The role of total hip arthroplasty (THA) for fracture in octogenarians remains unclear. Over a two-year period, 354 patients aged ≥ 80 years were admitted with a displaced intracapsular hip fracture. Using defined clinical guidelines, 38 patients underwent THA with a median age of 84 years, mean follow-up of 20 months. Primary outcomes were dislocation, 30-day and one-year mortality, revision surgery and periprosthetic fracture. There were no dislocations or periprosthetic fractures and patient survival was 97% at 30 days and 87% at one year. There was one revision for deep infection. This study demonstrates that THA for selected octogenarians can be performed safely, allows the majority of patients to return to independent living and has a low complication rate.

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Total Hip Arthroplasty (THA) for displaced intracapsular hip fracture has been shown to provide better function, lower re-operation rates and greater cost-effectiveness when compared to Hemiarthroplasty (HA) [1–3]. With an increasingly active and independent elderly population the use of THA for managing hip fracture is likely to increase. Recent UK guidance from the National Institute for Health and Clinical Excellence (NICE) has recommended total hip arthroplasty for this injury in patients who are able to walk independently and have no cognitive impairment [4]. Concerns remain about the suitability and safety profile of THA for elderly patients possibly due to the perceived greater risk of dislocation associated with THA when compared to Hemiarthroplasty [2]. There is debate regarding application of the available evidence which has led to widespread variations in treatment; patients in England and Wales are only one third as likely to receive a THA compared to an equivalent population in Sweden [5].

The purpose of this study was to establish the safety profile, survival and short-term results for patients of 80 years and over who received THA for fracture according to United Kingdom National guidelines [4]. Functional outcome scores such as the Oxford/Harris Hip Scores were not performed.

Keywords: hip fracture total hip arthroplasty trauma neck of femur elderly


The Conflict of Interest statement associated with this article can be found at http://dx.doi.org/10.1016/j.arth.2013.07.017.

Reprint requests: Will K.M. Kieffer, MBBS BSc MRCS (Eng), Department of Trauma and Orthopaedics, Fracture Clinic, Royal Sussex County Hospital, Eastern Road, Brighton, BN2 5BE.

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http://dx.doi.org/10.1016/j.arth.2013.07.017
Results
Demographics

Three hundred and fifty four patients 80 years and over were admitted with an intracapsular fractured neck of femur over the two-year period (See Fig. 1). There were 38 patients from this cohort selected for THA. Median age was 84 years. (Range 80–93). 14 patients were male, 24 were female. The surgical approach chosen and grade of the operating surgeon are shown in Table 1 whilst Table 2 shows ASA grade. Mean follow-up was 20 months (Range 12–33 months). Follow-up was by clinic appointments. The hemiarthroplasty cohort of the other

<table>
<thead>
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<th>Grade of Surgeon</th>
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<td>40</td>
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<tr>
<td>Associate Specialist</td>
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<td>15</td>
</tr>
<tr>
<td>Registrar</td>
<td>17</td>
<td>45</td>
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<tr>
<td>Surgical Approach</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Posterior</td>
<td>13</td>
<td>32</td>
</tr>
<tr>
<td>Anterolateral</td>
<td>25</td>
<td>68</td>
</tr>
</tbody>
</table>

Discussion

The management of hip fracture in elderly patients is an increasingly important aspect of Orthopaedic care worldwide. This study shows that THA is a safe and efficient use of resources when performed in selected patients over 80 years old. This represents a significant caseload for Orthopaedic services within the United Kingdom and is likely to increase in the future.

In the UK projections estimate that the incidence will rise from 70,000 patient events per year in the UK to 101,000 by 2020 [7]. The
potential cost of treating all fragility fractures in this patient population is £2.2 billion per year [8]. Several randomised studies have supported the use of arthroplasty over internal fixation of displaced intracapsular fractures [9–11]. Whether a patient undergoes THA or hemiarthroplasty remains controversial although the use of THA in independently mobile patients with displaced fractures has been supported by three randomised controlled trials in their short term results [1,12,13].

The benefits of THA over Hemiarthroplasty are balanced by an increased risk of dislocation, greater operative time and higher implant cost [14]. The dislocation rate after THA ranges from 2% to 20% [1,13,15–21] following fracture although this may be reducing as the use of larger head sizes becomes commonplace [22]. There were no dislocations in the group of patients we studied. Although the sample size was small, undoubtedly there was no evidence of a high dislocation rate in this group. In fact the dislocation rate after HA in our cohort was significant and doubtless has morbidity and mortality associated with it as evidenced by Blevitt et al [23] who suggested that 6 months post dislocation the mortality is 65%.

All of the factors used to select patients for THA are also independently associated with survival after hip fracture hence this cohort would be expected to demonstrate high rates of survival [24–26]. Indeed the survival is predictably high in this cohort (89.5% at 1 year). The aim of THA is to afford better post-operative function which we have shown by the high proportion of patients returning to independent living.

Phillips et al [27] reported the results of elective THA in patients over 90 years. 52% were able to return to their normal abode whilst 45% required prolonged rehabilitation. Encouragingly over 60% of our patients returned to their pre-morbid level of independence after hip fracture.

Patients selected for THA for fracture can have their procedure delayed or postponed whilst a suitably skilled surgeon becomes available in smaller centres which is frequently not the case for HA. This model of hip fracture care requires sufficient manpower to perform THA which might not be possible in all centres. In addition as the use of THA for fracture becomes more commonplace this will have implications for training and workforce planning which are yet to be defined. If the Australian model is to be followed where outcomes are measured against caseload then patients may be best served by a surgeon with significant experience in hip arthroplasty performing their surgery.

Delays to surgery impact on patient experience, mortality, length of stay and recently the attainment of the best practice tariff for hip fracture [28]. These factors may alter the cost–benefit ratio of THA compared with Hemiarthroplasty which was estimated at £3000 per patient [29]. We did not attempt to delineate the impact delay to surgery has on outcomes and survival.

Confounding factors in this study relate to the selection bias for THA versus HA. Whilst in our unit we try to quantify this with a scoring system, in many places it is down to surgeon discretion alone as to what implant a patient receives. These confounding factors are the basis for selection and those judged to be ‘less fit’ pre-morbidly are arguably more likely to have worse outcomes and prognoses. Hemiarthroplasty is not associated with lesser risk however as evidence exists regarding complications with one showing a 6 month mortality after dislocated hemiarthroplasty for fractured neck of femur as 65% [23] and another showing that of those patients who suffer a periprosthetic fracture 24% die prior to fracture union [30].

Future studies in this area

Hip fracture studies aiming to demonstrate long-term functional outcome must be very large as high rates of mortality leave only a small group of survivors for assessment. Bannister et al [31] had an overall mortality of 42% at a mean follow-up of 9 years and only a 4% loss to follow-up. Large multi-centred RCTs have similar difficulties [12,17,32] in maintaining large patient cohorts. One systematic review [2] was unable to conclude definitively that THA affords superior functional outcomes and lower re-operation rates when compared to HA. This ambiguity results from the distinct heterogeneity in the population in question. Matching patients for example comparison with a hemiarthroplasty group is very difficult as selection bias is the discriminator used to determine which patients are suitable for THA. Our cohort demonstrates this well as those patients who are often less fit and less likely to survive longer term to benefit from a THA are by default selected for HA, confounding their trend towards worse results.

Conclusions

Our findings, demonstrate that THA in suitably selected octogenarians can produce excellent short term results without a high risk of complication. However evidence regarding the long-term cost-effectiveness and patient related outcomes of these patients will require a much larger patient cohort.

An increasingly active elderly population now expects optimal functional capability following a fracture of the femoral neck. This study demonstrates that total hip arthroplasty for selected octogenarians affords a low complication rate with the majority of patients returning to independent living.

References

Appendix 23

Rogers BA, Carrothers AD.
Using patient-reported outcome measures to assess health-care quality.

Contribution by BA Rogers.
Concept & planning
Manuscript writing & editing

Citation Metrics
Web Of Science: 1
Google Scholar: 2
Altmetrics: 0
Tweets:
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Mendeley readers:
Using patient-reported outcome measures to assess health-care quality

The transparency of surgical outcomes data and the drive for quality has been highlighted since the public inquiry, led by Professor Ian Kennedy, into children’s heart surgery at the Bristol Royal Infirmary. This was formalized in Lord Darzi’s 2008 report High Quality Care for All, that proposed the NHS should: ‘systematically measure and publish information about the quality of care’. Subsequently the NHS White paper, Equity and Excellence: Liberating the NHS (Department of Health, 2010), set out the ambitions and aims of the NHS and in particular that it should provide: ‘...a service that offers care that is safe and of the highest quality.’

Patient-reported outcome measures are standardized, validated questionnaires that are completed by patients to measure their own functional status and general health. They were originally designed for use in clinical trials (Fitzpatrick et al, 1998). Since 2009, wider use of patient-reported outcome measures within the NHS has been proposed to augment mortality data from Hospital Episode Statistics, which are considered an insufficient measure of quality.

However, controversies exist regarding the widespread implementation, data collection and interpretation of patient-reported outcome measures within the UK and internationally (Dawson et al, 2010). This editorial considers some of the relevant issues inherent in collecting and analysing patient-reported outcome measures data.

Introduction of patient-reported outcome measures

Many scoring systems and questionnaires have been designed both to assess treatment effectiveness in the context of research and to quantify patient perspectives of care outcomes. The validity of this later use remains somewhat controversial (Judge et al, 2011). The outcomes-based definition of patient-reported outcome measures distinguishes them from questionnaires used to measure patients’ experience of the care process.

To date, patient-reported outcome measures data have been used in clinical trials, national audits (Williams et al, 2002) and registers for joint replacement (Malchau et al, 2005). However, since April 2009, it has been mandatory for NHS hospitals to collect patient-reported outcome measures data for four separate surgical procedures in the first instance: inguinal hernia repair, varicose vein surgery, hip and knee replacements. The aim is to achieve a quantifiable and transparent improvement in quality.

With the use in the context of audit and ‘registers’ to inform individual care and manage the performance of health-care providers, patient-reported outcome measures data are now becoming increasingly widespread at a local level as well as national level (Greenhalgh et al, 2005; Marshall et al, 2006).

Components of patient-reported outcome measures data

There are two principal components of patient-reported outcome measures data: 1. A measure of a patient’s perception of his/her general health (‘generic’ health status) 2. The patient’s perceptions of his/her health in relation to pathology (‘specific’ health status).

Patients complete patient-reported outcome measure questionnaires by rating their current health status in response to individual questions. Commonly used generic questionnaires include Short form 36, EQ5D, ASCOT and Perceived Impact of Problem Profile. Commonly used specific questionnaires include the Parkinson’s disease questionnaire, visual function questionnaire and Oxford hip and knee scores. The individual ratings are combined, usually one generic and one specific, to produce an overall score to represent an underlying phenomenon or ‘construct’, such as ‘perceived level of pain’ or ‘anxiety’.

The analysis of patient-reported outcome measures tends to focus on the amount of change that has occurred in the patient’s condition or his/her general health-related quality of life, as represented by a change in patient-reported outcome measure score following an intervention.

The collection of patient-reported outcome measures data outside the remit of clinical research risks a lack of clarity and focus, which may in turn result in sub-optimal data interpretation. Therefore clinicians and managers should be aware that the quality of both processes and outcomes can be audited (Table 1).

Collection of patient-reported outcome measures data

It is essential that there is a cogent reason for data collection and a defined duration of follow-up when no clear hypothesis or research question exists. Clearly stated inclusion and exclusion criteria will aid the standardization of data collection and interpretation. In addition, the data points

Table 1. Specific examples of the processes and outcomes that may be quantified with patient-reported outcome measures data

| Processes | Communication: improved communication between patient and health-care provider |
| Concordance: agreement between patient and health-care provider about problems and solutions |
| Provider behaviours: changes in health-care providers’ diagnosis and treatment of patient conditions |
| Patient behaviours: patient self-efficacy, adherence and behavioural change |
| Outcomes | Patient satisfaction: patient-reported satisfaction with the consultation, treatment or care overall |
| Health status: patients’ health and wellbeing as indicated by clinical measures or patient reports |
| Resource use: patients’ subsequent use of health and other services |
need to be clearly specified, e.g. are the data patient-specific or pathology-specific (i.e. one patient may have two arthritic knees).

The logistics of data collection should be clarified before the widespread implementation of patient-reported outcome measures, preferably with the use of a pilot study. In essence who, how, when and where is the data to be collected? In particular, has informed consent been obtained, is a written protocol available and is all the relevant documentation available in a variety of languages?

In order to minimize bias, mechanisms need to be in place to ensure that only the patients are responding. Further, the means of patient recruitment needs to be considered, e.g. including only patients attending the outpatients department risks selection bias, as there is likely to be a greater proportion of patients with problems attending. A mechanism is needed to reduce non-responders, incomplete or duplicated data. Finally, as with all confidential patient information, data storage must be secure, while remaining easily retrievable for analysis.

Potential benefits of patient-reported outcome measures data

The appropriate implementation and interpretation of patient-reported outcome measures data collection has several potential benefits. It can have a diverse role in altering how health problems are perceived and managed by patients and health-care providers. Patients are stimulated to present symptoms elicited in traditional consultations. Health professionals are encouraged to think beyond the conventional limitations in identifying problems and selecting solutions jointly with patients. There is also improved identification of goals and priorities over time between health professional and patients faced with complex, evolving and multifaceted problems. However, to date few academic studies have validated the role of the questionnaires currently used for patient-reported outcome measures data against these potential benefits.

Potential problems with patient-reported outcome measures data

The interpretation of patient-reported outcome measures data has an inconsistent impact on health status depending on the actual questionnaire used. For any single condition, the choice of patient-reported outcome measure questionnaire used will influence the study results. To increase provider understanding of patient needs, priorities and/or preferences, the most appropriate patient-reported outcome measures should be applied to accurately reflect these issues. However, the most commonly used patient-reported outcome measures currently only capture a single facet of patient health or were created without the involvement of patients. Therefore, they may not actually accurately reflect patients’ needs, priorities and preferences (Higgins and Carr, 2001). For example, questions relating to sports activity are not relevant to most elderly patients. While numerous measures are available (see www.proqolid.org), care is needed to ensure the most appropriate choice of data capture is used.

Conclusions

Clinicians should question what goals are achievable with the routine use of patient-reported outcome measures data for a specific patient population and whether all the potential benefits (processes and outcomes) are being used. More multidimensional and individualized measures, although more difficult to interpret, may help patient-reported outcome measures to optimize patient-centred care (Marshall, et al., 2006). Careful and thorough evaluation of patient-reported outcome measures will be required to ensure these tools enhance patient involvement (Greenhalgh, et al., 2005).

The widespread introduction and interpretation of patient-reported outcome measures data is not straightforward and will require auditing at local and national level since the definite advantages remain unclear.

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Arthroplasty and Trauma/Lower Extremity Reconstruction Surgery
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KEY POINTS

- Patient-reported outcome measures are standardized questionnaires that allow patients to measure their functional status and general health.
- Patient-reported outcome measures are being used throughout the NHS to evaluate health-care quality.
- Processes and outcomes may both be audited with patient-reported outcome measures.
- To afford valid information, the choice of questionnaire and the methods used to collect and interpret the data are critical.
- The definite advantages of patient-reported outcome measures remain unclear.
Appendix 24

Rogers BA, Alolabi B, Carrothers AD, Kreder HJ, Jenkinson RJ.
Can the pre-operative Western Ontario and McMaster score predict patient satisfaction following total hip arthroplasty?

**Contribution by BA Rogers.**

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HIP

Can the pre-operative Western Ontario and McMaster score predict patient satisfaction following total hip arthroplasty?

In this study we evaluated whether pre-operative Western Ontario and McMaster Universities (WOMAC) osteoarthritis scores can predict satisfaction following total hip arthroplasty (THA). Prospective data for a cohort of patients undergoing THA from two large academic centres were collected, and pre-operative and one-year post-operative WOMAC scores and a 25-point satisfaction questionnaire were obtained for 446 patients. Satisfaction scores were dichotomised into either improvement or deterioration. Scatter plots and Spearman’s rank correlation coefficient were used to describe the association between pre-operative WOMAC and one-year post-operative WOMAC scores and patient satisfaction. Satisfaction was compared using receiver operating characteristic (ROC) analysis against pre-operative, post-operative and δ WOMAC scores.

We found no relationship between pre-operative WOMAC scores and one-year post-operative WOMAC or satisfaction scores, with Spearman’s rank correlation coefficients of 0.16 and –0.05, respectively. The ROC analysis showed areas under the curve (AUC) of 0.54 (pre-operative WOMAC), 0.67 (post-operative WOMAC) and 0.43 (δ WOMAC), respectively, for an improvement in satisfaction.

We conclude that the pre-operative WOMAC score does not predict the post-operative WOMAC score or patient satisfaction after THA, and that WOMAC scores can therefore not be used to prioritise patient care.

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Total hip arthroplasty (THA) is one of the most commonly performed and successfully performed orthopaedic procedures, but predicting which patients will benefit most from surgery remains difficult and controversial.\(^1\) The routine collection of patient-reported outcome measures (PROMs) has been introduced in several countries, not only to quantify success but also as a possible means of defining a threshold for surgery.\(^1,2\) The focus has shifted from the technical aspects of surgery to outcome measures, such as implant survival, to PROMs, including the Oxford scores\(^1,3,4\) and Western Ontario and McMaster Universities (WOMAC) osteoarthritis index.\(^5,6\) These scores were introduced to compare outcomes in clinical trials and have subsequently been shown to be reliable and valid in that setting.\(^5,9,10\) The WOMAC osteoarthritis index assesses pain, stiffness and physical function in patients with osteoarthritis (OA) of the hip and knee.\(^11,12\) It consists of 24 items divided into three subscales and the total score ranges from 0 to 100, with 0 being the best possible score and 100 being the worst possible score.

Expanding the use of PROMs to prioritise patients for surgery is controversial and currently lacks a substantial base of evidence.\(^1\) A recent study based in the United Kingdom which prospectively analysed a cohort of 1523 total knee arthroplasties (TKAs) and 1784 THAs demonstrated that the pre-operative Oxford hip and knee scores did not predict post-operative patient satisfaction and should not be used to prioritise care.\(^1\)

Similar work comparing other ways of assessing outcome, such as the WOMAC score, has not been undertaken. In addition, the relationship between PROMs, satisfaction and objective activity scores remains unclear. The aim of this study was to assess to what extent the pre-operative WOMAC score can be used to predict WOMAC scores and satisfaction one year following THA.

Patients and Methods

We reviewed prospectively collected data from the SafeT (Safe Activities Following Elective THA) study (funded by the Canadian Institute of Health Research, grant number MOP84316), performed at two large academic...
This prospective multi-centre cohort study evaluates patient activities following THA.

We analysed the data for 446 patients who underwent THA and who were available for review one year post-operatively. A total of 217 patients (49%) were men. The average age of the patients at the time of surgery was 63 years (25 to 80) and their average body mass index (BMI) was 30 kg/m$^2$ (19 to 38). An uncemented THA was used in 394 patients (88%), a hybrid construct in 48 (11%) and a cemented THA in four (1%).

The bearing surfaces were metal-on-polyethylene (374 patients, 84%), ceramic-on-polyethylene (35 patients, 8%), metal-on-metal (35 patients, 8%), ceramic-on-ceramic (one patient 0.2%) and metal-on-ceramic (one patient, 0.2%).

Fellowship-trained surgeons performed all operations. All patients were aged < 80 years and underwent primary THA with similar post-operative rehabilitation regimes. Overall, 438 underwent surgery for OA. The WOMAC scores were completed pre- and one year post-operatively for all patients, who also completed a 25-point satisfaction questionnaire at these times. Data collection was done by trained research assistants independently of the clinicians.

All patients who had fully completed WOMAC and satisfaction scores at both times were included. Demographic data (age and gender), comorbidities, diagnosis and the indication for surgery were also recorded. Satisfaction scores were dichotomised into either improvement or deterioration, using a previously described method.

**Statistical analysis.** Spearman’s rank correlation coefficient and scatter plots were used to evaluate the correlation between the pre-operative WOMAC scores and the WOMAC scores and patient satisfaction one year post-operatively. Receiver operating characteristic (ROC) analysis was used to compare satisfaction scores against three polynomial variables, the pre-operative, post-operative and δ WOMAC scores. δ WOMAC was defined as the change between the pre- and one-year post-operative WOMAC scores. ROC analysis was also used to identify thresholds associated with patient satisfaction.

The area under the ROC curve (AUC) was interpreted as the possibility of correctly identifying whether or not patients were satisfied one year post-operatively, based on their pre-operative scores. This area ranges in value between 0.5 (useless test with no accuracy) and 1.0 (perfect accuracy).

**Results**

Data were collected for 446 patients who had completed both pre-operative and one-year post-operative WOMAC and satisfaction scores; 12 patients had been previously excluded because of incomplete data. The average pre- and post-operative and δ WOMAC and satisfaction scores are shown in Table I. A scatter plot analysis showed no relationship between the pre-operative WOMAC score and post-operative satisfaction (Fig. 1), or between the pre- and post-operative WOMAC scores (Fig. 2). Spearman’s rank correlation coefficient was −0.05 (95% confidence interval (CI) −0.08 to 0.18) between the pre-operative WOMAC score and the one-year post-operative satisfaction and 0.16 (95% CI 0.12 to 0.19) between the pre- and one-year post-operative WOMAC scores.

The ROC curve analysis showed that for an improvement in satisfaction, the AUC for the pre-operative WOMAC (Fig. 3), the post-operative WOMAC (Fig. 4) and the δ WOMAC scores (Fig. 5) was 0.54 (95% CI 0.48 to

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| Table I. The mean, standard deviation (SD) and range of the pre-operative, post-operative and δ Western Ontario and McMaster Universities osteoarthritis index (WOMAC) and satisfaction scores for all patients |
|-----------------|-----------------|-----------------|
| WOMAC score     | Satisfaction    |
| Pre-operative   |                 |
| Mean (SD) (range) | 51 (17) (2 to 94) | 22 (3) (6 to 25) |
| Post-operative  |                 |
| Mean (SD) (range) | 13 (15) (0 to 72) | 21 (4) (5 to 25) |
| δ                |                 |
| Mean (SD) (range) | 38 (3) (2 to 22) | 1 (1) (0 to 1)  |

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![Scatter plot of the pre-operative Western Ontario and McMaster Universities osteoarthritis index (WOMAC) scores against patient satisfaction one year after surgery.](image-url)
0.62), 0.67 (95% CI 0.59 to 0.73) and 0.43 (95% CI 0.38 to 0.43), respectively.

Discussion

This study shows that the pre-operative WOMAC score does not predict post-operative WOMAC scores or patient satisfaction with THA one year after surgery.

The goals of hip replacement surgery include pain relief, functional improvement and satisfaction.13 PROMs have been introduced as a means to quantify the success or otherwise of medical or surgical interventions, and also as a possible method of defining a threshold for intervention.1,2 However, the WOMAC score was initiated as a research tool to assess post-operative outcomes following hip and knee arthroplasty surgery. These PROMs are now commonly used to prioritise patients’ access to care, despite insufficient evidence for this purpose or a demonstrable correlation with patient outcomes or satisfaction.1,9-12 Furthermore, many studies have shown that pre-operative pain and function are not associated with satisfaction following surgery.14,15 In particular, Judge et al1 recently demonstrated that pre-operative Oxford hip and knee scores do not predict satisfaction, and concluded that these scores should not be used to prioritise patients for hip and knee arthroplasty surgery. Our findings are similar with regard to the use of the WOMAC scores in predicting outcome following THA.

The analysis of the ROC curves illustrates no threshold in the pre-operative, post-operative or WOMAC scores that predicts satisfaction. Even though the AUC of the post-operative WOMAC was higher than the pre-operative or δ WOMAC scores, it relates to a sensitivity of 64% and a specificity of 66%, both of which are poor. Also, the post-operative WOMAC score is a measure only available after surgery, and as such it can be of no use in stratifying patients before operation.

Quantifying satisfaction one year following surgery is appropriate, as previous studies have shown that satisfaction remains high beyond six months after both THA and TKA.16-18 Although most patients are satisfied following THA, a small proportion are not,14,19,20 and predicting such
patients is difficult. It has been reported that patients with inferior pre-operative mental health status and/or depression are more likely to be dissatisfied.14,21 Age, gender and comorbidities do not seem to be associated with patient satisfaction, 14-16,21,22 but a single study22 has shown increased age to be associated with dissatisfaction after THA, whereas poorer results in younger patients have been reported after TKA.13

Designing a dimensional assessment tool that includes patient-reported outcomes, pain, function, quality of life and satisfaction provides a predictive capacity for outcome and satisfaction would be highly beneficial. The ability to identify key factors associated with patient dissatisfaction or inferior outcomes is clearly important,14-16,21,22 and satisfaction and provides a predictive capacity for outcomes in total hip replacement. A comparison of hip outcomes in patients with and without THA, whereas poorer results in younger patients have been reported after TKA.13

References


