A multidisciplinary team approach to two-stage revision for the infected hip replacement

A MINIMUM FIVE-YEAR FOLLOW-UP STUDY

We report the five year outcomes of a two-stage approach for infected total hip replacement. This is a single-surgeon experience at a tertiary centre where the more straightforward cases are treated using single-stage exchange. This study highlights the vital role of the multidisciplinary team in managing these cases.

A total of 125 patients (51 male, 74 female) with a mean age of 68 years (42 to 78) were reviewed prospectively. Functional status was assessed using the Harris hip score (HHS). The mean HHS improved from 38 (6 to 78.5) pre-operatively to 81.2 (33 to 98) post-operatively. Staphylococcus species were isolated in 85 patients (68%).

The rate of control of infection was 96% at five years. In all, 19 patients died during the period of the study. This represented a one year mortality of 0.8% and an overall mortality of 15.2% at five years. No patients were lost to follow-up.

We report excellent control of infection in a series of complex patients and infections using a two-stage revision protocol supported by a multidisciplinary approach. The reason for the high rate of mortality in these patients is not known.

More than 10 000 revision total hip replacement (THR) procedures were performed in England, Wales and Northern Ireland according to their National Joint Registry report of 2013.1 The indication was infection in about 12% of these revisions.1

Infection following primary THR is a devastating complication with significant social and financial implications for both patients and healthcare organisations. Several forms of treatment have been described including early debridement,2 antibiotic therapy,3 single-stage revision to a cemented THR with antibiotic-loaded cement4 and a two-stage revision using either cemented5,6 or cementless components.7,8 Failure of treatment may lead to excision arthroplasty,9 arthrodesis10 or amputation.11

Different approaches may be used to achieve a high local concentration of antibiotics, maintain intact tissue planes and prevent soft-tissue contractures during the interval between stages in a two-stage procedure. These include the use of static and dynamic antibiotic-loaded cement spacers,5 which may be ready-made or hand-moulded at the time of the first stage,12 intramedullary cement spacers,13 cement balls14 and cement beads.7

The purpose of this study was to report the outcome of a two-stage revision protocol at a minimum follow-up of five years in an institution where the management of infected arthroplasty is guided by a multidisciplinary team.

Patients and Methods

We reviewed 125 consecutive patients who underwent two-stage revision THR between 2000 and 2008 by a single surgeon (FSH) at a tertiary centre. There were 51 men and 74 women meeting the diagnostic and inclusion criteria, with a mean age of 68 years (42 to 78). The mean follow-up was 8.6 years (5 to 13). The data were retrieved from a prospectively compiled database. The study had ethical approval.

All patients with an infected primary or revision THR and a minimum follow-up of five years were included in this study. We excluded those who underwent single-stage revision THR, which constitute about 20% of our revision workload, and revisions undertaken after failure of previous two-stage revision for infection elsewhere. A selective strategy was adopted for the treatment of infected THR by stratifying certain patients, including those with an uncomplicated problem (not immunocompromised, no systemic disease, no concurrent sepsis and no reinfection), with straightforward anatomy (no bone loss and no significant soft-tissue compromise) and an identified organism to be treated by single-stage revision, while reserving...
The diagnosis of infection was based on a detailed history, typically of pain and/or a discharging sinus. Confirmation of infection depended on aspiration of the hip and raised inflammatory markers; CRP > 10 mg/l (0 to 5) or an ESR > 30 mm/hr (0 to 15). A microbiological diagnosis was preferable prior to the first stage. All patients included in this study satisfied the criteria for diagnosing peri-prosthetic joint infection as proposed by the American Musculo-skeletal Infection Society. The multidisciplinary team included microbiologists, infectious disease specialists, orthopaedic surgeons, radiologists, physiotherapists and physicians who reviewed all patients, and their management was discussed at every stage in their pathway (Fig 1). The outcome of aspiration and biopsy was used to isolate the micro-organism and determine its antibiotic sensitivity and the most appropriate antibiotics for the first stage. Many tissue samples were sent at the time of this operation and helped to determine the type and duration of antibiotic treatment in the interval period, and the antibiotic cover required for the second stage.

Operative technique. The first stage involved removal of all implants and foreign material including cement and cement restrictors, followed by extensive debridement and irrigation with at least six litres of normal saline. A minimum of five samples were sent for microscopy, culture, sensitivity, gram staining and extended cultures. A dose of...
intravenous antibiotics was then given intra-operatively based on pre-operative microbiology results.

An antibiotic-loaded cement spacer, either dynamic or static, was inserted after changing drapes and equipment. The spacer usually contained 3 g of vancomycin and 2 g of gentamicin per 40 g sachet of Palacos R cement (Schering Plough Ltd, Labo nv, Belgium), unless otherwise indicated.

Following the first stage, a course of intravenous antibiotics, usually Teicoplanin, was commenced until the sensitivities of the intra-operative samples were available and discussed at the multidisciplinary meeting, at which point the antibiotic programme would be suitably adjusted. Patients usually received antibiotics for at least six weeks with sequential clinical, serological and microbiological assessment. We usually stopped antibiotics at least two weeks prior to the second stage to allow evaluation of the patient’s response when not taking antibiotics.

The decision to proceed to the second stage was based on decreasing serum levels of inflammatory markers (c-reactive protein (CRP) and erythrocyte sedimentation rate (ESR)). However, a normal CRP and ESR was not an absolute requirement pre-operatively. Nutritional markers were also monitored during the interval between the two stages, with an improvement in the serum levels of albumin and/or transferrin considered as important as a reduction in CRP and ESR.

A healthy dry surgical wound was a pre-requisite for proceeding to the second stage. Occasionally the particular circumstances of the patient dictated an earlier second stage; for example when they were unable to leave the hospital for social reasons, were in considerable pain following the first stage or were unwilling or unable to comply with the planned date for their second stage procedure.

We had a low threshold for repeating the first stage with a further debridement and irrigation if inflammatory markers remained elevated or the wound continued to discharge. During the second stage, we obtained gram stains and frozen sections intra-operatively if there was any doubt of persistent infection, otherwise we proceeded as planned. It was not standard practice to send frozen sections in every case.

Patients were seen in clinic two and six weeks, three, six and 12 months post-operatively and annually thereafter with clinical, radiological and serological assessment.

The Harris hip score (HHS) was used to assess the functional outcome.20 Radiographs for all patients were examined at each follow-up visit using the radiological criteria outlined by Johnston et al21 in cases of loosening of both acetabular and femoral components. Anteroposterior and lateral views of the ipsilateral femur were taken with the hip in neutral rotation and abduction. The radiographs were classified according to the degree of subsidence or radiolucency surrounding either component.7

Statistical analysis. Patients were dichotomised into two groups depending on their source of referral (in-house vs external referrals), complexity (very complex vs less complex) and number of revisions prior to this revision (first revision vs multiple revisions). The very complex cases were defined as those with polymicrobial infections +/- cases needing more than one first stage revision +/- externally referred +/- second or third revision cases. Statistical analysis was performed using SPSS version 17 software (SPSS Inc., Chicago, Illinois). The chi-squared test was used for data analysis to compare dichotomised groups and micro-organisms before and after 2004. Significance was set at a p-value < 0.05. Kaplan–Meier survival analysis was conducted to calculate survivorship.

Results
No deaths were reported between the first and second stages and no patients were lost to follow-up. For 64 patients (51.2%), this was the first revision, 40 patients (32%) had one prior revision and 21 (16.8%) had two prior revisions for reasons not related to infection. We identified the micro-organism pre-operatively in 101 patients (81%). In 11 patients (9%), it was identified post-operatively, and in 13 (10%) no organisms were isolated, however, they clinically had periprosthetic infection including some with draining sinuses found to be communicating with the prosthesis at operation. A second organism was isolated from the intra-operative samples in 14 patients (11%).

<table>
<thead>
<tr>
<th>Micro-organism</th>
<th>Before 2004</th>
<th>After 2004</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Staphylococcus aureus</td>
<td>20</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>Methicillin-resistant staphylococcus aureus</td>
<td>6</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td>Coagulase-negative staphylococcus</td>
<td>6</td>
<td>15</td>
<td>0.04*</td>
</tr>
<tr>
<td>Methicillin-resistant staph. epidermidis</td>
<td>4</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>Polymicrobial</td>
<td>4</td>
<td>12</td>
<td>0.038*</td>
</tr>
<tr>
<td>Streptococcus</td>
<td>6</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>No growth</td>
<td>8</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Gram-negative bacteria</td>
<td>5</td>
<td>14</td>
<td>0.031*</td>
</tr>
<tr>
<td>Anaerobic</td>
<td>3</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Fungal</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Mycobacterial</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

*chi-squared test
Gram-positive organisms accounted for most infections with *Staphylococcus aureus* and coagulase-negative Staphylococcus isolated in 85 patients (68%). Methicillin-resistant *Staphylococcus aureus* (MRSA) was isolated in 20 patients (16%) of whom 18 had complete eradication of infection five years post-operatively. We observed a changing trend before and after 2004, with more coagulase-negative staphylococcus species (six before and 15 after 2004, \( p = 0.04 \)) and Gram–negative bacteria (five before and 14 after 2004, \( p = 0.031 \)). More samples had polymicrobial growth after 2004 (four before and 12 after, \( p = 0.038 \)) indicating the complex nature of these infected cases.

Dynamic antibiotic-loaded spacers, constructed perioperatively, were used in 119 patients (95.2%). Static spacers were used in the remaining six (7.5%).

We repeated the first stage twice in 19 patients (15.2%) and three times in seven patients (5.6%). Only one of the 19 patients had a recurrent infection during the first post-operative year (with MRSA).

The mean time interval between stages was 9.2 weeks (3 to 36). All hips were thought to be clear of infection by the second stage based on inflammatory markers, wound healing and serology. All tissue samples obtained during the second stage were negative on microscopy and culture, except in 17 patients (13.6%). Of these, 16 grew one organism from only one of the five samples, and one grew two different organisms from different samples. These were not deemed significant by the multidisciplinary panel.

Antibiotic treatment continued until the second stage in five patients (4%) who were immunocompromised.

The posterior approach to the hip was used by the senior author (FSH) in all patients during both stages and cementless acetabular and femoral components were implanted at the second stage. Morsellised cancellous bone allograft was used in acetabular reconstruction in 37 patients (29.6%) using our standard impaction bone grafting technique.22

The mean HHS was 38 (6 to 78.5) pre-operatively and had improved to 81.2 (33 to 98) five years post-operatively. In six patients (4.8%) further infection arose, five occurring in the first post-operative year and one after six years. All patients remain under review except for 19 (15.2%) who died of causes unrelated to infection with a mean time to death from surgery of 3.84 years (1 to 8) post-operatively. In these 19 patients there had been no reported infection. The overall rate of control of infection five years post-operatively was 96%. The survivorship of these patients is illustrated in Figure 2. No further infection occurred in patients whose revision had included bone grafting.

There was no statistical difference in the rate of further infection among the dichotomised groups (Table II).

A total of three patients (2.4%) had a single dislocation treated successfully by closed reduction. One patient (0.8%) suffered a periprosthetic fracture in a fall and underwent a further revision. Two patients (1.6%) developed aseptic loosening of the acetabular component at six and seven years, respectively and underwent further revision. The rate of further revision surgery five years post-operatively, including those with recurrent infection, was 7.2%. A review of radiographs demonstrated no evidence of loosening with good bony ingrowth up to five years.

### Discussion

This study demonstrates the benefits of a multidisciplinary approach in obtaining a high rate of control of infection following complex revision THR for infection. The results at five years were excellent despite excluding the more straightforward cases that underwent a single-stage revision during this time period. Our cohort included complex tertiary cases and a significant number who had undergone several previous operations. We noted a changing trend in the isolated micro-organisms after 2004 with more polymicrobial infections. In spite of this, the survivorship five years post-operatively was 96%.

The 19 patients who died may be considered as a limitation of the study as they had not survived to be exposed to the risk of recurrent infection. Other limitations include the relatively small sample size and the fact that this cohort represents the experience of a single surgeon. The sample size, however, compares favourably with other previous studies (Table III).23–30

Two-stage revision is a well-established practice allowing more than one debridement and period of antibiotic therapy, with sensitivities being obtained prior to the second stage, and the freedom to use cementless components with or without bone grafting.

Good results have been reported following single-stage revision with antibiotic loaded cement but lower rates of
eradication of infection when cementless components are used.31 Winkler et al32 however, reported a mid-term rate of eradication of infection of 92% in 37 patients using antibiotic impregnated allograft and cementless components in single-stage revision.

A recent systematic review without meta-analysis showed similar rates of further infection in single- and two-staged procedures. However, better functional outcomes were noted using single-stage revision.33 The latter finding, however, was not statistically significant in most of the studies that were reviewed. We did not intend to compare these two procedures. Our purpose was merely to review the results of two-stage revision THRs undertaken for infection.

Table III shows the rates of control of infection that have been reported in the literature for two-stage revision using cementless components. The rates range from 79% to 100%,24 at a follow-up of between two and six years. Our rate of control at five years after two-stage revision for infection was 96%, with an improvement seen in functional outcome when assessed using the HHS.

We have taken five years as a reasonable time to assume that infection is eradicated but we recognise that it may recur later and recommend continued long-term follow-up in complex cases.

A potential disadvantage of two-stage revision is the reported morbidity and mortality. Berend et al12 showed that despite a high rate of control of infection two years post-operatively, using two-stage revision was associated with a high rate of mortality (7%; 14 hips) prior to the second stage. In our cohort, there were no deaths between the stages, and only one patient died during the first post-operative year, due to reasons not related to infection. The rate of mortality five years post-operatively was high (15.2%) and is probably related to the premorbid health of these patients. Our overall rate of mortality is similar to that reported by others. There are studies with follow-up of > five years reporting rates of mortality between 2.4%34 and 19%.26

Compared with the high failure rate (38%) reported by Berend et al12 in patients (n = 37 hips (18%)) with resistant staphylococcal infection, our two-stage technique supported by a multidisciplinary team shows a rate of eradication of 90%, with only two of 20 patients with MRSA becoming re-infected. This accounted for 33% of re-infections, with the remainder due to non-resistant organisms. Leung et al30 reported a failure rate of 21% following two-stage revision for infection with methicillin-resistant organisms. Volin et al35 reported clinical success with two-stage revision in the presence of resistant organisms, however, as expected, better results were shown with non-resistant organisms. In our study, 19 patients had two attempts at eradication of infection prior to the second stage and only one of these had a further infection with MRSA, demonstrating the ability to eradicate resistant organisms using this technique.

Two-stage revision can be used successfully in the presence of loss of bone requiring reconstruction. Hsieh et al36 used allograft and cemented components in 24 patients with an infected THR and a custom-made, antibiotic-loaded cement prosthesis as an interim spacer. They reported no further infection at a mean of 4.2 years (2 to 7) post-operatively.36 Similar results have been reported by others.7,23,37 We used morsellised allograft in 37 patients

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**Table II. Dichotomised data for the 125 patients**

<table>
<thead>
<tr>
<th>Dichotomised groups</th>
<th>Numbers</th>
<th>Re-infection</th>
<th>p-values*</th>
</tr>
</thead>
<tbody>
<tr>
<td>In-house referral</td>
<td>11</td>
<td>0</td>
<td>0.43</td>
</tr>
<tr>
<td>External referral</td>
<td>114</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Complex cases</td>
<td>81</td>
<td>3</td>
<td>0.43</td>
</tr>
<tr>
<td>Less complex cases</td>
<td>44</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>First revision</td>
<td>64</td>
<td>2</td>
<td>0.36</td>
</tr>
<tr>
<td>Second/third revision</td>
<td>61</td>
<td>4</td>
<td></td>
</tr>
</tbody>
</table>

*chi-squared test

**Table III. The reported rates of control of infection for two-stage revision arthroplasty of the hip in the literature (MRSA, methicillin-resistant *Staphylococcus aureus*; MRSE, Methicillin-resistant *Staphylococcus epidermidis*)**

<table>
<thead>
<tr>
<th>Study</th>
<th>Number of patients</th>
<th>Follow-up</th>
<th>Rate of control of infection (%)</th>
<th>Harris hip score (mean, range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haddad et al 20077</td>
<td>50</td>
<td>5.8 years</td>
<td>92</td>
<td>78 (54 to 92)</td>
</tr>
<tr>
<td>Koo et al 20018</td>
<td>22</td>
<td>44 months</td>
<td>95</td>
<td>Not reported</td>
</tr>
<tr>
<td>Berend et al 201312</td>
<td>186</td>
<td>53</td>
<td>83</td>
<td>Not reported</td>
</tr>
<tr>
<td>Wilson and Dorr 198923</td>
<td>13</td>
<td>&gt; 3 years</td>
<td>91</td>
<td>75 (range not reported)</td>
</tr>
<tr>
<td>Nestor et al 199244</td>
<td>34</td>
<td>47 months</td>
<td>82</td>
<td>Not reported</td>
</tr>
<tr>
<td>Fehring, Calton and Griffin 19925</td>
<td>25</td>
<td>41 months</td>
<td>92</td>
<td>81 (30 to 100)</td>
</tr>
<tr>
<td>Hoffman et al 200526</td>
<td>27</td>
<td>76 months</td>
<td>94</td>
<td>53 (36 to 68)</td>
</tr>
<tr>
<td>Kraay et al 200527</td>
<td>33</td>
<td>&gt; 2 years</td>
<td>92</td>
<td>Not reported</td>
</tr>
<tr>
<td>Masri et al 200728</td>
<td>29</td>
<td>&gt; 2 years</td>
<td>90</td>
<td>70 (42 to 100)</td>
</tr>
<tr>
<td>Fink et al 200929</td>
<td>36</td>
<td>35 months</td>
<td>100</td>
<td>90 (60 to 100)</td>
</tr>
<tr>
<td>Leung et al 201130</td>
<td>38</td>
<td>58 months</td>
<td>79 (MRSA &amp; MRSE)</td>
<td>Not reported</td>
</tr>
</tbody>
</table>
and cementless components, with no further infection in these patients and full bone-implant integration five-years post-operatively.

Certain aspects of two-stage revision remain controversial; for example, the timing of the second stage and the length of the interval between stages. The multidisciplinary team is useful in guiding this decision. Each patient is formally reviewed by the panel who formulate an individual treatment plan for the patient while maintaining collective responsibility. It is likely that the requirement for bacteriological advice that will be needed when dealing with infected THRs will continue to increase and will become more complicated.  

The decision-making at the time of the second-stage procedure is complex. The work published by the Rush University group on synovial aspiration and cell counts shows great promise in improving the accuracy of this decision.  

The management of the infected THR is an evolving field with particular focus on single-stage revision. However, with the increasing number of infections involving resistant, anaerobic, fungal and mycobacterial organisms, polymicrobial infection and bone loss, further research of the two-stage technique will be required. We found that, in spite of the complexity of the case mix, this procedure is effective in treating infected THRs. The reasons for the high rate of mortality in these patients is not understood. This study highlights that excellent results can be obtained using a two-stage revision, even after removal of the easier cases for single-stage treatment.

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References


