Two-stage revision of infected total knee replacements using articulating cement spacers and short-term antibiotic therapy

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We present a series of 48 patients with infected total knee replacements managed by the use of articulating cement spacers and short-term parenteral antibiotic therapy in the post-operative period. All patients had microbiological and/or histological confirmation of infection at the first stage of their revision. They all underwent re-implantation and had a mean follow-up of 48.5 months (26 to 85).

Infection was successfully eradicated in 42 of the 48 patients (88%). Six had persistent infection which led to recurrence of symptoms and further surgery was successful in eliminating infection in four patients. These rates of success are similar to those of other comparable series. We conclude that protracted courses of intravenous antibiotic treatment may not be necessary in the management of the infected total knee replacement.

In addition, we analysed the microbiological, histological and serological results obtained at the time of re-implantation of the definitive prosthesis, but could not identify a single test which alone would accurately predict a successful outcome.

The management of deep infection after total knee replacement (TKR) may be divided broadly into the use of component-retention or component-exchange procedures.

Component retention and debridement can be performed either arthroscopically¹ or as an open procedure,² the benefit of the latter being the ability to exchange the polyethylene insert. Varying levels of success have been reported for these procedures, but the earlier the diagnosis is made the higher is the chance of successful treatment.^{3,4}

Component-exchange surgery has been widely reported with different types of procedure,⁵ the use of spacer devices⁶ which may be static⁷ or mobile,^{8,9} and with differing periods of immobilisation and timing of the procedures. Most series report the prolonged use of antibiotics administered both locally and systemically. The advocates of spacer devices argue that the soft-tissue envelope is better preserved at the time of second-stage surgery. There are those who feel that the immobilisation achieved with static spacers complies better with the principle of resting the joint as part of the treatment of infection. Those who favour the use of an articulating spacer consider that movement is regained more readily after re-implantation of the definitive components.⁷

In our unit the management of these patients consists of two-stage debridement with the insertion of antibiotic-laden articulating cement spacers. Antibiotics are administered for two weeks after the first stage of surgery and until negative tissue cultures and histological reports are received after the second stage. We report the results of our experience of this treatment regime.

Patients and Methods

Between 1998 and 2003 two-stage reconstruction was undertaken by the senior author (RSJ) in a consecutive series of 48 patients with deep infection of a TKR. Data have been collected prospectively since 1998 and have now been reviewed retrospectively. There were no pre-operative exclusions from the series, although patients in whom a diagnosis of infection could not be established from microbiological or histological results were not included. All surgery was performed in the same laminar-flow theatres with disposable drapes and impervious gowns. A high-thigh tourniquet was used in all patients in whom the peripheral circulation was adequate and the body habitus allowed.

There were 28 men and 20 women with a mean age of 68.2 years (37.2 to 81.3). In 40 the initial TKR was for osteoarthritis and in eight

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Table I. Details of operations undertaken before primary knee replacement

Open reduction and fracture fixation	2
Patellar resurfacing	2
Patellectomy	2
High tibial osteotomy	2
Lateral release	1
Polyethylene insert exchange	1
Open washout	1
Howse procedure/tibial tuberosity realignment	1

for rheumatoid arthritis, four of whom were on immunosuppressive therapy with either steroids or methotrexate.

In 25 patients no surgery other than the TKR had been undertaken before this revision. In 11 patients some form of other soft-tissue or bony surgery had been conducted before the revision, one patient had two previous procedures (Table I). In six patients a previous revision for aseptic loosening had been undertaken, in five a previous revision for infection and in one patient two revisions had been performed as well as the initial primary joint replacement. A total of 41 standard condylar prostheses and seven stemmed revision prostheses had been used.

In 33 patients either diagnostic aspiration or arthroscopic biopsy was performed to confirm the diagnosis of infection. In the remaining 15, nine had rapid loosening of components and elevated inflammatory markers and were not investigated further before revision. The other six patients had discharging sinuses and again further investigation with invasive procedures was deemed to be unnecessary.

The mean time to revision was 3.3 years (5 months to 6 years), with 38 patients undergoing surgery within five years of their initial procedure. Ten patients presented at more than five years after their primary surgery.

The pre-operative diagnosis of infection was considered in the presence of certain clinical, serological and radiological findings. The inflammatory indices and plain radiographs were the main initial diagnostic aids. A total of 14 patients had technetium-99 scans which supported the diagnosis of infection and two had positive indium-111 scans. The definitive diagnosis of infection was confirmed by positive microbiological and histological findings from multiple deep and superficial tissue specimens taken at the time of surgery. Infection was diagnosed microbiologically when more than one tissue culture revealed similar organisms. Histological examination was performed on both frozen-section specimens at the time of surgery, and more formally at a later stage on fully-prepared specimens. The histological diagnosis was based on the presence of more than 10 neutrophil polymorphs per high power field.

These patients have been followed up annually both clinically and radiologically with none being lost to follow-up. We considered a successful outcome to be a functioning prosthesis with good relief from pain in the absence of clin-

ical evidence of infection. Radiological success was a stable prosthesis without evidence of progressive lucencies at the implant-bone interfaces. All patients with persistent discomfort were investigated using repeat inflammatory markers, bone scanning and aspiration when necessary to rule out recurrent infection.

A first-stage debridement with insertion of antibiotic-laden articulating polymethylmethacrylate spacers was performed. Using pre-fashioned latex moulds (Biomet, Warsaw, Indiana), spacers were fashioned using CMW cement with gentamicin (DePuy, Leeds, United Kingdom). One gram of vancomycin was added to each 40 g mix of cement. Intravenous vancomycin was administered for 14 days after surgery with adjustments made once cultures and sensitivities were available. The knee was immobilised in a straight-leg splint for the first five post-operative days after which it was mobilised and the patient encouraged to bear weight as tolerated using two elbow crutches.

Patients were re-admitted for a second-stage procedure once the inflammatory markers had improved and the soft tissue around the knee had softened. The mean time between stages was 4.3 months (6 weeks to 15 months). Nine patients had a delay of more than six months because of co-morbidities. Re-implantation took place if frozen-section specimens and the clinical appearance at the time of surgery were satisfactory. If the blood parameters and the clinical appearance of the knee failed to improve, a further debridement was undertaken.

At final re-implantation, a further debridement was performed after which the definitive components were secured with the same combination of antibiotic-laden cement. When the sensitivities from the first-stage specimens showed antibiotic resistance, the antibiotics in the cement were appropriately modified. Parenteral antibiotics were only administered until the intra-operative tissue culture and histological results were available from the second-stage surgery. If these cultures were found to be positive, systemic antibiotics were continued for a further two weeks.

Results

The mean follow-up was 48.5 months (26 to 85). One patient died of unrelated causes during follow-up. We successfully eradicated infection in 42 of the 48 patients. In the 25 patients in whom the only previous surgery on the knee had been the initial arthroplasty, our treatment was successful in 24. In the 23 with multiple previous procedures infection was eradicated in 18. There was one recurrent infection in the eight patients with rheumatoid arthritis and with a similar incidence of recurrence in patients with osteoarthritis.

Six patients had persistent infection, four of whom have undergone a successful further two-stage procedure. Two have been revised to a hinged prosthesis and two to an arthrodesis. The remaining two patients have declined further surgery preferring suppression of the infection with intermittent courses of antibiotics.

Table II. The organisms identified at the time of surgery

Organism	Number of patients
Coagulase negative staphylococcus*	30
<i>Staphylococcus aureus</i> *	5
<i>Beta-haemolytic streptococcus</i>	3
<i>Streptococcus faecalis</i>	2
<i>Pseudomonas</i> *	2
<i>Streptococcus oralis</i> *	2
MRSA*†	1
<i>Enterococcus faecalis</i>	1
<i>Staphylococcus xylosus</i>	1
<i>Streptococcus mitis</i>	1
<i>Streptococcus viridans</i>	1
<i>Staphylococcus simulans</i>	1
<i>Staphylococcus hyicus</i>	1

* denotes organisms identified in patients requiring a second debridement

† MRSA, methicillin resistant *Staphylococcus aureus*

Of the organisms found at the time of the first-stage surgery, coagulase-negative staphylococcus was the most frequently encountered, being found in 30 of the 48 patients (Table II). Multiple organisms were found in 11 patients.

It was considered necessary for six of the patients to undergo a repeat debridement between the first and second stages because of persistently elevated inflammatory markers and warmth and swelling of the knee. The organisms encountered in these patients are highlighted in Table II. Of these six patients, three had further positive cultures which in all cases revealed different organisms from those at the first-stage surgery.

At the time of second-stage surgery there were further positive cultures in 11 patients and two of these developed recurrent infection. Seven of these cultures revealed different organisms and four revealed persistent coagulase-negative staphylococcus. The remaining 37 patients had negative cultures at the time of second-stage surgery and of these, four developed recurrent infection.

The findings from the frozen sections performed at the time of the second-stage surgery indicated that in 33 patients there was no residual infection, but four of these developed recurrence of infection. In 14 patients it was thought that the frozen specimen could not exclude infection and two of these patients had recurrent infection.

The time interval between the first and second stages was less than six months in 39 patients, of whom five had recurrent infection. There was one recurrence in the nine patients who waited longer than six months for their second stage.

In 30 patients, modular stemmed revision prostheses were used for the reconstruction. Of the 48 patients 16 required rotating hinge prostheses and two were stabilised by arthrodesis nails. Both of these patients had previously undergone two previous revisions.

When considering the range of movement at follow-up there was a mean fixed-flexion deformity of 1° (0° to 15°). Five patients had a fixed-flexion deformity of more than 10°. The mean maximum flexion was 92° (30° to 120°) with only five patients having less than 80° of flexion. There was no association between the timing of the second-stage surgery and the range of movement achieved.

An analysis of the accuracy, and positive-predictive and negative-predictive values, for each of the investigations used is presented in Table III.

We have tried to determine which of the investigations were of most benefit at the time of the second-stage surgery. Neither the positive nor negative predictive values of microbiological cultures at the time of second-stage surgery were accurate enough to predict the recurrence of infection reliably. It would appear that the main role of microbiological specimens taken at the time of surgery was to define antimicrobial therapy at each stage. Their negative predictive value and specificity meant that negative results could be welcomed, but the overall accuracy of this test was still only 73%.

Frozen section was found to have a poor positive predictive value at the time of second-stage surgery. For the resources required, most surgeons would expect greater overall accuracy when using the results to determine whether or not to re-implant the definitive prosthesis. The negative predictive value for frozen section was similar when compared with that of previous studies,¹⁰ but still failed to identify four of the failures and was no more useful than the inflammatory indices.

The inflammatory markers were the best negative predictive investigation at the time of second-stage surgery, but their overall accuracy when considered with their positive predictive values meant that their usefulness was limited. Nevertheless, they remain one of the most accurate guides to a successful outcome.

Discussion

Initial observation of the overall rate of success of the method of treatment in our series suggests that the results may not be as favourable when compared with those of other published series. Most series report success rates

Table III. Value of investigations for diagnosing infection at second-stage surgery

Test*	Positive predictive value (%)	Negative predictive value (%)	Accuracy (%)
Microbiological culture	18	89	73
Frozen section	38	88	65
ESR + CRP	23	91	72

* ESR, erythrocyte sedimentation rate; CRP, C-reactive protein

ranging from 85% to 95%.^{7-9,11} However, in these reports multiply-operated patients made up only a small proportion of the cases as opposed to 52% in our series.

For those patients undergoing a first revision for infection with minimal previous surgery the success rate of this surgical technique was 96%. Two patients in this group required a repeat debridement and they had an infection with methicillin-resistant *Staphylococcus aureus* (MRSA) in one and multiple organisms in the other.

Previous studies looking specifically at the outcome of patients with multiply-operated knees have shown higher rates of failure even with prolonged treatment with antibiotics, some with rates of success as low as 41%.⁸ Our rate of success of 78% in this large group of patients compares favourably.

This disparity in the rate of successful eradication of infection appears to support the idea of different treatment regimes for different patterns of infection. It would appear that attention to the history of previous surgery and pre-operative microbiology results from aspirates may help to guide the surgeon in their choice of duration of antimicrobial treatment. However, given that there are no studies of the long-term outcome on significant numbers of multiply-operated knees, our results suggest that the treatment of deep infection around prosthetic joints is not simply a matter of adding more antibiotics.

We have found that within the limitations of this relatively small group there is no single investigation available at the time of re-implantation which can accurately predict the likelihood of a successful outcome. There were only 20 patients in whom all of the investigations were normal at the time of the second-stage surgery. One of these patients still went on to develop further infection. Of the 28 patients with at least one abnormal investigation at the time of second-stage surgery, 23 went on to a successful outcome. The further debridement undertaken at the time of second-stage surgery may well have contributed to these successes.

These results demonstrate that the available investigations can only play a limited part in reaching a decision and surgeons should be aware of this before relying too heavily on a single result to guide them. Our results do not support the quest for a full set of negative investigations before re-implantation since even this reassurance will not guarantee success.

When considering the infecting organisms we found that the overall distribution of organisms was similar to that of other series. Most were sensitive to our first-line antibiotics and there was only one case of MRSA infection. Given the small numbers of most organisms we were unable to identify specific organisms associated with the failure of this technique. It would appear that *Staph. aureus* may be associated with an increased need for repeat debridement and that coagulase-negative staphylococcus identified at the first stage is associated with positive cultures at the second stage. However, most of these patients had also had multiple previous operations which acted as a confounding variable.

Other studies¹² have suggested greater virulence of resistant organisms and multiple organism cultures, but we have been unable to add to this argument with our results.

Our study has shown the significance of previous interventions when considering a two-stage procedure. The greatest functional effect of multiple procedures seems to be a reduction in the quality and function of the extensor mechanism. For this reason, two of the multiply-revised knees required a modular arthrodesis nail as their definitive implant.

Although these are undoubtedly a different functional group they are included in this series since they demonstrate the application of this technique in the multiply-revised knee. We were unable to correlate the number of previous procedures with the post-operative range of movement. The final range of movement in this group compared well with that of other series⁶ with over 75% of patients achieving a minimum of 90° of flexion and 89% a minimum of 80°.

The timing of the second-stage surgery is often foremost in the patient's mind. There is often some pressure to expedite the second-stage surgery in order to return to a more normal way of life as soon as possible. We were unable to correlate either the likelihood of success or the final range of movement achieved with the interval between the two stages. During the study the interval between stages steadily increased from eight weeks in most of the early cases. Our perception was that re-exposure of the knee and the quality of the soft tissues was better if a minimum of approximately three months had elapsed between stages. This is now our target interval if the patient's general health allows.

Previous series looking at static spacers have identified a problem with further bone loss between stages with these devices.⁷ Like other authors^{8,9} we did not have any instances of significant further bone loss between stages using articulating spacers. There were only two complications relating to the use of these devices. Unlike previous authors⁸ we experienced one case each of subluxation of the femoral component and of the tibial tray, both after a period of two months. Both patients were managed by reducing their mobilisation and restricting weight-bearing.

When considering antibiotic therapy, most previous series demonstrating similar success rates have recommended the use of long-term antibiotics.^{8,13,14} The exact duration of these varied from six weeks most commonly, up to periods of several months. Recently, it has been reported that local treatment with short-term parenteral antibiotics provides comparable results with those of extended programmes.¹⁴ We feel that our results demonstrate equally well that prolonged antibiotic therapy may not be essential to the successful eradication of deep infection.

In conclusion, we have found that a two-stage technique of revision surgery in these difficult cases can produce satisfactory results. Expert microbiological advice needs to be available when planning re-implantation in order that

appropriate antibiotics are added to the cement for both stages. When considering the investigations available at the time of second-stage surgery, care should be taken interpreting the results since none is accurate enough to be conclusive. Despite all efforts it seems inevitable that there will be a persistent rate of failure and this information should be conveyed to patients before embarking on this challenging surgery.

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