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Assessing the Gold Standard: A Review of 253 Two-Stage Revisions for Infected TKA

Tahir Mahmud MBBS, FRCS(Tr&Orth), Matthew C. Lyons MBBS, FRACS, Douglas D. Naudie MD, FRCSC, Steven J. MacDonald MD, FRCSC, Richard W. McCalden MD, FRCSC

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Abstract

Background Periprosthetic joint infection has been the leading cause of failure following TKA surgery. The gold standard for infection control has been a two-staged revision TKA. There have been few reports on mid- to long-term survivorship, functional outcomes, and fate of patients with a failed two-stage revision TKA.

Questions/purposes Therefore, we determined (1) the mid-term survivorship of two-stage revision TKA, (2) the function of patients in whom infection was controlled, and (3) the outcome of patients with a failed two-stage revision due to recurrent infection.

Methods We retrospectively reviewed 239 patients who underwent 253 two-stage revision TKAs for periprosthetic infection. There were 239 patients (253 knees), 104 men and 135 women, with a mean age of 70 ± 10 years at the time of two-stage revision and a mean BMI of 31.53 ± 6.74 kg/m^2. During followup, we obtained WOMAC and The Knee Society Clinical Rating Scores and radiographs. The minimum followup was 1 year (median, 4 years; range, 1–17 years).

Results Thirty-three patients experienced a failed two-staged TKA. Sixteen patients experienced failure due to recurrent sepsis. There were 17 failures for aseptic causes.

Conclusion The overall infection-free survivorship for two-stage revision TKA was 85% at 5 years and 78% at 10 years.

Level of Evidence Level IV, therapeutic study. See the Guidelines for Authors for a complete description of levels of evidence.

Introduction

Infection has occurred in 1% to 2% of primary TKA surgeries and has been the leading cause of failure following TKA [33, 34, 40, 50]. The rate of periprosthetic infection has been declining over the last two to three decades, mostly due to operating room environments and operative techniques [17, 27, 40]. Various methods have been used in the initial treatment of periprosthetic knee infection, including irrigation and debridement [10, 11, 38], direct exchange arthroplasty [6, 16], and two-stage revision TKA with subsequent reimplantation [15, 18]. Incision and drainage has been an attractive option, with low cost and relatively low morbidity; however, the failure rate has been high, ranging between 61% and 82% [4, 5, 7, 23, 30, 35, 38, 39, 41, 44]. There has also been evidence suggesting that patients who failed a previous incision and drainage procedure were more likely to have a higher rate of failure with a subsequent two-stage revision arthroplasty [46]. Single-staged revision TKA for infection has not yet gained the level of support it has had for infected THAs [8, 43], despite two reports showing infection control rates of

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Each author certifies that his or her institution has approved the human protocol for this investigation, that all investigations were conducted in conformity with ethical principles of research, and that informed consent for participation in the study was obtained.

T. Mahmud (✉), M. C. Lyons, D. D. Naudie, S. J. MacDonald, R. W. McCalden
Division of Orthopaedic Surgery, University of Western Ontario & London Health Sciences Centre, University Campus, 339 Windermere Road, London, ON N6A 5A5, Canada
e-mail: drtahirmahmud@gmail.com

90.9% [6] and 89.2% [47]. Insall et al. [29] originally proposed the two-stage revision protocol for infected TKA, which many have considered the gold standard for control of deep periprosthetic infection [3, 49, 51]. This protocol involved the use of antibiotic loaded cement spacers for an interval period, with intravenous antibiotics and the use of antibiotic loaded cement for prosthesis fixation at the time of reimplantation. This two-stage strategy has seen infection-free survival rates of 80% to 100% [2, 3, 9, 10, 12–15, 18–22, 24–26, 29, 36, 39, 42, 45, 47–51]. However, these data require confirmation.

Therefore, we determined (1) the mid-term survivorship of two-stage revision TKA, (2) the function of patients in whom infection was controlled, and (3) the fate of patients who failed a two-stage revision due to recurrent infection.

Patients and Methods

We retrospectively reviewed all 239 patients who underwent 253 two-stage revision TKAs for periprosthetic infection between March 1993 and July 2010. The indications for two-stage surgery were: evidence of chronic infection (ie, symptoms of duration greater than 4 weeks) with an increased c-reactive protein (CRP), a positive culture report from joint aspiration and/or abnormal cell count, and/or intraoperative histology consistent with infection. The contraindications were: patients with documented infection unable to undergo surgery or patients without evidence of infection. For this study, we included any patient who had undergone a two-stage revision TKA procedure for a confirmed infection. Of the 239 patients (253 knees), 104 were men and 135 women, with a mean age of 70 ± 10 years at the time of two-stage revision TKA. The mean BMI was 31.53 ± 6.74 kg/m^2. Seventeen (7%) patients required a repeat first-stage procedure due to ongoing infection prior to reimplantation of the definitive prosthesis (Table 1). The minimum followup period was 12 months (median, 48 months; range, 12–276 months). No patients were lost to followup. We did not recall any patients for this study; all data were obtained from medical records and radiographs. Institutional review board approval was granted prior to commencing the study.

We took preoperative plain radiographs of all knees. All patients underwent preoperative blood tests, including a full blood count, erythrocyte sedimentation rate (ESR), and CRP. We performed knee fluid aspiration in all patients who had raised inflammatory markers 2 weeks after stopping oral antibiotics. Intraoperative frozen sections were obtained in cases where there was a high index of suspicion for infection despite negative preoperative knee aspiration findings.

The protocol for the first-stage procedure involved removing the prosthesis and cement, and sending five to six specimens for microbiology, including intramedullary specimens from both the femoral and tibial canals and swabs from the knee. All specimens were cultured for aerobic and anaerobic organisms. We then inserted either a static or an articulating polymethylmethacrylate (PMMA) spacer. Over the last decade, we estimated over 90% of our patients were treated with an articulating spacer. Only patients with massive defects or compromised knee stability were treated with nonarticulating spacers.

There were a number of different causative organisms at the time of the initial two-stage revision TKA (Table 2). There were a substantial number of patients with either no growth or unavailable bacterial information. This related to the fact that a substantial proportion of our patient cohort were referred to us from other institutions where records were not available and/or were already undergoing antibiotic treatment, thus compromising bacteriological specimens taken at our institution. We recorded the organisms cultured for patients with a failed two-stage revision TKA, along with the original

Table 1. Patient demographic data and summary of septic and aseptic failures

Demographic	Number
Number of patients	239 (253 knees)
Man-to-woman ratio	104:135
Median followup (years) (range)	4 (1–17)
Mean age (years)	70 ± 10
Mean BMI (kg/m^2)	32 ± 7
Number of repeat one-stage procedures	17 (7%)
Number of patients failing a two-stage revision	33 (13%)
Number of septic failures	16 (6%)
Number of aseptic failures	17 (7%)
Septic failures treated with:	
I&D + component retention and polyethylene exchange + suppressive antibiotics	4
I&D + component retention and polyethylene exchange	4
Suppressive antibiotics with no surgery	4
Above knee amputation	1
Repeat 2SR TKA	3
Number of repeat two-stage revisions	11 (in 11 patients)
Causes of aseptic failures:	
Loosening	7
Instability	5
Pain	2
Extensor mechanism failure	1
Osteolysis	1
Nickel allergy	1

I&D = open debridement.

Table 2. Organisms cultured preoperatively or at time of original resection

Organism	Number of knees
Staphylococcus	53
MSSA	40
MRSA	8
Streptococcus	7
Escherichia coli	3
Enterobacter	4
Serratia marcenses	3
Pseudomonas aeruginosa	2
Propionibacterium	2
Bacteroides	1
Clostridium	1
Multiorganism	5
No growth	68
No results available	56

MSSA = methicillin-sensitive Staphylococcus aureus; MRSA = methicillin-resistant Staphylococcus aureus.

Table 3. Causative organisms for repeat two-stage revision TKA

Patient	Revision organism	Repeat revision organism
1	MSSA	MSSA
2	Multiorganism	Multiorganism
3	Staphylococcus	Staphylococcus
4	MSSA	MSSA
5	No growth	No growth
6	No growth	No growth
7	Staphylococcus	Staphylococcus
8	Staphylococcus	Staphylococcus
9	MSSA	MSSA
10	MSSA	MSSA
11	Staphylococcus	Staphylococcus

MSSA = methicillin-sensitive Staphylococcus aureus.

causative organisms (Table 3). Staphylococcus sp. and methicillin-sensitive Staphylococcus aureus (MSSA) were the most common causative organisms in the index two-stage revisions and subsequent failed two-stage revision TKAs.

Patients received intravenous antibiotics for at least 6 weeks, at which point we stopped administering antibiotics. The patients underwent reimplantation when there was no evidence of active infection (usually 4–6 weeks after cessation of antibiotics), determined by a combination of physical examination, serology (CRP < 10 g/l, ESR $<$ 30 mm/hour), joint fluid aspiration (less than 3.0×10^9 cells per liter and no growth), and, when performed, intraoperative histology (less than 5 PMNs per high-powered field).

All patients underwent postoperative followup at 6 weeks, 3 months, 12 months, and yearly thereafter. At each visit, we obtained WOMAC [37] and The Knee Society Clinical Rating Scores [29]. All patients had standing AP, lateral, and skyline radiographs. From the patients' medical records, we collected the dates of all relevant surgeries, including the index procedure, first and second stage procedures, revision surgeries, and failure surgeries. We also recorded details of the infective organisms. The primary outcome variable was success or failure of a two-stage revision TKA. We recorded failures as any patient that required additional surgery for either septic or aseptic reasons following a two-stage revision. We defined septic failure as pain and/or a loose prosthesis with an increased CRP and a positive culture report from joint aspiration, and/or an abnormal cell count, and/or intraoperative histology consistent with infection. We also recorded the overall outcome for patients who failed a two-stage revision for infection.

We determined the Kaplan-Meier survivorships for aseptic and septic revision endpoints using SPSS® Version 17 (SPSS® Inc., An IBM® Company, Chicago, IL, USA).

Results

The overall infection-free survivorship for two-stage revision TKA was 85% at 5 years and 78% at 10 years (Fig. 1). Thirty-three (13%) patients failed a two-staged TKA: 16 due to recurrent sepsis and 17 due to aseptic causes (Table 1).

The preoperative WOMAC score, and The Knee Society Clinical Rating scores were 48 (± 21) and 64 (± 31), respectively. The postoperative WOMAC and The Knee Society Clinical Rating scores were 60 (± 21) and 129 (± 41), respectively. The difference between the pre- and postoperative WOMAC and The Knee Society Clinical Rating scores were 12 and 65, respectively.

Sixteen patients (16 knees) failed a two-staged revision TKA due to repeat infection (14/16 had positive cultures) at a median of 15 months (range, 5–84 months). Four of these 16 patients were successfully managed with open débridement and polyethylene exchange combined with chronic antibiotic suppression (eg, after 6 weeks of intravenous antibiotics, they were left on oral antibiotics permanently) and remained infection free at minimum of 4 years after surgery. We successfully treated one patient with peripheral vascular disease and a chronically discharging sinus over the knee with an above knee amputation. Eight of these 16 patients went on to repeat two-stage revision TKA following failure of initial management: four underwent open débridement and polyethylene exchange with a short course of postoperative

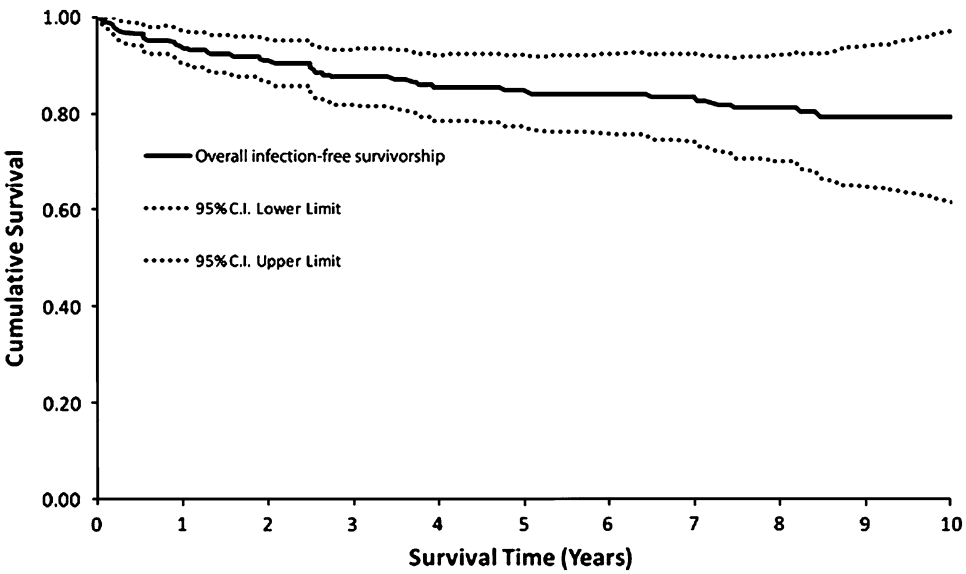

Fig. 1 The graph shows the overall infection-free survivorship for two-stage revision TKA.

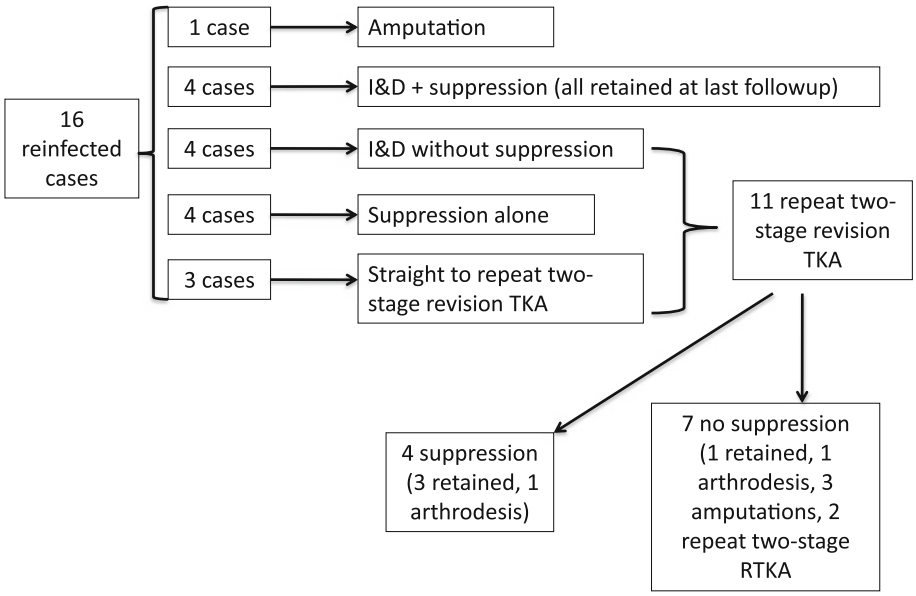

Fig. 2 The graph summarizes the treatment approach used for reinfected cases. I&D = open débridement.

antibiotics (eg, 6 weeks intravenous antibiotics which were then stopped), and four were treated with chronic antibiotic suppression alone. Three of the 16 patients underwent immediate repeat two-stage revision TKA (Fig. 2).

Of the 11 patients who underwent repeat two-stage revision TKA, four underwent chronic antibiotic suppression postoperatively, while seven did not. At a minimum of 2 years after surgery, three of the four patients who had undergone chronic antibiotic suppression still retained their prosthesis, whilst one patient with rheumatoid arthritis had sustained an extensor mechanism rupture and was subsequently treated with a knee fusion. Only one of the seven (14%) patients not receiving chronic antibiotic suppression still retained their prosthesis at the 2-year followup. The remaining six patients had undergone additional surgery with three above knee amputations, two repeat two-stage revision TKAs, and one knee fusion (Fig. 2).

Discussion

Infection has occurred in approximately 1% to 2% of primary TKA surgeries and has been the leading cause of failure following TKA [33, 34, 40, 50]. Surgeons have used various methods in the initial treatment of periprosthetic knee infection, including irrigation and débridement, direct exchange arthroplasty, and two-stage revision arthroplasty with subsequent reimplantation. There has been limited

data published regarding mid- to long-term survivorship and clinical outcomes following two-stage revision TKA, as well as the fate of patients who experienced a failed two-stage revision TKA.

Therefore, we determined (1) the mid-term survivorship of two-stage revision TKA, (2) the function of patients in whom infection was controlled, and (3) the fate of patients who experienced a failed two-stage revision due to recurrent infection.

We recognized the limitations to our study. First, while we collected the data prospectively, the study was a retrospective analysis and had the inherent limitations of a retrospective study design; specifically, the inability to obtain all data that may be helpful, such as the identification of the infecting organism and the total number and nature of surgical interventions the patients had all ready undergone prior to being referred to our center. Second, there were also a number of potential confounding factors, such as the use of static versus articulating antibiotic loaded spacers, the use of varying antibiotic regimes, a number of different surgeons performing the operative procedures, and patient comorbidities. Although this may have been the largest study looking at the outcomes of two-stage revision TKAs, we had inadequate power to stratify by these confounding factors to determine whether any influenced the control of infection. Third, there were 17 aseptic failures in which clinical examination findings, normal serology, negative aspiration results (absence of growth and cell count within normal limits), and frozen section were used to determine the absence of ongoing infection. However, no system or method is perfect, and certainly some aseptic failures could have represented ongoing infection. The patient with presumed metal allergy had a normal workup as above and was, therefore, a diagnosis of exclusion, although this also could have been a missed infection.

Our overall infection-free survivorship for two-stage revision TKA was 85% at 5 years and 78% at 10 years. The literature indicated that eradication of infection following a two-stage revision TKA has been successful in 85% to 95% of cases at short-term followup [15, 20, 24, 26, 29] (Table 4). Our 10-year survivorship results were similar to previously reported studies. Haleem et al. [18] published their 10-year survivorship results of 77% for implant revision for any cause in a series of 96 knees. Goldman et al. [15] reported on 64 knees treated with a two-stage revision protocol, and, despite not using antibiotic loaded cement, also reported a 10-year survivorship of 77%.

We demonstrated an improvement in the mean pre- and postoperative WOMAC and The Knee Society Clinical Rating scores, indicating an improvement in function following two-stage revision TKA when performed for infection. Other reports in the literature also supported our findings. Anderson et al. [1] reported an increase in the modified Hospital for Special Surgery scores following two-stage revision TKA. Haleem et al. [18] also reported an improvement in the median The Knee Society Score in their series.

When looking at the fate of patients failing a two-stage revision TKA, we found that chronic antibiotic suppression

Table 4. Success of two-stage revision TKA

Study	Year published	Number of successful patients (%)	Mean followup (months)	Resistant organism (%)	Definition of failure
Insall et al. [28]	1983	10/11 (91)	34	NR	Recurrence of infection
Wilde and Ruth [49]	1988	9/10 (90)	33	NR	Recurrence of infection
Booth and Lotke [2]	1989	24/25 (96)	25	NR	Recurrence of infection
Teeny et al. [48]	1990	10/10 (100)	42.5	NR	Recurrence of infection
Wilson et al. [50]	1990	16/20 (80)	34	NR	Recurrence of infection
Masri et al. [36]	1994	22/24 (92)	26	NR	Recurrence of infection
Goldman et al. [15]	1996	58/64 (91)	90	NR	Recurrence of infection
Hirakawa et al. [24]	1998	41/55 (75)	62	11	Recurrence of infection
Fehring et al. [13]	2000	51/55 (93)	36	NR	Recurrence of infection
Durbhakula et al. [12]	2004	22/24 (92)	33	20	Recurrence of infection
Haleem et al. [18]	2004	87/96 (91)	86	NR	Recurrence of infection
Cuckler [9]	2005	43/44 (98)	NR	11	Recurrence of infection
Hoffman et al. [26]	2005	44/50 (88)	30	4	Recurrence of infection
Hart and Jones [22]	2006	42/48 (88)	48.5	2	Recurrence of infection
Kurd et al. [32]	2010	70/96 (73)	34.5	50	Recurrence of infection
Mahmud et al. [current study]	2012	220/236 (93)	48	4	Recurrence of infection

NR = not recorded.

following repeat two-stage revision TKA was associated with an increased likelihood of prosthesis retention when compared to those patients not receiving chronic antibiotic suppression. Hanssen et al. [21] described the fate of 24 patients (24 knees) treated for reinfection following failed two-stage revision TKA. Their final outcome included 10 knees treated successfully with arthrodesis, five knees treated with suppressive antibiotics (four of these knees failed suppressive therapy), four above-the-knee amputations, three persistent pseudarthroses of the knee, one resection arthroplasty, and one uninfected prosthesis. Our experience of antibiotic suppression alone was poor, and this was reflected in the literature [17, 31, 52]. This method did not treat the infection definitively and only suppressed it, making it a treatment option only for patients who are not good surgical candidates for two-stage revision TKA. The disadvantages of this treatment included the development of resistant bacterial strains, antibiotic toxicity, and painful loosening of the prosthesis.

While the success of a two-stage revision TKA, regarding both controlling infection and improving functional outcomes, supported it as the treatment of choice, this review highlighted the difficulty in treating this complex group of patients. In addition, a careful review of patients who failed a two-stage revision TKA, while not representing large numbers, suggested that chronic antibiotic suppression combined with surgical intervention may be useful in achieving eventual success.

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