The Chitranjan Ranawat Award

Fate of Two-stage Reimplantation After Failed Irrigation and Débridement for Periprosthetic Knee Infection

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Abstract

Background Irrigation and débridement is an attractive low morbidity solution for acute periprosthetic knee infection. However, the failure rate in the literature is high, averaging 68% (range, 61%–82%). Patients who fail subsequently undergo two-stage reimplantation after a prolonged period of illness. This leads to higher surgical risk and further delays in rehabilitation and may contribute to failure of subsequent revision surgery.

Questions/purposes We determined the rerevision rate due to infection after two-stage reimplantation performed for failed irrigation and débridement of infected TKA.

Each author certifies that he or she has no commercial associations (eg, consultancies, stock ownership, equity interest, patent/licensing arrangements, etc) that might pose a conflict of interest in connection with the submitted article.

Each author certifies that his or her institution 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 as necessary. Data were collected at each institution. Data analysis was conducted at OrthoCarolina Research Institute.

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Methods We performed a multicenter retrospective review of periprosthetic knee infections treated with a two-stage procedure from 1994 to 2008. Selection criteria for the study included initial treatment with irrigation and débridement and subsequent two-stage revision surgery. Failure of two-stage revision was defined as the need for any additional surgery due to infection.

Results Of the 83 knees that had undergone previous irrigation and débridement, 28 (34%) failed subsequent two-stage revision and required reoperation for persistent infection.

Conclusions The failure rate in this series of two-stage revisions for periprosthetic knee infection in patients treated with previous irrigation and débridement is considerably higher than previously reported failure rates of two-stage revision. Factors affecting the failure rate may include host quality, thoroughness of débridement, and organism virulence. Patients and surgeons must understand that irrigation and débridement, while initially attractive, may lead to high failure rates of subsequent two-stage reimplantation.

Level of Evidence Level III, therapeutic study. See the guidelines online for a complete description of level of evidence.

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Introduction

Infection after TKA is a devastating complication that fortunately is rare, occurring in 1% to 2% of primary surgeries [21–23, 29, 37]. However, as the number of TKAs performed in the United States increases as projected over the next two decades, the number of infected cases will also increase [20, 22, 23]. The potential economic burden to our healthcare system is substantial [15, 20, 23] and strategies to treat and prevent total joint infections should be investigated.

Methods used for the initial treatment of periprosthetic knee infection include irrigation and débridement (I&D) with component retention (Table 1) [3–5, 7, 14, 19, 24, 26,

28, 30, 32, 35], direct-exchange arthroplasty [10, 34], and two-stage resection arthroplasty and reimplantation [1, 2, 6, 8, 9, 11–13, 16–18, 25, 27, 30, 33–37]. Two-stage revision, which includes interval use of antibiotic-loaded cement spacers and intravenous antibiotics and the use of antibiotic-loaded cement for prosthesis fixation at reimplantation, has become the gold-standard treatment in the United States, with infection-free survival rates of 80% to 100% (Table 2) [1, 2, 6, 8, 9, 11–13, 16–18, 25, 27, 30, 33–37].

I&D with retention of components is an attractive, low-cost, low-morbidity treatment for acute periprosthetic knee infection. However, the failure rate of this procedure is high, averaging 68% in the literature (61%–82%) (Table 1) [3–5, 7, 14, 19, 24, 26–28, 30, 32, 35, 37]. Patients who

Table 1. Failure of open irrigation and débridement for periprosthetic knee infection

Study	Failure (number of patients)	Definition of failure	Resistant organism
Hartman et al. [14] (1991)	20/33 (61%)	ROI with prosthesis removal	NR
Schoifet and Morrey [32] (1990)	24/31 (77%)	ROI	26%
Burger et al. [5] (1991)	32/39 (82%)	Clinical or radiographic signs of infection	18%
Deirmengian et al. [7] (2003)	20/31 (65%)	ROI	15%
Teeny et al. [35] (1990)	15/21 (71%)	ROI	NR
Rand (review) [28] (1993)	267/377 (71%)	ROI	NR
Bradbury et al. [3] (2009)	16/19 (84%)	Subsequent infection surgery	100%
Marculescu et al. [24] (2006)	53/99 (53%)	ROI	2%
Silva et al. [34] (2002)	357/530 (67%)	ROI	NR
Brandt et al. [4] (1997)	21/33 (64%)	ROI (same organism strain)	3%
Ivey et al. [19] (1990)	7/10 (70%)	Clinical or radiographic signs of infection	NR
Total	852/1253 (68%)		

ROI = recurrence of infection; NR = not reported.

Table 2. Success of two-stage revision for periprosthetic knee infection

Study	Success (number of patients)	Definition of failure	Resistant organism
Wilson et al. [37] (1990)	16/20 (80%)	ROI	NR
Insall et al. [18] (1983)	10/11 (91%)	ROI	NR
Haleem et al. [12] (2004)	87/96 (91%)	ROI	NR
Booth and Lotke [1] (1989)	24/25 (96%)	ROI	NR
Goldman et al. [11] (1996)	58/64 (91%)	ROI	NR
Fehring et al. [9] (2000)	51/55 (93%)	ROI	NR
Masri et al. [25] (1994)	22/24 (92%)	ROI	NR
Hofmann et al. [17] (2005)	44/50 (88%)	ROI	4%
Teeny et al. [35] (1990)	8/8 (100%)	ROI	NR
Hart and Jones [13] (2006)	42/48 (88%)	ROI	2%
Hirakawa et al. [16] (1998)	41/55 (75%)	ROI	11%
Wilde and Ruth [36] (1988)	9/10 (90%)	ROI	NR
Durbhakula et al. [8] (2004)	22/24 (92%)	ROI	20%
Cuckler [6] (2005)	43/44 (98%)	ROI	11%
Total	477/534 (89%)		

ROI = recurrence of infection; NR = not reported.

experience failure of I&D of an infected knee prosthesis are then subjected to a longer period of pain and swelling in the knee culminating in later two-stage revision surgery. Additionally, this delay in recovery can exacerbate other comorbid conditions and increase time away from family and work, thus having serious physical, emotional, and financial consequences for the patient. In failed patients, intraarticular bacteria that were incompletely removed at I&D persist until explantation occurs. We hypothesized more entrenched osteomyelitis may affect the success of subsequent two-stage reimplantation. We determined the rerevision rate of two-stage reimplantation performed for failed I&D of infected TKA. We posed the following research questions: (1) What is the rerevision rate of two-stage reimplantation performed after failed I&D of an infected TKA? (2) Do any differences exist between those who underwent a rerevision and those who did not with respect to age, gender, and patient health status? And (3) do any differences exist between those who underwent a rerevision and those who did not with respect to organism type, length of time between index procedure and I&D, and length of time between I&D and explantation?

Patients and Methods

We performed a multicenter study retrospective review of periprosthetic knee infections from 1994 to 2008 at five institutions. Institutional Review Board approval was obtained from each center. Cases were identified and selected by reviewing the medical records, practice management systems, and institutional total joint registries of patients with periprosthetic knee infection treated by two-stage revision surgery. Patients who had I&D with component retention before a two-stage revision surgery at a minimum of 2 years postoperatively were selected for inclusion in the study. Exclusion criteria included arthroscopic I&D procedures and draining sinus tracts.

Review of the orthopaedic literature was performed using the PubMed search engine. Individual search terms included “total knee infection, total knee debridement, and total knee two-stage”; studies not adhering to the treatment protocol (open irrigation and débridement or removal of the prosthesis, placement of either static or articulating antibiotic spacer, minimum 4 weeks intravenous antibiotics, and subsequent reimplantation) and those in languages other than English were excluded from this review.

Patient demographic data such as age at the date of initial I&D surgery, gender, and health status were recorded. The American Society of Anesthesiologists (ASA) physical status classification score was used as a proxy variable for health status [31]. Additionally, the dates of relevant surgical procedures, including the initial I&D, two-stage

procedures, and rerevision and failure surgeries, were recorded. The types of organisms at all infection procedures and the types of failure surgeries performed were documented. Multiorganism was used in cases in which different organisms were identified through different laboratory tests.

Between October 1994 and February 2008, 126 patients met the eligibility criteria. To minimize selection bias due to loss to followup, a strict followup protocol was defined. Lost to followup was defined as no clinical information available within 12 months before study initiation. All patients with inadequate followup data were contacted by letter and/or telephone. Patients were contacted a minimum of three times before categorized as lost to followup. Additionally, the Social Security Death Index was used to validate deceased patients.

Of the 25 patients lost to followup as previously defined, 13 of these patients were known to be infection free at an average followup of 39 months (range, 12–104 months). The remaining 12 patients did not have adequate postoperative clinical information available. Eighteen patients were deceased at the time of the study and did not have adequate followup data. Of the 18 deceased patients, 12 were known to be infection free at an average of 34 months (range, 4–103 months). It is unknown whether the remaining six patients were infection free. Therefore, the series included 83 patients who underwent two-stage reimplantation after an unsuccessful I&D. Including date of rerevision surgery and allowance for a 4-month annual visit window, the average followup for this group of patients was 50 months (range, < 1–151 months).

The diagnosis of periprosthetic infection was made based on a variety of clinical and laboratory assessments across centers. Preoperative laboratory assessments included C-reactive protein values, erythrocyte sedimentation rate, and synovial fluid analyses with polymorphonuclear cells. Additionally, intraoperative tissue cultures were analyzed for acute inflammation and the presence of gross purulence within the joint was documented. In cases where causative organisms were not identified, the presence of pus within the joint or positive intraoperative pathology led to the definitive diagnosis of periprosthetic infection. Medical records were retrospectively reviewed to verify the diagnosis of periprosthetic infection. Due to the retrospective design, no standard prospective protocol was used across centers.

The indications for proceeding to a two stage revision after recovery from the initial I&D included persistent pain, effusion, fever, or the presentation of a draining sinus. The two-stage revision protocol was consistent at each center. This consisted of removal of the prosthesis and all bone cement, thorough I&D, and placement of either a static or articulating antibiotic-loaded polymethylmethacrylate spacer (Stage I) followed by a minimum of 4 weeks of

culture-specific parenteral intravenous antibiotic treatment. Patients were reimplanted after a combination of physical examination, serology, joint fluid aspiration, and intraoperative pathology findings showing no evidence of continued infection (Stage II).

The primary outcome variable was success or failure of the two-stage revision procedure. More specifically, failure was defined as the need for any additional surgery due to infection and success was defined as no additional surgery required due to infection.

Additional variables analyzed included age, gender, organism type, and length of time between I&D and explantation. Patients with an ASA score of 1 or 2 were grouped together and considered in good health, while patients with scores of 3 or 4 were considered in poor overall health. Timing of infection was categorized as a dichotomous variable and defined as whether or not the initial I&D was performed in the first 4 weeks postoperatively or greater than 4 weeks postoperatively.

Descriptive statistics were calculated, including mean and frequency. Independent *t* tests were used to determine differences between successes and failures for continuous, normally distributed data. Mann-Whitney tests were used for ordinal data. Chi square tests were used to determine differences in proportions between dichotomous data.

Results

Of the 83 knees that had undergone previous I&D, 28 (34%) failed subsequent two-stage revision and required reoperation for persistent infection. Of the 28 patients who experienced failed two-stage reimplantation after I&D, 10 were left with a knee with less than desirable function (36%). Reoperation for infection included 15 repeat I&Ds, three fusions, four resection arthroplasties, three amputations, and two repeat two-stage reimplantations. One patient had an unknown procedure performed.

There was no difference with the numbers available between success (Table 3) and failure (Table 4) with respect to age ($p = 0.25$), gender ($p = 0.10$), or ASA grade ($p = 0.95$). Fifty-eight percent of both successful cases and failure cases had an ASA grade of 3 or 4.

The causative organisms of the 83 patients in this series were predominantly staphylococcus. Fifty-seven of the 83 patients were infected with these organisms. Fifteen of these 83 patients were known to be infected with resistant organisms (successful: Table 3; failed: Table 4). The average time between I&D and explantation was longer ($p = 0.03$) in the successful group (6.9 months) than in the failure group (3.6 months).

There was no association ($p = 0.29$) with failure in terms of whether the I&D procedure was performed within

4 weeks or greater than 4 weeks of the index procedure. Complete data related to the dates of the index and I&D procedures were available for 78 of the 83 patients (Successful: Table 3; failed: Table 4).

Discussion

I&D with component retention is an attractive low-morbidity option for periprosthetic knee infection. Success of I&D with or without polyethylene insert exchange is highly variable in the literature [3, 5, 7, 14, 26–28, 30, 32, 34, 37], with an average failure rate of 68% (range, 61%–82%).

Despite these high failure rates, this treatment option remains popular with surgeons and patients alike. Perceived advantages include a technically less demanding procedure that can be performed in a short period of time with low perioperative morbidity. It is also assumed by most advocates of this treatment option that, even if the procedure fails, little is lost in the recovery process.

Failure of open débridement adds substantial time to the recovery process, morbidity to the patient, and greater cost to the healthcare system. Of perhaps greater concern are the potential effects of failed I&D on the failure rate of subsequent two-stage reimplantation. We determined the rerevision rate due to infection of two-stage reimplantation after failed I&D.

A primary limitation of this study is related to observational, retrospective data collected across multiple centers and including multiple surgeons using a variety of surgical techniques. Selection bias is also possible, considering 25 patients were lost to followup despite an extensive search. There is a potential for misclassification bias related to the temporal sequence, ie, acute versus late, and treatment of infection. In some cases, exact dates of prior arthroplasty procedures and/or initial I&D were unknown, but we were able to document a month and year of these procedures. In five cases, dates of these procedures were missing entirely. A critical limitation of this study was the lack of a comparative group of patients who had a two-stage reimplantation without prior I&D. While our data set was sufficiently large for most evaluations, it was insufficient for stratified analyses such as organism type and timing of treatment that are relevant clinical factors associated with rerevision rates due to infection. On the other hand, including five centers from geographically diverse regions improves the generalizability of these data. Therefore, this study has generated important research questions to be addressed in continuing, multicenter studies conducted by this consortium.

Despite these limitations, we believe our data help to clarify the limited role I&D should play in the treatment of periprosthetic knee infection. The 34% failure rate noted in

Table 3. Successful cases

Patient	Age (years)	Gender	Side	ASA grade	Within 4 weeks of index procedure	Initial organism	Followup (months)
A2	85.99	Female	Right	4	Yes	MRSA	32.32
A4	67.86	Male	Left	3	Yes	Staphylococcus	34.82
A5	74.67	Female	Left	3	Yes	Staphylococcus	20.81
A11	63.54	Female	Right	2	Yes	Staphylococcus	151.33
A14	67.60	Female	Left	3	No	Staphylococcus	111.25
A15	72.73	Female	Right	Missing	No	Staphylococcus	136.80
A25	61.05	Male	Left	3	No	Escherichia coli	72.92
A28	60.34	Female	Right	3	No	Staphylococcus	87.48
A30	62.70	Male	Right	3	No	MRSA	79.23
A32	65.90	Male	Left	3	No	Missing	75.19
A33	58.29	Male	Right	2	Yes	Missing	76.31
A37	61.14	Male	Right	3	No	Staphylococcus	63.22
A38	50.45	Female	Right	3	No	Staphylococcus	53.10
A39	74.59	Female	Left	2	No	Multiorganism	59.80
A40	53.42	Female	Left	3	No	No growth	48.04
A41	60.58	Male	Right	3	No	Staphylococcus	82.13
A44	79.12	Female	Right	3	No	Staphylococcus	23.77
A46	61.49	Female	Left	2	No	MRSA	22.75
A48	64.44	Female	Left	2	No	Staphylococcus	145.58
A50	66.65	Female	Left	2	Yes	Staphylococcus	112.08
A52	65.88	Female	Right	2	Yes	Staphylococcus	140.28
B1	72.00	Female	Right	3	No	Streptococcus	123.58
B6	73.00	Female	Left	3	No	Staphylococcus	111.22
B7	56.00	Female	Left	2	No	Staphylococcus	102.77
B9	58.00	Male	Left	2	Missing	Staphylococcus	100.27
B10	73.00	Female	Left	3	Yes	Staphylococcus	82.03
B12	59.00	Male	Right	3	No	Streptococcus	77.65
B16	53.00	Female	Left	3	No	Staphylococcus	66.15
B20	58.00	Female	Left	2	Missing	Streptococcus	58.36
B22	82.00	Male	Right	3	Yes	Staphylococcus	45.01
B24	59.00	Male	Right	3	No	MRSA	30.71
C1	65.00	Male	Left	3	No	Staphylococcus	40.80
C2	72.00	Female	Right	3	No	Multi-organism	29.36
C5	77.00	Female	Left	3	No	Streptococcus	20.05
C8	52.00	Female	Left	2	No	Staphylococcus	78.25
C9	65.00	Male	Right	2	No	Pseudomonas aeruginosa	79.33
C11	73.00	Female	Left	3	Yes	Staphylococcus	63.48
C12	81.00	Male	Left	2	No	Staphylococcus	52.83
C13	66.00	Female	Left	2	No	Missing	57.34
C14	69.00	Female	Left	2	No	Staphylococcus	45.83
C15	61.00	Male	Left	3	No	Staphylococcus	46.42
C18	70.00	Male	Left	Missing	Yes	Staphylococcus	69.44
C19	75.00	Female	Right	2	Yes	Multiorganism	59.28
D4	37.00	Male	Right	4	Yes	Staphylococcus	68.45
D7	53.00	Male	Left	2	No	Staphylococcus	27.16
D8	60.00	Male	Left	2	No	Staphylococcus	82.16
D12	67.00	Male	Right	2	No	Staphylococcus	47.61

Table 3. continued

Patient	Age (years)	Gender	Side	ASA grade	Within 4 weeks of index procedure	Initial organism	Followup (months)
E3	80.00	Male	Right	3	No	Staphylococcus	101.42
E4	62.00	Male	Right	1	No	Propionibacterium acnes	85.81
E6	60.00	Female	Right	3	No	MRSA	29.69
E7	57.00	Male	Right	2	Yes	Staphylococcus	62.04
E9	71.00	Male	Right	2	Yes	Staphylococcus	53.59
E11	63.00	Male	Left	3	No	VRE	35.64
E12	71.00	Male	Right	3	Yes	Staphylococcus	26.37
E13	55.00	Male	Left	3	Yes	Staphylococcus	24.66

ASA = American Society of Anesthesiologists; MRSA = methicillin-resistant *Staphylococcus aureus*; VRE = vancomycin-resistant enterococci.

Table 4. Failure cases

Patient	Age (years)	Gender	Side	ASA grade	Within 4 weeks of index procedure	Initial organism	Rerevision organism	Time to failure (months)
A6	72.22	Male	Left	Missing	No	MRSA	Multiorganism	62.56
A7	75.05	Male	Left	Missing	No	Staphylococcus	Staphylococcus	97.38
A22	73.57	Male	Right	3	Yes	Staphylococcus	MSSA	3.22
A24	41.15	Female	Left	3	Yes	Candida	Multiorganism	50.01
A31	73.86	Male	Right	3	Yes	MRSA	MRSA	0.20
A34	61.30	Male	Left	2	No	No growth	Missing	49.18
A35	53.50	Female	Right	3	No	Missing	Staphylococcus	55.66
A36	83.87	Male	Left	3	No	Streptococcus	Streptococcus	6.51
A49	39.16	Male	Right	2	Yes	Staphylococcus	Staphylococcus aureus	3.85
B2	55.00	Male	Right	3	No	Serratia marcescens	Clostridium subterminale	1.94
B11	76.00	Male	Right	3	Missing	Streptococcus	Streptococcus	10.88
B14	64.00	Male	Left	2	Yes	Staphylococcus	No growth	0.33
B15	72.00	Female	Left	2	Missing	No growth	Proteus mirabilis	0.36
B17	61.00	Female	Left	3	Yes	MRSA	MRSE	0.69
B18	77.00	Female	Right	2	Yes	MRSA	MRSA	1.38
B25	59.00	Female	Right	3	No	Staphylococcus	No growth	3.78
C6	55.00	Male	Left	2	Yes	Staphylococcus	Staphylococcus	20.35
C10	57.00	Female	Right	2	No	VRE	Staphylococcus	14.93
D2	47.00	Male	Right	4	No	Multiorganism	Multiorganism	0.23
D5	58.00	Male	Left	2	No	Multiorganism	MRSE	8.81
D13	59.00	Male	Left	3	No	Staphylococcus	Multiorganism	12.20
D14	60.00	Female	Right	2	Missing	Staphylococcus	MRSA	0.99
D17	78.00	Female	Left	2	Yes	Multiorganism	MRSE	0.33
E2	69.00	Male	Right	3	No	MRSA	MRSA	36.79
E5	58.00	Male	Left	3	Yes	MRSE	MRSE	0.33
E8	49.00	Male	Right	2	No	MRSA	MRSA	9.14
E10	63.00	Male	Left	3	No	MRSA	MRSA	5.62
E14	59.00	Male	Left	3	No	Staphylococcus	Staphylococcus	0.39

ASA = American Society of Anesthesiologists; MRSA = methicillin-resistant *Staphylococcus aureus*; VRE = vancomycin-resistant enterococci; MRSE = methicillin-resistant *Staphylococcus epidermidis*.

this study raises some concern that utilizing I&D as the initial treatment for periprosthetic knee infection may compromise the success of two-stage reimplantation. In contrast, a literature review of two-stage reimplantation series demonstrates a failure rate that averages only 11% (range, 0%–25%) (Table 2). However, one must be cautious in directly comparing our data with such historical controls because it is unclear whether these series included patients who underwent I&D before the two-stage reimplantation.

Most authors state I&D is appropriate if one is dealing with an acute postoperative infection, ie, within 4 weeks of primary surgery, involves a sensitive organism, or occurs as an acute metastatic infection where I&D is performed within a few days of symptoms [2, 3, 5, 7, 14, 26–28, 30, 32–35]. However, the treating surgeon needs to be cognizant of the limitations of this treatment option, with an average failure rate reported in the literature of 68% (Table 1). In fact, this treatment option may substantially compromise the success of avoiding further revision surgeries due to infection if it fails.

In conclusion, patients and surgeons must understand I&D, while initially attractive, may lead to prohibitively high failure rates of two-stage reimplantation. I&D for periprosthetic infection with an initial failure rate of 68% in the literature and a subsequent failure rate of 34% after two-stage reimplantation should be used with caution.

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