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Clinical Outcomes and Infection Rates Following Revision Total Knee Arthroplasty: Aseptic Failure versus Septic Failure

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Background: It is controversial whether revision total knee arthroplasty (TKA) due to septic failure shows inferior clinical outcomes compared with TKA due to aseptic failure. Moreover, few studies have compared the infection rates after revision TKA between aseptic and septic failure. We aimed to compare the clinical outcomes and infection rates after aseptic and septic revision TKA.

Methods: Between April 2006 and May 2019, 68 and 26 patients underwent revision TKA due to aseptic failure (aseptic group) and septic failure (septic group), respectively. The postoperative range of motion (ROM), Western Ontario and McMaster Universities Osteoarthritis index, Knee Society Knee Score (KSKS), Knee Society Function Score (KSFS), and infection rates were compared between the two groups.

Results: The mean follow-up durations in the aseptic and septic groups were 44.4 and 54.8 months, respectively. The septic group showed inferior postoperative ROM (124.1° and 109.4°, $p = 0.004$), KSKS (88.9 and 78.8, $p = 0.001$), and KSFS (72.8 and 59.0, $p = 0.001$). Three patients of aseptic group had infection. Three patients of septic group had recurred infection (same pathogen with the first infection) and 1 patient had a new infection (different pathogen). The septic group showed slightly higher but not significantly different infection rates (4.4% and 15.4%, $p = 0.089$).

Conclusions: Revision TKA with septic failure showed inferior postoperative clinical outcomes compared with aseptic revision surgery. A slightly higher infection rate was observed in the septic group but it was not significantly different.

Keywords: *Revision arthroplasty, Knee, Infection, Outcome*

As primary total knee arthroplasties (TKAs) performed annually increase, the number of revision TKAs will inevitably increase.[1-3] Revision TKA is a challenging clinical area, and the outcomes are less satisfactory than those of primary TKA.[4] Recent Medicare data demonstrated an increase in annual revision TKAs from 9,650 in 1991 to 19,871 in 2010. Based on the National Hospital Discharge Survey and National Health Insurance System of the United States, revision TKA was projected to increase from 38,300 cases in 2005 to 268,200 cases in 2030 (an increase of 601%).[2,5]

Historically, periprosthetic joint infection, polyethylene wear, aseptic loosening, stiffness, and instability have been the leading causes of TKA failure.[6,7] Recent studies demonstrated that the most common etiology for revision TKA procedures was infection, which is a great challenge for surgeons.[7] Some studies reported that the mortality rate after septic revision was higher than that after aseptic revision;[8,9] however, it is still unclear whether revision

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TKA due to septic failure shows inferior clinical outcomes compared with TKA due to aseptic failure.[8,10-12] Moreover, few studies have compared infection rates after revision TKA between aseptic and septic failure.

Therefore, the purpose of the current study was to compare the clinical outcomes and infection rates after aseptic and septic revision TKA. We hypothesized that the clinical outcomes of septic revision TKA would be inferior to those of aseptic revision TKA and the infection rate of septic revision TKA would be higher than that of aseptic revision TKA.

METHODS

This study was performed in line with the principles of the Declaration of Helsinki. The protocol used to evaluate the radiographic findings and intraoperative data was approved by Institutional Review Board of Samsung Medical Center (No. SMC2021-07-120). Informed consent was obtained from all individual participants included in the study.

This study was a retrospective comparative design study. The data collected from first time revision TKAs performed by a single surgeon (YWM) between April 2006 and May 2019 were reviewed. Revision surgery was defined as any procedures, in which at least tibial or femoral components were exchanged. Patients were excluded if (1) they underwent polyethylene insert change alone among aseptic failures, (2) they underwent debridement surgery without component change among septic failures, (3) plain radiographs or clinical scores were unavailable or inadequate, and (4) the follow-up period was < 24 months. Patients were classified into two groups: aseptic and septic. The patients of aseptic group underwent one-stage revision TKA for aseptic reasons (e.g., aseptic loosening, stiffness, instability) and those of septic group underwent two-stage revision TKA for periprosthetic joint infection.

Periprosthetic joint infection was diagnosed based on indications of previous studies:[13,14] (1) abscess or sinus tract connected to the joint space; (2) positive culture from joint aspiration fluid; (3) purulence notified intraoperatively; or (4) abnormal joint fluid analysis, blood erythrocyte sedimentation rate, or C-reactive protein. Two-stage revision TKA was performed for infected TKA. The surgical protocol for infected TKA included removal of all components, meticulous debridement of soft tissues and bone, and insertion of an articulating cement spacer (mixed heat stable antibiotics). All-cement type articulating cement spacer was used rather than spacers containing bioinert materials. After 6–12 weeks, reimplantation of a new prosthesis was performed using the NexGen LCCK system (Zimmer-Biomet) or Scorpio TS system (Stryker). Aseptic revision TKA was defined as revision surgery due to aseptic failure of implant, instability, or stiffness. All aseptic revision cases underwent blood erythrocyte sedimentation rate or C-reactive protein test to rule out periprosthetic joint infection. If abnormal results were shown, joint fluid analysis was performed. Surgery for aseptic revision TKA was also performed using the same systems.

Clinical Assessment

The patients' demographic data were collected, including age, sex, body mass index (BMI), operated side (right or left), follow-up period, and time between index and revision surgeries. Clinical assessments using the range of motion (ROM), Western Ontario and McMaster University Osteoarthritis (WOMAC) index, Knee Society Knee Score (KSKS), and Knee Society Function Score (KSFS) were performed before surgery and at the final follow-up.[15,16] Further, the operative time and amount of blood drainage volume from the day of surgery to the second day after surgery were investigated. Peri- and postoperative complications were also assessed. The preoperative WOMAC index, KSKS, and KSFS were compared with those from the final follow-up. All pre- and postoperative clinical assessments were compared between the septic and aseptic groups. Periprosthetic joint infection was evaluated after the revision surgery. In the septic group, periprosthetic joint infection was defined as an infection after the second stage operation. The infection rates were also compared between the groups.

Statistical Analyses

The Shapiro-Wilk test was used to identify a normal distribution. The Mann-Whitney test or Student *t*-test was applied for continuous variables, and Fisher's exact test or the chi-square test was applied for categorical variables to compare outcomes between the two groups. A $p < 0.05$ was considered statistically significant. Data analysis was performed using the IBM SPSS software ver. 22.0 (IBM Corp., Armonk, NY, USA). This study had a power of at least 99.1% to detect a difference of at least 10.1 points with 8.5 (aseptic group) and 12.5 (septic group) points standard deviation in the mean KSKS ($\alpha = 0.05$).

RESULTS

A total of 94 patients were enrolled in this study (Fig. 1). Among them, 68 patients underwent revision surgery due to aseptic failure, and 26 underwent revision surgery due

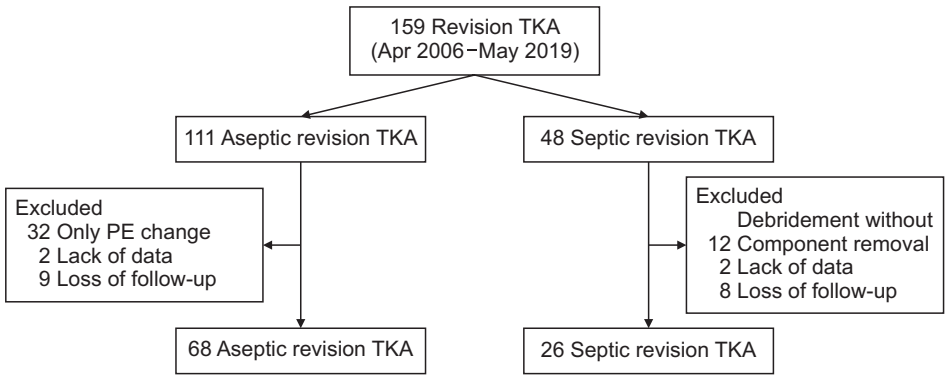

Fig. 1. Flowchart describing patient enrollment in the study. TKA: total knee arthroplasty, PE: polyethylene.

Table 1. Preoperative Data

Variable	Aseptic group	Septic group	*p*-value
Number of patients	68	26	-
Cause of revision			-
Loosening	57		
Instability	9		
Stiffness	2		
Age (yr)	72.1 ± 6.6 (54.3–85.8)	68.6 ± 8.8 (45.8–84.8)	0.071
Sex (male : female)	4 : 64	4 : 22	0.211
BMI (kg/m^2)	27.5 ± 4.5 (21.5–36.7)	25.9 ± 2.8 (20.5–35)	0.104
Direction (right : left)	44 : 24	15 : 11	0.635
Follow-up period (mo)	44.4 ± 25.1 (24–112)	54.8 ± 33.6 (24–153)	0.159
Time to revision (mo)	128.4 ± 72.1 (25–306)	44.3 ± 45.3 (10–216)	< 0.001
Preoperative ROM (°)	111.6 ± 16.8 (65–145)	105.8 ± 13.7 (75–130)	0.118
Preoperative WOMAC	49.6 ± 20.3 (16–87)	50.6 ± 21.0 (16–87)	0.825
Preoperative KSKS	50.5 ± 9.6 (15–70)	46.5 ± 18.8 (17–88)	0.310
Preoperative KSFS	41.2 ± 15.5 (10–70)	39.6 ± 18.6 (10–90)	0.675

Values are presented as mean ± standard deviation (range).
BMI: body mass index, ROM: range of motion, WOMAC: Western Ontario and McMaster University Osteoarthritis, KSKS: Knee Society Knee Score, KSFS: Knee Society Function Score.

to septic failure. In the aseptic group, 57 patients underwent surgery due to aseptic loosening, 9 due to instability, and 2 due to stiffness. There was no statistical difference between the two groups in terms of demographic data, including age, sex, BMI, operated side, and follow-up period. Only the time between index and revision surgeries was shorter in the septic group (mean value: aseptic group vs. septic group, 128.4 vs. 44.3; $p < 0.001$). The preoperative ROM, WOMAC index, KSKS, and KSFS were similar between the groups (Table 1).

In the aseptic group, the postoperative clinical outcomes (ROM, WOMAC index, KSKS, and KSFS) were significantly improved compared with the preoperative clinical outcomes. In the septic group, all postoperative outcomes were improved after revision surgery except for ROM (Table 2).

With respect to the postoperative outcomes, the septic group showed significantly lower ROM (mean value: 124.1° vs. 109.4°; $p = 0.004$), KSKS (88.9 vs. 78.8; $p = 0.001$), and KSFS (72.8 vs. 59.0; $p = 0.001$) than those of the asep-

Table 2. Comparison of Preoperative and Postoperative Clinical Values

Variable	Preoperative	Postoperative	*p*-value
All cases			
ROM	110.0 ± 16.2	120.0 ± 22.7	< 0.001
WOMAC	49.9 ± 20.4	9.6 ± 5.4	< 0.001
KSKS	49.4 ± 12.8	86.1 ± 10.7	< 0.001
KSFS	40.8 ± 16.3	69.0 ± 17.7	< 0.001
Aseptic group			
ROM	111.6 ± 16.8	124.1 ± 19.2	< 0.001
WOMAC	49.6 ± 20.3	9.8 ± 5.4	< 0.001
KSKS	50.5 ± 9.6	88.9 ± 8.5	< 0.001
KSFS	41.2 ± 15.5	72.8 ± 17.0	< 0.001
Septic group			
ROM	105.8 ± 13.7	109.4 ± 27.7	0.526
WOMAC	50.6 ± 21.0	9.4 ± 5.2	< 0.001
KSKS	46.5 ± 18.8	78.8 ± 12.5	< 0.001
KSFS	39.6 ± 18.6	59.0 ± 15.7	0.001

Values are presented as mean ± standard deviation.
ROM: range of motion, WOMAC: Western Ontario and McMaster University Osteoarthritis, KSKS: Knee Society Knee Score, KSFS: Knee Society Function Score.

Table 3. Comparison of Postoperative Results between Aseptic and Septic Groups

Variable	Aseptic group	Septic group	*p*-value
Postoperative ROM (°)	124.1 ± 19.2	109.4 ± 27.7	0.004
Postoperative WOMAC	9.8 ± 5.4	9.4 ± 5.2	0.788
Postoperative KSKS	88.9 ± 8.5	78.8 ± 12.5	0.001
Postoperative KSFS	72.8 ± 17.0	59.0 ± 15.7	0.001
Operative time (min)	170.4 ± 38.7	178.6 ± 22.3	0.309
Blood drainage volume (mL)	535.4 ± 294.5	563.0 ± 260.3	0.676
Infection cases	3 (4.4)	4 (15.4)	0.089
Other complications	Polyethylene change due to instability in 1 case	0	

Values are presented as mean ± standard deviation or number (%).
ROM: range of motion, WOMAC: Western Ontario and McMaster University Osteoarthritis, KSKS: Knee Society Knee Score, KSFS: Knee Society Function Score.

tic group. The blood drainage volume and operative time were similar between the two groups. The septic group showed a slightly higher infection rate (15.4%) than did the aseptic group (4.4%), although the difference was not statistically significant ($p = 0.089$) (Table 3). Three patients of the septic group had recurred infection (same pathogen with the first infection) and 1 patient had a new infection (different pathogen) (Table 4).

Table 4. Infection Cases after Revision Surgery

Age/sex	Cause of revision	Pathogen (if septic failure)	Time between primary and revision TKA (mo)	Pathogen (after revision TKA)
68/F	Septic failure	Methicillin-resistant *Staphylococcus aureus*	85	Methicillin-resistant *S. aureus*
70/F	Aseptic failure (loosening)		144	No growth
65/F	Septic failure	Methicillin-resistant Coagulase-negative *Staphylococci*	29	Methicillin-resistant coagulase-negative *Staphylococci*
59/F	Septic failure	Group G *Streptococcus*	56	Extended spectrum β-lactamase-producing *Escherichia coli*
81/M	Septic failure	*Streptococcus agalactiae*	28	*S. agalactiae*
70/F	Aseptic failure (loosening)		131	Methicillin-sensitive coagulase-negative *Staphylococci*
70/F	Aseptic failure (loosening)		161	Methicillin-sensitive *S. aureus*

TKA: total knee arthroplasty.

DISCUSSION

The principal findings of this study were as follows: (1) the septic failure group showed significantly inferior ROM, KSKS, and KSFS compared with the aseptic failure group and (2) the septic failure group showed a slightly higher infection rate than did the aseptic failure group without statistically significant difference after revision surgery (15.4% vs. 4.4%).

Previously, several investigations were conducted to determine whether revision TKA due to septic failure differs from that due to aseptic failure in terms of clinical outcomes; however, this is still unclear.[8,10-12,17,18] Although some authors demonstrated that septic revisions showed comparable clinical outcomes to aseptic revisions, we believe that the more popular opinion is that septic failure shows worse outcomes. Barrack et al.[17] reported that septic revisions were related to inferior ROM and clinical outcomes, although their satisfaction was similar between the two groups. Wang et al.[18] demonstrated that aseptic revisions achieved significantly better knee scores and ROM, although their pain and functional scores were similar. We believe that inferior ROM in septic revisions occurred due to two-stage surgery and that the functional outcomes were lower accordingly. Decreased ROM in two-stage surgery is inevitable; therefore, one-stage revision TKAs for periprosthetic joint infection are being attempted with limited indications (micro-organism and sensitivity determined, non-immunocompromised patients, and good tissue envelope) to avoid ROM limitation after surgery.[19,20] In this study, the septic failure group showed inferior ROM, KSKS, and KSFS, which supports the findings of the previous two studies.

It is generally accepted that the infection rate after revision TKA is considerably higher than that after primary TKA. Despite tremendous efforts, the overall failure rate of two-stage revision arthroplasty for infected TKA has been shown to range from 10% to 30%.[21-24] Whereas, the infection rate after revision TKA for aseptic reasons was 3%–7.5%.[25-27] Mortazavi et al.[10] compared the infection rate between septic and aseptic revision TKAs. In their study, the infection rate was fourfold higher in patients who underwent revision for infection (21%) than in those who underwent aseptic revision (5%). In our study, the infection rate was not significantly different. We think that the lack of statistical significance was related to the small volume of enrolled patients. A large volume study is needed in the future.

In this study, 4 patients were infected after revision surgery in the septic group. Among them, 3 patients were infected with the same pathogen with prior infection. In 2 patients, infections were caused by resistant organisms, and 1 was caused by *Streptococcus*. Both resistant organisms and streptococcal infections are known as risk factors for failure after exchange arthroplasty.[3,28] Special explanations are required for patients with infections caused by these strains.

There is no definitive evidence in terms of the optimal time interval between two-stage surgeries in septic failure TKA. Re-implantation of a new prosthesis is widely performed 6–8 weeks after removal and debridement surgery.[29,30] Recent studies reported that a short interval

(less than 4 weeks) showed similar results compared with a long interval (more than 4 weeks).[29,31] In our study, the patients were recommended 6–12 weeks interval in two-stage surgery. Based on previous studies, we think that the interval might not have a significant effect on the infection rate after revision TKA.

The current study has several limitations. First, the risk factors associated with periprosthetic joint infection, including sex, obesity, operative time, diabetes, and history of malignancy, could have influenced the infection of revision TKA in our study; however, they were not considered in this study. Second, the true incidence of infection in the cohort of this study was likely underestimated because there were patients with a follow-up period of only approximately 2 years. Third, the postoperative risk factors for infection, including hematoma or wound problems, were not evaluated. Fourth, because of its retrospective design, this study was potentially affected by confounding variables.

Revision TKA with septic failure showed inferior postoperative clinical outcomes compared with aseptic revision TKA. A slightly higher but not significantly different infection rate was observed in the septic group.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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