Early and Mid-Term Results of Two Stage Revision Arthroplasty in Infected Total Knee Arthroplasty Cases

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Abstract

Aim: Total knee arthroplasty is a treatment method to relieve pain and limitation of movement caused by many knee diseases such as degenerative arthritis. Our aim was to retrospectively evaluate the early and mid-term results of patients with infected total knee arthroplasty who underwent two-stage revision as a treatment method and to compare them with the literature.

Methods: Patients who were diagnosed with infected knee prosthesis in the Orthopedics and Traumatology clinic of our hospital between January 2004 and 2014 and decided to undergo two-stage revision as a treatment method were included in this study. Laboratory results, radiographs, American Knee Society clinical and functional scores were evaluated.

Results: Twenty knees of 19 patients were included in the study. The first stage of two-stage revision was performed in all patients and the second stage was performed in 17 patients. Of the 20 knees diagnosed with infected total knee arthroplasty, 3 had early, 6 had delayed, and 11 had late infection. Preoperative clinical score was 53.29 ± 9.51, postoperative 83.21 ± 9.51 ($p<0.001$); functional score was 40.88 (SD 20.48) preoperatively and 63.23 ± 30.81 ($p=0.018$) postoperatively. The mean degree of flexion was 68.52° ±19.34 preoperatively and 92.64° ±16.30 after revision ($p<0.001$). Compared to the pre-revision period, pain levels of all our patients decreased and walking distances increased

Conclusion: Two-stage revision surgery in infected total knee prostheses was found to be compatible with the literature in terms of eradication of infection, postoperative clinical and functional scores.

***Keywords**: Knee arthroplasty, knee prostheses, prosthetic joint infection*

1. Introduction

As a result of the increase in the number of prosthesis operations performed to reduce the pain caused by joint damage and to increase the reduced range of motion, the number of cases requiring revision is also increasing. The reasons for revision can be divided into two categories as septic and aseptic. In many centers, infection rates are 0.5%-1% after hip replacement and 1%-2% after knee replacement[1]. In a study conducted by Koh et al., the reoperation rate due to periprosthetic infection after total knee arthroplasty was reported as 2%, and half of these infections were reported to be observed in the first 2 years after primary arthroplasty[2]. Similarly, in other studies investigating periprosthetic joint infection, the infection rate after total knee arthroplasty is observed to be between 2% and 5%[3-5]. It is stated that increased body mass index, steroid therapy, diabetes, hypertension and rheumatoid arthritis cause predisposition to prosthesis infections in these patients[6]. There are treatment methods such as antibiotic suppression, flushing-debridement, resection arthroplasty, arthrodesis, one-stage or two-stage revision for patients with infected knee prosthesis. Although there has recently been a tendency towards single-stage revision, the two-stage revision method described by Insall et al. in 1983 is used in delayed, biofilm-formed periprosthetic joint infections. Today, two-stage revision is known to be the gold standard treatment[7-8]. This study aims to evaluate the early and mid-term outcomes of two-stage revision arthroplasty for infected total knee arthroplasty cases. Given the complexity of managing prosthetic joint infections and the limitations of alternative approaches, understanding the effectiveness of two-stage revision during these critical periods can provide valuable insights for

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clinical decision-making. By comparing our findings with existing literature, this study seeks to contribute to the ongoing optimization of treatment protocols for infected TKAs.

2. Materials and Methods

Patients who were diagnosed with infected knee prosthesis in the Orthopedics and Traumatology Clinic of Cumhuriyet University Faculty of Medicine between January 2004 and January 2014 and decided to undergo two-stage revision as the treatment method were selected as the study group. The diagnosis of total knee prosthesis infection was made based on the findings of pain, redness, increased temperature, presence of fistula mouth in the affected knee, findings of implant failure in 2-way direct radiographs, erythrocyte sedimentation rate above 30 mm/m and C reactive protein value above 20 mg/l, and findings of leukocytes and microorganisms in the aspiration material from the joint. The diagnosis was also supported by Technetium 99 scintigraphy. In addition, tissue cultures were taken from at least 3 regions during surgery and evaluated.

Patients included in the study were diagnosed with infected TKA based on clinical symptoms (e.g., redness, pain, or fistula), elevated inflammatory markers (ESR >30 mm/hour, CRP >20 mg/L), and microbiological or imaging findings consistent with infection. Exclusion criteria included insufficient follow-up duration (<6 months), incomplete records, or systemic conditions contraindicating surgery. The follow-up period of the selected patient with the shortest follow-up period was 6 months and it was aimed to give early and mid-term results. For this purpose, the files of the patients eligible for the study were retrospectively analyzed. Patients were contacted again and their last clinical status, laboratory results, radiographs and knee score questionnaires were renewed. Revision knee arthroplasty was performed in the second stage surgery in 18 of 20 knees in which spacers were applied. Then, appropriate antibiotic treatment was applied under the supervision of an infectious disease specialist according to the clinical characteristics of the patients and the microorganism. The duration of antibiotic treatment was decided according to clinical and laboratory results and continued. When infection recurred in one of these patients, arthrodesis was performed because the infection could not be eradicated despite one arthroscopic and two arthrotomic washing debridement and antibiotic spacer placement. The knees of two patients underwent a second washout debridement and antibiotic spacer placement due to intraoperative findings in favor of infection.

Although the infections of these two patients were eradicated during follow-up, revision operation could not be performed. All patients included in the study were contacted by telephone and were asked to come for follow-up. Except for the two patients who died due to other reasons during the follow-up period, all other patients were contacted again. Laboratory results, radiographs, American Knee Society clinical and functional scores were re-evaluated. These two patients who were exited were included in the study because their follow-up data for at least 12 months after the revision operation were available in their files. Pain, redness, increased temperature, presence of fistula mouth in the affected knee, findings of loosening in 2-way direct radiographs, findings of complete blood count, erythrocyte sedimentation value above 30 mm/L, C reactive protein value above 20 mg/L, and also Gram stain and culture-antibiogram from aspiration material from the joint were used to diagnose total knee prosthesis infection. Diagnosis was also supported by Technetium 99 scintigraphy. In addition, tissue cultures were taken from at least 3 regions during surgery and evaluated. The American Knee Society's knee clinical and functional score questionnaire was completed in all patients. Additional problems such as urinary tract infection and deep vein thrombosis were solved. Chronic problems such as diabetes mellitus and hypertension were controlled. Antibiotic therapy was initiated postoperatively based on intraoperative culture results and included agents such as cefazolin or vancomycin. In cases where cultures yielded no growth, empirical antibiotics targeting common pathogens (e.g., Staphylococcus aureus) were administered for 6 weeks. Low molecular weight heparin 0.4 cc once a day were started postoperatively. Haemovac drains were discontinued on the second postoperative day and wound dressings were continued every other day. After the drains were removed, patients were tried to be mobilized with double crutches as much as they could tolerate without loading the operated extremity. When the culture results of the materials taken during the operation were obtained, the patients were consulted to the Department of Infectious Diseases and antibiotherapy was organized according to their recommendations. Patients were called for 3rd and 6th week follow-up. Clinical status of the knee, ESR, CRP, and WBC results were evaluated at the controls. At the end of the 6th week, revision surgery was decided with the approval of the infectious diseases department for patients with regressed infection parameters and clinically resolved infection. If the laboratory results were not good, antibiotic treatment was continued. All patients who were decided for the second stage were prepared for surgery as in the first stage. The previously placed antibiotic spacer was removed. Any dead tissues inside or outside the joint were debrided and samples were taken for culture. In cases of doubt, intraoperative tissue samples were taken and gram staining was performed. If the result supported infection, the antibiotic spacer was reinserted and the protocol in the first stage was followed. If infection was not considered, revision knee prosthesis was placed with antibiotic cement. When intraoperative culture results were obtained, the infectious diseases department was consulted and antibiotherapy was arranged. Discharged patients were called for outpatient follow-up six weeks later. Two-way knee radiographs, ESR, CRP, WBC results were evaluated for loosening. Subsequent follow-ups were performed at one and a half months, third months, four and a half months, sixth months, ninth months, twelfth months and every six months thereafter.

Knee clinical and functional scores of all patients were evaluated preoperatively and postoperatively according to the American Knee Society questionnaire. In this questionnaire, the clinical score is the score value obtained by subtracting the negative scores of flexion contracture, hyperextension and alignment from the positive scores consisting of the degree of pain described subjectively by the patients, range of motion and stability of the joint in all directions. Functional score is the score obtained by subtracting the negative scores given according to the support used by the patient while walking from the positive scores brought by the success in walking and climbing stairs.

The statistical evaluation of the data obtained was done in a computer environment. Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) (14.0) software. In the analysis, descriptive statistical measures such as mean, median, standard error, minimum and maximum, as well as the significance of the difference between the two pairs was calculated in the comparison of the preoperative and postoperative data of the patients and the data during the period when they were called for control. The homogeneity of the variances was checked with the Levene test. The conformity of the numerical data to normal distribution was evaluated with the Shapiro-Wilk test. For variables showing normal distribution, independent two sample t-test, dependent sample t-test. In the study, $p<0.05$ was considered statistically significant.

The research was conducted in accordance with the 1975 Helsinki Declaration. Approval was obtained from the Cumhuriyet Uni-

versity Faculty of Medicine Ethics Committee (26/06/2014, nu.2014-06/10). After obtaining the permissions, the patients were informed about the study according to the Informed Voluntary Consent Form and their consent was obtained.

3. Results

The median age of the patients included in the study was 63 (minimum 48 - maximum 78) for males and 67.5 (minimum 51 - maximum 72) for females. A total of 20 knees, including the left knee of six patients, the right knee of 12 patients and both knees of one patient, were included in the study.18 patients underwent primary prosthesis in external centers and two patients underwent primary prosthesis in our clinic, and the indication for primary prosthesis was osteoarthritis. In the first stage operation, removal of the infected material, debridement and spacer placement were performed. New prosthesis implantation in the second stage was performed in 18 knees, but could not be performed in two patients. One of the 18 knees that underwent revision resulted in fistulising osteomyelitis despite all treatment applications and arthrodesis was performed. Another patient underwent a two-stage revision knee replacement procedure.

When we looked at the comorbidities of the 19 patients diagnosed with infected knee prosthesis; nine patients had diabetes, five patients had diabetes and hypertension, one patient had Parkinson's disease, and one patient had aortic and mitral valve replacement. In the next part of the findings, 17 knees of 16 patients who underwent two-stage revision as a result of an infected knee prosthesis and three patients who underwent arthrodesis will be reviewed. The median time from the application of the spacer to the second-stage operation was 68 days (minimum 41 to maximum 214) for both male and female patients. This period was median 71 days (minimum 41 to maximum 214) in men and median 67 days (minimum 48 to maximum 158) in women.

When the follow-up periods of male and female patients after the second stage surgery were evaluated, the median follow-up period was found to be 17 months (minimum 6.5 - maximum 102). This period was median 14 months (minimum 7,5 - maximum 102) in male patients and median 17 months (minimum 6,5 - maximum 32) in female patients (p=0,045). The ages, infection periods, follow-up periods and genders of the study patients are given comparatively in **Table 1**.

ESR, CRP and WBC parameters were evaluated as infection parameters. At the end of follow-up, a significant improvement in infection markers was observed: ESR decreased from 52.35 ± 25.7 mm/hour pre-spacer to 29.52 ± 12.16 mm/hour (p<0.001), while CRP decreased from 50.34 ± 54.39 mg/dL to 8.12 ± 4.49 mg/dL (p<0.001). WBC showed no significant change during follow-up (p=0.079). When we compared these values statistically, the lower CRP value before revision compared to the CRP value before spacer was significant with p<0.001. However, when we compared the CRP value at follow-up with the CRP value before revision, the p value was found to be p=0.011 (**Table 2**).

When the white blood cell values were analyzed, it was observed that the mean WBC value before spacer was 9428 ± 3757.92, the mean WBC value before revision was 7228 ± 1408.42, and the mean WBC value at follow-up was 7357 ± 1373.18. When these results were compared statistically, the p value between the first and second values was found to be p<0.001 and the p value between the second and third values was found to be p=0.079.

According to the culture results obtained perioperatively in the first stage; *Staphylococcus aureus* was grown in four patients, *Staphylococcus epidermidis* in three patients, *Pseudomonas aeruginosa* in two patients and *Gemella species* in one patient. There was no growth in the remaining seven patients.

The American Knee Society clinical and functional scores improved significantly, with clinical scores increasing from 53.29 ± 9.51 preoperatively to 83.21 ± 9.51 postoperatively (p<0.001) and functional scores rising from 40.88 ± 20.48 to 63.23 ± 30.81 (p=0.018). Patients achieved a significant increase in range of motion, with mean flexion improving from 68.52° ± 19.34 to 92.64° ± 16.30 (p<0.001). Likewise, when the mean flexion contracture was evaluated, it was reduced from 7.05° ± 12.12 before revision to 1.76° ± 4.98 after revision (p=0.018).

Table 1

Age, sex, duration of infection, follow-up of patients

	Male Mean/Median	Female Mean/Median	p	Total Mean/Median
Age at time of primary TKR /year	56.5 ± 13.3 53 (40-77.5)	62.25 ± 6.4 63.25 (50.5-71)	0.067	60.1 ± 9.6 62.5 (40-77.5)
TKR spacer interval/month	52.7 ± 52.02 47 (0.75-120)	31.1 ± 24.2 26.5 (1-79)	0.049	39.8 ± 38.1 26.5 (0.75-120)
Spacer revision time / day	101.2± 59.8 71 (41-214)	82.7 ± 35.6 67 (48-158)	0.099	90.35 ± 46.34 68 (41-214)
Period of follow-up/month	27.6 ± 33.3 14 (7.5-102)	19.1 ± 9.2 17 (6.5-32)	0.045	22.6 ± 21.96 17 (6.5-102)

TKR: Total knee replacement

Table 2

ESR, CRP, WBC means and statistical comparisons

	Before Spacer	Before Revision	Follow-up	p
ESR±SD (mm/hour)	52.35 ± 25.7a	33.70 ±13.61b	29.52 ±12.16c	p(a-b):<0.001 p(b-c):0.027
CRP±SD (mg/dl)	50.34± 54.39a	9.59 ±8.57b	8.12 ± 4.49c	p(a-b):<0.001 p(b-c):0.011
WBC±SD (mm3)	9428 ±3757	7228 ±1408	7357 ± 1373.18	p(a-b):<0.001 p(b-c):0.079

CRP: C - reactive protein, ESR: Erythrocyte sedimentation rate, WBC: White Blood Cell

4. Discussion

Total knee arthroplasty (TKA) is a surgical treatment method that is increasingly used in the world and in our country for the treatment of problems of the knee that cannot be solved with medical treatments, with successful results[9]. Diabetes, hypertension, rheumatoid arthritis, increased body mass index and steroid therapy have been shown to be major risk factors for infection after primary total knee arthroplasty[6]. When we look at the 19 patients with infected TKA in our study, we see that nine patients had diabetes and five patients had diabetes and hypertension, supporting that diabetes is a risk factor. ESR, CRP, WBC values are important in the diagnosis of infection. These parameters increase after surgical trauma even in the absence of infection and return to normal within weeks. Here, it is important that CRP value returns to normal more rapidly than ESR. Studies emphasize that ESR above 30 mm/hour and CRP above 20 mg/l should be interpreted in favor of infection[10].

Our study highlights the clinical utility of CRP and ESR as reliable markers for monitoring infection resolution during two-stage revision. The significant decrease in CRP values pre- and post-revision ($p<0.001$) supports its role as a sensitive indicator, consistent with findings in the literature. In contrast, WBC showed minimal changes and lacked statistical significance during follow-up, reflecting its limited specificity in diagnosing periprosthetic infections, as reported by Toossi et al. (2012)[11]. There is still inconsistency about the effectiveness of WBC values in distinguishing septic and aseptic loosening. There are studies reporting that preoperative WBC values are within the normal range in cases. CRP is reported in the literature to have high specificity and sensitivity. Since it has been reported that the CRP value alone can be misleading, it supports other clinical and laboratory findings. Although the ESR value is affected by many factors, it is included among the diagnostic criteria for various periprosthetic joint infections as a criterion supporting infection[12-15].

The gold standard for the diagnosis of infection is the examination of deep tissue cultures obtained intraoperatively[16]. In our study, intraoperative cultures were obtained during the first stage from all patients in whom two-stage revision was planned. Care was taken to obtain samples from at least three different sites from each patient. Despite this, 12 of 20 knees of 19 patients (60%) were cultured. There was no growth in eight knees (40%). In the literature, even if all the rules to be considered during culture collection are followed, the growth rate in cultures obtained is reported to be 65-94%[17]. 18 of 20 knees diagnosed with infected knee prosthesis should receive oral or parenteral antibiotherapy before admission, and antibiotherapy should be discontinued for at least two weeks before culture is taken; however, we believe that our culture results caused less growth than the rate stated in the literature because the optimum time could not be provided due to the heavy clinics of the patients and the density of patients requiring operation.

Staphylococcus aureus (22%), *coagulase-negative staphylococci* (22%), *alpha- and beta-haemolytic streptococci* (9% and 5%), *enterococci* (7%), *aerobic Gram-negative bacilli* (25%) and *anaerobes* (10%) were the most common microorganisms found in infected knee arthroplasties[18]. In our study, *Staphylococcus aureus* was grown in five patients, *Staphylococcus epidermidis* in four patients, *Pseudomonas aeruginosa* in two patients and *Gemella Species* in one patient.

When we examine the antibiotics used in the cement, we see that the use of vancomycin, tobramycin, teicoplanin, gentamicin is concentrated in the literature[19]. We used antibiotic cement prepared by adding 2 g teicoplanin to cement containing 40 g gentamicin in all our patients in accordance with the literature. No toxicity was seen in any of our patients and the infection was eradicated except for one patient who ended up with arthrodesis.

When the literature is analyzed in terms of the waiting time between the two stages, it is seen that there is actually no consensus on this period[20]. Although it is concluded that it will be difficult to eradicate the infection if this interval is short; it has been shown that long interval periods increase the rate of recurrent infection. In addition, it is known that bone mineral density decreases and muscle atrophy is more common in long interval periods, which makes rehabilitation difficult after the second stage operation. It has also been reported that the cost of treatment increases and patient satisfaction decreases due to long treatment times[21]. When we consider that the mean interval between the two stages in our patients was 90.35 days and the median was 68 days, we see that although it seems long at first glance according to the literature, it does not go beyond the given limits. The reasons for this long interval include the difficulty in ensuring the eradication of the infection due to the absence of culture growth in nearly half of our patients and empirical antibiotic treatment, the fact that one patient received treatment for deep vein thrombosis and two patients received treatment for urinary tract infection before revision, and the fact that our patients could not come to the controls at the desired times due to referral problems.

A 91% success rate was reported in the mid-long term results of another 71 centers in which two-stage revision was performed in 96 infected knee prostheses[22]. When we look at our patients, success was achieved in 16 of 18 knees in which two-stage revision was performed. In one patient, infection was observed in the early period and was treated with debridement and antibiotherapy, but arthrodesis was performed as it resulted in fistulized osteomyelitis with discharge in the follow-up. One of our patients underwent a second two-stage revision surgery due to reinfection. In this patient, the cause of reinfection was urinary tract infection secondary to hy-

pospadias and urinary tract infection was treated before the second revision and the infection was eradicated in the follow-up. After this case, complete urinalysis was routinely performed in all patients before both primary and revision surgeries. After two-stage revision surgery, 94% success rate was achieved and this rate is compatible with the literature. The results of two-stage surgery performed by Petis et al. on 245 infected total knee arthroplasties support the success of this method[23].

In the literature, non-infectious complications included aseptic loosening (19.7%), instability (11.6%), osteolysis (10.4%), arthrofibrosis (8.1%), polyethylene abrasion (7.7%), malposition (5.4%), patellar complication (3.1%), periprosthetic fracture (2.3%), pain (1.5%) and lack of extensor mechanism (0.8%)[24]. In our patients, one medial condyle fracture was seen as a complication and was fixed with a plate-screw, and one patient developed deep vein thrombosis during follow-up after the first stage. These complications, which are also seen in primary knee replacement operations, are within acceptable limits. Arthrodesis can be performed after unsuccessful total knee arthroplasty, loss of the extensor mechanism, or highly virulent periprosthetic infections that cannot be eradicated[25]. One of the patients in this study underwent arthrodesis because the infection could not be treated.

In this study using the American Knee Society scoring system, the mean preoperative clinical score increased from 53.29 (SD 9.51) to 83.21 (SD 9.51) postoperatively ($p<0.001$). The significant improvement in functional scores (40.88 to 63.23; $p=0.018$) and range of motion (68.52° to 92.64°; $p<0.001$) underscores the efficacy of two-stage revision in restoring joint function. These results align with Haleem et al.'s (2004) reported success rates of 91% for infection eradication, further validating this approach as the gold standard for managing infected TKAs.[22]. When we analyzed the flexion contracture, it was found that it decreased from 7.05° (SD 12.12) preoperatively to 1.76° (SD 4.98) postoperatively ($p=0.018$). Both the increase in range of motion and the improvement in flexion contracture were found to be consistent with the literature (Table 3). In the study conducted by Petis et al., improvement in knee scores was observed after two-stage revision surgery[23].

The pain score, another parameter we evaluated in our patients, decreased significantly postoperatively. While we had six patients with severe pain preoperatively, there were no patients with severe pain postoperatively. Similarly, walking distances increased significantly postoperatively. Preoperatively, two patients could not walk and seven patients could walk at home, postoperatively there were no more patients who could not walk and the number of patients who could walk at home decreased to two. This study's retrospective nature and single-center design limit the generalizability of the findings. Future research should focus on prospective, multicenter trials comparing one-stage and two-stage revisions. Additionally, evaluating long-term outcomes and cost-effectiveness would provide further insights into optimizing treatment protocols.

5. Conclusion

Antibiotics were given to our patients for the agents grown in the culture. If there was no growth in the culture, antibiotherapy was empirically organised to cover the most common agents *Staphylococcus aureus* and *Staphylococcus epidermidis*. The drugs were administered intravenously for at least two weeks and, if necessary, six weeks. In the following periods, antibiotherapy was discontinued or continued according to the clinical examination of the knee, ESR and CRP results.

This study demonstrates that two-stage revision arthroplasty is an effective and reliable method for managing infected total knee arthroplasty, achieving a 94% infection eradication rate and significant improvements in clinical and functional outcomes. The reduction in CRP and ESR levels pre- and post-revision underscores the utility of these markers in infection monitoring. Furthermore, the observed improvements in range of motion and flexion contracture highlight the procedure's potential to restore joint function. Our findings align with existing literature, supporting two-stage revision as the gold standard treatment for infected TKA. However, the relatively long spacer-to-revision intervals in this cohort emphasize the need for careful infection monitoring and individualized treatment planning. The study's retrospective nature and single-center design limit the generalizability of these findings, underscoring the need for prospective, multicenter studies to evaluate long-term outcomes and optimize treatment protocols. Future research should focus on comparing one-stage versus two-stage revisions and exploring strategies to reduce spacer intervals without compromising infection control.

Statement of ethics

This study was approved by the Ethics Committee of Cumhuriyet University Faculty of Medicine Ethics Committee (26/06/2014, nu.2014-06/10) The study was performed according to the Declaration of Helsinki.

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Conflict of interest statement

The authors declare that they have no conflict of interest.

Availability of data and materials

The data supporting the conclusion of this article will be available by the authors without undue reservation. Thesis number: 427031
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Author contributions

All authors contributed to the article.

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