

A retrospective comparative study of infection control rate and clinical outcome between open debridement using antibiotic-impregnated cement beads and a two-stage revision in acute periprosthetic knee joint infection

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Abstract

The aim of this study was to determine whether the infection control rate of a modified debridement, antibiotics, and implant retention (DAIR) protocol (DAIR with antibiotic-impregnated cement beads) is comparable to that of 2-stage revision for acute periprosthetic joint infection (PJI) after total knee arthroplasty (TKA). We also aimed to determine whether this modified DAIR technique produced better clinical results than those obtained using 2-stage revision in terms of functional outcome, range of motion (ROM), and patient satisfaction at 2 years after surgery.

This retrospective comparative study included patients who underwent modified DAIR (7 patients, 9 knees) or 2-stage revision (8 patients, 9 knees) for acute PJI of the knee joint. Infection control rate, functional outcome measured using Western Ontario and McMaster Universities Arthritis Index (WOMAC) score, ROM and patient satisfaction were compared between the two groups.

There was no difference in infection control rates between the modified DAIR and 2-stage revision groups (78% vs 78%, respectively). In contrast, surgical outcome in the modified DAIR group was tended to be better than 2-stage revision group, but it did not reach statistical significance. Median maximal range of flexion was 103° in the modified DAIR group and it was 90° in the 2-stage group ($P = .191$). In addition, the median WOMAC function score was 24 in the modified DAIR group and it was 30 in the 2-stage group ($P = .076$). Median patient satisfaction measured using visual analogue scale was 8 in the modified DAIR group and 5 in the 2-stage group ($P = .069$).

The infection control rates of the modified DAIR protocol and 2-stage revision protocol were similar for the treatment of acute PJI of the knee joint. However, the modified DAIR protocol could not provide substantially increased functional outcomes and patient satisfaction compared to 2-stage revision. Therefore, the modified DAIR technique should be considered to be of limited use in patients with high surgical morbidity.

Abbreviations: ASA = American Society of Anesthesiologists, BMI = body mass index, CRP = C-reactive protein, DAIR = debridement, antibiotics, and implant retention, IRB = institutional review board, PJI = periprosthetic joint infection, ROM = range of motion, TKA = total knee arthroplasty, VAS = visual analogue scale, WOMAC = Western Ontario and McMaster Universities Arthritis Index.

Keywords: functional outcome, infection control rate, open debridement, periprosthetic joint infection, two-stage revision

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This study protocol was approved by the ethics committee of the Samsung Medical Center. All participants gave their informed consent to assessing and using their data.

All participants gave their informed consent to publishing their data.

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1. Introduction

Many aspects of the surgical treatment of periprosthetic joint infection (PJI) after total knee arthroplasty (TKA) have not been established. Two-stage resection arthroplasty and revision is currently the treatment of choice.^[1] However, this technique is costly and time-consuming. Furthermore, the two major surgical steps required can cause considerable surgical morbidity and functional impairment after surgery.^[2–4] Thus, some surgeons prefer to first perform open debridement, antibiotics, and implant retention (DAIR) in patients with acute PJI.^[5–9] If the PJI can be successfully treated, this option may reduce surgical morbidity. However, the use of DAIR for PJI of the knee joint has been criticized because of its variable infection control rate even in cases of acute PJI.^[1,5,10] Therefore, new strategies are needed to reduce surgical morbidity and functional impairment while improving the infection control rate.

The additional use of antibiotic-impregnated cement beads may increase the success rate of DAIR for acute PJI of the knee joint. Factors previously reported to improve the success rate of PJI surgery include disrupting biofilm and increased antibiotic efficacy.^[11] Therefore, the antibiotic-impregnated cement beads may satisfy these conditions, as they can deliver higher dose of antibiotics to the knee joint than intravenous antibiotics.^[5] In a previous report, an improved infection control rate (90%) was reported using a technique consisting of 2-stage DAIR involving repeated debridement with antibiotic-impregnated cement beads.^[5] However, there are still insufficient data regarding the infection control rate of DAIR using antibiotic-impregnated cement beads.

DAIR for PJI may provide better functional outcomes and patient satisfaction after surgery for acute PJI following TKA than 2-stage revision.^[5] Two-stage revision is more costly than DAIR and increases the risk of surgical morbidity. In addition, range of motion (ROM) of the knee joint may decrease after 2-stage revision, regardless of whether static or mobile antibiotic-impregnated cement spacers are used during the first stage of surgery.^[2,12]

We sought to determine whether the infection control rate of a modified DAIR protocol (DAIR with antibiotic-impregnated cement beads) is comparable to that of 2-stage revision for acute PJI of the knee joint. In addition, we aimed to determine whether this modified DAIR technique produced better clinical results than those obtained using 2-stage revision in terms of functional outcome, ROM, and patient satisfaction at 2 years after surgery. We hypothesized that the infection control rate of our modified DAIR technique would be similar to that of 2-stage revision for acute PJI of the knee joint and that the clinical results of patients successfully treated using the modified DAIR technique would be better than those obtained using 2-stage revision.

2. Methods

This retrospective comparative study included patients who underwent modified DAIR (9 knees, 7 patients) or 2-stage revision (9 knees, 8 patients) for acute PJI of the knee joint with more than 2 years of follow-up after surgery. The inclusion criterion was a diagnosis of acute PJI after primary TKA. PJI was diagnosed using previously reported criteria.^[13] Acute PJI was defined as PJI in which the interval between infection onset and surgery was < 4 weeks, as several studies have revealed that open debridement can be an option for these patients.^[6] From March 2012 to July 2013, 40 patients (43 knees) with PJI after TKA

underwent surgical treatment. The exclusion criteria were as follows:

1. patients with classical DAIR without insertion of antibiotic-impregnated cement beads,
2. who have had multiple surgeries,
3. who died before the study evaluation,
4. with chronic PJI,
5. who had not completed a planned operation of 2-stage revision.

Among patients eligible for this study, 2 patients (2 knees) who underwent classical DAIR (i.e., without antibiotic-impregnated cement beads) and those who had undergone multiple operations for PJI before 2-stage revision at our hospital (6 knees; 6 patients) were excluded. Therefore, there were 10 knees (8 patients) in the modified DAIR group and 25 knees (24 patients) in the 2-stage revision group. One patient who died due to a disease unrelated to this surgery was excluded from the DAIR group. In the 2-stage group, 4 knees (4 patients) were excluded because of unplanned retention of prosthetic articulating spacers until evaluation for this study. In addition, 12 knees (12 patients) with chronic late infections were also excluded from the 2-stage revision group. Consequently, 7 patients (9 knees) were included in the modified DAIR group and 8 patients (9 knees) were included in the 2-stage revision group (Fig. 1). The differences were evaluated between patients in the modified DAIR and 2-stage revision groups in terms of age, sex, preoperative American Society of Anesthesiologists (ASA) classification, interval between primary TKA and PJI, duration of PJI symptoms, follow-up period after the second stage of surgery, and body mass index (BMI) using medical records. This study was approved by the institutional review board of the authors' hospital (IRB number: 2014-10-065-001). All participants gave their informed consent to assessing and using their data.

The treatment protocol of the DAIR group consisted of a 2-stage operation with retention of the prosthesis. Thorough debridement was performed, and antibiotic-impregnated cement beads were inserted during the first stage. The beads were simply removed during the second stage without repeated debridement. All of the surgeries were performed by a single surgeon (one of the authors) using a modified medial parapatellar approach with a tourniquet. During debridement, the polyethylene insert was changed in all patients. All of the synovium and necrotic soft tissues of the suprapatellar pouch and medial and lateral gutters were completely excised at once (Fig. 2). All retained components were scrubbed using a betadine solution. In addition, the joint was irrigated with diluted betadine solution and then with saline before the new polyethylene insert was replaced. Vancomycin-based antibiotic-impregnated cement beads were then placed in the medial and lateral gutters and suprapatellar space (Fig. 3). To make the beads, 4 g vancomycin and 2 g cefotaxime were added to 40 g bone cement (Simplex P bone cement; Stryker Orthopedics, Mahwah, NJ). Intravenous antibiotics were used for 6 weeks after the first stage of surgery, after which time the cement beads were surgically removed using part of a previous incision (Fig. 4). We routinely planned to remove all cement beads 6 weeks after the initial debridement. We did not perform additional debridement while removing the beads because it was the time the infection was completely eradicated when we decided to remove the beads. In addition, we wanted to reduce patients' surgical morbidity by using minimal invasive surgery by only removing the beads.

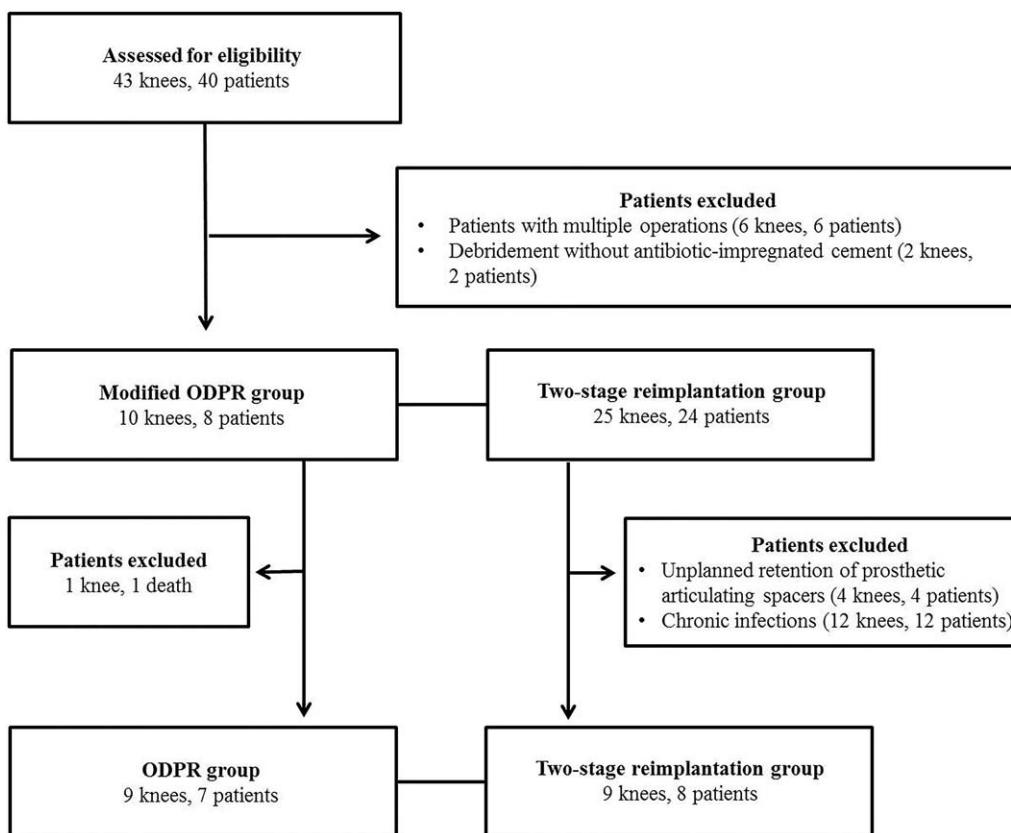


Figure 1. Flow chart of the patients included in the study.

The 2-stage revision protocol consisted of 2-stage operation with removal of all implants and foreign materials. All of the surgeries were performed by the same surgeon who performed the modified DAIR using the same surgical approach. The first stage of the operation included removal of all components and cement and thorough debridement of all necrotic bone and tissue. Copious irrigation using diluted betadine solution and saline was

performed. Removed femoral and tibial components were resterilized and used to make articulating temporary spacers. Bone cement impregnated with the same amount of antibiotic used in the DAIR group was used to fix the resterilized components. When the cement reached a doughy phase, it was used to coat the bony surface of the femur and tibia. Then, the resterilized femur and tibial components were inserted without

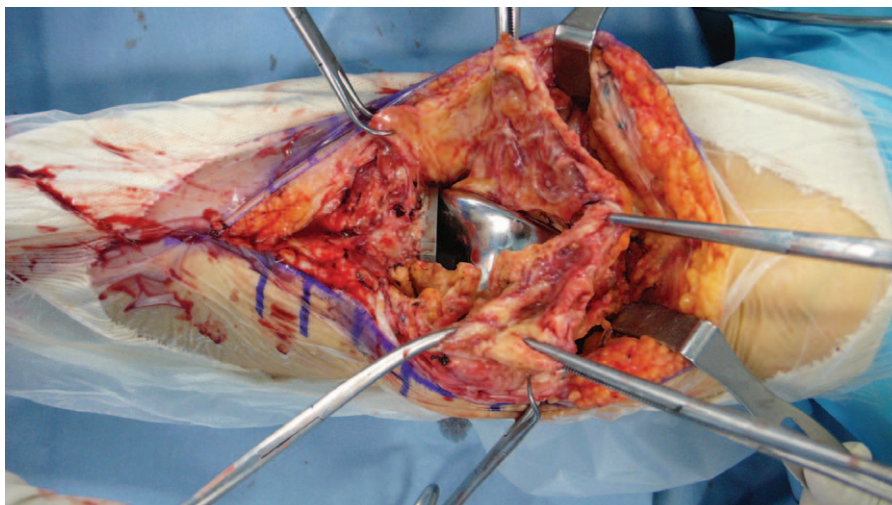


Figure 2. All of the synovium and necrotic soft tissues of the suprapatellar pouch and medial and lateral gutters were completely excised at once.

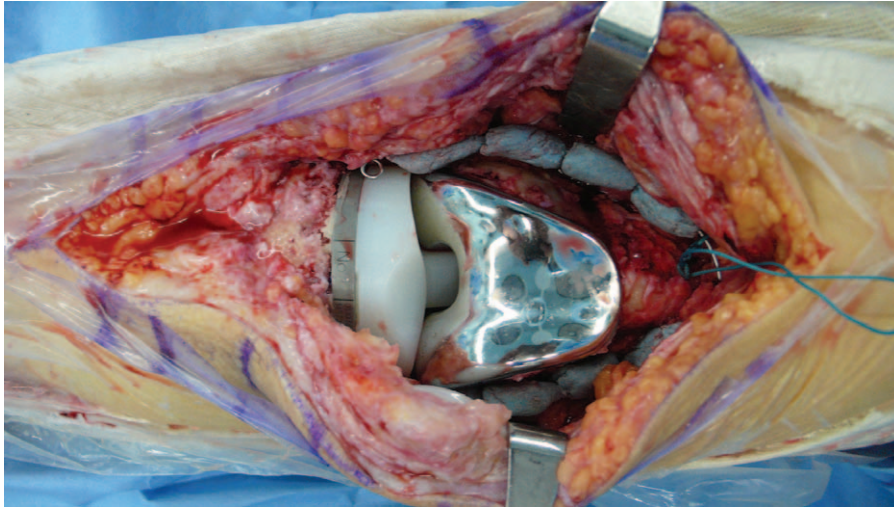


Figure 3. Vancomycin-based antibiotic-impregnated cement beads were placed in the medial and lateral gutters and suprapatellar space.

pressurization.^[14,15] The new polyethylene insert with an appropriate thickness was inserted (Fig. 5). Intravenous antibiotics were employed for 6 weeks after the first stage of surgery, after which time the patient was returned to the operating room for revision.^[16] We performed revision if the patient's serum C-reactive protein (CRP) level was less than 1.0mg/dL and no clinical signs and symptoms of persistent infection were present. All patients included in this study met the criteria for the revision. When we performed revision, the new implants were used after removing the implant reused for first stage operation.

The postoperative course was similar between the modified DAIR and 2-stage revision groups. During the first stage of surgery, a drain was kept in the joint until the amount of drainage was reduced < 50 mL/8 h. However, the drain was maintained no longer than 5 days after surgery. During the second stage, the drain was routinely removed on the second postoperative day. In every surgery, on the second postoperative day, all patients began ambulating with a walker. After the second stage of surgery,

patients were placed on variable courses of oral antibiotics (average of 6 months) (Tables 2 and 3).

Clinical outcome data were collected by reviewing medical records. We routinely followed up the patients 6 weeks, 3 months, 6 months, and 1 year, and annually thereafter, after the second stage of the operation. Clinical outcomes were assessed using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC). Flexion contracture and maximal flexion of the knee joint were measured using a goniometer with the patient supine. Each patient's satisfaction regarding the surgical outcome was evaluated at the last follow-up using a numerical satisfaction visual analogue scale (VAS) ranging from 0 to 10, where 0 indicated "very dissatisfied" and 10 indicated "very satisfied." Infections were considered to be controlled if serum CRP level was <1mg/dL with no clinical signs and symptoms of infection. Treatment failure was defined as the requirement for long-term prophylactic antibiotic therapy or additional surgery for recurrent infection.



Figure 4. The cement beads were surgically removed using part of a previous incision without additional debridement.

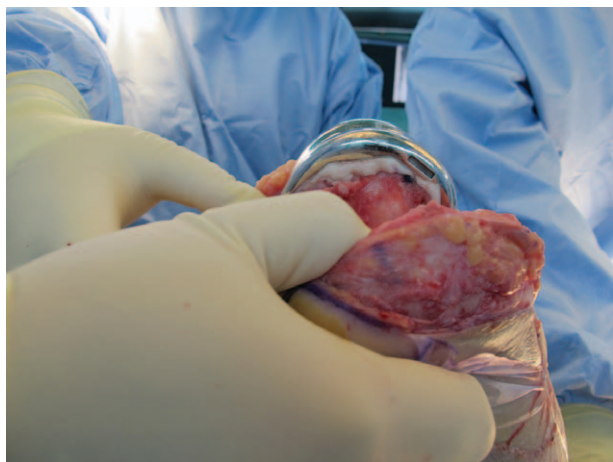


Figure 5. Bone cement impregnated with antibiotics was used to fix the resterilized components. When the cement reached a doughy phase, it was used to coat the bony surface of the femur and tibia. Then, the resterilized femur and tibial components were inserted without pressurization. The new polyethylene insert with an appropriate thickness was inserted.

Statistical analyses were performed using SPSS for Windows (version 18.0; SPSS Inc, Chicago, IL), and *P* values of <.05 were considered statistically significant. Differences in infection control rates between the modified DAIR and 2-stage revision groups were determined using Fisher’s exact test. Patient satisfaction and clinical outcomes (flexion contracture, maximal flexion WOMAC pain, stiffness, and function subscales) at the last follow-up visit are reported as medians and interquartile ranges. The significance of any differences between groups was determined using the Mann–Whitney *U* test.

3. Results

No differences were found between patients in the modified DAIR and 2-stage revision groups in terms of age, sex, preoperative ASA classification, interval between primary TKA and PJI, duration of PJI symptoms, and follow-up period after the second stage of surgery, with the exception of BMI (Table 1).

There was no difference in infection control rates between the modified DAIR and 2-stage revision groups (78% vs 78%, respectively; *P* = 1.000) (Tables 2 and 3). Five cases of methicillin-

resistant organisms (3 methicillin-resistant *Staphylococcus aureus* infections and 2 methicillin-resistant coagulase-negative staphylococci infections) were cultured in this study. There were 2 treatment failures in the DAIR group. One patient was successfully treated with subsequent 2-stage revision surgery. The other patient’s infection has been suppressed with long-term antibiotic treatment. There were 2 treatment failures in the 2-stage revision group. Both patients’ CRP levels remained elevated during the follow-up period; neither had any definite clinical signs and symptoms of recurrent PJI until the last follow-up visit. These patients have since been followed up without additional antibiotics or surgical treatments.

Surgical outcome in the modified DAIR group was tended to be better than 2-stage revision group, but it did not reach statistical significance. Median maximal range of flexion was 103° in the modified DAIR group and it was 90° in the 2-stage group (*P* = .191). In addition, the WOMAC function score was 24 in the modified DAIR group and it was 30 in the 2-stage group (*P* = .076). Median patient satisfaction measured using VAS was 8 in the modified DAIR group and 5 in the 2-stage group (*P* = .069) (Table 4).

4. Discussion

The principal findings of this study were that the modified DAIR technique achieved comparable infection control rates (78% vs 78%), however, functional outcome and patient satisfaction were not substantially improved.

Our findings support the hypothesis that infection control rates would be similar between the modified DAIR and 2-stage revision groups. The use of DAIR to treat PJI of the knee joint has received criticism due to its variable success rate (ranging from 24% to 100%).^[1] The considerable failure rate of DAIR may result from biofilm formation established shortly after infection.^[11] Thus, early surgery in cases of acute infection (i.e., before biofilm formation) has been generally used as indication for DAIR. In a previous study, the success rate of DAIR was higher in early postoperative infections than in acute hematogenous infections (81 vs 55%). In contrast, even for early postoperative infections, the failure rate of DAIR is as high as 63%.^[17] These factors most likely prevent surgeons from choosing DAIR to treat PJI after TKA. In the present study, we improved the infection control rate using antibiotic-impregnated cement beads. Our results are in line those of a previous study that used a similar 2-stage debridement

Table 1
Comparisons of demographic factors, interval between primary TKA and PJI, duration of PJI symptoms, and follow-up period between the modified DAIR and 2-stage revision groups.

Variables	Modified DAIR group Median (IQR)	Two-stage group Median (IQR)	<i>P</i>
Age (years)	75 (73–78)	74 (63–80)	.564
Sex (female:male)	9:0	7:2	.471
BMI (kg/m ²)	25.6 (23.2–27.9)	22.4 (22–25.3)	.046
Preoperative ASA classification			1.000
II	6	7	
III	3	2	
Interval from primary TKA to PJI (months)	2 (0.4–13.5)	13 (4–43)	.101
Duration of PJI symptoms (days)	4 (2–9)	10 (2–28)	.130
Follow-up period (months)	24 (14–29)	19 (14–25)	.561

Data are presented as the medians and the interquartile ranges except for sex and the preoperative ASA score. ASA=American Society of Anesthesiologists, BMI=body mass index, DAIR=debridement, antibiotics, and implant retention, IQR=interquartile range, PJI=periprosthetic joint infection, TKA=total knee arthroplasty.

Table 2**Patient data and inflammatory markers at the last follow-up in the modified DAIR group.**

Case	Sex	Age (years)	ASA class	Interval from TKA to PJI	Duration of PJI symptoms (days)	Microorganisms	IV antibiotics	Duration of oral antibiotics (months)	ESR (mm/h)/CRP (mg/dL)
1	F	77	3	14 days	2	MSSA	Cefazolin	Cefadroxil (3)	2/0.04
2	F	75	3	50 months	5	<i>Escherichia coli</i>	Ciprofloxacin	Ciprofloxacin (4)	32/1.34 (failure)*
3	F	72	2	15 months	1	<i>Streptococcus</i>	Ampicillin/sulbactam	Ciprofloxacin (3)	18/0.13
4	F	77	2	2 months	2	MSSA	Nafcillin → ampicillin/sulbactam†	Cefadroxil and rifampin (8)	29/0.13
5	F	79	2	7 days	4	MRSA	Vancomycin	Ciprofloxacin and rifampin (6)	25/0.42
6	F	79	2	7 days	4	MRSA	Vancomycin	Ciprofloxacin and rifampin (6)	25/0.42
7	F	74	3	12 months	12	MRCNS	Vancomycin	Ciprofloxacin (2)	18/0.03
8	F	74	3	12 months	12	MRCNS	Vancomycin	Ciprofloxacin (2)	Failure [§]
9	F	72	2	1 months	30	MRSA	Vancomycin	Ciprofloxacin and rifampin (1)	31/0.06

ASA = American Society of Anesthesiologists, CRP = C-reactive protein, DAIR = debridement, antibiotics and implant retention, ESR = erythrocyte sedimentation ratio, IV = intravenous, MRCNS = methicillin-resistant coagulase-negative staphylococci, MRSA = methicillin-resistant *Staphylococcus aureus*, MSSA = methicillin-sensitive *S aureus*, PJI = periprosthetic joint infection.

* This infection has been suppressed with long-term antibiotic therapy.

† Intravenous antibiotics were changed 4 weeks after the first stage of modified DAIR because of hepatotoxicity.

§ Two-stage reimplantation was performed in this case of recurrent PJI.

Table 3**Patient data and inflammatory markers at the last follow-up in the 2-stage revision group.**

Case	Sex	Age (years)	ASA class	Interval from TKA to PJI (months)	PJI symptom duration (days)	Microorganisms	IV antibiotics	Duration of oral antibiotics (months)	ESR (mm/h)/CRP (mg/dL)
1	F	60	2	13	3	MSSA	Cefazolin	Cefadroxil (3)	99/1.59 (failure)
2	F	74	2	8	25	<i>Escherichia coli</i>	Ciprofloxacin	Ciprofloxacin and rifampin (7)	18/0.06
3	F	81	3	30	30	No growth	Vancomycin	Ciprofloxacin (1)	14/0.09
4	F	81	3	30	30	No growth	Vancomycin	Ciprofloxacin (1)	14/0.09
5	F	78	2	100	2	<i>Ehria coli</i>	Ciprofloxacin	Ciprofloxacin (4)	9/0.14
6	M	69	2	2	3	MRSA	Vancomycin	Ciprofloxacin and rifampin (3)	9/0.63
7	M	58	2	56	3	MRSA	Vancomycin	Ciprofloxacin and rifampin (3)	22/1.18 (failure)
8	F	77	2	6	10	MRSA	Vancomycin	Levofloxacin and rifampin (5)	35/0.1
9	F	65	2	1	21	<i>Pseudomonas aeruginosa</i>	Tazocin	Ciprofloxacin (3)	62/0.81

ASA = American Society of Anesthesiologists, CRP = C-reactive protein, ESR = erythrocyte sedimentation ratio, IV = intravenous, MRSA = methicillin-resistant *Staphylococcus aureus*, MSSA = methicillin-sensitive *S aureus*, PJI = periprosthetic joint infection.

protocol with cement beads and achieved a 90% infection control rate.^[18] However, the indications for this modified DAIR technique remain unclear. DAIR should be used to manage acute PJI. Theoretically, this technique should be used to treat patients without compromised immunity and with PJI due to low-virulence organisms. However, the virulence of organisms is usually not confirmed before surgery, as DAIR must be performed in timely manner. In the present study, we encountered 5 cases of methicillin-resistant organisms (3

methicillin-resistant *S aureus* infections and 2 methicillin-resistant coagulase-negative staphylococci infections), 1 of which failed to be successfully treated. Our findings suggest that the modified DAIR technique can be used in cases involving methicillin-resistant organisms. However, because it is difficult to obtain concrete evidence from this small number of cases, further study is needed to support our conclusions.

Our findings did not support the hypothesis that the clinical results of successfully treated patients would be better with the modified DAIR technique than with 2-stage revision. Even though the modified DAIR technique can reduce surgical morbidity, 2 surgical steps are still required. Furthermore, during the radical debridement process, an imbalance can develop between flexion and extension gaps or between medial and lateral gaps. This imbalance often cannot be corrected by using a thicker polyethylene insert. In addition, the cement beads in the gutters of the knee joint can limit ROM of the joint. Thus, even though patient satisfaction tended to be higher with this technique, the objective functional outcome was not superior to that of the classical 2-stage revision technique.

This study has several limitations. First, the number of subjects was small and the follow-up period was relatively short. Thus, the statistical analyses of this study may have been underpowered, and the follow-up period may be insufficient to determine accurate infection control rates for both techniques. However,

Table 4**Comparison of clinical outcomes of the DAIR and 2-stage revision groups.**

Variables	DAIR group	Two-stage group	P
	Median (IQR)	Median (IQR)	
Flexion contracture (°)	2.5 (0–10)	0 (0–5)	.411
Maximal flexion (°)	103 (100–125)	90 (90–110)	.191
WOMAC score			
Pain	0 (0–3.8)	0.5 (0–1.3)	.929
Stiffness	2 (0–3.3)	3.5 (2–4)	.134
Function	24 (14.8–27.5)	30 (23.3–40)	.076
Patient satisfaction	8 (5.3–8)	5 (4–6)	.069

Data are presented as the medians and interquartile ranges.

DAIR = debridement, antibiotics and implant retention, IQR = interquartile range, WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index.

treatment of PJI using the modified DAIR is not the treatment method performed frequently. Thus, we think that our results are sufficient for a preliminary report and provide valuable information. Second, the allocation of the modified DAIR or 2-stage operation was not randomized. Even though we determined the surgical technique after having discussions with the patient about the advantages and disadvantages of each technique, a selection bias may have been present. It is possible that the modified DAIR was chosen for the treatment of patients with less severe clinical symptoms. However, we confirmed that there were no differences in demographic data, interval between primary TKA and PJI, duration of PJI symptoms, and follow-up period between the modified DAIR and 2-stage revision groups, suggesting that any possible selection bias was reduced. In addition, it is not easy to perform the randomized controlled trial in determining the surgical treatment of PJI because it is very serious complication after surgery. Thus, with lack of concrete evidence from the randomized controlled trial at this time, we think that retrospective studies can provide valuable information to readers. Third, 2 knees classified into the treatment failure in the 2-stage revision group show only elevated serum CRP level without need of additional treatment. If these knees are defined as successful in treatment, there may be differences in the infection control rate between the two groups. The strength of this study is that it reports the results of surgical treatment methods (DAIR with antibiotic impregnated cement beads) not had enough evidence in the literature.

In conclusion, the infection control rates of the modified DAIR protocol and 2-stage revision protocol were similar for the treatment of acute PJI of the knee joint. However, the modified DAIR protocol could not provide substantially increased functional outcomes and patient satisfaction compared to 2-stage revision. Therefore, the modified DAIR technique should be considered to be of limited use in patients with high surgical morbidity.

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