Original Article

Intraoperative Cement-on-Cement Antibiotic-Loaded Articulating Spacer for Treatment of Infected Total Knee Arthroplasty: Description and Results of A New Technique

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Background: Two-stage exchange revision total knee arthroplasty [TKA] is the gold standard for treating a chronically infected TKA. Application of a cement-on-cement antibiotic-loaded articulating spacer in the 1st stage exchange arthroplasty provides a good functional outcome during the interim between stages, easy surgical exposure for the 2nd stage exchange revision arthroplasty, and excellent infection eradication.

Objective: To describe the intraoperative use of a cement-on-cement antibiotic-loaded articulating spacer made with a new type of mold and evaluate the clinical results.

Materials and Methods: A retrospective case study was conducted of eight patients, mean age 71 years (range 62 to 84), who between 2011 and 2016 had been diagnosed with chronically infected TKA and who had undergone a two-stage exchange revision TKA using a cement-on-cement antibiotic-loaded articulating spacer. The mean time between the first and second stage operations was 4.5 months (range 3 to 7 months). The mean follow-up time was 26.75 months (range 12 to 40 months).

Results: No recurrence of infection was found in any of the patients. All functional outcomes improved compared to the preoperative period: Knee Society Score rose from 30 to 86, functional score increased from 16 to 81, and knee flexion increased from 68.2° to 104.7°. No spacer-related complications were seen in any of the patients.

Conclusion: Preliminary results, based on a small sample of eight patients, indicate that the technique of intraoperatively using a cement-on-cement antibiotic-loaded articulating spacer for treatment of chronically infected TKA provides good results in eradication of infection, improvement of functional outcome, and absence of spacer-related complications.

Keywords: Infected total knee arthroplasty, Cement spacer, Antibiotic-loaded articulating spacer, Chronic infection, Two-stage exchange, Revision total knee arthroplasty

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Infected total knee arthroplasty [TKA] is the one of the most devastating operative complications and is associated with increased morbidity and medical expense(1). One-stage exchange revision TKA is cost-effective and enhances patient recovery in otherwise healthy cases where there is an identifiable microorganism(2-4). Two-stage exchange revision TKA is the gold standard for treatment of chronically infected TKA and has a success rate exceeding 90% in unselected patients(2,3,5-7). Compared to one-stage exchange revision TKA, two-stage exchange revision TKA is suitable for a more diverse patient population,

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e.g., chronically infected TKA or infections with a drug resistant organism, patients with poor soft tissue around the knee, and immunocompromised patients. In cases of an infection of unknown etiology, re-debridement and re-insertion of an antibiotic-loaded cement spacer in a two-stage exchange arthroplasty increases the chance of infection eradication before insertion of the revision prosthesis(8,9).

In two-stage exchange revision TKA, the first stage consists of prosthesis removal, organism identification, debridement, and insertion of an antibiotic-loaded cement spacer, all of which are essential for a successful outcome. The antibiotic-loaded cement spacer allows soft tissue healing while minimizing soft tissue contractures. It also delivers high local doses of antibiotics for organism eradication prior to the second stage reimplantation(10,11). There is controversy, however, regarding the relative advantages of a static versus an articulating cement spacer in preventing soft tissue contractures and in controlling infection(12-14). The static antibiotic-loaded cement spacer can be inserted easily. It prevents knee movement, which facilitates microorganism eradication, but also it increases the risk of migration, fracture, bone loss, and patellar tendon injury, and is associated with a reduced postoperative range of motion [ROM](14-17). Immobilization of the knee between stages impedes the patient's daily activities during that period and results in quadriceps shortening and capsular contractures(17). Moreover, knee exposure in the second stage TKA revision may be challenging because of soft tissue contractures, requiring an extensile approach(18).

Articulating antibiotic-loaded cement spacers were developed to facilitate knee movement between the operative stages, to improve the patient's quality of life, and to prevent bone loss from spacer migration(17). Knee movement decreases the risk of soft tissue contractures, and thus simplifies exposure in the second stage revision TKA. Furthermore, an articulating spacer also facilitates patient rehabilitation after reimplantation(19,20).

The authors developed a new type of articulating spacer mold for producing articulating spacers for treating chronically infected TKA. The new mold consists of two silicone mold pieces, the femoral and the tibial articulating surface molds. This mold is intended to simplify the process of preparation of an intraoperative, cement-on-cement, antibiotic-loaded articulating cement spacer [ALACS]. The mold is reusable, making it cost efficient: it can be re-sterilized by gas sterilization.

Materials and Methods

A retrospective case study was conducted of patients who had been diagnosed with a chronically infected TKA and who had undergone a two-stage revision TKA with an intraoperative-made cement-on-cement ALACS between 2011 and 2016. We excluded patients who had been partially treated at other centers and those with less than one year of follow-up. The study was approved by Institutional Review Board of the university.

The primary objective of the study was to determine the success rate of infection eradication with the new mold. The secondary objectives were to obtain information on spacer-related complications and functional results using that mold as measured by Knee Society Score [KSS], functional score, and ROM in the preoperative period, between stages, and after the second operative stage.

All patients in the study had been diagnosed with a chronically infected TKA according to the Musculoskeletal Infection Society [MSIS] criteria 2011 for the diagnosis of periprosthetic joint infection(21). A definite periprosthetic joint infection [PJI] was diagnosed if any of the following were present: patients with a sinus tract communicating with the prosthesis, a pathogen was isolated by culture from at least two separate tissue or fluid samples obtained from the affected prosthetic joint, or if four of the following six criteria were present: elevated erythrocyte sedimentation rate [ESR] and serum C-reactive protein [CRP] concentration, elevated synovial fluid leukocyte count, elevated synovial neutrophil percentage (PMN%), presence of pus in the affected joint, isolation of a microorganism by culture from one sample of periprosthetic tissue or fluid, or >5 neutrophils per high-power field in five high-power fields on histopathologoic examination of periprosthetic tissue at x400 magnification.

Surgical technique for preparation of cement-on-cement ALACS

During the first stage, a standard medial parapatellar approach was used for surgical exposure. All of the prosthesis (femoral component, tibial component, polyethylene, and patella component) including cement were removed, followed by aggressive debridement and irrigation. At least five tissue samples from different sites were sent for aerobic culture. Diluted betadine solution was used to irrigate

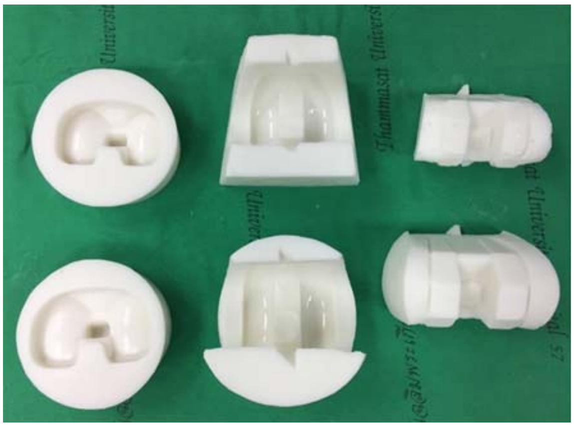

Figure 1. Silicon spacer molds for producing the femoral articulating surface cement and tibial articulating surface cement spacers.

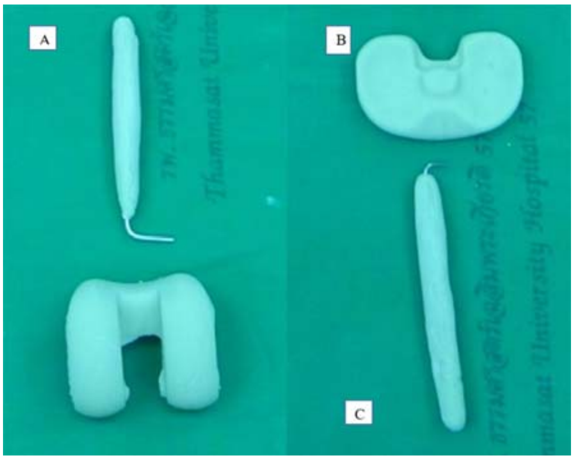

Figure 2. (A) Antibiotic-loaded femoral articulating cement; (B) antibiotic-loaded tibial articulating cement spacers; (C) antibiotic loaded intramedullary rod.

the wound and was then allowed to soak into the knee joint ≥5 minutes.

After an appropriate size of silicone cement spacer mold was determined (Figure 1), two batches of Palacos® bone cement (Heraeus Medical GmbH, Hanau, Germany) were prepared in addition to a high dose of combination antibiotics, chosen according to the surgeon's preference, i.e., either 4 g of vancomycin +4 g of fosfomycin (Fosmicin®, Meiji Pharmaceutical Co, Tokyo, Ltd, Japan) or 4 g of vancomycin +2 g of cetazidime/40 g of cement. The antibiotic powder and the polymethyl methacrylate particle cement powder were mixed together, then liquid methyl methacrylate monomer was added. After reaching the doughy phase, the antibiotic-loaded cement was packed and pressed into the femoral and the tibial component molds to create an articulating cement surface which was similar to the posterior stabilized femoral and tibial prostheses. Two 6 inch Kirschner wires were coated with the antibiotic cement mix before being inserted into the femoral and tibial medullary canals (Figure 2). After the femoral and tibial cement components had hardened, they were removed from the molds. Another batch of cement with antibiotics was mixed and applied in the early dough phase to the femoral articulating surface, then inserted into the distal femur. The coronal, sagittal and rotational alignment of the femoral articulating cement surface was determined and the molded pieces were left until the cement had cured. A third batch of cement with antibiotics was prepared and applied to the tibial articulating surface and inserted into the proximal tibia. The coronal and sagittal alignment of the tibial articulating surface was determined. Old meniscal scars were used as landmarks of the joint line. The soft tissue tension was set in extension. While the cement was hardening, the limb was distracted and held in full extension to create the correct alignment and to maximize soft tissue tension (Figure 3). The ROM, stability, and patellar tracking were assessed and recorded. A Hemovac drain was inserted and the wound was closed. Routine post-operative anteroposterior and lateral knee radiographs were made (Figure 4). A hinged knee brace was applied with a knee flexion limit of 90°. Partial weight bearing was allowed with a walker during the postoperative period. The Hemovac drain was removed on the second day after the operation.

After the 1st stage exchange arthroplasty, intravenous antibiotics were given until the infection was controlled. The antibiotics were selected either based on the culture and sensitivity results or selected empirically in the case of an unidentifiable microorganism. Symptoms and signs of infection, ESR, CRP as well as renal and liver functions were monitored periodically until the infection subsided. The ESR and CRP measurements were repeated for at least two weeks after the antibiotic course had been completed. During the 2nd stage revision TKA, the antibiotic-loaded cement spacers were removed and re-debridement was performed. New tissue cultures were obtained and examined. Following that, reimplantation of the new prosthesis with antibiotic-loaded cement was performed. Intravenous antibiotics were restarted and continued until tissue culture reports showed no

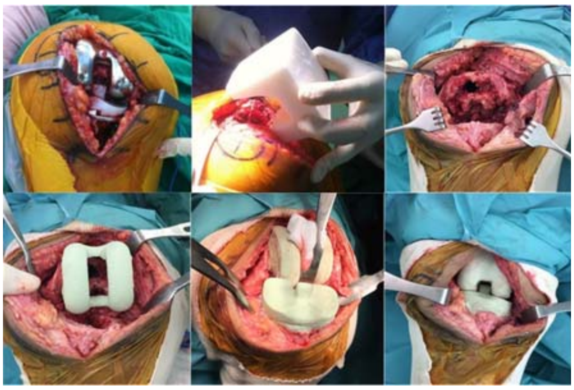

Figure 3. Replacement of a chronically infected TKA. The patient underwent a 1st stage revision TKA with a cement-on-cement, antibiotic-loaded, articulating spacer application to the distal femur and proximal tibia.

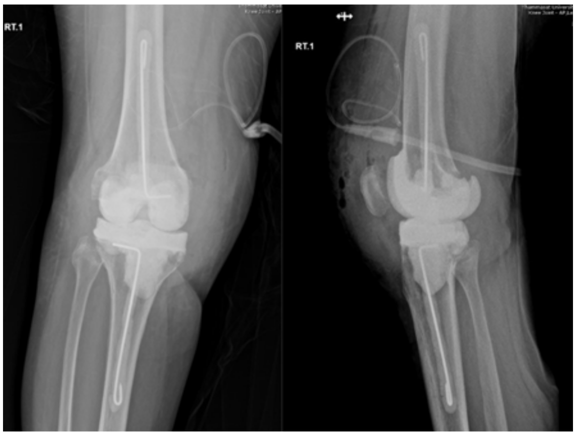

Figure 4. Postoperative knee radiograph after 1st stage exchange arthroplasty. (A) anteroposterior and (B) lateral views.

growth. A routine postoperative rehabilitation program was followed. All the patients were followed-up for at least one year after the revision arthroplasty. Reinfection rates, spacer related complications, KSS, knee ROM, and functional scores were recorded from the pre-operative period through the last follow-up appointment.

Results

The mean age of the eight patients (7 females) identified from hospital records had a mean age of 71.25 years (range 62 to 84). Mean follow-up time after the 2nd stage revision TKA was 26.8 months (12 to 40 months).

A total of four types of bacteria were identified following the first stage of prosthesis removal: coagulase-negative staphylococci, *Staphylococcus aureus*, *Enterobactor cloacae*, and *Escherichia coli* (Table 1). All prosthetic wounds were debrided prior to insertion of antibiotic-loaded cement. Four patients received vancomycin and ceftazidime, and the other four patients received vancomycin + fosfomycin.

The average period of intravenous and oral antibiotic usage was 11.8 weeks (range 4 to 28 weeks). Antibiotics were stopped an average of 7 weeks (range 2 to 18 weeks) before the second stage reimplantation. The mean time between the first and second stage operations was 4.5 months (range 3 to 7 months). No patients required re-debridement or re-insertion of a spacer. No complications related to the articulating antibiotics were encountered, including spacer fracture, dislocation, dislodgement and wound infections/dehiscence.

The biochemistry results were normal for all patients with the exception of one who developed antibiotic-induced hepatitis which was resolved when the type of antibiotic was changed. The levels of ESR and CRP over time are shown in Table 2. Knee ROM, KSS, and functional scores before the first stage, during the between stage, the 1st year after the 2nd stage revision, and at final follow-up are shown in Table 3. No relapses of infection occurred during follow-up.

Before the first stage surgery, seven patients needed to use a gait aid for walking. During the between stage, five patients could walk independently and three still needed a gait aid. One year after the second stage revision, seven patients were able to walk independently and one still needed a gait aid (which was associated with advanced age and cerebrovascular disease).

Discussion

Two-stage exchange revision TKA is the gold standard for treating chronically infected TKA. Whether to use a static spacer or to use an antibiotic-loaded articulating cement spacer to eradicate an infection and prevent soft tissue contractures is still controversial[14,19]. The main advantage of an ALACS is the knee mobility it allows between the operative stages, mobility which improves the patient's quality of life. Our study showed improvement of knee ROM and function in the between stage compared to baseline (83.8° vs. 68.2°). KSS (57.1 vs. 30) and the functional score (42.8 vs. 16.3) also increased after the 1st stage

Table 1. Demographic, clinical and bacteriological data of patients who underwent two-stage exchange revision total knee arthroplasty

Case	Age	Gender	Organism	Interval between stages (months)	Follow-up (months)
1	65	Female	*Enterobactor cloacae*	4.5	26
2	73	Male	Unknown	7	30
3	65	Female	Unknown	6	33
4	62	Female	Unknown	4	12
5	70	Female	*Staphylococcus aureus*	4	40
6	69	Female	*Escherichia Coli*	4.5	20
7	84	Female	*Coagulase negative staphylococcus*	3	19
8	82	Female	Unknown	3	34

Table 2. Erythrocyte sedimentary rate and C-reactive protein concentrations over time

Period	ESR (mm/Hr)	CRP (mg/L)
Preoperation	75.7 (52 to 105)	39.46 (22.49 to 87.10)
Before 2nd stage revision	32.5 (11 to 73)	3.56 (0.54 to 9.91)
3 months after 2nd stage revision	42.6 (28 to 67)	14.26 (3.63 to 31.4)
5 months after 2nd stage revision	31.5 (20 to 58)	6.74 (3.91 to 14.8)
1 year after 2nd stage revision	25 (14 to 35)	4.64 (0.73 to 9.26)

Table 3. Mean postoperative range of motion, Knee society, and functional scores

Period	Mean knee range of movement	Knee society score	Functional score
Preoperation	5.63° to 68.2°	30	16.3
Before 2nd stage revision	2.14° to 83.8°	57.1	42.8
1 year after 2nd stage revision	1.7° to 101.3°	77.6	75.3
Final follow-up	1.7° to 104.7°	85.8	81.3

operation compared to baseline. Moreover, improved ambulation was observed at the one year follow-up after the first operation. Our results are consistent with previous studies which also showed an improvement of between stage functional outcome in ALACS patients compared to those who received static spacers[14,22]. After the 2nd stage revision TKA, we also found incremental improvement in patient's ROM, KSS, and functional score compared to patients receiving static spacers, consistent with the findings of other studies[12,13]. Overall, we found functional outcomes with ALACS using the new molds to be superior to reported outcomes with static spacers. These findings are probably related to the articulating spacer maintaining soft tissue flexibility which, in turn, allows for better postoperative rehabilitation.

Our study found that intraoperative, cement-on-cement, antibiotic-loaded articulating spacers provided excellent infection control for up to one year after two-stage exchange revision TKA. Our results could also be related to adequate soft tissue debridement, high doses of combined antibiotics in the cement, and prolonged intravenous administration of antibiotics. Monitoring of renal function found no abnormalities, although one patient developed antibiotic-induced hepatitis which was resolved when the antibiotic was stopped. This good safety record is encouraging for older patients who may have other comorbidities. Larger studies have similarly reported a high rate of organism eradication without systemic complications using ALACS for infected TKAs(11,23,24).

We found no spacer-related complications, e.g., no spacer dislodging and no bone dislocation or fracture. The surgical technique of spacer production and implantation is critical for preventing complications. After preparing the articulating surface cement, another batch of antibiotic cement was prepared and secured the articulating surface cement to the bony surface while the cement was in the early dough stage. Early cement application increased interdigitation while preventing spacer dislodgement and bony erosion. The articulating cement spacer is associated with less bone loss compared to a static spacer for two-stage exchange revision TKA because it results in less motion between the spacer and the host bone during the between stage. Static spacers can move, dislodge, and cause bone erosion if there is not a high degree of immobilization. Appropriate articulating surface cement sizing, good component positioning, and tension setting are also crucial for the prevention of spacer dislocations and associated bone fractures. Restoring bone defects with cement and applying adequate tension by distracting the joint during the cement curing phase are essential. A recent systematic review showed lower knee ROM (mean 91° to 92°) when a static spacer was used compared to an articulating spacer (mean 100° to 101°)(12,13). This study achieved a mean ROM of 104.7° with ALACS. The limitations of our study were that there were the a very small number of cases and the relatively short follow-up - a mean of just one year.

Conclusion

Two-stage exchange revision TKA with intraoperative cement-on-cement, antibiotic-loaded articulating spacers for treating infected TKAs is effective for infection eradication as well as maintaining good functional status during the in between stage and beyond. This cement spacer application technique results in no spacer related complications. A high dose antibiotic combination in the cement mix, good wound debridement, and prolonged intravenous antibiotic administration are key to success with this technique. More studies are needed to conform these initial findings and to fine-tune the technique.

What is already known on this topic?

Two-stage exchange revision total knee arthroplasty [TKA] is the gold standard for treating a chronically infected TKA. Application of the cement-on-cement antibiotic-loaded articulating spacer in the 1st stage exchange arthroplasty has a good functional outcome in the between stage, easy surgical exposure for the 2nd stage exchange revision arthroplasty, and excellent infection eradication. Therefore, this study was conducted to report the surgical technique and clinical results of intraoperative-innovation of cement-on-cement antibiotic-loaded articulating spacer.

What this study adds?

Our study found that a two-stage exchange revision TKA with intraoperatively-innovation cement-on-cement, antibiotic-loaded articulating spacers for treating infected TKAs was effective for infection eradication, maintaining good functional status during the in between stage and beyond. With our cement spacer application technique, no spacer related complications were found. We believe high dose antibiotic combinations in the cement mix, good wound debridement, and prolong intravenous antibiotic administration were the key to our success. More studies are needed to see how this technique can be fine -tuned.

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Potential conflicts of interest

The authors declare no conflicts of interest.

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