

Outcomes of Patients Treated With Antibiotic-Loaded Acryl Bone Cement For Periprosthetic Hip Infection, Stratified By Cement Polymerization Temperature: A Retrospective Study

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Abstract

Background: Two-stage revision surgery using antibiotic-loaded acryl bone cement (ALAC) is an effective treatment for periprosthetic joint infection (PJI) after hip arthroplasty. However, ALAC has been reported to release different amounts of antibacterial agents, depending on the type of bone cement used. No previous study has examined patient outcomes based on the polymerization temperature of the bone cement used. This study aimed to compare the outcomes of patients who underwent a two-stage revision surgery using ALAC for PJI, stratified by the polymerization temperature of the bone cement used.

Methods: This study involved 23 joints in 23 patients treated with ALAC between 1993 and 2019. They were classified into normal (control group, n=12) and low polymerization temperature (L group, n=11) groups, respectively. Patient outcomes were compared between the groups.

Results: In both groups, the infection subsiding rate was 100%. The success rate of revision surgery at the 2-year follow-up was 82.6%. There was no difference between the groups in mean age, time to infection onset, patient general condition, presence of fistulas, or methicillin-resistant *Staphylococcus aureus* infection. However, the infection required less time to subside, and fewer beads or spacers were used in the L group than in the control group. The success rate of revision surgery was 66.7% and 100% in the control and L groups, respectively.

Conclusions: In the present study, two-stage revision surgery with ALAC in PJI was associated with a shorter infection subsidence period and fewer surgeries in the group treated with bone cement of low polymerization temperature than in the control group. The use of bone cement of low polymerization temperature in ALAC is an effective treatment option for PJI.

Background

In hip arthroplasty, periprosthetic joint infection (PJI) is a serious complication that occurs in approximately 1% of cases [1, 2]. PJI imposes a heavy financial and physical burden on patients, since treatment is administered over a long term [1, 2]. Antibiotic-loaded acryl bone cement (ALAC) is considered an effective treatment [3–5], and is mainly used for infection control and revision surgery in cases of PJI, showing good outcomes [1, 2, 6–9]. Antibacterial agents used in ALAC are selected based on the susceptibility of the causative bacteria [3, 10–12] and the recommended doses [3, 13]. The amount of antibacterial agents that is released in a sustained manner differs between bone cement types [14–16]. However, no previous study has examined treatment outcomes based on the temperature of bone cement polymerization. The present study aimed to compare outcomes of patients undergoing two-stage revision surgery using ALAC for periprosthetic hip infection, based on bone cement polymerization temperature.

Methods

This retrospective cohort study included 23 joints in 23 patients treated with ALAC between 1993 and 2019, including 17 women and 6 men, with the mean age of 72.8 years. Three cases involved early infection (0.7 months), and 20 cases involved late infection (59.8 months). This study included cases in which implant-conserving therapy such as continuous lavage was unsuccessful, requiring treatment with ALAC.

Different bone cement types were used for ALAC over the past decades. A total of 12 joints (4 joints treated with Simplex P® [Stryker Orthopedics, Mahwah, NJ, USA] during 1993-1998, and 8 joints treated with Zimmer bone cement® [Zimmer Biomet, Warsaw, Indiana, USA] during 1998-2010; normal polymerization temperature of bone cement) constituted the control group. Eleven joints treated after 2010 involved low-temperature polymerized bone cement (Cemex®, Tecres S.P.A Sommacampagna, Italy) and constituted the L group. Demographic characteristics of patients in the control and L groups are shown in Table 1. Treatment outcomes were compared between the groups. Since the time of surgery for each group was different, the results of revision surgery were examined at 2 years postoperatively.

Table 1
Demographic characteristics of patients in the control and L groups

	Hips	Control group	L group
Total, n (%)	23	12 (52.2)	11 (47.8)
Mean age, years (SD)	72.8 (9.02)	73.6 (9.25)	72.1 (9.14)
Female sex, n (%)	17	8 (66.7)	9 (81.8)
Surgical method			
THA, n (%)	15	8 (66.7)	7 (63.6)
BHA, n (%)	8	4 (33.3)	4 (36.4)
Reason for surgery			
OA, n (%)	13	6 (50)	7 (63.6)
ONFH, n (%)	2	1 (8.3)	1 (9.1)
RA, n (%)	2	1 (8.3)	1 (9.1)
Fracture, n (%)	6	4 (33.3)	2 (18.2)
THA, total hip arthroplasty; BHA, bipolar hip arthroplasty; OA, osteoarthritis; ONFH, osteonecrosis of the femoral head; RA, rheumatoid arthritis			

The variables of interest included time to infection onset, the causative organism (methicillin-resistant *Staphylococcus aureus* [MRSA] vs. other bacteria), presence of a fistula, general condition of the patient

(dichotomized using the American Society of Anesthesiologists [ASA] Physical Status classification ≥ 3 [17]), time to infection subsidence, number of surgeries, and success rate of revision surgery.

Cases in which revision surgery was not performed after the infection subsided were excluded. Infection was recognized as subsiding based on both negative joint fluid culture findings and C-reactive protein serum levels of <10 mg/L. We defined the time to infection subsidence as the period between the date of initial surgery and the point where laboratory parameters met the criteria for infection subsidence. Successful revision surgery was defined as cases in which no recurrence of infection was observed until the end of the follow-up period. The number of surgeries was defined as the number of times cement beads or cement spacers with ALAC were placed.

All statistical analyses were performed with EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan), which is a graphical user interface for R (R Foundation for Statistical Computing, Vienna, Austria) [18]. This modified version of the R commander includes statistical functions frequently used in biostatistics. Unpaired t-tests, Mann-Whitney U-test, and Fisher's exact test were used to determine the differences between the groups. P-values of <0.05 were considered as statistically significant.

All procedures involving human participants were performed following the ethical standards of the institutional and/or national research committees and 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The study design was approved by an ethics committee at our institution.

Results

The infection subsided in all cases, and the success rate of revision surgery at 2 years postoperatively was 82.6%. Revision surgery was not performed on two joints due to participant age and observed complications. Infection recurred in 2 of 21 joints after revision surgery; it subsequently subsided in one case after implant removal. In the other case, although the implant was removed, only fistula treatment was continued until the patient died of another disease. Vancomycin was administered in all cases in the L group. There was no significant difference between groups in age, time to infection onset, rate of complications or fistula, or the number of MRSA cases (Table 2). Time to infection subsidence and the number of surgeries were significantly lower in the L group than in the control group. The success rate of revision surgery was 66.7% and 100% in the control and L groups, respectively (Table 3). A case representative of the L group and treated with low-temperature polymerized bone cement for ALAC is shown in Fig. 1.

Table 2
Clinical characteristics of the patients in the control and L groups

	Control group	L group	P-value
Time to onset of infection, month (SD)	31.2 (36.5)	74.9 (69.8)	0.09*
Early infection, n (%)	3 (25)	0 (0)	
Late infection, n (%)	9 (75)	11 (100)	
General condition			
ASA ≥ class 3, n (%)	4 (33.3)	1 (9.1)	0.32**
ASA ≤ class 2, n (%)	8 (66.7)	10 (90.9)	
Culture			
MRSA, n (%)	4 (33.3)	2 (18.2)	0.64**
Others, n (%)	8 (66.7)	9 (81.8)	
Fistula, n (%)	3 (25)	3 (27.3)	1**
*Mann-Whitney U-test			
**: Fisher's exact test			
ASA, the American Society of Anesthesiologists Physical Status classification, MRSA, methicillin-resistant <i>Staphylococcus aureus</i>			

Table 3
Clinical outcomes in the control and L groups

	Control group	L group	P-value
Period until infection subsiding, weeks (SD)	26 (6.25)	8.82 (2.44)	<0.0001*¶
Number of beads or spacers with ALAC surgeries, n	2.42	1	0.00058**¶
Success rate of revision surgery at 2-year follow-up, %	66.70%	100%	0.093**
*Mann-Whitney U-test			
**Fisher's exact test			
¶Statistically significant			
ALAC, antibiotic-loaded acryl bone cement			

Discussion

The present study has revealed that in two-stage revision surgery using ALAC for PJI, the use of bone cement of a low polymerization temperature was associated with a shorter period to infection subsidence and a lower number of surgeries than those associated with the control cement type. The present study is the first to compare the outcomes of patients undergoing this type of treatment, depending on the polymerization temperature of the cement used.

Previous studies have shown that two-stage revision surgery using ALAC for PJI is associated with good outcomes; therefore, this approach is commonly used [1, 2, 6–9]. The success rate of two-stage revision surgery using ALAC has been reported in the range of 90%-100%; however, in this study, the overall revision surgery success rate was 82.6%. Nevertheless, the corresponding rate among patients treated with bone cement of low polymerization temperature was 100%; this estimate is similar or superior to those previously reported. This finding indicates that bone cement of a low polymerization temperature should be recommended for use in ALAC for PJI.

The optimal timing of revision surgery after implant removal remains unclear although it has been suggested that it requires the infection to be well controlled [19]. In this study, the criteria for infection control were reduction in C-reactive protein levels and negative bacterial culture findings in arthrocentesis, which remained constant over the entire period. Given these criteria, the number of surgeries and the time to infection subsidence were lower and shorter, respectively, in the L group than in the control group, suggesting that infection control was better in the former than in the latter group.

ALAC antibacterial agent composition is determined based on the susceptibility of the causative bacteria [3, 10–12]; the use of aminoglycoside antibiotics such as tobramycin, gentamicin, and vancomycin has been reported [13, 20–23]. Since bone cement usually polymerizes at temperatures in the range of 60–80°C, the selected antibacterial agents must have thermal stability [3]. Aminoglycoside antibacterial agents have high thermal stability, and premixed products are commercially available; however, the levels of antibacterial agents in each unit have been reported to vary between bone cement types [14–16]. Cemex®, which was used in this study, is a type of bone cement with low polymerization temperature [24, 25]. The amount of antimicrobial agent released from Cemex® has been shown as satisfactory under normal conditions [15]. In addition, in cases involving MRSA or unclear bacterial strains, it is often recommended to include vancomycin in ALAC as a broad-spectrum antibacterial agent [3, 10, 12]. The efficacy of antibacterial agents has been reported to decrease at a temperature of 80°C [26, 27]; meanwhile, at lower temperatures, bone cement may release a higher dose of vancomycin than it does otherwise [28]. The present study findings indicate that the use of bone cement of low polymerization temperature may prevent heat-associated inactivation of antibacterial agents.

The present study has some limitations. The patients in this study were divided into treatment groups according to the date of the surgery and bone cement type used. In addition, the present study included control group cases that were not treated with vancomycin, which may have biased the presented estimates.

In conclusion, the present study examined outcomes of patients with PJI treated with ALAC, involving bone cement of either normal or low polymerization temperature. In the present study, the time to infection subsidence and number of surgeries were lower among patients treated with bone cement of low polymerization temperature than among those in the control group. The use of bone cement with a low polymerization temperature in ALAC may be a clinically effective treatment option for PJI.

Abbreviations

PIJ, periprosthetic joint infection; ALAC, antibiotic-loaded acryl bone cement; MRSA, methicillin-resistant *Staphylococcus aureus*; ASA, American Society of Anesthesiologists

Declarations

Ethics approval: All procedures involving human participants were performed following the ethical standards of the institutional and/or national research committees and 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The study design was approved by an ethics committee at Kagawa University (Permit Number: 29-213).

Consent for publication: Informed consent was obtained from all participants included in the study, if participants are under 16, from a parent and/or legal guardian. Patients provided their informed consent to the publishing of their data and photographs.

Availability of data and materials: The datasets used and/or analysed during the current study available from the corresponding author on reasonable request.

Competing interests: The authors have no conflicts of interest to declare that are relevant to the content of this article.

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Figures

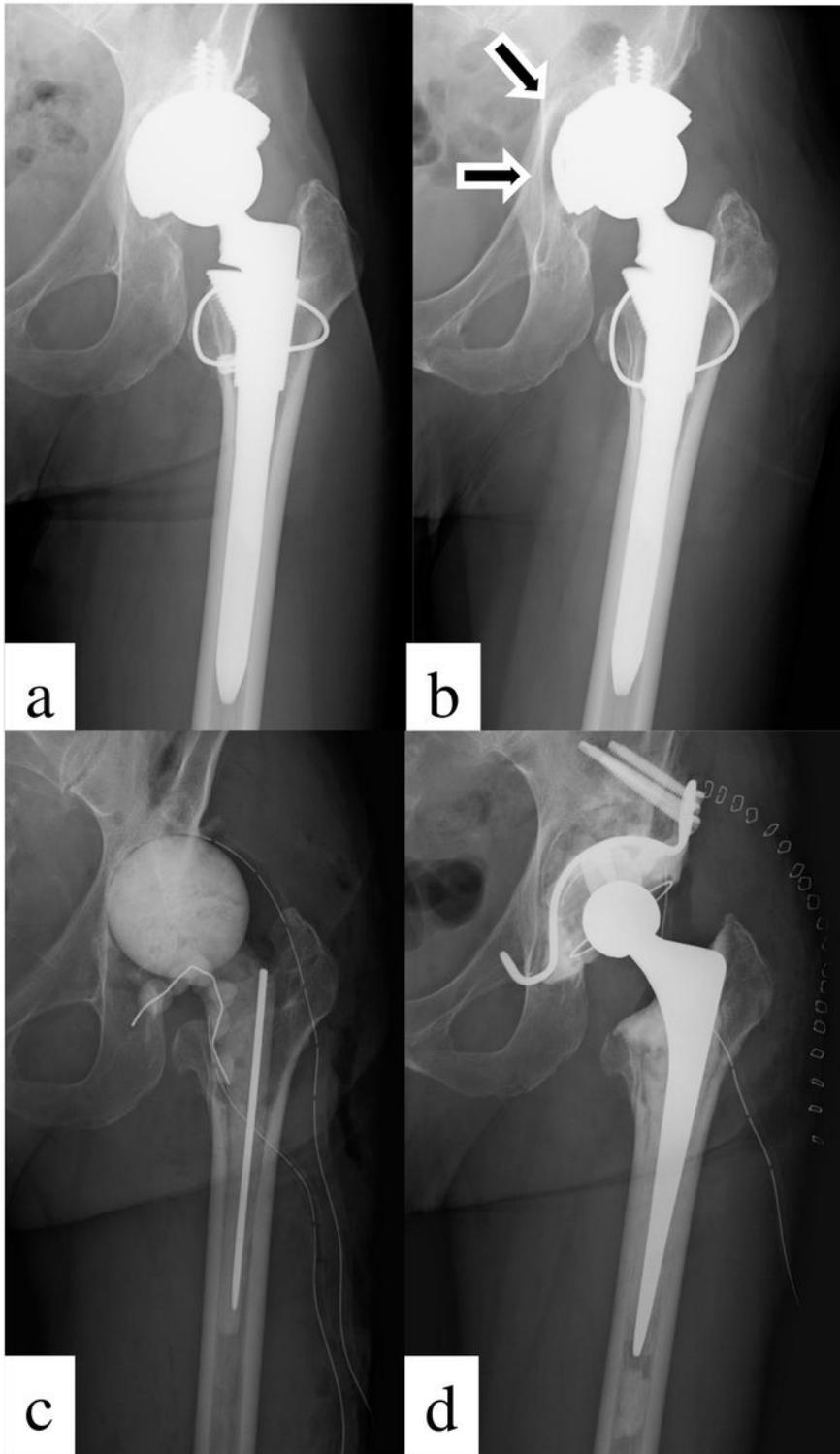


Figure 1

Representative case of the L group, treated with low-temperature polymerized antibiotic-loaded acryl bone cement. (a) A 61-year-old man underwent total hip arthroplasty (b) Developed infection (black arrow indicates implant loosening) (c) Implants were removed and a cement spacer using antibiotic-loaded acryl bone cement (Cemex®) was inserted (d) Eight weeks after the surgery with antibiotic-loaded acryl bone cement, revision surgery was performed

Supplementary Files

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- [ALACdata.xlsx](#)