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Research Article

Total Knee Arthroplasty: The Efficacy of Calcium Sulfate Beads in One-Stage Aseptic Revision

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ABSTRACT

Background: The risk of periprosthetic joint infection following revision total knee arthroplasty is high, as is the cost of care. Decreasing periprosthetic joint infection risk may include utilization of calcium sulfate beads. Calcium sulfate beads have been gaining momentum in treating infected joints because of their potential advantages, including antibiotic elution and dissolvability. However, literature documenting their utilization in aseptic revision is sparse. This study compares: 1) infection rates; 2) length of stay; 3) subsequent infection procedures; and 4) final surgical outcome between one-stage aseptic revision total knee arthroplasty patients who received calcium sulfate beads and those who did not.

Methods: We performed a retrospective chart review to identify patients who underwent aseptic one-stage revision total knee arthroplasty between January 2013 and December 2017. Outcomes collected included postoperative infection rate, length of stay, subsequent irrigation and debridement, and final surgical outcome, classified as a successful total knee arthroplasty reimplantation, a retained antibiotic spacer, or an above knee amputation. Chi-square analysis was used to analyze all categorical variables, while Student's t-testing was used for continuous variables. A p-value of 0.5 was set as the threshold for statistical significance.

Results: Calcium sulfate bead patients did not differ from non-calcium sulfate bead patients with regard to the number of postoperative infections (p=0.103), lengths of stay (p=0.210), irrigation and debridement procedures (p=0.063) and surgical outcome (p=0.085).

Conclusion: Patients who received calcium sulfate beads had analogous surgical outcomes and infection rates to non-calcium sulfate bead patients. The use of calcium sulfate beads in aseptic one-stage revision total knee arthroplasty may not be beneficial in preventing infection and reducing costs.

Introduction

The risk of periprosthetic joint infection (PJI) following revision total knee arthroplasty (TKA) has been reported to be nearly 28% [1, 2]. Additionally, revision costs are significantly inflated when complicated by infection, as the cost of explantation, reimplantation and total hospitalization can total over $110,000 [3, 4]. To decrease risk of PJI, surgeons investigated antibiotic delivery systems such as antibiotic-infused bone allografts and antibiotic-laden bone cement as preventive measures [5-8]. However, complications like periprosthetic fracture and reinfection have necessitated alternate methods of antibiotic delivery in joints to reduce infection risks [9-11].

Calcium sulfate beads (CSBs) are an antibiotic delivery device currently

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gaining momentum for treating infected joints [12, 13]. These beads are mixed with antibiotics, and designed to slowly elute the antibiotics over weeks once implanted [14–16]. The distinguishing feature of CSBs is their dissolvability, which may eliminate a nidus for bacterial growth [13,17]. For many surgical procedures, CSBs may be effective in preventing bacterial growth, biofilm formation, and filling tissue voids during healing [18–20]. Although potential benefits may exist, their utilization in joints reveals mixed results. Reports indicate that adverse side effects such as heterotopic ossification and wound drainage, may occur [17, 21]. Despite potential side effects, CSBs are currently under investigation as a means to decrease PJI risk in revision arthroplasty.

At our institution, CSBs are utilized to prevent PJI in one-stage aseptic revision. To date, few studies have reported the outcomes of CSBs in this population. For this reason, the present study investigates CSB utilization in aseptic revision TKA. Specifically, we compare: 1) infection rates; 2) length of stay; 3) subsequent infection procedures; and 4) final surgical outcomes between one-stage aseptic revision TKA patients who received CSBs and those who did not.

Methods

I Patient Selection

We performed a retrospective chart review to identify all patients who underwent revision TKA between January 1, 2013 and December 31, 2017 at a single institution with current procedural terminology (CPT) codes 27487, or 27488. Patients were included if their revision procedure was planned as a one-stage, the procedure was secondary to aseptic implant failure (i.e. instability, aseptic loosening, periprosthetic fracture, dislocation, pain), and if they received preoperative joint aspiration/culture to ensure the absence of active infection prior to undergoing revision. Patients were excluded if they were undergoing a primary or conversion arthroplasty, if they had a diagnosis of PJI, showed signs of infection prior to revision, or had less than two years of follow-up. Patients were further stratified based upon receipt of adjunctive calcium sulfate beads. The average follow-up for all patients was two years. Patient level demographics, including age, race, sex, McPherson Host status, American Society of Anesthesiologists (ASA) status, smoking status, alcohol dependency, and body mass index (BMI) were collected from the charts.

II Preparation of Calcium Sulfate Beads

In patients receiving CSBs, calcium sulfate powder (Stimulan, Biocomposites Inc, Wilmington, North Carolina, USA) was mixed with 1g of vancomycin powder, 0.6g of tobramycin powder, and 10 mL of sterile water to form a paste. The paste was spread onto a 4.8mm diameter bullet mat to harden into beads. Once dried, the beads were removed from the mat and inserted around the joint space after component implantation and before wound closure. All patients received standardized institutional postoperative care.

Table 1: Demographic characteristics in aseptic revision TKA patients who were and were not implanted with antibiotic-impregnated calcium sulfate beads.

TKA	No calcium sulfate beads	Calcium sulfate beads	P-value
Total Number (n)	57	49	
Mean age at initial revision (yrs) (S.D.)	63.8 (11.9)	64.2 (9.9)	0.827
Female (%)	39 (68.4%)	24 (49.0%)	**0.049**
Race:			0.857
White	31 (54.4%)	24 (49.0%)	
Black	25 (43.9%)	24 (49.0%)	
Hawaiian	1 (1.8%)	1 (2.0%)	
ASA:			0.821
2	9 (15.8%)	10 (20.4%)	
3	44 (77.2%)	36 (73.5%)	
4	4 (7.0%)	3 (6.1%)	
McPherson Host status:			0.861
Type A	19 (33.3%)	14 (28.6%)	
Type B	33 (57.9%)	30 (61.2%)	
Type C	5 (8.8%)	5 (10.2%)	
Current smoker (%)	13 (22.8%)	5 (10.2%)	0.120
Current alcohol dependency (%)	1 (1.8%)	1 (2.0%)	0.999
Mean BMI (kg/m^2) (S.D.)	36.0 (8.4)	34.8 (8.0)	0.432

III Patient Demographics

A total of 106 patients were included for analysis (Table 1). There were 57 revision TKA patients who did not receive CSBs, compared to 49 revision TKA patients who did. The mean age at the time of revision for patients who did not receive CSBs was 63 years, while the mean age of patients who received CSBs was 64 years (p=0.827). There were more females in the non-CSB group than the CSB group (68.1% non-CSB vs. 49.0% CSB, p=0.049), but there was no significant difference found in the racial distribution (White: 54.4% non-CSB vs. 49.0% CSB, p=0.857). There were no significant differences found in ASA score (ASA score 2: 15.8% non-CSB vs. 20.4% CSBs, p=0.0821), or in McPherson Host status scores (Type B: 57.9% non-CSB vs. 61.2% CSB, p=0.861). There were no differences in the proportions of current smokers (22.8% non-CSB vs. 10.2% CSB, p=0.120) or the proportion of patients with current alcohol dependence (1.8% non-CSB vs. 2.0% CSB, p=0.999). The mean BMI was not significantly different between groups (36.0 kg/m^2 non-CSB vs. 34.8 kg/m^2 CSB, p=0.432).

IV Outcomes

The primary outcome collected was postoperative infection rate, defined as subsequent irrigation and debridement(s) (I+D) or positive culture following one-stage revision. Secondary outcomes measured included length of stay (LOS), the number of I+Ds performed, and final surgical outcome, classified as a successful TKA reimplantation, a retained antibiotic spacer, or an above knee amputation (AKA).

V Statistical Analysis

Chi-square analysis was used to analyze all categorical variables, while Student's t-testing was used for continuous variables. A p-value of 0.5 was set as the threshold for statistical significance. All statistical analysis was performed using SPSS version 25 (IBM Corporation; Armonk, New York, USA).

Results

The non-CSB cohort did not significantly differ from the CSB cohort in number of postoperative infections (14.0% non-CSB vs. 4.1% CSB, p=0.103) (Table 2). There were no differences in LOS between the two groups (2.81 days non-CSB vs. 2.55 days CSB, p=0.210). There were very few patients requiring a postoperative I+D procedure in both groups (mean I+Ds: 0.39 non-CSB vs. 0.10 CSB, p=0.063). No significant differences were seen in the final surgical outcomes, with 86.0% of the non-CSB cohort having a successful TKA, 12.3% having an antibiotic spacer and 1.8% having an AKA, compared to 98.0% of patients in the CSB cohort having a successful TKA, 2.0% having an antibiotic spacer and 0.0% having an AKA (p=0.085).

Table 2. Comparison of outcomes between aseptic revision TKA patients who were and were not implanted with antibiotic-impregnated calcium sulfate beads.

TKA	No calcium sulfate beads	Calcium sulfate beads	P-value
Infection (%)	8 (14.0%)	2 (4.1%)	0.103
Mean length of stay (days) (range)	2.81 (1 to 5)	2.55 (1 to 4)	0.210
Mean number of I&Ds after revision surgery (range)	0.39 (0 to 3)	0.10 (0 to 3)	0.063
Final surgical outcome:			0.085
Total knee arthroplasty	49 (86.0%)	48 (98.0%)	
Antibiotic spacer	7 (12.3%)	1 (2.0%)	
Above-knee amputation	1 (1.8%)	0 (0%)	

Discussion

One-stage revision is effective in restoring joint function for TKA patients after aseptic loosening [22]. However, this procedure carries a risk of developing a subsequent periprosthetic joint infection [2,23,24]. In order to reduce the occurrence of postoperative infection, surgeons have employed the use of antibiotic delivery adjuncts, including antibiotic calcium sulfate beads. This study investigated the outcomes of CSBs in patients undergoing one-stage aseptic revision TKA. Our results revealed no significant difference in postoperative infection rates, I+Ds, LOS and final surgical outcome between CSB and non-CSB patients. These results suggest that the utilization of CSBs may not be advantageous in aseptic TKA.

There exist some limitations in this study. First, the number of patients in each cohort may be too low to detect true differences in outcomes. However, these numbers are comparable to contemporary institutional studies investigating the use of dissolvable beads for infection treatment and prevention. Additionally, we found a slightly significant difference in the percentage of females in each group. Finally, the retrospective nature of this study does not allow for assertions of causality, and may have some unintentional bias in that more complicated cases may have been selected to receive CSBs. Despite these limitations, this study is one of the few comparative studies on in vivo use of CSBs in aseptic revision arthroplasty, and adds valuable information to the literature.

Other investigational studies have been conducted assessing CSBs as means of eradicating infection in TKA. A study by Lum and Pereira evaluated 56 hip and knee arthroplasty patients who received CSBs for infection prevention or eradication [25]. Of their 12 aseptic TKA revisions, they had one case of intra-articular ossification that required surgical I+D and exchange of the polyethylene liner. In one revision TKA, there was a case of persistent wound drainage that resolved without surgical intervention. Additionally, Kallala and Haddad studied 15 hip and knee revision patients that were implanted with CSBs in an observational case series [26]. They found that one patient had clinical signs of infection with raised inflammatory markers at final follow-up. They also found that three patients developed transient hypercalcemia, with one developing symptoms requiring treatment, while another patient developing asymptomatic heterotopic ossification. These studies highlight the side effects associated with CSBs, and reflect our findings that CSBs are only marginally more effective than standard of care. However, none of these studies compared outcomes between CSB and control patients. The present study strengthens the results previously demonstrated with our comparison design.

The literature on CSB use in aseptic revision TKA is scant, but correlates with the results reported in the present study. McPherson et al. conducted a case series with 250 revision arthroplasty patients treated with CSBs, of which 66 were aseptic TKA [17]. They reported six aseptic knee complications, including two cases of failure due to infection and one case of wound drainage. There were no cases of heterotopic ossification in any aseptic TKA patients. More recently, Kallala et al. prospectively evaluated 755 revision TKA and THA patients who were implanted with CSBs, of which 25 were revised for aseptic reasons [21]. In the TKA patients, there were 21 cases of wound drainage, 22 cases of hypercalcemia, and five cases of heterotopic ossification. Approximately 19 TKA patients seemed to have had septic failures, though this was not

clearly mentioned. Upon further analysis, there was a significant effect of bead volume (p=0.0014) and systemic host grade (p=0.0021) on the presence or absence of complications. However, neither study utilized a control group to compare the efficacy of CSBs in revision surgery. Due to the potential side effects previously described, and the equivocal results of the present study, CSBs may be an added unnecessary cost in aseptic revision that does not enhance surgical outcomes.

Conclusion

Finding an effective method to prevent PJI in revision TKA is an ongoing struggle. The present study assessed the utilization of antibiotic-impregnated calcium sulfate beads as an antibiotic delivery device in aseptic revision surgery. We demonstrated that patients who received CSBs during aseptic revision TKA had analogous surgical outcomes and infection rates to patients who did not receive CSBs. The use of CSBs in the context of aseptic one-stage revision TKA may be of no additional benefit in preventing infection and reducing the costs associated with PJI.

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Conflicts of Interests

Ronald E. Delanois, MD is a board/committee member of the Baltimore City Medical Society, and has received research support from Flexion Therapeutics, Orthofix, Inc., Stryker, Tissue Gene, and United Orthopedics.

James Nace, DO is a member of the editorial/governing board for Journal of Arthroplasty, Journal of the American Osteopathic Medicine Association, Orthopedic Knowledge Online, and Journal of Knee Surgery. He also receives research support from Stryker.

All other authors declare that there are no conflicts of interest.

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