Clinical effects of two-stage joint replacement on septic arthritic knee

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Abstract

Objective: To assess the clinical effect of two staged joint replacement for the treatment of septic arthritic knee and the therapeutic differences between antibiotic cement beads and the tibial plateau spacer.

Methods: 26 patients (27 knee joints) treated with spacer (antibiotic cement beads or the tibial plateau spacer) for septic arthritis knee were retrospectively reviewed between 2014 and 2018. At the first stage, thoroughly debridement and irrigation with self-made antibiotic cement beads or tibial plateau spacer was performed; After that, systemic antibiotic treatment was followed; when the infection was surely eliminated, Two-stage TKA was performed. Knee mobility (range of motion, abbreviated to ROM) and function (HSS scores system) were evaluated before surgery, in the interval period, and after joint replacement.

Results: All patients finished follow-up and the follow-up time was 27.3 months (12-54 months). 23 patients (24 knee joints) completed the staged surgery as expected, 3 patients in the beads group gave up the second-stage operation after infection elimination. Each group has one patient replaced with a homotypic spacer, and all patients eventually cleared the infection. None of the patients had a recurrent infection. The mobility and HSS scores of the two groups were significantly improved post-operation (p<0.05). There was no significant difference in mobility between the two groups (p=0.153). The HSS score of the tibial plateau spacer group had a better trend of improvement after TKA (p= 0.054).

Conclusion: Two-stage TKA is an efficacious way for septic arthritic knees, which can effectively control infection and improve knee function.

Introduction

Septic arthritic knee (SAK) is a relatively low incidence disease while has a high risk of disability and mortality [1]. There is currently no universally agreed ideal treatment strategy, and its treatment still faces great challenges [2]. Traditional treatment methods include knee incision or arthroscopic cleaning/irrigation/drainage based on systemic antibiotic treatment [3]. Even if anti-infective treatment against SAK is timely and appropriate, permanent joint destruction and persistent
infections are still common [4]. For SAK cases with false infection control, rescue treatments, such as fusion and amputation, are often adopted [5, 6]. In recent years, there have been occasional reports of a method similar to the second-stage revision [7-10] for the treatment of SAK, including first-stage debridement and implantation of static or articulated spacer to control infection and second-stage initial total knee replacement to restore knee function [2; 5; 11-16].

Previous relevant studies are limited to case reports and small-sample-size studies, and lack the comparisons of spacer types. This study observed the effects of various spacers based on the same staging joint replacement surgery strategy, aiming to further demonstrate the effectiveness of staged joint replacement for the treatment of SAK and to explore and analyze the efficacy differences of different spacers.

Materials And Methods
General Information
This study was approved by the ethics committee of the PLA General Hospital. Twenty-six SAK patients (27 joints) treated in the Department of joint surgery of our hospital from March 2014 to April 2018 were retrospectively collected (Table 1). Three patients who did not complete the second-stage replacement were excluded. Of the remaining 23 patients (24 joints), 6 were males (7 joints) and 17 were females (17 joints). The average age was 61.6 years (45-75 years). Nine patients (9 joints) were treated with antibiotic-containing tibial plateau spacer (group A), and 14 patients (15 joints) were treated only with antibiotic cement beads (group B). In group A, 1 patient had a history of open knee surgery, 5 patients had a history of knee injection, 1 patient had a history of arthroscopy, 2 patients had unknown infection, and 8 patients had positive cultures (3 patients had fungal infection); In group B, 3 patients with a history of trauma, 5 patients had a history of knee injection, 3 patients had a history of arthroscopy, 3 patients had unknown infection causes, and 6 patients had positive cultures (1 patient had fungal infection, and 1 patient had mixed infection). All the patients were followed up for an average of 27 months.
### Table 1

Basic information of the patients before surgery

| Grouping (No) | Gender/age(years) | Affected side | Preoperative HSS | Preoperative ROM | Reason of knee infection | Results of culture |
|---------------|-------------------|---------------|------------------|------------------|--------------------------|-------------------|
| A1            | F/70              | L             | 32               | 40               | history of knee injection | Candida albicans   |
| A2            | F/60              | L             | 48               | 100              | history of knee injection | Candida fris       |
| A3            | F/69              | L             | 35               | 40               | history of knee injection | Candida parapsilosis |
| A4            | F/65              | L             | 41               | 20               | unknown                   |                   |
| A5            | M/70              | L             | 35               | 95               | History of arthroscopy   | Micrococcus luteus |
| A6            | F/68              | R             | 61               | 85               | unknown                   | Propionibacterium acnes |
| A7            | M/58              | L             | 36               | 61               | history of knee injection |                   |
| A8            | M/75              | R             | 30               | 85               | history of knee injection |                   |
| A9            | M/45              | L             | 14               | 70               | History of knee incision for nail removal |                   |
| Average of group A | 4 M/5 F 64.4 | 7L/2R | 36.9 | 66.2 |                   |                   |

| B1            | F/63              | R             | 46               | 110              | history of knee injection |                   |
| B2            | F/66              | R             | 28               | 50               | unknown                   |                   |
| B3            | F/58              | L             | 8                | 40               | unknown                   | Staphylococcus aureus |
| B4            | F/49              | R             | 46               | 90               | History of arthroscopy   |                   |
| B5 (two sides)| M/62              | R             | 27               | 20               | History of trauma         | Gram-positive bacilli |
| B6            | F/71              | L             | 23               | 45               | unknown                   | Staphylococcus aureus |
| B7            | F/71              | L             | 32               | 40               | history of knee injection | Staphylococcus aureus |
| B8            | F/58              | R             | 30               | 30               | History of arthroscopy   | Aspergillus flavus |
| B9            | M/55              | R             | 45               | 60               | history of knee injection |                   |
| B10           | F/57              | R             | 20               | 20               | history of knee injection | Staphylococcus surface and Staphylococcus hominis |
| B11           | F/66              | R             | 40               | 40               | history of knee injection |                   |
| B12           | F/48              | L             | 35               | 60               | history of knee injection |                   |
| B13           | F/57              | R             | 19               | 60               | history of knee injection |                   |
| B14           | F/55              | R             | 35               | 40               | history of knee injection |                   |
| Average of group B | 2M/12F 59.7 | 5L/10R | 30.4 | 47.7 |                   |                   |
| Sum           | 6M/17F 61.6       | 12L/12R       | 32.9             | 54.6             |                          |                   |

**Diagnostic criteria of SAK [15]**

The diagnosis was combined with individual medical history, together with the symptoms and signs of clinical infection (painful effusion, restricted mobility, elevated skin temperature, or the presence of the same sinus as the joint); elevated serum inflammation markers (C-reactive protein [CRP > 10 mg /
dL, erythrocyte sedimentation rate [ESR] > 30 mm / h), polymorphonuclear (PMN) cell count percentage > 90%); imaging-revealed narrowing of joint space and destruction of articular cartilage; surgery-revealed purulent slip in joint cavity, synovial membrane, or tissue; frozen sections (> 5 neutrophils / HPF) of suspicious infection during surgery, positive results of synovial fluid or tissue culture.

Inclusion criteria
1) the patient should be confirmed SAK; 2) Anti-infection or other surgical methods were not effective; 3) the patient had obvious knee joint pain and limited joint movement. X-ray of knee joint before surgery indicated degenerative changes of knee joint; 4) the patient had preoperative evaluation of being able to tolerate surgery and had no mental illness. 5) the patient fully understood the meaning and risks of secondary surgery and signed relevant medical documents.

Exclusion criteria
1) the patient had still good knee function and the symptoms were mild; 2) the patient had complicated infection of other parts (lung, urinary system, femur, tibia, etc.); 3) the patient can’t complete secondary replacement.

Treatment
Stage I surgery: The median incision and lateral medial approach of the patella used in conventional TKA were performed. During the operation, 3 to 5 suspicious infected tissues in different parts were sampled for rapid intraoperative frozen slice examination, the results of which in all patients indicated that the knee joint was infected. Thorough debridement and repeated flushing with hydrogen peroxide, iodine, and saline was then performed within the reach of surgical field. For the patients in group A (antibiotic methyl-methacrylate cement polymer, Heraeus Medical GmbH, Wehrheim / Ts., Germany), the tibial plateau was performed 9-mm osteotomy to fully expose and clean the joint capsule. A temporary prepared tibial plateau was fixed on the tibial plateau (Fig. 1A); and the antibiotic cement beads were placed on the front and sides of the knee capsule (Fig. 1B). The strategy for antibiotic use was the same in the two groups. For the patients with unidentified pathogen, 4 g of vancomycin powder (VIANEX SA, Athens, Greece) + 2 g of meropenem (Sumitomo
Dainippon Pharma Co. Ltd., Osaka, Japan) were placed in 40 g of bone cement; For the patients with known culture results before surgery, appropriate doses of antibiotics or antifungal drugs according to the results of drug sensitivity test were added. Negative pressure drainage tube was applied after the surgery was completed.

After surgery, the affected knee joint was kept straight, and the drainage tube was withdrawn when the drainage was less than 50 ml / day and clear. After drainage tube withdrawal, partial weight-bearing activities were allowed under the protection of knee braces. After surgery, 6-week routine intravenous broad-spectrum antibiotics (when the culture result was negative) or corresponding sensitive antibiotics was administrated; then, oral antibiotics was administrated for at least 6 weeks or until the clinical symptoms and signs disappeared and ESR/CRP returned to normal (Fig. 2). Once the clinical indexes were normal for two times, the spacer can be removed for knee joint replacement.

Stage 2 surgery: The same original knee incision and original approach were used in the Stage 2 knee replacement surgery. After exposing the joints, 3 to 5 soft tissues of different parts were sampled for rapid intraoperative frozen slice examination. The results showed that the joint replacement can be performed as planned when the infection was ruled out. After removing the spacer, the joint cavity was fully washed and cleaned, and the surgery was then completed according to the method of initial knee joint replacement. Because tibial plateau osteotomy had been completed in the patients with tibial plateau placer having been placed in Stage 1 surgery, this step can be omitted in Stage 2.

Postoperative treatment and functional exercise were performed in accordance to conventional TKA. If the patient's interval clinical evidence or Stage 2 intraoperative freezing slice test indicated persistent knee infection, the same bone cement spacer as before should be replaced again in combination with systemic antibiotic for continuous anti-infective treatment. One patient in each group received such spacer replacement.

Data collection

1) the patients’ hospital medical history, relevant medical history, and relevant test results, as well as previous invasive knee operations, time, effects, and outcome, were reviewed; 2) the patients’ mobility and knee function scores (HSS scoring system) before and after surgery in hospital were
3) the patients were followed up after joint replacement, reviewed the X-ray images of the knee joint, blood routine, ESR, CRP, joint mobility, and HSS score.

**Statistical analysis**

To evaluate the efficacy of staged surgery in each group, univariate analysis (ANOVA) was used to compare the differences in ROM and functional score (HSS) before surgery, during the interval period, and after replacement. The SNK-t test was then used to compare the functional and activity differences in each group between any two periods. In order to compare the differences in the efficacy between the two groups, the independent-sample t test was used to compare the function and ROM at the same period. All data results were analyzed using SPSS 20.0 with $P < 0.05$ being considered as statistical significance.

**Results**

A total of 26 patients (27 knees) completed Stage 1 spacer implantation. Of these, 2 patients with antibiotic cement beads were satisfied with their knee function recovery after their knee infection was controlled and rejected Stage 2 surgery after the beads were withdrawn; one patient with antibiotic cement beads abandoned Stage 2 knee replacement due to financial unaffordability after the infection was controlled; the preoperative information of the remaining 23 patients (24 joints) are shown in Table 1.

One patient in each group was re-debrided and replaced with a spacer due to persistent infection during the interval period, and after the infection was controlled, they both Stage 2 knee replacement. By the follow-up, all the 23 patients (24 joints) had no recurrence of infection.

**Comparison of knee joint HHS score and ROM**

Before surgery, the average HSS scores of the patients in group A and group B were 36.9 (14–61) and 30.5 (8–46), respectively, ($p = 0.208$, no significant difference); the average ROMs of knees of the patients in group A and group B before surgery were 66.2 ° (20 ° -100 °) and 47.7 ° (20 ° -95 °), $p = 0.116$, and there was no statistical significance.

**Comparison of knee HHS score and ROM during the interval period**

In the interval period, the average HSS score of group A was significantly improved to 58.9 points (41–73 points), and the average HSS score of group B was also significantly improved to 45.5 points
(23–73 points), which both showed statistical significance than those before surgery; however, the knee function score of group A were significantly higher than that of group B (p = 0.025).

The average ROM of group A slightly decreased to 57.8° (20° -110°), and the decrease was small and had no statistical significance. The average ROM of group B was significantly improved to 69.7° (range: 10° -100°). There was no statistical significance in ROM between group A and group B during the interval period, p = 0.328.

Comparison of knee HHS score and joint mobility after Stage 2 surgery

The average follow-up time after Stage 2 surgery was 27.3 months (12–54 months). At the last follow-up, the average HSS score of group A improved significantly to 90.5 points (83–95 points), and the average ROM increased to 109.4° (85° -130°). The average HSS score of group B significantly improved to 80.9 points (63–95 points), and the average ROM increased to 96° (65° -130°). There was no statistical significance in the HHS score (p = 0.054) and ROM (p = 0.153) between the two groups after stage 2 joint replacement.

Discussion

Treatment of SAK is different from knee infections and periprosthetic infections. For acute knee infections, arthroscopic surgery is currently used [1]; for chronic joint infections or osteomyelitis, knee debridement is more suitable [5]; for periprosthetic infections, the generally accepted treatment is Two-stage revision surgery [17, 18]. However, for SAK, there is still no unified treatment strategy, and it is very challenging [19]. In response to this problem, a small number of studies have proposed staged joint replacement strategies similar to the two-stage revision. The treatment concept is the same as that of the two-stage revision. In the first stage, controlling the infection by debridement and implantation of antibiotic cement spacer. After the infection is controlled, Stage 2 total knee replacement surgery is performed to restore the knee joint.

Although research available for reference is limited, existing studies have shown that staged joint replacement can bring satisfactory infection control rate and knee function recovery against SAK, which is a promising treatment strategy for SAK. Nazarian has reported 14 cases of non-articular spacer for staged joint replacement against chronic SAK with a success rate of 100% [5]. Shaikh also
reported 15 cases with SAK who all used joint-type spacer, among whom one case failed and was replaced with the same type of spacer, and another two cases refused to remove the spacer for stage 2 joint replacement due to satisfactory function after the infection was cured [14]. Yi et al reported 17 cases of severe knee infection with joint-type spacer, and only 1 failed [16]. Inadequately, previous reported staged operations have completed a large amount of osteotomy during the first stage of surgery, which is not conducive to the preservation of bone mass; and if the spacer is left in the body for a long period of time, there is a risk of its loosening or fragmentation, followed by the abrasion of bone mass. Studies have shown that long intervals can cause biofilm formation on the surface of the spacer and further cause continuous infection or reinfection [20]. Therefore, this study proposes the optimization with antibiotic cement beads and tibial plateau spacer. A total of 23 patients (24 joints) were performed spacer implantation in this study. 9 patients (9 joints) were implanted tibial plateau spacer and 14 patients (15 joints) were implanted antibiotic cement beads. One case in each group failed infection control and was replaced the same type of spacer during the interval period. After combined with systemic antibiotics, all the patients' infection was effectively controlled. Compared with articulated spacer, tibial plateau spacer can achieve a thorough debridement while retain more bone mass. The results show that whether using antibiotic cement beads or tibial plateau spacer as the local spacer, satisfactory knee infection control can be achieved, and the Stage 2 knee replacement surgery is especially for those with joint destruction or severe joint function impairment. However, for patients with SAK, the risk of directly performing joint replacement to form PJL is extremely high. The premise of staged knee replacement surgery must be the control of knee infection, otherwise the failure rate of knee replacement will increase significantly. Theoretically, tibial plateau osteotomy has been performed during the implantation of tibial plateau spacer, which can expose the joint cavity more fully and allow more thorough debridement of posterior joint capsule, which is not possible by simply placing antibiotic cement beads. Due to limited sample size, this study did not find a difference in infection clearance between the two debridement methods. For patients using antibiotic cement beads, knee replacement can be temporarily suspended if the knee joint function is satisfactory after infection control, which is not applicable to patients who have had
osteotomy and tibial plateau spacer.

There are still some limitations in this study. First, this retrospective study included a small number of cases and did not perform random grouping, which was limited by the low incidence of this disease and the lack of uniform treatment. However, we have included all our SAK patients eligible for stage 2 surgery in the past 4 years. The total number of cases has exceeded the previous reports. This study included two types of spacer for subgroup comparison. Secondly, the duration of follow-up in this study varies, and certain patients did not reach more than 2 years of follow-up. The long-term efficacy still needs further follow-up; however, all the patients' clinical manifestations, examination indicators, and intraoperative frozen slice test before replacement and confirmed the control of infection, and there was no sign of recurrent infection at follow-up for at least 1 year.

Conclusions
The use of staged joint replacement for the treatment of SAK, whether tibial plateau spacer or antibiotic cement beads, can effectively control infection; joint replacement surgery after infection control can restore the knee joint satisfactorily. antibiotic cement beads are more recommended for patients who are unsure of further joint replacement after knee infection control.

Declarations

**Abbreviation**

SAK, septic arthritic knee; TKA, total knee arthroplasty; HSS, Hospital for special surgery; ROM, range of motion; PJI, periprosthetic joint infection.

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**Availability of data and supporting materials**
The datasets supporting the conclusions of this article are included within the article and its supplementary materials.
Ethics approval
This study was approved by the ethics committee of the PLA General Hospital.

Author contributions
MN, JF and JYC designed the study and proofread the manuscript. TD, ELN, and CX conceived of and designed the study, collected and analyzed the data, and wrote the paper. XL, WC and GQZ revised the draft and generated the figures. All authors read and approved the final manuscript.

Conflicts of interest
The authors declare no conflict of interest.

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Figures

A  B

Figure 1

A: tibial plateau spacer implantation; B: antibiotic cement beads implantation.
Figure 2

A: X-ray of the knee joint after tibial plateau spacer implantation; B: X-ray of the knee joint after antibiotic cement beads implantation.