Two-stage Exchange Arthroplasty is a Viable Treatment for Periprosthetic Joint Infection in Inflammatory Diseases

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Abstract

Aims

The aims of this study were to identify the differences in (1) serum markers, synovial indicators and pathology results and (2) treatment outcomes following two-stage exchange arthroplasty between patients with or without inflammatory diseases.

Patients and Methods

A retrospective review of 182 prosthetic joint infection patients who underwent two-stage exchanged arthroplasty from 2014 to 2017 was conducted. PJI was diagnosed by using the MSIS criteria. Serum biomarkers, synovial fluid, organism and pathology results at the time of the PJI diagnosis and reimplantation were reviewed and compared between patients with or without inflammatory diseases. Treatment success was defined according to the Delphi consensus criteria; Kaplan-Meier survivorship curves of the patients were generated and compared. The mean clinical follow-up duration was 33.9 months (15.9 to 51.9) in the no inflammatory group and 35.5 months (16.2 to 54.8) in the inflammatory group.

Results

There was no difference in the biomarkers, pathology results or organism profile at the time of the PJI diagnosis. Regarding reimplantation, the patients with inflammatory diseases had a higher serum erythrocyte sedimentation rate and C-reactive protein, interleukin-6, and fibrinogen values than those without inflammatory diseases. However, there was no difference in the synovial white blood cell counts between groups. The total treatment success rate was 91.3% (92% for individuals with inflammatory diseases and 91.2% for the controls). The survivorship of the inflammatory disease group was comparable with that of the control group.

Conclusion

Two-stage exchange arthroplasty is a viable treatment option for PJIs with inflammatory diseases. Individuals with PJIs and inflammatory diseases have higher serum inflammatory biomarker levels at reimplantation, which may make determining the timing of reimplantation difficult. In contrast, synovial analysis may be more reliable.
Background

Inflammatory diseases are chronic systemic autoimmune diseases that mainly include rheumatoid arthritis (RA), psoriatic arthritis (PSA), juvenile idiopathic arthritis (JIA), ankylosing spondylitis (AS), and systemic lupus erythematosus (SLE). The prevalence of inflammatory diseases is rarely low, with a rate ranging from 0.05–1% in the general population\(^1\). Although several studies have suggested a decreasing trend in the occurrence of inflammatory diseases\(^2,3\), there are a considerable number of individuals with inflammatory diseases with severe arthritis who are candidates for total joint arthroplasty (TJA)\(^4\).

Prosthetic joint infection (PJI) is a devastating complication that develops after TJA with an incidence of 1–3% following primary TJA and 3–5% following revision TJA\(^5−9\), which leads to a tremendous burden for individual patients as well as the global health care industry\(^10\). Many studies have attempted to identify potential risk factors for PJI. For example, individuals with a medical history of an inflammatory disease have been shown to be independently associated with more than 4 times as many subsequent PJIs than those with osteoarthritis due to the long-term use of disease-modifying anti-rheumatic drugs (DMARDs)\(^11\), biological drugs and corticosteroids\(^12−17\).

The management of PJI remains challenging. Two-stage exchange arthroplasty remains the “gold standard” for chronic PJI in North America and East Asia\(^18,19\), with success rates ranging from 65 to 100%\(^20\). Due to the low incidence of inflammatory diseases, there are limited data on the outcomes following two-stage exchange arthroplasty for individuals with PJI and inflammatory diseases. In the clinic, surgeons frequently consider patients with inflammatory diseases to have inferior outcomes than those without inflammatory diseases. However, to the best of our knowledge, no study has been conducted to compare the outcomes between patients with or without inflammatory diseases. Additionally, whether the current thresholds of inflammatory biomarkers can be applied in patients with inflammatory diseases at PJI diagnosis remains unknown.

In this study, we investigated (1) whether there were any differences in the serum indicators, cultures and pathology results between patients with and without inflammatory diseases and (2) whether
patients with inflammatory diseases have a poor prognosis after two-stage revision surgeries compared to those without inflammatory diseases.

Methods

Patients

We retrospectively reviewed the database of our hospital to identify all patients who underwent two-stage revision for PJI after total knee arthroplasty (TKA) or total hip arthroplasty (THA). A total of 226 patients (228 joints) underwent two-stage revision between 2014 and 2017, of which 28 patients (12.3%) suffered from inflammatory diseases (including rheumatoid arthritis, psoriatic arthritis and ankylosing spondylitis). The diagnoses of inflammatory diseases were made on the basis of the Assessment of SpondyloArthritis International Society’s criteria for AS\textsuperscript{21}, 2010 Rheumatoid Arthritis Classification Criteria for RA\textsuperscript{22}, and criteria proposed by Taylor for psoriatic arthritis\textsuperscript{23}. All inflammatory disease patients underwent medical therapy involving DMARDs, biological drugs or corticosteroids in the rheumatology department, and the inflammatory diseases were not active or showed low levels of activity before surgery.

In the no inflammatory disease group, 13 patients were excluded because they did not meet the Musculoskeletal Infection Society (MSIS) criteria\textsuperscript{24} for PJI, 12 patients were excluded because they did not undergo two-stage revision, and 15 patients were excluded due to a follow-up period of less than 1 year. In the inflammatory disease group, 3 patients who did not meet the MSIS criteria for PJI were excluded, and 1 patient was excluded because he or she did not undergo two-stage revision.

Therefore, a total of 182 patients (77 knees and 107 hips) were included in the final analyses; of these, 24 patients (8 knees and 17 hips) were diagnosed with inflammatory diseases, including 12 with rheumatoid arthritis, 8 with ankylosing spondylitis and 4 with psoriatic arthritis (Fig. 2).

The medical records were reviewed manually in detail to determine whether there were any differences between patients with and without inflammatory diseases in the demographic data (sex, age, body mass index [BMI], and type of joint [knees or hips]) or American Society of Anesthesiologists (ASA) score. We included comorbidities as defined by the international consensus
on PJI\textsuperscript{24} and other risk factors, including hepatitis and cardiovascular disease\textsuperscript{25}. The serologic test results (including erythrocyte sedimentation rate [ESR], C-reactive protein [CRP], interleukin-6 [IL-6], fibrinogen, d-dimer), pathology results, and organism culture test results were compared between the two groups at the time of resection and reimplantation.

Treatment protocol

An institutional standard protocol for two-stage procedures was performed\textsuperscript{26}. The timing of implantation was based on the following criteria: no clinical signs of infection, a well-healed surgical wound, and a declining trend in the inflammatory markers. A period of at least 2 weeks of antibiotic holiday before the second-stage surgery was stipulated. The median interval between the 1st stage and 2nd stage was 126.00 (25.00 to 1203.00) days in the no inflammatory disease group and 126.00 (37.00 to 391.00) days in the inflammatory disease group (P = 0.998).

Definition of the endpoints and treatment success

Primary endpoints for this study were defined as follows: 1. spacer exchange because of infection recurrence; 2. Reinfection (according to MSIS criteria) after reimplantation; 3. long-term antibiotic suppression at the time of the last follow-up; and 4. death related to PJI.

We determined treatment success using the following Delphi consensus criteria\textsuperscript{27,28}: 1. infection eradication, characterized by a healed wound without fistula, drainage, pain, or infection recurrence caused by the same organism strain; 2. no subsequent surgical intervention for infection after reimplantation surgery; and 3. no occurrence of PJI-related mortality.

Statistical analysis

All of the statistical analyses were performed with the statistical software package R (http://www.R-project.org, The R Foundation). The categorical data were summarized as the absolute value and percentage. The continuous data are presented as the mean and standard deviation (SD). The demographic and clinical characteristics were compared between groups with the Student’s t-test if the data were normally distributed; if the data were not normally distributed, the Mann-Whitney test was used for continuous variables and the chi-square test or Fisher’s exact test was used for
categorical variables. Kaplan-Meier survivorship curves with treatment failure as an endpoint were generated. Differences in survivorship between patients with or without inflammatory diseases were assessed using the log-rank test. A retrospective power analysis was calculated based on the 5-year survival rates. A p-value less than 0.05 was considered significant.

Results

General Information

The patient characteristics are shown in Table 1. There was no significant difference in age, sex, ASA, type of surgery, joint function score, or smoking habits between the inflammatory disease and no inflammatory disease groups. Interestingly, patients in the inflammatory disease group had a higher prevalence of renal disease than the control group (20.00% VS 2.52%, p = 0.003), while there was no significant difference in the other relevant risk factors according to our analysis. More alcohol abusers were found in the inflammatory diseases group (28.00% VS 8.18%, p = 0.009), indicating the need for more effective management.

Table 1 Patients data and demographics

| Patient characteristics | Non-inflammatory diseases [n=159] | Inflammatory diseases (n=25) | P-value |
|-------------------------|----------------------------------|-----------------------------|---------|
| Mean age, years (SD)    | 57.12 (14.70)                    | 55.96 (14.77)               | 0.737   |
| Mean BMI, kg/m² (SD)    | 25.26 (3.74)                     | 23.49 (4.17)                | 0.031   |
| Mean ASA (SD)           | 2.08 (0.41)                      | 2.12 (0.33)                 | 0.608   |
| Gender, n (%)           |                                   |                             |         |
| Female                  | 77 (48.43)                       | 13 (52.00)                  | 0.740   |
| Male                    | 82 (51.57)                       | 12 (48.00)                  |         |
| Joint, n (%)            |                                   |                             | 0.283   |
| Knee                    | 69 (43.40)                       | 8 (32.00)                   |         |
| Hip                     | 90 (56.60)                       | 17 (68.00)                  |         |
| Comorbidity, n (%)      |                                   |                             |         |
| Diabetes                | 25 (15.72%)                      | 2 (8.00%)                   | 0.541   |
| Hepatitis               | 6 (3.77%)                        | 1 (4.00%)                   | 1.000   |
| Cardiovascular          | 16 (10.06%)                      | 2 (8.00%)                   | 1.000   |
| Malignancy              | 8 (5.03%)                        | 0 (0.00%)                   | 0.601   |
| Renal                   | 4 (2.52%)                        | 5 (20.00%)                  | 0.003   |
| Alcohol abuse           | 13 (8.18%)                       | 7 (28.00%)                  | 0.009   |
| Mean joint function score (SD) | 40.85 (17.41)           | 36.52 (17.99)               | 0.323   |

BMI, body mass index; ASA, American society of anesthesiologists; joint function score, measured by The Hospital for Special Surgery (HSS) score for knee and Harris score for hip.

Lab, Microbiology and Pathology Tests at Spacer Insertion

We retrospectively collected and analysed all data from the database on the lab, culture and pathology tests for both groups at the time of spacer insertion. The results are shown in Table 2. No
significant differences were found in the lab test results. However, all inflammatory indicators were elevated according to the MSIS criteria. The most common organism was resistant PJ (35/159, 22.15%), followed by coagulase-negative staphylococcus (25/159, 15.82%), in the no inflammatory disease group. The most common culture result in the inflammatory disease group was coagulase-negative staphylococcus (4/25, 16.67%). The positive pathology rate was 62.77% in the no inflammatory disease group and 73.68% in the inflammatory disease group.
Table 2

|                      | No inflammatory diseases (n = 159) | Inflammatory diseases (n = 25) | P-value |
|----------------------|-----------------------------------|--------------------------------|---------|
| **Serum biomarkers, mean (SD)** |                                   |                                |         |
| CRP (mg/l)           | 29.9 (33.4)                       | 23.3 (22.4)                    | 0.552   |
| IL-6 (pg/ml)         | 30.03 (97.49)                     | 22.54 (34.22)                  | 0.991   |
| ESR (mm/h)           | 44.34 (26.76)                     | 38.27 (22.14)                  | 0.370   |
| Fibrinogen, (g/l)    | 5.05 (1.30)                       | 4.83 (1.12)                    | 0.164   |
| D-dimer, (g/ml)      | 1.92 (1.44)                       | 1.23 (0.64)                    | 0.106   |
| Mean Synovial WBC, 10^9/ml (SD) | 23994.78 (30090.00) | 20571.67 (34426.31) | 0.406   |
| **Microbiology results, n (%)** |                                   |                                |         |
| Staphylococcus aureus | 17 (10.76)                       | 2 (8.33)                       | 1.000   |
| Coagulase negative Staphylococcus | 25 (15.82)         | 4 (16.67)                      | 1.000   |
| Enterococcus faecalis | 7 (4.43)                        | 1 (4.17)                       | 1.000   |
| Streptococcus        | 5 (3.16)                         | 1 (4.17)                       | 0.577   |
| Gram negative bacillus | 12 (7.59)                     | 2 (8.33)                       | 1.000   |
| Resistant PJI        | 35 (22.15)                       | 2 (8.33)                       | 0.172   |
| Fungal PJI           | 11 (6.96)                        | 0 (0.00)                       | 0.364   |
| Polymicrobial PJI    | 12 (7.59)                        | 2 (8.33)                       | 1.000   |
| Other organisms      | 5 (3.16)                         | 0 (0.00)                       | 1.000   |
| Positive pathology*, n (%) | 100 (62.77)              | 18 (73.68)                     | 0.753   |
| Sinus tract, n (%)   | 43 (27.22)                       | 7 (28.00)                      | 1.000   |
| **Serum results, mean (SD)** |                                   |                                |         |
| CRP (mg/l)           | 8.0 (16.6)                       | 16.8 (16.3)                    | 0.003   |
| IL-6 (pg/ml)         | 11.85 (79.33)                    | 25.32 (40.51)                  | 0.032   |
| ESR (mm/hr)          | 14.70 (14.36)                    | 26.00 (21.60)                  | 0.001   |
| Fibrinogen (g/l)     | 3.47 (0.83)                      | 4.12 (1.01)                    | 0.003   |
| D-dimer (ug/ml)      | 1.71 (1.34)                      | 3.02 (3.07)                    | 0.105   |
| Mean synovial WBC, 10^9/ml (SD) | 1467.14 (1856.46) | 1279.33 (1283.43) | 0.839   |
| **Microbiology results, n (%)** |                                   |                                |         |
| Staphylococcus aureus | 2 (1.26)                       | 0 (0.00)                       | 1.000   |
| Gram negative bacillus | 7 (4.40)                        | 1 (4.17)                       | 1.000   |
| Resistant PJI        | 2 (1.26)                         | 1 (4.17)                       | 0.346   |
| Fungal PJI           | 2 (1.26)                         | 0 (0.00)                       | 1.000   |
| Other organisms      | 5 (3.14)                         | 0 (0.00)                       | 1.000   |
| Positive Pathology*, n (%) | 30 (18.95)               | 3 (10.52)                      | 0.570   |
| Sinus tract, n (%)   | 6 (3.77)                         | 0 (0.00)                       | 1.000   |

ESR, erythrocyte sedimentation rate; CRP, c-reactive protein; IL-6, interleukin-6; positive pathology, greater than five neutrophils per high-power field in five high-power fields observed from histologic analysis of periprosthetic tissue at 400 magnification.

Lab, Microbiology and pathology Tests at Reimplantation

Table 3 shows the lab, microbiology and pathology test results at reimplantation for the two groups.

Several inflammatory indicators were observed to be significantly higher in the inflammatory disease group than in the control group, including the serum CRP, IL-6, ESR, fibrinogen, and d-dimer values.

The mean CRP and IL-6 levels were 16.8 mg/l and 25.32 pg/ml, respectively, in the inflammatory
disease group. The mean ESR, fibrinogen and d-dimer levels were 26.00 mm/hr, 4.12 g/l and 3.02 ug/ml, respectively. However, the synovial WBC count showed satisfactory consistency between the two groups. The mean synovial WBC count was 1467.14*10^9/ml in the no inflammatory disease group and 1279.33*10^9/ml in the inflammatory disease group (p = 0.839). The culture positive rate was low at the time of reimplantation. Only 1 case of gram-negative bacillus and 1 case of MRSA were identified in the inflammatory diseases group. The positive pathology rate was 18.95% in the no inflammatory disease group and 10.52% in the inflammatory disease group (p = 0.570).

| Serum results, mean (SD) | No inflammatory diseases (n=159) | Inflammatory diseases (n=25) | P-value |
|--------------------------|----------------------------------|-----------------------------|---------|
| CRP (mg/l)               | 8.0 (16.6)                       | 16.8 (16.3)                 | 0.003   |
| IL-6 (pg/ml)             | 11.85 (79.33)                    | 25.32 (40.51)               | 0.032   |
| ESR (mm/hr)              | 14.70 (14.36)                    | 26.00 (21.60)               | 0.001   |
| Fibrinogen (g/l)         | 3.47 (0.83)                      | 4.12 (1.01)                 | 0.003   |
| D-dimer (ug/ml)          | 1.71 (1.34)                      | 3.02 (3.07)                 | 0.105   |
| Mean synovial WBC, 10^9/ml (SD) | 1467.14 (1856.46) | 1279.33 (1283.43) | 0.839   |

| Microbiology results, n (%) | No inflammatory diseases (n=159) | Inflammatory diseases (n=25) | P-value |
|-----------------------------|----------------------------------|-----------------------------|---------|
| Staphylococcus aureus       | 2 (1.26)                         | 0 (0.00)                    | 1.000   |
| Gram negative bacillus      | 7 (4.40)                         | 1 (4.17)                    | 1.000   |
| Resistant PJJ               | 2 (1.26)                         | 1 (4.17)                    | 0.346   |
| Fungal PJJ                  | 2 (1.26)                         | 0 (0.00)                    | 1.000   |
| Other organisms             | 5 (3.14)                         | 0 (0.00)                    | 1.000   |
| Positive Pathology*, n (%)  | 30 (18.95)                       | 3 (10.52)                   | 0.570   |
| Sinus tract, n (%)          | 6 (3.77)                         | 0 (0.00)                    | 1.000   |

Table 3 Lab tests and culture results among patients with and without inflammatory diseases at reimplantation

Patients’ Follow-up

According to the Delphi consensus criteria, the failure rate was 8.8% (14/159) in the no inflammatory disease group and 8.0% (2/25) in the inflammatory disease group. The mean duration of follow-up was 33.9 months (15.9 to 51.9) in the no inflammatory disease group and 35.5 months (16.2 to 54.8) in the inflammatory disease group (Table 4). No significant difference in the joint function score was
observed in the PJI without inflammatory disease group or PJI with inflammatory disease group (p = 0.084).

Overall, the survivorship of the individuals free from PJI in the no inflammatory disease group was 93.08% (95% CI, 89.22 to 97.11%) at 1 year and 90.39% (95% CI, 85.58 to 95.47%) at 5 years, and the survivorship of the individuals free from PJI in the inflammatory disease group was 96.00% (95% CI, 88.62 to 100.00%) at 1 year and 86.40% (95% CI, 69.23 to 100.00%) at 5 years (Fig. 1). No significant difference was found between the two groups in the probability of survival (p = 0.89).

Discussion

Prosthetic joint infection (PJI) is a devastating complication, and inflammatory diseases have been reported to be an important risk factor for PJI in many articles\textsuperscript{11–14}. The diagnosis of PJI depends on the combination of the culture results, lab test results, clinical symptoms and pathology results. Classic serological markers, including ESR and CRP, are widely used in diagnoses, and serum fibrinogen was suggested to be useful in diagnoses in a study by LI R et al\textsuperscript{29}. Many articles have researched the utility of lab, culture and pathology tests in diagnosing PJI prior to two-stage revision\textsuperscript{30–32}. However, to the best of our knowledge, no studies have compared the differences in the indicator values, culture test results and pathologies between patients with and without inflammatory diseases, mainly because of the rarity of inflammatory diseases in individuals with PJI. According to our research, inflammatory disease patients show no significant difference in the serum biomarkers or synovial WBC count at the time of spacer insertion. The average ESR, CRP and synovial WBC count values are all above the thresholds in the MSIS criteria, indicating that the MSIS criteria are also optional standards for diagnosing inflammatory disease patients. The average fibrinogen levels in both groups were higher than 4.10 g/l, which is in accordance with the results reported by LI R et al\textsuperscript{29}, suggesting that fibrinogen is a helpful indicator for both patients with and without inflammatory diseases. Coagulase-negative staphylococci were the most common organisms in the inflammatory disease group in our research, while no significant difference was found in the type or ratio of microorganisms. An excessive focus on the elevation of the inflammatory indictors caused by
the inflammatory diseases was shown to be unnecessary, as the infection activated the immune system and led to even higher levels of the biomarkers in individuals with well-controlled inflammatory diseases.

At the reimplantation stage, there is no gold standard for the diagnosis of PJI, and the MSIS criteria are considered to have low sensitivity because of long-term antibiotic suppression\textsuperscript{32}. However, we found a significant difference between the no inflammatory disease and inflammatory disease groups in the serum markers. The average CRP and IL-6 levels were clearly elevated, even though the inflammatory diseases of all patients included in the analysis showed low levels of activity. The synovial WBC count showed good consistency between the two groups and was less affected by the immune changes caused by the inflammatory diseases. Many articles have explained the elevation in serum and synovial IL-6, ESR, and CRP in patients with inflammatory diseases\textsuperscript{33,34}, causing ultrahigh sensitivity in diagnosing PJI before insertion. Significant differences in the inflammatory indicators in the inflammatory disease group were observed in our research, which may sometimes mislead clinical doctors and make it difficult to distinguish inflammatory disease related PJIs using serum biomarkers alone. In addition, fibrinogen recommended by LI R et al\textsuperscript{29} failed to distinguish inflammatory diseases and PJIs at reimplantation due to its elevation in both inflammatory diseases and PJIs. However, synovial fluid is a local immune response that is less influenced by inflammatory diseases. The recommended marker is the synovial WBC count at the time of reimplantation because of its good agreement between patients with and without inflammatory diseases. XIE K et al\textsuperscript{31} reported that the synovial IL-6 level showed higher sensitivity and specificity than the serum IL-6 level in diagnosing PJI, but more research is required to determine whether the synovial IL-6 level is less affected by inflammatory diseases. More research is needed to identify the thresholds of synovial indicators for diagnosing PJIs in individuals with inflammatory diseases and PJIs.

Two-stage revision is widely reported to be a viable procedure for prosthetic joint infection\textsuperscript{10,35,36}, and patients with inflammatory diseases suffer from a higher risk of infections than those without inflammatory diseases. However, we found that inflammatory diseases and PJIs can be resolved, and
the survivorship in individuals with PJIs and inflammatory diseases was as high as 86.4% (95% CI, 69.2 to 100%) in our hospital. Regarding joint function, apparent improvement was observed between the perioperative and postoperative procedures. Infections were resolved, malformations were corrected, and pain was relieved in individuals with inflammatory diseases and PJIs after two-stage revision. Two-stage revision is still the most viable choice for PJIs with and without inflammatory diseases. Considering the long-standing nature of inflammatory diseases even after reimplantation, reasonable medical treatment is necessary. However, the long-term use of DMARDs, biological drugs and corticosteroids increases the risk of PJI and causes renal function damage. The balance between the control of inflammatory diseases, renal function and PJI should be deeply considered by clinicians. There were several limitations in our research. First, this was a retrospective study, and certain biases of retrospective studies cannot be avoided. Although we reviewed most cases that were documented, some errors may exist. Second, a limitation of the study is the small number of patients with inflammatory diseases and PJIs. Therefore, we did not divide the patients into rheumatoid arthritis, psoriasis and ankylosing spondylitis groups to analyse them separately, which may have resulted in an underpowered study. In addition, the inflammatory disease group in this study only consisted of RA, AS and PAS patients, while patients with other conditions, such as systemic lupus erythematosus, need to be studied further. Third, all inflammatory disease patients in our research received medical treatment to control the inflammatory diseases, and no active inflammatory diseases were visible. The level of activity of the inflammatory diseases may affect the failure rate and lab indicators, which should be confirmed in future studies. Fourth, although guidelines for two-stage procedures were implemented in our hospital, the different methods of treatment management conducted by different surgeons may introduce bias. Finally, the minimum 1-year follow-up period was limited in indicating long-term outcomes.

Conclusion
Two stage revision is the viable treatment to cure both inflammatory diseases PJIs and non-inflammatory diseases PJIs. Infection eradicated, malformation corrected and function improved was observed in IDs PJIs after two stage revision. Though MSIS criteria, fibrinogen and IL-6 all reveal
feasible diagnosis utility of PJI before spacer insertion, synovial WBC was considered more accurate than other biomarkers at reimplantation. The elevation of serum markers causing by persistent PJI or IDs should be differentiated by clinicians at reimplantation stage. Further studies with larger cohorts are needed to validate long term survivorship in patients with inflammatory diseases patients and find more accurate biomarkers to diagnose persistent PJI combining with inflammatory diseases at reimplantation.

**Abbreviations**
RA, rheumatoid arthritis; PSA, psoriatic arthritis; JIA, juvenile idiopathic arthritis; AS, ankylosing spondylitis; SLE, systemic lupus erythematosus; TJA, total joint arthroplasty; PJI, Prosthetic joint infection; DMARDs, disease-modifying anti-rheumatic drugs; TKA, total knee arthroplasty; THA, total hip arthroplasty; BMI, body mass index; MSIS, Musculoskeletal Infection Society; ASA, American Society of Anesthesiologists; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; IL-6, interleukin-6; WBC, white blood cell; SD, standard deviation; PMN, polymorphonuclear; CNS, coagulase negative staphylococci; HSS, the hospital for special surgery knee score

**Declarations**

*Ethics approval and consent to participate*
This study was approved by the Ethics Committee of the General Hospital of People's Liberation Army and in accordance with the standards of the National Research Council. Written informed consent was obtained from all participants.

*Consent for publication*
Not applicable.

*Availability of data and materials*
We do not wish to share our data, because some of the patient’s data regarding individual privacy, and according to the policy of our hospital, the data could not be shared with others without permission.

*Competing interests*
The authors declare that they have no competing interests
Authors’ contributions

| Contributors | Roles |
|--------------|-------|
| Qiao Jiang   | Manuscript writing; Data collection; Data analysis; Study conceive; Participated in the design of the study; Data interpretation; Project coordination |
| Chi Xu       | Study conceive; Participated in the design of the study; Data interpretation; Project coordination |
| Jun Fu       | Data collection; Data analysis; Study conceive; Participated in the design of the study; Data interpretation; Project coordination |
| Wei Chai     | Data curation; Investigation; Methodology; Visualization; Writing - review & editing |
| Li-Bo Hao    | Data curation; Investigation; Methodology; Validation; Writing - review & editing |
| Yong-Gang Zhou | Data curation; Validation; Methodology; Validation; Writing - review & editing |
| Ji-Ying Chen | Project administration; Supervision; Writing - review & editing |

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Figures
Figure 1

Kaplan-Meier survival curve regarding treatment failure of two-stage exchange arthroplasty when stratifying by the inflammatory diseases and no inflammatory diseases

$p = 0.89$
Flowchart of details of patients underwent two stage reimplantation