Changes in Serum Markers Failed to Predict Persistent Infection after Two-stage Exchange Arthroplasty

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Abstract

Background Two-stage exchange arthroplasty is a viable choice for prosthetic joint infection (PJI). After removing the infected prosthesis and implanting an antibiotic-loaded spacer in the first stage, the proper timing of reimplantation is crucial for successful treatment. To date, there is no gold standard to evaluate the eradication of PJI before reimplantation. A combination of serum indicators, synovial blood white cell (WBC) counts, culture results, intraoperative histology, and clinical symptoms is widely used to guide the timing of reimplantation. However, the proper timing of reimplantation is not clearly defined. We investigated whether: (1) serum indicators, which included the erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), interleukin-6 (IL-6) and fibrinogen, were useful indicators for predicting the failure of reimplantation; and (2) primary culture results were related to serum marker changes?

Method A retrospective review of 109 patients treated with two-stage exchange arthroplasty from 2014 to 2017 was conducted. The inclusion criteria included the following: 1. a minimum of a 2-year follow-up or failure of treatment within this period; 2. complete record of serum biomarkers; and 3. met the Musculoskeletal Infection Society criteria (MSIS) when diagnosed PJI. Serum biomarkers and organism results at the onset of PJI diagnosis and reimplantation were reviewed. Treatment success was defined according to the Delphi consensus criteria with a minimum follow-up of 2 years, and the receiver operator characteristic (ROC) was used to examine the usefulness of changes in four serum markers for predicting failure.

Results When predicting persistent PJI, the area under the ROC curves (AUC) demonstrated that both the percent change and value change of serum markers were poor indicators. When comparing exact values of serum markers during reimplantation, the values of CRP and fibrinogen were significantly higher in the reinfection group. Besides, initial causative organism didn't influence the normalization of serum markers.

Conclusion Either the value change or percent change of serum markers were not useful for determining the timing of reimplantation, and initial causative organism didn't influence the normalization of serum markers. Persistent PJI after TJA was still difficult to diagnose.

Introduction

The management of prosthetic joint infection (PJI) is a challenging problem for clinicians, with a high prevalence after total joint arthroplasty (TJA)[1, 2]. In North America and East Asia, two-stage exchange arthroplasty is widely applied for chronic PJIs after TJA[3, 4]. After removing the infected prosthesis and implanting an antibiotic-loaded spacer in the first stage, the proper timing of reimplantation is crucial for successful treatment[5]. Currently, there is no "gold standard" to evaluate the eradication of PJI before reimplantation. The combination of serum indicators, synovial white blood cell (WBC) counts, culture results, intraoperative histology, and clinical symptoms is widely used to guide the timing of reimplantation.

The elevated erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) are minor criteria in MSIS criteria for predicting PJI[6–11]. A definite PJI is present when: 1. Two positive periprosthetic cultures with phenotypically identical organisms, or 2. A sinus tract communicating with the joint, or 3. Having three of the following minor criteria: (1) Elevated serum CRP AND ESR; (2) Elevated synovial fluid WBC count OR ++change on leukocyte esterase test strip; (3) Elevated synovial fluid polymorphonuclear neutrophil percentage (PMN%); (4) Positive histological analysis of periprosthetic tissue; (5) A single positive culture. However, the reliability and utility of both indicators has been questioned by several studies. Due to their unclear threshold cutoff levels, the normalization of both markers was reported to fail predict PJI control[5–7, 11]. Several other serum biomarkers have been studied by researchers. Interleukin-6 (IL-6) was suggested to be useful in diagnosing PJI[12–14], and Hoell et al reported the high utility of IL-6 in predicting reimplantation failure[15]. Li et al reported that fibrinogen had good performance in the diagnosis of PJI[16]. However, more research is needed to determine the accuracy and reliability of these serum indicators for predicting the proper timing of reimplantation.

Instead of a numerical threshold, a downward trend in serum markers was useful for determining the proper timing of reimplantation was with the approval of the majority in the 2018 International Consensus Meeting. However, the opposite result was found that by Stambough et al[17]. Stambough et al[17] found the area under the receiver operator curves was 0.530 for the percent or delta change of the ESR and 0.482 for the change of CRP when predicting persistent PJI, indicating that both were poor markers. Considering the value of fibrinogen and IL-6 in diagnosing PJI, changes in these serum markers may be useful for predicting failure after reimplantation. In addition, instead of percent changes, the usefulness of the value changes in serum markers should be investigated.

As contradictory results exist regarding whether changes in serum markers can guide the timing of reimplantation in two-stage exchange arthroplasty after total joint arthroplasty (TJA), we investigated whether: (1) serum indicators, which included the erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), interleukin-6 (IL-6) and fibrinogen are useful for predicting infection eradication; and (2) correlations between primary culture results and serum marker changes.

Methods

Patients

After receiving Institutional Review Board approval, we retrospectively reviewed all patients who underwent two-stage reimplantation between 2014 and 2017 (n=226). All patients were confirmed to have chronic PJI, and acute hematogenous and perioperative infections were excluded[18]. The exclusion criteria were as follows: 1. uncertain changes in serum indicators in these patients[11, 19, 20], which included fungal PJI (n=7), patients with potential inflammatory rheumatic disease (n=26), and septic arthritis (n=30); 2. incomplete recordings of serologic markers at the time of resection or reimplantation (n=26); and 3. less than the minimum 2-year follow-up or no reinfection occurrence within this period (n=15). In this study, the MSIS criteria[21] were considered the gold standard reference for diagnosing PJI

before resection, and 13 PJIs were excluded for not meeting the MSIS criteria. The inclusion criteria included the following: 1. a minimum a 2-year follow-up or failure of treatment within this period; 2. complete record of serum biomarkers; and 3. met the MSIS criteria when diagnosed with PJI. There was a total of 109 patients (56 hips and 53 knees) in final analysis with complete records of serum biomarkers, and all patients met the MSIS criteria when diagnosed with PJI.

We reviewed all medical records of patients in detail, which included sex, age, gender, joint, American Society of Anesthesiologists (ASA) score, risk factors, surgical history of the same site, pathology results, and organism culture results. Values of four main serum biomarkers including serum ESR, CRP, fibrinogen and IL-6, were determined before resection and reimplantation. We used STA-R Evolution® analyzer (Stago Diagnostica, Asnieres, France) to gauge fibrinogen and D-dimer levels and expressed in gram per liter (g/L) and microgram per milliliter ($\mu\text{g/mL}$), respectively[22]. And ESR and CRP were measured by the Westergren method and nephelometric immune assay, respectively[23]. The threshold values were 30 mm/hr for ESR and 10 mg/L for CRP according to the MSIS criteria[21], and the upper limit was 12 pg/mL for IL-6 and 4.01 mg/mL for fibrinogen[16, 24] when diagnosing PJI. The change in serum indicators was evaluated by the percent change (using values of serum markers at the time of reimplantation divided by values at the time of resection) and value change (using values of serum markers at the time of resection minus values at the time of reimplantation).

Treatment protocol

All patients underwent an institutional standard two-stage exchange arthroplasty, including the removal of the prosthesis, placement of an antibiotic-loaded articulating cement spacer and thorough debridement at the time of the first stage procedure. Vancomycin (2-4 g per 40 g) and meropenem (1-2 g per 40 g) were mixed in polymethylmethacrylate (PMMA) spacers. Four to six samples for aerobic, anaerobic and fungal culture and there to five samples for histology analysis were obtained intraoperatively from the periprosthetic membrane and other periprosthetic tissues in which infection was suspected. After the insertion of cement, all patients received 6-8 weeks of intravenous antibiotics depending on culture sensitivity reports. For patients with culture negative results ($n=11$), broad-spectrum antibiotic therapy was used. At least 2-week antibiotic holiday was stipulated before reimplantation. During the second-stage revision, the antibiotic-loaded cement was removed. Sterilized saline water (4-6 L) was used to irrigate the joint after thorough debridement. Three to five samples were sent for frozen sectioning, and aerobic and anaerobic cultures according to the surgeons' suspicion.

Definition of persistent PJI and treatment success

Persistent PJI for this study was defined as :1. Re-infection after reimplantation, based on MSIS criteria, 2. Long-term antibiotic suppression after reimplantation, 3. Death relating to PJI, 4. Met the MSIS criteria at the time of reimplantation.

We determined treatment success using the Delphi-based consensus criteria[25, 26], which matches the following: 1. 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; 3. no occurrence of PJI-related mortality.

Statistical analysis

All of the statistical analyses were performed with the statistical software packages R (<http://www.R-project.org>, The R Foundation). Categorical data were summarized as absolute values and percentage. Continuous data were presented as median and interquartile range (IQR). The demographic and clinical characteristics between groups were compared with the use of the Student's *t*-test if they were normally distributed or the Mann-Whitney test if not normally distributed for continuous variables and the chi-square test or Fisher's exact test for categorical variables. Receiver operating characteristic (ROC) curves were generated to determine the diagnostic value of each test for the assessment of persistent PJI. The area under the curve (AUC) was calculated. Discriminatory value of ROC curves was interpreted as excellent (AUC 0.9–1), good (0.8–0.89), fair (0.7–0.79), poor (0.6–0.69), or fail/no discriminatory capacity (0.5–0.59)[27]. Youden's J-statistic was used to attempt to determine a threshold value for each serologic marker. A *p*-value less than 0.05 was considered significant.

Results

General information and patients' follow-up

Demographic information and follow-up results are shown in Table 1. There were 54 (49.5%) males and 55 females (50.5%). The mean age was 60.4 ± 12.7 years in the success group and 60.3 ± 14.4 years in the re-infected group. The mean BMI was 25.4 ± 3.7 kg/m² in the success group compared with 25.6 ± 3.9 kg/m² in the reinfected group. Fifty-six hips and fifty-three knees were included in the analysis. Though the difference was not significant (*p*=0.007), the prevalence of sinus occurrence tended to be higher in the reinfection group (53.3%) than in the success group (27.7%).

The mean follow-up year was 3.1 (range, 2.00 to 5.70 years) years in the success group and 1.4 (range, 0.07 to 4.43 years) years in re-infected group. The interval of spacer insertion was 168.0 (range, 32 to 529 days) days in the success group and 162.7 (range, 45 to 491 days) days in reinfection group. There were 15 patients re-infected after reimplantation in two-stage exchange arthroplasty, and the total success rate was 86.2%.

Organism analysis

Details of the causative organism at the set of spacer and culture results at the time of reimplantation in reinfected patients are shown in Table 2. Resistant organisms (including methicillin-resistant *Staphylococcus aureus*, methicillin-resistant *S. epidermidis* and vancomycin-resistant enterococcus) were the most common causative bacteria for initial PJI (32,29.4%). The rest of the causative organisms included 21 (19.3%) coagulase-negative *Staphylococcus* (CNS), 18 (16.5%) *Staphylococcus aureus*, 5 (4.6%) *Enterococcus faecalis*, 4 (3.7%) *Streptococcus*, 5 (4.6%) Gram-negative *Bacillus*, 3 (2.8%) other

organisms and 10 (9.2%) polymicrobial organisms. Eleven (10.1%) patients had negative culture results but were diagnosed with PJI according to the MSIS criteria. At the time of reimplantation, the culture result of reinfected patients included 1 (0.9%) CNS, 2 (1.8%) gram-negative Bacillus, 2 (1.8%) MRSA, 1 (0.9%) fungal PJI, 1 (0.9%) other organism and 8 (7.2%) unidentified organisms.

Was there any difference in values of serum markers between the success and reinfection groups?

The values of the ESR, IL-6, CRP and fibrinogen were compared between success patients and reinfection patients. The details of each serum marker are shown in Table 3. At the time of PJI diagnosis, the reinfection group exhibited significantly higher values for all four serum markers. At reimplantation, higher values of CRP and fibrinogen were observed, while the IL-6 and ESR were comparable, indicating that higher values of CRP and fibrinogen may be related to reinfection. The accurate cut-off value of CRP and fibrinogen requires further research.

Can the percent change or value change in serum markers guide the timing of reimplantation?

Table 5 shows the percent change and value change from resection to reimplantation. No significant difference was found in either the value change or percent change of serum markers. Furthermore, we generated a receiver operator curve (ROC) for the value change (figure 1) and percent change (figure 2) of serum markers. The area under the receiver operator curve (AUC) was 0.543 for CRP, 0.572 for IL-6, 0.621 for the ESR and 0.463 for fibrinogen for predicting failure based on the value change, demonstrating that all of these serum markers were poor indicators. However, the AUC exhibited acceptable utility for the combination (AUC=0.709) of the ESR, CRP, IL-6 and fibrinogen. With regard to the percent change for determining the timing of reimplantation, the AUC indicated that CRP (AUC=0.521), IL-6 (AUC=0.472), the ESR (AUC=0.413), fibrinogen (AUC=0.552) and their combination (AUC=0.630) were all not useful markers. As a result of the low sensitivity and specificity caused by the wide distribution of changes in inflammatory levels, a threshold value could not be calculated by Youden's J-statistic.

Do microbial culture results influence the value or percent change of serum markers?

A comparison of the difference in the value change and percent change of serum markers between resistant PJI (including MRSA, MRSE, VRE) and sensitive organisms is shown in Table 5. Reinfected patients showed a lower value change and a higher percent change for the ESR. The subgroup analysis between culture negative PJI and PJI with identified organisms is shown in Table 6. No significant difference was found in either the value change or the percent change of all four serum markers.

Discussion

PJI is still a challenging problem after total joint arthroplasty, and two-stage exchange arthroplasty has been proven to be a useful treatment for prosthetic joint infection after total joint arthroplasty, with a success rate ranging from 65% to 100%[28]. The proper timing of reimplantation is crucial to the survival after reimplantation. Considering the unreliability of clinical symptoms, delayed pathology results and

scarcity of synovial fluid, serum biomarkers still play an important role in predicting persistent infection after reimplantation. Though several authors failed to determine the threshold of the ESR and CRP[6, 7, 10], the utility of fibrinogen and IL-6 for predicting failure after reimplantation was reported in some articles[13, 22].

Our research investigated the value change and the percent change of four common serum markers (the ESR, CRP, IL-6 and fibrinogen) between resection and reimplantation. The AUC was no more than 0.70 for all serum markers, and the combination of serum markers did not improve the diagnostic usefulness, indicating that neither the value change nor percent change of these four serum markers were useful for determining the timing of reimplantation. A higher value of CRP was observed at both resection and reimplantation, and elevated fibrinogen at reimplantation seemed to be related to increased failure rate. In addition, resistant PJI or negative culture results were not associated with changes in serum markers.

We found that preresection CRP and IL-6 were significantly higher in the reinfection group. In addition, the values of fibrinogen and ESR tended to be significant. This is not surprising given that the utility and threshold of the four serum markers have been thoroughly studied[16, 24, 29, 30]. However, at the time of reimplantation, values of CRP and fibrinogen were significantly higher in reinfection patients. Kusuma et al[6] reported 76 PJIs after total knee arthroplasty, and the AUC was 0.62 for the ESR and 0.39 for CRP. Xu et al[22] also investigated 109 hips in patients who underwent two stage exchange arthroplasty. They found that the value of fibrinogen may be a promising marker for predicting persistent PJI, and the threshold of fibrinogen was 3.61 g/L. Qu et al[31] reported high specificity but low sensitivity when the threshold of IL-6 was set at 8.12 pg/mL, and the AUC was 0.59. The value of serum markers may be useful for predicting reinfection after two-stage exchange arthroplasty, but further study is needed to determine their accurate thresholds. Besides, other serum markers, such as procalcitonin, TNF- α and D-dimer, were reported to be useful by several articles[24, 32, 33].

Instead of a numerical threshold value, the International Consensus Meeting recommended that the downtrend of serological tests and results of synovial analysis should be used to determine the optimal timing of reimplantation. However, two traditional serum markers (the ESR and CRP) were studied by Stambough et al[26], and the AUC for the percent change in Stambough et al was 0.530 for the ESR and 0.482 for CRP. Ghanem et al[7] studied a consecutive series of 109 patients who underwent two-stage resection arthroplasty for infected TKA. The total success rate was 79% in their cohort. The value change of the ESR and CRP was depicted by the ROC, and the AUC was 0.503 for the ESR and 0.545 for CRP. Both Stambough et al and Ghanem et al came to conclusions that opposed the ICM recommendations. We did, however, include the change of IL-6 and fibrinogen in our analysis. We found that neither the value change nor the percent change of these four laboratory markers was a suitable indicator for predicating re-infection after two-stage exchange reimplantation. A downward trend in serum markers was not significantly associated with the eradication of infection, and this result may change the traditional beliefs of surgeons.

In addition, no obvious correlations were observed between culture results and changes in serum markers. Though a significantly lower value change in the ESR was observed in resistant PJI, it could be ascribed to the high virulence of MRSA, MRSE and VRE. Regarding culture-negative organisms, all serum markers in our study showed no differences with confirmed PJI. Berbari et al[34] reported 897 PJI, of whom 60 patients were culture negative. The 5-year estimate of survival free of treatment failure was 94% for patients treated with two-stage exchange. There was not a higher recurrence rate for culture-negative PJI if full-dose antibiotics were used.

To date, the accurate diagnosis of the eradication of infection is still difficult for clinicians. As our study proved that changes in four common serum markers had low utility for predicting persistent PJI, other useful ways, such as new biomarkers, biochemistry, and histology, should be proposed to detect infection. The combination of clinical symptoms, the value of serum markers, frozen sections, and synovial fluid WBC counts is still the most reliable method for surgeons to determine the timing of reimplantation.

There were several limitations in our study. First, this was a retrospective study and certain biases of retrospective studies cannot be avoided. Although we reviewed most cases in the study, some mistakes may have existed. Second, because there is no “gold standard” for diagnosing persistent PJI after reimplantation, we combined culture result and follow-up result to identify re-infection. Thus, we constructed a broad definition for failure of the 2- stage exchange procedure and the subsequent PJI surgery after reimplantation might be indicative of a new infection rather than a persistent PJI. Third, several surgeons in our hospital conducted the surgery. Though institutional guidelines for therapy have been approved, differences still exist in the management of patients. Fourth, it was a single-institution study with a limited sample size and, as a result, has limited external validity. Only 15 patients developed the treatment failure during the follow-up, which might be an insufficient sample size. However, we set strict inclusion criteria. Thus, changes in inflammatory markers are only affected by joint infection, and the statistical result may be reliable.

Conclusion

We have shown that either the value change or percent change of serum markers failed to diagnose persistent infection after reimplantation. Besides, initial causative organism didn't influence the normalize of serum markers. Persistent PJI after TJA was still difficult to diagnose, and the combination of clinical symptoms, histology analysis, organism culture results in addition to serology, synovial fluid analysis should continue to use to diagnose persistent PJI during reimplantation.

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

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Not applicable.

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
Xue Yang	Data collection; Data analysis; Study conceive; Participated in the design of the study; Data interpretation; Project coordination
Chi Xu	Data curation; Investigation; Methodology; Visualization; Writing - review & editing
Wei Chai	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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Tables

	Success (n=94)	Failure (n=15)	P-value
Demographic information			
Follow-up (years)	3.1 ± 1.1	1.4 ± 1.3	<0.001
Age (years)	60.4 ± 12.7	60.3 ± 14.4	0.826
BMI (kg/m ²)	25.4 ± 3.7	25.6 ± 3.9	0.937
Interval of spacer (days)	168.0 ± 136.5	162.7 ± 113.3	0.996
Male	43 (45.7%)	11 (73.3%)	0.056
Hip	49 (52.1%)	7 (46.7%)	0.784
Sinus	26 (27.7%)	8 (53.3%)	0.070
Comorbidities			
Diabetes	19 (20.2%)	3 (20.0%)	1.000
Hepatitis	3 (3.2%)	1 (6.7%)	0.452
Cardiovascular	10 (10.6%)	2 (13.3%)	0.670
Carcinoma	5 (5.3%)	1 (6.7%)	1.000
Previous surgical history	23 (24.5%)	6 (40.0%)	0.220
Nephropathy	2 (2.1%)	0 (0.0%)	1.000
Smoking	14 (14.9%)	1 (6.7%)	0.689
Alcohol abuse	5 (5.3%)	1 (6.7%)	1.000
ASA>2	11 (11.7%)	3 (20.0%)	0.405

Table 1 Patients' demographic information and comorbidities associated with failure after two-stage exchange arthroplasty

BMI, Body mass index; ASA, American Society of Anesthesiologists

Cultured organism	Number
At the time of PJI diagnosis	
<i>Staphylococcus aureus</i>	18 (16.5%)
Coagulase-negative <i>Staphylococcus</i>	21 (19.3%)
<i>Enterococcus faecalis</i>	5 (4.6%)
<i>Streptococcus</i>	4 (3.7%)
Gram-negative <i>Bacillus</i>	5 (4.6%)
Resistant organisms	32 (29.4%)
Polymicrobial PJI	10 (9.2%)
Other organism	3 (2.8%)
Culture negative	11 (10.1%)
At the time of reimplantation	
Coagulase-negative <i>Staphylococcus</i>	1 (0.9%)
Gram-negative <i>Bacillus</i>	2 (1.8%)
Resistant organisms	2 (1.8%)
Fungal PJI	1 (0.9%)
Other organism	1 (0.9%)
Unidentified	8 (7.2%)

Table 2 Initial cause of prosthetic joint infection and culture results of re-infected patients at the time of reimplantation

	Success (n=94)	Failure (n=15)	P-value
Preresection			
CRP (mg/l)	26.0 ± 29.1	39.5 ± 24.2	0.008
IL-6 (pg/ml)	18.8 ± 18.1	25.2 ± 10.4	0.008
ESR (mm/hr)	42.0 ± 25.4	53.1 ± 22.5	0.091
Fibrinogen (g/l)	4.9 ± 1.2	5.5 ± 1.0	0.105
Pre-reimplantation			
CRP (mg/l)	5.3 ± 6.8	17.1 ± 24.2	0.025
IL-6 (pg/ml)	4.9 ± 4.6	8.9 ± 8.3	0.102
ESR (mm/hr)	13.7 ± 10.8	15.1 ± 11.3	0.597
Fibrinogen (g/l)	3.4 ± 0.7	3.9 ± 1.0	0.033

Table 3 Values of serum markers at the time of resection and reimplantation in prosthetic joint infection

	Success (n=94)	Failure (n=15)	P-value
Value change of serum markers			
CRP (mg/l)	21.2 ± 29.4	21.6 ± 32.9	0.595
IL-6 (pg/ml)	30.9 ± 12.6	16.3 ± 15.9	0.374
ESR (mm/hr)	28.3 ± 22.3	38.1 ± 22.4	0.135
Fibrinogen (g/l)	1.5 ± 1.2	1.5 ± 1.6	0.647
Percent change of serum markers			
CRP (%)	43.2 ± 55.8	51.6 ± 55.7	0.795
IL-6 (%)	51.9 ± 81.7	51.6 ± 63.0	0.725
ESR (%)	40.9 ± 32.7	30.3 ± 22.8	0.283
Fibrinogen (%)	74.9 ± 45.6	75.0 ± 24.9	0.515

Table 4 Value changes and percent changes of serum markers between resection and reimplantation in prosthetic joint infection

	Sensitive organisms (n=77)	Resistant organisms (n=32)	P- value
Value change of serum markers			
CRP (mg/l)	22.3 ± 31.4	19.1 ± 23.0	0.920
IL-6 (pg/ml)	35.1 ± 13.3	14.1 ± 14.0	0.572
ESR (mm/hr)	33.3 ± 22.7	20.8 ± 19.5	0.006
Fibrinogen (g/l)	1.6 ± 1.4	1.4 ± 1.1	0.585
Percent change of serum markers			
CRP (%)	46.6 ± 55.0	38.8 ± 57.6	0.389
IL-6 (%)	53.6 ± 78.8	47.6 ± 80.8	0.269
ESR (%)	34.7 ± 27.0	50.8 ± 38.8	0.038
Fibrinogen (%)	76.2 ± 49.7	72.0 ± 21.3	0.894

Table 5 Value change and percent change in sensitive organisms versus resistant organisms in initial prosthetic joint infection

	Negative culture (n=98)	Identified organism (n=11)	P- value
Value change of serum markers			
CRP (mg/l)	22.8 ± 30.1	15.9 ± 12.1	0.984
IL-6 (pg/ml)	30.8 ± 11.8	12.2 ± 15.0	0.556
ESR (mm/hr)	29.6 ± 22.5	29.9 ± 23.7	0.960
Fibrinogen (g/l)	1.5 ± 1.3	1.6 ± 1.3	0.798
Percent change of serum markers			
CRP (%)	45.0 ± 57.8	38.8 ± 30.4	0.644
IL-6 (%)	52.1 ± 82.5	49.3 ± 39.8	0.421
ESR (%)	40.0 ± 32.4	34.7 ± 24.6	0.759
Fibrinogen (%)	75.3 ± 45.2	71.7 ± 19.4	0.944

Table 6 Value changes and percent changes in patients with negative cultures versus identified organisms in initial prosthetic joint infection

Figures

Figure 1

Receiver operator curves for the value change of serum markers for predicting failure after two-stage exchange arthroplasty: A. The erythrocyte sedimentation rate (yellow line), interleukin-6 (green line), C-reactive protein (blue line) and fibrinogen (purple line). The black line depicts 50% sensitivity and specificity. B. The combination of these four serum markers (blue line).

Figure 2

Receiver operator curves for the percent change of serum markers for predicting failure after two-stage exchange arthroplasty. A. The erythrocyte sedimentation rate (yellow line), interleukin-6 (green line), C-reactive protein (blue line) and fibrinogen (purple line). The black line depicts 50% sensitivity and specificity. B. The combination of these four serum markers (blue line).

Supplementary Files

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