

# The Utility of Synovial Fluid Interleukin-10 in Diagnosing Chronic Periprosthetic Joint Infection: A Prospective Cohort Study

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**Background:** Diagnosing chronic periprosthetic joint infection (PJI) is challenging. Synovial fluid interleukin-10 (SF IL-10), an anti-inflammatory cytokine produced by leukocytes, plays a pivotal role in inflammation and infection regulation. However, limited research has explored the diagnostic potential of SF IL-10 in chronic PJI patients.

**Objective:** The study aimed to investigate the relationship between SF IL-10 and incidence of chronic PJI, and to evaluate its diagnostic reliability.

**Design and Methods:** We analyzed data from 137 patients who underwent revision surgery for aseptic loosening or chronic PJI between 2017 and 2019 in our hospital. PJI diagnoses followed the 2013 International Consensus Meeting criteria. We measured serum ESR, serum CRP, SF PMN%, SF WBC and SF IL-10 levels, using logistic regression and receiver operating characteristic (ROC) curves to evaluate associations and diagnostic accuracy.

**Results:** Demographic data showed no significant differences. However, SF IL-10 levels differed significantly between groups. Logistic regression indicated a strong association between SF IL-10 and chronic PJI (OR = 1.11, 95% CI 1.05~1.17,  $p < 0.001$ ). At a cut-off of 10.305 pg/mL, SF IL-10 had an area under the ROC curve (AUC) of 0.891, with 92.16% sensitivity and 77.91% specificity. Adding SF IL-10 to traditional models improved risk prediction for chronic PJI (net reclassification improvement [NRI]: 0.167 [0.023 ~ 0.312]; integrated discrimination improvement [IDI]: 0.160 [0.096 ~ 0.224]).

**Conclusion:** Higher SF IL-10 levels were significantly associated with chronic PJI in revision surgery patients, and incorporating SF IL-10 into the traditional risk model enhanced its predictive value for chronic PJI in these patients.

**Keywords:** periprosthetic infection, synovial fluid, interleukin-10, C-reactive protein, erythrocyte sedimentation rate

## Introduction

Periprosthetic joint infection (PJI) significantly hinders arthroplasty success, which stands as the foremost cause of revisions in total knee arthroplasty and ranks third for revisions in total hip arthroplasty.<sup>1,2</sup> The incidence of PJI has gradually increased over time, ranging from 0.5% to 2.0%,<sup>3,4</sup> imposing a substantial burden on both patients and the healthcare system.<sup>3,5-8</sup> Therefore, timely and accurate diagnosis of PJI is crucial.

However, diagnosing PJI, especially in chronic cases, remains challenging due to the absence of typical clinical characteristics and the lack of a completely definitive test.<sup>9</sup> ESR and CRP have been suggested as diagnostic criteria for PJI.<sup>10</sup> However, approximately 4% of chronic PJI cases exhibit normal ESR and CRP levels, attributed to the presence of low-virulence pathogens.<sup>11,12</sup> Implant sonication, next-generation sequencing (NGS), and 16s rRNA metagenomics were used to improve PJI diagnosis,<sup>13-16</sup> which did enhance accuracy but not yet been incorporated into routine clinical practice due to their high costs and limited applicability.<sup>17</sup> Recent efforts to precisely diagnose PJI have focused on synovial fluid biomarkers. Evaluation of

inflammatory markers such as alpha-defensin, calreticulin, leukocyte esterase, IL-6, IL-1 $\beta$ , IL-4, IL-8, and CD-64, as well as combined biomarker diagnostics, demonstrated superior diagnostic performance compared to routine clinical laboratory testing.<sup>18–26</sup> The diagnosis of PJI has evolved significantly over the years, with various diagnostic criteria proposed and refined. The 2013 International Consensus Meeting (ICM) criteria, which were later updated in 2018, represent key milestones in standardizing PJI diagnosis. These criteria have significantly enhanced diagnostic confidence and supported more effective treatment strategies. They integrate key synovial fluid biomarkers, such as alpha-defensin and leukocyte esterase, which have become essential components of the current diagnostic approach. The inclusion of these markers has markedly improved diagnostic precision, particularly in chronic and complex cases where conventional markers may yield inconclusive results. However, the diagnostic accuracy for PJI remains suboptimal, highlighting the need for the exploration of new methods to further improve diagnostic precision.

Interleukin-10 (IL-10), produced by various leukocytes, inhibits Th1, NK, and macrophage activity, serving as a key anti-inflammatory cytokine during infections.<sup>27</sup> Studies have shown significantly elevated IL-10 levels in conditions such as central nervous system catheter *Staphylococcus epidermidis* infection,<sup>28</sup> Gram-negative sepsis,<sup>29</sup> bacterial systemic inflammatory response syndrome,<sup>30,31</sup> and *Streptococcus pneumoniae* infection,<sup>32</sup> highlighting its reliable diagnostic role. The imbalance between anti-inflammatory and pro-inflammatory cytokines may characterize chronic periprosthetic joint infection (PJI).<sup>33</sup> Therefore, synovial fluid IL-10 could potentially serve as a biomarker for diagnosing chronic PJI. However, the specific role of synovial fluid interleukin-10 (IL-10) in PJI diagnosis, especially in chronic cases, remains underexplored, with limited studies and small sample sizes reported in the literature.<sup>21,34</sup> Further research focusing on SF IL-10 in chronic PJI cases is warranted to enhance diagnostic capabilities in this challenging clinical scenario.

Consequently, this study aims to explore the impact of SF IL-10 on chronic PJI in suspected patients and to assess whether combining SF IL-10 with traditional risk indicators improves risk stratification.

## Materials and Methods

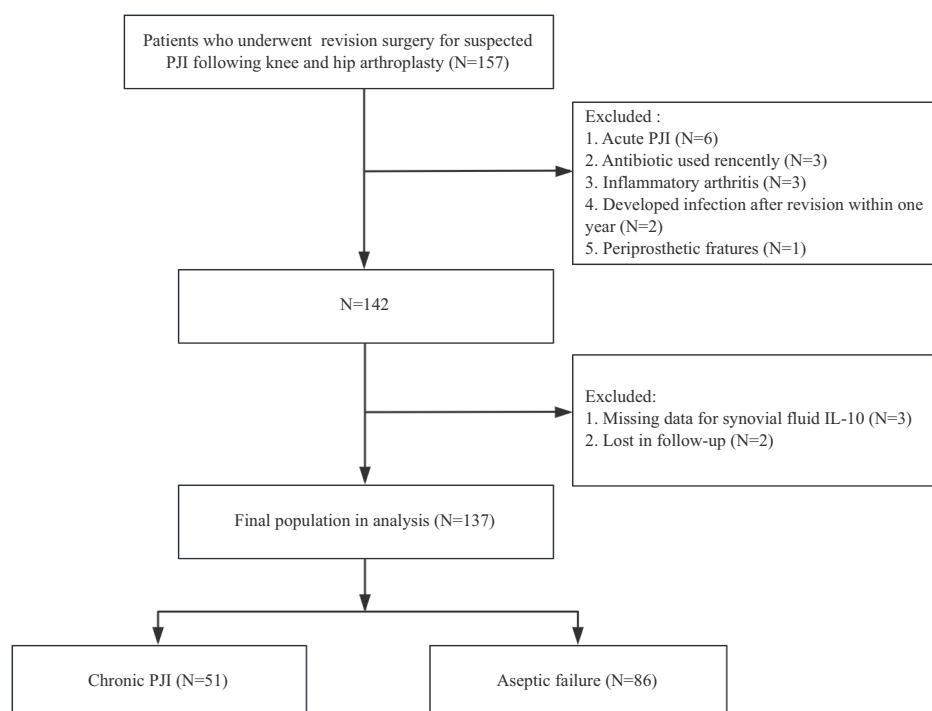
### Study Population

The research study obtained ethical approval from the institutional ethics board, and all participants provided informed consent before their inclusion. Between January 2018 and August 2019, we conducted a prospective cohort study involving 137 admitted patients underwent revision surgery for suspected PJI following knee and hip arthroplasty. The diagnosis of PJI adhered to the 2013 International Consensus Meeting (ICM) criteria.<sup>10</sup> Additionally, infections were categorized as “chronic”, occurring more than 3 months from the index implantation.<sup>10</sup> Aseptic revisions were defined as single-stage revisions performed for non-infectious causes (including loosening, wear, instability, malalignment, adverse local tissue reactions, or other aseptic reasons) in cases that did not subsequently fail due to infection or necessitate additional surgery on the same joint.<sup>22</sup> To minimize confounding factors affecting the expression of inflammatory markers, the following were excluded from this study: patients with acute PJI, rheumatoid arthritis, gout, pneumonia, urinary tract infections, malignancy, and those who had used antibiotics within the past two weeks (Figure 1).

Demographic information, including age, gender, weight, height, body mass index (BMI), and surgical approach, were meticulously collected and subjected to analysis. On the day prior to surgery, blood samples for erythrocyte sedimentation rate (ESR) analysis and C-reactive protein (CRP) serological testing were obtained from the cubital vein. Synovial fluid samples were procured before revision surgery for assessing synovial fluid interleukin-10 (SF IL-10), synovial fluid polymorphonuclear neutrophil percentage (SF PMN%), Synovial fluid white blood cell (SF WBC) and cultures. All specimens were processed and submitted for analysis within 2 hours of collection. During the revision surgery, three tissue samples were collected from each patient for both standard and prolonged microbiological culture. Subsequently, these samples were appropriately categorized into either the chronic infection group or the aseptic failures group.

### Sample Determination

The synovial fluid sample (2 mL) was collected in tubes with anticoagulant, ethylene diamine tetraacetic acid (EDTA), and then centrifuged (2000rpm, ten minutes, 4°C). The supernatants were retained, and all cell and pellet contents were discarded. Synovial fluid was treated with hyaluronidase (Merck, Darmstadt, Germany) to decrease viscosity. The levels



**Figure 1** Flowchart for patient selection.

of IL-10 in the synovial fluid were determined using the IMMUNOLITE 1000 Immunoassay System (SIEMENS Healthcare, Erlangen, Germany). Synovial fluid WBCs and PMNs were examined by a haematology analyzer (Sysmex XE-5000 haematology analyzer, Sysmex, Japan). The particle-enhanced turbidimetric immunoassay with the HITACHI 7600 Series Automatic Biochemical Analyzer (Hitachi, Tokyo, Japan) and a diagnostic kit provided by DiaSys Diagnostic Systems GmbH (Shanghai, China) were used to examine the CRP.

## Statistical Analysis

Categorical data were presented as counts (*n*) and percentages (%) and analyzed using chi-square tests. For continuous data, means  $\pm$  standard deviations were used for normally distributed variables, and medians with interquartile ranges (IQRs) for non-normal distributions, analyzed using one-way ANOVA and Kruskal–Wallis tests, respectively. We used univariate and multivariate logistic regression to explore the association between synovial fluid IL-10 (SF IL-10) and chronic periprosthetic joint infection (PJI). In this study, covariates were selected based on prior research, clinical importance, and the frequency of observed outcomes. Multivariate models were adjusted for gender, age, BMI, ESR, CRP, SF PMN%, SF WBC according to these criteria. Diagnostic values were compared with independent-samples *t*-tests and Fisher's exact tests. Youden's J statistic determined the best SF IL-10 threshold for diagnosing chronic PJI. ROC curves assessed whether including SF IL-10 enhanced the predictive capability of models with identified risk factors (gender, age, BMI, ESR, CRP, SF PMN% and SF WBC). DeLong's test compared AUCs between models. NRI and IDI were used to evaluate the additional predictive value of SF IL-10. Significance was set at  $p < 0.05$ . Results are presented as odds ratios (OR) with 95% confidence intervals (CI). Statistical analyses were performed two-sided using R version 4.2.3 (<http://www.R-project.org>, The R Foundation), Free Statistics software version 1.9, and MedCalc version 13.2.2.

## Results

Out of the 137 patients included in the study, 51 were diagnosed with chronic PJI, while the remaining 86 were classified as aseptic failures. In the PJI group, there were 27 males and 24 females, with a mean age of  $65.02 \pm 6.89$  years and an

average BMI of  $23.19 \pm 3.45$  kg/m<sup>2</sup>. The aseptic failures group consisted of 49 males and 37 females, with a mean age of  $66.55 \pm 7.00$  years and an average BMI of  $23.26 \pm 3.66$  kg/m<sup>2</sup>. There were no statistically significant differences in age, gender, or BMI between the two groups ( $p > 0.05$ ) (Table 1).

Before revision surgery, serum CRP, serum ESR, and SF IL-10 levels were significantly higher in the chronic PJI group compared to the aseptic failures group (Table 2). The median SF IL-10 level was 26.53 pg/mL (15.50 to 39.28 pg/mL) in the chronic PJI group, compared to 4.89 pg/mL (1.52 to 9.28 pg/mL) in the aseptic failures group ( $p < 0.001$ ) (Table 2). Similarly, the median ESR was 36.00 mm/h (15.50 to 50.50 mm/h) in the PJI group and 20.00 mm/h (11.00 to 34.00 mm/h) in the aseptic failures group ( $p < 0.001$ ) (Table 2). The median serum CRP was 20.10 mg/L (14.40 to 29.10 mg/L) in the chronic PJI group, compared to 6.93 mg/L (3.35 to 18.00 mg/L) in the aseptic failures group ( $p < 0.001$ ) (Table 2). The median SF PMN% was 73.44 (56.20 to 81.73) in the chronic PJI group, compared to 56.74 (51.46 to 70.10) in the aseptic failures group ( $p < 0.001$ ) (Table 2). The median SF WBC was  $404.66 \times 10^7/L$  (330.26 to  $492.44 \times 10^7/L$ ) in the chronic PJI group, compared to  $194.31 \times 10^7/L$  (126.11 to  $310.17 \times 10^7/L$ ) in the aseptic failures group ( $p < 0.001$ ) (Table 2).

**Table 1** Demographic Data for the Study Population

	Total (n=137)	Aseptic (n=86)	Chronic PJI (n=51)	P value
Age (year)	65.98±6.97	66.55±7.00	65.02±6.89	0.217
Weight (kg)	60.73±9.68	61.00±9.96	60.27±9.26	0.673
Height (cm)	161.82±7.78	162.07±7.67	161.41±8.02	0.634
BMI (kg/m <sup>2</sup> )	23.23±3.57	23.26±3.66	23.19±3.45	0.903
Gender				0.646
Male	76 (55.47%)	49 (56.98%)	27 (52.94%)	0.579
Female	61 (44.53%)	37 (43.02%)	24 (47.06%)	
Joint type				
Knee	71 (51.82%)	43 (50.00%)	28 (54.90%)	0.579
Hip	66 (48.18%)	43 (50.00%)	23 (45.10%)	

**Note:** Variables are expressed as Mean ± SD, or Numbers (Percentage).

**Abbreviation:** BMI, Body mass index.

**Table 2** Analysis of Inflammatory Markers in Patients with Infected and Aseptic Revision Arthroplasty

Inflammatory Marker	Hip + Knee			
	Total (n=137)	Aseptic (n=86)	Chronic PJI (n=51)	P value
SF IL-10 (mmol/L)				
Median	9.45	4.89	26.53	<0.001
P25, P75	(4.35, 19.78)	(1.52, 9.23)	(15.50, 39.28)	
ESR (mm/h)				
Median	25.00	20.00	36.00	<0.001
P25, P75	(13.00, 39.00)	(11.00, 34.00)	(15.50, 50.50)	
CRP (mg/L)				
Median	15.00	6.93	20.10	<0.001
P25, P75	(4.52, 23.30)	(3.35, 18.00)	(14.40, 29.10)	
SF PMN%				
Median	60.15	56.74	73.44	<0.001
P25, P75	(52.70, 78.50)	(51.46, 70.10)	(56.20, 81.73)	
SF WBC ( $10^7/L$ )				
Median	284.80	194.31	404.66	<0.001
P25, P75	(154.66, 411.38)	(126.11, 310.17)	(330.26, 492.44)	

**Abbreviations:** CRP, C-reactive protein; ESR, Erythrocyte sedimentation rate; SF IL-10, Synovial fluid Interleukin-10; SF PMN%, Synovial fluid polymorphonuclear neutrophil percentage; SF WBC, Synovial fluid white blood cell.

In model 1, SF IL-10 showed a significant association with the incidence of chronic PJI (OR = 1.10; 95% CI = 1.06~1.14;  $p < 0.001$ ) (Table 3). After adjusting for potential risk factors in model 2, SF IL-10 remained an independent risk factor for PJI in patients undergoing revision surgery (OR = 1.11; 95% CI = 1.05~1.17;  $p < 0.001$ ) (Table 3).

To evaluate the discriminatory power of these inflammatory markers between chronic PJI and aseptic failure, we generated Receiver Operating Characteristic (ROC) curves for serum CRP, serum ESR, SF PMN%, SF WBC and SF IL-10. Detailed diagnostic characteristics are provided in Table 4. The area under the ROC curve (AUC) for serum ESR was 0.682 (95% CI = 0.585~0.778), for serum CRP, the AUC was 0.728 (95% CI = 0.646~0.811), for SF PMN %, the AUC was 0.690 (95% CI = 0.592~0.789), and for SF WBC, the AUC was 0.840 (95% CI = 0.775~0.906). Synovial fluid IL-10 demonstrated superior discrimination with an AUC of 0.891 (95% CI = 0.836~0.947). Using Youden's index, the optimal cutoff point for synovial fluid IL-10 to differentiate PJI from aseptic failure was 10.305 pg/mL, yielding a sensitivity of 0.922 and a specificity of 0.779. In contrast, serum CRP showed a sensitivity of 0.941 and a specificity of 0.512, serum ESR had a sensitivity of 0.412 and a specificity of 0.942, SF PMN% had a sensitivity of 0.431 and a specificity of 0.942, and SF WBC had a sensitivity of 0.824 and a specificity of 0.744 (Table 4).

To assess the incremental effect of SF IL-10 in predicting chronic PJI, we evaluated the ROC curves of the baseline risk model, which included traditional risk factors (gender, age, BMI, ESR, CRP, SF PMN%, and SF WBC), and the model incorporating SF IL-10 (Figure 2). A significant difference was observed between the baseline risk model (AUC: 0.915) and the model with SF IL-10 (AUC: 0.960) ( $p = 0.007$ ) (Figure 2). The more sensitive metrics, category-free net reclassification improvement (NRI) and integrated discrimination improvement (IDI), are detailed in Table 5. These findings showed that incorporating SF IL-10 significantly enhanced the predictive value of the baseline model for patients suspected of PJI following hip and knee replacement surgery (NRI = 0.167; 95% CI: 0.023~0.312; IDI = 0.160; 95% CI: 0.096~0.224).

**Table 3** Multivariate Logistic Regression to Evaluate the Association Between SF IL-10 and Chronic PJI

Variable	Events/N	Model 1			Model 2		
		OR	95% CI	p	OR	95% CI	p
SF IL-10	137	1.10	1.06~1.14	<0.001	1.11	1.05~1.17	<0.001

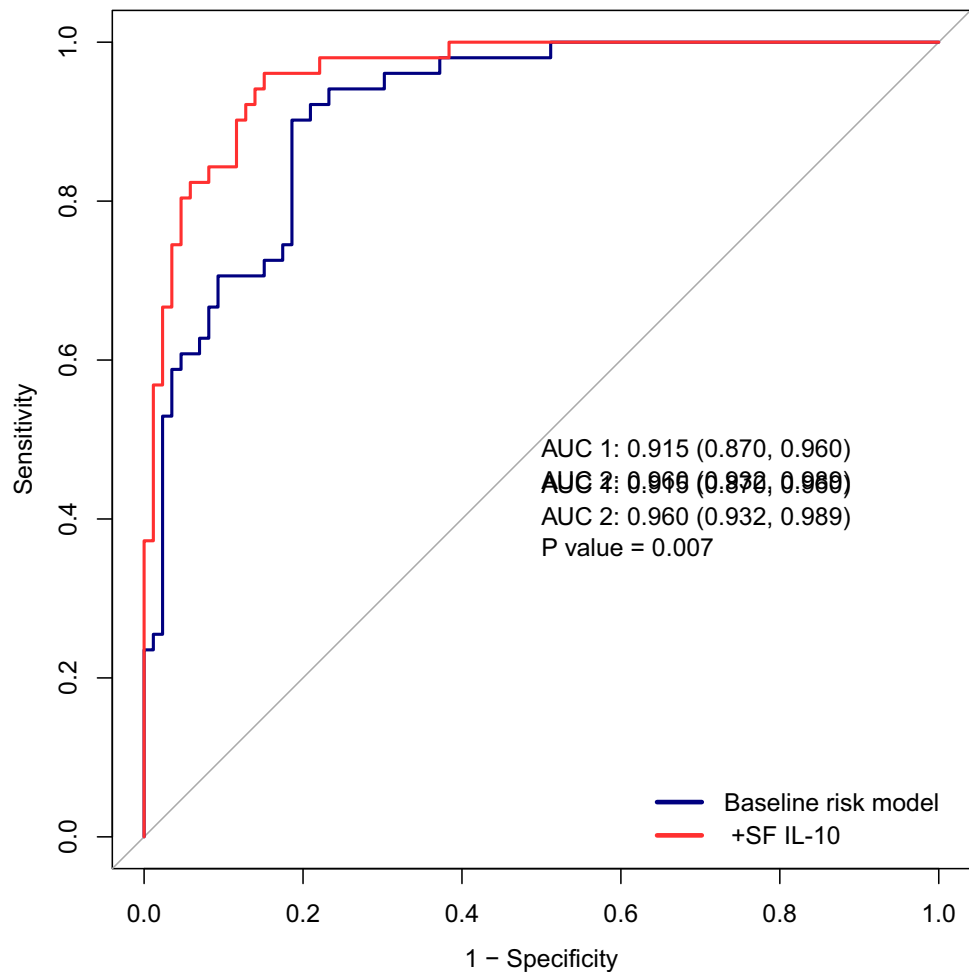
**Notes:** Model 1: unadjusted model. Model 2: adjusted for gender, age, BMI, ESR, CRP, SF PMN%, SF WBC.

**Abbreviations:** OR, odds ratio; CI, confidence interval; p, p-value; SF IL-10, Synovial fluid Interleukin-10.

**Table 4** Sensitivity, Specificity, PPV, NPV, and Accuracy of Inflammatory Markers

Parameters	ESR (mm/h)	CRP (mg/L)	SF PMN%	SF WBC ( $10^7/L$ )	SF IL-10 (pg/mL)
AUC (95% CI)	0.682 (0.585, 0.778)	0.728 (0.646, 0.811)	0.690 (0.592, 0.789)	0.840 (0.775, 0.906)	0.891 (0.836, 0.947)
Cut-off level	41.500	8.165	80.510	307.317	10.305
Sensitivity	0.412	0.941	0.431	0.824	0.922
Specificity	0.942	0.512	0.942	0.744	0.779
PPV	0.808	0.533	0.815	0.656	0.712
NPV	0.730	0.936	0.736	0.877	0.944
Accuracy	0.745	0.672	0.752	0.774	0.832

**Abbreviations:** CRP, C-reactive protein; ESR, Erythrocyte sedimentation rate; SF IL-10, Synovial fluid Interleukin-10; AUC, Area under the curve; CI, Confidence interval; PPV, Positive predictive value; NPV, Negative predictive value.



**Figure 2** Receiver operating characteristic curves (ROC) of the SF IL-10 as a predictive marker to diagnose chronic PJI.

# Discussion

Chronic periprosthetic joint infection (PJI) is typically indicated by a localized chronic inflammatory environment around joint prostheses and adjacent tissues, featuring the infiltration of various inflammatory cells and the accumulation of inflammatory mediators.<sup>14,35,36</sup> Diagnosing chronic PJI is complex and often challenging to differentiate from aseptic loosening, despite various organizations and societies developing different criteria for defining PJI in the last decade.<sup>10,37–40</sup> Our research explored the relationship between SF IL-10 and chronic PJI in patients following hip and knee replacement surgeries. The key findings were: (1) SF IL-10 had a strong association with chronic PJI; (2) elevated SF IL-10 levels corresponded to an increased risk of chronic PJI, even after adjusting for confounders; and (3) the inclusion of SF IL-10 to the baseline risk model significantly improved its predictive value for chronic PJI.

**Table 5** C-Statistics, NRI and IDI for the Incremental Predictive Value and Predictive Power of Different Models in Diagnosing PJI

Model	C-statistic (95% CI)	p	NRI (95% CI)	p	IDI (95% CI)	p
Baseline risk model	0.915 (0.870, 0.960)		Ref.		Ref.	
+ SF IL-10	0.960 (0.932, 0.989)	0.007	0.167 (0.023, 0.312)	0.023	0.160 (0.096, 0.224)	0

**Note:** Baseline risk model: Gender, Age, BMI, ESR, CRP, SF PMN%, SF WBC.

**Abbreviations:** NRI, Net reclassification index; IDI, integrated discrimination improvement; SF IL-10, Synovial fluid Interleukin-10.



The sensitivities and specificities of ESR and CRP ranged from 41.2% to 94.1% and 51.2% to 94.2%, respectively, while the sensitivities and specificities of SF PMN% and SF WBC ranged from 43.1% to 82.4% and 74.4% to 94.2%, respectively. These findings are consistent with reports in the literature.<sup>41,42</sup> The SF IL-10 assay out-performed all of these laboratory tests for diagnosing chronic PJI. Specifically, the optimal threshold for SF IL-10 to independently diagnose chronic PJI was 10.305 pg/mL, with an AUC of 0.891, a sensitivity of 92.20%, and a specificity of 77.90%. Notably, incorporating SF IL-10 into a baseline risk model significantly enhanced its predictive ability, evidenced by an increase in the AUC from 0.775 to 0.916. The adjusted model with SF IL-10 also showed an NRI of 0.494 and an IDI of 0.266, with the differences reaching statistical significance. And these suggest a potential impact of SF IL-10 on chronic PJI.

Our findings align with several previous studies, which show that SF IL-10 is elevated in PJI patients and plays a positive role in diagnosing PJI. For example, in a prospective study involving 14 cases of periprosthetic joint infection (PJI) and 37 cases of aseptic loosening, the authors found that the mean level of IL-10 in the synovial fluid of patients with aseptic loosening was 4.1 pg/mL. In contrast, the PJI group had a significantly higher mean SF IL-10 level of 32.6 pg/mL.<sup>43</sup> In another cohort study consisting of 75 patients with postoperative pain after shoulder arthroplasty, researchers observed that synovial IL-10 levels were significantly elevated in the infected group compared to the non-infected group. The optimal threshold for SF IL-10 was 28.1 pg/mL, with an AUC of 0.76 for diagnosing PJI in the shoulder joint, a sensitivity of 0.72, and a specificity of 0.82.<sup>34</sup> In another study that included 107 subjects, the authors evaluated the diagnostic performance of 23 synovial fluid biomarkers for detecting PJI after hip or knee arthroplasty. SF IL-10 was significantly higher in the PJI group than in the aseptic failure group. The optimal cut-off value of SF IL-10 for diagnosing PJI was 14.58 pg/mL, with an AUC of 0.800 ( $p=0.0001$ ), a sensitivity of 62%, and a specificity of 88%.<sup>21</sup> However, other studies have shown that SF IL-10 and the incidence of PJI was not significantly correlated.<sup>44</sup> The debate may be due to differences in sample sizes, follow-up durations, PJI diagnostic criteria, pathogenic microbial species, and how confounders are controlled. In contrast to earlier studies, our research includes a larger sample with adequate statistical power and comprehensive adjustments for confounders like age, gender, BMI, ESR, CRP, SF PMN% and SF WBC. This approach strengthens the evidence that SF IL-10 is an independent risk factor for chronic PJI and enhances predictive accuracy. Our study expands the current understanding on the diagnostic role of SF IL-10 among patients with suspicious chronic PJI for previous clinical research. And it further offers important population-based evidence supporting the involvement of SF IL-10 in diagnosing chronic PJI.

IL-10, as an anti-inflammatory cytokine, offers unique advantages in diagnosing periprosthetic joint infection (PJI) compared to traditional pro-inflammatory markers. While pro-inflammatory markers (eg, IL-6, IL-1 $\beta$ ) are effective for detecting acute infections, they may not be as sensitive for chronic or low-grade infections.<sup>45</sup> IL-10's role in immune regulation allows for better identification of these infections, where inflammation is less pronounced.<sup>45,46</sup> Additionally, its lower interference from non-infectious conditions further enhances diagnostic accuracy, particularly when used in combination with existing markers.<sup>45,47</sup>

Several mechanisms may explain the observed associations between SF IL-10 and chronic PJI. Infection site signals induce myeloid-derived suppressor cells (MDSCs) to expand and recruit, making them the predominant leukocyte population at PJI sites.<sup>48</sup> MDSCs stimulate IL-10 production,<sup>48</sup> which inhibits T cell activation and programs macrophages toward an anti-inflammatory phenotype.<sup>49,50</sup> This prevents the sufficient activation of antimicrobial mechanisms, promoting bacterial persistence. *Staphylococcus aureus* is a leading cause of biofilm-associated prosthetic joint infection (PJI). Its metabolite, lactate, can act as a virulence factor by inhibiting histone deacetylase 11 (HDAC11) and activating histone deacetylase 11 (HDAC6). This action on the proximal region of the IL-10 promoter (−87 to −7) promotes IL-10 production by biofilm-associated MDSCs and macrophages. The increased IL-10 production facilitates biofilm formation, thereby sustaining the infection.<sup>36</sup> Further studies are needed to clarify the specific molecular mechanisms responsible for the increased levels of SF IL-10 in chronic PJI.

However, the study has several notable limitations. Firstly, being a single-center observational study, the findings should be interpreted with caution. Secondly, the exclusion of missing data and the low incidence of PJI may have led to an underestimation of the effect. Consequently, larger, multi-center studies are needed for further validation. Thirdly, the potential influence of unmeasured or unknown confounding factors, such as the time interval between primary and revision surgery, cannot be excluded, and may account for some of the observed associations. Additionally, as the study

was conducted in a single region of China, the findings may not be generalizable to other populations. Further research is required to confirm these results in diverse settings.

## Conclusion

In patients undergoing revision surgery for suspected PJI following knee and hip arthroplasty, SF IL-10 was significantly associated with chronic PJI incidence, with higher levels correlating with an increased risk. Additionally, incorporating SF IL-10 into the baseline risk model improved its predictive performance for chronic PJI. To confirm these findings, further prospective, large-scale, multi-center studies are needed. Moreover, the mechanisms behind the observed relationship warrant additional investigation.

## Abbreviations

PJI, Prosthetic joint infection; IL-10, Interleukin-10; PMN%, Polymorphonuclear neutrophil percentage; WBC, White blood cell; ROC, Receiver operating characteristic; CRP, C-reactive protein; ESR, Erythrocyte Sedimentation Rate; SF, Synovial fluid; CI, Confidence interval; PPV, Positive predictive value; NPV, Negative predictive value; AUC, Area under the curve; MSIS, Musculoskeletal Infection Society; ICM, International Consensus Meeting; IDSA, Diseases Society of America; EBJIS, European Bone and Joint Infection Society.

## Data Sharing Statement

The data that support the findings of this study are available from the corresponding author, Ning Hu, upon reasonable request.

## Ethics Approval and Consent to Participate

Our study was conducted in accordance with the Declaration of Helsinki. This study was approved by the institutional ethics board of The First Affiliated Hospital of Chongqing Medical University (Chongqing, China) at 26 September 2018 (local ethical committee ref. no: 20187101), and patients signed informed consent before enrolled into the study. The prospective study was registered in the Chinese Clinical Trial Registry, (registration number: ChiCTR1800020440), and approval date is 29 December 2018.

## Consent for Publication

All patients gave consent for publication.

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## Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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## Disclosure

Authors, cooperators, and sponsors have no potential conflict of interest.

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