Serum White Blood Cell Count and Differential Do Not Have a Role in the Diagnosis of Periprosthetic Joint Infection

Nader Toossi, MD, Bahar Adeli, BA, Mohammad R. Rasouli, MD, Ronald Huang, BS, and Javad Parvizi, MD, FRCS

Abstract: Serum white blood cell (WBC) count and neutrophil differential are frequently ordered during preoperative workup of suspected cases of periprosthetic joint infection (PJI). However, their roles in diagnosis of PJI have remained unclear despite previous studies. In this study, preoperative serum WBC and neutrophil percentages were retrieved from hospital charts. The diagnostic cutoff point determined by receiver operating characteristic curve analysis was 7800 cells/μL with 55% sensitivity and 66% specificity for WBC count, whereas the cutoff value for neutrophil percentage was 68% with 52% sensitivity and 75% specificity. Our study confirms the long-held belief that serum WBC count and differential has minimal role in routine workup of patients with suspected PJI. **Keywords:** periprosthetic joint infection, total joint arthroplasty, serum WBC count, serum neutrophil percentage.

Many decades have passed since Charnley [1] reported an infection rate of more than 9% after total hip arthroplasty. Because of the use of prophylactic antibiotics, clean air operating rooms, and a number of other strategies, the incidence of periprosthetic joint infection (PJI) has declined remarkably to be as low as 1% [2,3]. Despite this trend, PJI has remained one of the most challenging complications of total joint arthroplasty. Treatment of PJI is costly because of the subsequent need for reoperation, and the lengthy hospitalization often required eradicating the infection [4].

Presently, there is no universally accepted diagnostic test that is absolute or reliable for detection of PJI [5]. Hence, diagnosis of PJI is made based on clinical suspicion, serologic tests, imaging studies, and isolation of organisms from joint culture samples [3,5-7]. In recent years, studies have demonstrated that other inflammatory markers such as C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), interleukin 6, procalcitonin, and tumor necrosis factor α may also play a role in diagnosis of PJI [5,8-11].

Elevation of the serum white blood cell (WBC) count (WCC) and neutrophil differential has been the hallmark for diagnosis of many infections [12]. Thus, it is reasonable to assume that the level of WBC and neutrophil differential in serum may also be elevated with PJI. Using the latter reasoning, clinicians have routinely ordered WBC and differential in patients suspected of PJI. A number of previous studies have cast doubt on the value of blood WCC and differential for diagnosis of PJI. A recent meta-analysis by Berberi et al [13] detected a pooled sensitivity of 45% and specificity of 87% for WCC in diagnosis of PJI.

Part of the problem with interpretation of the literature relates to the fact that different definition of PJI was used by each study, which influences the accuracy of a diagnostic test. Furthermore, none of the studies evaluated the accuracy of WCC and differential in isolation. This study, using a single institutional database in a consecutive series of patients, was designed to address many of the shortcomings of the current literature to determine the role of serum WCC and differential in diagnosis of PJI. A standard definition for PJI was applied to all patients, and receiver operating characteristic (ROC) curves were used to determine the statistical parameters for the test.

From the Department of Orthopedics, Rothman Institute of Orthopedics at Thomas Jefferson University Hospital, Philadelphia, Pennsylvania.
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Reprint requests: Javad Parvizi, MD, FRCS, Department of Orthopedics, Rothman Institute of Orthopaedics, Thomas Jefferson University Hospitals, 925 Chestnut St, 2nd 26 Floor, Philadelphia, PA, 19107.

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Methods and Material

After obtaining approval of the institutional review board, the computerized and prospective database on all revision total joint arthroplasties was reviewed to identify all patients who underwent surgery for failure of either total knee arthroplasty or total hip arthroplasty. The registry consisted of 1856 revision surgeries performed on 1543 patients (817 females) at our institution between January 2003 and August 2010. The mean age of the patients at the time of surgery was 66 years with an SD of 12 years (range, 25-96 years).

Using strict institutional criteria [14], 751 joints were found to have PJI. There were 463 knees and 288 hips in our septic revision group, and female patients comprised 49% of this group. In the aseptic group, there were 687 hips and 418 knees, and 54% of the patients were female. Patients were diagnosed to have PJI if they fulfilled one of the following criteria:

1. Positive culture:
   a More than 5 colonies on 1 plate
   b Light growth and greater in a single culture
   c Very light growth on 2 cultures if pathogen has the same resistance profile
   d 3 positive cultures in broth
2. Intraoperative purulence
3. Draining sinus tract

or 3 of the following 4:

a. ESR greater than 30 mm/h
b. CRP greater than 10 mg/L
c. Synovial WCC greater than 1760 cells/μL or 10 700 cells/μL acute postoperative (from synovial fluid)
d. Synovial neutrophils percentages greater than 73% or 89% acute postoperative (from synovial fluid)

The database was explored to extract all relevant data including the level of serum WCC and neutrophil differential. All patients had a record of their preoperative WCCs, but there were 572 patients for whom differential had not been ordered preoperatively, leaving 930 patients in whom both the serum WCC and neutrophil differential were available. The mean time interval from preoperative blood sampling to revision surgery was 12 days with an SD of 8 days. Forty-three percent of patients in aseptic group and 33% in septic group did not have any differentials.

Statistical Analysis

All statistical analyses were performed using Medcalc software version 11.6.1 (MedCalc Software, Mariakerke, Belgium). The mean and 95% confidence interval (95% CI) of WCCs and neutrophil percentages of the infected and noninfected cases were determined, and independent-samples Student t test was used to compare mean WCC and neutrophil percentage. $P < .05$ (2-sided) was considered to be statistically significant. We constructed ROC curves to determine the area under the ROC curve (AUC) and cutoff value for WCC and neutrophil percentage. The AUC, which implies the diagnostic accuracy of the test, was calculated. An AUC of 1 demonstrates an ideal test with a 100% sensitivity and specificity, whereas an AUC of less than 0.5 indicates that the diagnostic test is not useful. The ROC curve constructed correlates the true-positive and false-positive rates for a series of data points. Finding a point on the curve nearest to the top left corner of the diagram meant the most optimum for determining cutoff point. We determined cutoff points for WCC and neutrophil percentage as such. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) for the corresponding cutoff value were calculated. In addition, PPV and NPV were calculated for combination of WCC and neutrophil percentage results. For this purpose, a binary variable was defined. If both WCC and neutrophil percentage had predicted infection based on obtained cutoff points, the new variable was coded as "septic." If both of them refuted infection, the variable value was coded as "aseptic."

Because of the high prevalence of infected joints, we calculated the Bayesian positive and negative predictive values for each test in addition to conventional predictive values using the following formulae [15]:

$$\text{Bayesian PPV} = (\text{Sensitivity} \times \text{Prevalence}) / \{(\text{Sensitivity} \times \text{Prevalence}) + [(1-\text{Specificity}) \times (1-\text{Prevalence})]\}$$

$$\text{Bayesian NPV} = [(\text{Specificity} \times (1-\text{Prevalence})] / \{[(1-\text{Sensitivity}) \times \text{Prevalence}] + [\text{Specificity} \times (1-\text{Prevalence})]\}$$

Results

The prevalence of PJI in this cohort was found to be 40%. The mean of serum WCC in infected joints was 9236 cells/μL (95% CI, 8896-9575 cells/μL), whereas the mean for the noninfected group was 7331 cells/μL (95% CI, 7204-7458 cells/μL). There was statistically significant difference between 2 groups regarding mean WCC ($P < .001$). The mean of neutrophil percentage for the noninfected and infected joints were 63% (95% CI, 62.2%-63.6%) and 69% (95% CI, 67.5%-70%) respectively. There was statistical difference between the 2 means ($P < .001$).

The AUC for WCC was 0.637 (95% CI, 0.614-0.659), and that for neutrophil percentage was 0.652 (95% CI, 0.623- 0.679). The cutoff points were found to be 7800 cells/μL for WCC and 69% for neutrophil percentage (Fig.; available online at www.arthroplastyjournal.org). The sensitivity and specificity for WCC were 55% (95%