The Journal of Arthroplasty xxx (2017) 1–5

Contents lists available at ScienceDirect

The Journal of Arthroplasty

journal homepage: www.arthroplastyjournal.org

Original Article

Utility of Synovial White Blood Cell Count and Differential Before Reimplantation Surgery

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ARTICLE INFO

Article history:
Received 31 October 2016
Received in revised form
10 March 2017
Accepted 28 March 2017
Available online xxx

Level of Evidence:
Diagnostic, level II

Keywords:
periprosthetic joint infection
PJI
2-stage exchange
reimplantation
white blood cell count

ABSTRACT

Background: Determining optimal timing of reimplantation during 2-stage exchange for periprosthetic joint infection (PJI) remains elusive. Joint aspiration for synovial white blood cell (WBC) count and neutrophil percentage (PMN%) before reimplantation is widely performed; yet, the implications are rarely understood. Therefore, this study investigates (1) the diagnostic yield of synovial WBC count and differential analysis and (2) the calculated thresholds for persistent infection.

Methods: Institutional PJI databases identified 129 patients undergoing 2-stage exchange arthroplasty who had joint aspiration before reimplantation between February 2005 and May 2014. Persistent infection was defined as a positive aspirate culture, positive intraoperative cultures, or persistent symptoms of PJI—including subsequent PJI-related surgery. Receiver-operating characteristic curve was used to calculate thresholds maximizing sensitivity and specificity.

Results: Thirty-three cases (33 of 129; 25.6%) were classified with persistent PJI. Compared with infection-free patients, these patients had significantly elevated PMN% (62.2% vs 48.9%; $P = .03$) and WBC count (1804 vs 954 cells/μL; $P = .04$). The receiver-operating characteristic curve provided thresholds of 62% and 640 cells/μL for synovial PMN% and WBC count, respectively. These thresholds provided sensitivity of 63% and 54.5% and specificity of 62% and 60.0%, respectively. The risk of persistent PJI for patients with PMN% >90% was 46.7% (7 of 15).

Conclusion: Synovial fluid analysis before reimplantation has unclear utility. Although statistically significant elevations in synovial WBC count and PMN% are observed for patients with persistent PJI, this did not translate into useful thresholds with clinical importance. However, with little other guidance regarding the timing of reimplantation, severely elevated WBC count and differential analysis may be of use.

The treatment and management of periprosthetic joint infection (PJI) with 2-stage exchange remains suboptimal owing to the absence of a "gold standard" diagnostic method demonstrating the eradication of the joint infection. Recent investigations have provided substantial knowledge regarding the workup and diagnosis of acute and chronic PJI [1,2]. Yet, effective therapy and treatment remain elusive. In North America, the 2-stage exchange arthroplasty remains the preferred method for treatment of chronic PJI [3]. Even with complete prosthetic removal and implantation of an antibiotic spacer with delayed reimplantation, the rate of recurrent PJI remains unacceptable [4–6].

There have been numerous substantial attempts to improve the effectiveness of the 2-stage exchange for PJI. These efforts have included attempts to identify persistent infection before reimplantation with the use of primary and secondary markers of infection. Previous analyses have investigated the effectiveness of these markers—erythrocyte sedimentation rate and C-reactive protein (CRP) [7,8], serum white blood cell (WBC) count [5], aspiration culture [9], and tissue frozen section [10,11]—with little benefit. This has left the arthroplasty surgeon with little guidance on the appropriate timing for reimplantation. Often, the surgeon relies on variables rooted in clinical acumen to determine the appropriate time for reimplantation, which include the time duration from performing the resection arthroplasty to the completion of antibiotic therapy, and the subjective clinical status of the soft tissues around the affected joint.

One or more of the authors of this paper have disclosed potential or pertinent conflicts of interest, which may include receipt of payment, either direct or indirect, institutional support, or association with an entity in the biomedical field which may be perceived to have potential conflict of interest with this work. For full disclosure statements refer to http://dx.doi.org/10.1016/j.arth.2017.03.068.

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http://dx.doi.org/10.1016/j.arth.2017.03.068
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Therefore, establishing effective tests to guide reimplantation is an imperative step in improving the efficacy of the 2-stage exchange treatment. Synovial WBC count and neutrophil percentage (PMN%) have proven essential in the initial diagnosis of PJI [12–14]. Therefore, it is postulated that synovial fluid analysis may possibly detect persistent PJI before reimplantation. This study investigates (1) if an association exists between synovial fluid parameters and persistent PJI during 2-stage exchange and (2) the thresholds of the synovial parameters that are indicative of persistent PJI.

Materials and Methods

Following institutional review board approval, this study was undertaken. For this analysis, patients undergoing 2-stage exchange with joint aspiration of their spacer before reimplantation were identified. From 2 institutions, 128 2-stage exchanges with complete joint aspirate analysis before reimplantation were identified between February 2005 and April 2014. These patients had an average age of 65.6 years (range, 34-82 years), 65 were male (50.8%; 65 of 128), and 40 were hips (31.3%; 40 of 128). Twelve patients (9.4%; 12 of 128) had interstage procedures (eg, spacer exchange). A total of 137 aspirations were performed in these patients. All patients underwent prosthetic resection with insertion of an antibiotic-loaded cement spacer. Patients then received a varied course of antibiotics managed by the infectious disease team. In general, antibiotics were ceased 2 weeks before reimplantation which occurred on average 140.1 days (range, 46-885 days) after resection. Aspiration was performed before arthrotomy for reimplantation and sent for fluid cell count, differential analysis, and culture. The average time between aspiration and reimplantation was 18.1 days (range, 0-101 days).

First, the impact of aspiration timing on the cell count and differential analysis was investigated. The average time from latest surgery (resection with spacer insertion or spacer exchange) to aspiration was 115.2 days (range, 15-778 days). For this analysis, the cohort was limited to those patients without positive cultures during the second-stage procedure or infectious failure after reimplantation (n = 90). The fluid WBC count and PMN% were each plotted against time from the most recent surgery. Subsequently, the correlation between the 2 outcomes (WBC count and PMN%) and the time since last surgery was determined. This allowed for an understanding of the impact that surgical insult in 2-stage exchange had on fluid analysis results.

To study the relationship between joint aspiration analysis of a spacer and persistent PJI in 2-stage exchange arthroplasty, a consistent definition of persistent PJI was necessary. As culture has been a poor indicator of persistent PJI, a clinical definition was adopted. We constructed a broad definition for failure of the 2-stage exchange procedure which included positive cultures of the aspirate fluid, positive cultures at the time of reimplantation, and/or subsequent surgery for PJI after reimplantation. However, we are aware that subsequent PJI surgery after reimplantation might be indicative of a new infection rather than a persistent PJI. Hence, we constructed a narrow definition for failure of the 2-stage procedure limited to include only those patients with positive cultures at the time of reimplantation or subsequent surgery that have bacterial pathogens similar to the ones cultured at the time of resection of implants. This narrowed definition was compared with only those patients without any subsequent signs of PJI (ie, no subsequent surgery for PJI by any infecting organism). Five patients (3.9%; 5 of 128) had <6 months follow-up postreimplantation at the time of this analysis and therefore were not included in the analysis of persistent PJI. For patients with multiple aspirations in the interstage period, the most recent aspiration before reimplantation was included in the study.

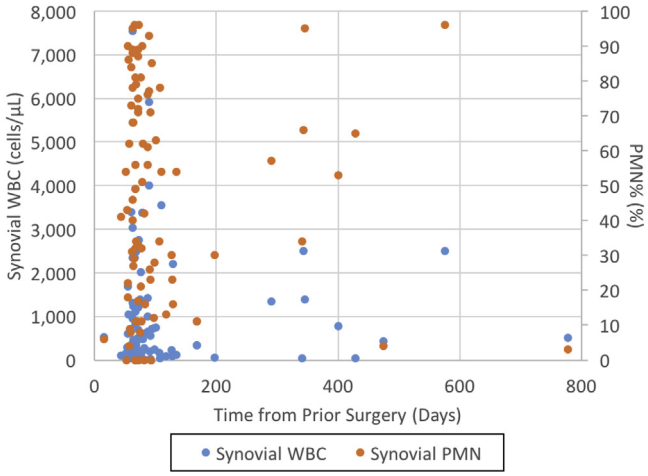

Fig. 1. Scatter plot of synovial white blood cells (WBC) and neutrophil percentage (PMN%) against time from last surgery. This graph shows no significant association between time and resulting synovial fluid cell count analysis. This analysis only included patients without positive cultures or recurrent infection after reimplantation.

After analyzing for statistical differences in fluid cell count and differential analysis for failed vs successful 2-stage exchange, an attempt to develop a useful clinical threshold for synovial WBC count and PMN% before reimplantation was conducted. For each definition of the aforementioned failure (narrow and broad), a receiver-operating characteristic (ROC) curve was used to calculate the accuracy and appropriate threshold for synovial WBC count, synovial PMN%, and synovial absolute neutrophil count (ANC). In addition, each synovial fluid parameter was separated by values into bins (collections of cases segregated by the respective synovial fluid parameter), and the incidence of failure was calculated for each bin.

Simple means with 95% confidence intervals were calculated to assess the differences in fluid WBC count and PMN% between the failed and the successful 2-stage exchange cases. A Student *t* test was used to determine the statistical strength of differences between failed and successful cases. As mentioned, an ROC curve was used to calculate the optimum threshold of fluid WBC count and PMN% to identify persistent PJI before reimplantation. The threshold was calculated using Youden J statistic. The area under the curve (AUC) was also used as an indicator of the test accuracy, in addition to standard parameters (sensitivity, specificity, true-positive rate, and false-positive rate). To further analyze the relationship between synovial cell count and persistent PJI, the ranges were equally divided into 6 groups by percentile and graphed with their incidence of persistent PJI.

Results

The time duration from surgery before reimplantation (ie, resection procedure or spacer exchange) to the date of joint aspiration did not correlate with either the synovial WBC count (R = 0.002; $P = .99$; Fig. 1) or PMN% (R = −0.06; $P = .60$). When defining failure of the 2-stage exchange arthroplasty using the aforementioned broad definition, synovial WBC count, PMN%, and ANC were significantly elevated before reimplantation in patients who failed compared with those with a successful procedure (Table 1). Similar findings were observed when we used the narrow definition—although the difference in PMN% was no longer statistically significant ($P = .08$). Analysis of prereimplantation serologic tests (erythrocyte sedimentation rate and CRP) demonstrated no