

3-2014

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## Recommended Citation

Zmistowski, BS, Benjamin; Higuera, MD, Carlos; Liu, BA, Jane; Barsoum, MD, Wael; Mendelis, BA, Joseph; Della Valle, MD, Craig; and Parvizi, MD, Javad, "Threshold for Synovial Cell Count and Neutrophil Differential in Diagnosis of Periprosthetic Knee Infection: A Multi-Institutional Study" (2014). *Rothman Institute Conference Posters*. Paper 1.  
<http://jdc.jefferson.edu/rothinsposters/1>

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# Threshold for Synovial Cell Count and Neutrophil Differential in Diagnosis of Periprosthetic Knee Infection: A Multi-Institutional Study



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## INTRODUCTION

Synovial fluid analysis is an important tool in the work-up of suspected periprosthetic joint infection (PJI). Yet, there is conflicting guidance for the analysis of synovial fluid aspiration, including a lack of uniform thresholds for white blood cell (WBC) count and neutrophil percentage (PMN%)<sup>1-3</sup>. Therefore, a multi-institutional study was undertaken to reassess these thresholds, compare preoperative versus intraoperative sample collection, and assess variation in results between institutions.

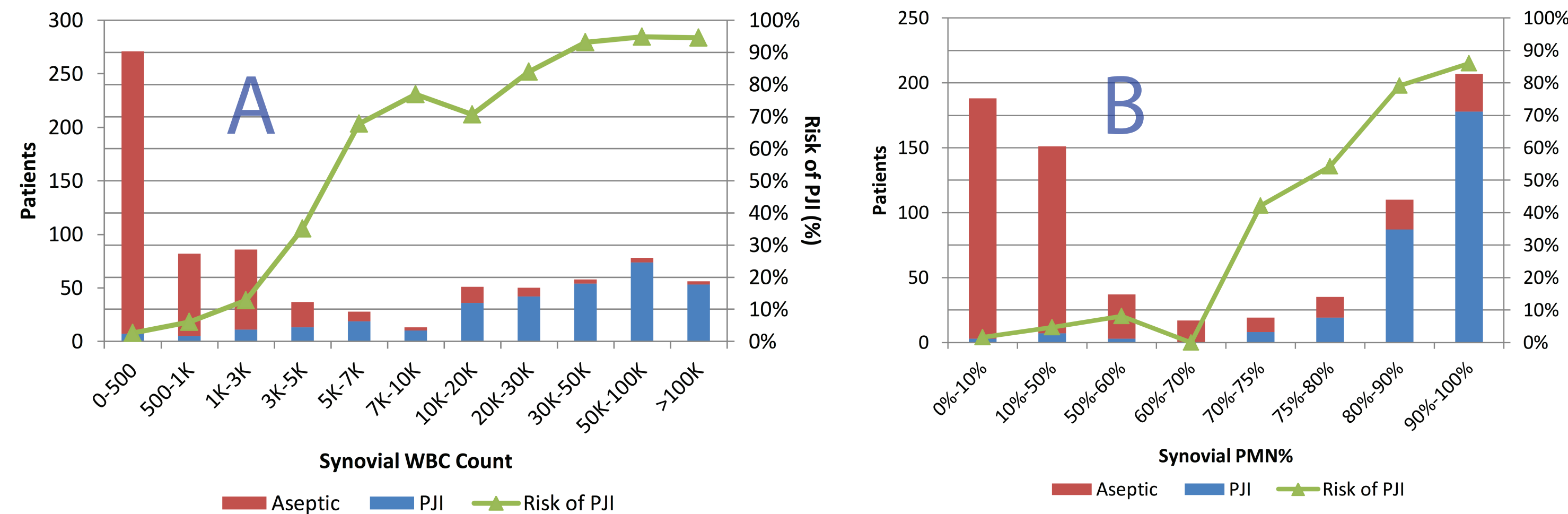
## METHODS AND MATERIALS

The definition of PJI provided by the Musculoskeletal Infection Society (MSIS) was utilized to classify patients as septic or aseptic<sup>4</sup>. Three institutions provided 782 (305 septic; 39.0%) patients with knee aspiration undergoing revision at a minimum of 6 weeks from index surgery on the affected joint. A receiver operating characteristic (ROC) curve with Youden's J statistic was used to calculate the optimum thresholds for diagnosing PJI. Synovial fluid results were compared between institutions. A subset of 73 patients with both pre- and intraoperative aspirations served to investigate any differences in aspiration timing.

## REFERENCES

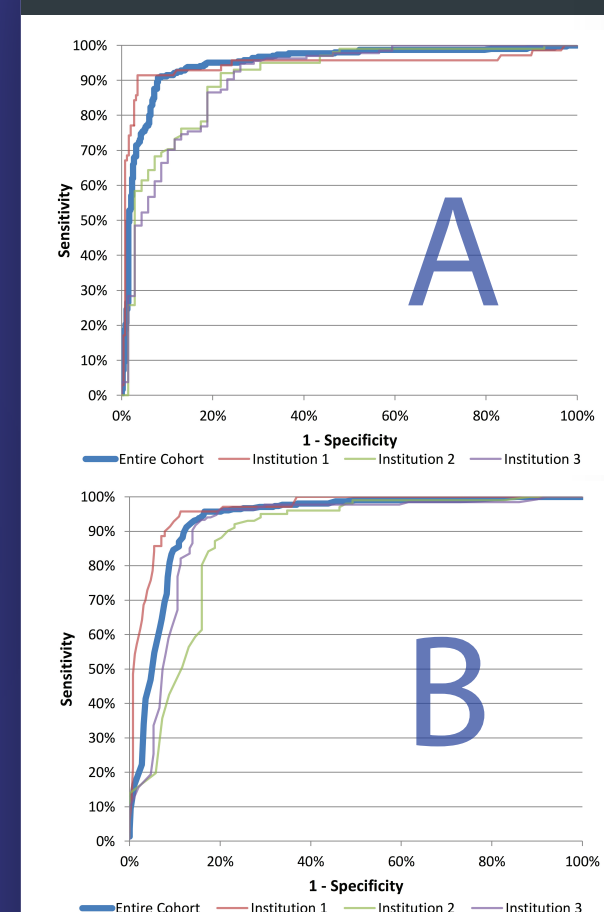
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## FIGURE 1



Distribution of (A) white blood cell (WBC) count and (B) neutrophil percentage (PMN%) results with resulting risk of periprosthetic joint infection (PJI). Bars represent number of patients stratified by PJI versus aseptic diagnosis. The line represents the proportion of patients with PJI in the representative range.

## FIGURE 2



Receiver operating characteristic (ROC) curves for synovial (A) white blood cell count and (B) neutrophil percentage. The primary curve represents the compiled cohort with minor curves for each institution.

## TABLE 1: CELL COUNT AND DIFFERENTIAL ACCURACY

	Threshold	Number	Sensitivity	Specificity	PPV	NPV	Accuracy
<b>Synovial WBC Count</b>							
Entire Cohort	5,286	782	90.8%	92.0%	87.9%	94.0%	91.6%
Within 40% of Threshold	N/A	38	66.7%	91.3%	83.3%	80.8%	81.6%
Institution 1	5,500	327	91.4%	96.5%	87.7%	97.6%	95.4%
Institution 2	7,941	170	88.1%	81.2%	87.3%	82.4%	85.3%
Institution 3	5,125	285	90.3%	90.7%	89.6%	91.3%	90.5%
<b>Synovial PMN%</b>							
Entire Cohort	78%	782	93.1%	85.1%	80.7%	95.1%	88.6%
Within 10% of Threshold	N/A	74	78.9%	33.3%	55.6%	60.0%	56.8%
Institution 1	76%	327	92.9%	90.3%	72.2%	97.9%	90.8%
Institution 2	83%	170	87.1%	81.2%	87.1%	81.2%	84.7%
Institution 3	77%	285	91.8%	85.4%	84.8%	92.1%	88.4%

The calculated thresholds of synovial WBC and PMN% and their respective diagnostic accuracy are shown for the entire cohort and stratified by institution. As well, diagnostic accuracies are reported for a subset of patients with aspirate results near the calculated threshold for both synovial WBC and PMN%.

PPV=Positive predictive value; NPV=Negative predictive value; WBC=White blood cell; PMN%=Neutrophil percentage.

## RESULTS

From the entire cohort, an area under the curve (AUC) of 0.95 and 0.93 with thresholds of 5,286 cells/ $\mu$ L and 78% for synovial WBC count and PMN%, respectively, was found (Table 1; Figure 2). A gradual increase in the proportion of patients with PJI was observed with increasing WBC count and PMN% with the transition occurring over 1,000-30,000 cells/ $\mu$ L and 70-80 PMN% (Figure 1).

Mean WBC count ( $p=0.01$  for infected and  $p=0.02$  for uninfected) and PMN% ( $p<0.001$  for uninfected) were significantly different between institutions. The calculated thresholds for each institution ranged from 5,125 to 7,941 cells/ $\mu$ L and 76% to 83% for synovial WBC count and PMN%, respectively.

An appreciable, yet non-significant, rise in WBC count from pre- to intraoperative aspiration was noted for both septic (29,375 vs. 42,915;  $p=0.14$ ) and aseptic (8,553 versus 9,869;  $p=0.87$ ) cases. The diagnostic accuracies for pre- versus intra-operative synovial WBC count were indistinguishable (AUC=0.89 vs 0.93;  $p=0.46$ ). In addition, a strong correlation between pre- and intraoperative aspiration was found for both WBC count ( $R=0.71$ ;  $p<0.001$ ) and PMN% ( $R=0.81$ ;  $p<0.001$ ).

## DISCUSSION

Synovial fluid WBC count and PMN% were reaffirmed as accurate markers of PJI with new calculated thresholds. However with values near these thresholds, it is important to appreciate the gradual transition of PJI risk resulting in poor diagnostic accuracy. Significant differences in timing of joint aspiration were not appreciated and the cell counts correlated over multiple aspirations. Yet, significant variation was noted between treating institutions. Inter-institutional variability and the gradual transition in PJI risk likely account for the wide range of calculated thresholds in the literature.