Synovial fluid analyses exhibit a high intraindividual variation in periprosthetic joint infections of the knee

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INTRODUCTION:

Synovial fluid analyses like leucocyte cell count (LC) and polymorphonuclear percentage (PMN%) represent an essential part in the diagnosis of periprosthetic joint infections (PJI). Interestingly, it is unknown if these parameters are subject to a time-dependent intraindividual variance that potentially could affect the diagnostic assessment.

METHODS:

We conducted a retrospective, double-center study of prospectively collected data including 35 consecutive patients with confirmed PJI of the knee and two joint aspirations at different timepoints (t1 and t2). Exclusion criteria were timespan >120 days between t1 and t2, or meanwhile performed intraarticular injections, surgeries or concomitant antibiotic medication. Absolute LC and PMN% as well as percentual change between t1 and t2 was evaluated. Percentage of missed PJI cut-off thresholds according to MSIS and EBJIS criteria and sub-analysis between low- and high virulent pathogen associated PJI were conducted, too.

RESULTS:

In total, seventy synovial fluid samples of 35 patients were analyzed (20 women, 15 men). The median age at the time of surgery was 71 years (range, 39 - 94 years; SD 13 years). The average time between the first and second joint aspiration was 33 ± 31 days [0 - 111 days]. 17.1% of the cases received an DAIR, 31.4% a one-stage and 51.4% a two-stage septic revision as surgical procedure.

Mean LC of all 70 samples was 19.969 n/µl ± 27.035 n/µl [300 – 135.000 n/µl], mean PMN% was 65% ± 28% [6% - 97%]. There was no significant difference between first and second LC and PMN% measurement despite the median percentual variability was 58% [2-1775] for LC and 11% [0-442] for PMN% (Table 1, p=0.062).

There was no relationship between in-between time interval and percentual change of LC (Pearson = -0.186, p=0,221) but a moderate correlation between length of time interval and percentual change of PMN% (Pearson = 0.471, p=0.004).

Seven (20%) patients showed discrepant LC values either below or above the PJI threshold of 3000 leucocytes /µl depending on the time of aspiration. In contrast, for PMN%, this was evident in 4 (11%) patients.

As automated cell count in body fluids shows an overall imprecision up to 20% a sub-analysis was performed including only cases with LC changes > 20% between both aspirations. 27 of 35 cases (77,1%) demonstrated a relevant change of LC > 20%. There was no significant difference between first and second LC and PMN% despite the median percentual variability was 73% [20-1775] for LC and 11% [0-442] for PMN% (Table 2).

17 cases (48.6%) were identified as low-virulent pathogen caused PJI, 18 cases (51.4%) as high-virulent pathogen caused PJI. The average LC was significantly higher in high-virulent associated PJI than in low-virulent pathogen associated PJI (33,382 n/µl ± 31,913 [397-135000] vs. 5767 n/µl ± 6630 [300-23,340], p <0.001). So did PMN% (82% ±18 [14-97] vs. 48% ± 27 [6-93], p <0.001).

Variability of PMN% was significant less in high-virulent pathogen associated PJI (p=0.008, Table 3).

DISCUSSION AND CONCLUSION:

The findings of our study have significant clinical implications. LC and PMN% values appear to be related to organism type and virulence, exhibiting high intra-individual variability over time. Orthopedic surgeons should be aware of the high rate of false-negative results, particularly in low-grade PJI. Given the inherent variation, the necessity of a multifaceted diagnostic approach (clinical features, blood work, microbiology, synovial analysis, histology) as outlined in current PJI definition criteria is crucial . To date, there is no single diagnostic test with high sensitivity and specificity for detecting low-grade PJI. Emerging diagnostic tools, such as pathogen-specific biomarkers, reverse transcription-quantitative polymerase chain reaction, and metagenomic next-generation sequencing of synovial fluid, show promise but are still in early stages of evaluation. Until these methods are refined, LC should be regarded as less accurate compared to PMN%. However, in cases of low-grade infections, both synovial LC and PMN% have less diagnostic power than generally assumed.

Table 1: Overall comparison of LC and PMN% between first and second aspiration

	1.Aspiration	2.Aspiration	Mean Difference absolut	Significance
LC [n/µl]	18,262 ± 24,061 7695 [397-102,000]	21,676 ± 29,972 9887 [300-135,000]	11,630 ± 23,800 3200 [45-127,800]	0.272
PMN [%]	63 ± 31 % 77 [6-97]	68 ± 26 77 [14-96]	11 ± 11 6 [0-40]	0.053

Data presented as average ± SD and Median [range] as not distributed normally. Leucocyte Cell Count (LC), polymorphonuclear percentage (PMN%)

Table 2 Sub-analysis and comparison of LC and PMN% between first and second aspiration in cases with percentual LC change > 20% between aspirations

	1.Aspiration	**2.Aspiration**	**Mean Difference absolut**	**Significance**
LC [n/µl]	13,924 ± 18,251 7500 [397-81,700]	18,217 ± 27,988 9300 [300-135,000]	14,168 ± 26,587 3950 [273-127,800]	0.195
PMN [%]	61 ± 32 % 75 [6-97]	68 ± 24 75 [17-96]	12 ± 11 8 [0-40]	0.069

Data presented as average ± SD and Median [range] as not distributed normally. Leucocyte Cell Count (LC), polymorphonuclear percentage (PMN%)

Table 3: comparison LC and PMN% variability (in absolute and percentual change) between first and second aspiration between low- and high-virulent pathogen associated PJI

	low-virulent	**high-virulent**	**Significance**
Leucocyte Cell Count (LC)			
Variability in %	88 ± 151 46 [2-662]	155 ± 408 67 [4-1775]	0.987
polymorphonuclear percentage (PMN%)			
Variability in %	77 ± 108 40 [6-441]	22 ± 65 5 [0-279]	0.008