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 \pm 27.035 n/µl [300 – 135.000 n/µl], mean PMN% was 65% \pm 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: Or	verall comparison of	LC and PMN% betw	een first and secon	d aspiration		Table 2 Su	b-analysis and compa	iri
	1.Aspiration	2.Aspiration	Mean Difference absolut	Significance		aspiration	1 Asniration	
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		LC	13,924 ± 18,251	
PMN [%]	63 ± 31 % 77 [6.97]	68 ± 26 77 [14-96]	11±11 6[0.40]	0.053		[n/µl]	7500 [397-81,700]	Ľ
Data presentes	i as average ± SD and N	fedian [range] as not distrib	outed normally. Leucoc	yte Cell Count (I	.C),	[%]	61 ± 32 % 75 [6-97]	
polymorphona	clear percentage (PMN%)				Data presente	d as average ± SD and M sclear percentage (PMN%)	ed
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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
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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				