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Are Synovial Inflammatory Markers Increased in Patients Who Have Aseptic Total Hip Arthroplasty Dislocation Indicated for Revision?

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ABSTRACT

Background: Previous studies have speculated on elevated synovial inflammatory markers in patients undergoing surgical revision for total hip arthroplasty (THA) dislocation. However, this assumption is based on small patient series and a full investigation according to International Consensus Meeting (ICM) criteria has not yet been performed.

Methods: Patients who had aseptic THA dislocation indicated for revision surgery were identified retrospectively. Only patients who had available diagnostic workup according to ICM 2018 criteria, including preoperative and intraoperative parameters, were included. For comparison, we analyzed a matched cohort of patients indicated for aseptic THA revision for other conditions. The 2 cohorts each consisted of 55 patients and were not different regarding age, sex, BMI, or implant fixation.

Results: There was no difference in synovial white blood cell count (2,238 ± 2,544 versus 2,533 ± 3,448 c/μL; $P = .601$), alpha-defensin quotient (0.14 ± 0.11 versus 0.19 ± 0.28; $P = .207$), or polymorphonuclear neutrophil percentage (% PMN) (36.7 ± 22.6 versus 31.3 ± 24.5%; $P = .312$) between the groups. In the dislocation cohort, 20% of patients had a synovial white blood cell count of 3,000 c/μL or higher, compared with 18% in the control cohort. However, all patients in the dislocation cohort were below the cutoff for alpha-defensin or % PMN.

Conclusion: In patients who have aseptic THA dislocation, synovial inflammatory markers are not elevated compared with patients undergoing aseptic revision for other complications. A detailed preoperative analysis of synovial inflammatory markers using ICM criteria appears critical in patients who have a THA dislocation to exclude periprosthetic joint infection.

Level of Evidence: Level III, retrospective, comparative study.

There is a noticeable increase in the number of arthroplasties worldwide, leading to a potential increase in complications associated with this surgical procedure. Dislocation is a common complication after total hip arthroplasty (THA) [1], with an annual incidence of around 2% [2]. Individual reasons for dislocation are diverse and include malpositioning, impingement, neuromuscular disease (eg, Parkinson's disease, epilepsy), trauma, fractures, spine pathologies, and nonosteoarthritis indications for THA such as hip osteonecrosis or femoral neck fracture [3–6]. Treatment of dislocation often requires surgical revision to restabilize the joint and minimize the risk of further dislocations. In patients scheduled for revision, concomitant periprosthetic joint infection (PJI) should be ruled out by preoperative joint aspiration with synovial fluid analysis, as the therapeutic concept differs with the presence of a PJI (eg, 2-stage versus 1-stage revision, antibiotic treatment) [7]. In supposedly

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aseptic revisions, dislocation has been identified as the most common reason for occult PJI [8]. It is also possible that PJI accompanied by septic loosening leads to implant migration or muscular insufficiency and thus may be the cause of the dislocation [9].

Diagnostic criteria for PJI were inconsistent until standardized criteria were developed by the Musculoskeletal Infection Society (MSIS) and the Infectious Diseases Society (IDSA) [10,11]. In 2013 and 2018, these criteria were revised and adapted by the International Consensus Meeting (ICM) and its definition is now based on a scoring system including preoperative assessment of laboratory inflammatory markers such as serum c-reactive protein (CRP), synovial white blood cell (WBC) count, alpha-defensin, and percentage of polymorphonuclear neutrophils (% PMN), as well as microbiological and histological analyses of intraoperatively obtained tissue samples, among others [12]. Meanwhile, there is still some debate in the literature about the optimal cutoff values for individual inflammatory markers [13,14] and the impact of other conditions such as THA dislocation [15]. To date, there is 1 study showing that synovial WBC count is increased in patients suffering from THA dislocation [15], postulating that THA dislocation could be a cause for false-positive results regarding PJI diagnosis. However, this previous study assessed only a subset of inflammatory markers in a rather small cohort of 28 patients.

In this study, we aimed to assess additional inflammatory markers based on ICM 2018 criteria (including alpha-defensin and % PMN) in a larger cohort of patients who had a THA dislocation. We also aimed to investigate the potential association between the time interval from dislocation to synovial fluid analysis and inflammatory markers. Our overall aim was to improve preoperative clinical decision-making in these patients. Specifically, we aimed to answer the following questions [1]: Are synovial inflammation markers increased in aseptic THA dislocation compared with aseptic revisions for other conditions? [2] Is there a divergence between synovial WBC count and other markers such as synovial alpha-defensin? [3] Is there a time-dependent variation in synovial inflammatory markers in relation to the time between dislocation and synovial fluid analysis?

Materials and Methods

Study Cohort

We performed a retrospective analysis of patients treated surgically for THA dislocation at our institution between January 1, 2015, and December 31, 2022. We are affiliated with a large rehabilitation facility that admits patients after THA from several regional hospitals. A total of 66 radiologically confirmed THA dislocations scheduled for revision THA were identified during this period (Figure 1). To be included, patients had to have available serum CRP, synovial WBC count, and alpha-defensin data. Nine patients who had missing documentation of serum CRP (n = 1), or *punctio sicca* (dry tap) (n = 8) were excluded, resulting in 57 patients. Furthermore, 2 patients who had a THA dislocation and multiple positive microbiological cultures were diagnosed with PJI, leaving 55 patients for final analysis (Figure 1). Osteoarthritis was the indication for primary THA in all patients. Metal-on-metal bearings had not been used in any of the patients in the previous surgery. None of the patients had a history of septic arthritis.

For comparison, a total of 55 consecutive patients who had an aseptic complication scheduled for revision surgery were retrospectively identified. The individual diagnoses included aseptic loosening, polyethylene (PE) wear, or acetabular bone defects; however, dislocation was considered as exclusion criterion. Otherwise, the same inclusion and exclusion criteria were applied as for the aseptic dislocation cohort.

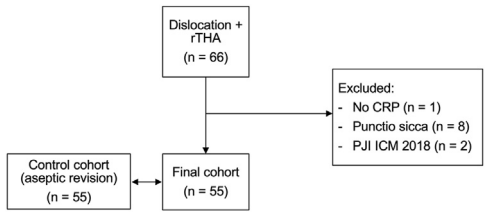

Fig. 1. Flowchart. Retrospective identification of the study population, consisting of patients with total hip arthroplasty dislocation in whom revision surgery was performed and diagnostic workup based on international consensus meeting criteria was available. rTHA, revision total hip arthroplasty; CRP, c-reactive protein; PJI, periprosthetic joint infection; ICM, international consensus meeting.

We evaluated several clinical parameters such as age, sex, body mass index (BMI), type of implant fixation, prosthesis survival, and time interval between dislocation and synovial fluid analysis. In addition, we analyzed whether the procedure was the first revision (ie, primary revision) or whether multiple THA revisions had been performed in the past.

Synovial Fluid and Tissue Sample Analysis

To establish the aseptic origin and to exclude chronic PJI in both cohorts, the scoring system according to ICM 2018 criteria was applied [12,16]. A sinus tract and 2 or more positive microbiological samples with the same pathogen immediately allowed the diagnosis of PJI (ie, major criteria). There were 6 tissue samples obtained during revision surgery, of which 5 and 1 were used for microbiological (conventional cultures) and histological analysis (paraffin sections), respectively. The incubation time of all microbiological samples was 14 days with daily control of bacterial growth. Furthermore, the following parameters were assessed serving as minor criteria: Serum CRP (>10 mg/L; 2 points), synovial WBC count (>3,000 c/μL; 3 points) or synovial alpha-defensin quotient (>1; 3 points), % PMN (>80% ; 2 points), histological assessment (tissue sample positive; 3 points), microbiology (1 of 5 tissue samples positive; 2 points). Cell count analyses were carried out in an automated fashion. For % PMN, we used a cutoff of 80% [16]. Synovial alpha-defensin was measured by Enzyme-linked Immunosorbent Assay (ELISA, CD Diagnostics, Claymont, DE) and was expressed as a quotient. Only patients who had less than 6 points were included. Although not included in the 2018 ICM criteria, we additionally included the absolute synovial PMN count, with a cutoff value of 3,300 c/μL as previously reported [17].

Sample Size Calculations and Statistical Analyses

Sample size calculation was performed using G*Power 3.1 (University of Düsseldorf, Düsseldorf, Germany) [18] based on the results of a previous study [15], which showed that the synovial WBC count is increased in the dislocation group compared to an aseptic THA revision group (1,721.5 ± 2,335.5 c/μL versus 615.6 ± 367.1 c/μL; $P = .015$). These results correspond to an effect size of Cohen's d = 0.662. With an alpha level set at 0.05, a power of 0.8, and an expected medium effect (d = 0.662), a required total sample size of n = 74 (n = 37 each group) was determined to detect differences in synovial WBC count between the dislocation group and the aseptic revision group (unpaired 2-sided *t*-test).

Statistical analyses and visualizations were performed using Statistical Product and Service Solutions (SPSS) Statistics 29.0 (IBM, Armonk, NY) and GraphPad Prism 9.5.0 (GraphPad Software, San Diego, CA). After confirming normal distribution, we used unpaired 2-tailed *t*-tests for comparison of 2 groups. Comparison of categorical data was performed using Fisher's exact tests. Linear

regression analyses were performed to analyze the relationship of the time interval between dislocation and synovial fluid analysis and individual inflammatory markers (such as synovial WBC count, alpha-defensin, serum CRP, and % PMN). In addition, multiple linear regression models (enter method) were applied to evaluate the predictive value of the independent variables age, sex, BMI, prosthesis survival, and time between dislocation and synovial fluid analysis on synovial WBC count and % PMN (dependent variables). In addition to general model properties (R^2, adjusted R^2, F, and P value), individual regression coefficients (B, β, and P value) were calculated. The level of significance was defined as $P < .05$. Exact P values are reported unless $P < .001$. All data are presented as absolute values, means ± standard deviation (±SD), or medians with 95% confidence interval.

Results

Comparison of Inflammatory Markers Between the Dislocation and Control Cohort

The 2 cohorts (aseptic dislocation and aseptic control) each consisted of 55 patients and were not different regarding age (mean 76 years (range, 44 to 90) versus mean 73 years (range, 42 to 92; $P = .06$), sex ratio (each 35 women and 20 men; $P > .999$), BMI (mean 27.8 kg/m^2 (range, 18.4 to 43.7) versus mean 27.5 kg/m^2 (range, 19.4 to 42.5); $P = .117$), presence of rheumatoid arthritis (4 versus 6 patients; $P = .742$), and implant type or fixation (Table 1). Prosthesis survival time was shorter in the dislocation cohort compared to the control cohort (mean 6.2 years (range, 0.0 to 30.3) versus mean 13.8 years (range, 0.2 to 33.2); $P < .001$).

We found higher serum CRP values in the dislocation cohort (19.4 ± 31.5 versus 8.2 ± 19.6 mg/L; $P = .026$). Of the dislocations, 42% of patients had a CRP of 10 mg/L or higher (ie, the ICM cutoff), compared to 18% in the control cohort (Figure 2A). For synovial WBC count, both groups showed similar values (2,238 ± 2,544 versus 2,533 ± 3,448 c/μL; $P = .601$), with 20% of the dislocations and 18% of the controls being above the ICM cutoff of 3,000 c/μL (Figure 2B). The ICM scores of 2 to 5 ("possibly infected") were found in 32 (58%) of the patients who had a dislocation and in 21 (38%) of the patients who had an aseptic revision due to other indications ($P = .056$) when only preoperative diagnostic measures were considered (Table 1). However, synovial alpha-defensin quotient, % PMN, and absolute PMN count, were above the defined cutoff in the dislocation cohort in 0, 0, and 2%, respectively. No differences were detected in these markers compared to the control group (Figure 2C through E).

To identify possible causes for increased synovial WBC count, we evaluated individual data of all patients with WBC count >3,000 c/μL. In the dislocation cohort, the number of dislocations ranged from 1 to 7, and the underlying clinical conditions included cup loosening, malpositioning, or polyethylene wear (Table 2). Similar conditions were also seen in the aseptic control group with increased WBC count (Table 3).

Time-dependent Effects

The median interval between dislocation and synovial fluid analysis was 15 days (95% confidence interval: 5 to 21 days). There were 6 patients who underwent synovial fluid analysis more than 2 months after dislocation. These patients had initially decided on a nonoperative approach and presented to us again for surgical revision due to pain or subjective instability. To examine potential time-dependent effects, we restricted the time frame between dislocation and synovial fluid analysis to 30 days for our analyses (n = 40). There was no association with serum CRP, synovial WBC count, or alpha-defensin quotient (Figure 3A through C). For % PMN, we were able to detect a weak negative time-dependent association, indicating decreasing % PMN counts with the time between dislocation and synovial fluid analysis ($R^2 = 0.26$, $P = .004$) (Figure 3D). A multiple linear regression model confirmed this relationship between time between dislocation until synovial fluid analysis and synovial % PMN (Table 4). In addition, a sex-specific effect could be shown, with men having higher synovial % PMN counts. However, other possible influencing factors such as prosthesis survival or BMI could not be confirmed as independent predictors on either WBC count or % PMN.

Influence of the Number of Dislocations and Revisions on Inflammatory Markers

On average, 2.3 dislocations occurred per patient before revision was indicated. We analyzed the influence of the number of dislocations on synovial inflammatory markers. For this purpose, the cohort was divided into patients with 1 dislocation and more than 1

Table 1
Comparison of Demographic, Clinical, and Laboratory Characteristics Between the Dislocation and Aseptic Revision Control Cohort.

Characteristics (Unit)	Dislocation n = 55	Aseptic Revision n = 55	*P* Value
Mean age (y)	76 (44 to 90)	73 (42 to 92)	.060
Sex ratio (W/M)	35/20	35/20	>.999
Mean BMI (kg/m^2)	27.8 (18.4 to 43.7)	27.5 (19.4 to 42.5)	.117
Rheumatoid Arthritis (n)	4	6	.742
Prosthesis survival (y)	6.2 (0.0 to 30.3)	13.8 (0.17 to 33.2)	**<.001**
Dual mobility cup (n)	3	3	>.999
Cup screw fixation/reinforcement device (n)	16	17	>.999
Modular neck (n)	9	5	.392
Uncemented/cemented cup (ratio)	50/5	50/5	>.999
Uncemented/cemented stem (ratio)	34/21	36/19	.843
Serum CRP (mg/L)	19.4 (±31.5)	8.2 (±19.6)	**.026**
Synovial WBC (c/μL)	2,238 (±2,544)	2,533 (±3,448)	.601
Synovial alpha-defensin (quotient)	0.14 (±0.11)	0.19 (±0.28)	.207
Synovial %PMN	36.7 (±22.6)	31.3 (±24.5)	.312
Synovial abs. PMN (c/μL)	902 (±1,027)	1,084 (±1,808)	.584
Preoperative ICM score	1.44 (±1.37)	1.16 (±1.64)	.345
"Possibly infected" (n)	32	21	.056
Final ICM score	1.70 (±1.52)	1.46 (±1.78)	.423

Bold indicates significant differences.
W: women, M: men, BMI: body mass index, CRP: c-reactive protein, WBC: white blood cell count, PMN: polymorphonuclear neutrophils, ICM: international consensus meeting.

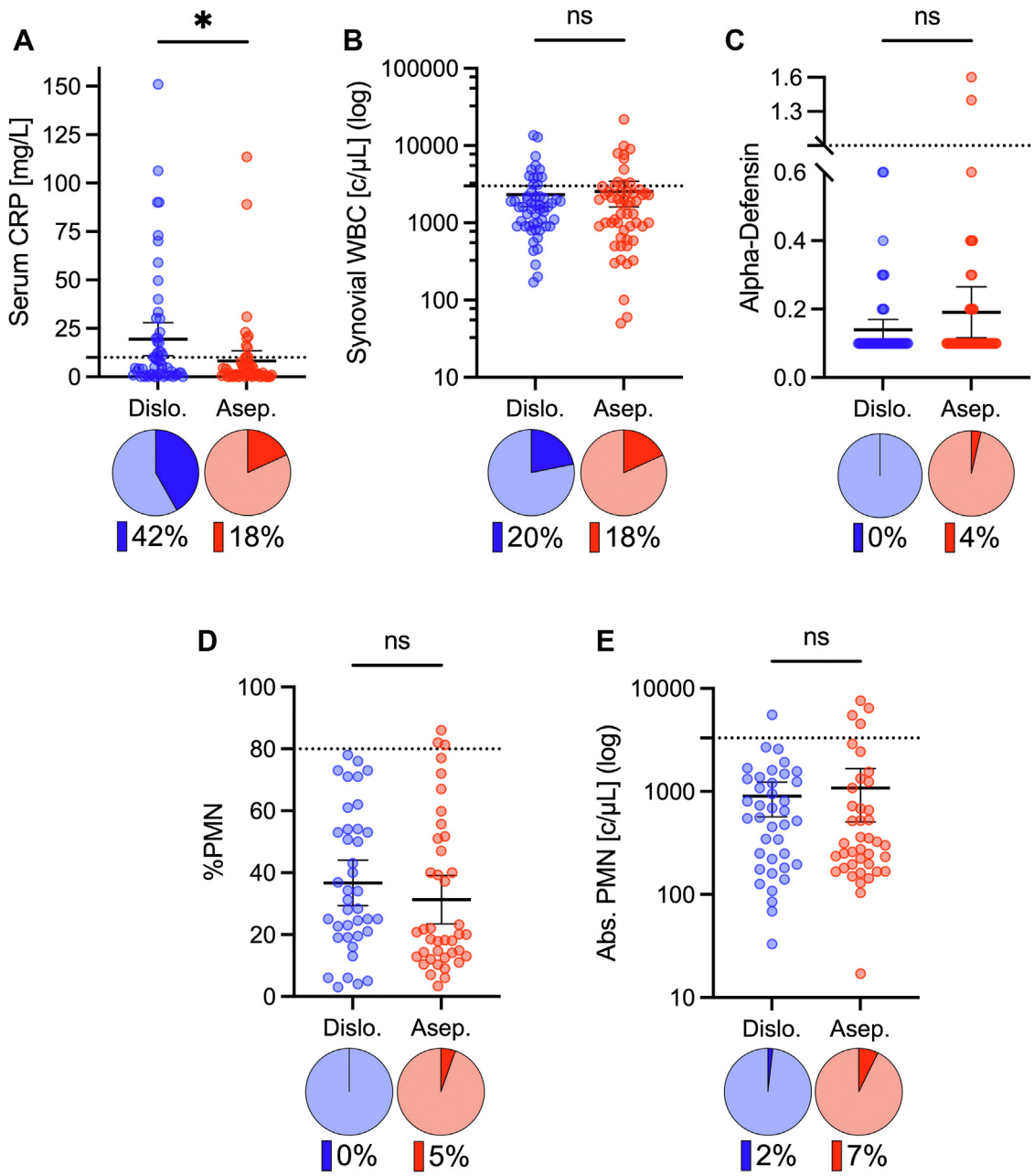

Fig. 2. Comparison of serum and synovial inflammatory markers between the dislocation and aseptic revision cohort. (A) Serum c-reactive protein (CRP), (B) synovial white blood cell (WBC) count, (C) synovial alpha-defensin quotient, (D) percent synovial polymorphonuclear neutrophil (% PMN) cell count, and (E) absolute synovial PMN count. The cutoff value of 3,300 c/µL for absolute synovial PMN is based on [17]. Median with 95% confidence interval is displayed. *$P < .05$, ns, not significant.

dislocation. There was no difference in any of the inflammatory markers (Supplemental Table 1). We also compared inflammatory markers between patients who underwent revision for the first time and those who underwent multiple revisions. Again, none of the inflammatory markers differed between the 2 subgroups. However, both the dislocation cohort and the control cohort showed a trend toward lower synovial WBC counts in patients who had multiple revisions (Supplemental Table 2).

Discussion

While the individual causes for THA dislocation are diverse, PJI should be excluded in patients scheduled for revision surgery [11]. It has been unclear whether patients who have aseptic THA dislocation exhibit elevated synovial inflammatory markers, which would preclude the application of current diagnostic PJI criteria. In this study of 55 patients who had aseptic THA dislocation, we did not observe an increase in synovial inflammatory markers compared to a control group of age-matched, sex-matched, and BMI-matched patients indicated for aseptic revision for other conditions. Moreover, there were no time-dependent effects with respect to the interval of dislocation and assessment of inflammatory markers, except for a notable negative association with % PMN. These results are clinically relevant, as the established synovial inflammatory markers appear suitable to exclude PJI in patients who have aseptic THA dislocation. In this context, it must be noted that there is no single preoperative parameter with a perfect diagnostic accuracy to confirm and exclude PJI. In our cohort, 20% of

Table 2
Individual Presentation of Patients With False-Positive Synovial White Blood Cell (WBC) Count in the Dislocation Cohort.

Pat.	Age (y)	Prosthesis Survival (y)	Dislo. - SFA (days)	Count Dislo. (n)	Specifics	Serum CRP (mg/L)	Syn. WBC (c/μL)	AD (Quotient)	% PMN	Abs. PMN (c/μL)	Histo.	MiBi.	ICM 2018 Score
1	83	18	35	4	PE wear	1.3	5,500	0.1	25	1,375	neg.	sterile	3
2	78	0	1	3	Cup loosening	49.6	7,300	0.3	76	5,548	neg.	sterile	5
3	70	1	6	1	Malpositioning	1	4,000	0.1	4	160	neg.	sterile	3
4	75	8	63	2	Malpositioning	4	4,053	0.1	/	/	neg.	sterile	3
5	61	9	17	7	None	1	3,126	0.1	54	1,688	neg.	sterile	3
6	72	16	192	4	PE wear	0.6	12,800	0.1	21	2,688	neg.	sterile	3
7	75	2	122	2	PE wear	70	4,891	0.1	/	/	neg.	sterile	5
8	89	16	0	1	PE wear	4.3	3,100	0.2	40	1,240	neg.	sterile	3
9	78	15	3	2	Cup loosening	3	3,900	0.6	/	/	neg.	sterile	3
10	60	0	1	2	Malpositioning	5.1	3,800	0.1	51	1,938	neg.	sterile	3
11	75	5	56	5	Malpositioning	1	13,500	0.1	19	2,565	neg.	sterile	3

Pat.: patient, Dislo.: dislocation, SFA: synovial fluid analysis, PE: polyethylene, CRP: c-reactive protein, WBC: white blood cell count, AD: alpha-defensin, PMN: polymorphonuclear neutrophils, Histo: histology, MiBi: microbiology, ICM: international consensus meeting.

Table 3
Individual Presentation of Patients With False-Positive Synovial White Blood Cell (WBC) Count in the Aseptic Revision Control Cohort.

Pat.	Age (y)	Prosthesis Survival (y)	Specifics	Ser. CRP (mg/L)	Syn. WBC (c/μL)	AD (Quotient)	% PMN	Abs. PMN (c/μL)	Histo.	MiBi.	ICM 2018 Score
1	74	5	Loosening, femoral defect	10	3,300	0.1	6	198	neg.	sterile	5
2	63	26	PE wear	5.6	9,000	0.1	15	1,350	neg.	sterile	3
3	79	22	PE wear	0	6,800	0.1	18	1,224	neg.	sterile	3
4	78	29	Acetabular defect	0	7,900	0.1	81	6,399	neg.	sterile	5
5	79	14	Acetabular defect	0	3,368	0.1	86	2,896	neg.	sterile	5
6	58	4	Loosening	4.5	4,900	0.1	15	735	neg.	sterile	3
7	73	5	Loosening	5.3	21,800	0.1	21	4,578	neg.	sterile	3
8	82	11	Loosening, acetabular defect	16	9,900	0.2	77	7,623	neg.	sterile	5
9	66	6	Loosening	1	3,177	0.1	/	/	neg.	sterile	3
10	72	3	Loosening	5.2	7,600	0.3	72	5,472	neg.	sterile	3

Pat.: patient, PE: polyethylene, CRP: c-reactive protein, WBC: white blood cell count, AD: alpha-defensin, PMN: polymorphonuclear neutrophils, Histo: histology, MiBi: microbiology, ICM: international consensus meeting.

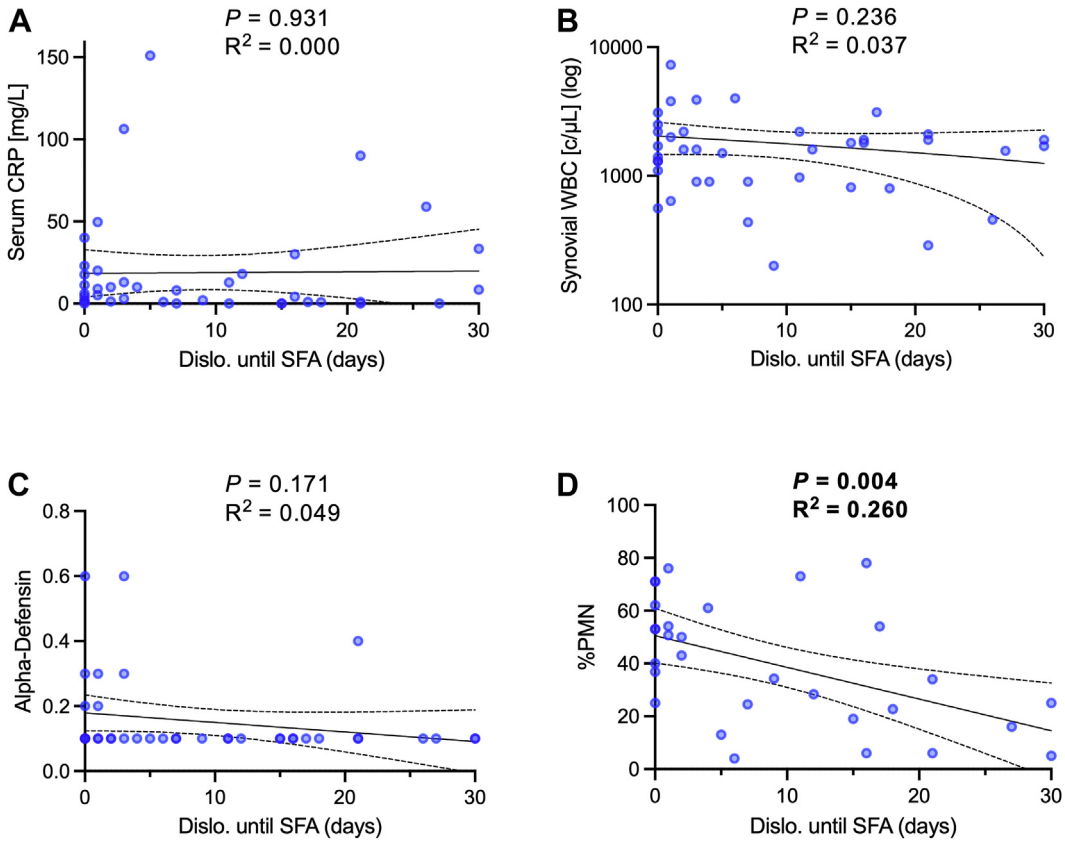

Fig. 3. Time-dependent trends of laboratory inflammatory markers between dislocation and synovial fluid analysis SFA. (A-D) Associations between time interval from dislocation to synovial fluid analysis and measurement of serum c-reactive protein (CRP), synovial white blood cell (WBC) count, synovial alpha-defensin quotient, and percent synovial PMN count. Linear regression analyses were performed in all panels. A period of up to 30 days after dislocation was covered in this analysis. Exact *P* values and R^2-values are shown.

patients who have aseptic THA dislocation had elevated synovial WBC counts, but a similar frequency was detectable in the control group. Application of synovial alpha-defensin or % PMN allowed exclusion of PJI in patients who have THA dislocation before surgical revision compared with the full set of ICM 2018 parameters after intraoperative sampling.

Previous Investigations on Inflammatory Markers in THA Dislocation

To the best of our knowledge, there is only 1 other study that has previously assessed synovial inflammatory markers in patients who have aseptic THA dislocation [15]. In contrast to our findings, the authors showed increased synovial WBC counts in these patients. They speculated on possible reasons including shearing of the head, injuries to soft tissue or bone caused by dislocation, and the influence of PE wear. While the previous study was limited to 28 patients and other synovial markers such as alpha-defensin had not been determined, the parameter % PMN also showed no differences compared to an aseptic control group without dislocation.

Explanations for Elevated WBC Count

In our study, 20% of the patients in the dislocation cohort and 18% in the control cohort had a WBC count above the ICM 2018 cutoff (>3,000 c/µL). We assume that PE wear especially led to the increased synovial WBC count detected in both the dislocation and

Table 4
Multiple Linear Regression Model Analyzing Independent Factors Associated With Synovial White Blood Cell (WBC) Count and Percent Synovial Polymorphonuclear Neutrophils (% PMN) in the Dislocation Cohort.

Parameter	Synovial WBC (c/µL)			Synovial % PMN		
	B	β	*P*	B	β	*P*
(Constant)	4,773.079		.126	104.361		.034
Age (y)	−21.301	−0.142	.465	−0.629	−0.235	.165
Sex (W = 0, M = 1)	−111.743	−0.041	.825	18.735	0.390	**.024**
BMI (kg/m^2)	−36.461	−0.159	.438	−0.372	−0.083	.632
Prosthesis survival (y)	2.041	0.012	.943	−0.327	−0.116	.449
Dislocation until SFA (d)	−34.128	−0.249	.177	−1.138	−0.483	**.004**
	R^2 = 0.061			R^2 = 0.486		
	R^2 adjusted = −0.077			R^2 adjusted = 0.379		
	F (5, 34) = 0.441, *P* = .817			F (5, 24) = 4.537, ***P*** = **.005**		

Bold indicates significant differences.
W: women, M: men, BMI: body mass index, SFA: synovial fluid analysis, WBC: white blood cell count, PMN: polymorphonuclear neutrophils.

control group. In accordance with this assumption, a recent study comparing WBC counts in different indications for aseptic revision found that PE wear was shown to account for the largest proportion of WBC count >3,000 c/μL [19]. These authors further noted that a large proportion of patients had a WBC count of >3,000 c/μL, regardless of the indication for aseptic THA revision. In our cohort, some patients who did not have PE wear also had increased WBC counts. These collective findings suggest that a sole evaluation of synovial WBC count is not reliable for excluding PJI in patients who have aseptic THA dislocation as well as other aseptic complications.

Role of Other Inflammatory Markers

Because of the above-mentioned limitations of synovial WBC count, it is important to assess other inflammatory markers in the context of aseptic THA dislocation. Synovial alpha-defensin is a comparatively reliable laboratory parameter that is included in the 2018 ICM criteria, but also lacks optimal sensitivity [20]. In the dislocation cohort, none of the patients were above the cutoff value for synovial alpha-defensin. For % PMN and absolute PMN count, none and 1 patient, respectively, were above the cutoff value, underscoring that this parameter is equally reliable compared with alpha-defensin, as previously demonstrated [17]. The only inflammatory marker for which we found higher values in the dislocation cohort was serum CRP, which may reflect the trauma associated with dislocation accompanied by a systemic inflammatory response. In only 1 patient, the time between the previous surgery and the CRP measurement was less than 14 days, which makes it unlikely that the surgery was the cause of the CRP elevation. While CRP is indeed an important screening tool and has always been included in the criteria for diagnosis of PJI [21–23], there are also false-positive and false-negative outcomes [24]. Therefore, synovial analyses are recommended, particularly when CRP levels are elevated [25].

Time-dependent Effects

As patients experiencing recurrent dislocations are typically not prioritized for emergency revision surgery, the timing of preoperative synovial fluid analysis may vary. We expected time-dependent effects, that is, that the trauma resulting from the dislocation is associated with a temporary increase in inflammatory markers. We were unable to confirm this association for most parameters, but the detected negative association of the time between dislocation and synovial % PMN may suggest a local inflammatory response directly related to dislocation.

Number of Dislocations and WBC Count

We hypothesized that patients who had multiple dislocations would have lower values of synovial inflammatory markers because of an attenuated inflammatory response due to joint laxity. However, there were no differences between patients who had one and patients who had multiple dislocations. Regarding the influence of the number of previous revisions, no differences in any of the other inflammatory markers could be detected.

Potential Limitations

Our study is limited by the rare occurrence of dislocations with concomitant presence of PJI. We excluded only 2 patients who had a dislocation and PJI according to ICM 2018 criteria. Indeed, to calculate the diagnostic accuracy of inflammatory markers for the presence of PJI in the dislocation cohort only, more patients who had a dislocation and PJI would have had to be included. In our study we compared inflammatory parameters to a control group of patients who had other aseptic complications and additionally used the cutoff values defined according to ICM 2018. A limitation of our study is that most revision surgeries were performed in patients who have THA dislocations in whom the previous surgery was performed at another institution. A further limitation of our study is that the surgical approach of the previous procedure was not known in all patients, although the posterior approach was used in most patients. Although we believe that, for example, the surgical approach and implants used have minor influences on synovial inflammatory markers, these may be confounding factors. Another limitation of our study is that although matching of preoperative with full ICM criteria (including intraoperative/postoperative assessment) was performed, even these gold-standard criteria do not have perfect diagnostic accuracy, and thus PJI may not have been correctly excluded in all patients. Other methods for PJI diagnosis, including sonication and intraoperative frozen sections, were not used. We performed conventional histological assessment on paraffin sections of periprosthetic tissue. Furthermore, we used automated cell count analyses, the results of which may be influenced by various factors, such as hemarthrosis due to dislocation [26].

Conclusions

In patients who have aseptic THA dislocation, synovial inflammatory markers are not elevated compared with patients undergoing aseptic revision for other complications. Irrespective of dislocation, synovial WBC count exceeds the cutoff of 3,000 c/μL in approximately one-fifth of patients. Since none of the patients exceeded the cutoff for % PMN and alpha-defensin, a detailed preoperative analysis of synovial inflammatory markers using the ICM criteria appears critical in patients who have THA dislocation to exclude PJI.

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Appendix/Supplemental Material

Supplemental Table 1
Comparison of Clinical and Laboratory Characteristics in Patients With the First Dislocation Versus Patients With Multiple Dislocations.

Characteristics (Unit)	Dislocation = 1 n = 13	Dislocation >1 n = 42	*P* Value
Prosthesis survival (y)	6.9 (±8.0)	5.8 (±1.7)	.640
Serum CRP (mg/L)	28.4 (±36.8)	16.7 (±29.5)	.243
Synovial WBC (c/μL)	1,758 (±986)	2,386 (±2,854)	.442
Alpha-defensin (quotient)	0.16 (±0.10)	0.13 (±0.11)	.424
% PMN	34 (±27)	38 (±22)	.650
Abs. PMN (c/μL)	615 (±513)	987 (±1,130)	.348

CRP: c-reactive protein, WBC: white blood cell count, PMN: polymorphonuclear neutrophils.

Supplemental Table 2
Comparison of Demographic, Clinical, and Laboratory Characteristics in Patients Undergoing the First Versus Multiple THA Revisions.

Characteristics(unit)	Dislocation Cohort			Aseptic Revision Cohort		
	First Revision n = 29	Multiple Revisions n = 26	*P* Value	First Revision n = 34	Multiple Revisions n = 21	*P* Value
Age (y)	77.1 (±7.2)	75.0 (±11.3)	.407	71.5 (±10.2)	74.9 (±6.9)	.181
No. Dislocations	2.3 (±1.1)	2.5 (±1.7)	.762	/	/	/
Serum CRP (mg/L)	15.9 (±24.7)	23.4 (±37.8)	.384	7.1 (±15.7)	9.9 (±24.9)	.617
Synovial WBC (c/μL)	2,769 (±3,295)	1,645 (±1,063)	.102	3,024 (±4,145)	1,737 (±1,632)	.181
Alpha-defensin (quotient)	0.11 (±0.05)	0.17 (±0.15)	.061	0.18 (±0.24)	0.21 (±0.39)	.699
% PMN	36 (±25)	38 (±21)	.825	34 (±26)	27 (±22)	.434
Abs. PMN (c/μL)	974 (±1,266)	808 (±619)	.625	1,326 (±1,978)	634 (±1,396)	.253
ICM 2018 score	2.0 (±1.8)	1.4 (±1.2)	.136	1.9 (±1.9)	0.7 (±1.4)	**.014**

Bold indicates significant differences.
Comparisons were performed individually for the dislocation group and the aseptic revision group.
No.: number, CRP: c-reactive protein, WBC: white blood cell count, PMN: polymorphonuclear neutrophils, ICM: international consensus meeting.