Clinical characteristics of Culture-Negative Periprosthetic Joint Infections: Findings from an International PJI Registry

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INTRODUCTION: Culture-negative periprosthetic joint infections (CN-PJI) remain a major problem within the field of orthopaedic infections. The clinical features of CN-PJI and its risk factors remain poorly defined in the literature. The purpose of this multicenter study was to elucidate the characteristics of CN-PJI.

METHODS: This was a retrospective multicenter cohort study as part of the Orthopaedic Device Infection Network (ODIN). Using real-world data from 5 institutions across Australia, the Netherlands, and United States, 563 cases of PJI (470 culture-positive; 93 culture-negative) were queried from the ODIN database between 1995 and 2021. Patients with CN-PJI had negative cultures on preoperative aspiration, blood, or intraoperative cultures. Patient demographics, history of surgery on the infected joint, presenting symptoms, operative details, preoperative laboratory values, and intraoperative findings were recorded. Prior antibiotic usage was not collected. Multivariable logistic regression was used to determine the association between these variables and culture negativity.

RESULTS: The incidence of CN-PJI was 16.5%. Univariate analysis revealed that patients with CN-PJI were more likely to be female, more often had a revision arthroplasty or prior PJI, had a longer duration of symptoms, and were less likely to present with fever, wound dehiscence or wound necrosis; they also had lower hemoglobin and serum CRP (p<0.05 for all). Using multivariate regression to control for confounders, the only factor significantly associated with CN-PJI was a duration of symptoms of >12 weeks (OR 2.24, 95% CI 1.008–4.964, p=0.048).

DISCUSSION AND CONCLUSION: Utilizing real-world data from an international PJI registry, this study found that patients with a prolonged duration of symptoms were twice as likely to have negative cultures, supporting the traditional belief that CN-PJI presents in a more insidious fashion. This supportive clinical data should be used to guide the selection of advanced investigations.

Table. Multivariate analysis for factors associated with positive cultures

Variable	Odds Ratio	95% lower	95% upper	p-value
Sex				
Male	ref			
Female	0.6640597	0.3976883	1.108847	0.118
CCI	1.059536	0.9324037	1.204003	0.375
Joint				
Hip	ref			
Knee	0.7641202	0.4702972	1.241512	0.277
Endoprosthesis	2.08468	0.730969	5.945384	0.169
Infection onset				
Early	ref			
Chronic	1.123176	0.5980934	2.109242	0.718
Late-acute	2.019977	0.5455319	7.479501	0.291
Fever	1.318879	0.6044494	2.877731	0.486
Duration of symptoms				
<4 weeks	ref			
4-12 weeks	0.4139182	0.1682861	1.018078	0.055
>12 weeks	0.4490751	0.202682	0.9949991	**0.049**
Hemoglobin	1.005751	0.9981095	1.01345	0.140
ESR	1.000555	0.9911097	1.01009	0.908
CRP	1.000148	0.9994466	1.000851	0.677

CCI, Charlson comorbidity index; *ESR*, erythrocyte sedimentation rate; *CRP*, C-reactive protein;
*Reference category: culture-negativity