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Hip and Knee Section, What is the Definition of a Periprosthetic Joint Infection (PJI) of the Knee and the Hip? Can the Same Criteria be Used for Both Joints?: Proceedings of International Consensus on Orthopedic Infections



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What is the definition of a periprosthetic joint infection (PJI) of the knee and the hip? Can the same criteria be used for both joints?

Recommendation:

See [Figure 1: Proposed 2018 ICM criteria for PJI](#).

Level of Evidence: Moderate

Delegate Vote: Agree: 68%, Disagree: 28%, Abstain: 4% (Super Majority, Weak Consensus)

Rationale:

The introduction of the Musculoskeletal Infection Society (MSIS) criteria for periprosthetic joint infection (PJI) in 2011, which was later altered by the 2013 consensus meeting, resulted in immense

improvements in diagnostic confidence and research collaboration [1]. In recent years, numerous serum and synovial markers have been evaluated and become widely available [2–14]. Moreover, publications in recent years show different sensitivity and specificity for the various tests used [4,14], and highlight the value of a high pretest probability in the overall diagnosis [9,15,16]. These advancements in the field call for the modification of current diagnostic criteria to an evidence-based one.

In a recent multi-institutional study [17], we proposed a new definition considering the relative and quantitative weight of established markers as well as newer markers [7,9,11]. The new diagnostic criteria also consider chronicity and invasiveness of the diagnostic tests, making the preoperative diagnosis of infection easier compared to previous definitions. By using a stepwise approach in developing the current criteria, which was based on the current American Academy of Orthopaedic Surgeons (AAOS) guidelines [18], we were able to provide relative weights for each diagnostic marker/finding. The threshold for infection of the combined score was determined in a way that would keep false positives to a minimum (threshold for infection), but also reduce false negatives (threshold for not infected). By performing this in a stepwise manner, we were able to maximize sensitivity in early stages of the work-up (to avoid under-diagnosis) and to maximize specificity in later stages (to avoid over-diagnosis).

This proposed definition showed a high level of performance using an independent multi-institutional cohort for validation and a better performance compared to previous MSIS and International Consensus Meeting (ICM) definitions. The new criteria demonstrated a sensitivity of 97.7% compared to the MSIS (79.3%) and ICM

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Major criteria (at least one of the following)	Decision
Two positive growth of the same organism using standard culture methods	Infected
Sinus tract with evidence of communication to the joint or visualization of the prosthesis	

Minor Criteria	Threshold		Score	Decision
	Acute [€]	Chronic		
Serum CRP (mg/L)	100	10	2	Combined preoperative and postoperative score: ≥6 Infected 3-5 Inconclusive* <3 Not Infected
<i>or</i> D-Dimer (ug/L)	Unknown	860		
Elevated Serum ESR (mm/hr)	No role	30	1	
Elevated Synovial WBC (cells/μL)	10,000	3,000	3	
<i>or</i> Leukocyte Esterase	++	++		
<i>or</i> Positive Alpha-defensin (signal/cutoff)	1.0	1.0		
Elevated Synovial PMN (%)	90	70	2	
Single Positive Culture			2	
Positive Histology			3	
Positive Intraoperative Purulence [¥]			3	

[€] These criteria were never validated on acute infections. [¥] No role in suspected adverse local tissue reaction. *Consider further molecular diagnostics such as Next-Generation Sequencing

Fig. 1. Proposed 2018 ICM criteria for PJI.

definition (86.9%), with a similar specificity of 99.5%. It also enables one to reach an earlier diagnosis compared to previous criteria, as more than 80% of the PJI cases using the new definition were diagnosed prior to surgery. This enhances the importance of a joint aspiration prior to surgery and supports it becoming the cornerstone of diagnosing PJIs. Another novel finding of the present definition is the introduction of patients in which a diagnosis is inconclusive. These patients are often encountered in clinical practice and represent a real diagnostic challenge. Pointing out this unique group or “gray area” of patients promotes awareness in both clinical practice and the need for further research focused at this cohort.

One major limitation of this study is an inherent selection bias. Defining PJI based on major criteria for developing the scoring system may have affected the thresholds of different markers and has the potential to under-diagnose more overt infections. That being said, 30% of the cohort used for developing the scoring system had coagulase-negative *Staphylococcus* which is not considered to cause a major immune response. Moreover, we validated the scoring system on an external cohort of infected and noninfected patients, independent from any previous criteria. In this group of patients, there were many culture negatives and so called “low grade infections” and the new criteria demonstrated a high sensitivity of 97.7%. This further validates the utility of the new definition in more overt infections.

The criteria have been reviewed and altered by a group of recognized international experts who are also delegates of the ICM in 2018. We wish to point out some important facts related to the newly proposed definition of PJI:

1. The proposed definition was developed and validated on a cohort with chronic PJI. Patients with acute PJIs and acute hematogenous PJIs (with <6 weeks of symptoms) were excluded from this study since we were not able to define a proper control group for them. A control group for acute infections would be patients following joint replacement undergoing a serum and synovial fluid investigation but proven not to be infected—isolating and defining the control cohort is challenging and rare. Different thresholds for acute infections have been suggested in the literature and we used the previous ICM thresholds for the parameters used. Although we believe these new criteria should apply also for acute and acute hematogenous infections, both the scoring system and the proposed thresholds require further validation on this specific population.
2. In this study, we used conventional cultures to diagnose and define positive growth. We did not use sonication or novel techniques such as Next-Generation Sequencing. More sensitive microbiological investigation methods are likely to reveal a potential infection in the absence of elevated serum and/or synovial markers. As these novel methods for isolation of organisms become more widespread, the newly proposed criteria should be validated once again.
3. For the current definition, a decision tree index (Gini) was used to point out the thresholds for the various markers evaluated that would provide maximal sensitivity and specificity for each marker based on chronicity and the pretest probability. When these thresholds were similar to the previous ICM definition, we

used the earlier one to ease its implementation. It should be pointed out that a variety of thresholds have been proposed in the literature and may be different from the ones proposed here. These differences may be attributed to the fact that we wanted to maximize sensitivity in early stages of the work-up and to maximize specificity in more advanced stages.

4. The present scoring system is not designed or intended to be used as a guide for which tests should be ordered; rather, it should be used as a tool to diagnose patients when a panel of tests are already available. Not all tests are needed to use this proposed definition and a preoperative diagnosis can be made without the need for intraoperative findings.
5. The proposed definition was developed and validated on both PJI cases of the knee and the hip. Although several publications have noted differences in the thresholds for synovial markers in PJI cases of the hip and the knee, we believe that the differences are minor. Thus, the new definition has not made a distinction between hip and knee PJI. Nevertheless, future studies should explore such potential difference between knee and hip PJIs.
6. Newer markers, such as the serum D-dimer, have not been sufficiently studied, and while we had sufficient data to analyze the new markers and include them in the definition, more work is needed to further validate their role in the diagnosis of PJIs. Moreover, their role and thresholds in diagnosing acute PJIs still remain unknown.
7. In patients with adverse local tissue reactions, crystalline deposition arthropathy, inflammatory arthropathy flares, infections with slow growing organisms, and patients under antibiotic treatment, the proposed criteria may be inaccurate. Moreover, there may be situations when a patient is infected and does not meet the diagnostic criteria and vice versa. Clinical judgment should still prevail and guide physicians in the management of patients.

Additionally, we wish to disclose that since its introduction earlier this year, the new diagnostic criteria have additionally been validated in patients treated in Japan and Brazil, as well as 84 patients from around the globe using a designated chatbot.

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