LABUPDATE no. 70

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SYNOVIAL FLUID C-REACTIVE PROTEIN (CRP)
Mnemonic: CRPSY

Background

Periprosthetic joint infection (PJI) remains one of the most serious complications following joint arthroplasty and is a leading cause of revision surgery.[1] Early and accurate diagnosis is essential to optimise patient management and clinical outcomes. Synovial fluid analysis plays a central role in distinguishing infectious from non-infectious joint inflammation. However, conventional diagnostic approaches such as microbial culture may be limited by delayed turnaround times, and reduced sensitivity in low-grade infections and prior antibiotic exposure.[2] In this context, synovial fluid C-reactive protein (CRP) has emerged as a highly sensitive adjunctive biomarker to support the diagnosis of PJI.[3,4]

Sample Handling

Synovial fluid specimens should be collected into a clear tube without preservatives or additives. Although every effort will be made to perform synovial fluid CRP testing, highly viscous samples may not be suitable for analysis.

Diagnostic Utility

The Musculoskeletal Infection Society (MSIS) and the International Consensus Meeting on Musculoskeletal Infection (ICM 2018) diagnostic criteria for PJI (Table 1) use a weighted scoring system based on major and minor criteria.[5] A definitive diagnosis is established by the presence of a major criterion (a sinus tract communicating with the prosthesis or two positive cultures of the same organism) or by achieving a cumulative score of ≥6 from minor criteria. Within this framework, synovial CRP is included as a weighted minor criterion. A synovial CRP concentration >6.9 mg/L contributes 1 point toward the total diagnostic score. Synovial CRP provides a localised measure of inflammation within the joint, and evidence suggests that local CRP concentrations may demonstrate greater specificity than serum levels due to increased vascular and synovial permeability at the site of infection.[6] When interpreted alongside other biomarkers and clinical findings, synovial CRP enhances overall diagnostic accuracy, particularly in cases where other findings are inconclusive. It should be regarded as supportive evidence within the scoring system rather than as a standalone diagnostic test.[3-6]

Table 1: ICM criteria for PJI definition[5]

Major criteria	Decision
Two positive cultures of the same organism	Infected
Sinus tract communicating with joint OR visualisation of the prosthesis	

		Minor criteria	Score	Decision
Preoperative	Blood	Serum CRP >10 mg/L or Plasma D-dimer > 0.86 mg/L	2	≥6 Infected
		Whole blood ESR >30 mm/h	1	2-5 Possibly infected [a]
	Synovial fluid	Synovial WBC count >3000 cells/µL or synovial LE ≥2+	3	
		Positive synovial alpha-defensin	3	0-1 Not infected
		Synovial PMN% >80%	2	
		Synovial CRP >6.9 mg/L	1	

	Inconclusive preoperative score or dry tap	Score	Decision
Intraoperative	Preoperative score	-	≥6 Infected
	Positive histology [b]	3	4-5 Possibly infected
	Positive intraoperative purulence	3	≤3 Not infected
	Single positive culture	2	

ICM, international consensus meeting; PJI, periprosthetic joint infection; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; WBC, white blood cell; LE, leukocyte esterase; PMN%, polymorphonuclear percentage.
[a] For patients with inconclusive minor criteria, operative criteria can also be used to fulfil definition for PJI.
[b] Greater than 5 neutrophils per high-power field in 5 high-power fields observed from histologic analysis of periprosthetic tissue at 400x magnification.

Important Interpretation Note

The MSIS and ICM criteria define a synovial fluid CRP concentration >6.9 mg/L as supportive of PJI.[5] However, increasing evidence indicates that assay-specific cut-off values should be applied.[7] Recent studies emphasise the importance of laboratory-specific validation and the establishment of method-dependent thresholds.[7,8] CRP measurement is known to be assay-dependent, and it has been demonstrated in published data that optimal diagnostic cut-off values vary according to the analytical platform used.[7,8] In our laboratory, the Beckman AU high-sensitivity CRP (hsCRP) assay is utilised for synovial CRP measurement. An assay-specific threshold of 4.45 mg/L is applied on the basis of published literature and internal validation data.[7] With this method, improved diagnostic performance has been demonstrated at this lower decision limit (sensitivity 86.1%, specificity 87.1%). All results should be interpreted in conjunction with clinical findings, imaging studies, microbiological results, synovial fluid leukocyte count and differential, and additional serum biomarkers. Synovial CRP should be regarded as a supportive diagnostic parameter within the comprehensive PJI scoring framework.

KEY MESSAGES

- Synovial fluid CRP testing is now available, and the mnemonic is CRPSY.
- It is used as a supportive biomarker for the diagnosis of PJI.
- An assay-specific cutoff of 4.45 mg/L is recommended to support the diagnosis of PJI.
- Results must be interpreted in the full clinical context.

References

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