HK11: In doubtful cases for periprosthetic joint infection, what is the best intraoperative test to confirm or refute the diagnosis?

Seyed Mohammad Javad Mortazavi, Pooya Hosseini-Monfared, Mohammed Kamal Abdelnasser, Mahmoud M Abdel Karim, Mohamed Elkabbani, Thanh Tu Dao, Irene Katharina Sigmund, Jacem Saadana, NK Hung Truong, Parag Sanchez

Response/Recommendation: The best intraoperative tests to confirm or refute the PJI based on the diagnostic accuracy, availability, time to result, and cost efficiency are leukocyte esterase, synovial fluid analysis, and frozen section.

Strength of recommendation: Moderate
Delegate Vote:

Rationale:

Reliable intraoperative diagnostic tests are essential for guiding appropriate treatment, minimizing unnecessary procedures, and improving patient outcomes, particularly in preoperative unclear cases. Diagnosis of periprosthetic joint infection (PJI) relies on a combination of tests on serum and synovial fluid as well as tissue samples. Because of the lack of a single absolute test for the diagnosis of PJI, the combination of these tests provides some degree of certainty related to the presence or absence of PJI in a painful prosthetic joint (REF-ICM definition and other references).put these in However, despite performing these tests occasionally, diagnosis of PJI is not possible, or an unexpected finding during revision surgery prompts surgeons to seek additional data to confirm or refuse the diagnosis of PJI. The question posed above is seeking tests that can easily be performed during surgery in order to provide additional data.

To answer the above question, a comprehensive systematic review was conducted. Using the MeSH terms developed by librarians, the Medline, Scopus, Web of Science, and Embase databases were searched to identify relevant studies. 964 potentially eligible studies were identified. After screening by two observers, 887 were excluded, leaving 77 studies for inclusion in this review (**Table 1)**.

Table 1: Summary of pooled diagnostic accuracy metrics for intraoperative tests used in the detection of PJI

Test	Number of Studies	Total Patients	Number of PJI cases	Pooled Sensitivity (%)	Pooled Specificity (%)	Pooled LR+	Pooled LR-	DOR	Availability	Time to Results	Cost
Alpha Defensin	15	1,259	333	85.78	96.29	18.58	0.11	119.25	Limited	<15 minutes	High
Frozen Section	27	3,755	649	71.47	93.85	9.20	0.28	33.97	Moderately available	>1 hour	Moderate
Calprotectin	11	786	262	90.08	89.77	7.33	0.11	73.84	Limited	<15 minutes	Moderate
Leukocyte Esterase	14	1,368	384	82.52	93.75	7.95	0.15	54.82	Widely available	<15 minutes	Low
Synovial Fluid Analysis	7	636	200	79.44	85.59	5.26	0.21	26.36	Widely available	15 minutes – 1 hour	Low
PCR – Synovial Fluid	4	341	161	67.38	88.65	-	-	-	Limited	>1 hour	High
PCR – Tissue Samples	6	381	209	83.7	98.68	16.85	0.12	143.98	Limited	>1 hour	High
PCR – Sonication Fluid	3	228	107	63.2	84.1	-	-	-	Limited	>1 hour	High
D-Lactic Acid	2	258	86	(83-86)	(82-100)	-	-	-	Moderately available	15 minutes – 1 hour	Moderate
NGAL	1	86	23	92	83	-	-	-	Limited	15 min – 1 hour	High
IL-6 Lateral Flow	1	26	-	46.88	97.62	-	-	-	Limited	<15 minutes	High

Pooled LR +: pooled positive likelihood ratio, Pooled LR -, Pooled negative likelihood ratio; DOR: Diagnostic Odds Ratio.

PCR= mmm; NGAL =. Mmm; put in rest of abbreviations

Based on our analyses of the studies, the tests that can be performed during surgery, both from the perspective of time and need logistics, were included in the final recommendation.

Alpha Defensin

Alpha defensin demonstrates high specificity (96.29%) and good sensitivity (85.78%), with the advantage of being performed intraoperatively using lateral flow devices for rapid results and reduced operator dependency compared to histopathology [1-15]. However, its use is limited by the high cost of commercial test kits and the potential for false positives in cases of metallosis or inflammatory arthropathies, though these occurrences are rare.

Histopathology and Frozen Section

Frozen section is a traditional and widely used intraoperative method that allows direct visualization of polymorphonuclear leukocytes (PMNs) in tissue, providing valuable diagnostic insights [6, 9, 16-40]. However, it is operator-dependent, requires an experienced pathologist, and has moderate sensitivity (71.47%) with a risk of sampling error.

Calprotectin

Calprotectin offers high sensitivity (90.08%) and good specificity (89.77%), with lateral flow test kits enabling rapid intraoperative results similar to alpha defensin [41-51]. However, its use is limited by less available data compared to alpha defensin and potential issues with cost and availability depending on the setting.

Leukocyte Esterase

Leukocyte esterase (LE) is a rapid and inexpensive diagnostic option for periprosthetic joint infections (PJI), utilizing a readily available urine dipstick test with reasonable specificity (93.75%) and sensitivity (82.52%) [22, 27, 52-63]. However, its subjective colorimetric interpretation can lead to errors, and its sensitivity is limited for detecting low-grade infections.

Synovial Fluid Analysis

Synovial fluid aspiration and evaluation of WBC and PMN counts were suggested as a diagnostic tool for PJI. The pooled sensitivity and specificity of the synovial fluid analysis were 79.44 and 85.59% based on the results of four studies [1, 43, 51, 52, 59, 64].

Polymerase chain reaction testing

A PCR ***(polymerase chain reaction) test*** on tissue samples offers the highest diagnostic accuracy, with excellent specificity (98.68%) and good sensitivity (83.7%), making it especially valuable for identifying difficult-to-culture and low-virulence pathogens [5, 7, 11, 35, 65-75]. However, its use is limited by the need for specialized molecular biology facilities, higher costs, and limited availability as a rapid intraoperative test.

Other Tests

Other tests including D-lactic acid, NGAL, and IL-6 lateral flow have limited evidence or practical constraints that restrict their routine use in diagnosing periprosthetic joint infections (PJI) [5, 52, 53, 76, 77]. Using D-lactic acid shows promise as a biochemical marker, but lacks robust studies and is not widely available intraoperatively. A NGAL test demonstrates high sensitivity (92%) in

a single study but lacks validation across cohorts. The IL-6 lateral flow test offers rapid point-of-care testing with high specificity (97.62%) but suffers from very low sensitivity (46.88%) and limited supporting evidence, reducing its standalone utility.

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