Synovasure® Diagnostics

2018 ICM Proposed Criteria for Diagnosing PJI

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Newly proposed criteria for PJI by the 2nd ICM.

Voting at the 2018 ICM Meeting showed that in the absence of any major criteria, not only was alpha defensin a valuable complement to existing diagnostic minor criteria for PJI but was also given significant individual test weight in the newly proposed scoring system for diagnosing PJI, as can be seen in the table below:

2018 ICM Definition of PJI:

Major Criteria includes:	Decision
Two positive periprosthetic cultures with phenotypically identical organisms	Infected
A sinus tract communicating with the joint	

Institution	Threshold		Score	Decision
	Acute*	Chronic		
Serum CRP (mg/L)	100	10	2	Combined preoperative and postoperative score: ≥ 6 = Infected 4-5 = Inconclusive** ≤ 3 = Not Infected
or				
D-Dimer (µg/L)	Unknown	860		
Elevated Serum ESR (mm/hr)	No role	30	1	
Elevated Synovial WBC (cells/µL)	10,000	3,000	3	
or				
Leukocyte Esterase	++	++		
or				
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	

Proceed with caution in: Adverse local tissue reaction, crystal deposition disease and slow growing organisms.

**Further studies needed to validate a specific threshold.*

***Consider further molecular diagnostics such as next-generation sequencing.*

****Has no role in patients with suspected adverse local tissue reaction.*

Key Takeaways

- ***Alpha defensin is recommended as important diagnostic marker for PJI***
- ***Alpha defensin lateral flow/rapid test device is recommended for use in PJI diagnostics***
- ***Alpha defensin is part of the newly proposed ICM PJI algorithm with a high score of 3 points***

Role of Alpha Defensin in Supporting PJI Diagnosis

What is the International Consensus Meeting on Periprosthetic Joint Infection?

The International Consensus Meeting (ICM) on Periprosthetic Joint Infection (PJI) addresses the wide variation globally for prevention, diagnosis and treatment of PJI. Currently, a single test that serves as the "gold standard" to aid in the diagnosis of PJI does not exist. As a result, a wide spectrum of tests to diagnose the condition are utilized.

In August 2013, the 1st International Consensus Meeting (ICM) convened to address the global variations in prevention, diagnosis and treatment of PJI. The 400 global experts in attendance voted, with strong consensus, on criteria proposed in the summer of 2011 by a MSIS workgroup to define infection and allow for a more standardized approach to supporting the diagnosis of PJI. The criteria included:

2013 ICM Definition of PJI[1]

Major Criteria includes:	Decision
Two positive periprosthetic cultures with phenotypically identical organisms	Infected
A sinus tract communicating with the joint	

Minor Criteria	Threshold		Decision
	Acute	Chronic	
Elevated Serum ESR (mm/hr) and Serum CRP (mg/L)	N/A 100	30 10	PJI is present if at least 3 out of 5 minor criteria exist
Elevated Synovial WBC (cells/µL) or Leukocyte Esterase	10,000 + or ++	3,000 + or ++	
Elevated Synovial PMN (%)	90	80	
Positive Histological Analysis of Periprosthetic Tissue	> 5 neutrophils per high power field in 5 high power fields (x400)	> 5 neutrophils per high power field in 5 high power fields (x400)	
Single Positive Culture			

The 2nd International Consensus Meeting on Musculoskeletal Infection (2018)[2]

In July 2018, the 2nd ICM convened, comprising of 546 global delegates in attendance, to evaluate and vote, in real-time, on modifications to the 2013 criteria. Among the 652 questions considered for the meeting, three (3) were related to the role of alpha defensin and, specifically, Synovasure Diagnostics:

Question (as posed to delegates):

What is the role of alpha defensin in the diagnosis of PJI?

Recommendation by ICM: Measurement of alpha defensin in synovial fluid is a valuable complement to existing diagnostic criteria for PJI.

Delegates were provided with the following clinical study data on the topic[3]:

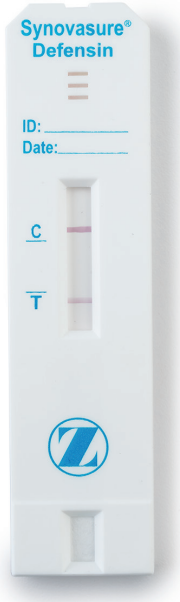
Institution	N	Gold Standard	Sensitivity	Specificity
Rothman Institute	156	MSIS Criteria	97% (36/37)	96% (107/112)
Mayo Arizona	61	MSIS Criteria	100% (33/33)	95% (83/87)
Cleveland Clinic	111	MSIS Criteria	100% (24/24)	98% (53/54)
ENDO Klinik	156	MSIS Criteria	97% (28/29)	97% (123/127)
Cleveland Florida	70	MSIS Criteria	97% (34/35)	97% (34/35)
Combined	**547**		**98.1% (95%CI: 95-100%)**	**96.4% (95%CI: 94-98%)**

Delegate Voting: Super Majority | Strong Consensus

Question (as posed to delegates)

Are point-of-care/rapid tests for diagnosing periprosthetic joint infections (PJIs) validated and useful?

Recommendation by ICM: Yes, there are several useful point-of-care tests which can be added to the diagnostic workup of PJIs. A number of studies support the usefulness and reliability of the leukocyte esterase (LE) test strip and the alpha defensin lateral flow test kit. Diagnostic criteria for PJIs should be updated and consider inclusion of these tests.



Synovasure Lateral Flow is the only rapid test available on the market that utilizes Alpha Defensin biomarker to diagnose PJI equating to more reliable results.

Delegates were provided with the following clinical study data on the topic[3]:

Author	N	PJIs	Gold Standard	Sensitivity (95%CI)	Specificity (95%CI)
Berger *et al.*	121	34	MSIS	97% (85-100)	97% (90-99)
Gehrke *et al.*	223	76	MSIS	92% (84-97)	100% (97-100)
Renz *et al.*	212	45	MSIS	84% (71-94) 94% (excluding sinuses)	96% (92-99)

Note: Smaller studies were deemed difficult to draw conclusions from due to very small numbers (N) and very large confidence intervals.[4]

Delegate Voting: Super Majority | Strong Consensus

References

1. Parvizi J, Gehrke T; International Consensus Group on Periprosthetic Joint Infection. Definition of periprosthetic joint infection. J Arthroplasty. 2014 Jul;29(7):1331. doi:0.1016/j.arth.2014.03.009. Epub 2014 Mar 21.
2. Second International Consensus Meeting (ICM) on Musculoskeletal Infection (Website). https://icmphilly.com/
3. Part II: Hip and Knee. https://icmphilly.com/document/icm-2018-hip-and-knee-document/
4. Bauer, T. *et al.* Hip and Knee Section, Diagnosis, Laboratory Tests: Proceedings of International Consensus on Orthopedic Infections. The Journal of Arthroplasty. Publication. doi: 10.1016/j.arth.2018.09.019.

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