Critères diagnostiques microbiologiques

Faut il utiliser un score diagnostique ?

Amittimus nostrum latinum !

Didier Tandé, Claudie Lamoureux, Luc Quaesaet

La Team brestoise

Quelques mots d'Histoire …

- **Au commencement il y avait … 2009**

Recommandations de pratique clinique

Infections ostéo-articulaires sur matériel

(prothèse, implant, ostéosynthèse)

Texte court

Organisées par

la Société de Pathologie Infectieuse de Langue Française (SPILF)

Quelques mots clés…

L'existence d'une **fistule** à proximité de la prothèse **affirme l'infection** jusqu'à preuve du contraire **(niveau3).**

L'absence de signes inflammatoires cliniques locaux et généraux **ne permet pas d'éliminer** une infection sur prothèse **(niveau 2).**

Aucun paramètre biologique n'est à lui seul spécifique de l'infection sur prothèse.

Il est fortement recommandé de réaliser une radiographie standard même si 50 % d'entre-elles restent normales et s'il **n'existe aucun signe radiographique formel** d'infection sur matériel **(grade B).**

Il est recommandé, dans tous les cas, de réaliser un examen anatomopathologique intéressant le tissu osseux et la synoviale.

2.5.1 Infection certaine

- Présence d'une **fistule** au contact de la prothèse ou de l'implant **(niveau 3),**
- Présence de pus dans l'articulation ou au contact de la prothèse ou de l'implant **(avis d'expert)**,
- Présence **d'au moins 3 prélèvements** … positifs au(x) même(s) bactérie(s) **appartenant à la flore cutanée** … et dont l'isolement pose la question d'une éventuelle contamination **(niveau 2)**,
- Présence **d'au moins 1 prélèvement positif** … à une bactérie n'appartenant pas à la flore cutanée et pour lequel **la question d'une contamination ne se pose pas** … **(avis d'expert)**.

2.5.2 Infection probablement exclue ou non détectable

En l'absence de fistule ou de pus dans l'articulation ou au contact de l'implant, une infection est considérée **comme probablement exclue ou non détectable** s'il existe l'un des critères suivants :

- **tous les prélèvements per opératoires sont stériles** (à condition d'avoir été réalisés après 15 jours d'arrêt de toute antibiothérapie) et lorsqu'il n'existe **aucun signe histologique** d'infection **(niveau 2)**,

- **1 seul prélèvement per opératoire est positif à un germe de la flore cutanée** … **sans signe histologique** d'infection et avec **moins de 65 % de polynucléaires neutrophiles** dans le liquide de ponction articulaire **(niveau 2)**.

- Dans ces 2 situations, **une CRP < 10 mg/**l peut conforter l'absence d'infection**.**

HAUTE AUTORITÉ DE SANTÉ

SYNTHÈSE DE LA RECOMMANDATION DE BONNE PRATIQUE

Prothèse de hanche ou de genou : diagnostic et prise en charge de l'infection dans le mois suivant l'implantation

Mars 2014

Repérage et diagnostic de l'infection sur prothèse dans le mois suivants l'implantation

Algorithme

- Repérage d'une infection précoce
- Quels sont les signes cliniques en faveur de l'infection
- Quelle place pour les examens complémentaires dans le diagnostic ?
- Place de la bactériologie

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AE	Les signes cliniques locaux qui **affirment** l'infection sur prothèse sont : • écoulement purulent ; • abcès ; • fistule.
AE	Il est recommandé de réaliser un dosage du taux sérique de la CRP devant l'existence de signes cliniques évocateurs. Si le diagnostic n'est pas établi, il est recommandé de répéter le dosage du taux sérique de la CRP.
AE	Aucun examen d'imagerie n'est nécessaire pour le diagnostic d'infection précoce. Seule l'échographie peut être utile pour guider une ponction au niveau de la hanche.
AE	**En cas de doute diagnostique**, il est recommandé de réaliser systématiquement et rapidement une ponction articulaire à visée diagnostique et bactériologique. Cette ponction doit être réalisée même s'il y a une antibiothérapie préalable. Un résultat négatif n'élimine pas le diagnostic d'infection, il faut alors répéter la ponction après une « fenêtre » (suspension de l'antibiothérapie) d'au moins 72 h.
AE	Il est nécessaire d'informer le laboratoire et de traiter sans délai les prélèvements au laboratoire. L'acheminement, l'accueil du prélèvement au laboratoire, la qualité des cultures, les techniques additionnelles et la conservation des souches sont décrits en annexe 3. En cas de difficulté d'acheminement (supérieur à 2 h), il est recommandé d'ensemencer directement une partie du liquide articulaire sur flacons d'hémoculture. L'analyse cytologique (recherche de polynucléaires neutrophiles altérés et de microcristaux) doit être systématique si les conditions le permettent.

Enfin il est arrivé …

Clin Orthop Relat Res (2011) 469:2992–2994
DOI 10.1007/s11999-011-2102-9

Clinical Orthopaedics and Related Research®
A Publication of The Association of Bone and Joint Surgeons®

SYMPOSIUM: PAPERS PRESENTED AT THE 2010 MEETING OF THE MUSCULOSKELETAL INFECTION SOCIETY

New Definition for Periprosthetic Joint Infection

From the Workgroup of the Musculoskeletal Infection Society

Javad Parvizi MD, Benjamin Zmistowski BS, Elie F. Berbari MD, Thomas W. Bauer MD, PhD, Bryan D. Springer MD, Craig J. Della Valle MD, Kevin L. Garvin MD, Michael A. Mont MD, Montri D. Wongworawat MD, Charalampos G. Zalavras MD

The intention of this proposal is to have a **"gold standard"** definition for PJI that can be **universally adopted by all physicians, surveillance authorities** (including the Centers for Disease Control medical and surgical journals, the medicolegal community)

The panel acknowledged, **in certain low-grade infections** (ie, Propionibacterium acnes), several of **these criteria may not be routinely met despite the presence of PJI**.

Definition of Periprosthetic Joint Infection

Based on the proposed criteria, definite PJI exists when:

(1) There is a sinus tract communicating with the prosthesis; or

(2) A pathogen is isolated by culture from **at least two separate tissue or fluid** samples obtained from the affected prosthetic joint; or

(3) **Four of the following six criteria exist**:

(a) Elevated serum erythrocyte sedimentation rate (ESR) and serum C-reactive protein (CRP)
(b) Elevated synovial leukocyte count,
(c) Elevated synovial neutrophil percentage (PMN%),
(d) Presence of purulence in the affected joint,
(e) Isolation of **a microorganism in one culture** of periprosthetic tissue or fluid, or
(f) Greater than five neutrophils per high-power field in five high-power fields observed from histologic analysis of periprosthetic tissue at x400 magnification.

Mais : PJI may be present if fewer than four of these criteria are met.
Isolation of **a single virulent organism** such as *S. aureus* **may represent** a PJI

Diagnosis and Management of Prosthetic Joint Infection: Clinical Practice Guidelines by the Infectious Diseases Society of America[a]

IDSA GUIDELINES

Clinical Infectious Diseases 2013;56(1):1–10

Douglas R. Osmon,[1] Elie F. Berbari,[1] Anthony R. Berendt,[2] Daniel Lew,[3] Werner Zimmerli,[4] James M. Steckelberg,[1] Nalini Rao,[5,6] Arlen Hanssen,[7] and Walter R. Wilson[1]

What preoperative evaluation and intraoperative testing should be performed to diagnose PJI and **what is the definition of PJI?**

The presence of a **sinus tract** **definitive evidence** of PJI (B-III).

Histopathologic examination **highly suggestive evidence** of PJI (B-II).

The presence of **purulence** **definitive evidence** of PJI (B-III).

≥ 2 intraoperative cultures **definitive evidence** of PJI.

A virulent microorganism in a single specimen may also **represent PJI**.

Mais

The presence of PJI is possible even if the above criteria are not met

The clinician should use his/her clinical judgment to determine if this is the case after reviewing all the available preoperative and intraoperative information (B-III).

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■ SPECIALTY UPDATE: ARTHROPLASTY

Proceedings of the International Consensus on Periprosthetic Joint Infection

J. Parvizi, T. Gehrke, A. F. Chen

Bone Joint J 2013;95-B:1450–2.

Question 1A: What is the definition of periprosthetic joint infection (PJI)?

Consensus

PJI is defined as:

- Two positive periprosthetic cultures with phenotypically identical organisms, or
- A sinus tract communicating with the joint, or
- Having three of the following minor criteria: **(5)**

  - Elevated serum C-reactive protein (CRP) AND erythrocyte sedimentation rate (ESR)
  - Elevated synovial fluid white blood cell (WBC) count OR ++change on leukocyte esterase test strip
  - Elevated synovial fluid polymorphonuclear neutrophil percentage (PMN%)
  - Positive histological analysis of periprosthetic tissue
  - A single positive culture **(?)**

Delegate Vote

Agree: 85%, Disagree: 13%, Abstain: 2% (Strong Consensus)

- 400 spécialistes en IOA de 52pays
- 15 groupes de travail selon thématiques
- Analyse de la littérature, débats, proposition d'un consensus
- Soumis au vote de l'assemblée générale

Mais

Clinically, PJI **may be present without meeting these criteria**, specifically in the case of less virulent organisms (e.g., P. acnes).

Alors pourquoi des scores …

Existing guidelines were largely generated by expert opinions and **have not been validated.**

Furthermore, while relatively specific, there is **concern about the sensitivity** of the current definitions .

Although definite evidence or major criteria for infection are identical between the different definitions, the **supportive evidence or minor criteria differ and are less agreed upon.**

Moreover, publications in the recent years have shown **different weights** (sensitivity and specificity) for the various tests used.

Invasiveness of the tests in the previous criteria : this can make the preoperative diagnosis of infection extremely difficult.

Parvizi 2018

The Journal of Arthroplasty 33 (2018) 1309–1314

Contents lists available at ScienceDirect

The Journal of Arthroplasty

journal homepage: www.arthroplastyjournal.org

The 2018 Definition of Periprosthetic Hip and Knee Infection: An Evidence-Based and Validated Criteria

Javad Parvizi, MD [a,*], Timothy L. Tan, MD [a], Karan Goswami, MD [a], Carlos Higuera, MD [b], Craig Della Valle, MD [c], Antonia F. Chen, MD, MBA [a], Noam Shohat, MD [a,d]

- Elaboration d'un système de score en prenant en compte les poids respectifs des tests :

  684 PJI et 820 aseptiques en Rétrospectif

- Validation externe :

  222 PJI et 200 aseptiques en Rétrospectif

- Inclusions :

  Infections chroniques uniquement

  Critères majeurs uniquement

- Comparaison avec les anciennes définitions

Table 2
Simple Importance Based on Random Forest and Beta Coefficients Derived From a Multivariate Regression Analysis of Each Step.

Step	Random Forest	Beta	Standard Error	*P* Value	Score
Step 1					
Serum CRP >1 mg/dL[a]	198	2.48	0.28	<.001	2
Serum D-dimer > 860 ng/mL[a]	134	2.41	0.62	<.001	2
Serum ESR >30 mm/h	112	1.39	0.29	<.001	1
Step 2					
Synovial WBC count >3000 (cells/μL)[a]	109	2.65	0.80	.001	3
Synovial alpha-defensin	79	2.64	1.24	.041	3
Synovial LE (++)[a]	63	2.56	1.02	.017	3
Synovial PMN% >80%	47	1.73	0.92	.121	2
Synovial CRP >6.9 mg/L	22	0.85	1.12	.449	1
Step 3					
Histology[b]	17	3.21	1.02	.002	3
Purulence	12	3.47	1.32	.007	3
Single culture	8	2.25	1.45	.122	2

CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; LE, leukocyte esterase; PMN%, polymorphonuclear %; WBC, white blood cell.

[a] The following demonstrated a high collinearity ($r > 0.7$) and thus were grouped into a single criterion in the final model.

[b] Greater than 5 neutrophils per high-power field in 5 high-power fields observed from histologic analysis of periprosthetic tissue at 400× magnification.

Table 4
Proposed Thresholds Based on the 2013 ICM Combined With Current Findings.

Marker	Chronic (>90 d)	Acute (<90 d)
Serum CRP (mg/dL)	1.0	10
Serum D-dimer (ng/mL)	860	860[a]
Serum ESR (mm/h)	30	-
Synovial WBC count (cells/μL)	3000	10,000
Synovial PMN (%)	80	90
Synovial CRP (mg/L)	6.9[a]	6.9
Synovial alpha-defensin (signal-to-cutoff ratio)	1.0	1.0

CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; ICM, International Consensus Meeting; PMN, polymorphonuclear; WBC, white blood cell.

[a] Further studies are needed to validate a specific threshold.

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

		Minor Criteria	Score	Decision
Preoperative Diagnosis	Serum	Elevated CRP *or* D-Dimer	2	≥6 Infected
		Elevated ESR	1	
	Synovial	Elevated synovial *WBC count or LE*	3	2-5 Possibly Infected [a]
		Positive alpha-defensin	3	
		Elevated synovial PMN (%)	2	0-1 Not Infected
		Elevated synovial CRP	1	

	Inconclusive pre-op score *or* dry tap [a]	Score	Decision
Intraoperative Diagnosis	Preoperative score	-	≥6 Infected
	Positive histology	3	4-5 Inconclusive [b]
	Positive purulence	3	
	Single positive culture	2	≤3 Not Infected

Fig. 1. New scoring based definition for periprosthetic joint infection (PJI). Proceed with caution in: adverse local tissue reaction, crystal deposition disease, slow growing organisms. CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; LE, leukocyte esterase; PMN, polymorphonuclear; WBC, white blood cell. [a]For patients with inconclusive minor criteria, operative criteria can also be used to fulfill definition for PJI. [b]Consider further molecular diagnostics such as next-generation sequencing.

>80% des PJI diagnostiquées AVANT la chirurgie

Aspiration = pierre angulaire du diagnostic

Table 5

Patients in Whom the Proposed Criteria May Be Inaccurate.

Red Flag Patients
Adverse local tissue reaction (ALTR)
Crystalline deposition arthropathy
Inflammatory arthropathy flare
Infection with slow growing organisms[a]

[a] Such as *Propionibacterium acnes*, coagulase negative *Staphylococcus*, and others.

Consider further molecular diagnostics such as NGS

Table 3

Performance of the New Definition Compare With the Traditionally Used Musculoskeletal Infection Society (MSIS) and International Consensus Meeting (ICM) Criteria.

Criteria	PJI Cohort (n = 222)			Aseptic Cohort (n = 200)			Sensitivity (95% CI)	Specificity (95% CI)
	True Positives	False Negatives	Inconclusive	True Negative	False Positives	Inconclusive		
MSIS (2011)	176 (79.3%)	46 (20.7%)	-	199 (99.5%)	1 (0.5%)	-	79.3% (73.4-84.4)	99.5% (97.3-99.99)
ICM (2013)	193 (86.9%)	29 (13.1%)		199 (99.5%)	1 (0.5%)		86.9% (81.8-91.1)	99.5% (97.3-99.99)
New definition (2018)	212 (95.5%)	5 (2.3%)	5 (2.3%)	195 (97.5%)	1 (0.5%)	4 (2.0%)	97.7% (94.7-99.3)	99.5% (97.2-99.99)

CI, confidence interval; PJI, periprosthetic joint infection.

Finally, while we show an excellent performance, clinical judgment should still prevail and guide physicians in management of patients

A t-on avancé ?

The Journal of Arthroplasty 33 (2018) 1309–1314

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The Journal of Arthroplasty 34 (2019) S325–S327

Contents lists available at ScienceDirect

The Journal of Arthroplasty

journal homepage: www.arthroplastyjournal.org

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

Noam Shohat, Thomas Bauer, Martin Buttaro, Nicolaas Budhiparama, James Cashman, ...

MSIS

ICM

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

	Minor Criteria	Score	Decision
Preoperative Diagnosis – Serum	Elevated CRP *or* D-Dimer	2	≥6 Infected
Preoperative Diagnosis – Serum	Elevated ESR	1	
Preoperative Diagnosis – Synovial	Elevated synovial *WBC count or LE*	3	2-5 Possibly Infected [a]
Preoperative Diagnosis – Synovial	Positive alpha-defensin	3	
Preoperative Diagnosis – Synovial	Elevated synovial PMN (%)	2	0-1 Not Infected
Preoperative Diagnosis – Synovial	Elevated synovial CRP	1	

	Inconclusive pre-op score *or* dry tap [a]	Score	Decision
Intraoperative Diagnosis	Preoperative score	-	≥6 Infected
Intraoperative Diagnosis	Positive histology	3	4-5 Inconclusive [b]
Intraoperative Diagnosis	Positive purulence	3	
Intraoperative Diagnosis	Single positive culture	2	≤3 Not Infected

Fig. 1. New scoring based definition for periprosthetic joint infection (PJI). Proceed with caution in: adverse local tissue reaction, crystal deposition disease, slow growing organisms. CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; LE, leukocyte esterase; PMN, polymorphonuclear; WBC, white blood cell. [a]For patients with inconclusive minor criteria, operative criteria can also be used to fulfill definition for PJI. [b]Consider further molecular diagnostics such as next-generation sequencing.

≠

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
or				
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	
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	

[€] 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

DELEGATE VOTE: Agree: 68%, **Disagree: 28%**, Abstain: 4% (Super Majority, Weak Consensus)

*En 2013 : Delegate Vote Agree: 85%, **Disagree: 13%**, Abstain: 2% (Strong Consensus)*

Peut on critiquer Javad ?

- Pas validé pour les infections aigües
- Elaboré et validé avec des cultures ‘’conventionnelles’’
- Cut-off non différenciés pour PTH et PTG
- D-Dimers sériques pas assez étudiés
- Critères peut être inadaptés dans certaines situations (cf avant)
- At last but not the least : ICM ≠ MSIS 2018
  - ☞ ICM = score combiné préop + intraop
  - ☞ validation du score faite sur les critères de la 1ère version
  - ☞ pas de validation sur la version de l’ICM 2018 ???

The Journal of Arthroplasty 32 (2017) S232–S235

Contents lists available at ScienceDirect

The Journal of Arthroplasty 2017

journal homepage: www.arthroplastyjournal.org

Complications - Infection

Diagnosing Periprosthetic Joint Infection: And the Winner Is?

Alisina Shahi, MD, Timothy L. Tan, MD, Michael M. Kheir, MD, Dean D. Tan, Javad Parvizi, MD, FRCS *

Conclusion: Based on our findings, it appears that among the minor diagnostic criteria, **LE has the best performance**.

Contents lists available at ScienceDirect

The Journal of Arthroplasty 2021

journal homepage: www.arthroplastyjournal.org

Leukocyte Esterase Versus ICM 2018 Criteria in the Diagnosis of Periprosthetic Joint Infection

Emanuele Chisari, MD [a], Steven Yacovelli, MD [a], Karan Goswami, MD [a], Noam Shohat, MD [a, b], Paul Woloszyn, BS [a], Javad Parvizi, MD, FRCS [a, *]

The Journal of Arthroplasty xxx (2021) 1–6

Utiliser le cut-off LE1+ (trace ou absence) pour exclure
Utiliser le cut-off LE2+ quasi spécifique de l'infection

Contents lists available at ScienceDirect

The Journal of Arthroplasty 2021

journal homepage: www.arthroplastyjournal.org

Which International Consensus Meeting Preoperative Minor Criteria is the Most Accurate Marker for the Diagnosis of Periprosthetic Joint Infection in Hip and Knee Arthroplasty?

Ali Levent, MD [a, b], Michael E. Neufeld, MD, MSc [a], Pongsiri Piakong, MD [a, c], Christian Lausmann, MD [a], Thorsten Gehrke, MD [a], Mustafa Citak, MD, PhD [a, *]

The diagnostic performance of preoperative minor criteria was **outstanding (PMN%, alpha defensin, white blood cell count**) or excellent (leukocyte esterase, serum C-reactive protein).
PMN% showed the best diagnostic utility (area under the curve) and should have an increased weight-adjusted score in the ICM scoring system.

2018

Alpha Defensin Lateral Flow Test for Diagnosis of Periprosthetic Joint Infection

Not a Screening but a Confirmatory Test

Nora Renz, MD, Katsiaryna Yermak, MD, Carsten Perka, MD, and Andrej Trampuz, MD

α-défensine rapide et Sp ≥ 95% mais Se limitée

⇨ test de confirmation

The Journal of Arthroplasty xxx (2021) 1–7

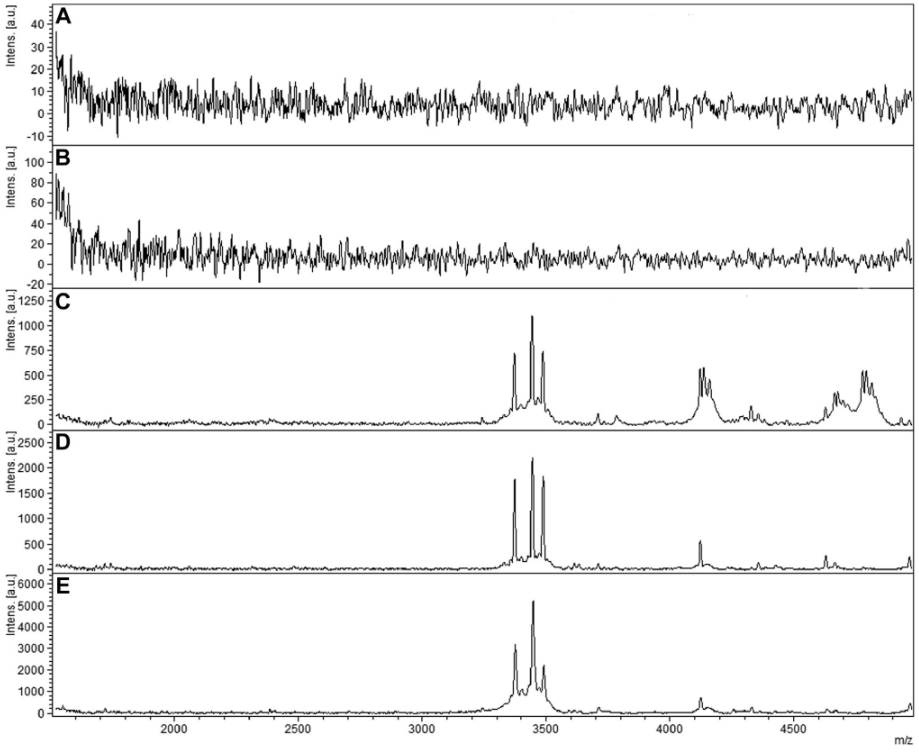
Contents lists available at ScienceDirect

The Journal of Arthroplasty

journal homepage: www.arthroplastyjournal.org

"Accuracy and Cost-Effectivenss of a Novel Method for Alpha Defensins Measurement in the Diagnosis of Periprosthetic Joint Infections"

Raffaele Iorio, PhD [a, b], Edoardo Viglietta, MD [a, b, *], Daniele Mazza, MD [b], Andrea Petrucca, PhD [d], Marina Borro, PhD [a, c], Santino Iolanda, PhD [a, d], Maurizio Simmaco, PhD [a, c, d], Andrea Ferretti, PhD [a, b]



Designed by Lénaïg Tandé

138 patients avec révision

MSIS 2018 >>> 59 Prothèses infectées

Test MT : positif pour 55/59 des infectées
: négatif pour 76/79 des non infectées

Se = 93% Sp = 96% VPN = 95% VPP = 95%

Journal of Clinical Medicine

MDPI

Concept Paper

The W.A.I.O.T. Definition of High-Grade and Low-Grade Peri-Prosthetic Joint Infection

2019

Carlo Luca Romanò [1,2], Hazem Al Khawashki [3], Thami Benzakour [4], Svetlana Bozhkova [5,6], Hernán del Sel [7], Mahmoud Hafez [8], Ashok Johari [9], Guenter Lob [10], Hemant K Sharma [11], Hirouchi Tsuchiya [12] and Lorenzo Drago [13,*] on behalf of The World Association against Infection in Orthopedics and Trauma (W.A.I.O.T.) Study Group on Bone and Joint Infection Definitions

Journal of Clinical Medicine

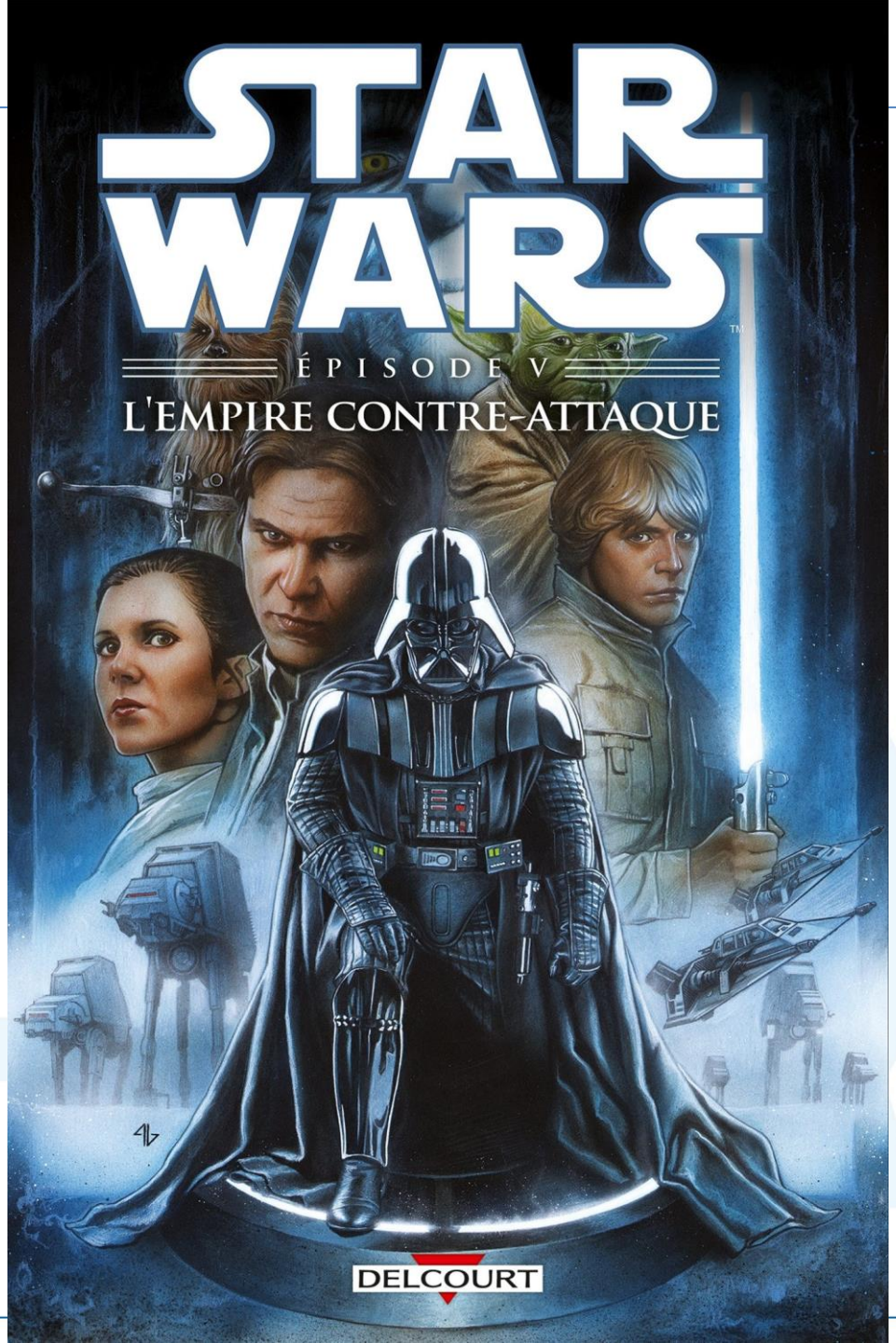
MDPI

Article

The W.A.I.O.T. Definition of Peri-Prosthetic Joint Infection: A Multi-center, Retrospective Validation Study

2020

Svetlana Bozhkova [1,2], Virginia Suardi [3], Hemant K Sharma [4], Hiroyuki Tsuchiya [5], Hernán del Sel [6], Mahmoud A. Hafez [7], Thami Benzakour [8], Lorenzo Drago [9] and Carlo Luca Romanò [10,11,*] on behalf of The World Association against Infection in Orthopedics and Trauma (W.A.I.O.T.) Study Group on Bone and Joint Infection Definitions



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Pourquoi une nouvelle définition ?

- ➢ Au moins 5 définitions en 10 ans
- ➢ pas de vrai test référence sur lequel se comparer >>> biais dans les classifications
- ➢ Des tests parfois chers et non disponibles
- ➢ Résultats ‘’inconclusives’’
- ➢ Pas prise en compte de l’imagerie

☞ **Proposition d’un nouveau score basé sur la capacité des test à exclure ou à inclure le diagnostic**

- ➢ Choix des cut-off des tests pour :

  une Se maximale (≥90%) pour exclure : Rule OUT

  une Sp maximale (≥90%) pour inclure : Rule IN

Un test Rule OUT négatif = -1

Un test Rule IN positif = +1

Les scores des tests Rule OUT positifs et des tests Rule IN négatifs sont cotés 0.

à Se égales même poids et à Sp égales même poids

Table 10. Rule In and Rule Out tests of the modified WAIOT PJI.

Definition.	Rule In Tests	Rule Out Tests
Clinical examination	Draining sinus or exposed joint prosthesis *	
Serum	IL-6 (>10 pg/mL) ** PC (>0.5 ng/mL) ** D-Dimer (>850 ng/mL) **	ESR (>30 mm/h) *** CRP (>10 mg/L) ***
Synovial fluid	Cultural examination ** WBC (>3000/mL) ** LE (++) ** AD immuunoassay (>5.2 mg/L) or lateral flow test **	WBC (>1500/µL) *** LE (++) *** AD immunoassay (>5.2 mg/L) ***
Imaging	Combined leukocyte and bone marrow scintigraphy **	Tc99 bone scan ***
Histology	Frozen section (5 neutrophils in ≥3 HPFs **	

* If positive, consider as infected; ** Positive Test Scores +1; *** Negative Test Scores −1. Abbreviations: WAIOT: World Association against Infection in Orthopedics and Trauma; ESR: Erythrocyte sedimentation rate; CRP: C-reactive protein; IL-6: Interleukin-6; WBC: White blood cell count; PC: Procalcitonin; LE: Leukocyte esterase strip (++); AD: Alpha-defensin; HPFs: High power fields (×400).

Table 9. Modified WAIOT Definition of peri-prosthetic joint infection (PJI). The presence of a sinus or an exposed implant is considered as a pathognomonic sign of infection.

	No Infection	Contamination	BIM	LG-PJI	HG-PJI
Clinical presentation	One or more condition(s), other than infection, can cause the symptoms or the reason for reoperation (e.g., wear debris, metallosis, recurrent dislocation or joint instability, fracture, malposition, neuropathic pain)		Sinus tract or exposed implant, or ≥1 of the followings: otherwise "unexplained" pain, swelling, stiffness		Sinus tract or exposed implant or ≥2 of the followings: pain, swelling, redness, warmth, *Functio laesa*
Positive rule in minus Negative rule out tests	<0	<0	<0	≥0	≥1
Post-operatively confirmed if	Negative cultural examination	One pre- or intra-operative positive culture, with negative histology	Positive cultural examination (preferably with anti-biofilm techniques) and/or positive histology		

Abbreviations: WAIOT: World Association against Infection in Orthopedics and Trauma; BIM: Biofilm-related implant malfunction; LG-PJI: Low-grade peri-prosthetic joint infection; HG-PJI: High-grade peri-prosthetic joint infection.

Validation sur 210 patients

Moyenne de **3,1±1 tests Rule OUT et 2,7±0,9 tests Rule IN**

6 diagnostics pré/intra op **pas confirmés** en post op soit **97,1 % de confirmation**

it should be noted, that several **biomarkers can be falsely positive** for PJI, in patients with concurrent local or systemic inflammatory conditions (e.g., rheumatological disease, pneumonia, acute urinary tract infections, deep vein thrombosis, etc.)

■ ARTHROPLASTY

The EBJIS definition of periprosthetic joint infection

A PRACTICAL GUIDE FOR CLINICIANS

*"… ICM 2018, but was **supported by only 68%** of delegates. **It was not endorsed** by the MSIS or the EBJIS."*

We did not apply scores to our test criteria as the literature is highly heterogenous and scores would be arbitrary at best.

- Problème de sensibilité des critères
- Problème des infections torpides (low grade) sous diagnostiquées
- Aucun test ou même combinaison ne donne une décision infecté / non infecté
- Aide à la recherche avec des classements clairs et aide à la validation de nouveaux traitement

Qualités requises :

- diagnostic de la grande majorité des infections : basé sur la grande Se des tests
- pas de sur-diagnostic : grande Sp des tests
- simple à appliquer
- aide à décision en temps réel
- tests largement disponibles
- acceptable par les cliniciens
- évolution possible avec l'amélioration des connaissances

	Infection Unlikely (all findings negative)	Infection Likely (two positive findings)[a]	Infection Confirmed (any positive finding)
Clinical and blood workup			
Clinical features	Clear alternative reason for implant dysfunction (e.g. fracture, implant breakage, malposition, tumour)	1) Radiological signs of loosening within the first five years after implantation 2) Previous wound healing problems 3) History of recent fever or bacteraemia 4) Purulence around the prosthesis[b]	Sinus tract with evidence of communication to the joint or visualization of the prosthesis
C-reactive protein		> 10 mg/l (1 mg/dl)[c]	
Synovial fluid cytological analysis[d]			
Leukocyte count[c] (cells/µl)	≤ 1,500	> 1,500	>3,000
PMN (%)[c]	≤ 65%	> 65%	> 80%
Synovial fluid biomarkers			
Alpha-defensin[e]			Positive immunoassay or lateral-flow assay[e]
Microbiology[f]			
Aspiration fluid		Positive culture	
Intraoperative (fluid and tissue)	All cultures negative	Single positive culture[g]	≥ two positive samples with the same microorganism
Sonication[h] (CFU/ml)	No growth	> 1 CFU/ml of any organism[g]	> 50 CFU/ml of any organism
Histology[c,i]			
High-power field (400x magnification)	Negative	Presence of ≥ five neutrophils in a single HPF	Presence of ≥ five neutrophils in ≥ five HPF
			Presence of visible microorganisms
Others			
Nuclear imaging	Negative three-phase isotope bone scan[c]	Positive WBC scintigraphy[i]	

Infection likely = there is a significant risk that an infection may be present

Classe **la plus difficile à définir** mais la **plus importante** >>> on doit s'interroger à nouveau !

Beaucoup de conditions limitent les interprétations !

Summary Key

a. Infection is only likely if there is a positive clinical feature or raised serum C-reactive protein (CRP), together with another positive test (synovial fluid, microbiology, histology or nuclear imaging).

b. Except in adverse local tissue reaction (ALTR) and crystal arthropathy cases.

c. Should be interpreted with caution when other possible causes of inflammation are present: gout or other crystal arthropathy, metallosis, active inflammatory joint disease (e.g. rheumatoid arthritis), periprosthetic fracture, or the early postoperative period.

d. These values are valid for hips and knee periprosthetic joint infection (PJI). Parameters are only valid when clear fluid is obtained and no lavage has been performed. Volume for the analysis should be > 250 µL, ideally 1 ml, collected in an EDTA containing tube and analyzed in <1h, preferentially using automated techniques. For viscous samples, pre-treatment with hyaluronidase improves the accuracy of optical or automated techniques. In case of bloody samples, the adjusted synovial WBC= synovial $WBC_{observed}$ – [WBC_{blood} / RBC blood x $RBC_{synovial\ fluid}$] should be used.

e. Not valid in cases of ALTR, haematomas, or acute inflammatory arthritis or gout.

f. If antibiotic treatment has been given (not simple prophylaxis), the results of microbiological analysis may be compromised. In these cases, molecular techniques may have a place. Results of culture may be obtained from preoperative synovial aspiration, preoperative synovial biopsies or (preferred) from intraoperative tissue samples.

g. Interpretation of single positive culture (or < 50 UFC/ml in sonication fluid) must be cautious and taken together with other evidence. If a preoperative aspiration identified the same microorganism, they should be considered as two positive confirmatory samples. Uncommon contaminants or virulent organisms (e.g. *Staphylococcus aureus* or Gram negative rods) are more likely to represent infection than common contaminants (such as coagulase-negative staphylococci, micrococci, or *Cutibacterium acnes*).

h. If centrifugation is applied, then the suggested cut-off is 200 CFU/ml to confirm infection. If other variations to the protocol are used, the published cut-offs for each protocol must be applied.

i. Histological analysis may be from preoperative biopsy, intraoperative tissue samples with either paraffin, or frozen section preparation.

j. WBC scintigraphy is regarded as positive if the uptake is increased at the 20-hour scan, compared to the earlier scans (especially when combined with complementary bone marrow scan).

A méditer …

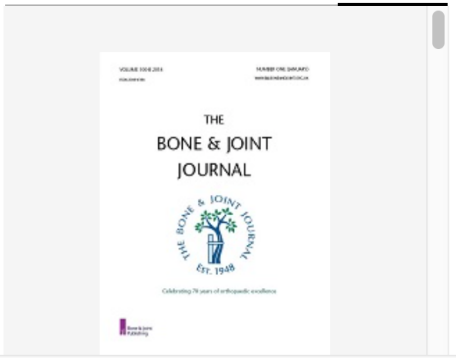
The Bone & Joint Journal, VOL. 104-B, NO. 1 | General Orthopaedics 2021 normal

Figures References Related Details

Should all patients with a culture-negative periprosthetic joint infection be treated with antibiotics?

a multicentre observational study

Maxime van Sloten, Joan Gómez-Junyent, Tristan Ferry, Nicolò Rossi, Sabine Petersdorf, Jeppe Lange, Pablo Corona, Miguel Araújo Abreu, Olivier Borens, Ovidiu Zlatian, Dhanasekaran Soundarrajan, S. Rajasekaran. ... See all authors



- **Diagnostics posés selon : MSIS, ICM et EBJIS**
- 1556 infections chroniques
- 70 ont donné lieu à des **cultures stériles** en per op
- 34 ne sont pas traitées par antibiothérapie
- **Pas de différence dans le devenir** :

  ni sur les infections
  ni sur les changements de matériel

Questions ?

- En dehors de la possibilité d'accès aux tests
- Toutes les classifications Scores ou pas Scores :
  - Cas inclassables : likely ou inconclusive
  - Vraies infections : avec tests / marqueurs négatifs
  - Non infections : avec tests / marqueurs positifs
  - Diagnostics positifs possibles **avec 0 ou 1 culture positive**
- Renforcer la place de l'histologie ?
- Quelle place pour la microbiologie hors cas évidents (≥2 cultures positives) ?
  - C'est quoi un prélèvement positif ?
  - nombre de milieux – liquide ou solide – abondance de la culture ?

Question (centrale ?) non résolue (parmi d'autres) :

Qui a raison pour la définition du critère majeur entre 2 ou 3 prélèvements positifs à potentiels contaminants…

jamais étudié, et jamais remis en question

La France s'aligne, mais a-t-elle raison ?

2

3

Quelle est la place des microbiologistes dans ces consensus ?

ces critères *pourraient* avoir un intérêt …

- Principalement dans les infection chroniques à diagnostic difficiles / descellement supposés mécaniques et **cultures peu concluantes**
- Ces scores / marqueurs notamment synoviaux peuvent-être une aide
- Sous réserve d'un nouveau marqueur magique, il n'y aura jamais de critères ON / OFF
- **Le sens clinique doit toujours primer**
- Ces incertitudes renforcent la nécessité d'**une discussion pluridisciplinaire de qualité**
- Nécessité de techniques nouvelles à valider : NGS !
- Il faut rester humble et accepter que l'on puisse se tromper :

  => équilibre parfois précaire entre « en faire trop » et « pas assez »
- Comparaisons internationales et publications les rendent nécessaires
- **A tester en revisitant nos cultures en parallèle >>>> cf PHRC**