Infezioni di protesi osteoarticolari

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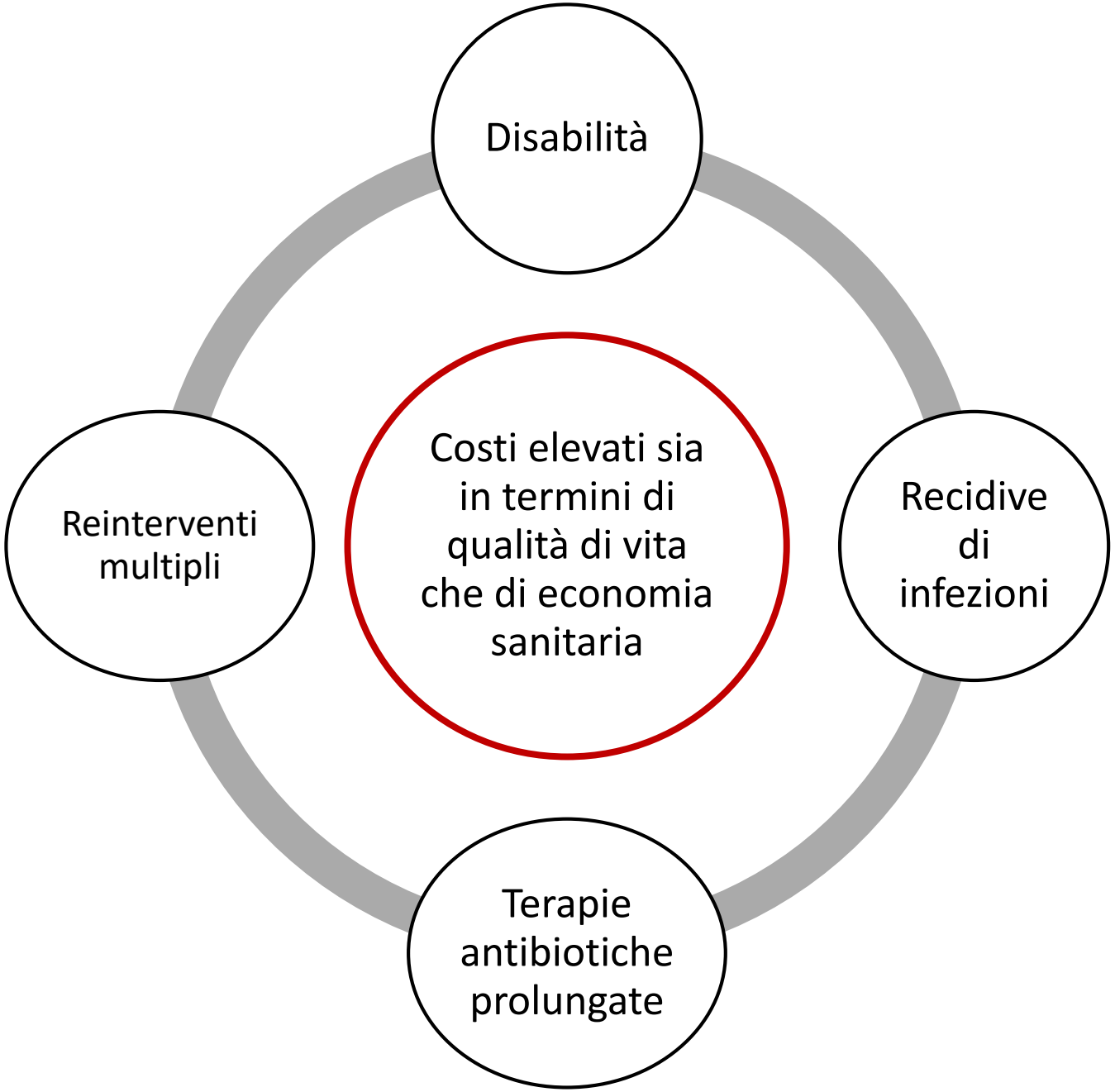
Disabilità
Reinterventi multipli
Costi elevati sia in termini di qualità di vita che di economia sanitaria
Recidive di infezioni
Terapie antibiotiche prolungate

Epidemiologia

- Incidenza 1-2% negli interventi di protesi primarie (in Italia secondo i dati ECDC del 2017 0.8% anca e 0.6% ginocchio)
- Prevalenza 2% a 10 aa
- Incidenza10-20% negli interventi di revisione
- Mortalità: 26% a 5 aa dopo revisione per PJI

Impatto

- Aumentato rischio di morbidità
- Riduzione della qualità di vita
- Causa di fallimento di protesi (terza nel ginocchio e spalla e quarta nell'anca)
- Potenziale compromissione della funzione articolare con diminuzione del livello di mobilità e deambulazione

Original article

Progression and projection for hip surgery in France, 2008-2070: Epidemiologic study with trend and projection analysis

Roger Erivan [a,*], Guillaume Villatte [a], Julien Dartus [b,c], Nicolas Reina [d], Stéphane Descamps [a], Stéphane Boisgard [a]

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[c] *Service d'Orthopédie, Hôpital Roger Salengro, Centre Hospitalier et Universitaire de Lille, place de Verdun, 59037 Lille, France*
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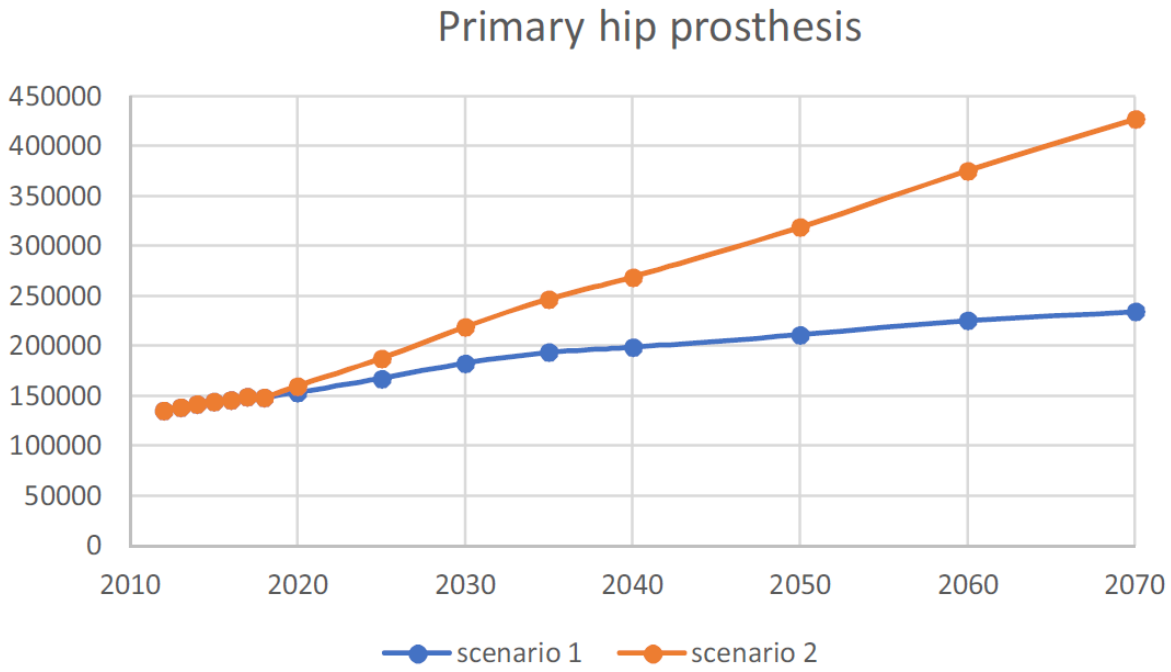
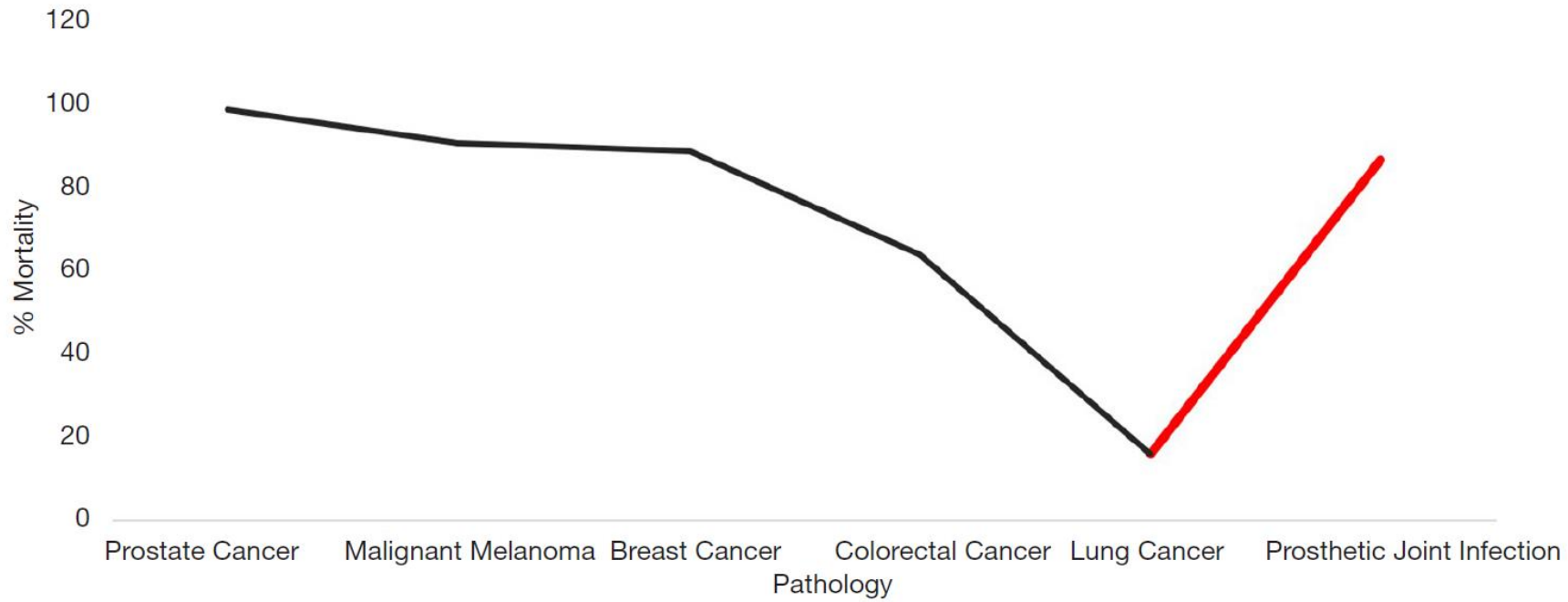


Un incremento atteso per gli interventi di protesi d'anca primaria dal 41.9% al 114%

The mortality associated with PJI compared to common cancers



Ann Joint 2021;6:25 | http://dx.doi.org/10.21037/aoj-2020-pji-11

Outline


Diagnosi
Strategia chirurgica
Tp antibiotica
Reimpianto
Strategie al fallimento

Definizione di infezione protesica

Mancanza di un test di riferimento unico (*benchmark*) e assenza di una definizione univoca e universalmente accettata di infezione peri-protesica

La diagnosi di IPP sia attualmente basata su un approccio multimodale, in cui il “peso” dei singoli dati diagnostici nel determinare la diagnosi definitiva e estremamente variabile nei diversi studi e nelle diverse definizioni.

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]

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	

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

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

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

The EBJIS definition of periprosthetic joint infection

A PRACTICAL GUIDE FOR CLINICIANS

	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[j]	

Bone Joint J **2021;103-B(1):18–25.**

The European Bone and Joint Infection Society definition of periprosthetic joint infection is meaningful in clinical practice: a multicentric validation study with comparison with previous definitions

Acta Orthopaedica

EBJIS preoperative unlikely result shows 89%(CI 84–93) sensitivity and 90% (CI 85–93) negative predictive value (NPV)

ICM 2018 preoperative not infected result shows 85% (CI 79–90) sensitivity and 87% (CI 82–90) NPV
IDSA preoperative not infected result shows 56% (CI 48–65) sensitivity and 77% (CI 74–80) NPV
MSIS 2013 preoperative not infected result shows 66% (CI 57–74) sensitivity and 85% (CI 81–88) NPV

Within EBJIS, the rate of subsequent PJI during follow up was significantly lower in the non-infected cohort: 8% (20/255); when compared with the confirmed: 17% (33/195), (RR = 2, CI 1–4); or likely infection: 23% (5/22), (RR =3, CI 1–10) cohorts.

The proportion of culture-negative infections was significantly different among classifications ($p < 0.001$). It was higher in EBJIS (28%) than in ICM 2018 (19%) or IDSA (19%), and lowest using the MSIS 2013 (9%).

Acta Orthopaedica 2023; 94: 8–18

Esame del liquido sinoviale:
il miglior «single test»
se effettuato in assenza di tp atb da almeno 2 settimane

1. Colturale per aerobi e anaerobi
2. Conta dei leucociti
3. Percentuale dei neutrofili
4. Test alfa defensina→ ELISA migliore in SENS e SPEC del lateral-flow test, costoso. Utile dopo tp atb, non inficiata dalla contaminazione con sangue; sensibile nei batteri a bassa virulenza. Falsi positivi gotta.
5. Esterasi leucocitaria
6. Ricerca genomica→ pannello molecolare sindromico (Biofire)

Isolamento microbiologico

Improved Diagnosis of Prosthetic Joint Infection by Culturing Periprosthetic Tissue Specimens in Blood Culture Bottles

Trisha N. Peel,[a,b] Brenda L. Dylla,[a] John G. Hughes,[a] David T. Lynch,[a] Kerryl E. Greenwood-Quaintance,[a] Allen C. Cheng,[c,d] Jayawant N. Mandrekar,[e] Robin Patel[a,f]

Inoculare il liquido sinoviale e/o campioni di tessuto periprotesico in flaconi da emocolture per aerobi e anaerobi aumenta la sensibilità in modo significativo

Prolungare il tempo di incubazione a 10-14 giorni incrementa sensibilmente la possibilità di isolare patogeni difficile e a lenta crescita come gli anaerobi

Quando possibile sospendere la terapia antibiotica per almeno due settimane prima del campionamento

1. I campioni di tessuto dovrebbero essere ottenuti con una dissezione netta, evitando l'uso di elettrocauterizzazione per ridurre il rischio di falsi positivi conseguenti ad artefatti termici all'analisi istopatologica
2. Prelevare dalle aree con segni più evidenti di infezione e da diverse aree del campo operatorio
3. Cambiare gi strumenti ad ogni campionamento per ridurre il rischio di contaminazione crociata

Clinical Infectious Diseases Advance Access published December 6, 2012

IDSA GUIDELINES

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

Almeno 3 campioni

- da prelevare dal tessuto maggiormente sospetto per infezione
- Inoculare in flaconi da emocolture per aerobi e anaerobi

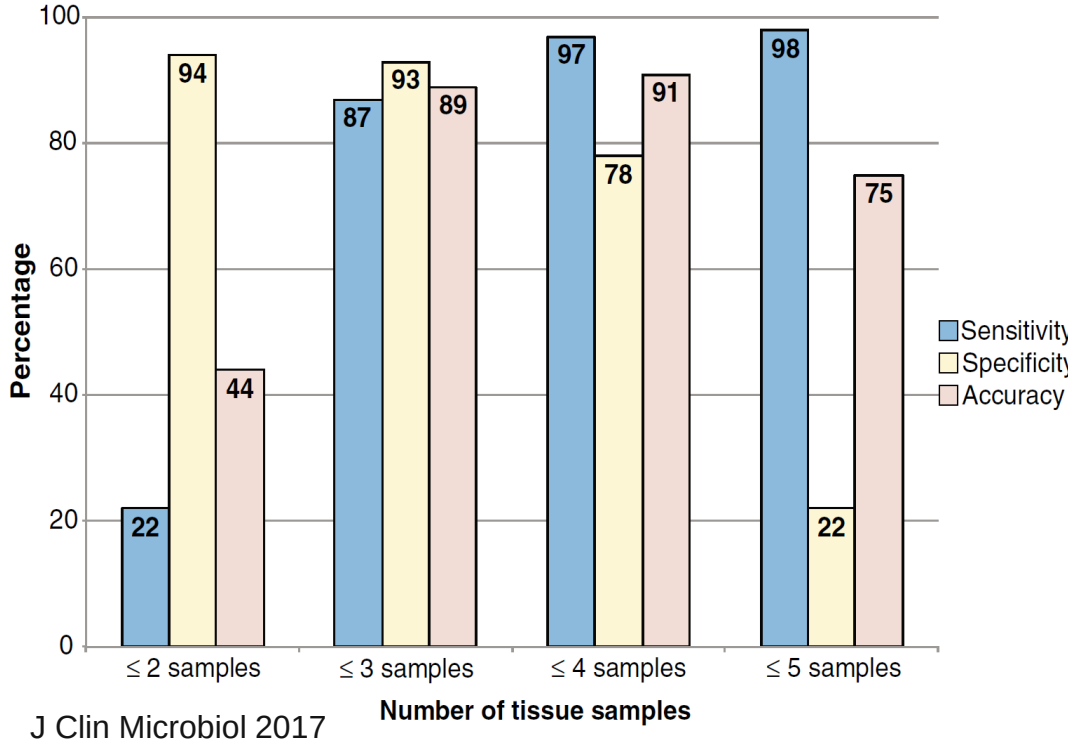
Meglio 5 o 6

Optimal Periprosthetic Tissue Specimen Number for Diagnosis of Prosthetic Joint Infection

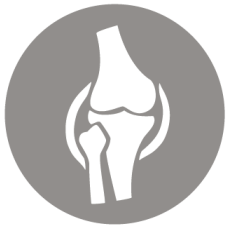
Trisha N. Peel,[a,b] Tim Spelman,[c] Brenda L. Dylla,[a] John G. Hughes,[a] Kerryl E. Greenwood-Quaintance,[a] Allen C. Cheng,[b,d] Jayawant N. Mandrekar,[e] Robin Patel[a,f]

Prelevare oltre 5 o 6 campioni non incrementa l'accuratezza diagnostica

Ottimale 3 campioni di tessuto periprotesico



J Clin Microbiol 2017



BIOFIRE®
JOINT INFECTION (JI) PANEL

1 Test. 39 Target in ~ 1 Ora.

BATTERI GRAM-POSITIVI

Anaerococcus prevotii/vaginalis
Clostridium perfringens
Cutibacterium avidum/granulosum
Enterococcus faecalis
Enterococcus faecium
Finegoldia magna
Parvimonas micra
Peptoniphilus
Peptostreptococcus anaerobius
Staphylococcus aureus
Staphylococcus lugdunensis
Streptococcus spp.
- *Streptococcus agalactiae*
- *Streptococcus pneumoniae*
- *Streptococcus pyogenes*

BATTERI GRAM-NEGATIVI

Bacteroides fragilis
Citrobacter
Enterobacter cloacae complex
Escherichia coli
Haemophilus influenzae
Kingella kingae
Klebsiella aerogenes
Klebsiella pneumoniae group
Morganella morganii
Neisseria gonorrhoeae
Proteus spp.
Pseudomonas aeruginosa
Salmonella spp.
Serratia marcescens

LIEVITI

Candida spp.
- *Candida albicans*

GENI DI RESISTENZA AGLI ANTIMICROBICI

Carbapenemasi
IMP
KPC
NDM
OXA-48-like
VIM

ESBL
CTX-M

Resistenza alla Meticillina
*mec*A/C e MREJ (MRSA)

Resistenza alla Vancomicina
*van*A/B

Campione

0.2mL di liquido sinoviale

Performance: Sensibilità del 91.7% e Specificità del 99.8% [1]

US FDA-cleared | CE 2797

Diagnostica metagenomica

BJR

INFECTION

Metagenomic next-generation sequencing of synovial fluid demonstrates high accuracy in prosthetic joint infection diagnostics

MNGS FOR DIAGNOSING PJI

Bone Joint Res 2020;9(7):440–449.

AMERICAN SOCIETY FOR MICROBIOLOGY | Journal of Clinical Microbiology®

BACTERIOLOGY

Check for updates

Direct Detection and Identification of Prosthetic Joint Infection Pathogens in Synovial Fluid by Metagenomic Shotgun Sequencing

Morgan I. Ivy,[a] Matthew J. Thoendel,[b] Patricio R. Jeraldo,[c] Kerryl E. Greenwood-Quaintance,[a] Arlen D. Hanssen,[d] Matthew P. Abdel,[d] Nicholas Chia,[c] Janet Z. Yao,[c] Aaron J. Tande,[b] Jayawant N. Mandrekar,[e] Robin Patel[a,b]

September 2018 Volume 56 Issue 9 e00402-18

Sindromico e metagenomica: Quando, dove, come

- Colturali negativi
- Infezioni polimicrobiche e da patogeni difficili
- Paz immunodepressi
- PJI early candidata a DAIR
- Pre-reimpianto?

Article

Impact and Modification of the New PJI-TNM Classification for Periprosthetic Joint Infections

Andre Lunz [1,*], Burkhard Lehner [1], Moritz N. Voss [1], Kevin Knappe [1], Sebastian Jaeger [1], Moritz M. Innmann [1], Tobias Renkawitz [1] and Georg W. Omlor [1,2]

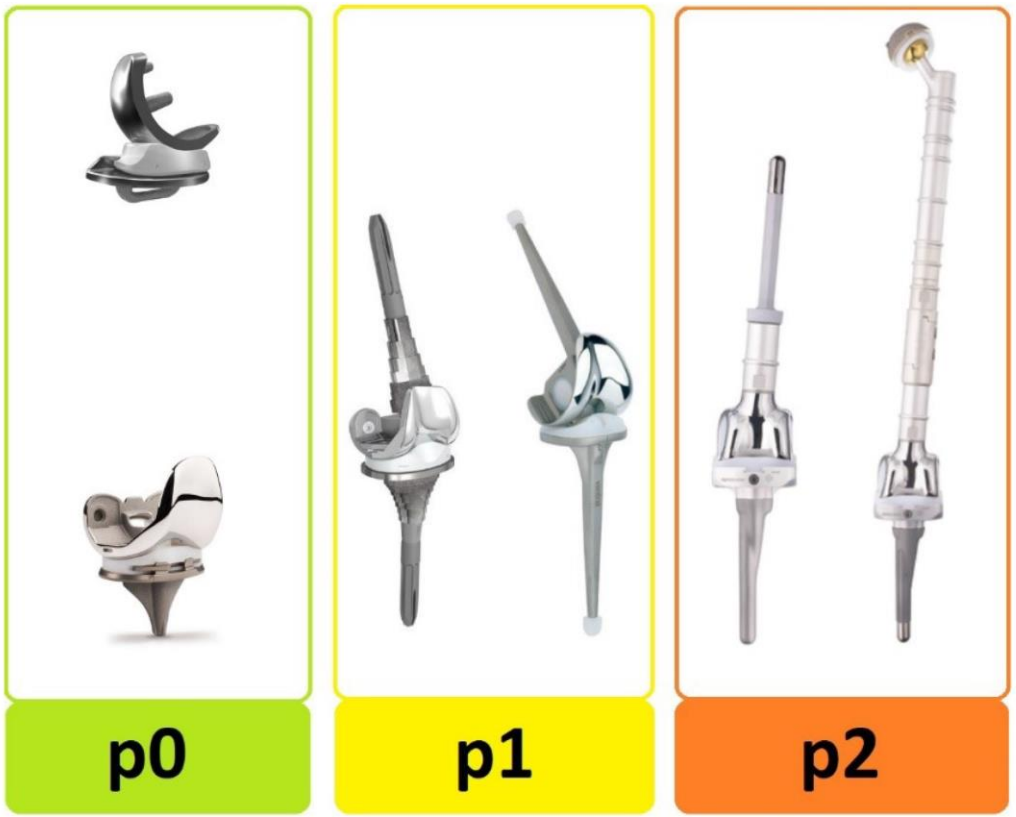
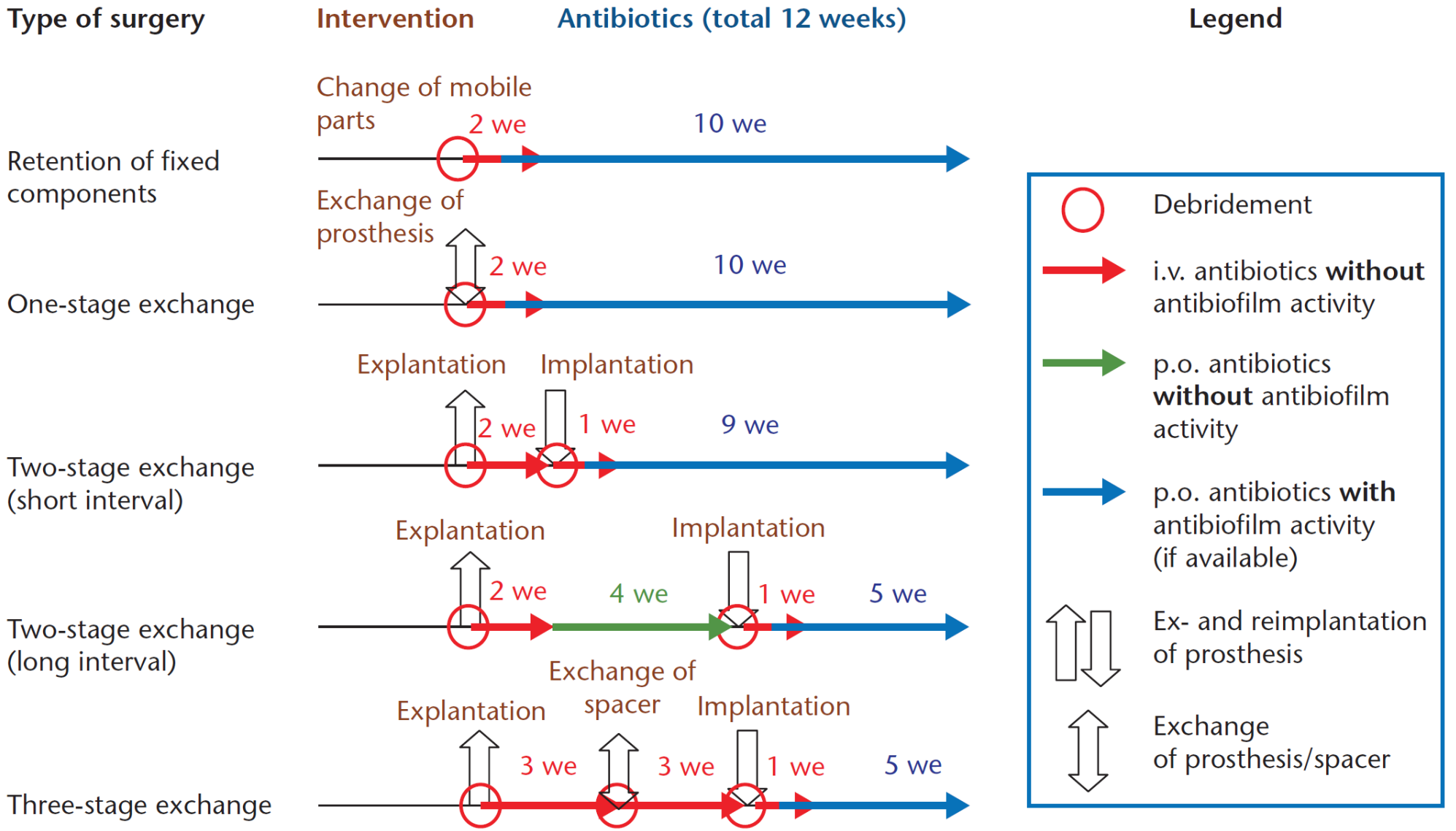


Figure 1. Type of infected prosthesis at time of diagnosis. The "p-status" distinguishes between: p0 = standard implant, p1 = revision implant, and p2 = megaprosthesis.

p	**Prosthesis**	
	p0	Standard implant
	p1	Revision implant
	p2	Megaprosthesis
T	**Tissue condition**	
	T0	Soft tissue in good clinical condition
	T1	Soft tissue in bad clinical condition without fistula
	T2	Fistula or significant soft tissue defect
N	**Non-human cells**	
	N0	Immature biofilm (=acute PJI)
	N1	Mature biofilm and "non-difficult-to-treat" bacteria
	N2	Mature biofilm and "difficult-to-treat" germs
M	**Morbidity**	
	M0	≤ ASA-II
	M1	ASA-III
	M2	≥ ASA-IV

SURGICAL PROCEDURES

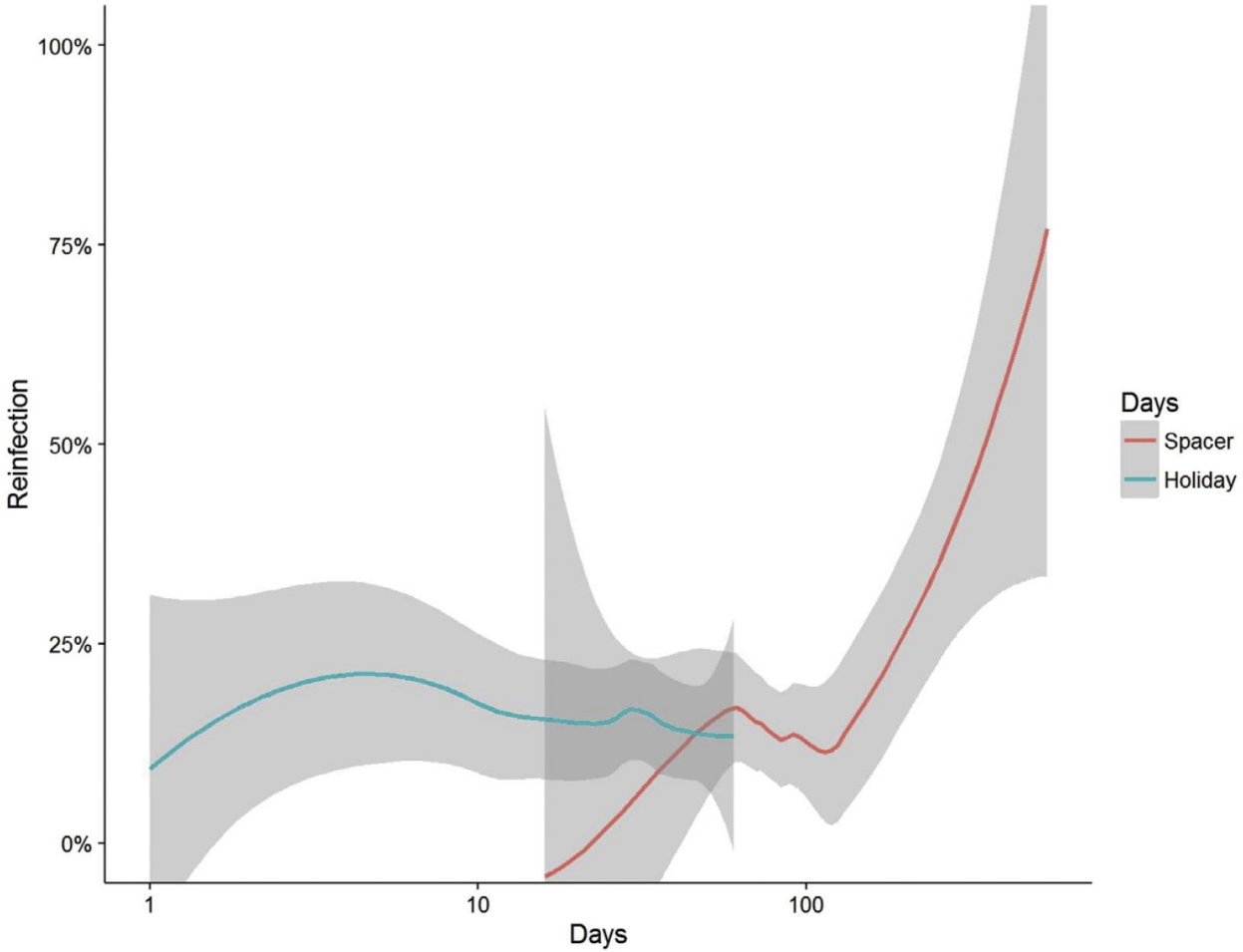


Se colturali intraoperatori del reimpianto risultassero positivi, estendere la terapia a 12 settimane (equivalente a revisione one-stage)

EFORT Open Rev 2019;4:482-494.

Determining the Role and Duration of the "Antibiotic Holiday" Period in Periprosthetic Joint Infection

Timothy L. Tan, MD [a], Michael M. Kheir, MD [a], Alexander J. Rondon, MD, MBA [a], Javad Parvizi, MD, FRCS [a,*], Jaiben George, MBBS [b], Carlos A. Higuera, MD [b], Noam Shohat, MD [a,c], Antonia F. Chen, MD, MBA [a]



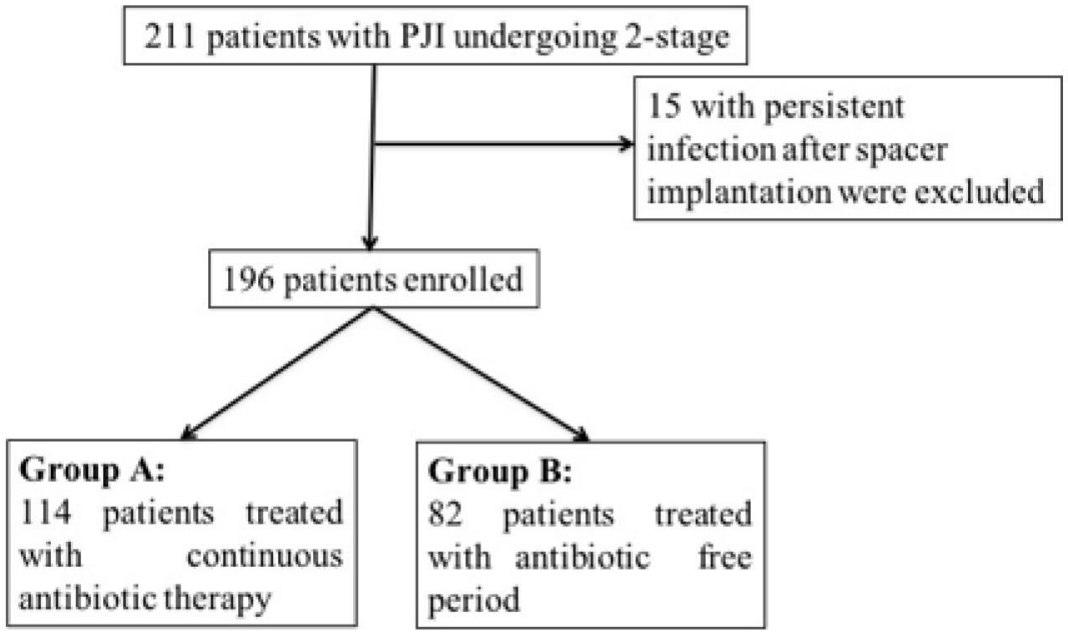
Studio retrospettivo
Dal 2000 al 2014
Arruolati 785 pz sottoposti a revisione two-stage

La durata del BS era significativamente associata al rischio di reinfezione.
41,5% fallimenti durante il trattamento atb
58.5% durante il periodo libero da antibiotici
La durata del periodo antibiotic-free non correlava in modo significativo con il rischio di recidiva di PJI dopo reimpianto

T.L. Tan et al. / The Journal of Arthroplasty 33 (2018) 2976–2980

Continuous antibiotic therapy can reduce recurrence of prosthetic joint infection in patient undergoing 2-stage exchange

Ascione T, Balato G[1], Mariconda M[1], Rotondo R[2], Baldini A[3], and Pagliano P



Favorable outcome was achieved for 169 (86%) patients (91% and 79% in Groups A and B, respectively).

Conclusions. Treatment with continuous antibiotic therapy ameliorated success rate, permitting a better outcome in immunocompromised and reducing the time to reimplantation. Continuous antibiotic therapy can be considered a valid option for the treatment of patients with PJI undergoing 2-stage exchange

The Journal of Arthroplasty (2019), doi: https://doi.org/10.1016/j.arth.2018.12.017

What Markers Best Guide the Timing of Reimplantation in Two-stage Exchange Arthroplasty for PJI? A Systematic Review and Meta-analysis

Yong Seuk Lee MD, PhD, Navin Fernando MD, FRCS, Kyung-Hoi Koo MD, PhD, Hyun Jung Kim MPH, PhD, Hamed Vahedi MD, Antonia F. Chen MD, MBA

Twelve parameters were examined, including serum erythrocyte sedimentation (ESR) rate, serum C-reactive protein (CRP), serum white blood cell (WBC) count, synovial fluid Gram stain, synovial fluid culture, synovial fluid sonication culture, synovial fluid WBC, synovial fluid polymorphonucleocyte percentage (PMN%), tissue Gram stain, tissue culture, positron emission tomography scan, and leukocyte scan.

Conclusions This meta-analysis suggests that no single marker was superior to all the others, and none (when used alone) is likely sufficient to confirm control of infection after the first stage of a two-stage protocol for PJI.

Clin Orthop Relat Res (2018) 476:1972-1983

Synovial Cell Count Before Reimplantation Can Predict the Outcome of Patients with Periprosthetic Knee Infections Undergoing Two-stage Exchange

Tiziana Ascione MD[1,2], Giovanni Balato MD, PhD[3], Massimo Mariconda MD[3], Francesco Smeraglia MD[3], Andrea Baldini MD[4], Cristiano De Franco MD[3], Giuseppe Pandolfo PhD[5], Roberta Siciliano PhD[6], Pasquale Pagliano MD[2,7]

Table 2. Diagnostic parameters of synovial fluid WBC count and PMN percentage at the proposed threshold

Parameter	WBC count	PMN percentage	WBC count ≥ 934cells/μL, PMN percentage ≥ 52%
Proposed threshold	934 cells/μL	52%	
Sensitivity	0.82 (95% CI 0.71-0.89)	0.82 (95% CI 0.71-0.89)	0.66 (95% CI 0.52-0.74)
Specificity	0.82 (95% CI 0.71-0.89)	0.78 (95% CI 0.67-0.86)	0.92 (95% CI 0.83-0.96)
Positive predictive value	0.41 (95% CI 0.30-0.52)	0.36 (95% CI 0.26-0.547)	0.54 (95% CI 0.43-0.65)
Negative predictive value	0.98 (95% CI 0.89 0.99)	0.97 (95% CI 0.89-0.99)	0.94 (95% CI 0.86-0.98)
Area under the curve	0.87 (95% CI 0.79-0.96)	0.84 (95% CI 0.73-0.95)	0.70 (95% CI 0.60-0.95)

Is long time to reimplantation a risk factor for reinfection in two-stage revision for periprosthetic infection? A systematic review of the literature

Jan Puetzler*, Martin Schulze, Georg Gosheger, Jan Schwarze, Burkhard Moellenbeck† and Christoph Theil†

Department of Orthopaedics and Tumor Orthopaedics, University Hospital Muenster, Muenster, Germany

The two-stage revision arthroplasty is a common treatment option for chronic periprosthetic infection (PJI). The time to reimplantation (TTR) reported in the literature varies substantially from a few days to several hundred days. It is hypothesized that longer TTR could be associated with worse infection control after second stage. A systematic literature search was performed according to Preferred Reporting items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, in Pubmed, Cochrane Library and Web of Science Core Collection in clinical studies published until January 2023. Eleven studies investigating TTR as a potential risk factor for reinfection met the inclusion criteria (ten retrospective and one prospective study, published 2012–2022). Study design and outcome measures differed notably. The cutoff points above which TTR was regarded as "long" ranged from 4 to 18 weeks. No study observed a benefit for long TTR. In all studies, similar or even better infection control was observed for short TTR. The optimal TTR, however, is not yet defined. Larger clinical studies with homogeneous patient populations and adjustment for confounding factors are needed.

doi: 10.3389/fsurg.2023.1113006

Problematiche aperte

1. Gestione delle PJI in team multidisciplinari dedicati
2. Definizione dell'infezione protesica, quando considerarla early o late
3. Scelta del miglior trattamento antibiotico possibile (biofilm, penetrazione ossea, sinergie, attività battericida, tollerabilità e sostenibilità)
4. Come definire un'infezione «eradicata» e decidere il timing ottimale del reimpianto
5. Per quanto proseguire la terapia dopo reimpianto
6. Prolungare il follow-up
7. Organizzarsi per eventuale strategie alternative, come i batteriofagi