La Gestione Appropriata
delle Infezioni in Riabilitazione:
indicazioni strategiche

Cona (Fe) 20 Giugno 2019

Aula Congressuale

Le infezioni osteoarticolari e protesiche

SILVIO BORRE’ DIVISIONE MALATTIE INFETTIVE –VERCELLI-

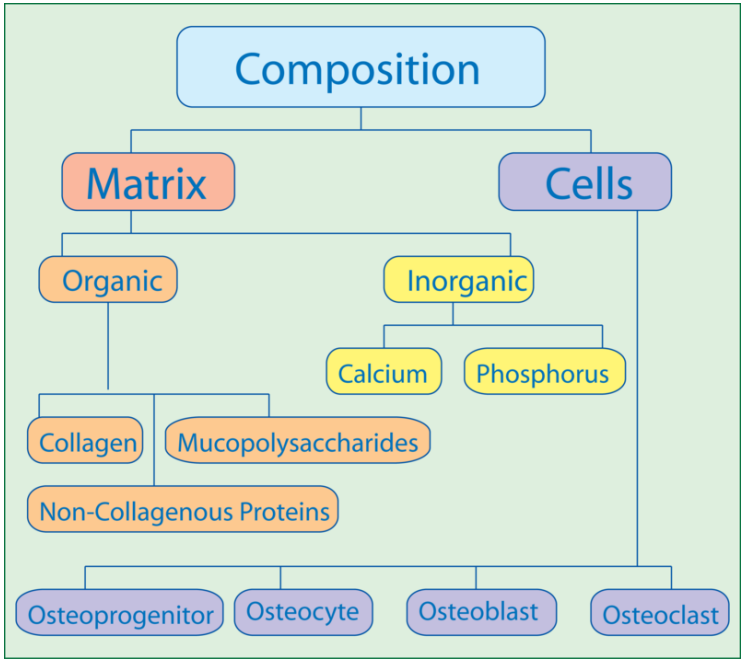
My disclousures

- **Speaker/chairman**

  - Pfizer, Nordic, MSD, Gilead, Sanofi, Angelini

Bone and joint infections are painful for patients and frustrating for both them and their doctors

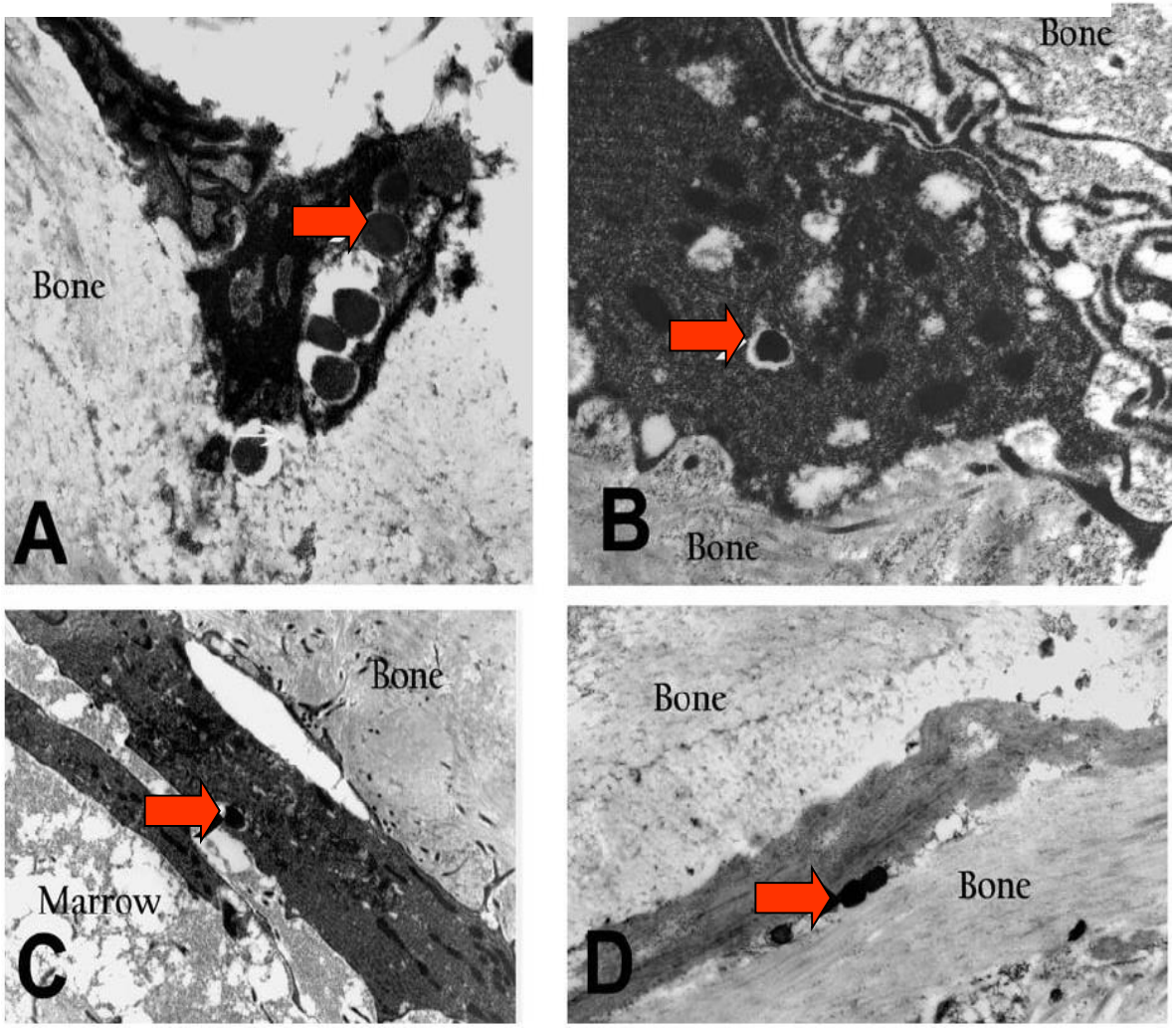
The high success rates of antimicrobial therapy in most infectious diseases have not yet been achieved in bone and joint infections owing to the **physiological and anatomical characteristics of bone.**



Waldvogel F.A. et al.: Osteomyelitis Lancet Vol. 364, Issue 9431, 369 - 379, 24 July 2004

INTRACELLULAR SURVIVAL

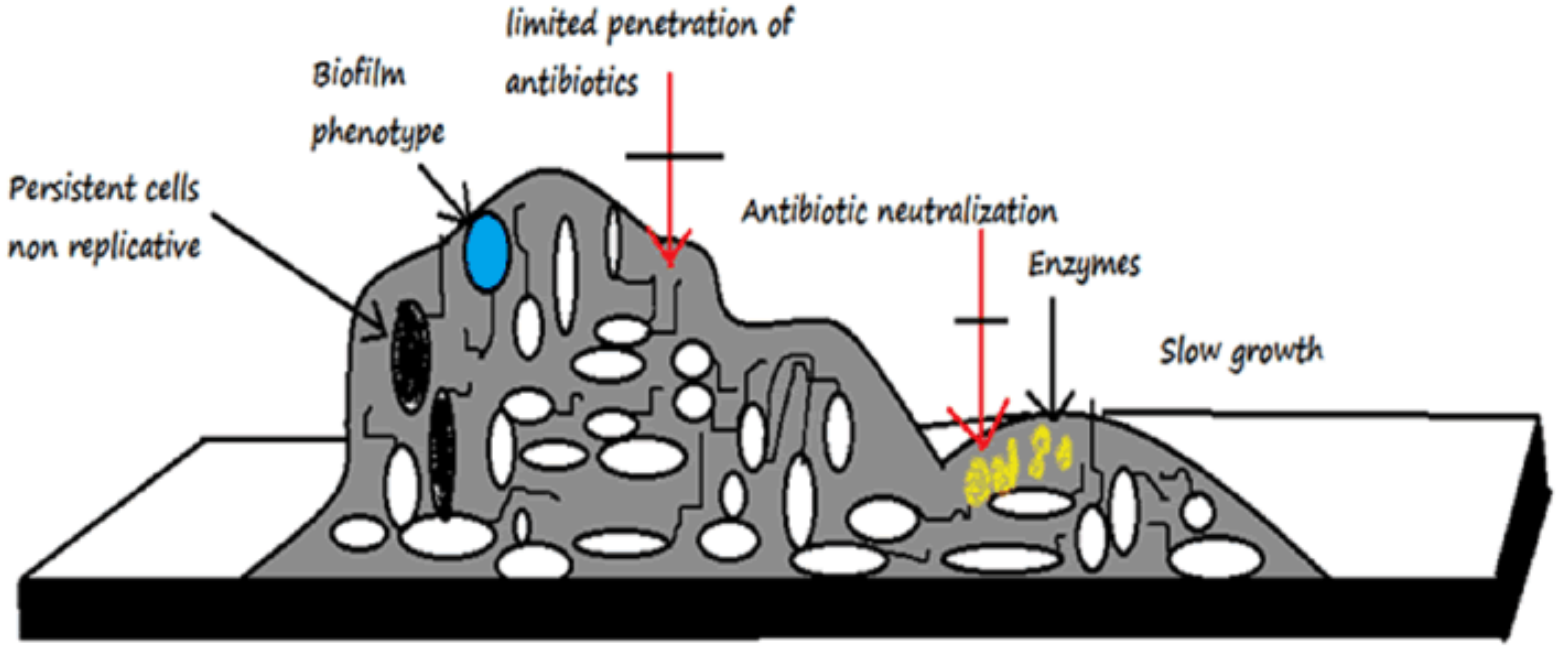
Evidence of an intracellular reservoir in osteocytes (A,B), osteoblasts (C) bone matrix (D) of a patient with recurrent osteomyelitis



Bosse et al., J Bone Joint Surg Am. 2005; 87:1343-7

Bacterial biofilms: from the natural environment to infectious diseases

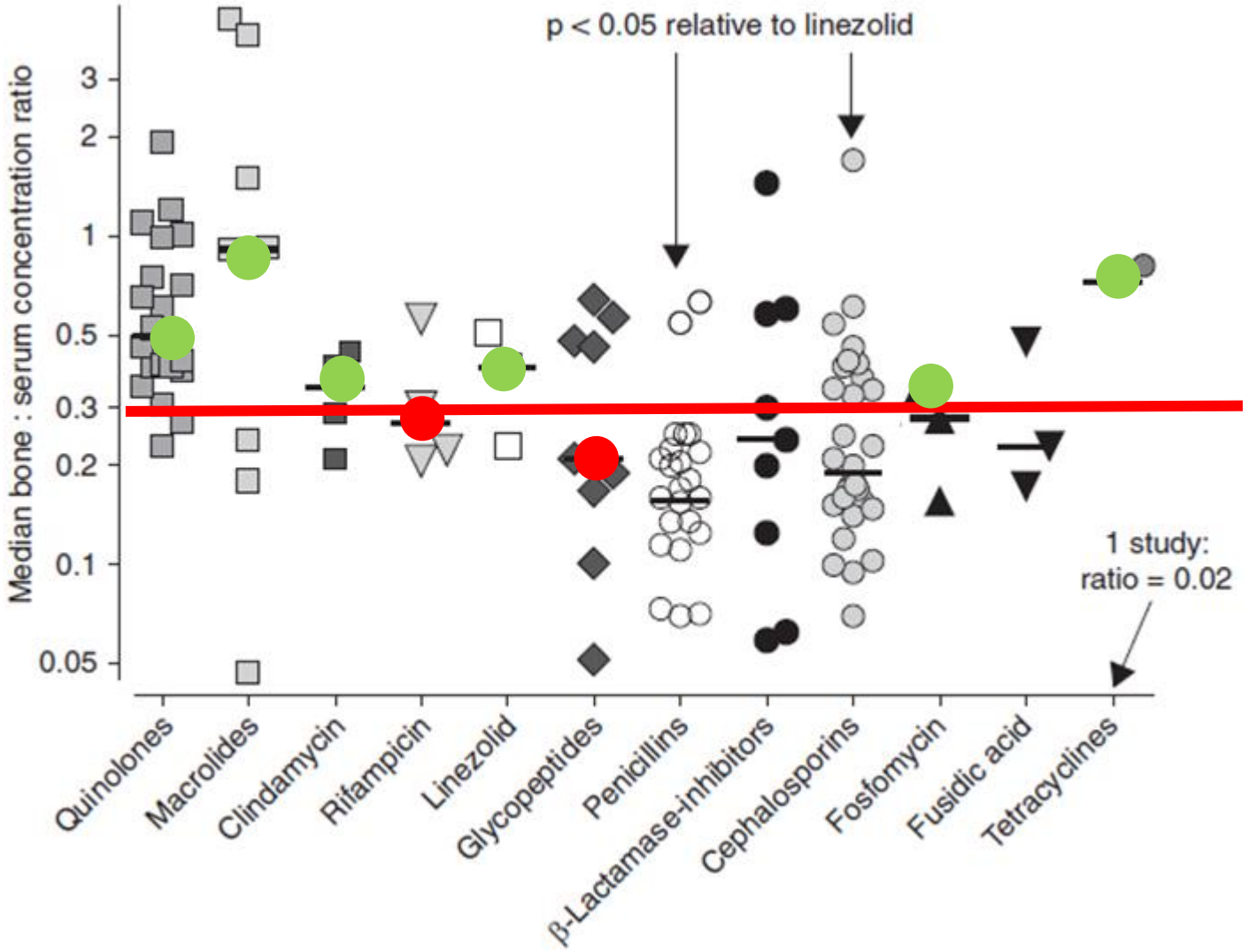
	Components	Percentage of matrix
1	Microbial cells	2-5%
2	DNA and RNA	<1-2%
3	Polysaccharides	1-2%
4	Proteins	<1-2% (including enzymes)
5	Water	Up to 97%



. Description of the key mechanisms involved in antibiotic resistance such as enzyme causing neutralizations,presence of persistent (non-dividing) cells and biofilm phenotype

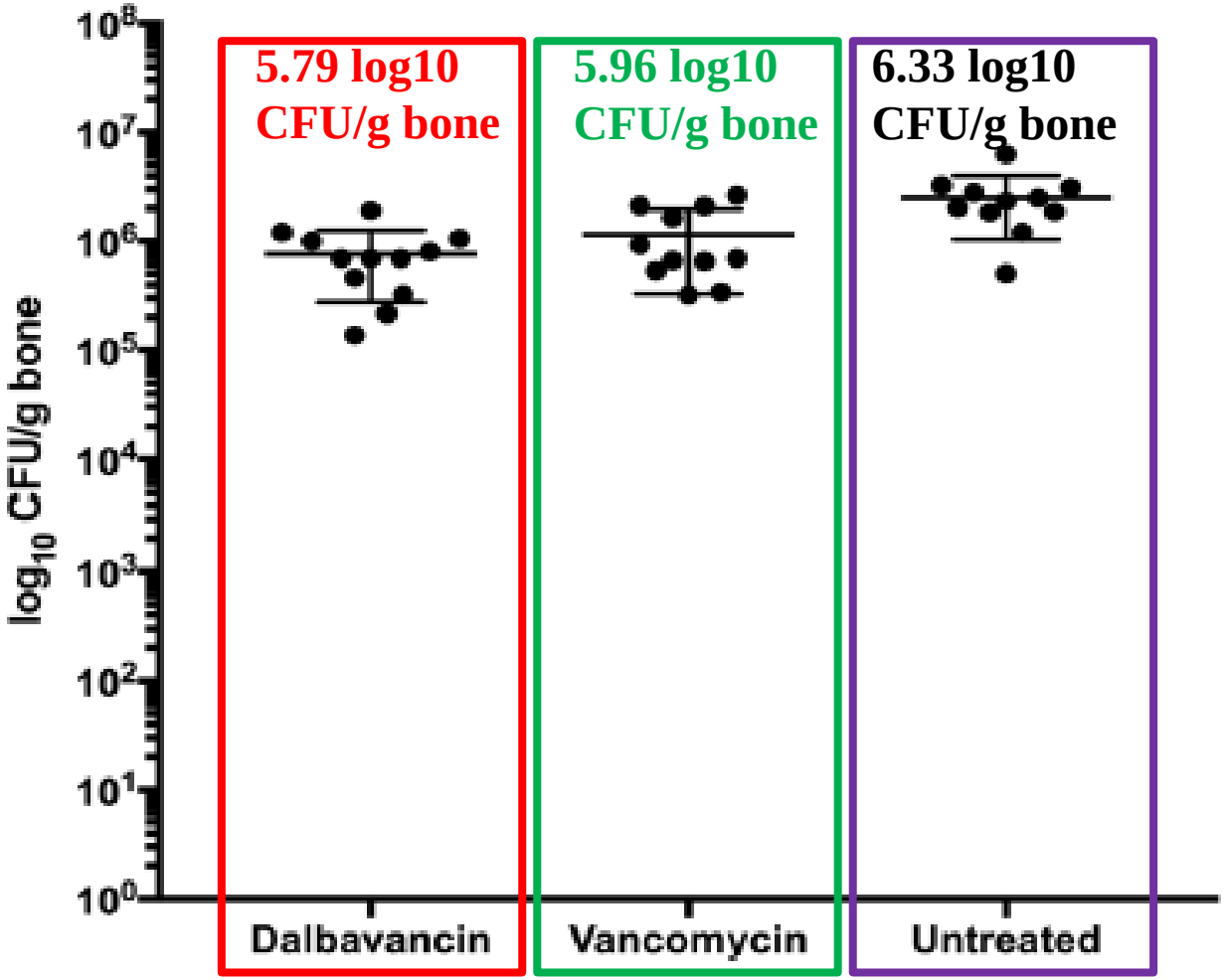
Hall-Stoodley L. et al.: Nat Rev Microbiol. 2004 Feb;2(2):95-108.

Penetration of Antibacterials into Bone
Pharmacokinetic, Pharmacodynamic and Bioanalytical Considerations

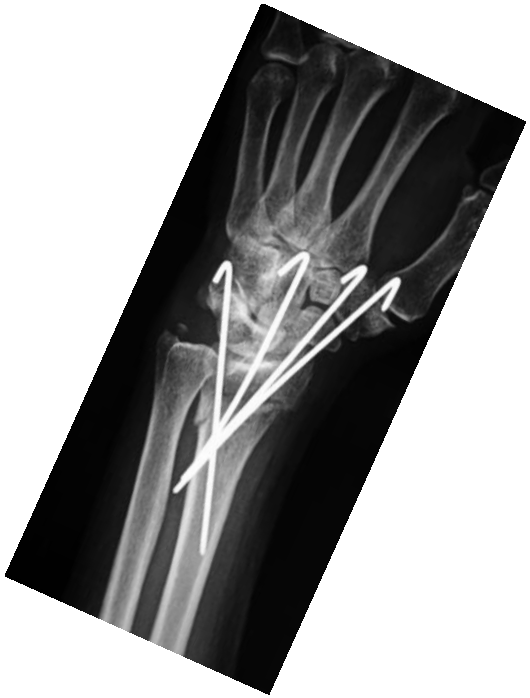


Landersdorfer CB et al.:Clin Pharmacokinet 2009; 42(2):89-124

Dalbavancin for treatment of implant-related methicillin resistant *Staphylococcus aureus* osteomyelitis in an experimental rat model



Kussmann et al. 2018



Mean bacterial counts in log10 CFU/g bone (±SD) from osseous tissue after a four-week treatment period with dalbavancin, vancomycin or without treatment in an experimental implant-related MRSA osteomyelitis in rats

Médecine et Maladies Infectieuses Volume 48, Issue 4, June 2018, Pages 256-262

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Médecine et maladies infectieuses

Médecine et maladies infectieuses xxx (2017) xxx–xxx

Original article

Key features of bone and joint infections following the implementation of reference centers in France☆,☆☆

Points clés des infections ostéoarticulaires depuis la labellisation des centres de référence en France

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Received 6 February 2017; received in revised form 7 June 2017; accepted 8 February 2018

Overall bone and joint infections (BJI), device-associated BJI and complex BJI patients, and hospitalizations, 2008 vs. 2013, France.

	Overall BJIs				Device-associated BJIs				Complex BJIs	
	2008		2013		2008		2013		2013	
	n	%	*n*	%	*n*	%	*n*	%	*n*	%
Patients' demographic data	28.453		37.252		9.353	33[b]	12.952	35[b]	2.776	7.5[b]
Age (years), mean(median [min-max])	63.1 (66 [15–105])		65.4 (69 [15–104])		64 6 (69 [15–105])		66.2 (69 [15–104])		62 (65 [15–104])	
Sex-ratio M/F	1.54		1.60		1.17		1.15		1.60	
Male	17	60.6	23	61.6	5.043	53.9	6.930	53.5	1.694	61.0
Female	11	39.4	14	38.4	4.310	46.1	6.022	46.5	1.082	39.0
Device-associated BJI	9.353	32.9	12.952	34.8	9.353	100.0	12.952	100.0	1.786	64.3
Hospital case fatality	1.322	4.6	1.928	5.2	410	4.4	593	4.6	73	2.6
Rehospitalization	4.599	17.0	6.481	18.3	1.883	20.1	2.638	20.4	927	33.4
Diagnosis codes										
Septic arthritis	15.052	52.9	18.658	50.1	6.590	70.5	8.993	69.4	1.828	65.9
Osteomyelitis	9.676	34.0	13.629	36.6	1.518	16.2	2.246	17.3	786	28.3
Spondylodiscitis	2.666	9.4	3.670	9.9	186	2.0	418	3.2	119	4.3
Not indicated	1.059	3.7	1.295	3.5	1.059	11.3	1.295	10.0	43	1.5
Cost (€) per patient, mean (median)	8.014 (5.526)		11.305 (8.904)		8.905 (6.025)		11.758 (9.728)		17248 (13.073)	
Hospital stays	36.097	0.21[a]	48.386	0.27[a]	11.451	32[b]	16.214	34[b]	3.301	6.8[b]
Public sector hospitalization	28	78.8	40	82.2	7.923	69.2	12	74.6	3.3234	98.0
Reference center hospitalization	11	30.9	16	32.8	3.448	30.1	5.448	33.6	3.002	90.9
Surgical ward stays	20	55.0	27	56.4	8.513	74.3	12	74.5	2.715	82.3
ICU stays	2.106	5.8	3.350	6.9	624	5.4	991	6.1	236	7.2
Z76800 code (2013 only)	–	–	3.301	6.8	–	–	2.033	12.5	3.301	100.0
Micro-organisms	14	39.9	31	63.7	4.708	41.1	11.077	68.3	2.542	77.0
Bacteria	14	97.7	30	98.3	4.668	99.2	10.998	99.3	2.522	99.2
Polymicrobial infection	1.591	11.0	6.116	19.8	502	10.7	1.716	15.5	576	22.7
Staphylococci	9.425	65.4	21	67.6	3.570	75.8	8.484	76.6	1.961	77.1
Streptococci	2.208	15.3	5.678	18.4	687	14.6	1.636	14.8	452	17.8
Gram-negative bacilli	2.370	16.5	8.104	26.3	788	16.7	2.373	21.4	656	25.8
Resistance	485	3.4	7.974	25.9	183	3.9	2.925	26.4	918	36.1
LOS (days),mean (median [min–max])	17.5 (11 [1–421])		17.5 (12 [1–442])		18.9 (13 [1–421])		18.2 (13 [1–441])		22.2 (15 [1–386])	

BJI: bone and joint infection; ICU: intensive care unit: LOS: length of stay.

[a] % of overall stays within the same year. [b] % of overall BJI inpatients/stays.

Arthroplasty: good and bad

Arthroplasty numbers worlwide	~ 5 millions
Yearly trend	5% increase
Arthroplasty revision rate	5% - 10%
Infected revision rate	11% - 40%
Infection rate (primary)	1% - 4%

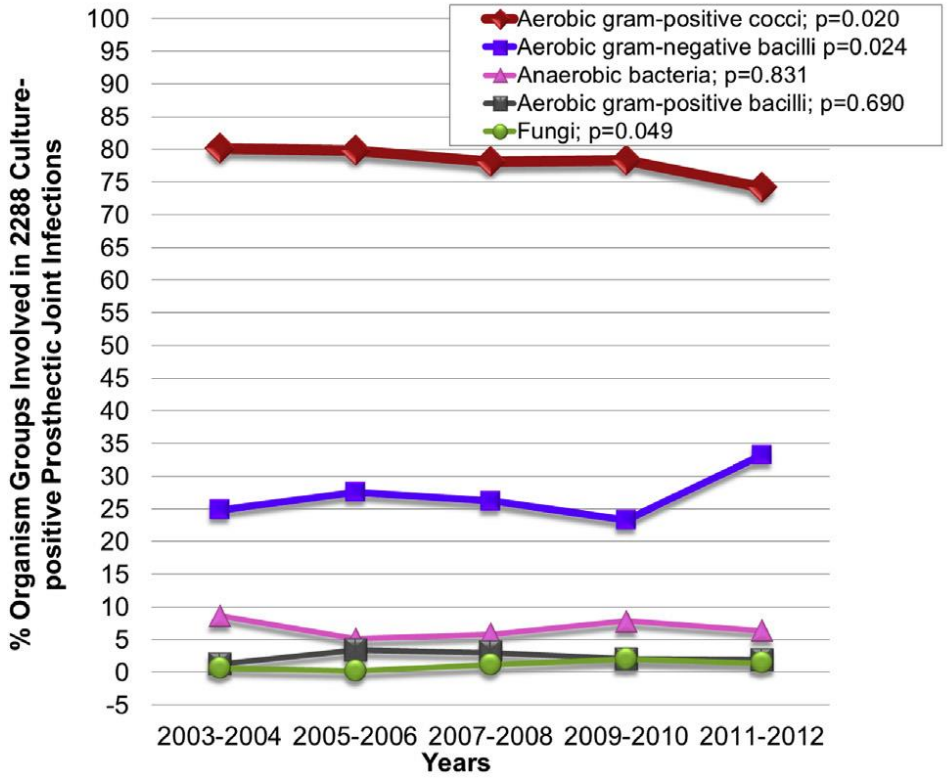
Infected revision rate

	THA	TKA	References
UK	20.3%	25.6%	*NJR report - 2011*
Norway	12.5%	11.3%	*NAR report - 2010*
USA	14.8%	25.2%	*JBJS (Am) - Bozic 2009; CORR – Bozic 2010*
Canada (early 2Y)	32%	39%	*JCC – Singh 2016*
Japan	16%	32.8%	*NJR report - 2017*

Time trends in the aetiology of prosthetic joint infections: a multicentre cohort study

2524 consecutive adult patients with a diagnosis of PJI. microbiological diagnosis:2288 cases (90.6%).

(a



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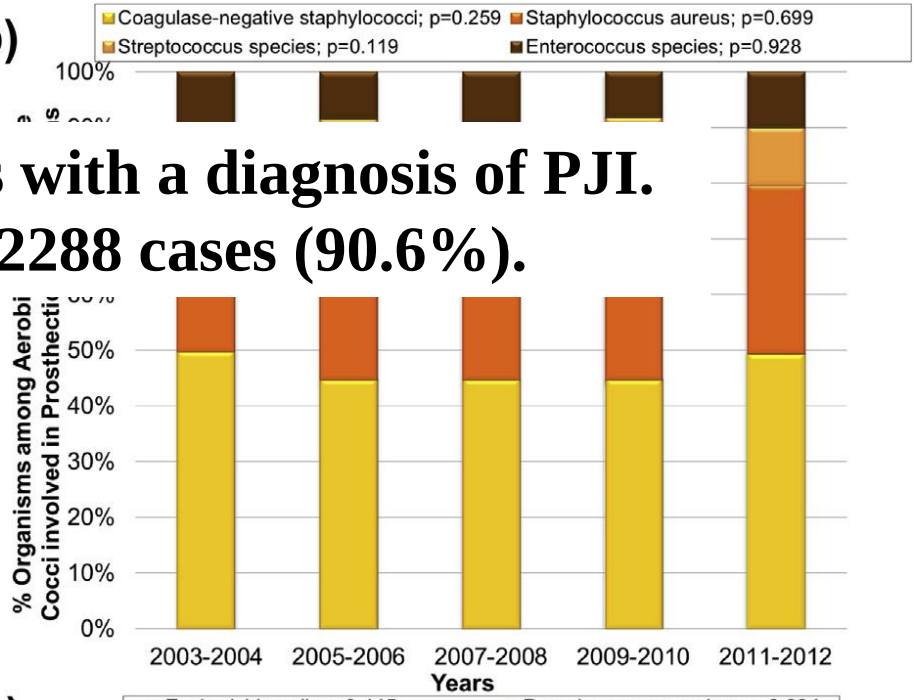

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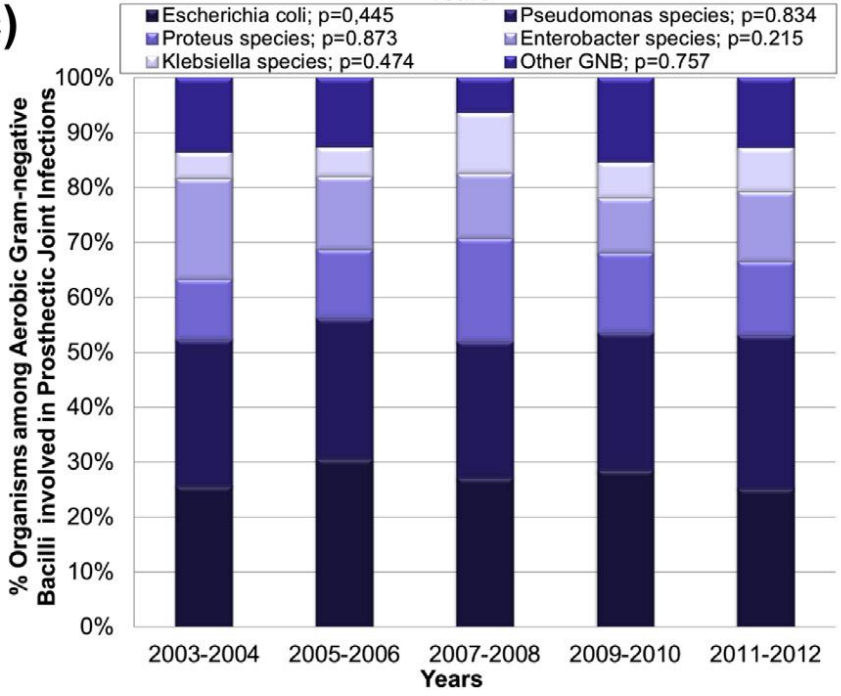
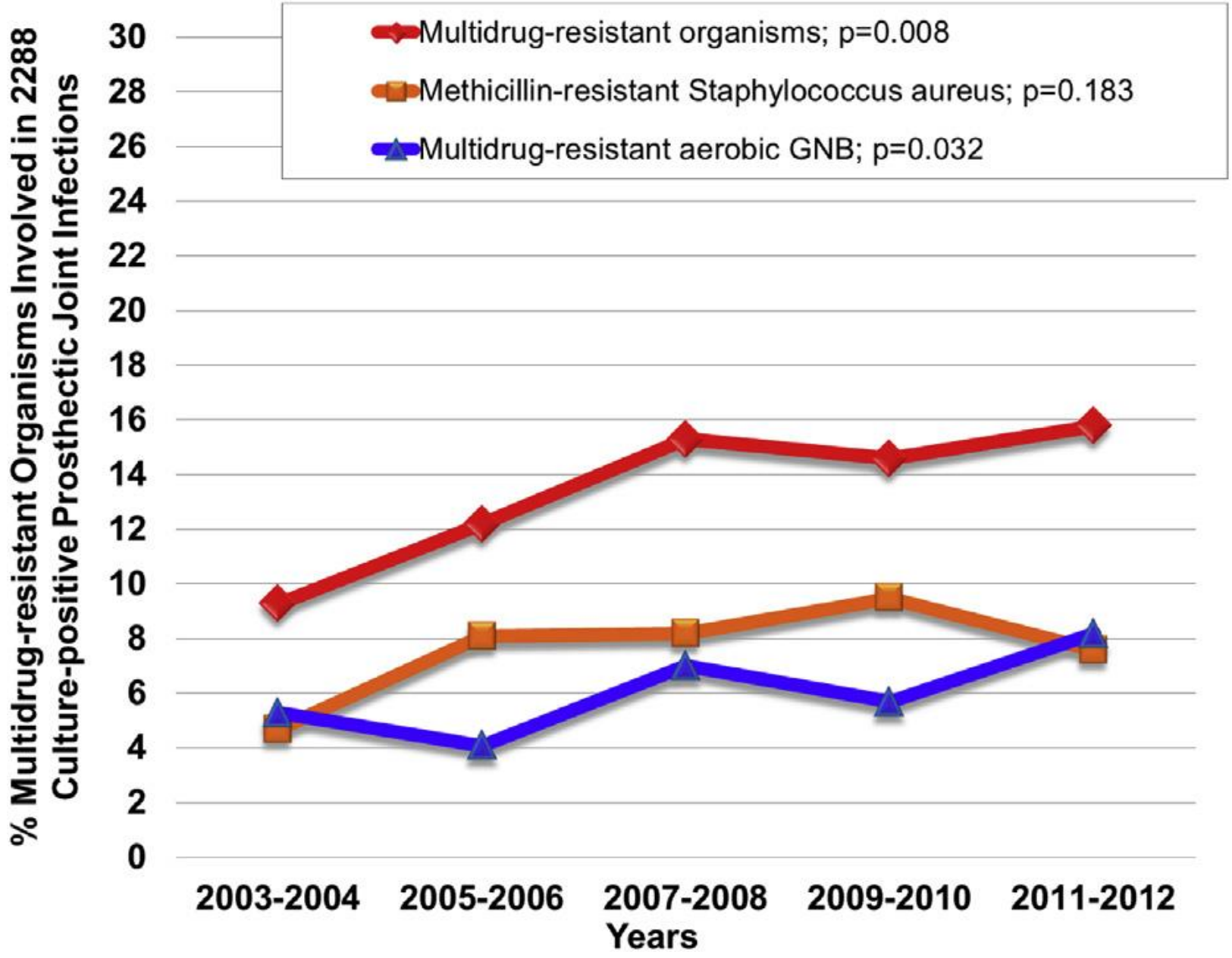
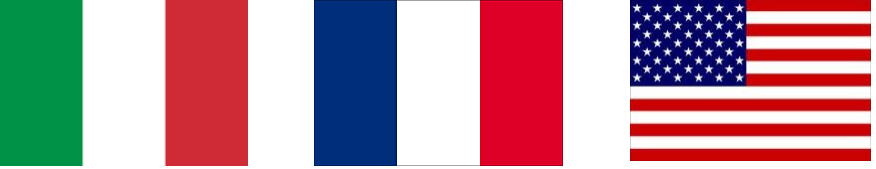


N. Benito et al. / Clinical Microbiology and Infection 22 (2016) 732.e1e732.e8


% Multidrug-resistant Organisms Involved in 2288 Culture-positive Prosthectic Joint Infections
30
28
26
24
22
20
18
16
14
12
10
8
6
4
2
0
Multidrug-resistant organisms; p=0.008
Methicillin-resistant Staphylococcus aureus; p=0.183
Multidrug-resistant aerobic GNB; p=0.032
2003-2004
2005-2006
2007-2008
2009-2010
2011-2012
Years


-Cellularità
- Colturale
LA STORIA DEL PAZIENTE
LA CLINICA
-Biomarker
- Esterasi leucocitaria
- α-defensina
GB VES PCR
- PCT IL-6
Rx
- Scintigrafia Tc Leu N.C.
- ECO TC RM (PET)
+++ colturali
Es.istologico



DIAGNOSTICA

“LA CLINICA CON LA STORIA DEL PZ “”

non tutte le protesi dolorose sono una PTJ,
ma la segnalazione di cicatrizzazione problematica,
di ematomi post-chirurgici più volte drenati,
la persistenza di secrezione sierosa dalla ferita,
il dolore comparso durante riabilitazione,
il dolore presente anche a riposo
devono far pensare ad una infezione

➢ *Le attuali linee guida per la diagnosi e il trattamento delle infezioni articolari protesiche di spalla fanno riferimento a quelle di anca e ginocchio :*
le infezioni protesiche di spalla spesso differiscono da quelle dell'anca e del ginocchio a causa della **natura “indolente” degli organismi** incriminati nella maggior parte delle complicanze infettive e per le **differenti condizioni anatomiche** dopo impianto di protesi

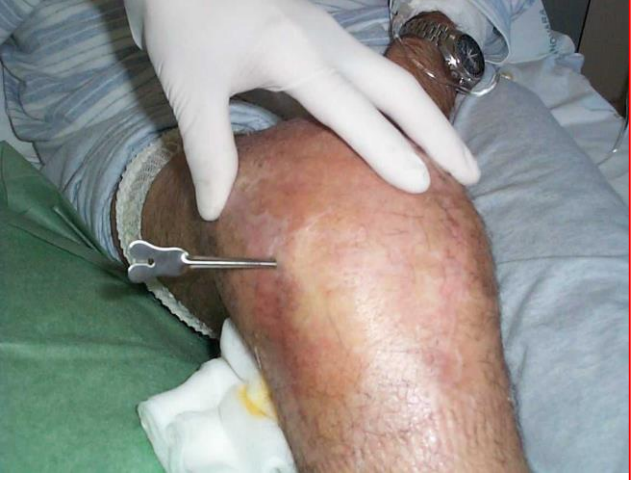
VES e PCR aumentati sembrano fornire la miglior sensibilità e specificità diagnostica (A-III).

Plain radiographs should be performed in all cases of suspected PJI. Magnetic resonance imaging (MRI), computed tomography (CT), and nuclear imaging currently do not have a direct role in the diagnosis of PJI but may be helpful in the identification of other causes of joint pain/failure. Strong (*93*)
International Consensus on Periprosthetic Joint Infection

routine per diagnosticare PJI (B-III).

Una artrocentesi diagnostica dovrebbe essere eseguita in tutti i Pz
- con sospetta PJI acuta
- con protesi dolorosa cronica anche senza > VES e/o PCR (A-III)

Analisi del liquido sinoviale:
- N° totale GB e % PMN, Esterasi leucocitaria / α-defensina
-Coltura per microrganismi aerobi ed anaerobi (A-III).
- ***La sospensione della terapia antibiotica per almeno 2 settimane prima della raccolta liquido sinoviale > la probabilità di identificare organismo (B-III)***



IDSA

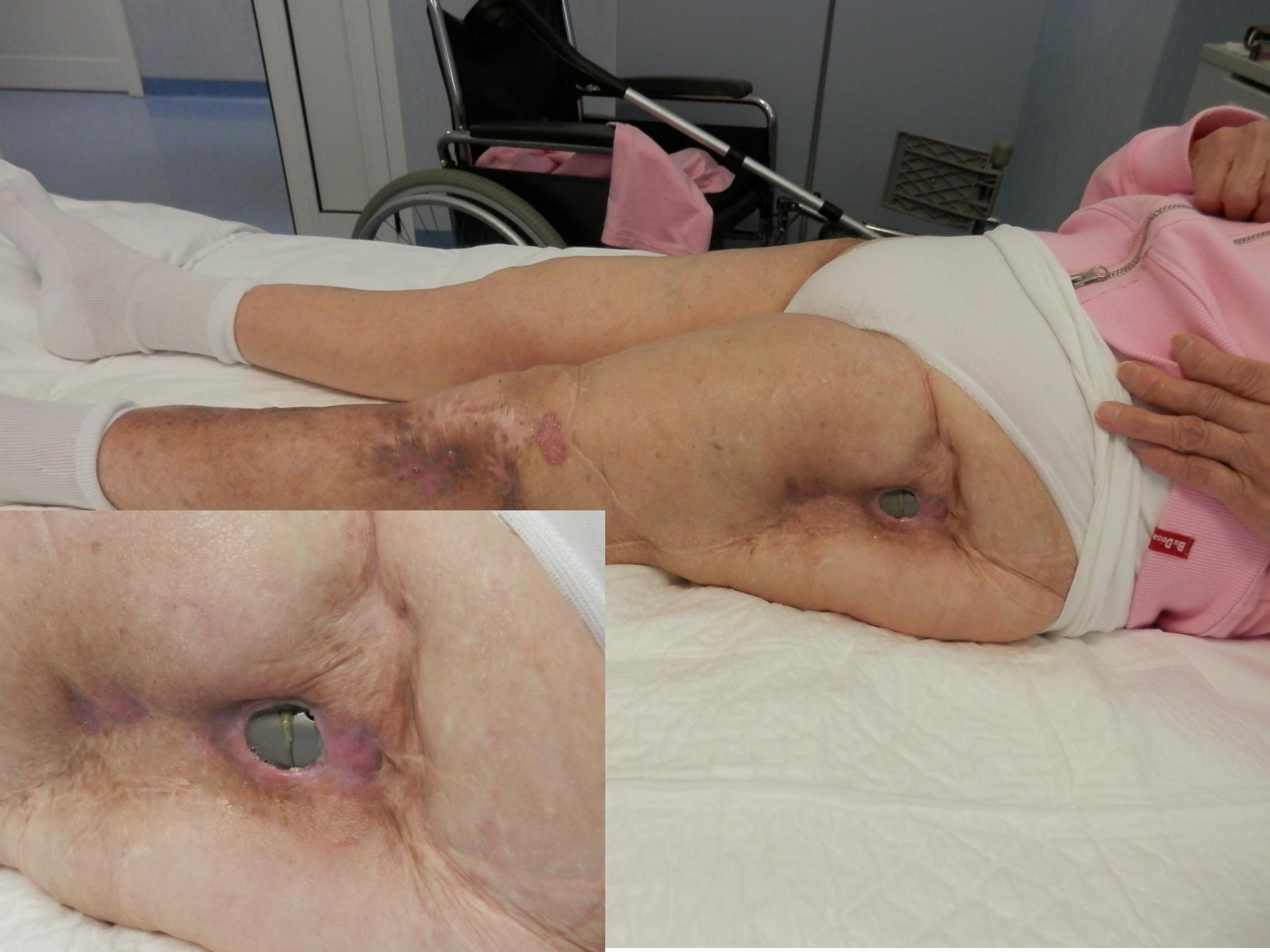
PJI is present when one of the following criteria is present:

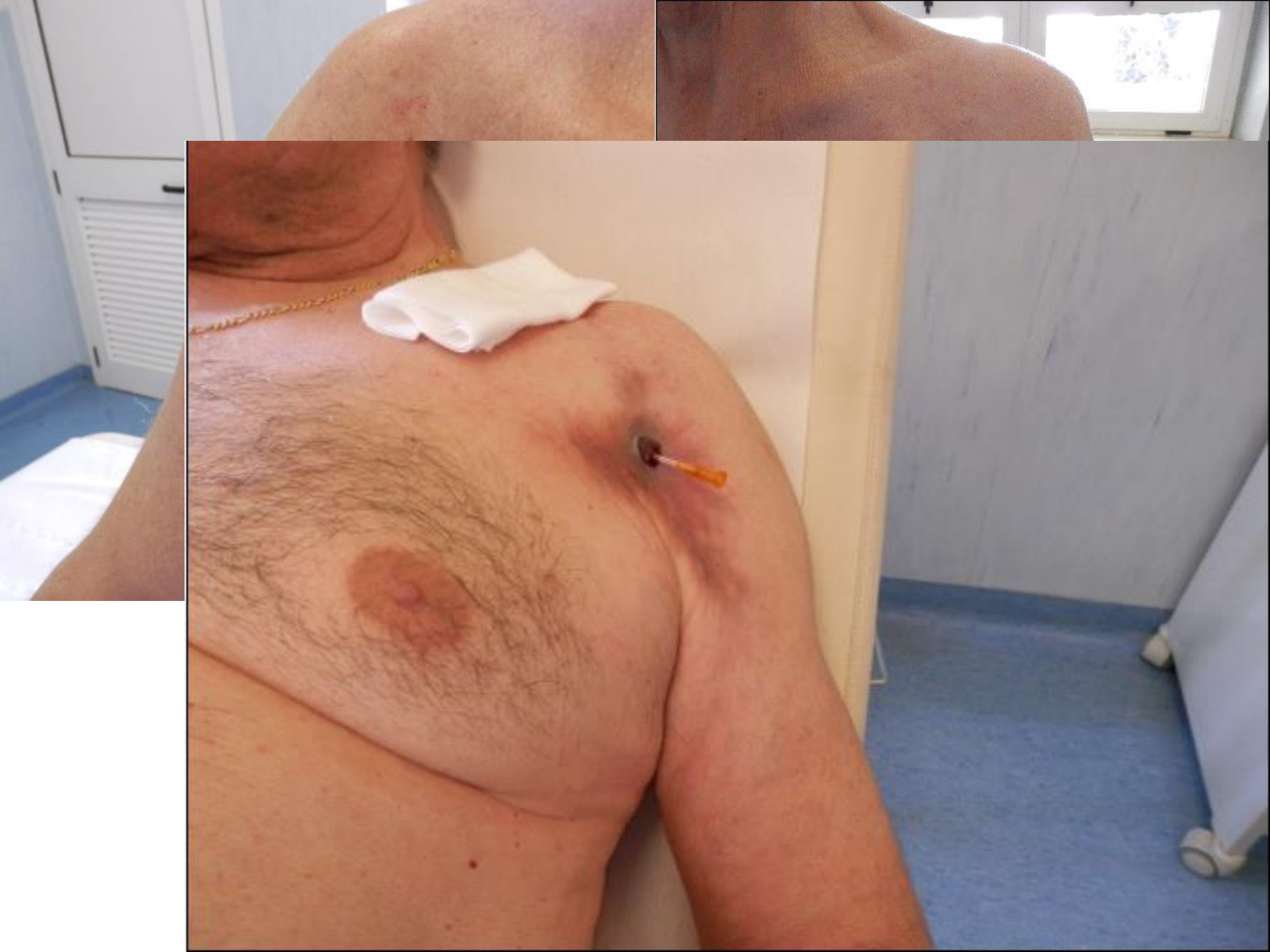
- Sinus tract communicating with prosthesis
- Presence of purulence
- Acute inflammation on histopathologic evaluation of periprosthetic tissue
- Two or more positive cultures with same organism (intraoperatively and/or preoperatively)
- Single positive culture with virulent organism

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	

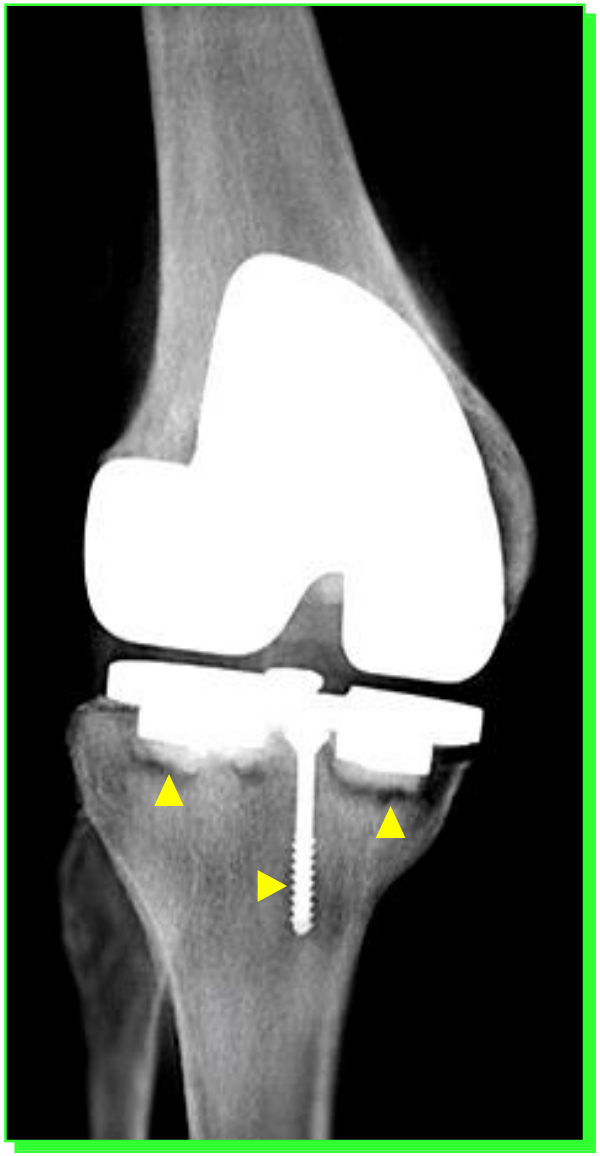
Minor Criteria	Threshold		Score	Decision
	Acute[€]	Chronic		
Serum CRP (mg/L)	100	10	2	Combined preoperative and postoperative score: ≥6 Infected 3-5 Inconclusive* <3 Not Infected
or				
D-Dimer (ug/L)	Unknown	860		
Elevated Serum ESR (mm/hr)	No role	30	1	
Elevated Synovial WBC (cells/μL)	10,000	3,000	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	

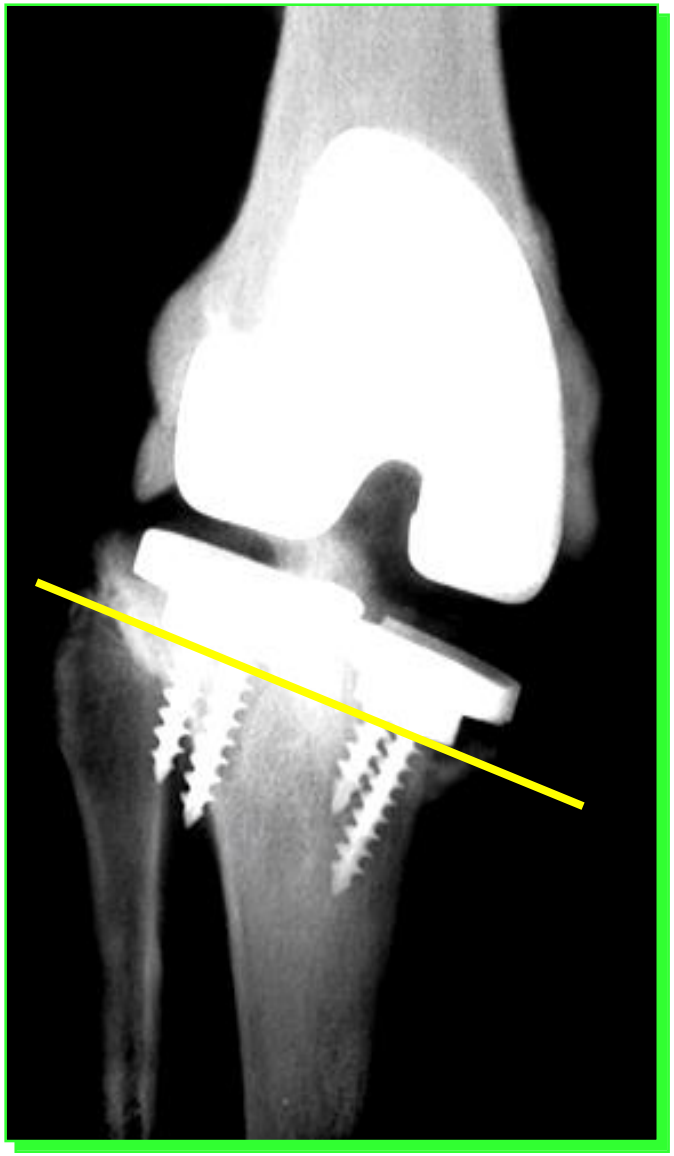
[€] These criteria were never validated on acute infections. ¥ No role in suspected adverse local tissue reaction. *Consider further molecular diagnostics such as Next-Generation Sequencing

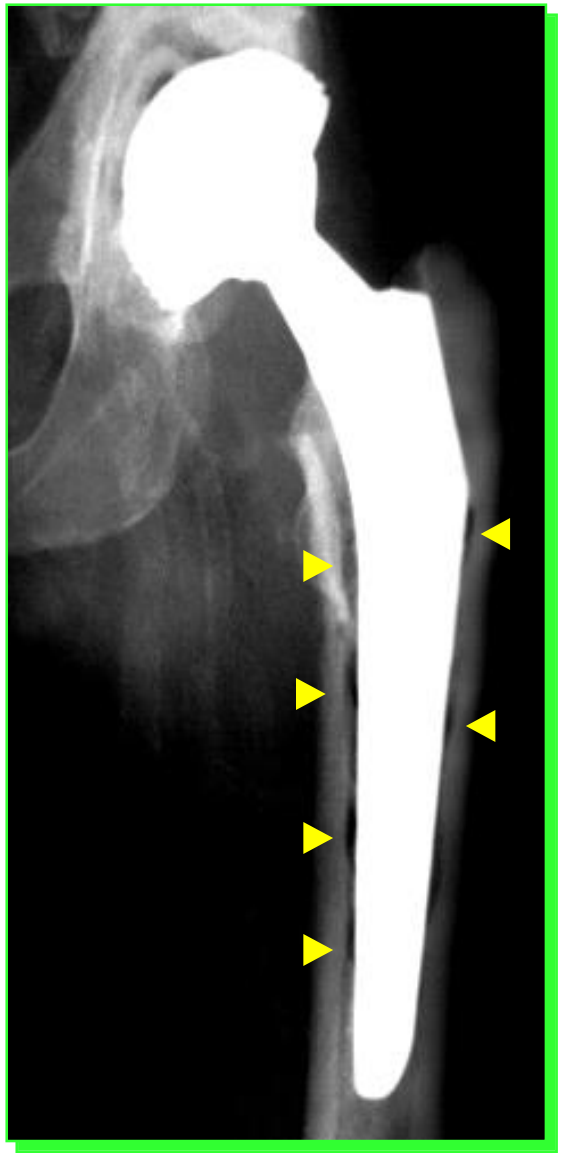


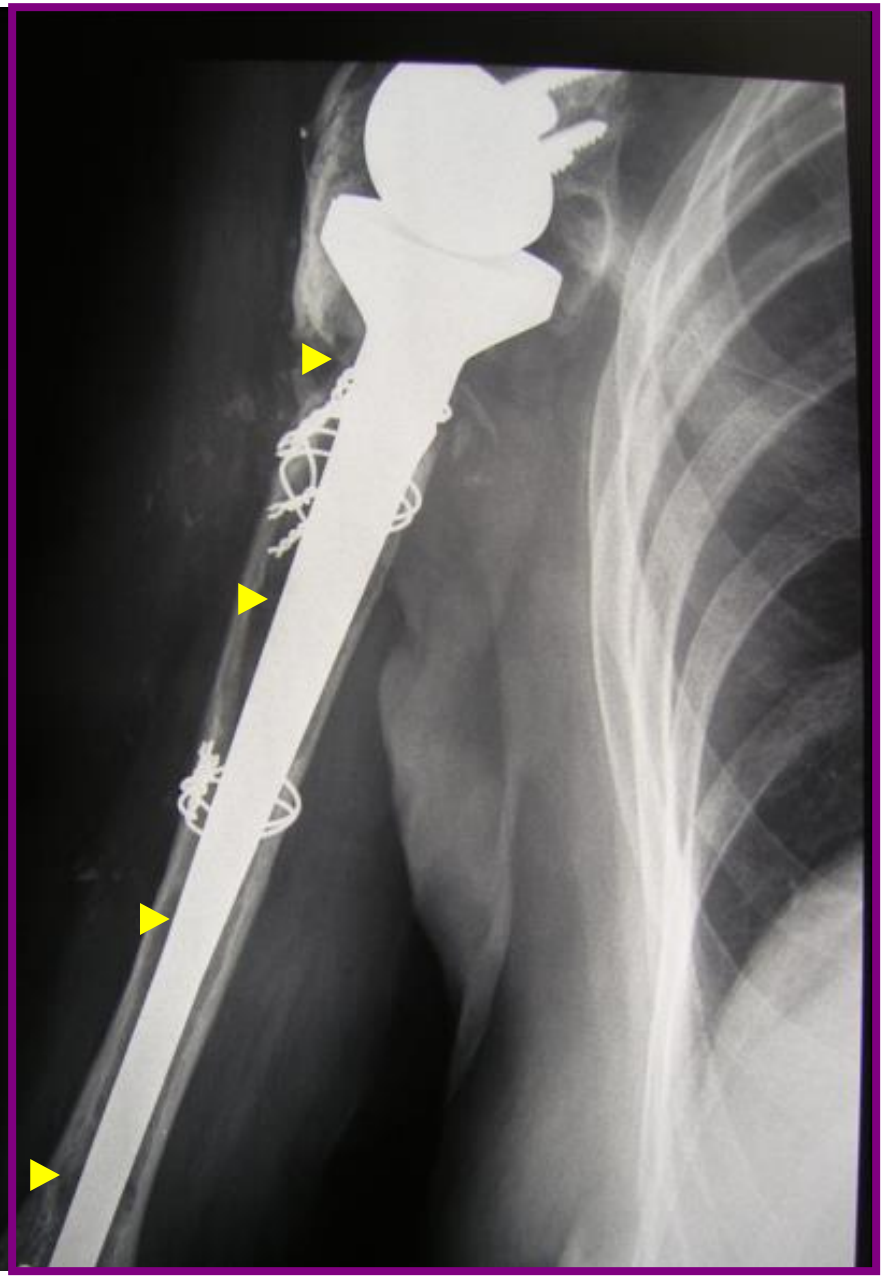


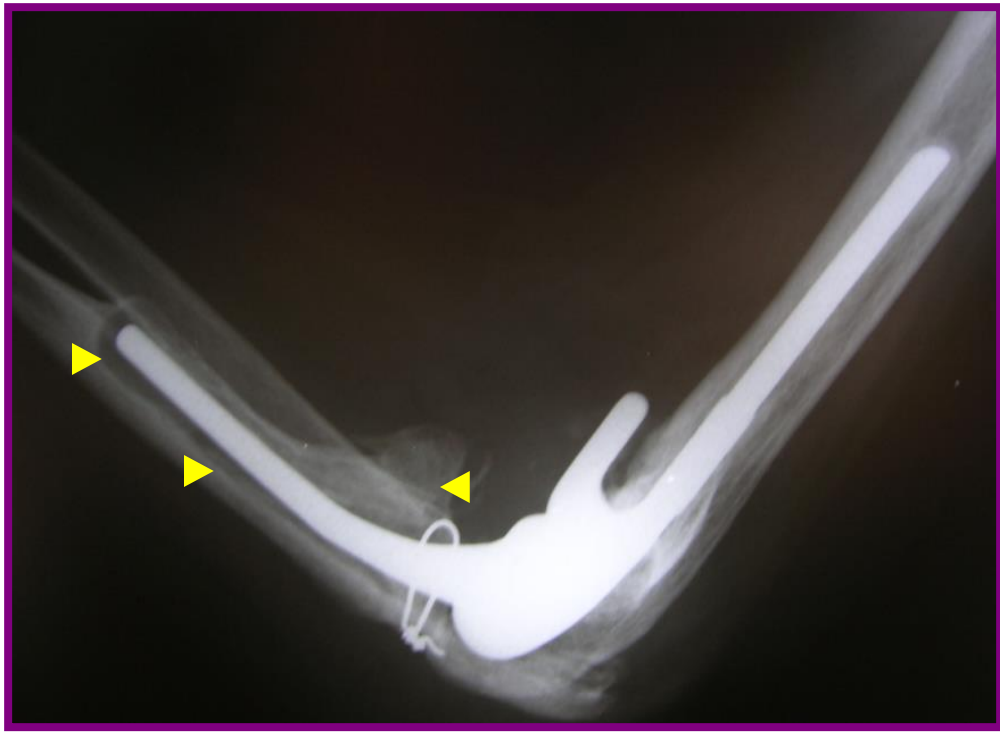
SEGNI RADIOGRAFICI











European Journal of Nuclear Medicine and Molecular Imaging (2019) 46:971–988
https://doi.org/10.1007/s00259-019-4263-9

GUIDELINES

Consensus document for the diagnosis of prosthetic joint infections: a joint paper by the EANM, EBJIS, and ESR (with ESCMID endorsement)

Alberto Signore[1,5] · Luca Maria Sconfienza[2,3] · Olivier Borens[4] · Andor W. J. M. Glaudemans[5] · Victor Casar-Pullicino[6] · Andrej Trampuz[7] · Heinz Winkler[8] · Olivier Gheysens[9] · Filip M. H. M. Vanhoenacker[10] · Nicola Petrosillo[11] · Paul C. Jutte[12]

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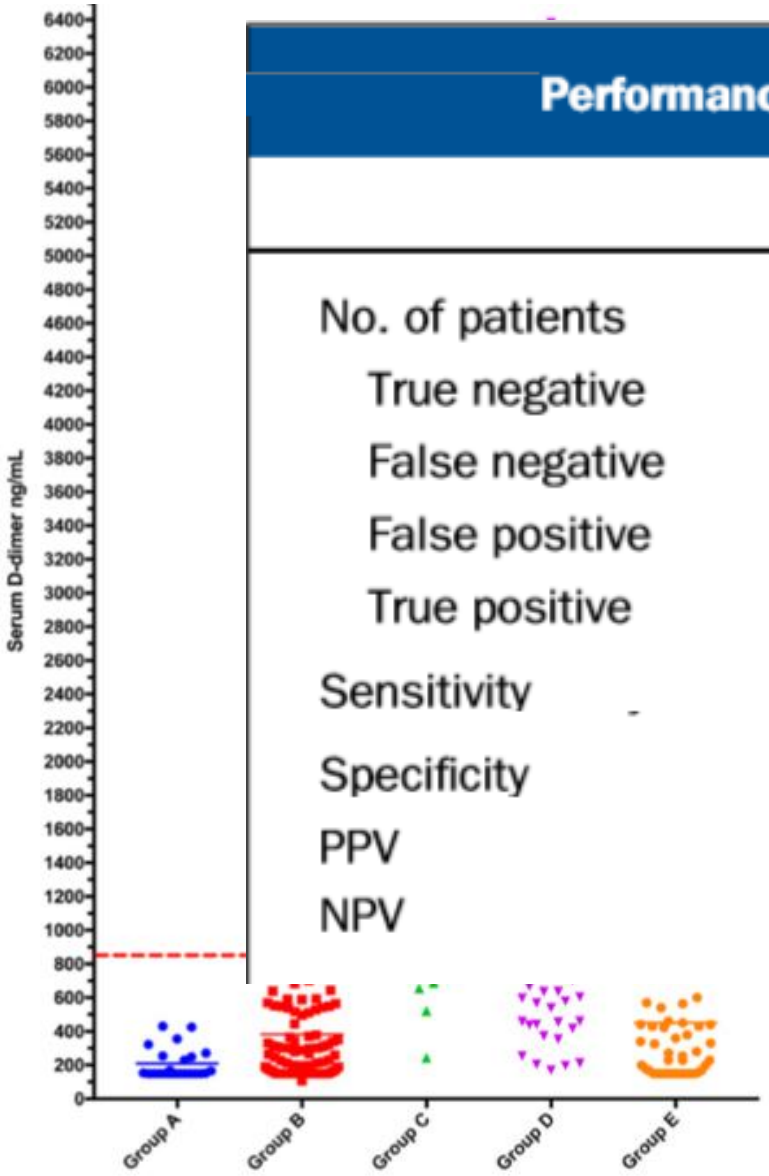
Table 1 Advanced radiological techniques

	Ultrasound	Computed tomography	Magnetic resonance
Pros	May be useful in monitoring soft tissue extension of infection and for soft tissue biopsies Widely available and low cost	Needed as a guide for bone biopsy Widely available and medium cost	High diagnostic accuracy using new sequences without interference from the prosthesis Widely available and medium cost Radiation-free
Cons	Low sensitivity and specificity for bone infection	Possible striking artefacts due to the metal nature of prosthesis Overall lower diagnostic accuracy than MR High radiation exposure Possible side effects from contrast agent	Peri-implant edema may occasionally suggest false-positive findings

Table 2 Advanced nuclear medicine techniques

	^{99m}Tc-MDP/HDP bone scan	^{99m}Tc-anti-granulocyte scan (IgG/Fab AGA)	^{99m}Tc-HMPAO/^{111}In-oxine-WBC scan	[^{18}F]FDG-PET/CT
Pros	High sensitivity Useful as screening method in chronic infections Widely available and low cost	High sensitivity and specificity; however, generally lower than for WBC scan Data support the preferential use of IgG over Fab in chronic infections. Widely available and medium cost Often to be used coupled with bone marrow scan and/or bone scan	High sensitivity and specificity Data support preferential use in acute infections Poor availability and medium cost Often to be used coupled with bone marrow scan SPECT/CT images improve accuracy	High sensitivity
Cons	Low specificity Moderate radiation exposure	Possible contraindications for IgG and HAMA induction Moderate radiation exposure IgG scan requires a late acquisition at 20 h p.i.	Moderate radiation exposure Always requires a late acquisition at 20 h p.i. Blood manipulation Needs an approved laboratory and method and trained personnel	Low specificity High radiation exposure Difficult interpretation of images Poor availability and high cost

Serum D-Dimer Test Is Promising for the Diagnosis of Periprosthetic Joint Infection and Timing of Reimplantation



Performance of Serum Tests for Diagnosing PJI*

	ESR	CRP	D-Dimer
No. of patients			
True negative	109	111	128
False negative	15	12	6
False positive	30	28	10
True positive	41	44	51
Sensitivity	73.21%	78.57%	89.47%
Specificity	78.42%	79.86%	92.75%
PPV	57.75%	61.11%	83.61%
NPV	87.90%	90.24%	95.52%

Parvizi J. Et al J Bone Joint Surg Am. 2017;99:1419-27

Leukocyte esterase analysis in the diagnosis of joint infection: Can we make a diagnosis using a simple urine dipstick?

Table 2 Specificity, sensitivity, positive predictive value, negative predictive value, accuracy and 95 % confidence interval

	Sensitivity*	Specificity	PPV**	NPV***	Accuracy
Total	100 (80–100)	91.9 (77–98)	87.0 (65–97)	100 (87–100)	94.7
Periprosthetic	100 (79–100)	97.0 (79–100)	95.0 (73–100)	100 (87–100)	98.2
Native	100 (55–100)	50 (9–91)	33.3 (2–87)	100 (20–100)	60

*All result in percent; $\frac{100}{(80\text{–}100)}$ indicates a sensitivity of 100 with 95 % confidence interval of 80 to 100 %

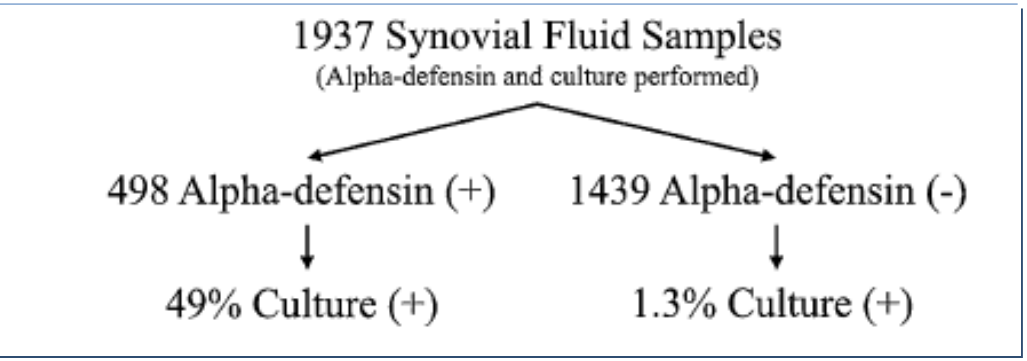
**PPV=positive predictive value

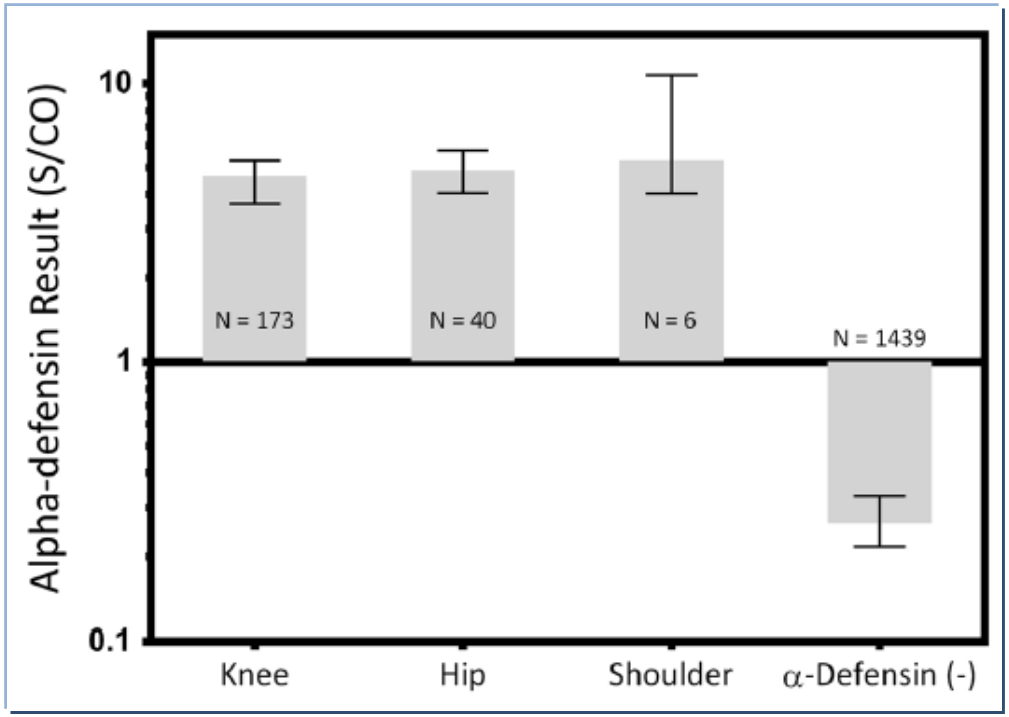
***PNPV=Negative predictive value

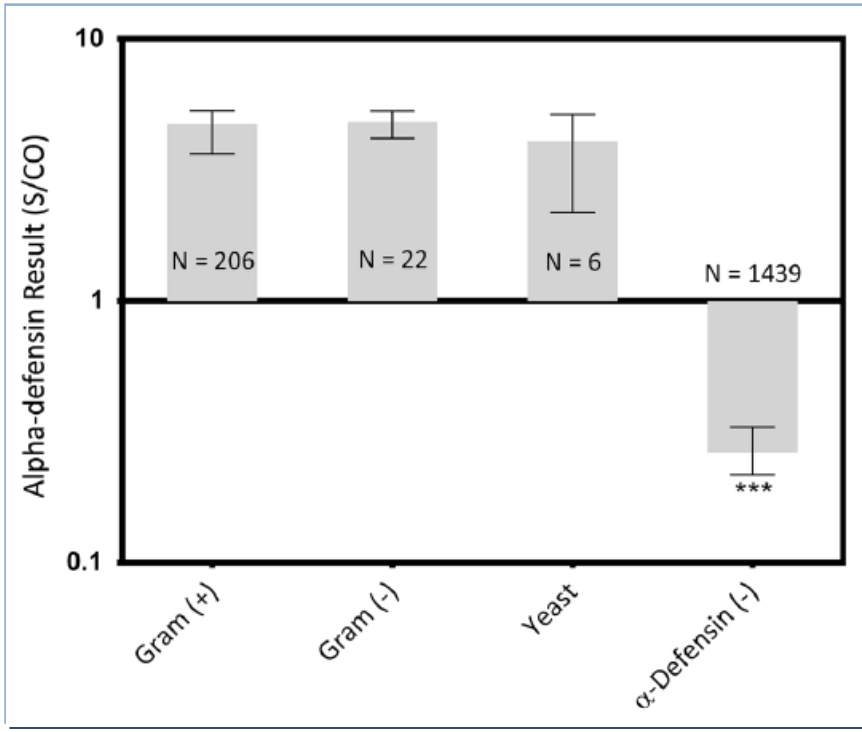
- Our test results confirm that the leukocyte esterase test can accurately detect PJI and that it can be used as a part of the traditional PJI workup.
- In the assessment of native joints, its high negative predictive value suggests that it is a valuable tool in excluding native joint septic arthritis.

Otis C. Colvin et al.:Skeletal Radiol (2015) 44:673–677

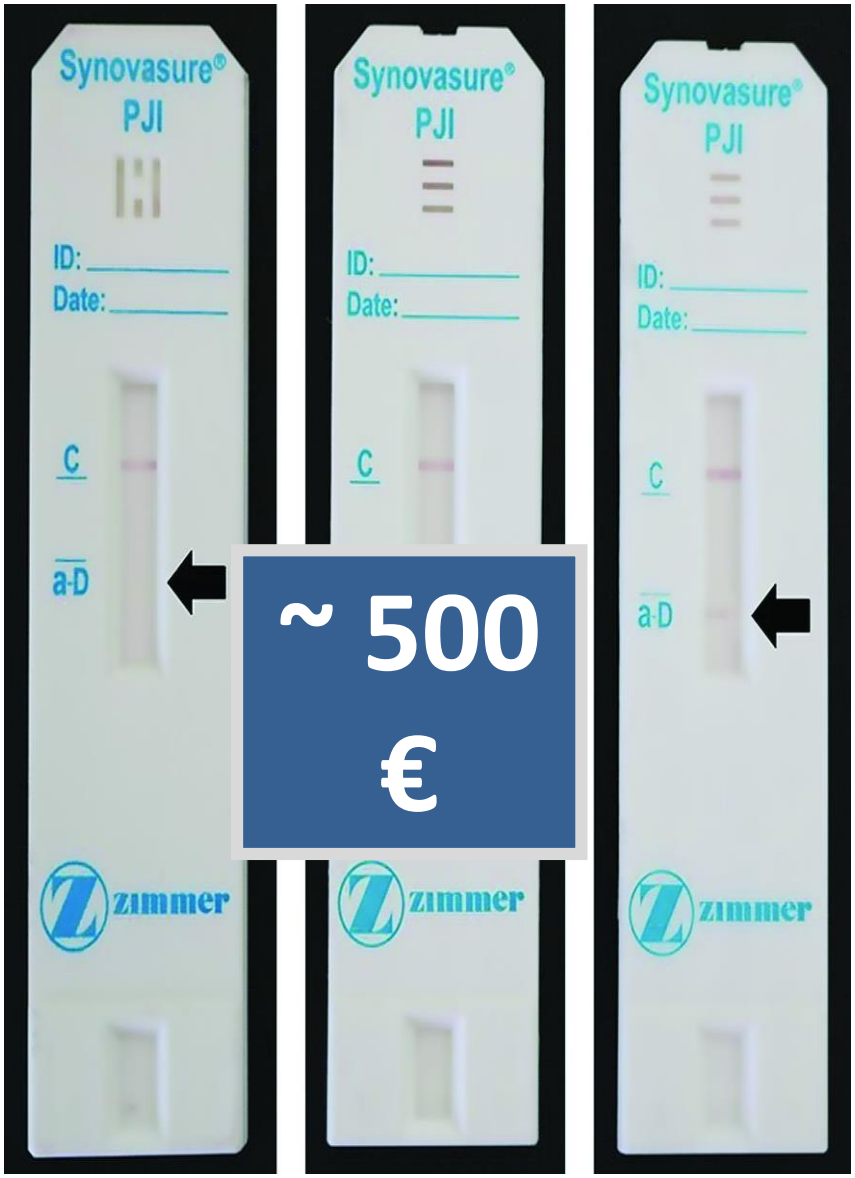
The Alpha-defensin Test for Periprosthetic Joint Infection Responds to a Wide Spectrum of Organisms







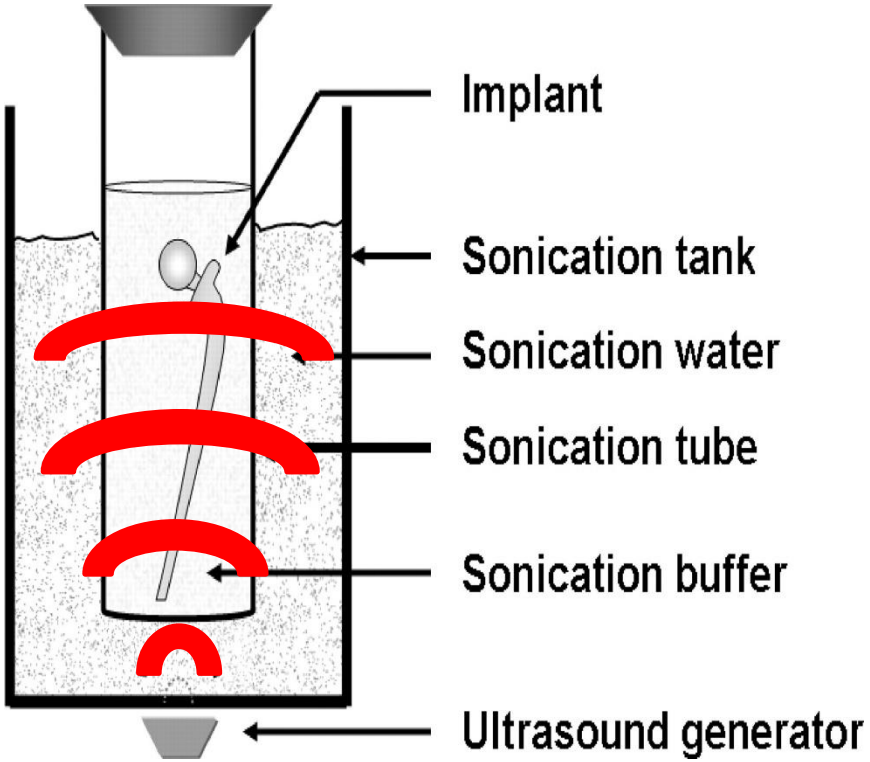
Deirmengian C. et al.:Clin Orthop Relat Res (2015) 473:2229–2235


Synovasure®
PJI
ID:
Date:
C
a-D
zimmer
~ 500
€


<0,50
€


-Cellularità
- Colturale
- Esterasi leucocitaria
- α-defensina
- Calprotectina
LA STORIA DEL PAZIENTE
LA CLINICA
GB VES PCR
DDimero
Rx
- Scintigrafia Tc Leu N.C.
- ECO TC RM (PET)
+++ colturali
Es.istologico
IDENTIFICAZIONE DEL PATOGENO

Monsen 2008



Sonicazione

Clinical Orthopaedics and Related Research. 476(1):137–145, JAN 2018
DOI: 10.1007/s11999.0000000000000060, PMID: 29389758
Issn Print: 0009-921X
Publication Date: 2018/01/01

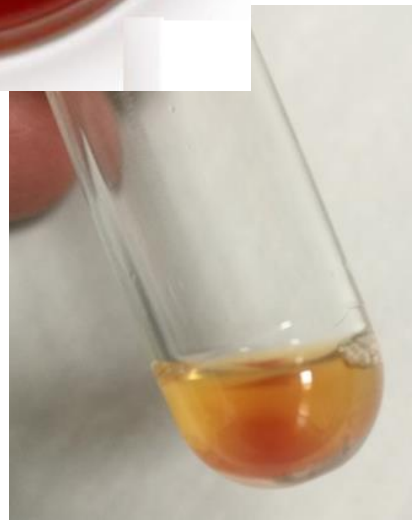
Is Treatment With Dithiothreitol More Effective Than Sonication for the Diagnosis of Prosthetic Joint Infection?

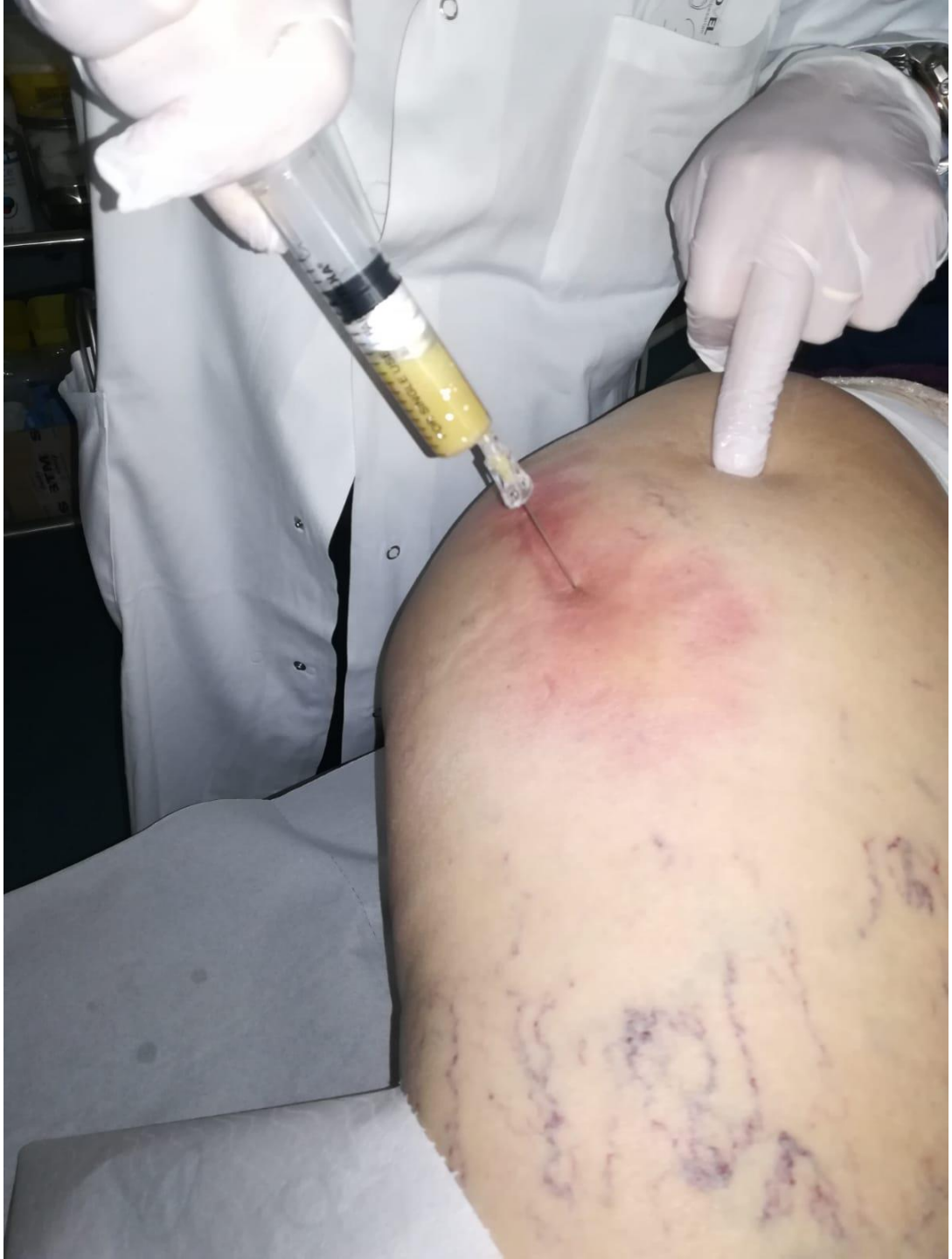
Andrea Sambri; Matteo Cadossi; Sandro Giannini; Giovanni Pignatti; Maurilio Marcacci; Maria Pia Neri; Alessandra Maso; Elisa Storni; Simonetta Gamberini; Susanna Naldi; Arianna Torri; Silvia Zannoli; Martina Tassinari; Michela Fantini; Giuseppe Bianchi; Davide Donati; Vittorio Sambri

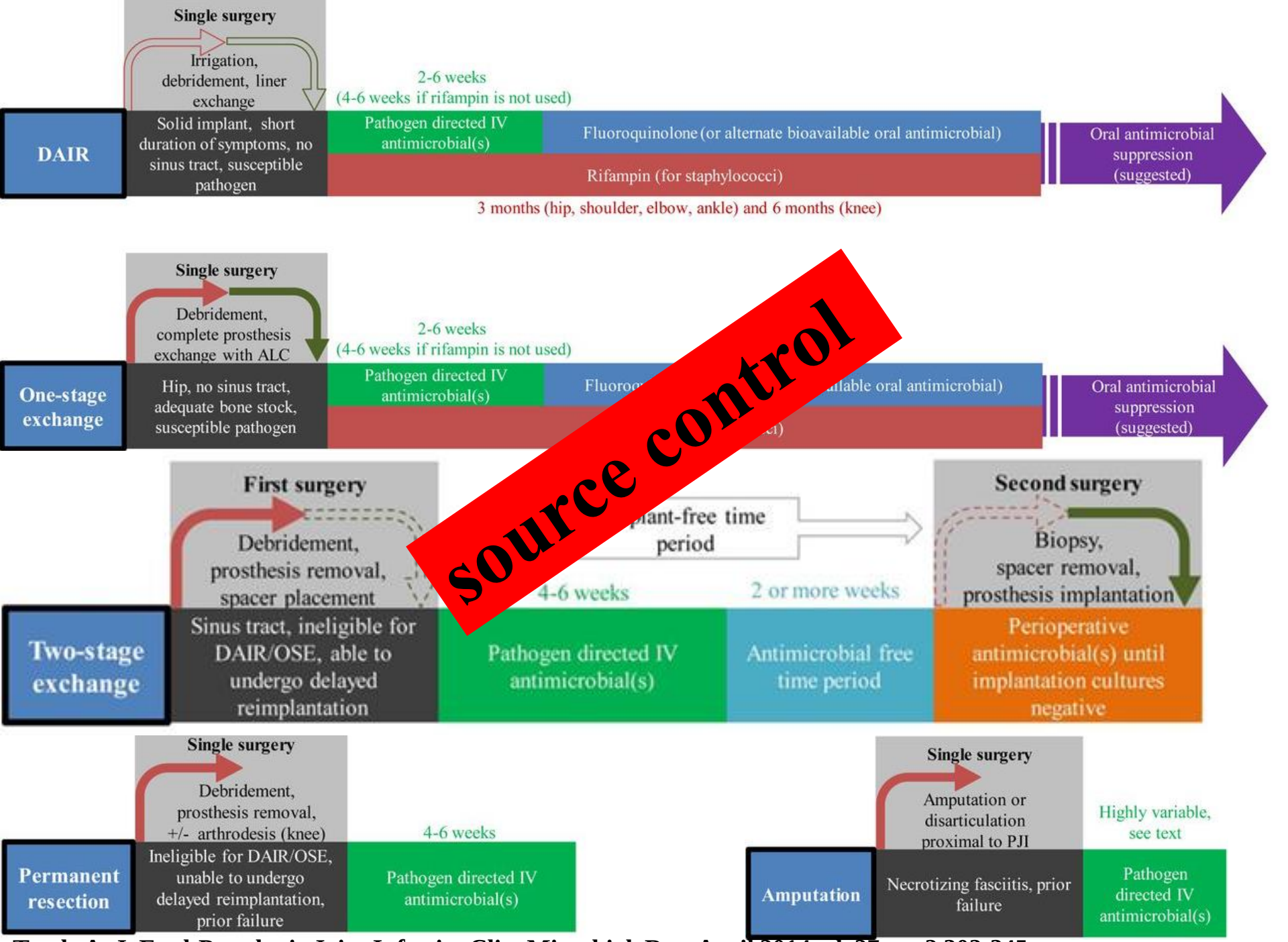
In this randomized study, we found **no difference in sensitivity between DTT and sonication for the detection of PJI**, and both of those tests were more sensitive than standard tissue cultures. Thus, cultures of sonication or DTT fluid should be considered important additional tools to standard cultures for definition of PJI and should be considered together with other criteria, especially in settings where infection is not suspected before revision surgery.


BACTEC


BBL™ Fluid
Thioglycollate
Medium
IVD





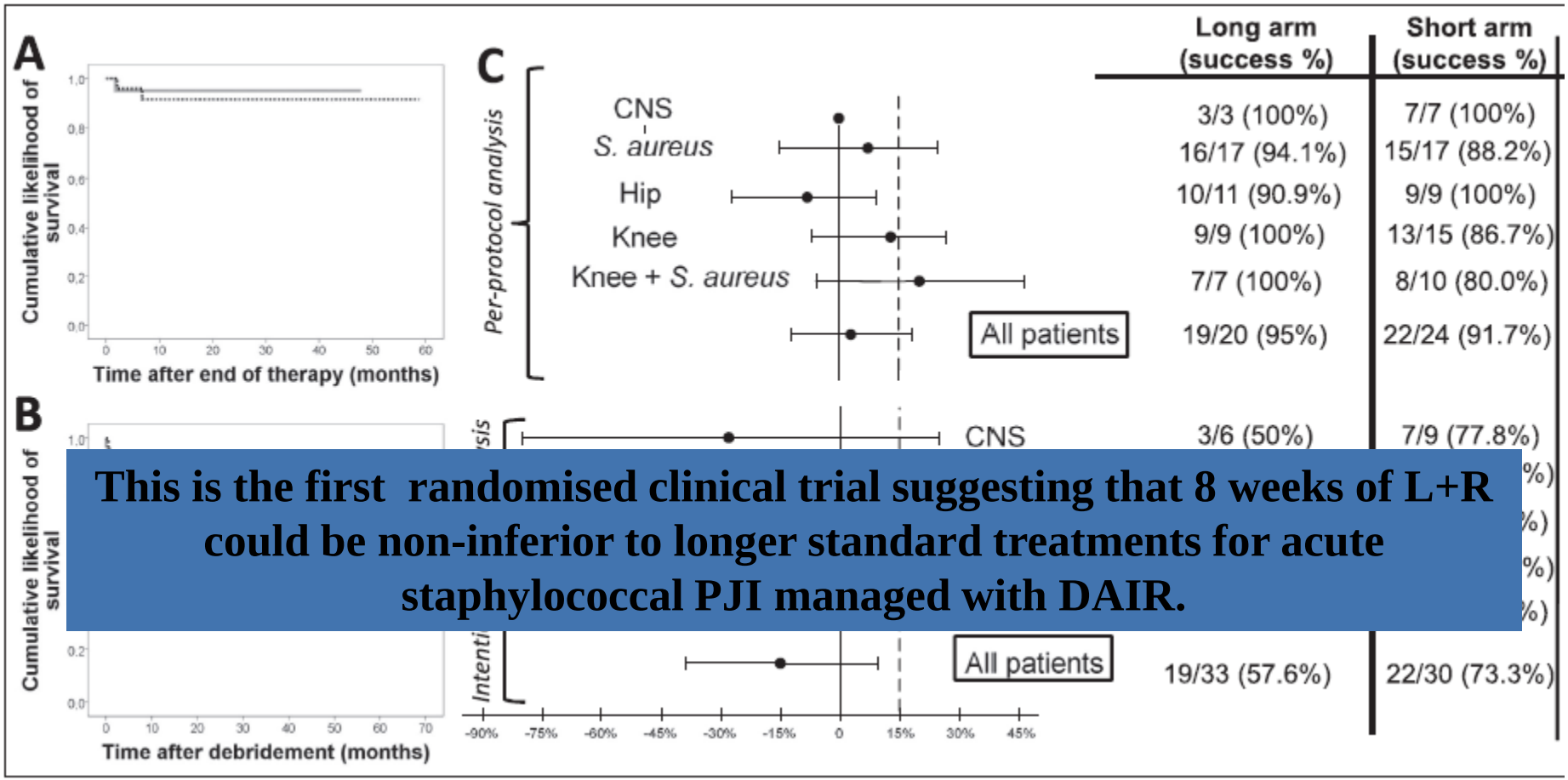


Tande A. J. Et al:Prosthetic Joint InfectionClin. Microbiol. Rev. April 2014vol. 27 no. 2 302-345

Debridement and polyethylene exchange
Antibiotic
Implant **R**etention

Are 3-6 months necessary?
IV/OS…….?

SHORT- VERSUS LONG-DURATION LEVOFLOXACIN PLUS RIFAMPICIN FOR ACUTE STAPHYLOCOCCAL PROSTHETIC JOINT INFECTION MANAGED WITH IMPLANT RETENTION: A RANDOMISED CLINICAL TRIAL



This is the first randomised clinical trial suggesting that 8 weeks of L+R could be non-inferior to longer standard treatments for acute staphylococcal PJI managed with DAIR.

J. Lora-Tamayo et al. / International Journal of Antimicrobial Agents 48 (2016) 310–316

International Journal of Infectious Diseases

Contents lists available at ScienceDirect

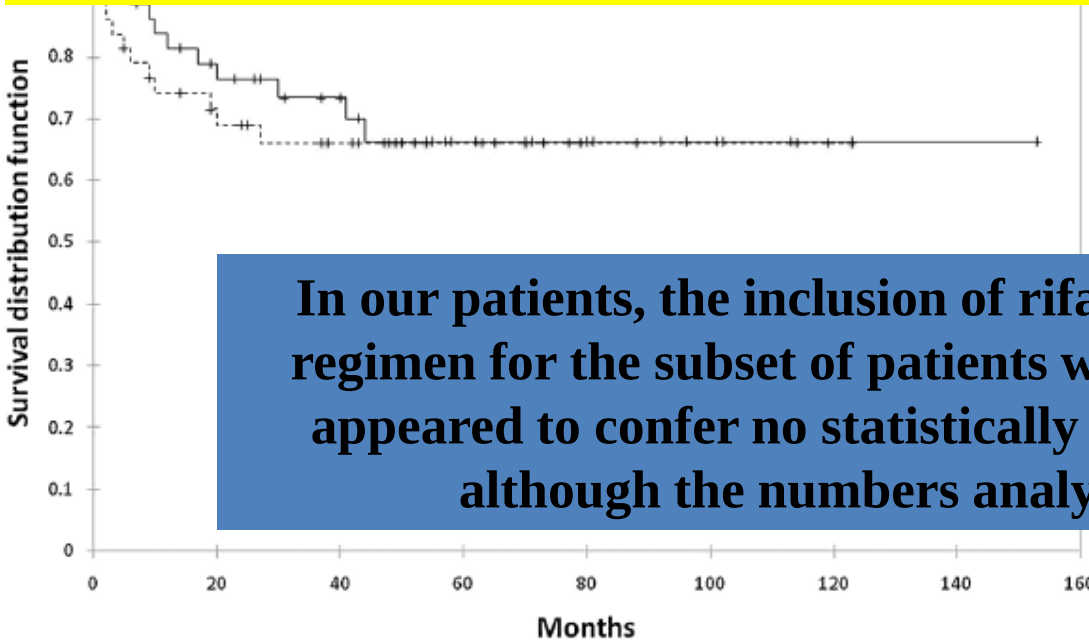
International Journal of Infectious

journal homepage: www.elsevier.com/loc

ELSEVIER

87 patients
debridements were performed within
3 weeks of symptom

60 patients with PJI (**69%**) remained in **remission**, with no significant difference between hip and knee cases (73.3% vs. 59.3%, 95% confidence interval (CI), 0.20–1.38), or between patients receiving **6 compared with 12 weeks of antibiotic treatment** (70.5% vs.67.4%, 95%CI 0.27–2.10, p = 0.60). **MRSA was isolated from 13.8%** of infections and **this was the only variable associated with a poorer outcome** (remission in 41.7% vs. 73.3% for those with other pathogens, 95%CI 0.05–0.77, p = 0.02).



In our patients, the inclusion of rifampin in the antibiotic regimen for the subset of patients with S. aureus infection appeared to confer no statistically significant advantage although the numbers analysed were small

Kaplan Meier remission curve for patients treated for 6 or 12 weeks with antibiotics

Rifampicin might be most effective during the first days after debridement, the time period in which new biofilm formation on the surface of the implant needs to be prevented

*Therefore in our tertiary institution for orthopedic implant surgery, all patients with an acute staphylococcal PJI who underwent a DAIR were treated with **only five days of rifampicin** in combination with at least 6 weeks of betalactam/glycopeptide antibiotics, both started intraoperatively*

Journal of Infection
Volume 76, Issue 5, May 2018, Pages 498-500

Outcome of acute staphylococcal prosthetic joint infection treated with debridement, implant retention and antimicrobial treatment with short duration of rifampicin

Henk Scheper ✉, Daphne van Hooven, Michiel van de Sande, Robert van der Wal, Martha van der Beek, Leo Visser, Mark de Boer, Rob Nelissen

Show more

https://doi.org/10.1016/j.jinf.2018.01.009

Table 2
Subgroup analyses of outcome of DAIR and 5 days of rifampicin for acute staphylococcal PJI.[a]

	n	Complete cure[b]	Functional cure[c]
All patients	41	63%	76%
Patients without megaprosthesis	27	70%	78%
Hip PJI	18	83%	89%
Knee PJI	9	44%	56%
Patients with a megaprosthesis[d]	14	50%	71%
All patients with steroids/anti-TNF/MTX	11	46%	55%

[a] Acute: symptoms or last operation/revision < 8 weeks.
[b] Complete cure: absence of infection and a stable retained implant for at least six months after stopping antibiotic therapy.
[c] Functional cure: stable prosthesis in situ but with chronic suppressive antimicrobial therapy.
[d] Mega prosthesis: patients with bone- or soft-tissue tumors.
Anti-TNF: tumor necrosis factor inhibitors, MTX: methotrexate.

Does Prior Failed Debridement Compromise the Outcome of Subsequent Two-Stage Revision Done for Periprosthetic Joint Infection Following Total Knee Arthroplasty?

Cumulative Survival Rates.

	F-DAIR Group (%) (n = 88)	DTSR Group (%) (n = 96)	Overall (%) (N =
6 mo	90.90	94.79	91.84
1 y	82.95	88.54	
2 y	79.54	85.41	
5 y	77.27	84.37	.98
10 y	76.13	84.37	80.43

beginning of the end of DAIR?

A failed-DAIR procedure before a 2 ion TKA is associated with a higher probability of failure (**almost twice the ris** d to those undergoing a direct two stage revision . This is also associated wit nctional outcome scores, lower ROM, and higher wound-related complication t should be emphasized to the patient to make an informed decision.

A highe e of patients with MRSA and *Pseudomonas* infection were noted in the failed DAIR gro p. Also, the chances of eradication of these organisms are diminished in the prior failed debridement group compared to those undergoing a direct 2-stage surgery. We recommend that patients with PJIs caused by these organisms should undergo an early 2-stage revision.

Rajgopal A. et al.: J Arthroplasty 2018 Aug;33(8):2588-2594.

Debridement and polyethylene exchange
Antibiotic
Implant **R**etention


DAIR
Daptomycin 850 mg q 24 h 5 weeks

Provenienza: VIN VC MALATTIE INFETTIVE

Data Di Accettazione **08/11/2016** Ore: 14:45
Data Nascita: 21/07/1957 Età: 59 Anni

Routine

Richiesta: **154064**

Descrizione Analisi	*Risultato*	*U. di Misura*	*Int. di Riferimento*	*Metodo*

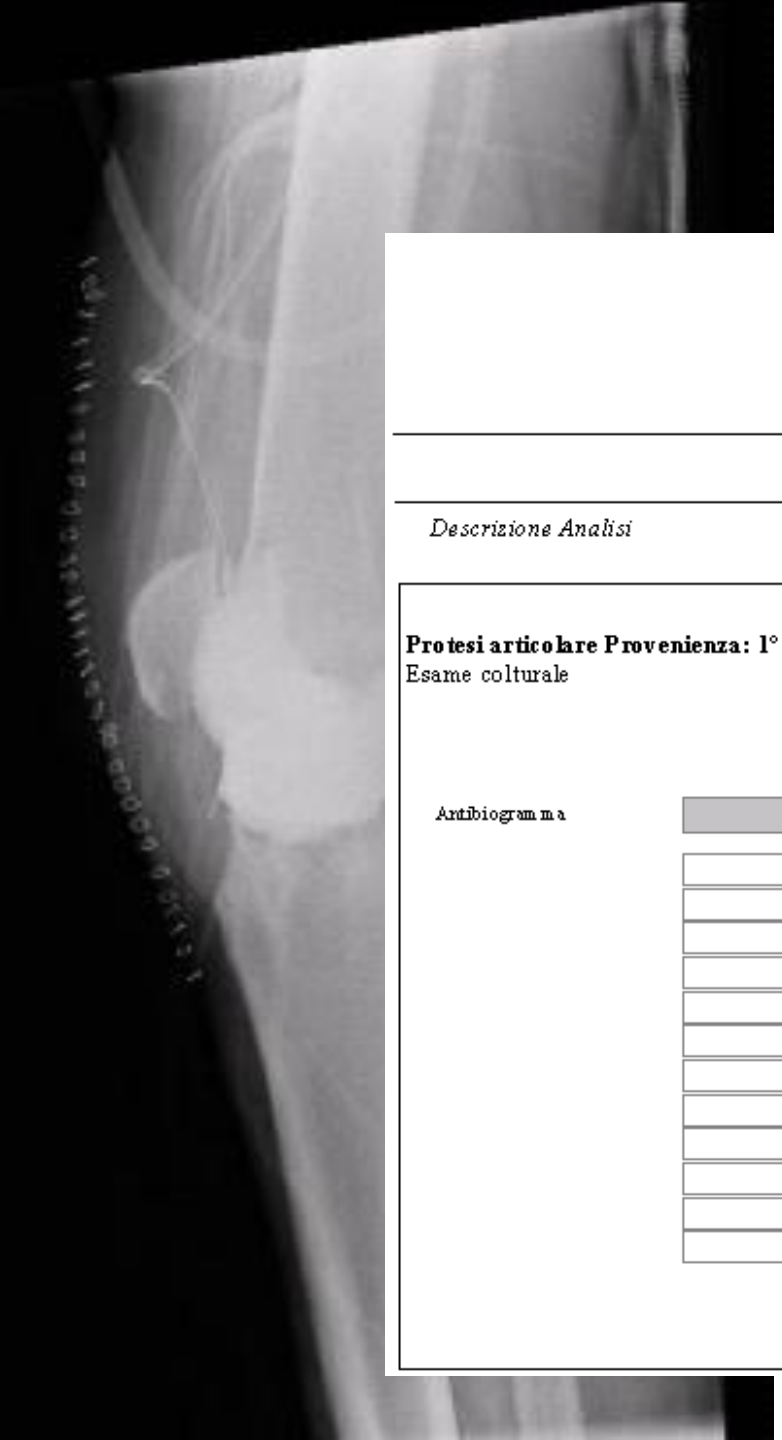
Liquido articolare Provenienza:
Ricerca areobi/miceti **Positivo/a**

	Microorganismo	*Carica*
1	Pseudomonas aeruginosa	

Antibiogramma

ANTIBIOTICI	1	*MIC*
Amikacina	S	<=4
Cefepime	S	2
Ceftazidima	S	2
Ciprofloxacina	S	<=0,25
Colistina	S	<=1
Gentamicina	S	<=1
Imipeneme	S	2
Levofloxacina	S	<=0,5
Meropeneme	S	0,25
Piperacillina	S	<=4
Piperacillina-tazobattame	S	<=4/4
Tobramicina	S	<=1

S=Sensibile, R=Resistente, I=Intermedio



Provenienza: VOT VC ORTO.-TRAUMA.

Data Di Accettazione **18/11/2016** Ore: 12:15
Data Nascita: 21/07/1957 Età: 59 Anni

Routine

Richiesta: **158984**

Descrizione Analisi	*Risultato*	*U. di Misura*	*Int. di Riferimento*	*Metodo*

Protesi articolare Provenienza: 1° campione

Esame colturale **Positivo/a** (Colturale)

Microorganismo *Carica*

1 Pseudomonas aeruginosa

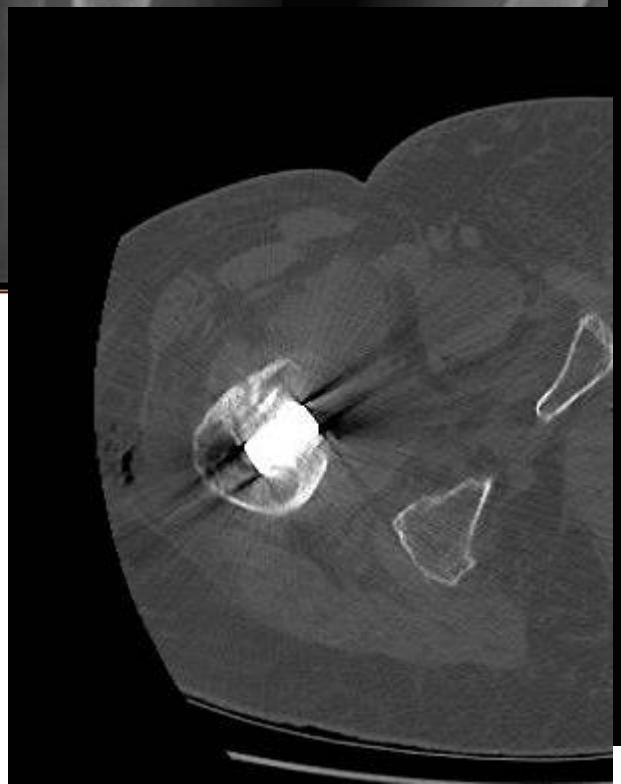
Antibiogramma

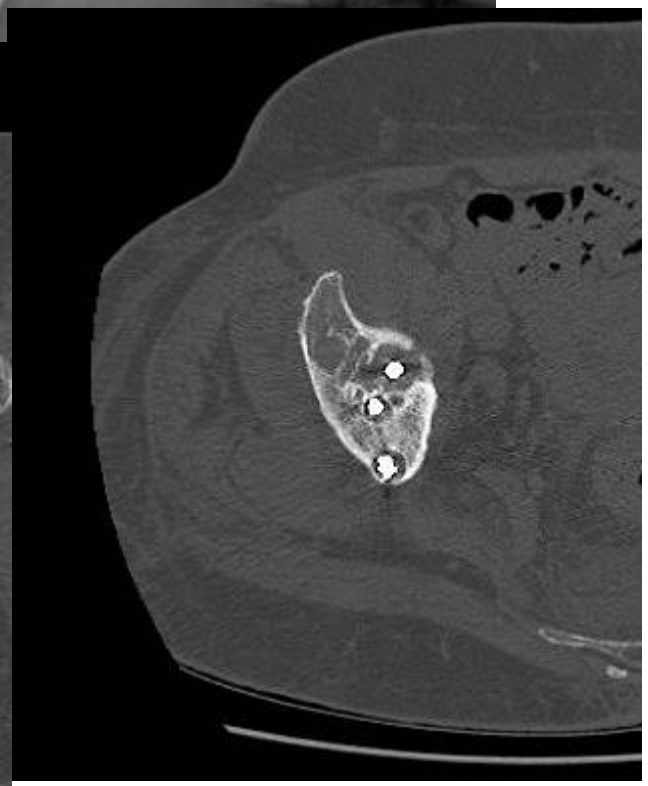
ANTIBIOTICI	1	*MIC*
Amikacina	S	<=4
Cefepime	S	4
Ceftazidima	S	4
Ciprofloxacina	S	<=0,25
Colistina	S	<=1
Gentamicina	S	2
Imipeneme	S	2
Levofloxacina	S	1
Meropeneme	S	0,25
Piperacillina	S	8
Piperacillina-tazobattame	S	<=4/4
Tobramicina	S	<=1

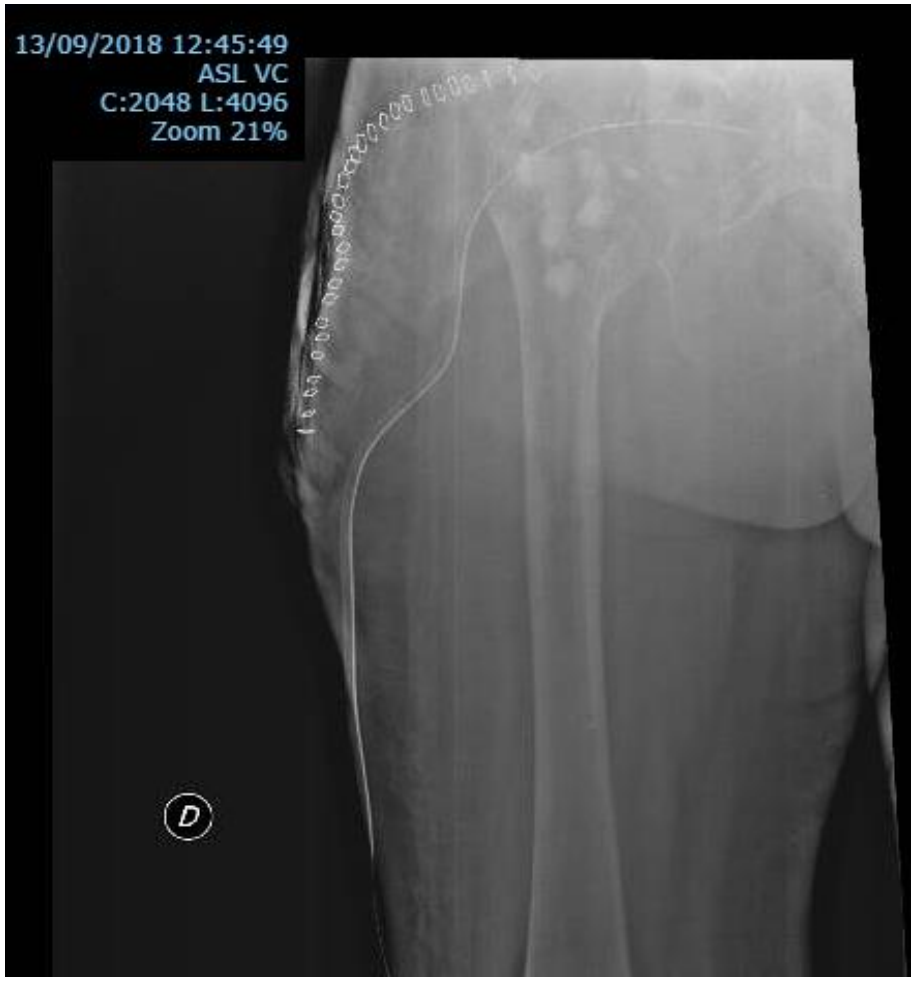
S=Sensibile, R=Resistente, I=Intermedio

Sepsi da MRSA dopo 4 mesi da reimpianto PTH trattata con Daptomicina 700 mg die da 9 gg

Trasferita per persistenza febbre dolore e flogosi anca dx







Altro Provenienza: 2° campione

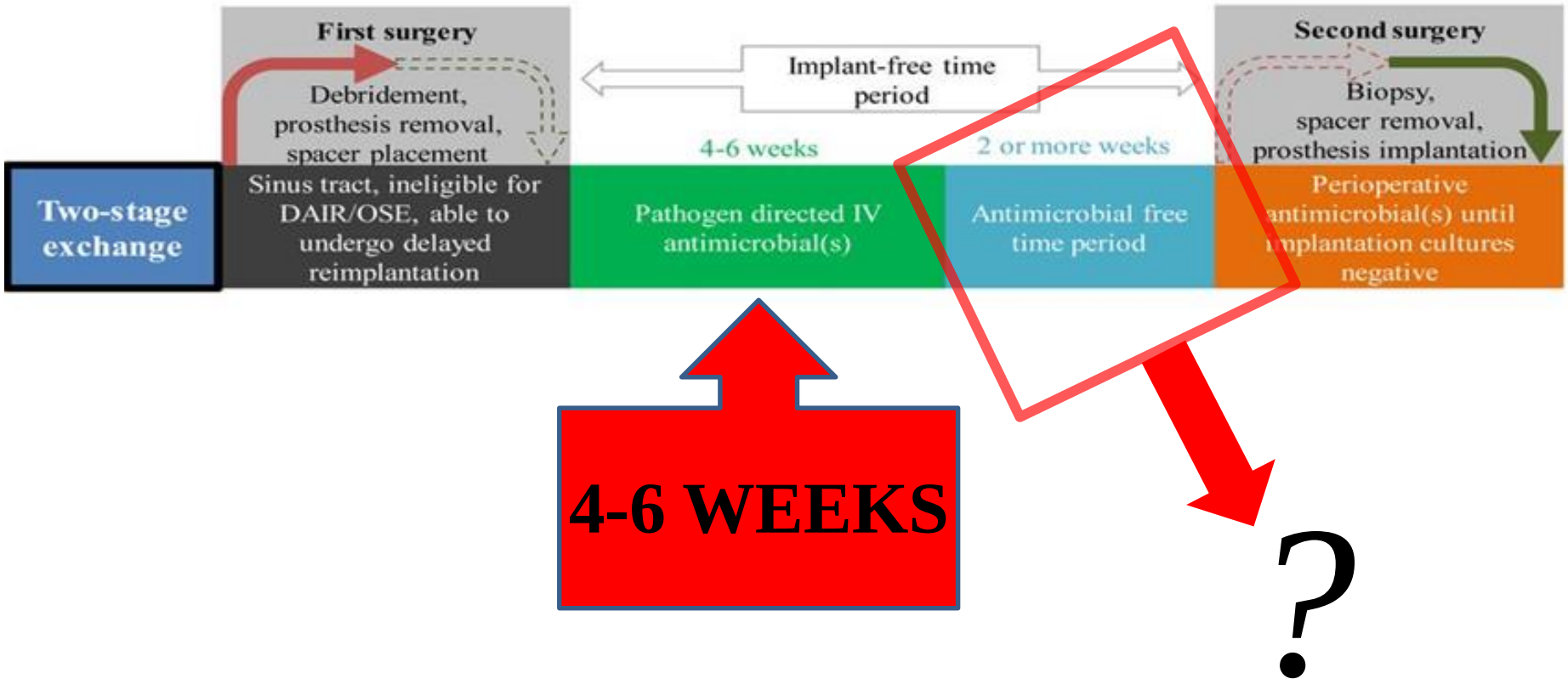
Esame colturale **Positivo/a**

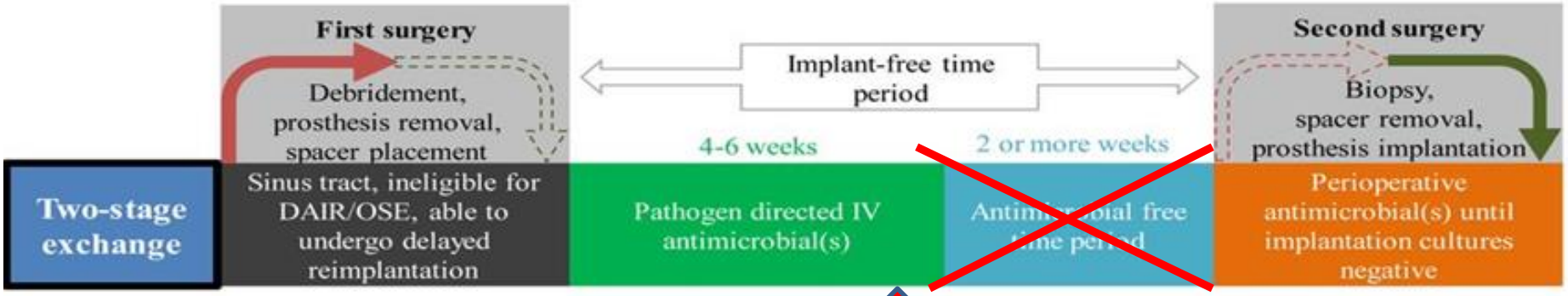
Microorganismo

Klebsiella pneumoniae ssp pne

Antibiogramma

ANTIBIOTICI	I	*MIC*
Amikacina	R	>16
Amoxicillina-clavulanato (f)	R	>32/2
Ampicillina	R	>8
Cefepime	S	<=1
Cefotaxima	R	>4
Ceftazidima	R	>8
Cefuroxime	R	>8
Ciprofloxacina	R	>1
Colistina	S	<=1
Ertapenem	R	>1
Fosfomicina c/G6P	S	<=16
Gentamicina	S	2
Imipeneme	R	>8
Levofloxacina	R	>2
Meropeneme	R	>8
Piperacillina	R	>16
Piperacillina-tazobattame	R	>16/4
Tigeciclina	I	2
Tobramicina	R	>4
Trimetoprima-sulfametoxazolo	R	>4/76


First surgery
Debridement, prosthesis removal, spacer placement
Implant-free time period
Second surgery
Biopsy, spacer removal, prosthesis implantation
4-6 weeks
2 or more weeks
Two-stage exchange
Sinus tract, ineligible for DAIR/OSE, able to undergo delayed reimplantation
Pathogen directed IV antimicrobial(s)
Antimicrobial free time period
Perioperative antimicrobial(s) until implantation cultures negative
4-6 WEEKS
?



6-8 WEEKS

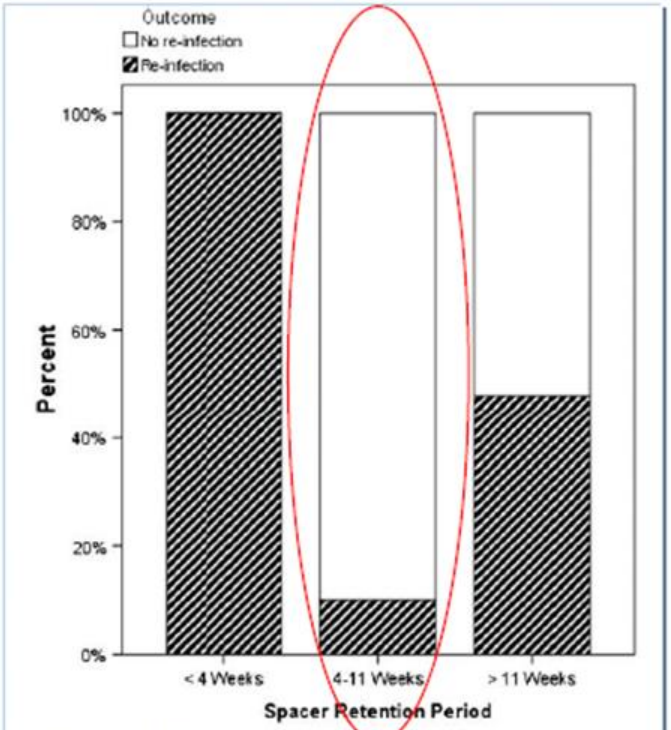


Fig. 1 Reinfection-rates depending on time of spacer-retention in patients who have undergone two-stage revision arthroplasty

International Orthopaedics (SICOT) (2015) 39:1731-1736

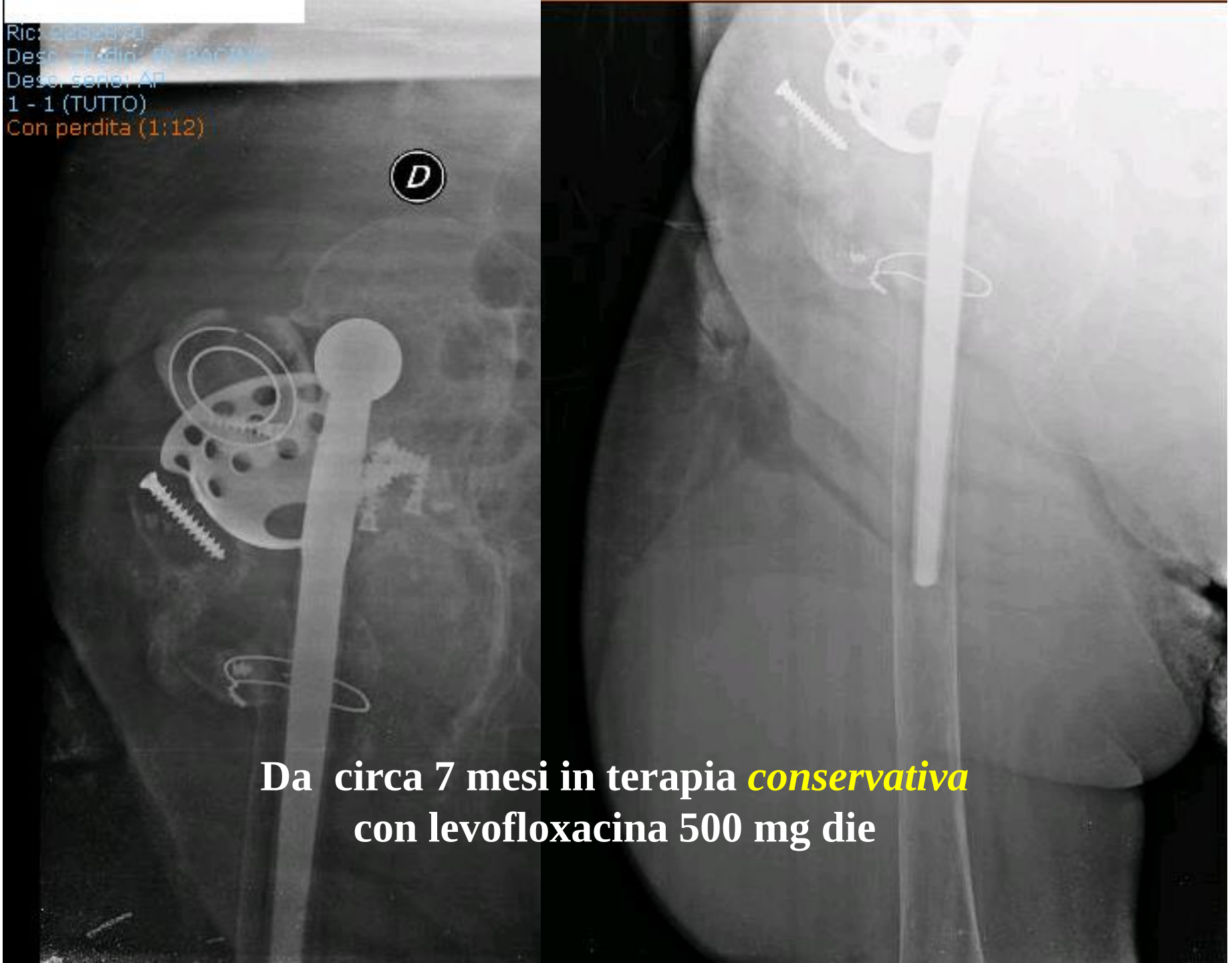
TERAPIA ANTIBIOTICA *CONSERVATIVA* CRONICA

- **Controindicazioni all'intervento / rifiuto del Pz**
- **Elevata sensibilità del patogeno ad antibiotici orali**

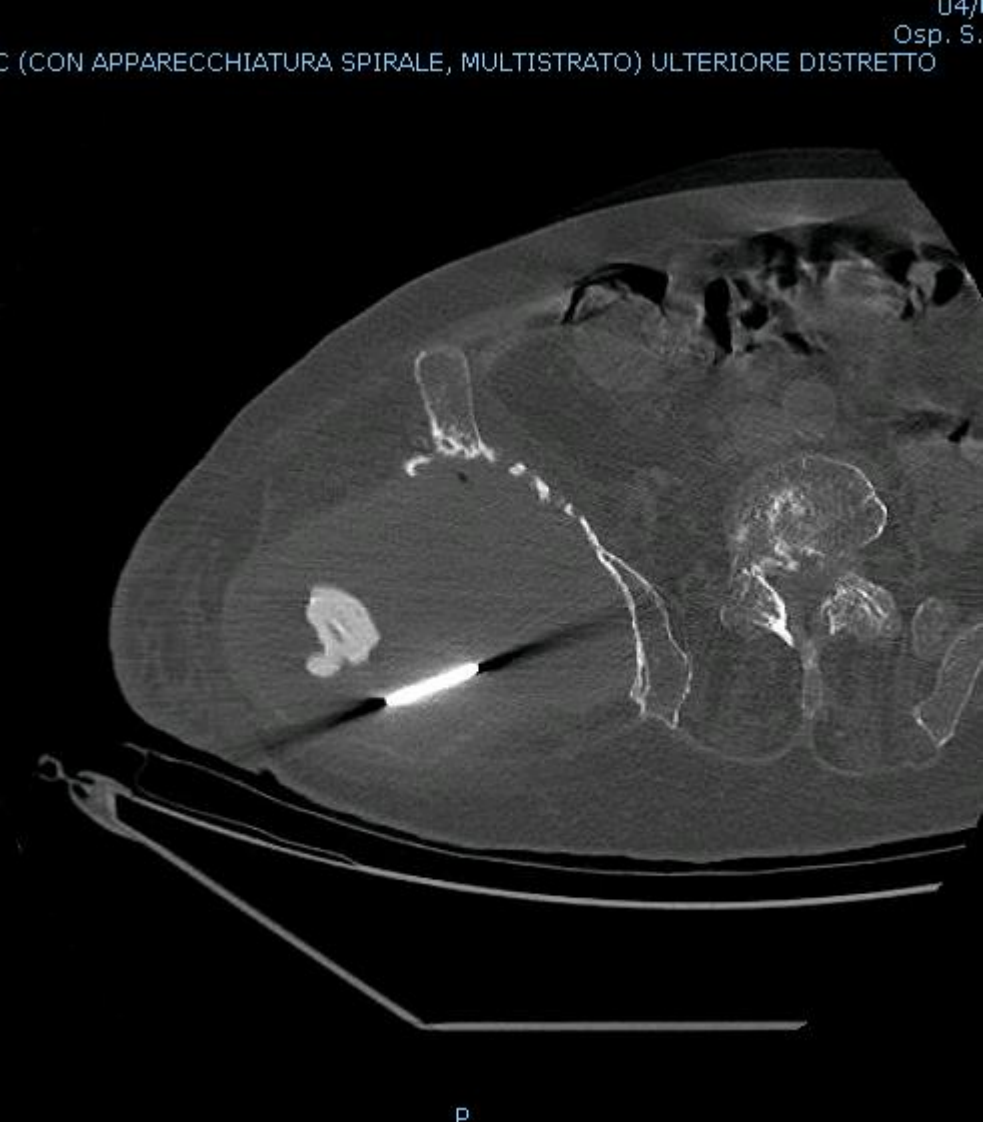
…… o Ultra-long acting ev

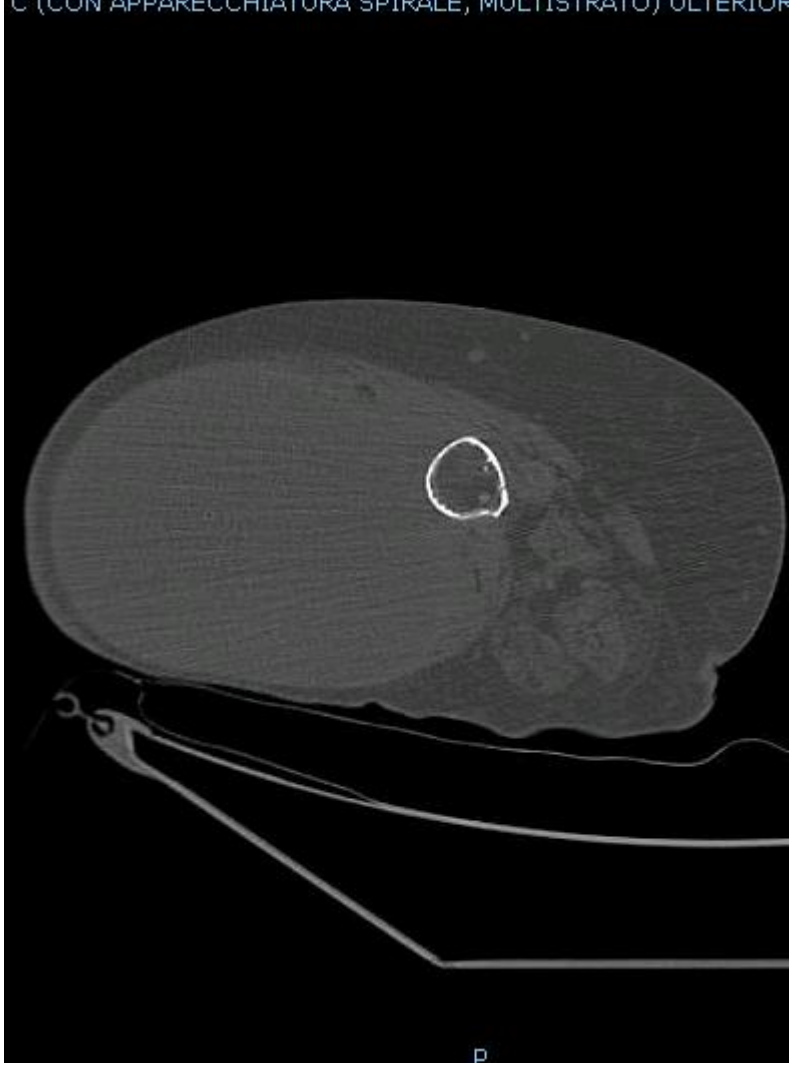
- **Buona tollerabilità parenchimi / paziente alla terapia prescelta**
- **Protesi stabile**

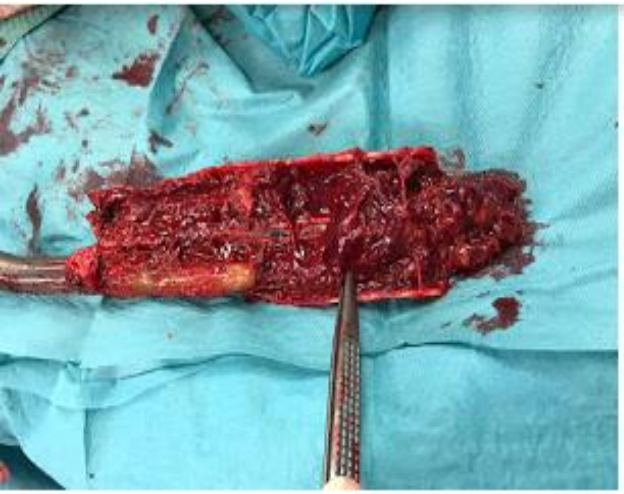
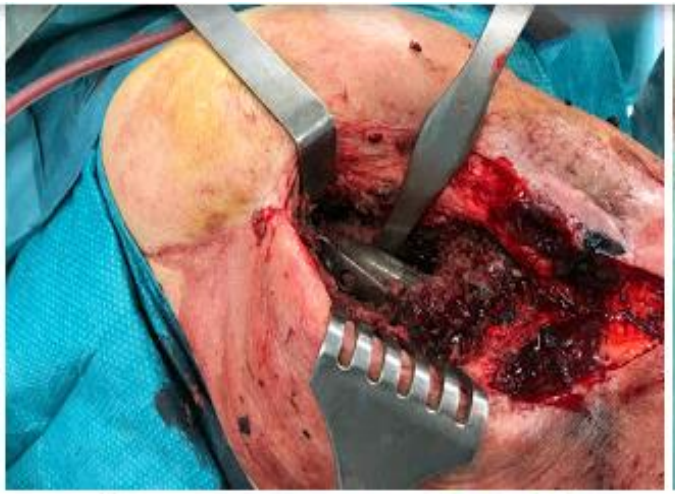
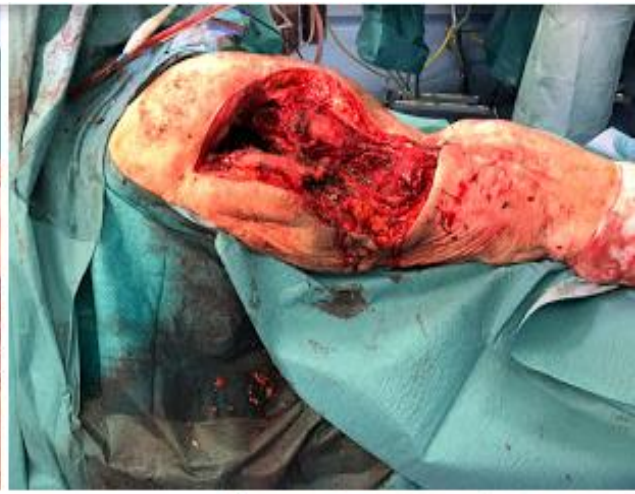
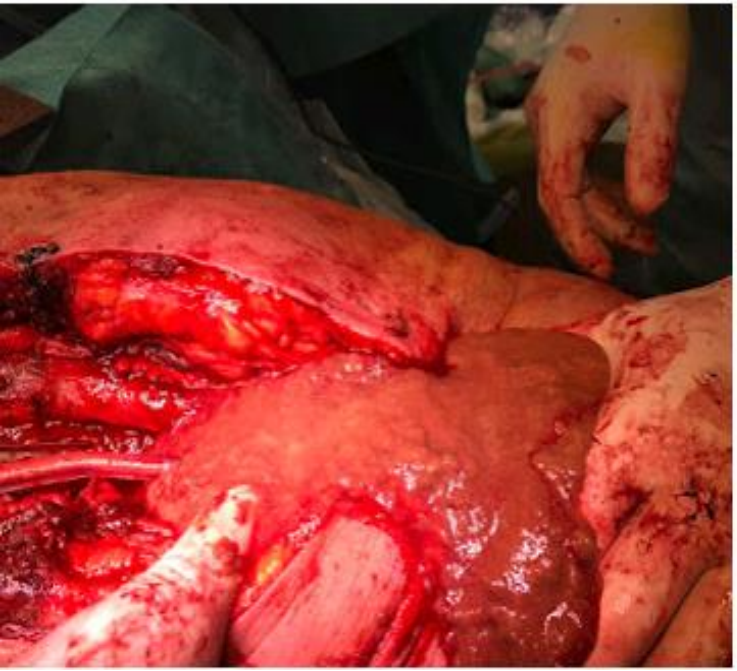
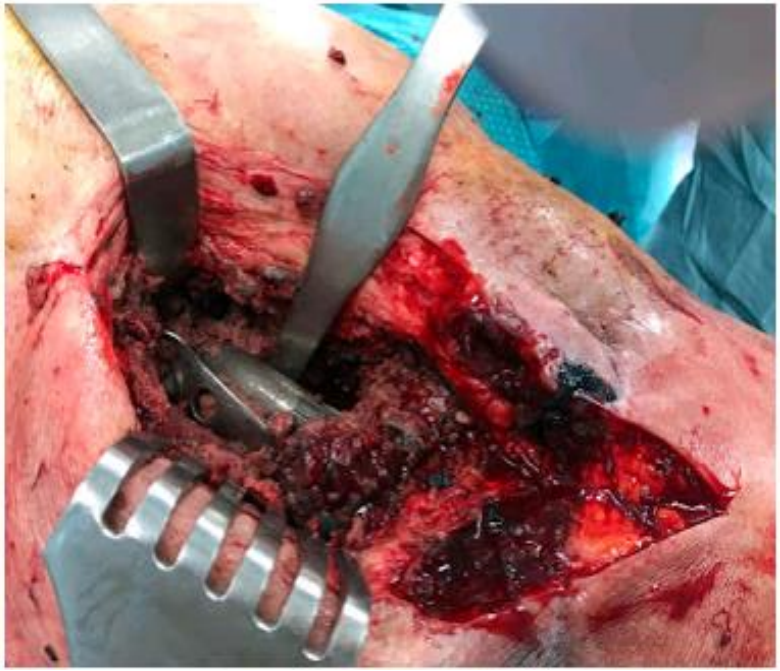
MONITORAGGIO BIOCHIMICO/MICROBIOLOGICO / RADIOLOGICO

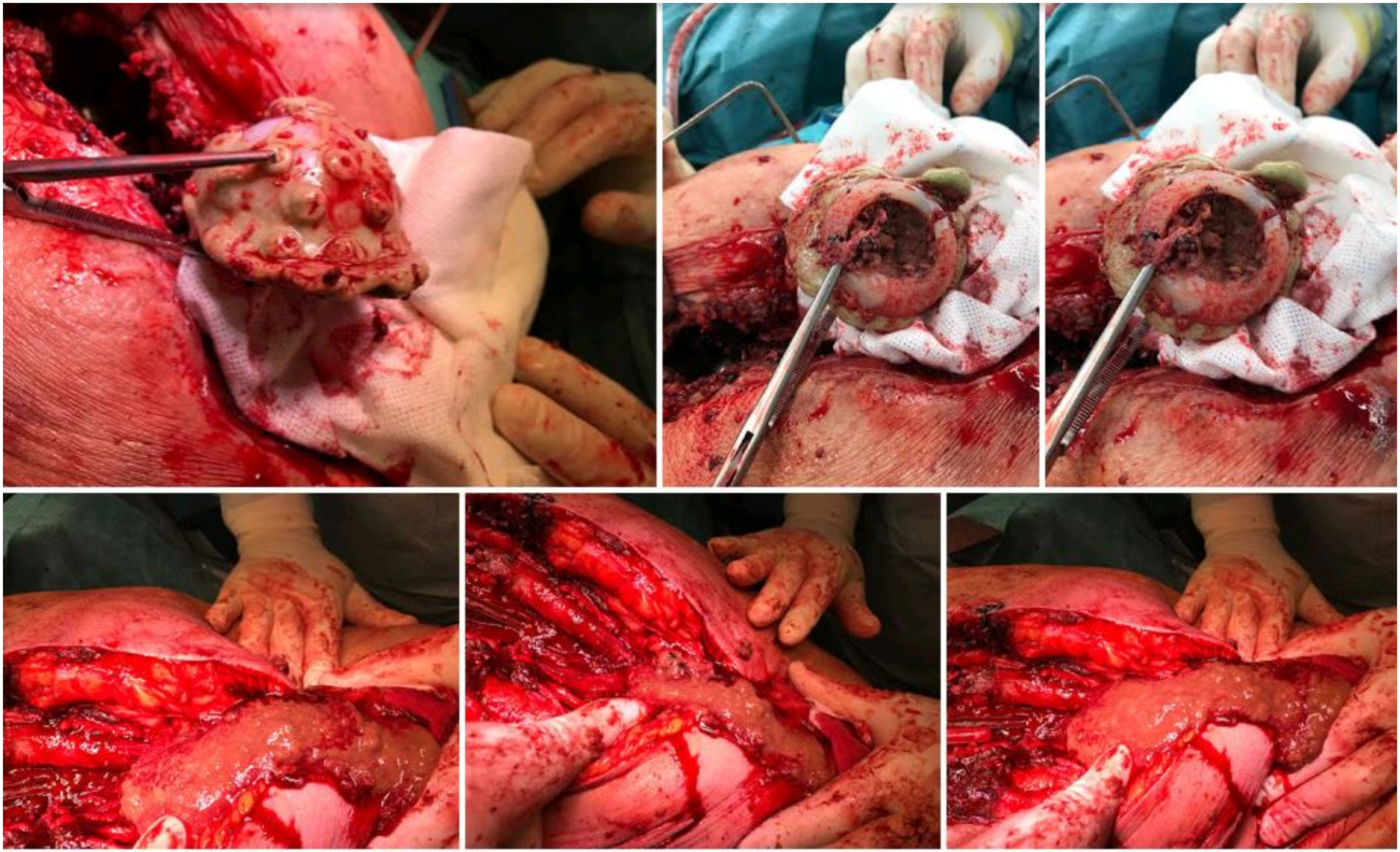


Da circa 7 mesi in terapia *conservativa*
con levofloxacina 500 mg die


04/
Osp. S.
C (CON APPARECCHIATURA SPIRALE, MULTISTRATO) ULTERIORE DISTRETTO
P


C (CON APPARECCHIATURA SPIRALE, MULTISTRATO) ULTERIOR
P

Altro Provenienza: 1° campione

Esame colturale **Positivo/a** (Colturale)

	Microorganismo	*Carica*
1	Proteus mirabilis	
2	Kleb. pneumo. ssp pneu.	

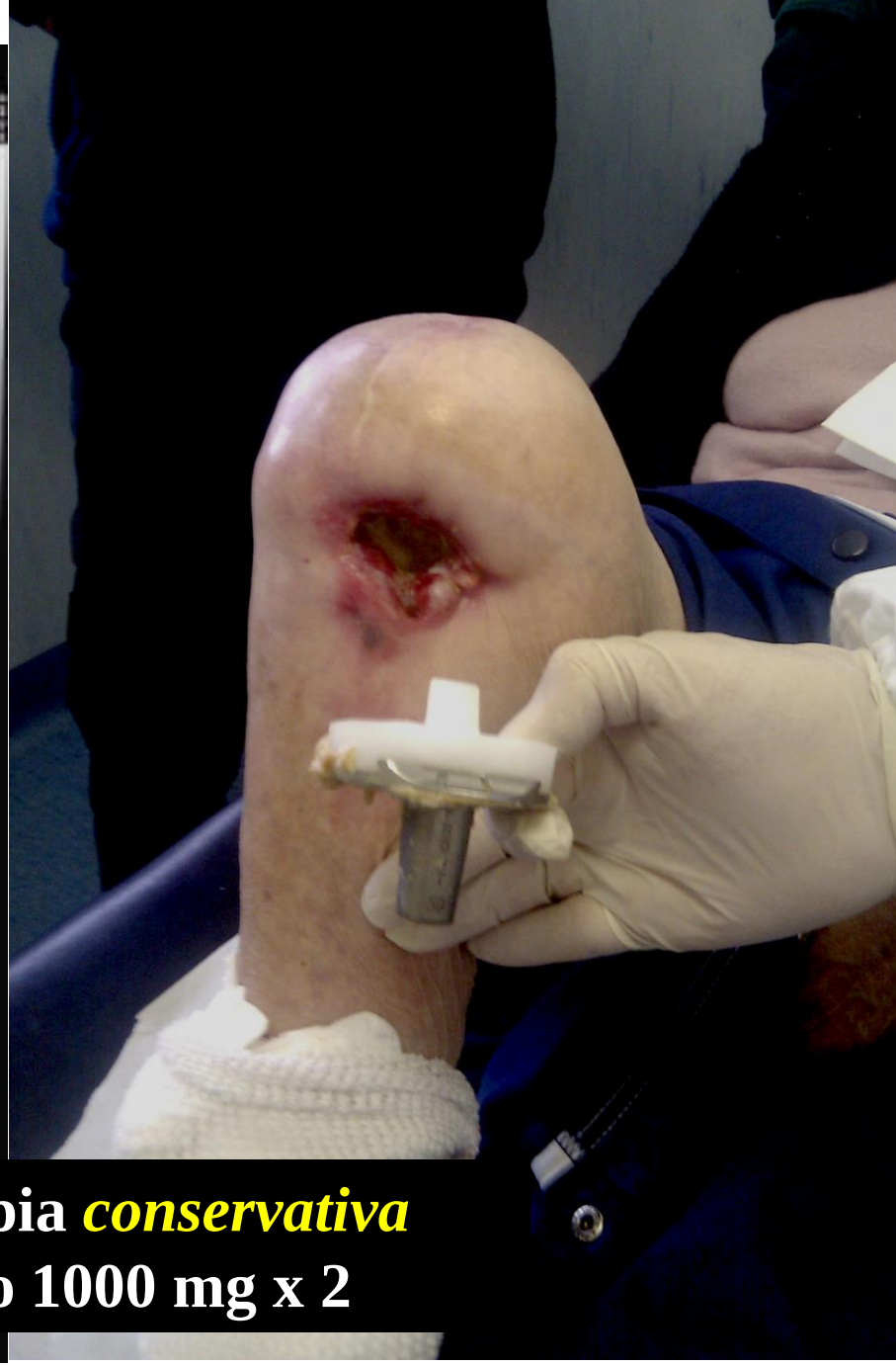
Antibiogramma

ANTIBIOTICI	1	*MIC*	2	*MIC*
Amikacina	S	8	S	<=4
Amoxicillina-clavulanato (f)	R	>32/2	R	>32/2
Ampicillina	R	>8	R	>8
Cefepime	I	2	S	<=1
Cefotaxima	R	>4	R	>4
Ceftazidima	R	>8	R	>8
Cefuroxime	R	>8	R	>8
Ciprofloxacina	R	>1	R	>1
Colistina	R	>4	S	<=1
Ertapenem	S	<=0,25	R	>1
Fosfomicina c/G6P	S	<=16	S	<=16
Gentamicina	R	>4	R	>4
Levofloxacina	R	>2	R	>2
Meropeneme	S	<=0,5	I	8
Piperacillina	R	>16	R	>16
Piperacillina-tazobattame	S	<=4/4	R	>16/4
Tigeciclina	R		R	>2
Tobramicina	R	>4	R	>4
Trimetoprima-sulfametoxazolo	R	>4/76	R	>4/76
Imipeneme			I	8

S=Sensibile, R=Resistente, I=Intermedio

Altro

Test screening carbapenemasi **Positivo/a**



Da cirrca 1 anno in terapia *conservativa*
amoxicillina /clavulanato 1000 mg x 2

procedura di salvataggio **, ultima opzione in presenza di una grave infezione, scarsa quantità o qualità di tessuto osseo o dopo il fallimento di interventi di protesi anca. rimozione della testa femorale sino al piccolo trocantere /rimozione protesi e la sutura dei tessuti molli associati**

----- il recupero funzionale completo può essere limitato-----

In letteratura non sono presenti linee guida condivise riguardo il protocollo riabilitativo da seguire dopo un intervento di Girdlestone

Septic Arthritis of Native Joints

Septic arthritis of native (nonprosthetic) joints *is uncommon but not rare*, with approximately **2 cases per 100,000 people per year.**

Table 1
Microbiology of 505 cases of septic arthritis in large series reporting data from 1999–2013

Bacteria	Number (%)
Staphylococci	282 (56)
Methicillin-sensitive *Staphylococcus aureus* (MSSA)	214 (42)
Methicillin-resistant *S aureus* (MRSA)	51 (10)
Coagulase-negative staphylococci	17 (3)
Streptococci	83 (16)
Unspecified streptococcal species	56 (11)
Viridans streptococci	7 (1)
Streptococcus pneumoniae	5 (1)
Other streptococcal species	15 (3)
Gram-negative rods	78 (15)
Pseudomonas aeruginosa	30 (6)
Escherichia coli	14 (3)
Proteus species	5 (1)
Klebsiella species	5 (1)
Others	21 (4)
Others	62 (12)
Polymicrobial	25 (5)
Anaerobes	3 (0.6)
Mycobacterium tuberculosis	9 (1.8)
Neisseria gonorrhoeae (gonococcus)	6 (1.2)
Miscellaneous	19 (4)

Risk factors for septic arthritis of native joints

- Preexisting joint diseases
  - Rheumatoid arthritis
  - Gout and pseudogout
  - Osteoarthritis
  - Lupus
  - Trauma
  - Recent surgery
- Diabetes mellitus
- Intravenous drug use
- Cirrhosis
- End-stage renal disease
- Prednisone and other immunosuppressive medications
- Skin diseases
  - Psoriasis
  - Eczema
  - Skin ulcers
- Human bite (fight bite)

John J. Ross Infect Dis Clin N Am 31 (2017) 203–218

- Today, septic arthritis is managed with antibiotics combined with joint drainage by arthroscopy, arthrocentesis, or arthrotomy. Drainage decompresses the joint, improves blood flow, and removes bacteria, toxins,and proteases.
- **Arthrocentesis should be repeated daily until effusions resolve and cultures are negative.**
- **Surgical drainage is indicated for septic arthriti he hip , failure to respond after 5 to 7 days of antibiotics and arthroce oft tissue extension of infection.**
- The shoulder joint should be drained cally or under radiologic guidance.
- Patients with sternoclavicular s often respond poorly to medical management, especially wh therapy is delayed. Thoracic surgery should be consulted in these pati ess the need for sternoclavicular joint excision and pectoralis flap grafting.

source control

- **A recent study showed a significant benefit of dexamethasone therapy in preventing disabi o data exist to recommend its u**
- **Aggressive rehal ctures and muscle atrophy. *Patients should be mobilized as soon as pain allows***

4 WEEKS

Expanded Version of the Gustilo Classification System of Open Fractures

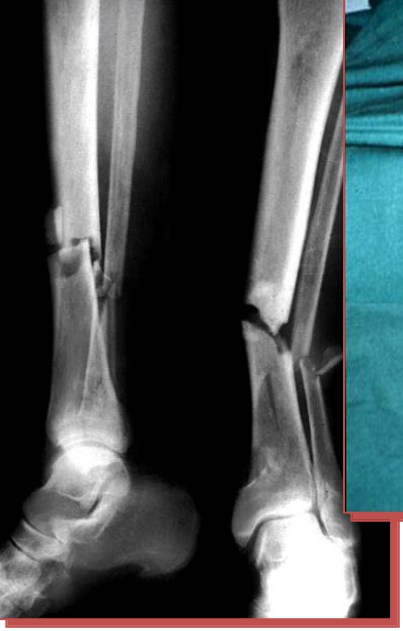
Feature	Fracture Type I	II	IIIA	IIIB	IIIC
Wound size, cm	<1	>1	>1	>1	>1
Energy	Low	Moderate	High	High	High
Contamination	Minimal	Moderate	Severe	Severe	Severe
Deep soft tissue damage	Minimal	Moderate	Severe	Severe	Severe
Fracture comminution	Minimal	Moderate	Severe/ segmental fractures	Severe/ segmental fractures	Severe/ segmental fractures
Periosteal stripping	No	No	Yes	Yes	Yes
Local coverage	Adequate	Adequate	Adequate	Inadequate	Adequate
Neurovascular injury	No	No	No	No	Yes
Infection rate	0%-2%	2%-7%	7%	10%-50%	25%-50%

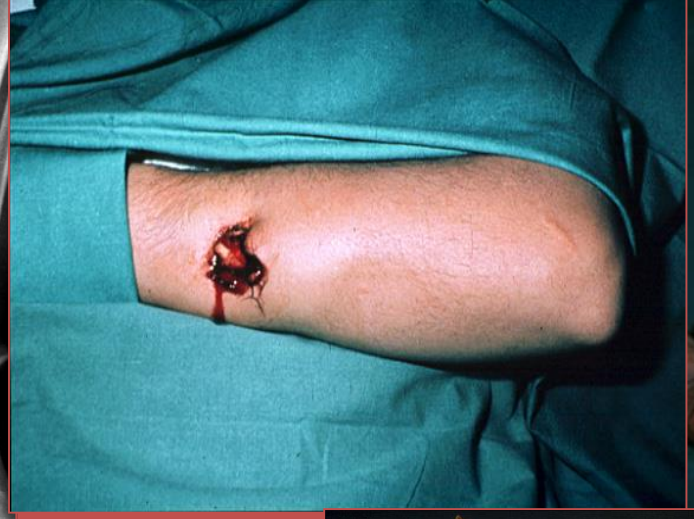
.Gustilo RB et al.:The management of open fractures. ***J Bone Joint Surg Am. 1990; 72(2):299-304***

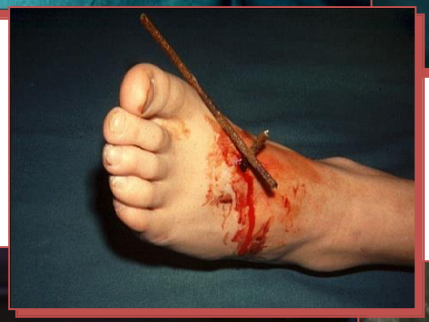
.Gustilo RB et al.: Prevention of infection in the treatment of one thousand and twenty-five open fractures of long bones: retrospective and prospective analyses. ***J Bone Joint Surg Am. 1976; 58(4):453-45***

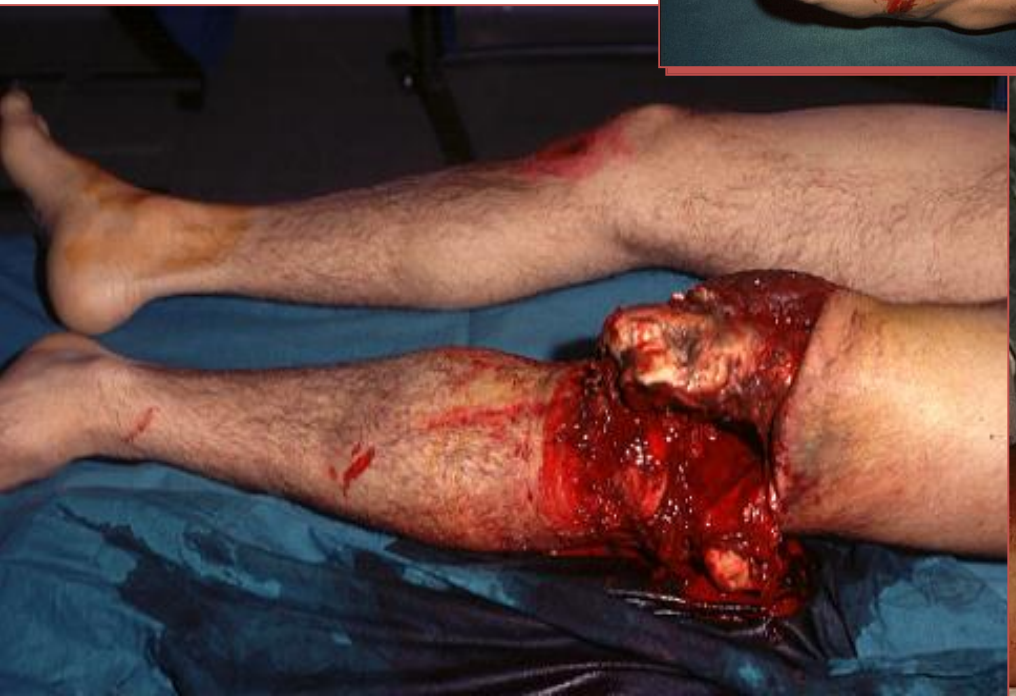
.Gustilo RB et al Problems in the management of type III (severe) open fractures: a new classification of type III open fractures. ***J Trauma. 1984; 24(8):742-746.***

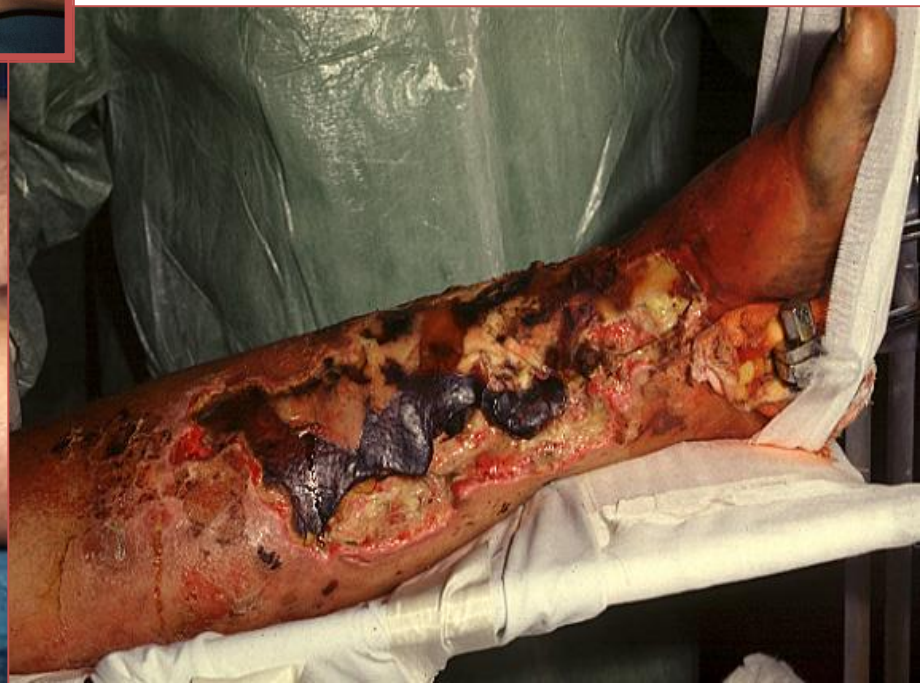
.Kim PH et al. In brief: Gustilo- Anderson classification [corrected]. ***Clin Orthop Relat Res. 2012; 470(11):3270-3274***



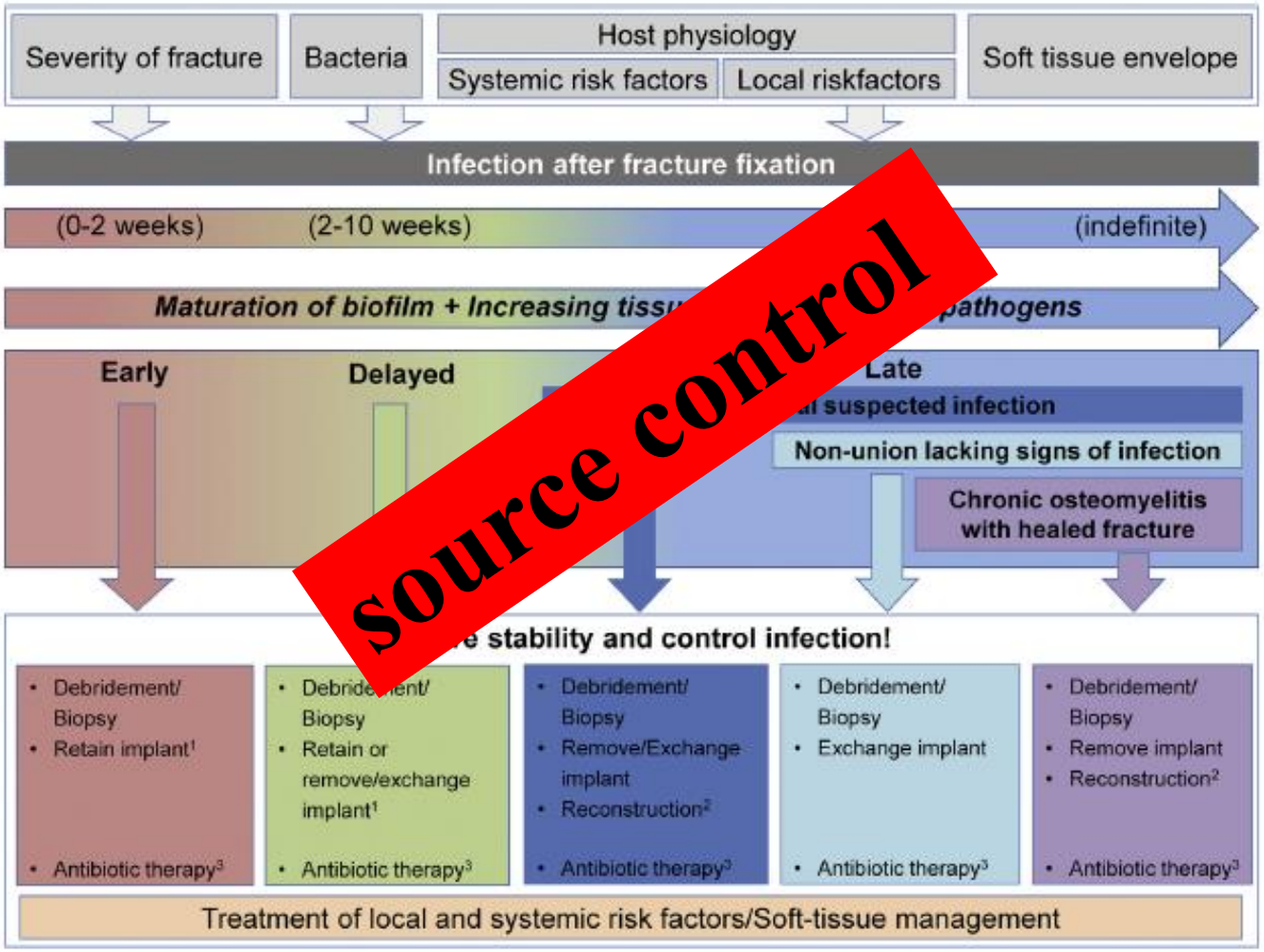








INFECTION AFTER FRACTURE FIXATION: CURRENT SURGICAL AND MICROBIOLOGICAL CONCEPTS



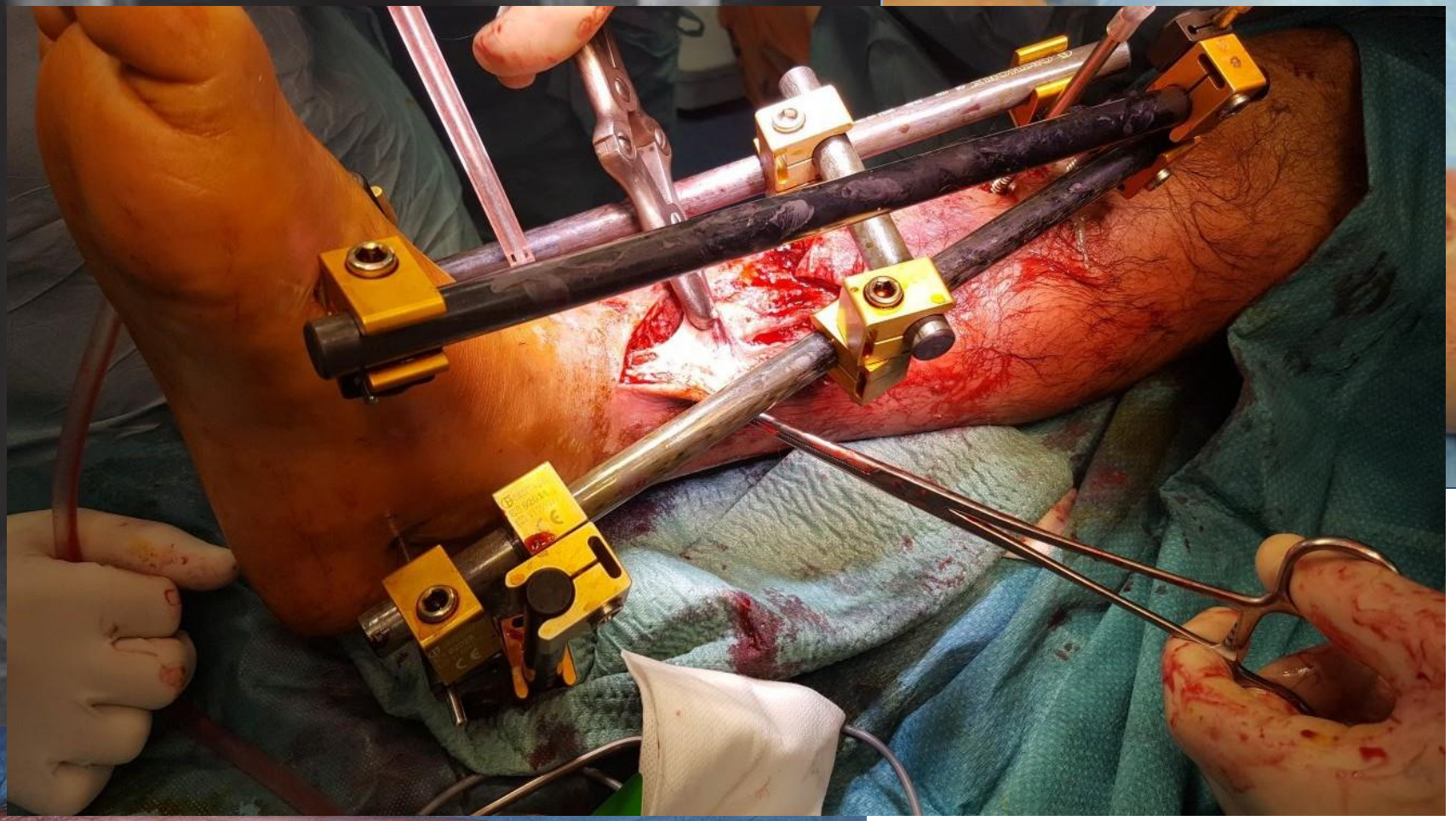
Pathophysiology, classification and treatment algorithm of IAFF.

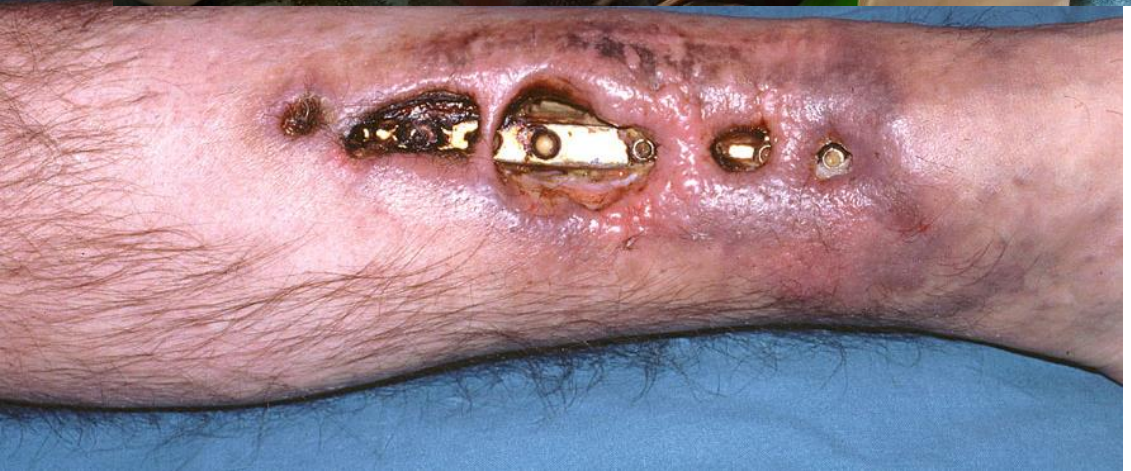
[1] See Table 4: Factors favoring implant removal and exchange

[2] Reconstruction can be carried out in a single step (with implant exchange) or in multiple stages; after resection of necrotic soft-tissue and bone a multidisciplinary approach will often be required

[3] Antibiotic therapy should be chosen in collaboration with an infectious disease specialist (especially in polymicrobial infections or proof of difficult to treat pathogens)

W.J. Metsemakers et al. / Injury, Int. J. Care Injured (2016)





TERAPIA ANTIBIOTICA

?

SE

- TEMPI BREVI PER CONSOLIDAMENTO (~ 30 gg)
IDENTIFICAZIONE PATOGENO

TERAPIA ANTIBIOTICA MIRATA
FINO A STABILIZZAZIONE FRATTURA

risoluzione flogosi tessuti molli
riduzione/arresto processo osteolitico

guargione

RIMOZIONE APPARECCHIO
ESTESA PULIZIA
TRATTAMENTO ANTIBIOTICO: durata
4-6 settimane

SE

-TEMPI LUNGHI PER CONSOLIDAMENTO (>30) - MANCATA IDENTIFICAZIONE PATOGENO

- PATOGENO MDR

- PRESENZA DI SEQUESTRO

RIMOZIONE OSTEOSINTESI

ESTESA PULIZIA /OSTEOTOMIA

IMMOBILIZZAZIONE ALTERNATIVA

CONSIDERARE SE TRATTAMENTO ANTIBIOTICO (4-6 settimane)

Etiologic Diagnosis of Chronic Osteomyelitis

A Prospective Study

Andres F. Zuluaga, MD, MSc; Wilson Galvis, MD; Juan G. Saldarriaga, MD; Mari[illegible]o, MD; Beatriz E. Salazar; Omar Vesga, MD

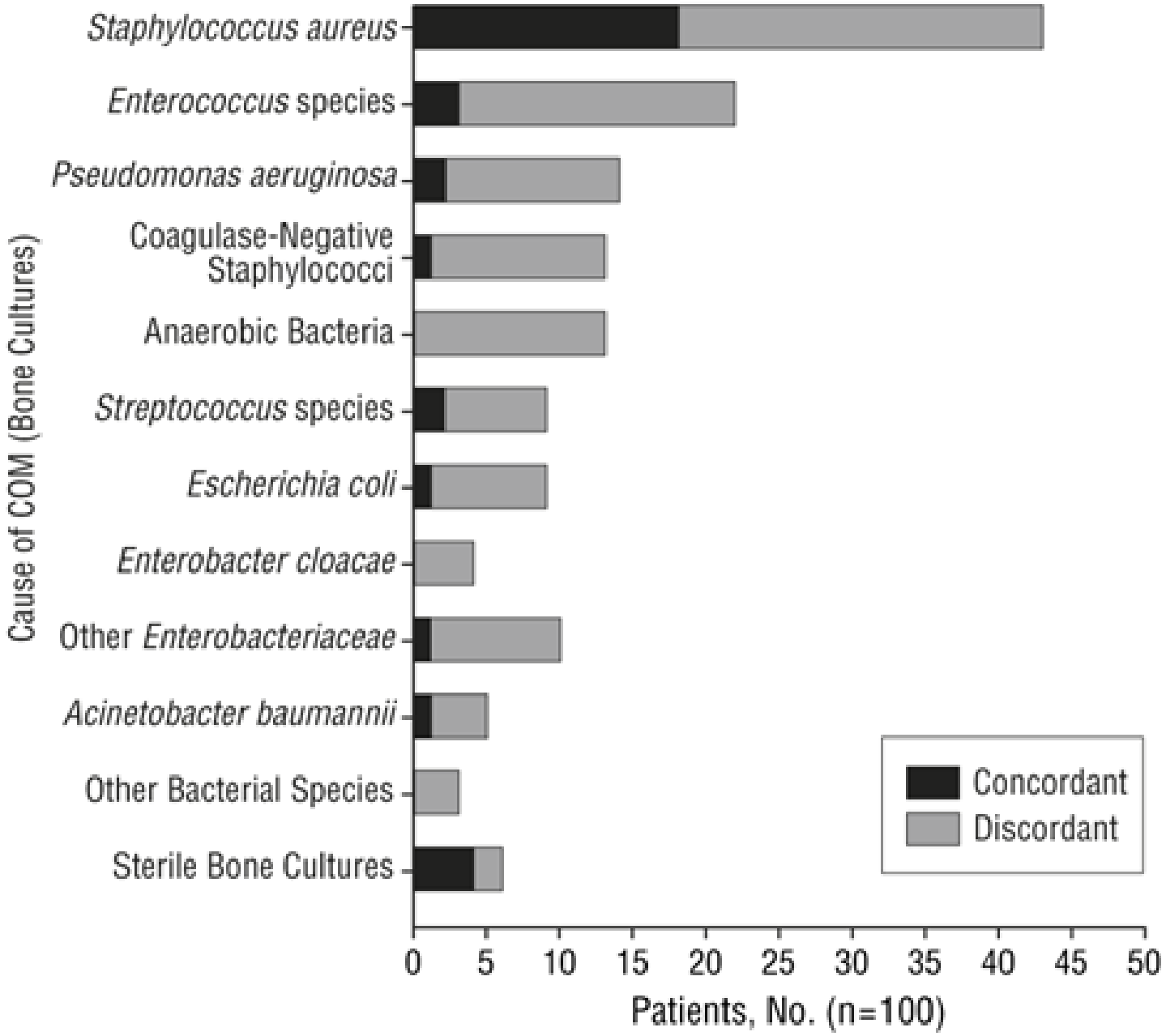
Arch Intern Med. 2006;166(1):95. doi:10.1001/archinte.166.1.95.

100 Pz con diagnosi clinica di [illegible]omielite cronica

l'identificazione dell'agente nel [illegible] dei casi, compresi i batteri anaerobi (14%). Colture di [illegible]pioni non-osso e osso diedero risultati identici nel 30% dei [illegible]enti, (>concordanza in osteomielite cronica causata da Staphy[illegible]occus aureus -42%- rispetto a tutte le altre [illegible]e batteriche -22%-).

INDICAZIONE DISATTESA

L'dentifi[illegible]one dell'agente eziologico di oste[illegible]elite cronica richiede la cultura dell'osso infetto


Staphylococcus aureus
Enterococcus species
Pseudomonas aeruginosa
Coagulase-Negative Staphylococci
Anaerobic Bacteria
Streptococcus species
Escherichia coli
Enterobacter cloacae
Other Enterobacteriaceae
Acinetobacter baumannii
Other Bacterial Species
Sterile Bone Cultures
Cause of COM (Bone Cultures)
Concordant
Discordant
0
5
10
15
20
25
30
35
40
45
50
Patients, No. (n=100)

Referto Ambulatoriale

Redatto dal Dottor **in data 09/02/2018 13:10**

Cognome e Nome:
Sesso: **F**
Data di nascita:

quesito diagnostico:
OSTEOMIELITE GIA' POLITRATTATA

Sig.ra

Paziente con ulcere croniche gamba sinistra, connettivite indifferenziata, fibrosi polmonare con ipertensione polmonare post-embolica, anemia cronica multifattoriale, ipotiroidismo.
Ricovero in Medicina Interna per osteomielite gamba sinistra per cui in data 13/10/2016 inizia terapia con teicoplanina e doxiciclina indicativamente per 2 mesi.
Trasferita in ospedale minore, dove il 13/12/2016 viene sospesa la terapia, nonostante il controllo la scintigrafia con leucociti marcati risulti anocra positivo.
Dal 29/12/2016 al 16/01/2017 ricovero in Malattie Infettive per neutropenia da sovradosaggio di teicoplaninemia (che era stata sospesa il 13/12!), osteomielite gamba sinistra con ulcera cronica, connettivite indifferenziata, fibrosi polmonare con ipertensione polmonare post-embolica, anemia cronica multifattoriale e ipotiroidismo.
Durante il ricovero, in data 5/01/2017, viene avviata terapia con teicoplanina e ceftriaxone che la Paziente ha proseguito in ADI sino al 10/05/2017, in quanto le scintigrafie del 22/02 e 29/03 risultavano positive, invece quella del 27/04 risultava bonificata.
Il 30/05 ripete scintigrafia con leucociti che risulta nuovamente positiva e dal 12/06 assume terapia con levofloxacina e doxiciclina; l'11/08 controlla scintigarfia con leucociti che risulta positiva e dal 6/09 modifica la terapia: sospende levofloxacina e doxiciclina e riprende teicoplanina e ceftriaxone.
Prosegue tale terapia fino al 6/12/2017, nel frattempo la scintigrafia del 6/11 era ancora positiva.
Il Curante controlla scintigrafia il 30/01/2018: positiva.
Non si imposta alcuna terapia antibiotica e si indirizza la Paziente alla Vostra C.A.
Compiltata oggi DEM per Rx tibia sin.
Si rimane a disposizione per ogni chiarimento.
Cordiali saluti

9 scintigrafie con LEU +

Maschio 82 aa

Diabete in insulina, Parkinson, extrasistolia (b-bloccanti)

- Feb 2016 frattura femore dx – IVU nel post-operatorio
- Nov 2016 dolore anca dx (scinti Leu+ per mobilizzazione settica)
- 2018 TC: migrazione protesi nella piccola pelvi

--> amoxi-clav + cipro da Feb a Giu 2018

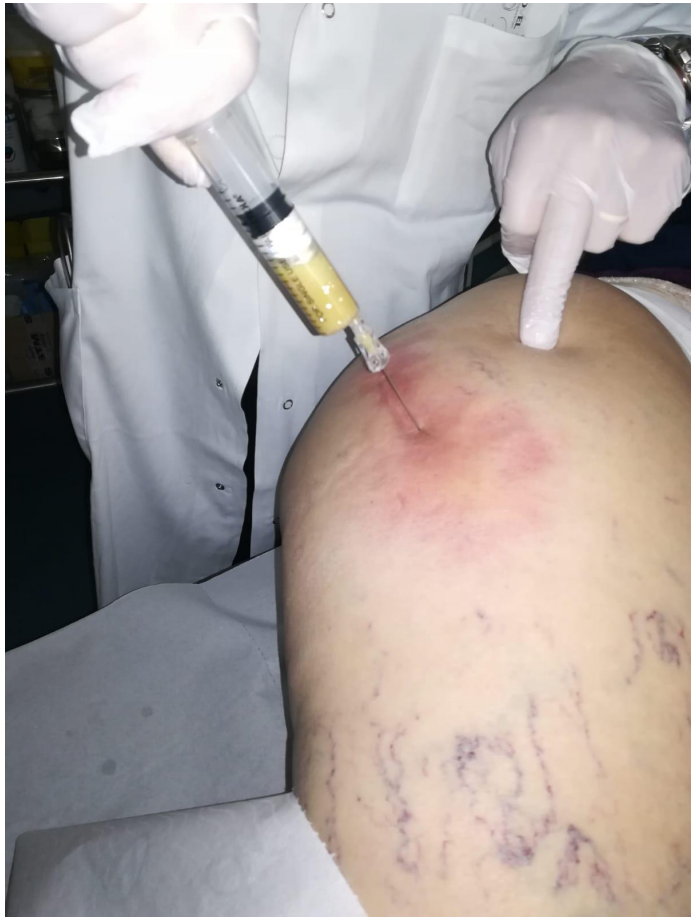
→dalbavancina + cipro da Giu a Dic 2018 (fino a marzo?)

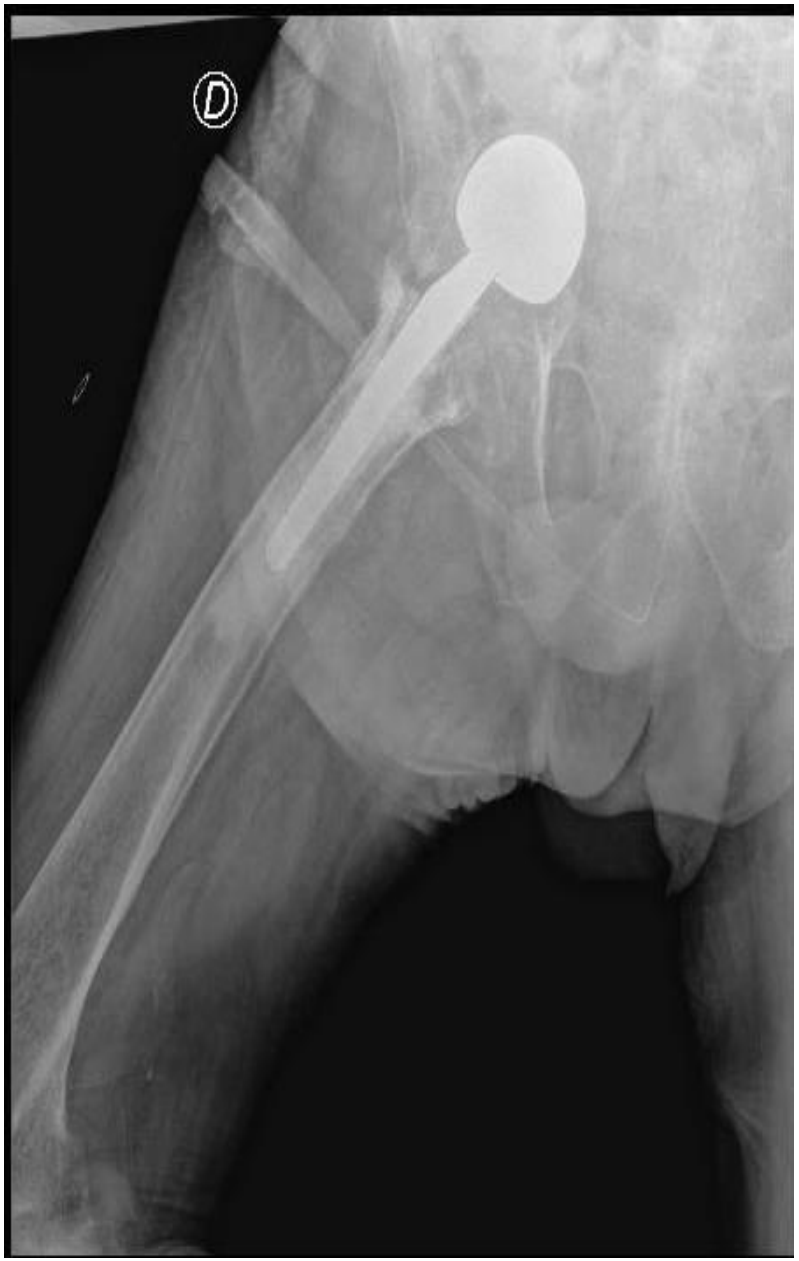
[dalbavancina 1500 mg D1 + 1500 D8 poi 1500 una volta ogni due mesi]

- Mar 2019 sospende antibiotici su indicazione MYOS
- Fine aprile 2019 sepsi da Proteus ESBL e ricovero presso altro ospedale (Geriatria) –> KPC -
- --> inizia ertapenem + teicoplanina (a domicilio)

- 10/06/2019 ricovero VC -> KPC+
- WBC 8570, PCR 6.61 (lim 0.8), creatinina 0.57

Alla faccia del Bicarbonato di Sodio

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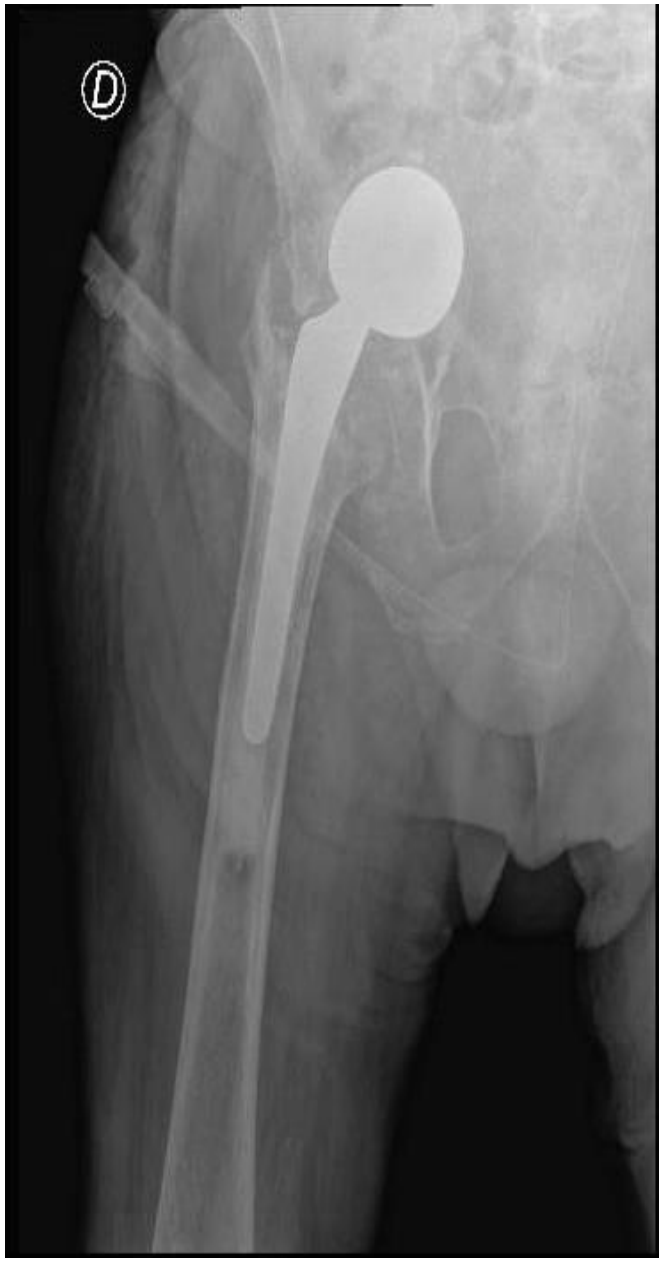
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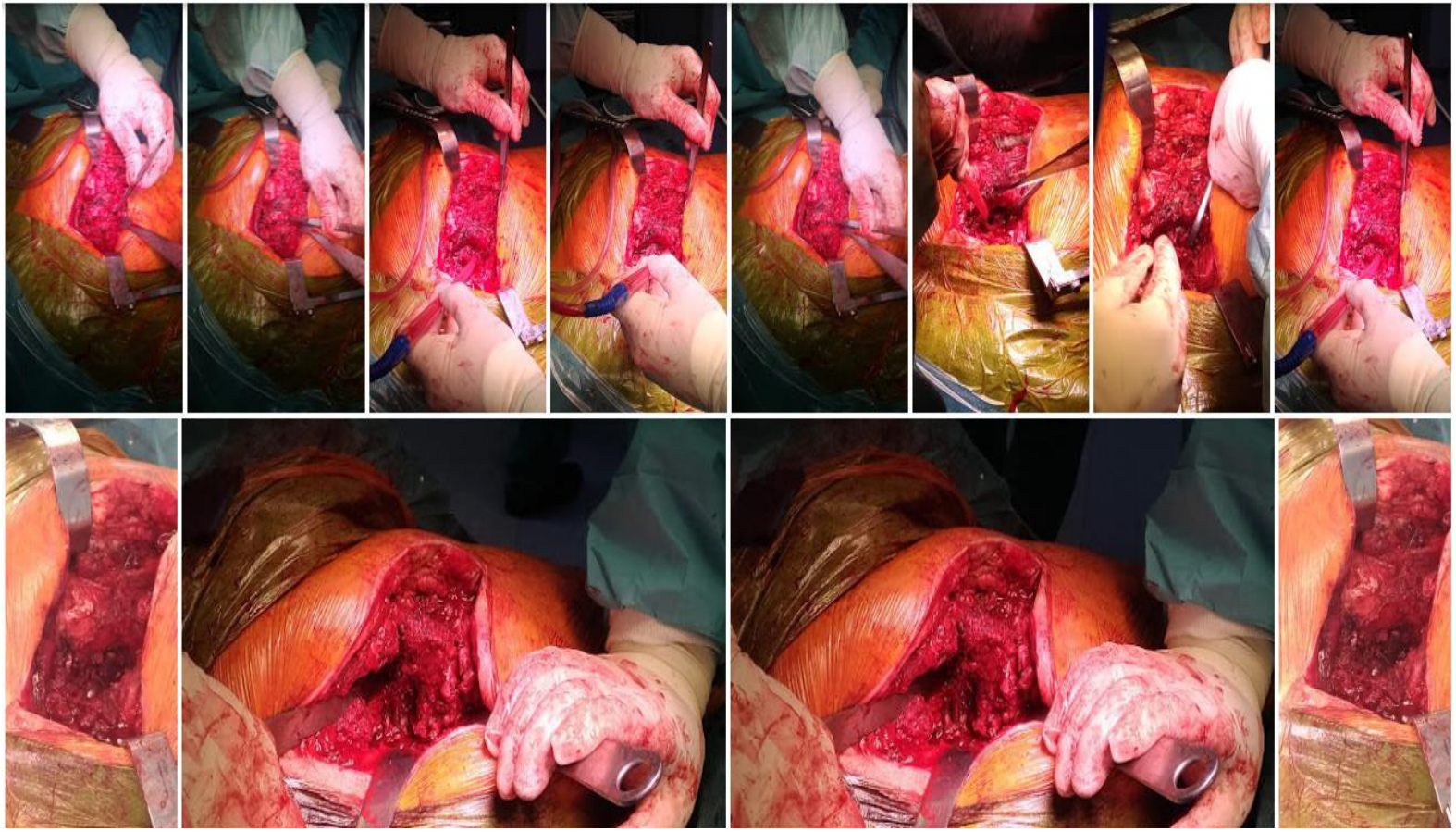

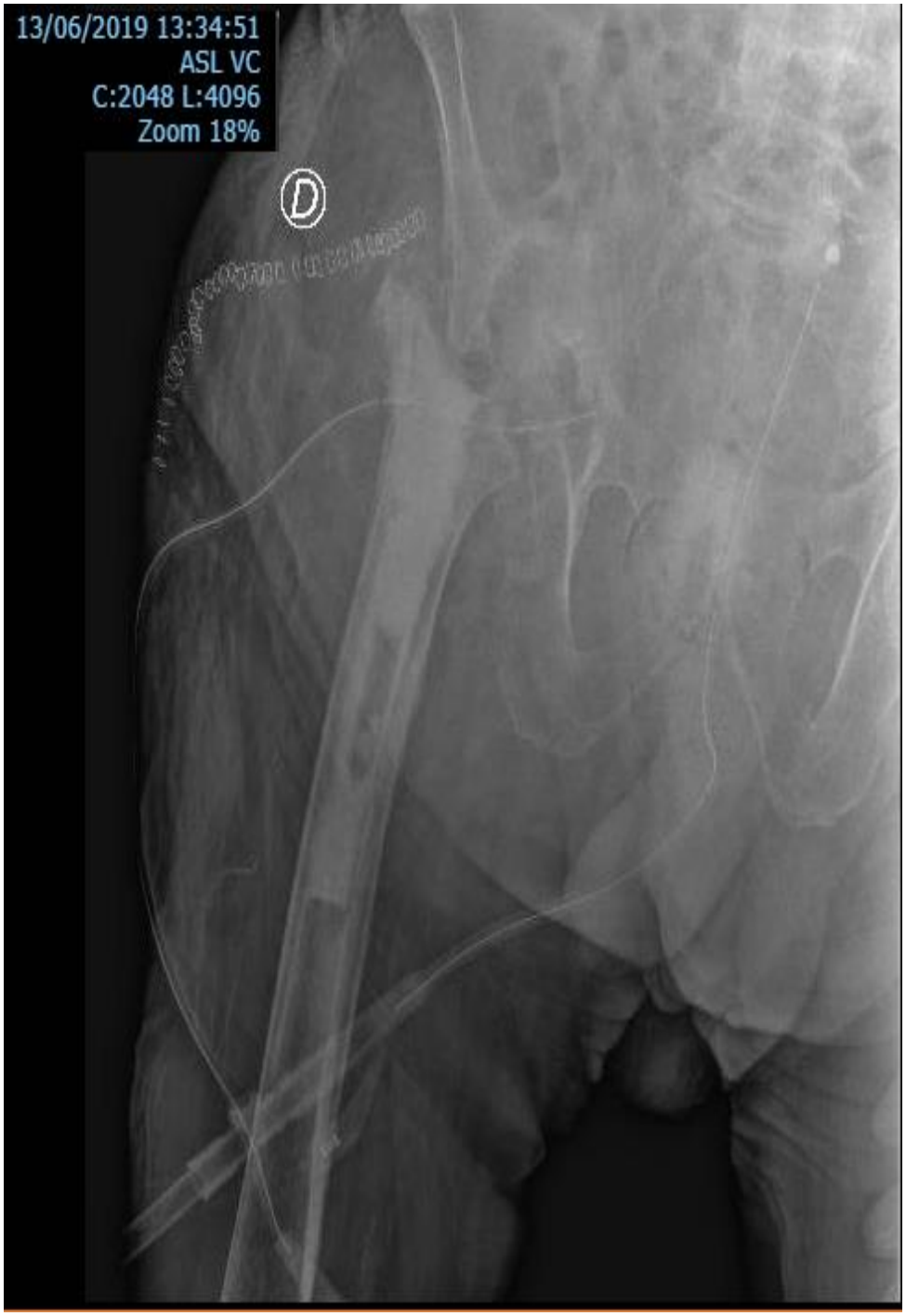
13/06/2019 13:34:51
ASL VC
C:2048 L:4096
Zoom 18%
D

Sesso M Data di Stampa: 18/06/2019 Ore: 16:06 Data Di Accettazione **12/06/2019** Ore: 14:00

Altro Provenienza: 3° campione

Esame colturale **Positivo/a** (Colturale)

Microorganismo *Carica*

Ceppo 1 Proteus mirabilis

Ceppo produttore di beta-lattamasi a spettro esteso (ESBL); ad eccezione dei carbapenemi, la terapia con beta-lattamici (incluse cefalosporine a spettro esteso, aztreonam e combinazioni con inibitori) potrebbe risultare scarsamente efficace o inefficace

Ceppo 1 *Proteus mirabilis*

			MIC Breakpoint		
Antibiotici	*MIC*	*S/I/R*	*S<= *	*R>*	*Note*
Amikacina	2	**S**	*8*	*16*	
Amoxicillina/Acido Clavu	8	**S**	*8*	*8*	
Cefotaxime	>32	R	*1*	*2*	
Ceftazidime	2	I	*1*	*4*	
Ciprofloxacina	>2	R	*0.5*	*1*	
Colistina	>8	R	*2*	*2*	
Ertapenem	<=0,12	**S**	*0.5*	*1*	
Fosfomicina	>128	R	*32*	*32*	
Gentamicina	>8	R	*2*	*4*	
Meropenem	<=0,25	**S**	*2*	*8*	
Piperacillina/Tazobactam	<=4	**S**	*8*	*16*	
Tigeciclcina	4				
Trimetoprim/Sulfametoxazo	>160	R	*2*	*4*	