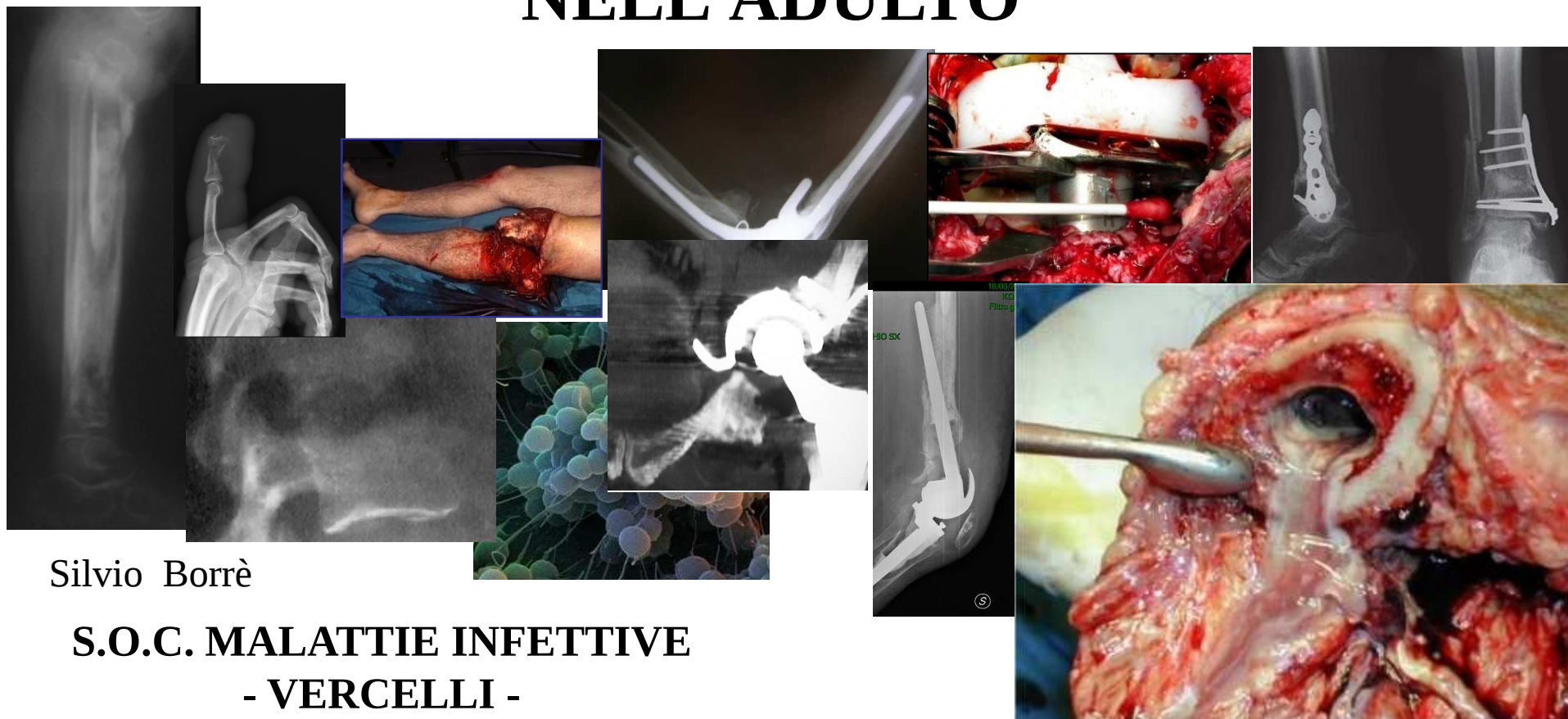




LA TERAPIA DELLE OSTEOMIELITI NELL'ADULTO



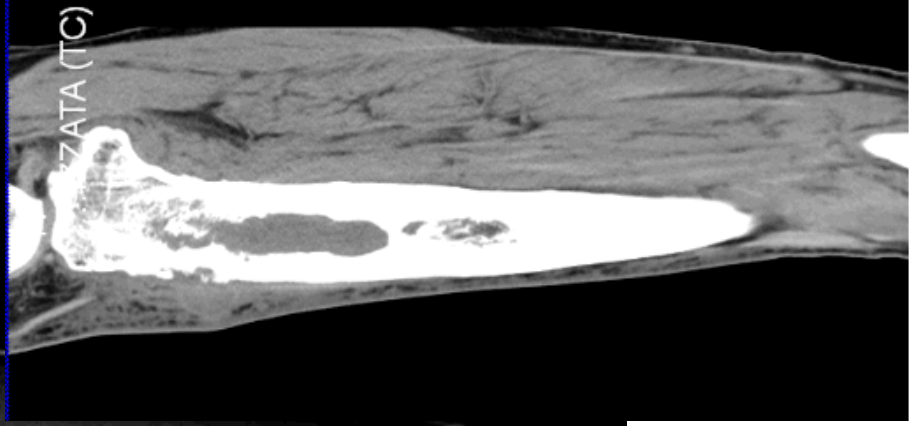
Silvio Borrè

**S.O.C. MALATTIE INFETTIVE
- VERCELLI -**

H
COQ - OSPEDALE - OMEGNA
...IZZATA (TC) DEL GINOCCHIO E GAMBA SN
09/03/2018



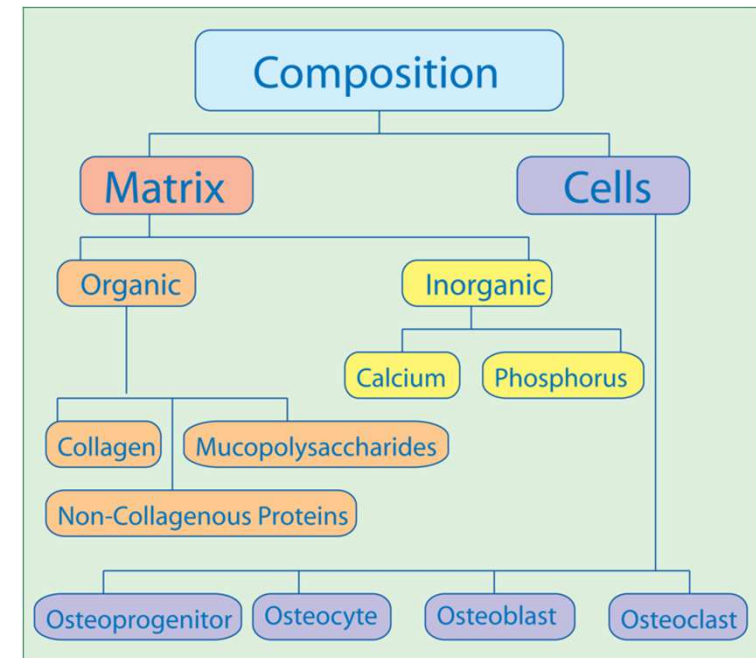
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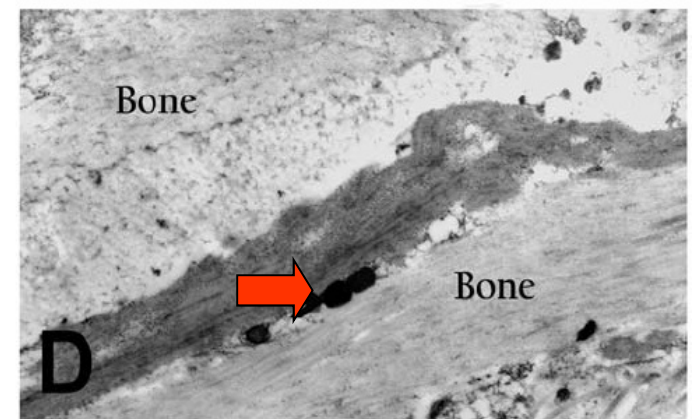
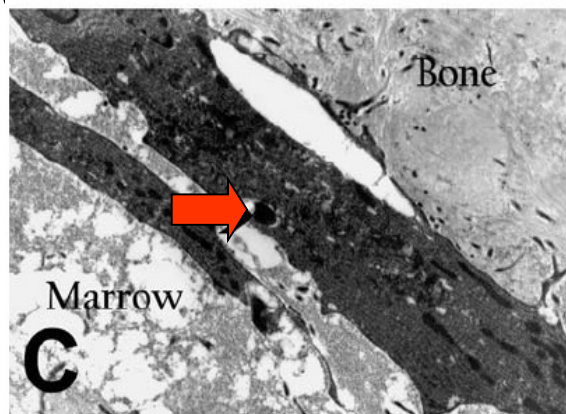
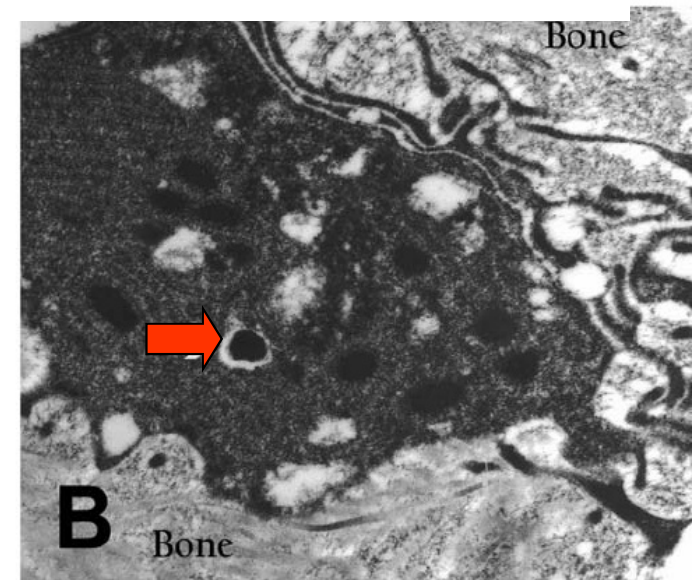
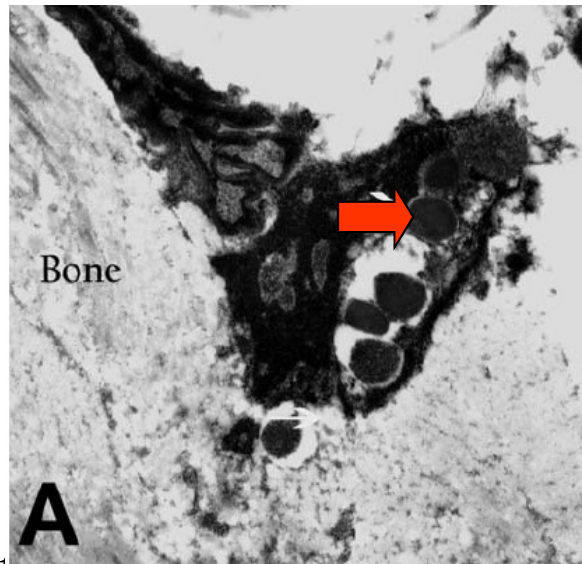
Bone and joint infections are painful for patients and frustrating for both them and their doctors

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**



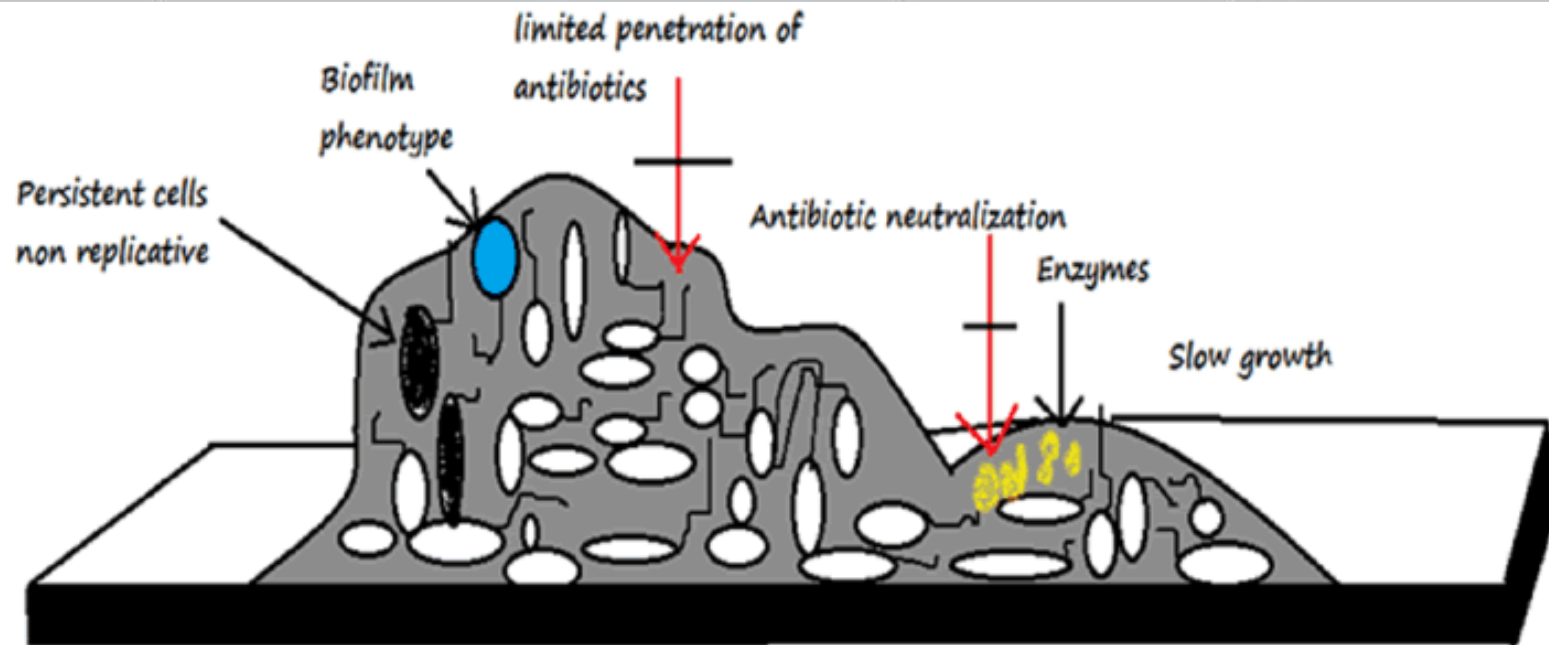
INTRACELLULAR SURVIVAL

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



Bacterial biofilms: from the natural environment to infectious diseases

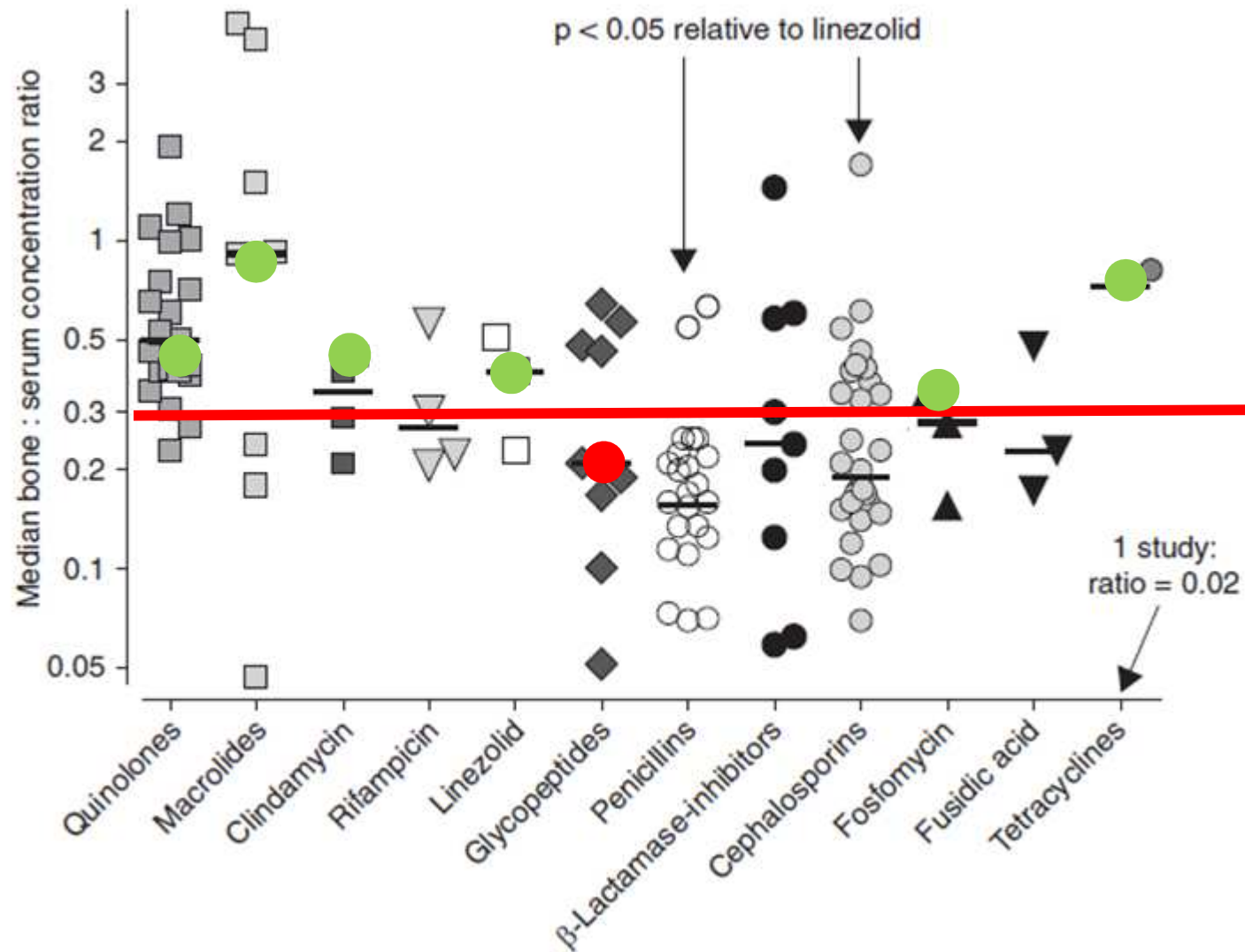
	Components	Percentage of matrix
1	Microbial cells	2-5%
2	DNA and RNA	<1-2%
3	Polysaccharides	1-2%
4	Proteins	<1-2% (including enzymes)
5	Water	Up to 97%



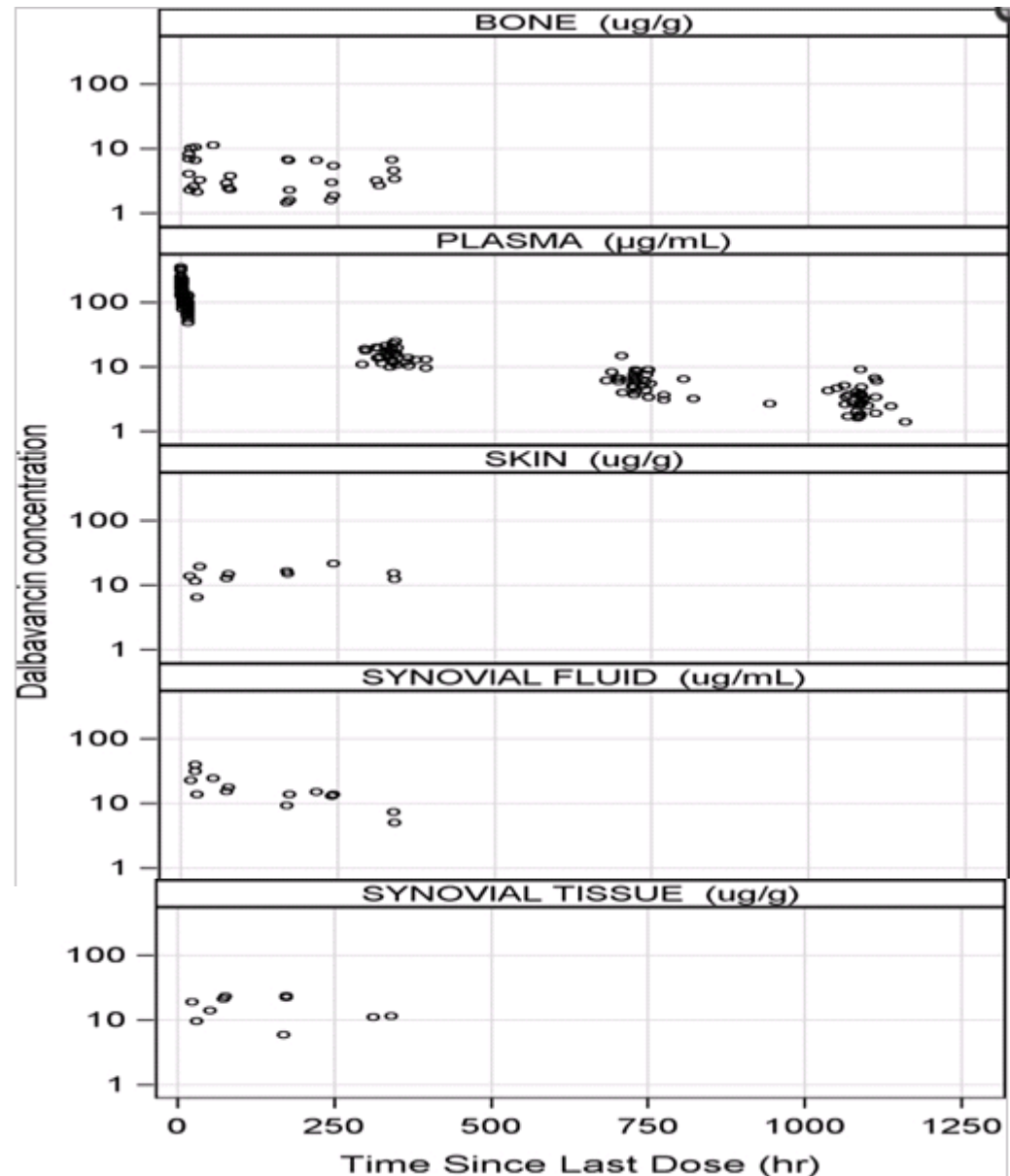
- . Description of the key mechanisms involved in antibiotic resistance such as enzyme causing neutralizations, presence of persistent (non-dividing) cells and biofilm phenotype

Penetration of Antibacterials into Bone

Pharmacokinetic, Pharmacodynamic and Bioanalytical Considerations



Extended-Duration Dosing and Distribution of Dalbavancin in to Bone and Articular Tissue



Dalbavancin concentrations in plasma, bone, and related tissues.



Contents lists available at ScienceDirect

Diagnostic Microbiology and Infectious Disease

journal homepage: www.elsevier.com/locate/diagmicrobio



In vitro activity of dalbavancin against biofilms of staphylococci isolated from prosthetic joint infections



Javier Fernández ^{a,b,c}, Kerryl E. Greenwood-Quaintance ^a, Robin Patel ^{a,d,*}

^a Division of Clinical Microbiology, Department of Laboratory Medicine and Pathology, Mayo Clinic, Rochester, MN, USA

^b Department of Functional Biology, Section of Microbiology, University of Oviedo, Oviedo, Spain

^c Service of Microbiology, Hospital Universitario Central de Asturias, Oviedo, Spain

^d Division of Infectious Diseases, Department of Medicine, Mayo Clinic, Rochester, MN, USA

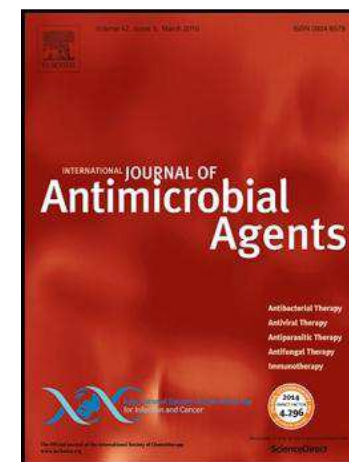
The *in vitro* activity of dalbavancin was tested against biofilms of 171 staphylococci associated with prosthetic joint infection.

Dalbavancin minimum biofilm bactericidal concentration (MBBC) values were:
MBBC50 for *Staphylococcus aureus* and *Staphylococcus epidermidis*, **1 µg/mL**;
MBBC90 for *S. aureus*, **2 µg/mL**;
MBBC90 for *S. epidermidis*, **4 µg/mL**.

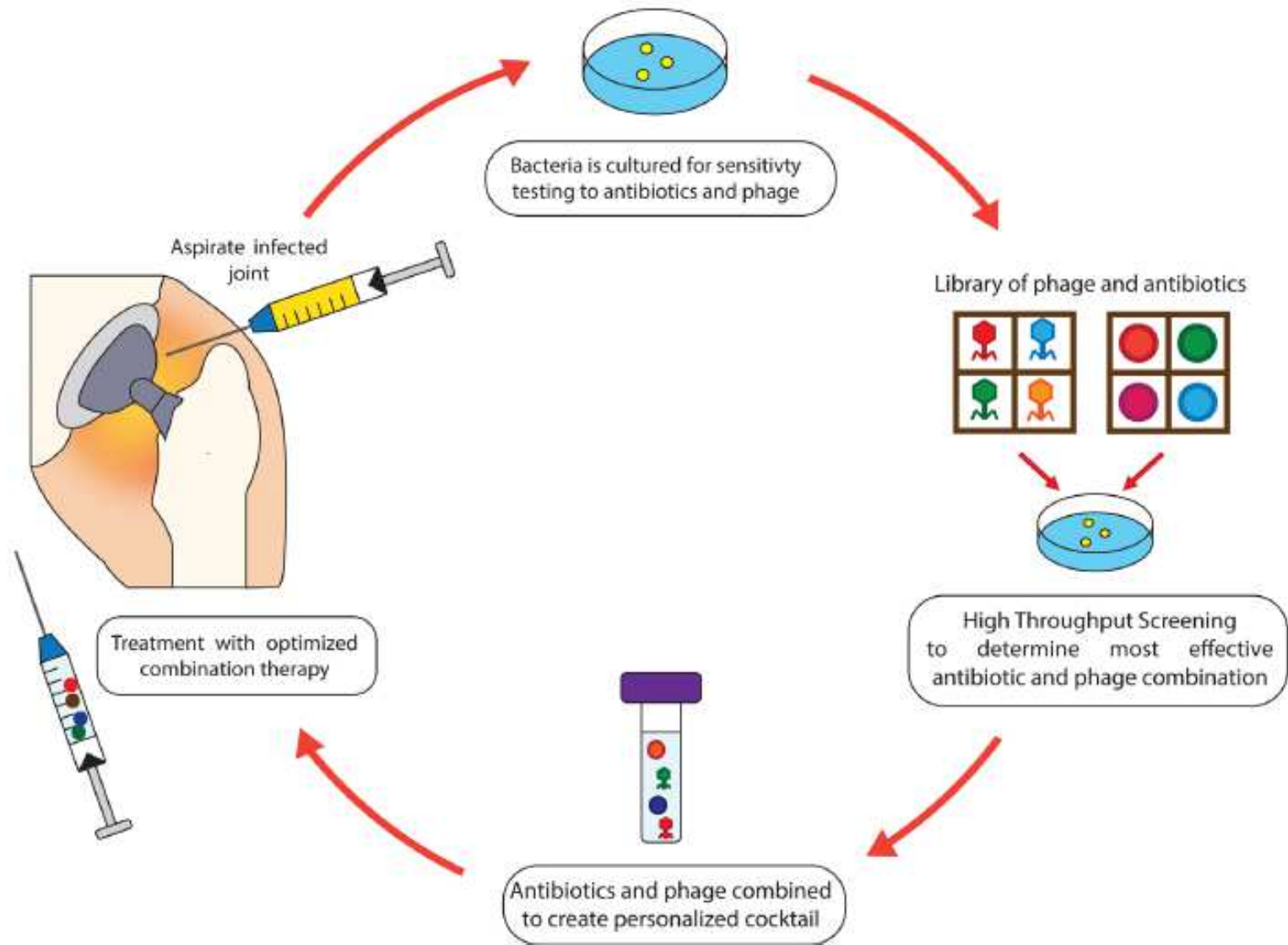
previous study for the same set of isolates, showing that the
vancomycin MBBC50 and MBBC90 were both ≥ 128 µg/ml
tedizolid MBBC50 and MBBC90 were both > 32 µg/ml (Schmidt-Malan et al., 2016).

Dalbavancin in the treatment of different gram-positive infections: a real-life experience

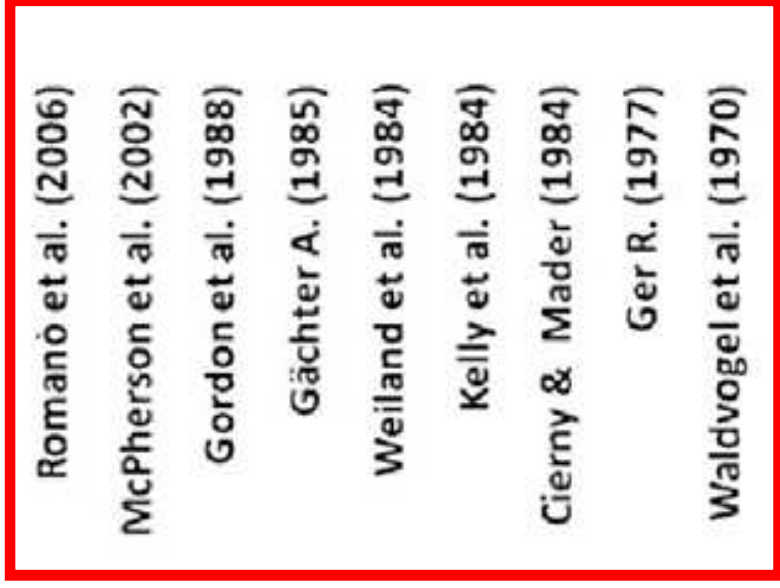
Treatment outcomes by primary infection type (n=69)



Current Review— The Rise of Bacteriophage as a Unique Therapeutic Platform in Treating Peri-Prosthetic Joint Infections



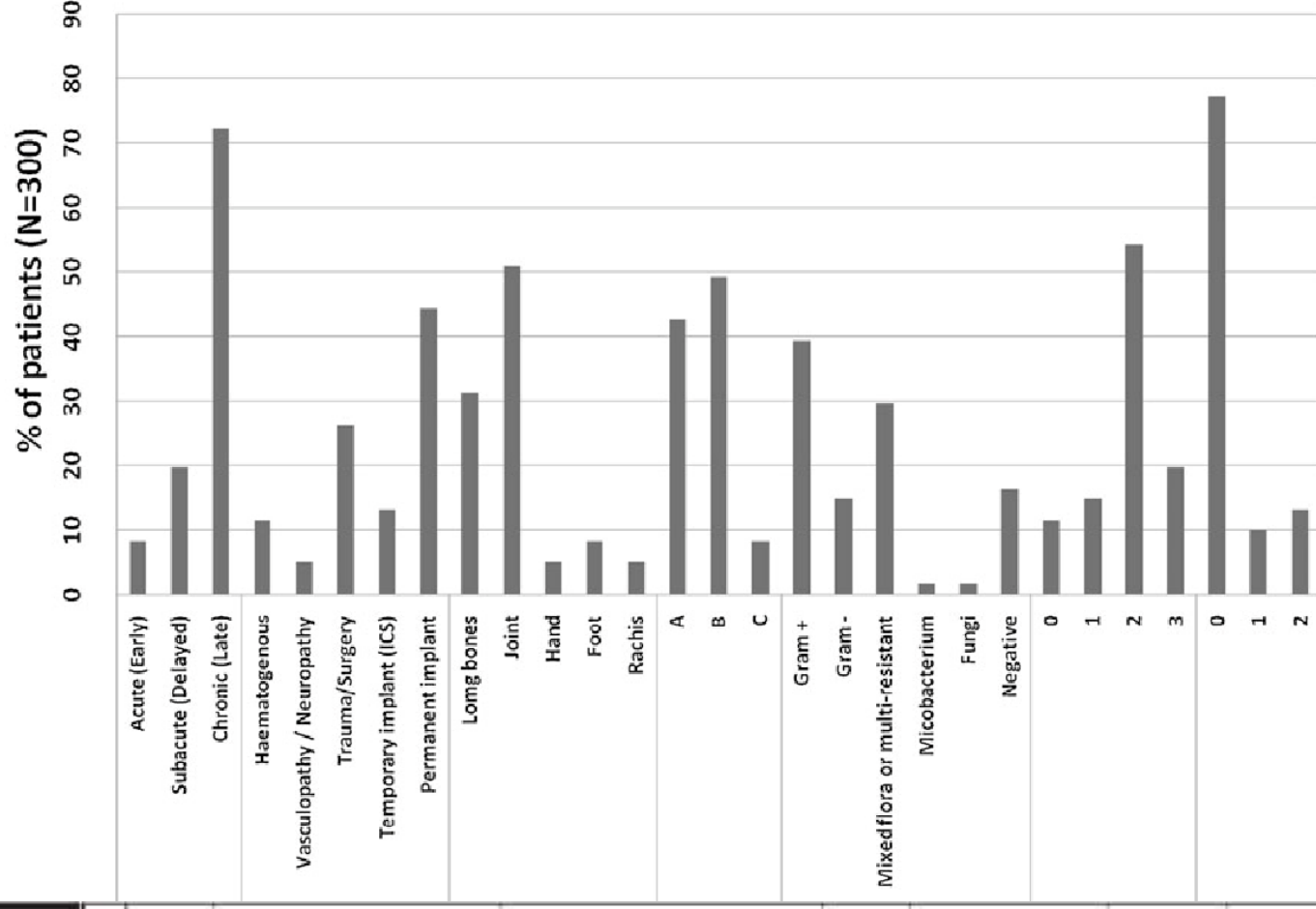
Authors	Year of first publication	Main object of classification	Classified items
Waldvogel et al.	1970	Osteomyelitis	Duration Acute Chronic Etiopathogenesis Hematogenous osteomyelitis Osteomyelitis secondary to contiguous focus of infection No generalized vascular disease Generalized vascular disease Soft tissue Type I, simple sinus Type II, chronic superficial ulcer Type III, multiple sinuses Type IV, multiple skin-lined sinuses Anatomo-pathological Stage 1, medullary osteomyelitis Stage 2, superficial osteomyelitis Stage 3, localized osteomyelitis Stage 4, diffuse osteomyelitis Host Type A, normal Type B, compromised (local and/or systematic) Type C, treatment worse than the disease Etiopathogenesis Hematogenous osteomyelitis Posttraumatic (united fracture) Posttraumatic (nonunited fracture) Post-surgical Anatomo-pathological Type I, open, without evidence of bone infection Type II, circumferential, cortical, and endosteal infection Type III, cortical and endosteal infection associated with segmental bone Anatomo-pathological Stage I, opacity of fluid, redness of the synovial membrane, no radiographic changes Stage II, severe inflammation, fibrinous deposition, pus, no radiological changes Stage III, thickening of the synovial membrane, compartment formation, no radiological changes Stage IV, aggressive pannus with infiltration of the cartilage, undermining the cartilage, radiological sign of subchondral osteolysis, possible osseous erosions, and cysts Bone defect Type A, tibial defects and nonunions without significant segmental loss Type B, tibial defects of <3 cm, intact fibula Type C, tibial defects of >3 cm, no intact fibula
Gier R.	1977	Osteomyelitis	
Cierny and Mader	1984	Long bone osteomyelitis	
Kelly et al.	1984	Osteomyelitis	
Gächter A.	1985	Septic arthritis (knee)	
Gordon et al.	1988	Osteomyelitis (tibia)	



Authors	Year of first publication	Main object of classification	Classified items
McPherson et al.	2002	Implant-related infections (hip prosthesis)	Duration I, early postoperative (<4 weeks from surgery) II, hematogenous (<4 weeks duration) III, late chronic (>4 weeks duration) Host Type A, uncompromised Type B, compromised (one to two compromising factors) Type C, significantly compromised (more than two compromising factors) Bone defect Type 1, cavitory defect Type 2, epiphyseal defect Type 3, segmental defect Anatomo-pathological Type I, stable osteosynthesis, with callus progression Type II, stable osteosynthesis, with scarce or absent callus progression Type III, no callus formation and unstable osteosynthesis
Romano et al.	2006	Osteomyelitis Septic arthritis Implant-related infections	
Romano et al.	2006	Implant-related infections (osteosynthesis)	

Table V: The Seven-Item Comprehensive Classification System proposed by Romanò, et al.¹⁵

Item	Characteristic
Clinical presentation	Acute/sub-acute/chronic Early/delayed/late
Aetiopathogenesis	Haematogenous Vasculopathy/neuropathy Temporary implant ICS classification Type I Type II Type III Permanent implant
Anatomo-pathology	Rachis Hand Long bones Type 1 Type 2 Type 3 Type 4 Foot Joint
Host type / age	A/B/C <2 yr / <14 yr / >14 yr
Microorganism	Gram + Gram - Mixed or multi-resistant Mycobacterium Negative
Bone defect	Type I Type II Type III A/B/C
Soft tissue defect	No soft tissue defect Soft tissue defect (cm ³) With or without exposed bone



OSTEOMIELEITE VERTEBRALE ematogena

INCIDENZA COMPLESSIVA: 2,4 / 100 000 *

< 20 anni 0,3 / 100 000

50-70 anni 3,5 / 100 000

> 70 anni 6,5 / 100 000

1 Episodio / 215 pazienti / anno dialisi **

***Staphylococcus spp.* 40%**

Batteriemia 68%⁺

Endocardite 9%

Decesso 3%

*** Grammatico - Guillon Direction generale de la sante 2012**

****Abid S et al. Infective spondylodiscitis in patients on high-flux hemodialysis and on-line hemodiafiltration Hemodial Int. 2008 Oct;12(4):463-70.**

⁺Bernard L. et al: Lancet 2015; 385: 875–82

2015 Infectious Diseases Society of America(IDSA) Clinical Practice Guidelines for the Diagnosis and Treatment of Native Vertebral Osteomyelitis in Adults



**recommend a total duration of 6 weeks of
parenteral or highly bioavailable oral
antimicrobial therapy for most patients with
bacterial NVO (strong, low).**

Antibiotic treatment for 6 weeks versus 12 weeks in patients with pyogenic vertebral osteomyelitis: an open-label, non-inferiority, randomised, controlled trial

	6-week regimen (n=176)	12-week regimen (n=175)	Total (n=351)
Microbiological diagnosis			
Blood culture	119 (68%)	121 (69%)	240 (68%)
CT-vertebral biopsy	67 (38%)	71 (41%)	138 (39%)
Perioperative surgical biopsy	9 (5%)	10 (6%)	19 (5%)
Microbiological identification			
<i>Staphylococcus aureus</i> †	69 (39%) 3 MRSA	76 (43%) 5 MRSA	145 (41%)
Coagulase-negative <i>Staphylococcus</i> ‡	29 (16%)	32 (18%)	61 (17%)
<i>Streptococcus</i> spp	32 (18%)	31 (18%)	63 (18%)
<i>Enterococcus</i> spp	11 (6%)	15 (9%)	26 (7%)
Enterobacterial spp	22 (13%)	16 (9%)	38 (11%)
Anaerobia	7 (4%)	6 (3%)	13 (4%)
Other Gram-negative bacteria	6 (3%)	4 (2%)	10 (3%)
Other <i>Streptococcus</i>	4 (2%)	4 (2%)	8 (2%)

Bernard L. et al: Lancet 2015; 385: 875–82

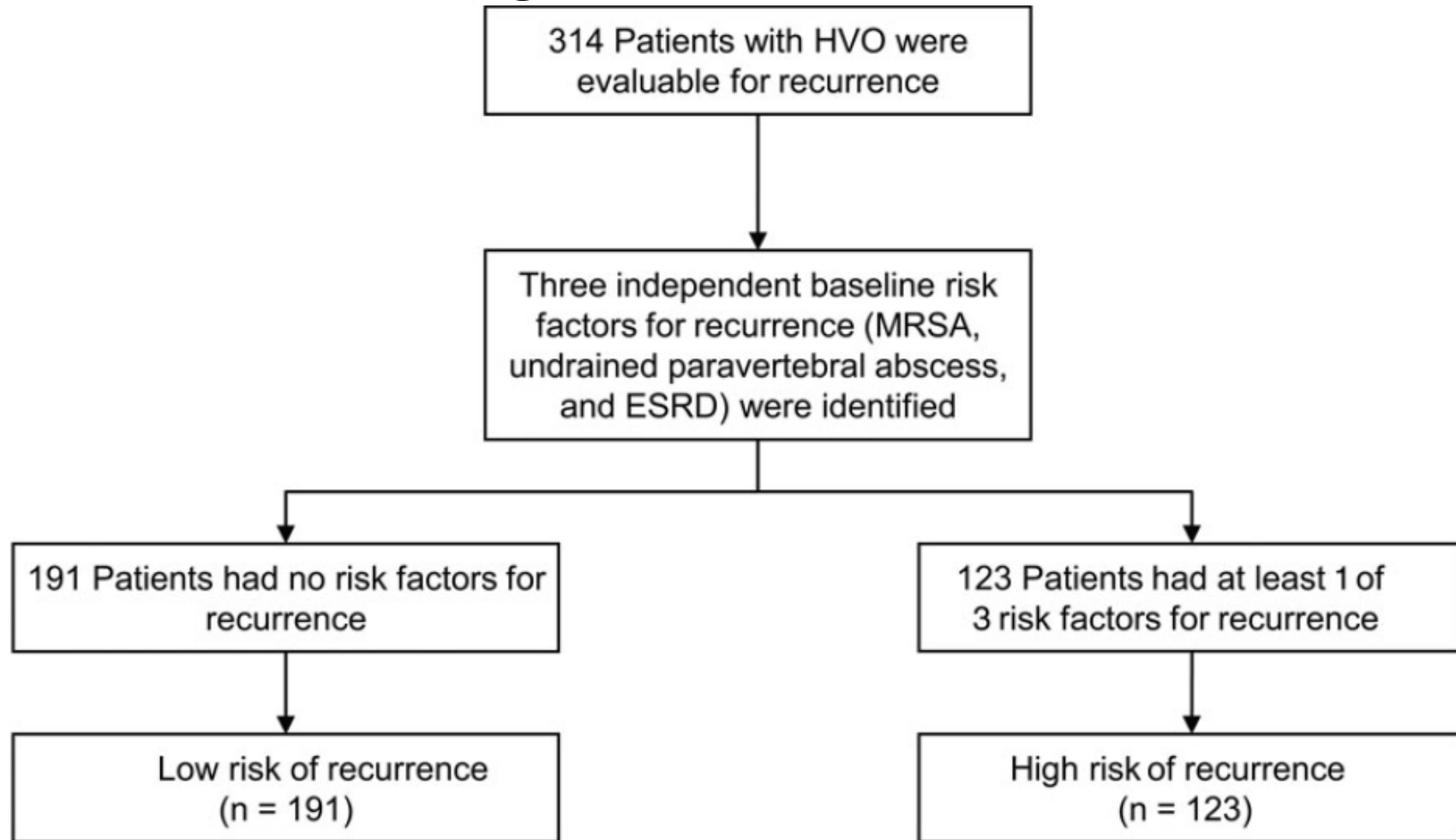
Antibiotic treatment for 6 weeks versus 12 weeks in patients with pyogenic vertebral osteomyelitis: an open-label, non-inferiority, randomised, controlled trial

	6-week regimen	12-week regimen	Difference in proportion of patients ^a	95% CI
Intention-to-treat analysis, n	176	175		
Cured	160 (90.9%)	159 (90.9%)	+0.1	-6.2 to 6.3
Cured and alive†	156 (88.6%)	150 (85.7%)	+2.9	-4.2 to 10.1
Cured without further antibiotic treatment‡	143 (80.7%)	141 (80.6%)	-0.1	-8.3 to 8.5
Per-protocol analysis, n	171	171		
Cured	156 (91.2%)	155 (90.6%)	-0.6	-7.1 to 5.9
Cured and alive†	133 (91.1%)	126 (92.0%)	-0.9	-7.7 to 6.0
Cured without further antibiotic treatment‡	NA	NA	NA	NA

Table 2: Primary outcome analyses of patients with vertebral osteomyelitis according to duration of antibiotic treatment

Thus..... in patients with pyogenic vertebral osteomyelitis, our results show that 12 weeks of antimicrobial treatment has no clinical advantage over 6 weeks of treatment

Optimal Duration of Antibiotic Therapy in Patients With Hematogenous Vertebral Osteomyelitis at Low Risk and High Risk of Recurrence



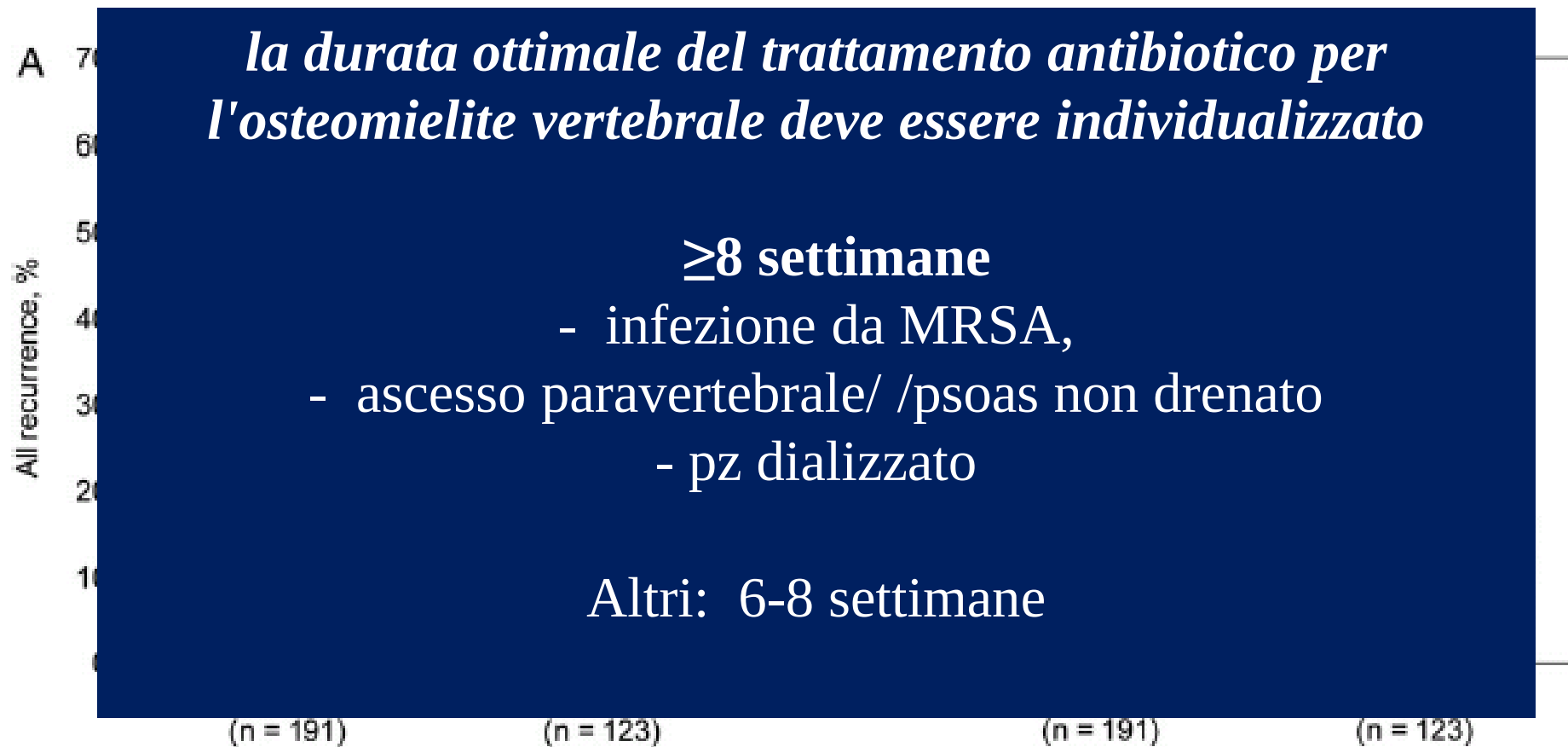
ESRD, end-stage renal disease; HVO, hematogenous vertebral osteomyelitis

Table 2. Bacteria Isolated From 345 Patients With Hematogenous Vertebral Osteomyelitis

Organisms	All Isolates (n = 345)
<i>Staphylococcus aureus</i>	203 (58.8)
Methicillin-susceptible <i>S. aureus</i>	115 (33.3)
Methicillin-resistant <i>S. aureus</i>	88 (25.5)
Gram-negative bacteria	75 (21.7)
<i>Escherichia coli</i>	38 (11.0)
<i>Klebsiella pneumoniae</i>	14 (4.0)
<i>Enterobacter</i> species	5 (1.4)
Nontyphoidal <i>Salmonella enterica</i>	4 (1.2)
<i>Pseudomonas aeruginosa</i>	4 (1.2)
Other gram-negative bacteria ^a	10 (2.9)
<i>Streptococcus</i> species	39 (11.3)
Viridans group streptococci	20 (5.8)
<i>Streptococcus agalactiae</i>	13 (3.8)
<i>Streptococcus pneumoniae</i>	4 (1.1)
Other streptococci ^b	2 (0.6)
Coagulase-negative staphylococci ^c	10 (2.9)
<i>Enterococcus</i> species	10 (2.9)
Anaerobe ^d	5 (1.5)
Other ^{c,e}	1 (0.3)
Polymicrobials ^f	2 (0.6)



Optimal Duration of Antibiotic Therapy in Patients With Hematogenous Vertebral Osteomyelitis at Low Risk and High Risk of Recurrence



Pyogenic Vertebral Osteomyelitis and Antimicrobial Therapy:

***It's Not Just the Length,
but
Also the Choice***

Parenteral Antimicrobial Treatment Native Vertebral Osteomyelitis

IDSA GUIDELINE

Microorganism	First Choice ^a	Alternatives ^a	Comments ^b
Staphylococci, oxacillin susceptible	Nafcillin ^c sodium or oxacillin 1.5–2 g IV q4–6 h or continuous infusion or Cefazolin 1–2 g IV q8 h or Ceftriaxone 2 g IV q24 h	Vancomycin IV 15–20 mg/kg q12 h ^d or daptomycin 6–8 mg/kg IV q24 h or linezolid 600 mg PO/IV q12 h or levofloxacin PO 500–750 mg PO q24 h and rifampin PO 600 mg daily ^[122] or clindamycin IV 600–900 mg q8 h	6 wk duration
Staphylococci, oxacillin resistant ^[123]	Vancomycin IV 15–20 mg/kg q12 h (consider loading dose, monitor serum levels)	Daptomycin 6–8 mg/kg IV q24 h or linezolid 600 mg PO/IV every 12 h or levofloxacin PO 500–750 mg PO q24 h and rifampin PO 600 mg daily ^[122]	6 wk duration
<i>Enterococcus</i> species, penicillin susceptible	Penicillin G 20–24 million units IV q24 h continuously or in 6 divided doses; or ampicillin sodium 12 g IV q24 h continuously or in 6 divided doses	Vancomycin 15–20 mg/kg IV q12 h (consider loading dose, monitor serum levels) or daptomycin 6 mg/kg IV q 24 h or linezolid 600 mg PO or IV q12 h	Recommend the addition of 4–6 wk of aminoglycoside therapy in patients with infective endocarditis. In patients with BSI, physicians may opt for a shorter duration of therapy. Optional for other patients ^[124, 125] . Vancomycin should be used only in case of penicillin allergy.
<i>Enterococcus</i> species, penicillin resistant ^e	Vancomycin IV 15–20 mg/kg q12 h (consider loading dose, monitor serum levels)	Daptomycin 6 mg IV q 24 h or linezolid 600 mg PO or IV q12 h	Recommend the addition of 4–6 wk of aminoglycoside therapy in patients with infective endocarditis. In patients with BSI, physicians may opt for a shorter duration of aminoglycoside. The additional of aminoglycoside is optional for other patients ^[124, 125] .
<i>Pseudomonas aeruginosa</i>	Cefepime 2 g IV q8–12 h or meropenem 1 g IV q8 h or doripenem 500 mg IV q8 h	Ciprofloxacin 750 mg PO q12 h (or 400 mg IV q8 h) or aztreonam 2 g IV q8 h for severe penicillin allergy and quinolone-resistant strains or ceftazidime 2 g IV q8 h	6 wk duration Double coverage may be considered (ie, β-lactam and ciprofloxacin or β-lactam and an aminoglycoside).
Enterobacteriaceae	Cefepime 2 g IV q12 h or ertapenem 1 g IV q24 h	Ciprofloxacin 500–750 mg PO q12 h or 400 mg IV q12 hours	6 wk duration
β-hemolytic streptococci	Penicillin G 20–24 million units IV q24 h continuously or in 6 divided doses or ceftriaxone 2 g IV q24 h	Vancomycin IV 15–20 mg/kg q12 h (consider loading dose, monitor serum levels)	6 wk duration Vancomycin only in case of allergy.
<i>Propionibacterium acnes</i>	Penicillin G 20 million units IV q24 h continuously or in 6 divided doses or ceftriaxone 2 g IV q24 h	Clindamycin 600–900 mg IV q8 h or vancomycin IV 15–20 mg/kg q12 h (consider loading dose, monitor serum levels)	6 wk duration Vancomycin only in case of allergy.
<i>Salmonella</i> species	Ciprofloxacin PO 500 mg q12 h or IV 400 mg q12 h	Ceftriaxone 2 g IV q 4 h (if nalidixic acid resistant)	6–8 wk duration

Abbreviations: BSI, bloodstream infection; IV, intravenous; PO, take orally; q, every.

^a Antimicrobial dosage needs to be adjusted based on patients' renal and hepatic function. Antimicrobials should be chosen based on in vitro susceptibility as well as patient allergies, intolerances, and potential drug interactions or contraindications to a specific antimicrobial.

^b Recommend Infectious Diseases Society of America guidelines for monitoring of antimicrobial toxicity and levels ^[126].

^c Flucloxacillin may be used in Europe.

^d Vancomycin should be restricted to patients with type I or documented delayed allergy to β-lactams.

^e Daptomycin, linezolid, or Synercid may be used for vancomycin-resistant enterococci.

Diagnostic value of MRI and 18F-FDG-PET/CT related to the timing of the imaging procedure

	≤ 14days of start of symptoms	>14 days of start of symptoms	Total
MRI	29	39	68
→ Sensitivity	50 (28.3–71.8)	82 (61.9–93.6)	67 (52.5–80.0)
→ Specificity	86 (42.2–97.6)	83 (51.6–97.4)	84 (60.4–96.4)
PPV	92 (61.5–98.6)	92 (73.0–98.7)	92 (77.5–98.2)
NPV	35 (14.3–61.7)	67 (38.4–88.1)	50 (31.9–68.1)
Accuracy	58 (40.0–76.0)	82 (69.9–94.1)	72 (61.3–82.7)
¹⁸ F-FDG-PET/CT	32	36	68
→ Sensitivity	96 (79.6–99.3)	96 (78.8–99.3)	96 (86.0–99.4)
→ Specificity	100 (58.9–100)	92 (61.5–98.6)	95 (73.9–99.1)
PPV	100 (85.6–100)	96 (78.8–99.3)	98 (88.9–99.7)
NPV	88 (47.4–97.9)	92 (61.5–98.6)	90 (68.3–98.5)
Accuracy	97 (91.1–100)	94 (86.2–100)	96 (91.3–100)

C. Smids et al.: A comparison of the diagnostic value of MRI and 18F-FDG-PET/CT in suspected spondylodiscitis Infection (2017) 45:41–49

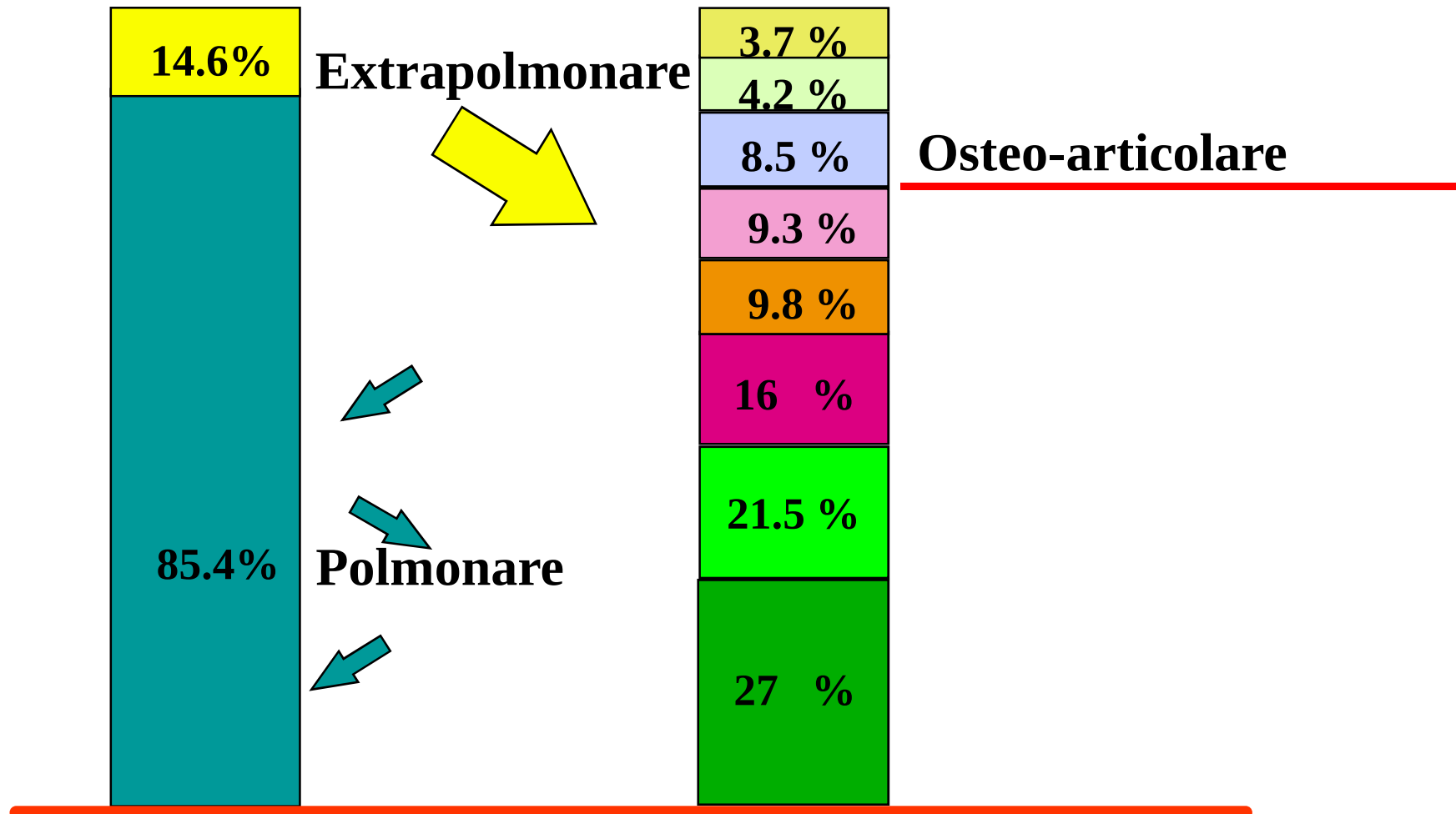
IMAGING

FDG PET/CT is useful for the interim evaluation of response to therapy in patients affected by haematogenous spondylodiscitis

Cristina Nanni, Luca Boriani, Caterina Salvadori



ORGANI “BERSAGLIO” DELL’INFEZIONE DA *M. tuberculosis*



The course of spinal tuberculosis (Pott disease): results of the multinational, multicentre Backbone-2 study

35 centri (Turchia, Egitto, Albania e Grecia) 314 pazienti arruolati 2000 - 2013

Durata media sintomi/diagnosi: 78 giorni

Lombare (56%), toracico (49%) toraco-lombare (13%) 8% lesioni non contigue

Trattamento medico 103 pazienti (33%)

Trattamento medico e chirurgico (diagnostico e / o terapeutico) 211 pazienti (67%)

Mortalità 2%

**Sequela (25% dei casi): 11% cifosi, 6% gibbo, 5% scoliosi, 5% paraparesi,
5% paraplegia 4% deficit sensitivo**

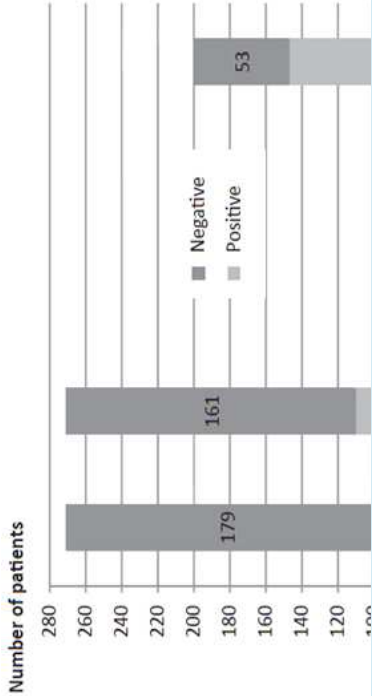
morbilità correlata al ritardo diagnostico/terapeutico

Treatment	Value
Treatment	
INH, RIF, PRZ, EMB	261 (83)
INH, RIF, PRZ, STM	22 (7)
INH, RIF, PRZ, EMB, STM	29 (9)
Corticosteroid therapy	13 (4)
Missing data	2 (1)
Duration of therapy (months)	11.6 ± 2.5
Surgical intervention	
Percutaneous biopsy with or without abscess drainage	211 (67)
Open abscess drainage	100 (47)
	34 (16)

Treatment
 INH, RIF, PRZ, EMB
 INH, RIF, PRZ, STM
 INH, RIF, PRZ, EMB, STM
 Corticosteroid therapy

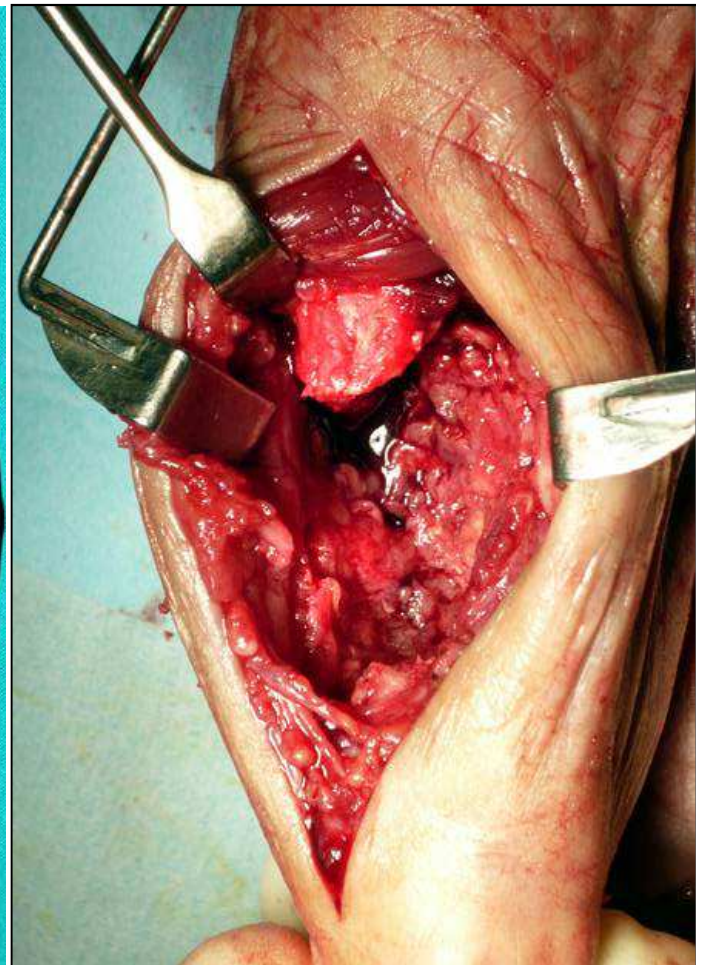
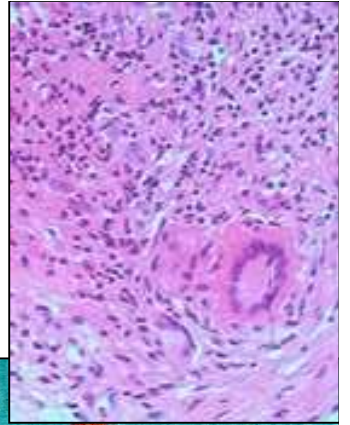
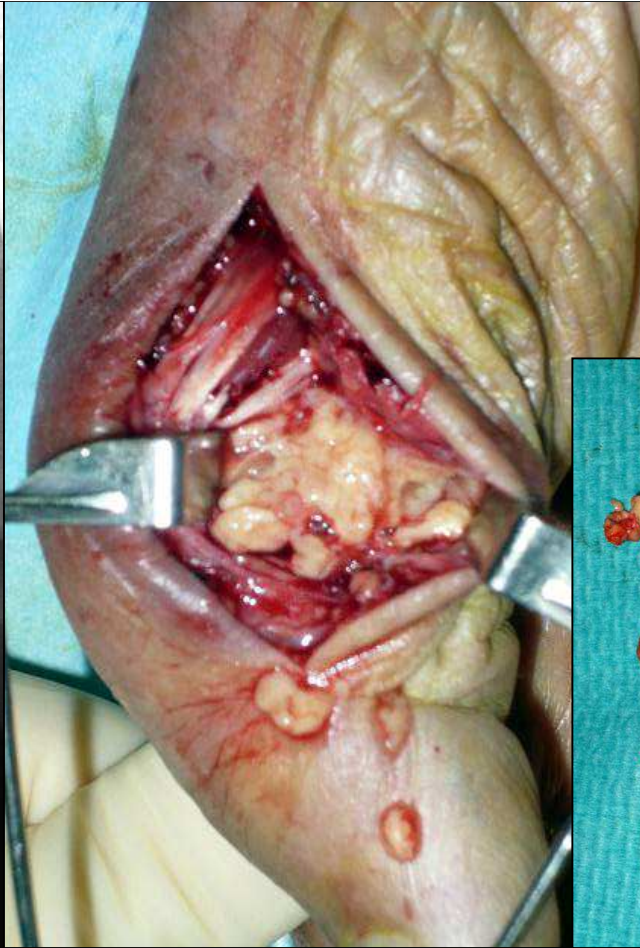
Missing data

Duration of therapy (months)
 Surgical intervention

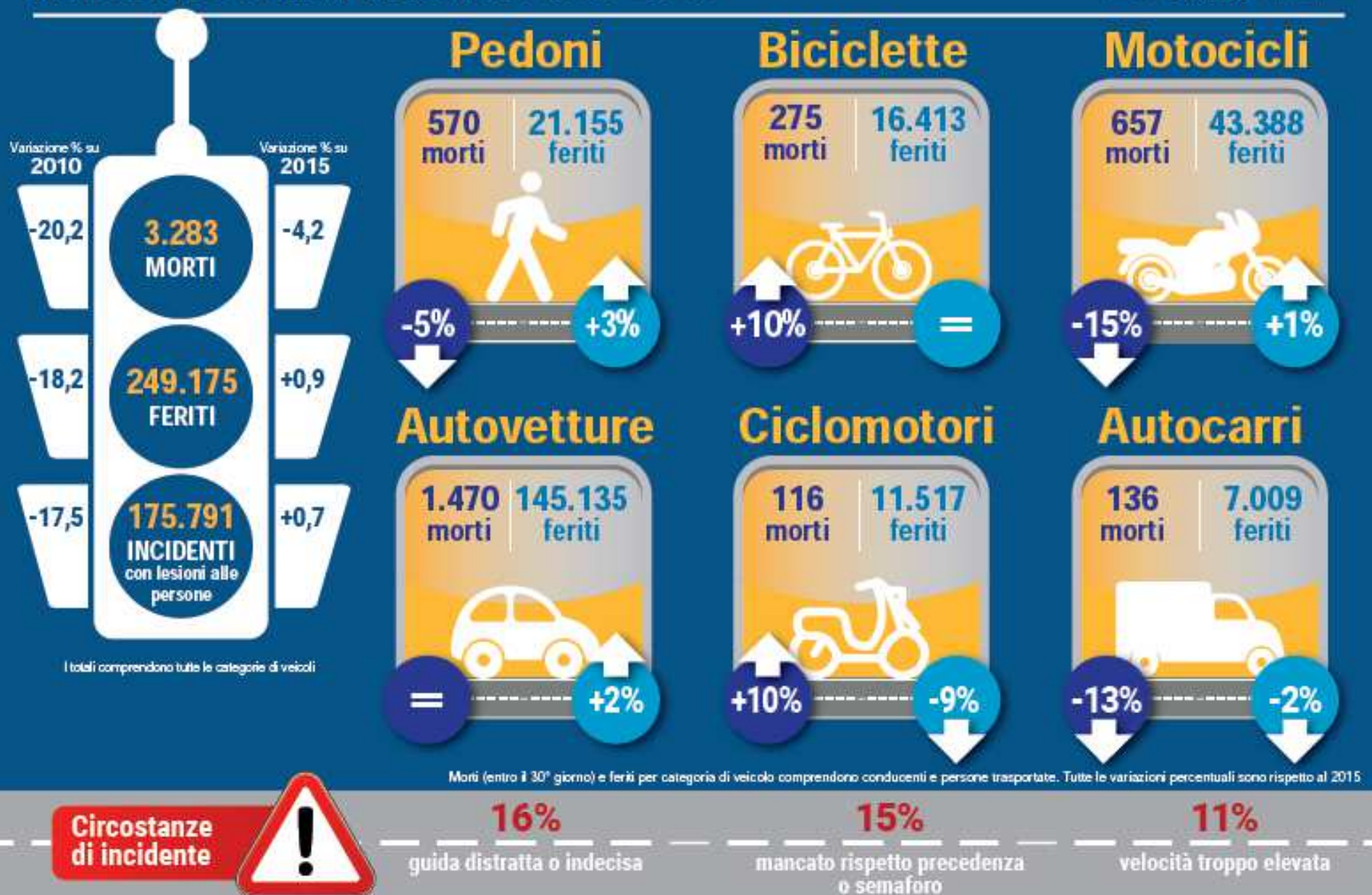


261 (83)
 22 (7)
 29 (9)
 13 (4)
 2 (1)
 11.6 ± 2.5
 211 (67)

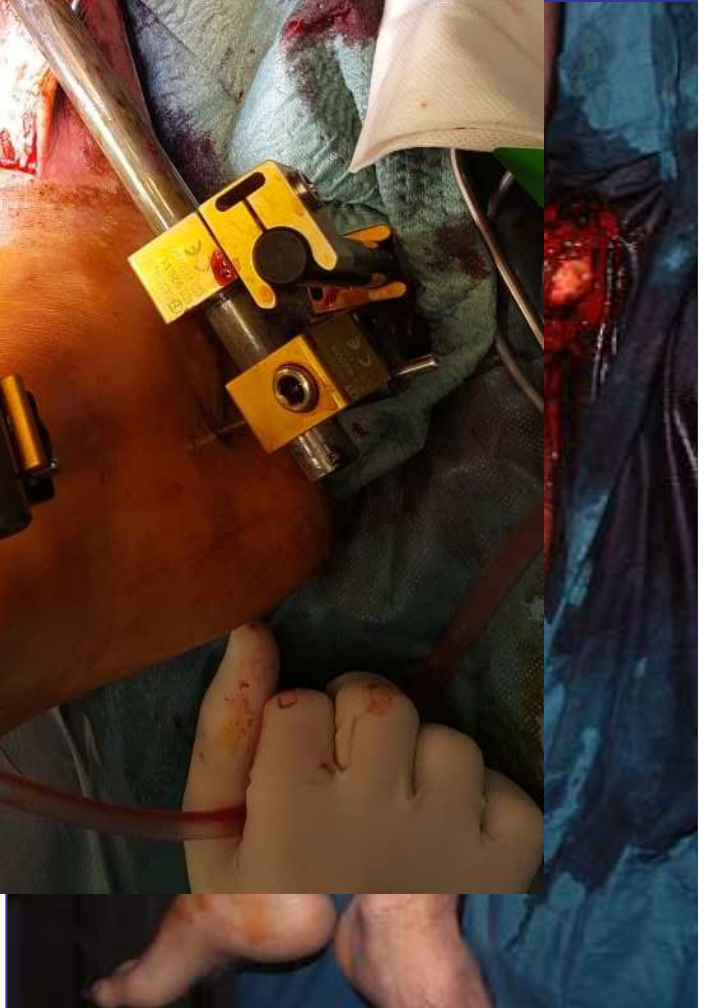
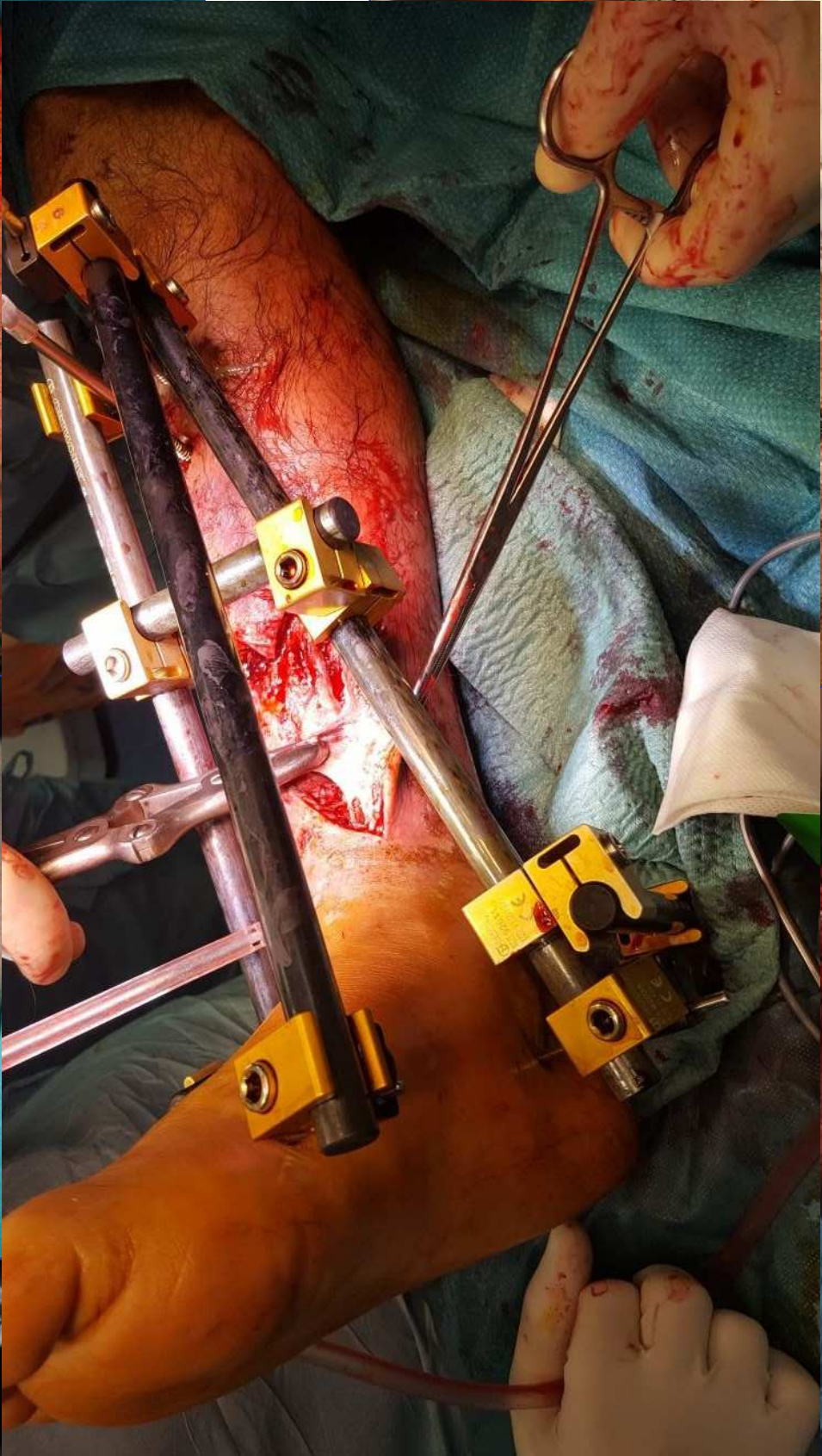
Time to ESR normalization	28 (120, 30)
Follow-up imaging results	
Cure	48 (15)
Radiologic improvement	137 (44)
Worsening of radiologic findings	13 (4)
Unfavourable outcomes	84 (27)
Mortality	7 (2)
Posttreatment sequelae ^a	77 (25)
Kyphosis	35 (11)
Gibbus deformity	18 (6)
Motor weakness	17 (5)
Paraplegia	17 (5)
Scoliosis	15 (5)
Loss of sensation	12 (4)
Kyphoscoliosis	3 (1)
Vertebral compression fracture	2 (0.6)
Persistent pain	2 (0.6)
Urinary retention	1 (0.3)
Polyneuropathy	1 (0.3)



Incidenti stradali in Italia. Anno 2016



27 luglio 2017.



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%

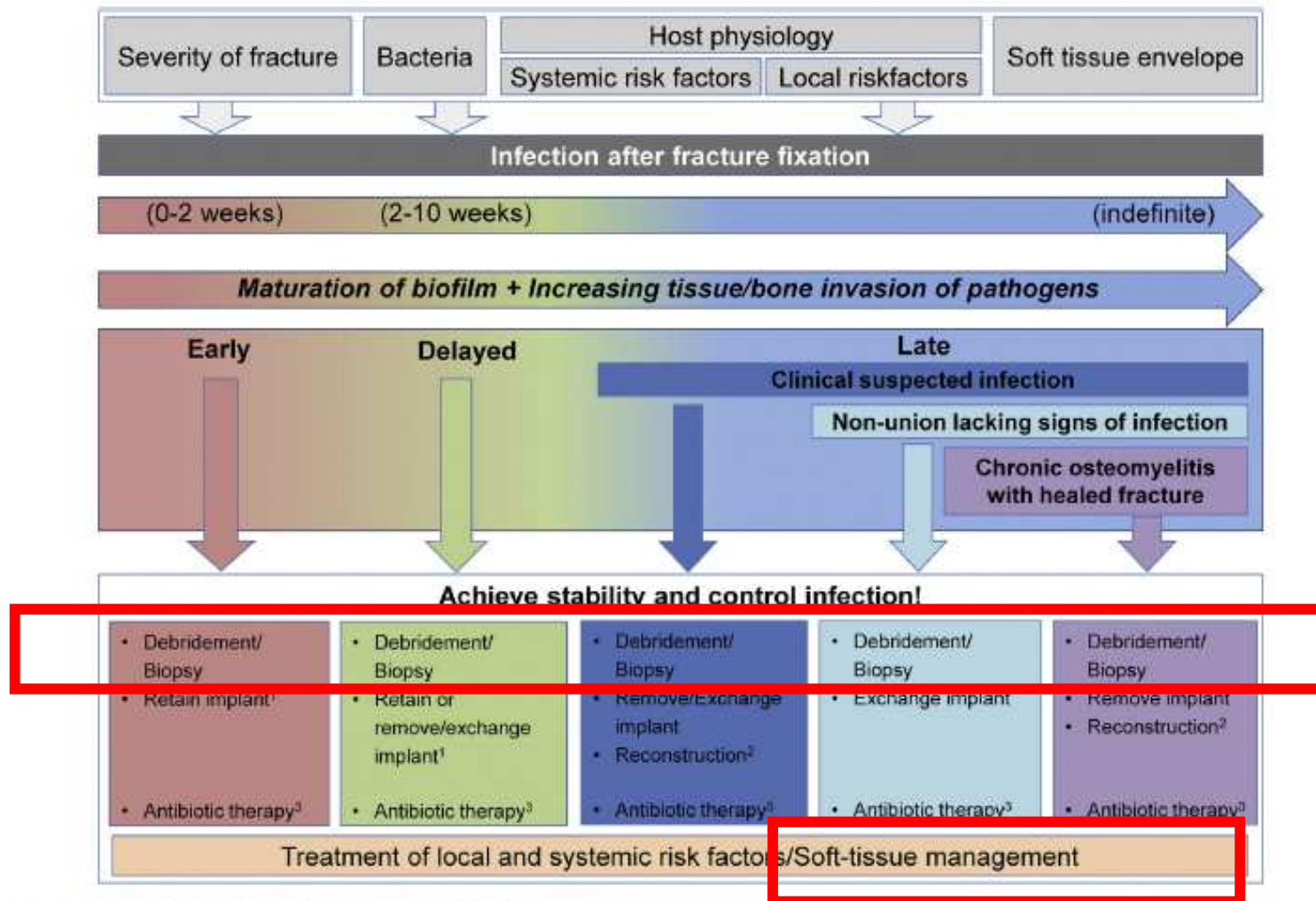
.Gustilo RB et al.:The management of open fractures. *J Bone Joint Surg Am.* 1990; 72(2):299-304

.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)

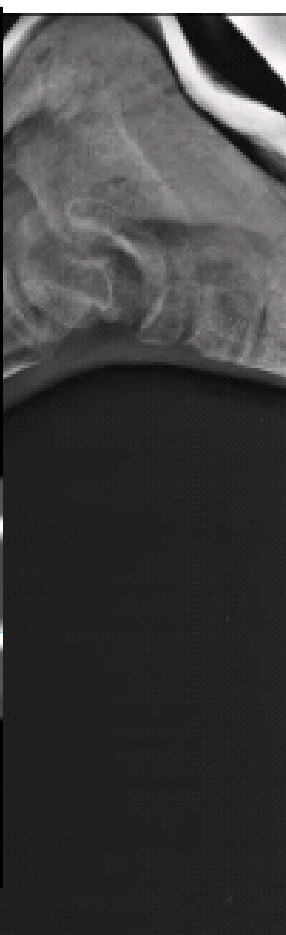
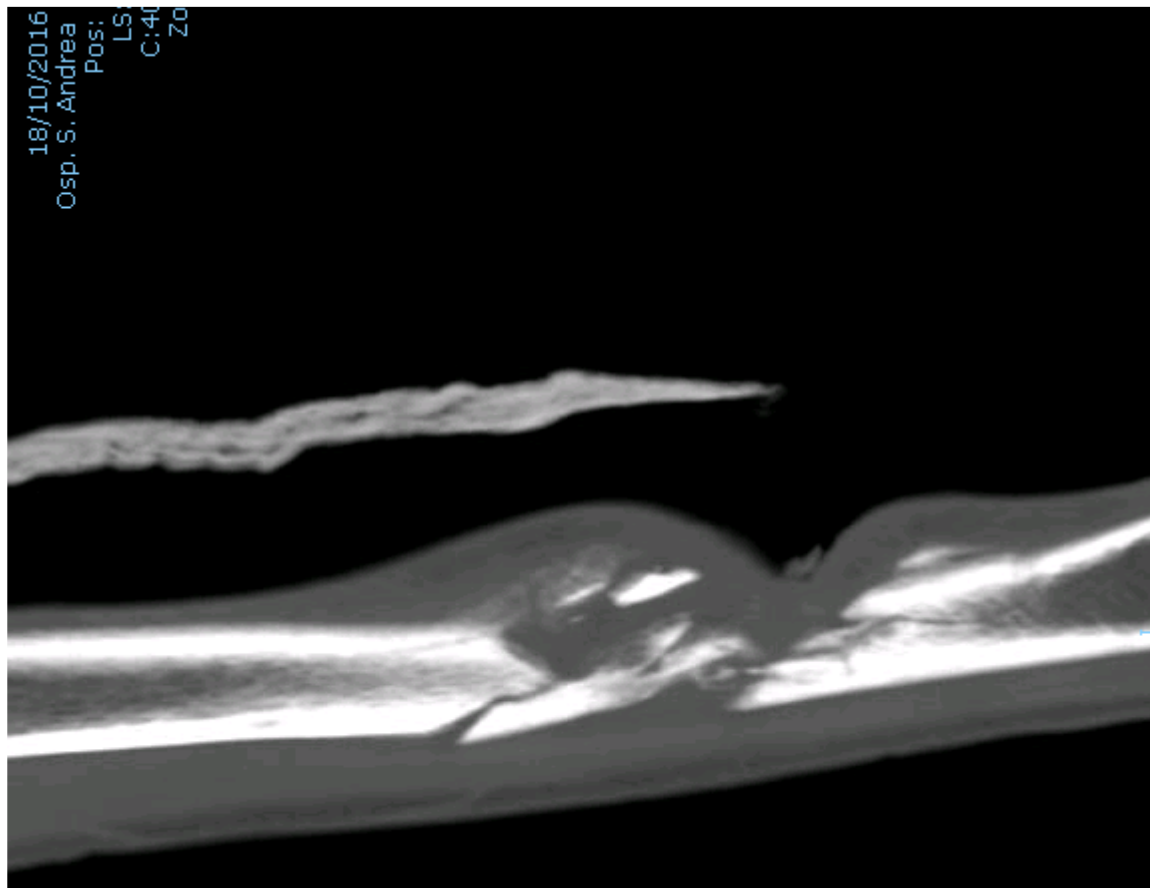


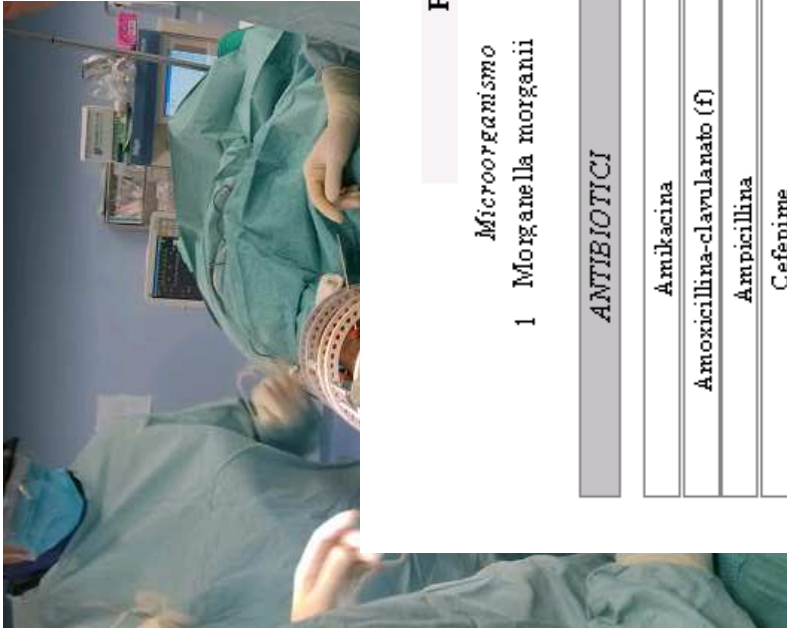
**TERAPIA
ANTIBIOTICA**

?



18/10/2016
Osp. S. Andrea
Pos:
LS
C:40
Zo

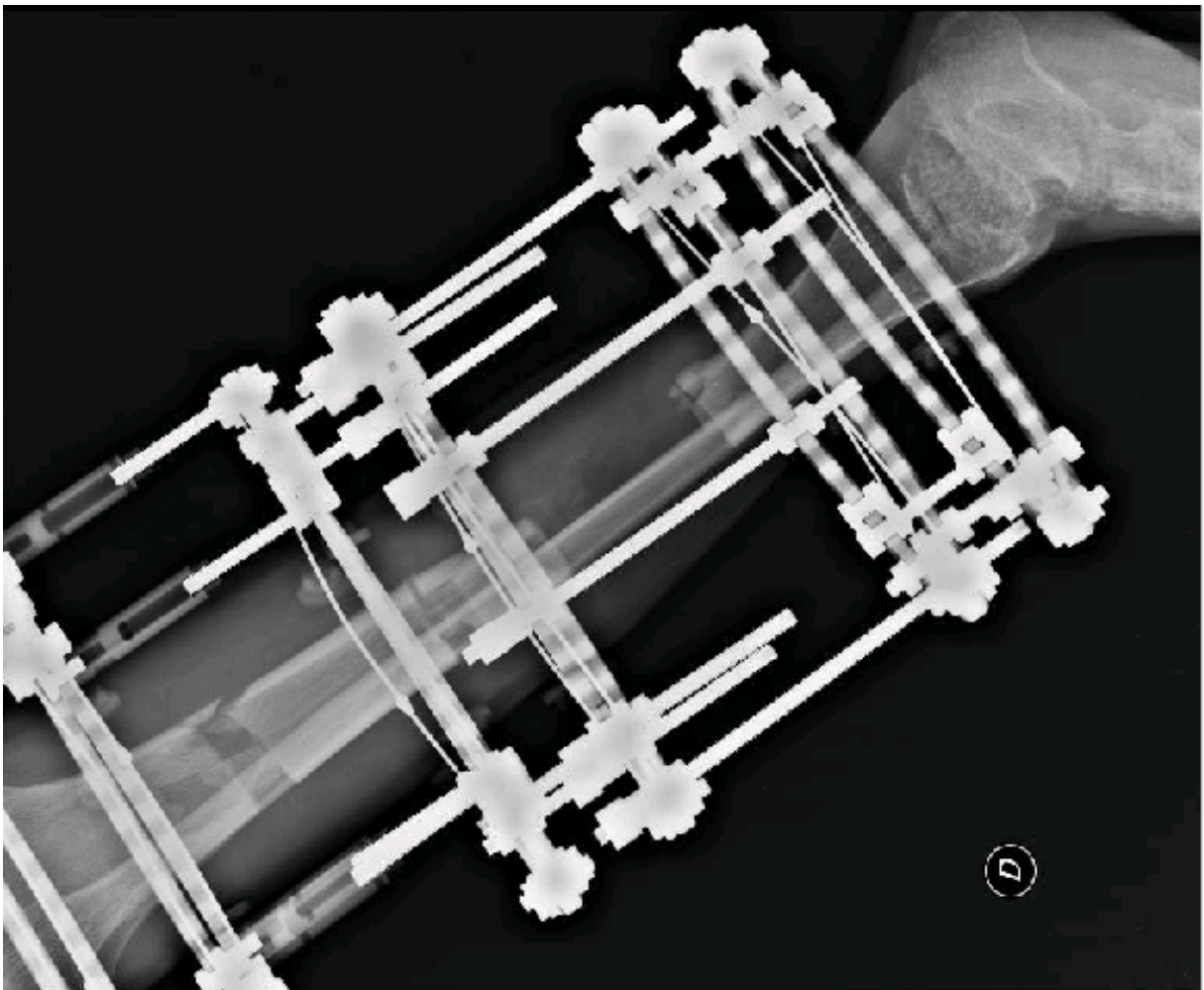




Positivo/a
Microorganismo
 1 Morganella morganii *Carica*

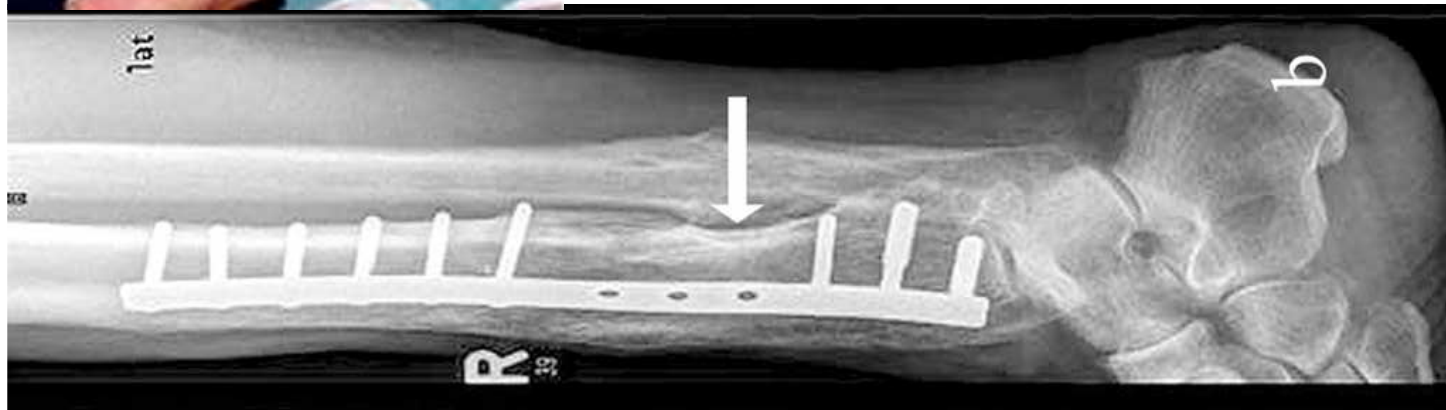
ANTIBIOTICI	I	MIC
Amikacina	S	≤4
Amoxicillina-clavulanato (f)	R	>32/2
Ampicillina	R	>8
Cefepime	S	≤1
Cefotaxima	R	>4
Ceftazidima	R	>8
Ciprofloxacina	R	>1
Colistina	R	>4
Ertapenem	S	≤0.25
Fosfomicina c/G6P	R	>64
Gentamicina	R	>4
Imipeneme	I	8
Levofloxacina	R	2
Meropeneme	S	≤0.12
Piperacillina-tazobattam	S	≤4/4
Tigeciclina	R	1
Tobramicina	R	>4
Trimetoprima-sulfametossolo	R	>4/76

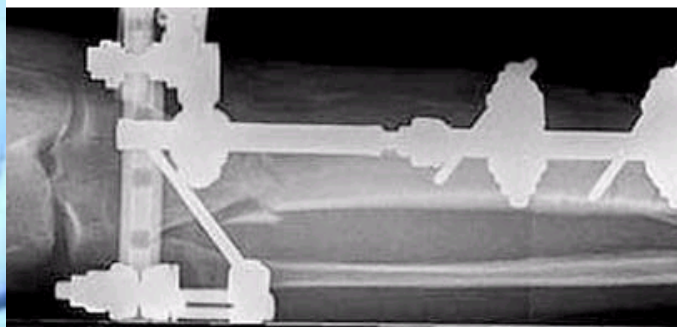
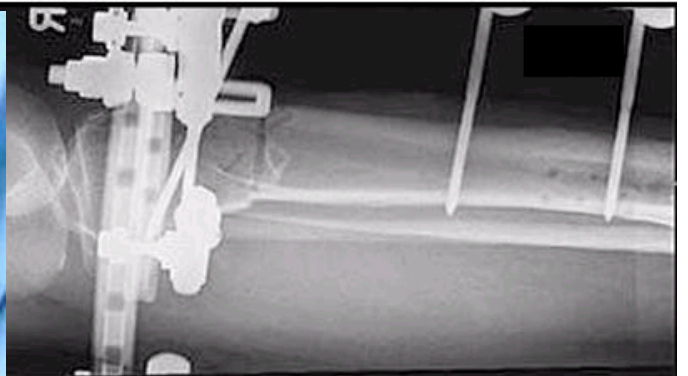
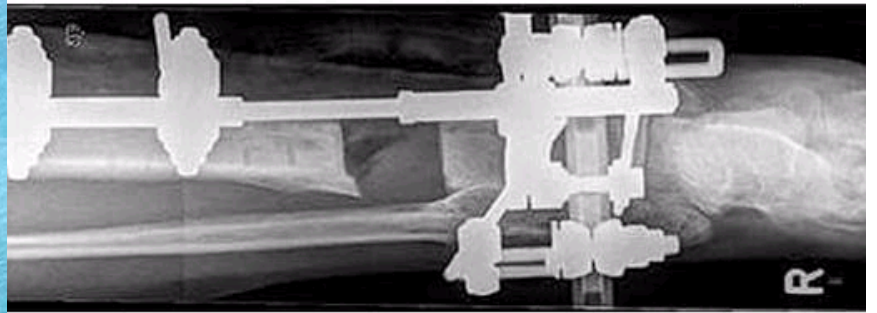
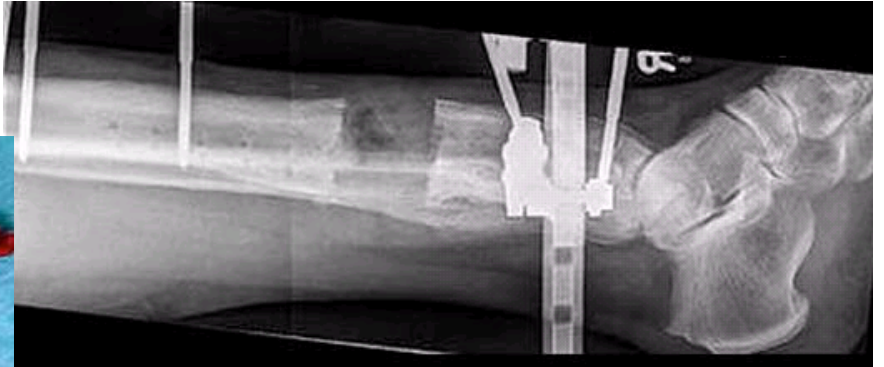
S= Sensibile, R= Resistente, I= Intermedio

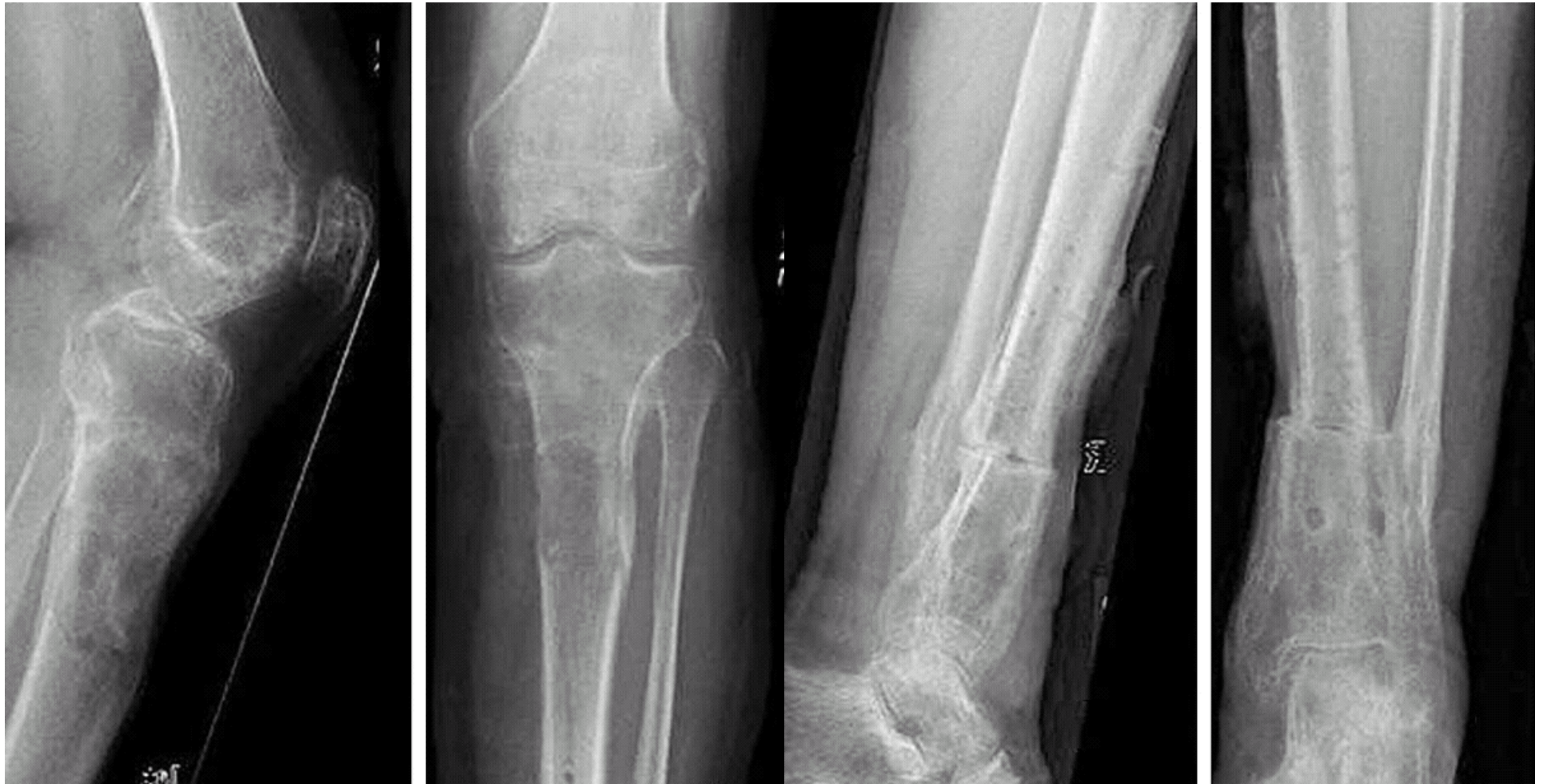


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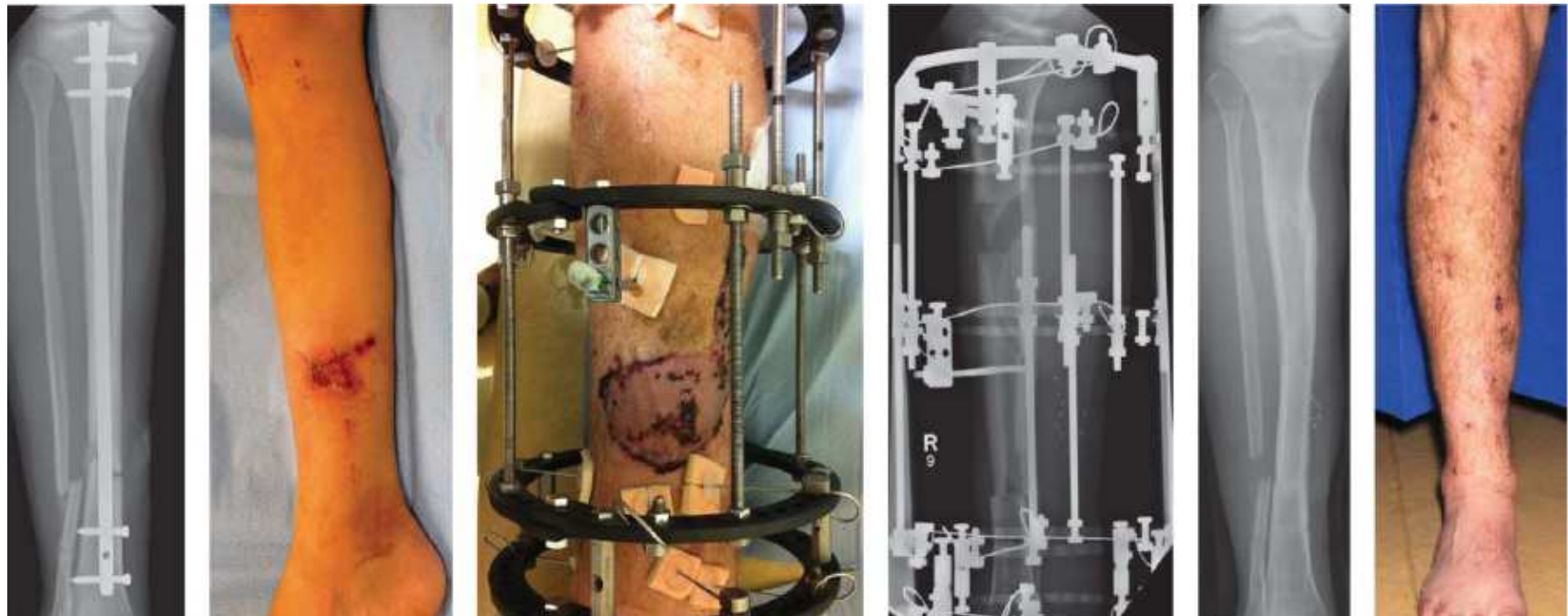
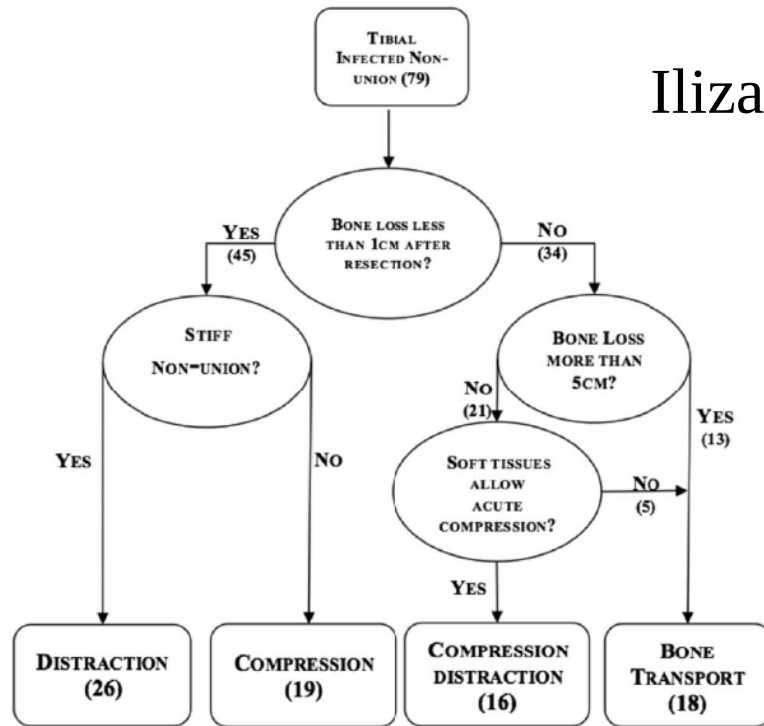


dopo 9 mesi

**Il trasporto viene terminato e il fissatore esterno viene
rimosso.**

Ilizarov Treatment Protocols in the Management of Infected Nonunion of the Tibia

J Orthop Trauma Volume 31, Number 10 Supplement, October 2017



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 LUNGI 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)**





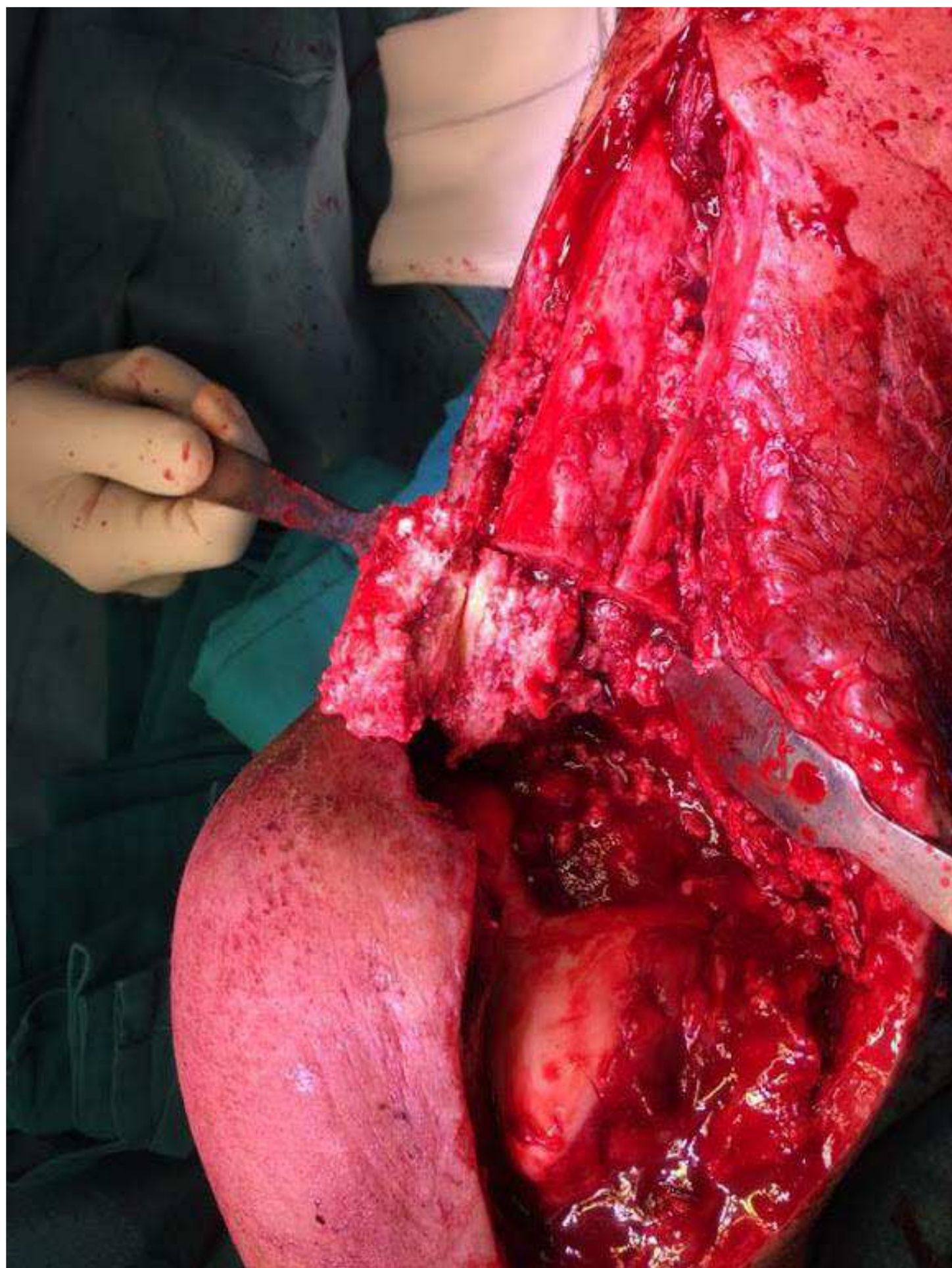
Marchi, Liborio
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5/13/1971
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Desc. serie: AP
ID plastro: 910437975
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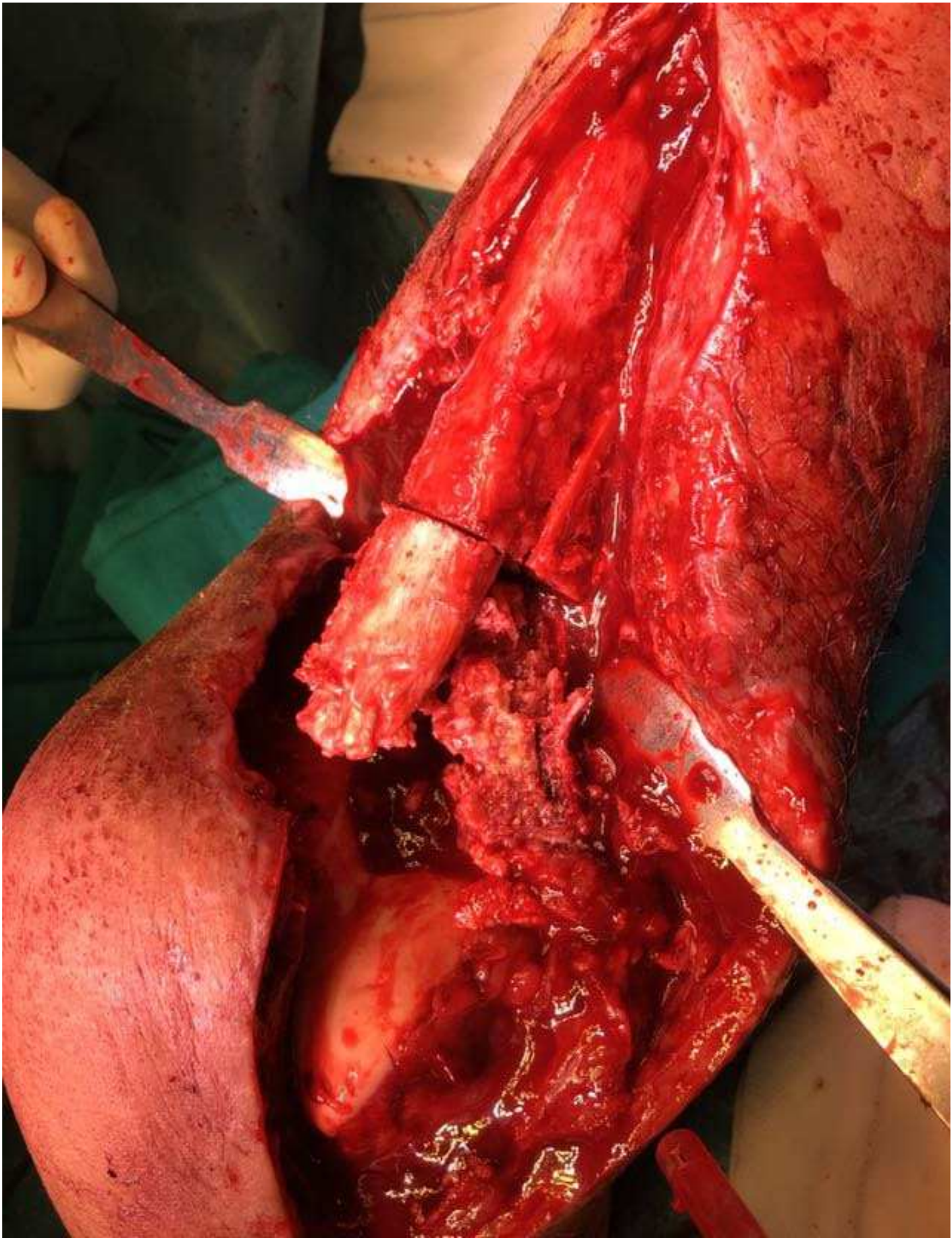
29/11/2017 11:39:38

ASL VC
KODAK CR0975
41% Pixel
DFOV 42.0 x 42.0 cm











Altro Provenienza: 2° campione
Esame culturale

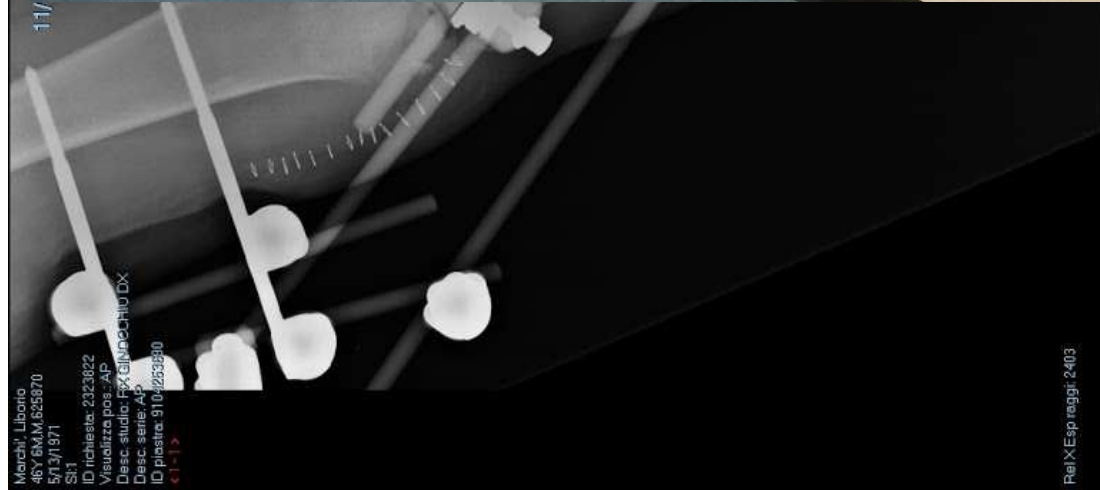
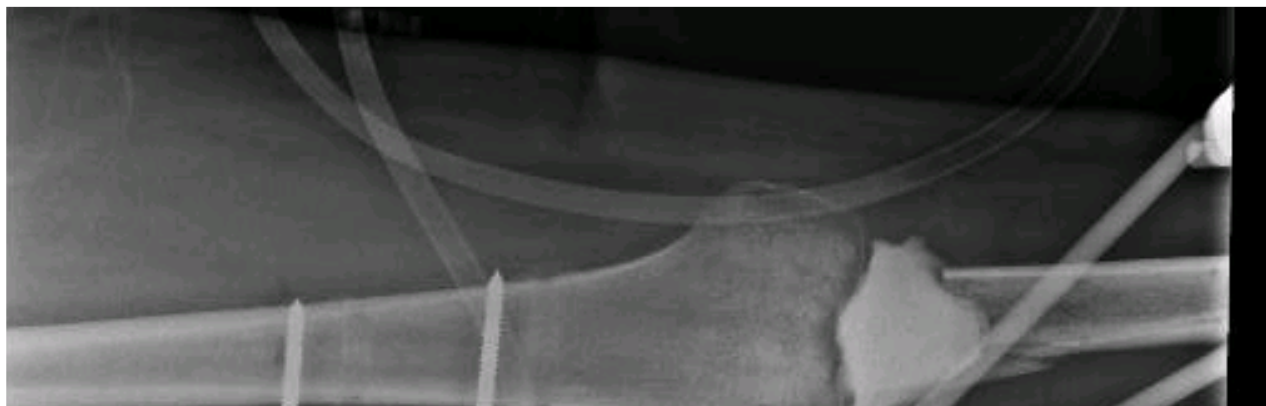
Positivo/a
Microorganismo *Carica*
1 *Klebsiella pneumoniae* ssp pne

Altro Provenienza: 3° campione
Esame culturale

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

Antibiogramma

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



Marchi Libero
46Y6MAM625870
5/13/1971
S11
ID richiesta: 2323822
Visualizza pos: AP
Desc studio: T2X GINocchio DX
Desc serie: AP
ID piastra: 9104263090
11/

Piel X Esp raggi 2403

August 2017

Centers for Disease Control and Prevention Guideline for the Prevention of Surgical Site Infection, 2017

Sandra I. Berríos-Torres, MD¹; Craig A. Umscheid, MD, MSCE²; Dale W. Bratzler, DO, MPH³; et al

» [Author Affiliations](#) | [Article Information](#)

JAMA Surg. 2017;¹

By 2030, the infection risk for hip and knee arthroplasty is expected to increase **from 2.18% to 6.5% and 6.8%**, respectively

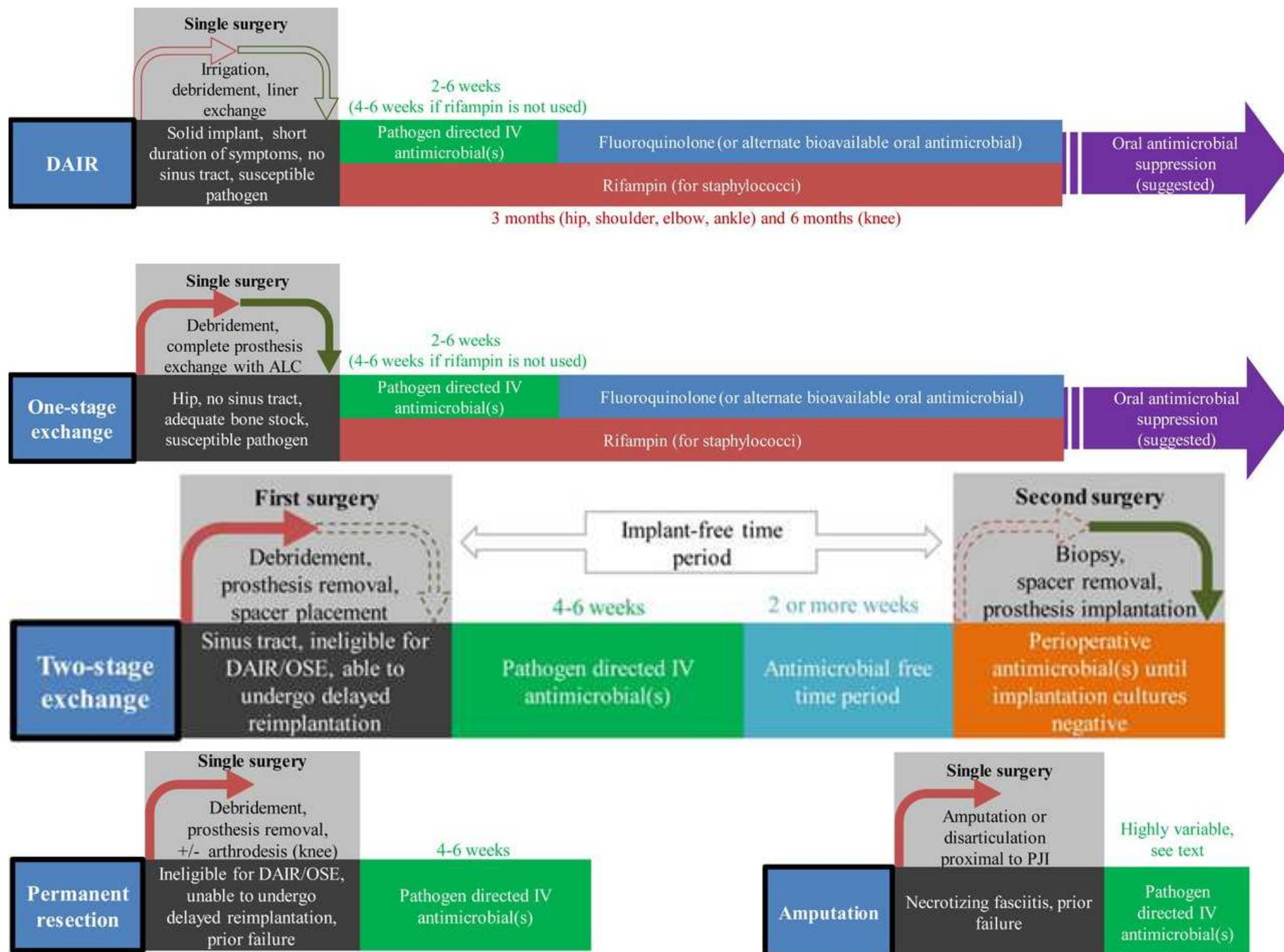
PJI :DIFFERENTI STRATEGIE MEDICHE E CHIRURGICHE

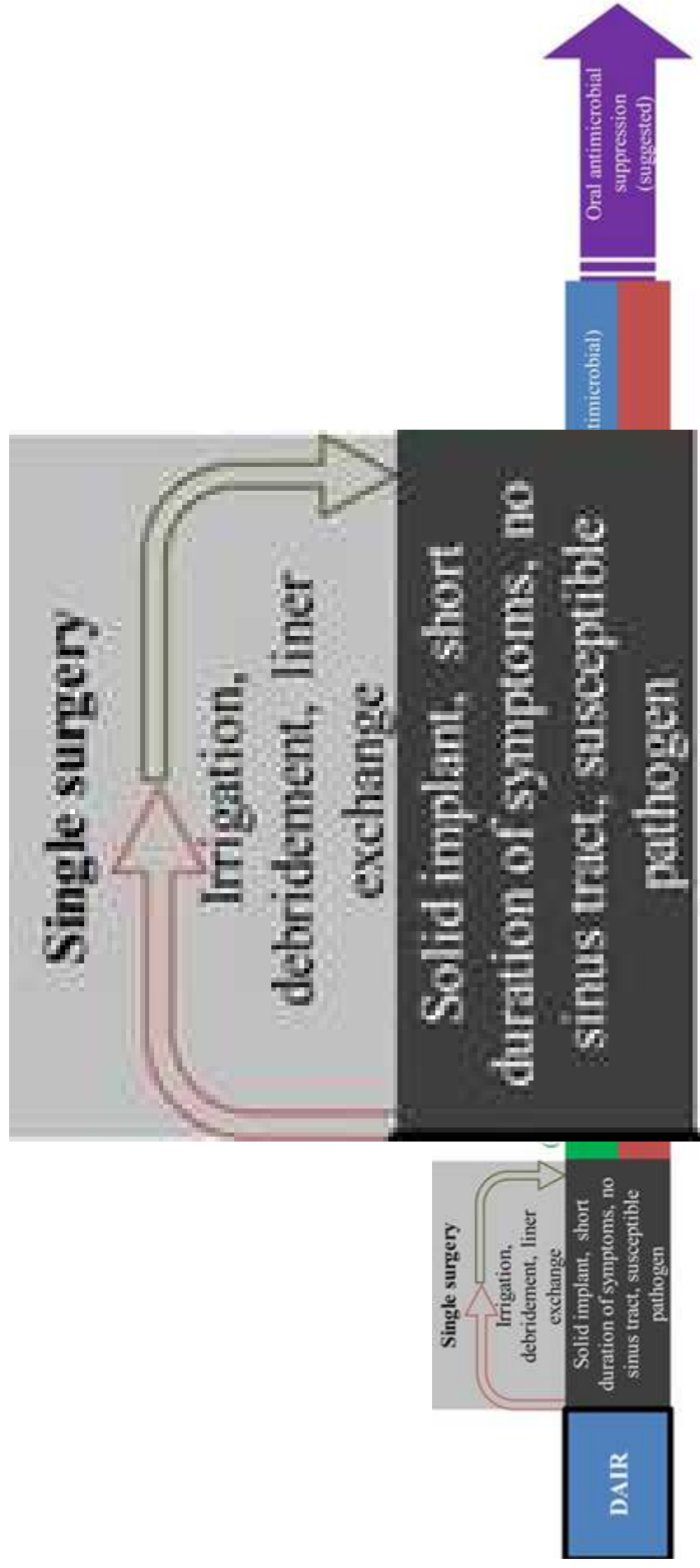
- debridement, sostituzione polietilene senza rimozione della protesi
- sostituzione in 1 o 2 tempi chirurgici
- rimozione senza reimpianto - Gilderstone -/artrodesi ginocchio
- amputazione/disarticolazione
- terapia antimicrobica soppressiva cronica senza intervento chirurgico

L'obiettivo di ogni strategia chirurgica è rimuovere tutto il tessuto infetto e parte o tutto l'impianto per diminuire carica batterica e biofilm permettendo alla terapia antibiotica post-operatoria di eradicare la restante infezione .

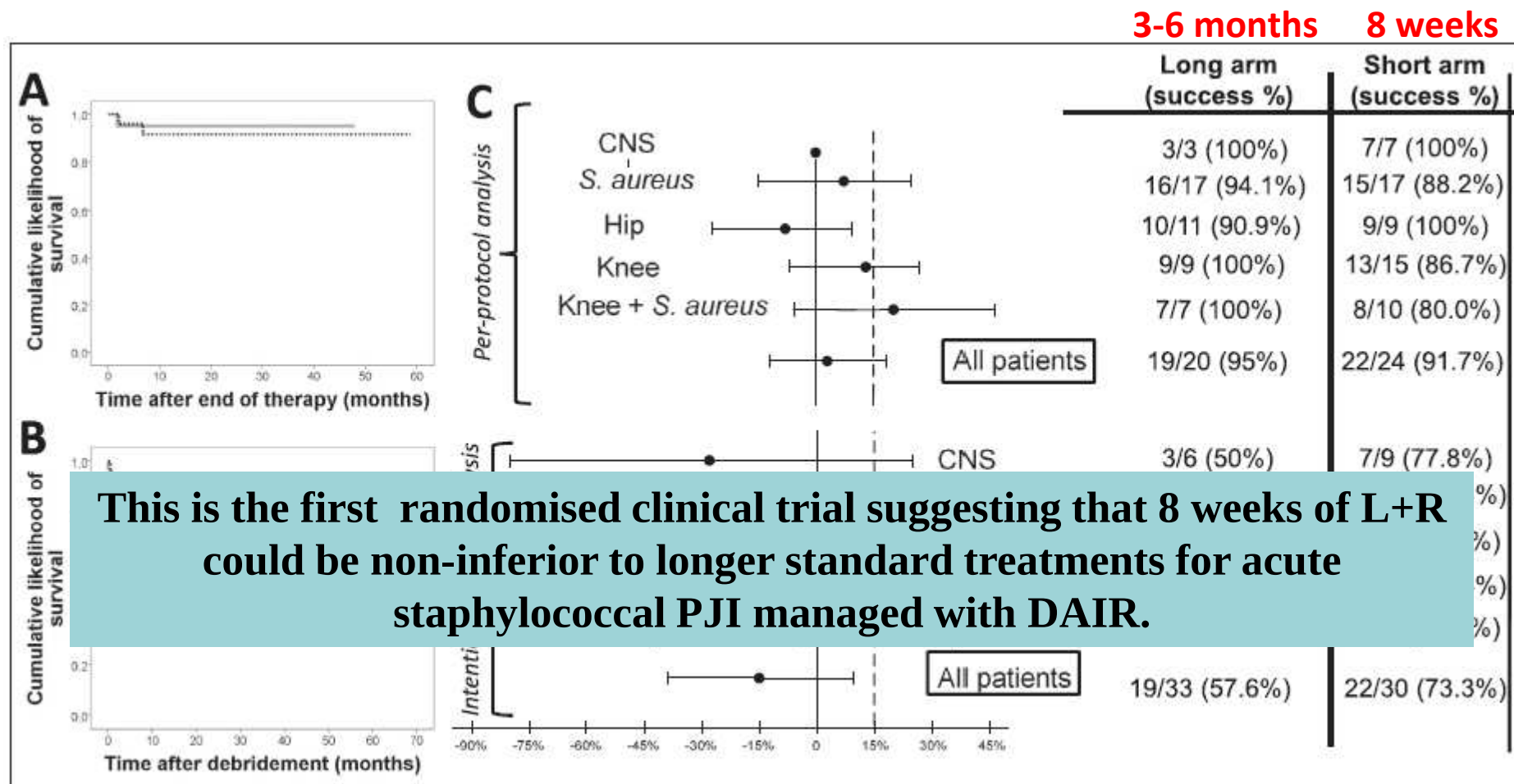
 Se la diagnosi eziologica è certa l'approccio chirurgico potrà essere eseguito con Pz in trattamento antibiotico mirato

 Se la diagnosi eziologica certa non è stata ottenuta, non somministrare antibiotici fino ad esecuzione di prelievi multipli intraoperatori





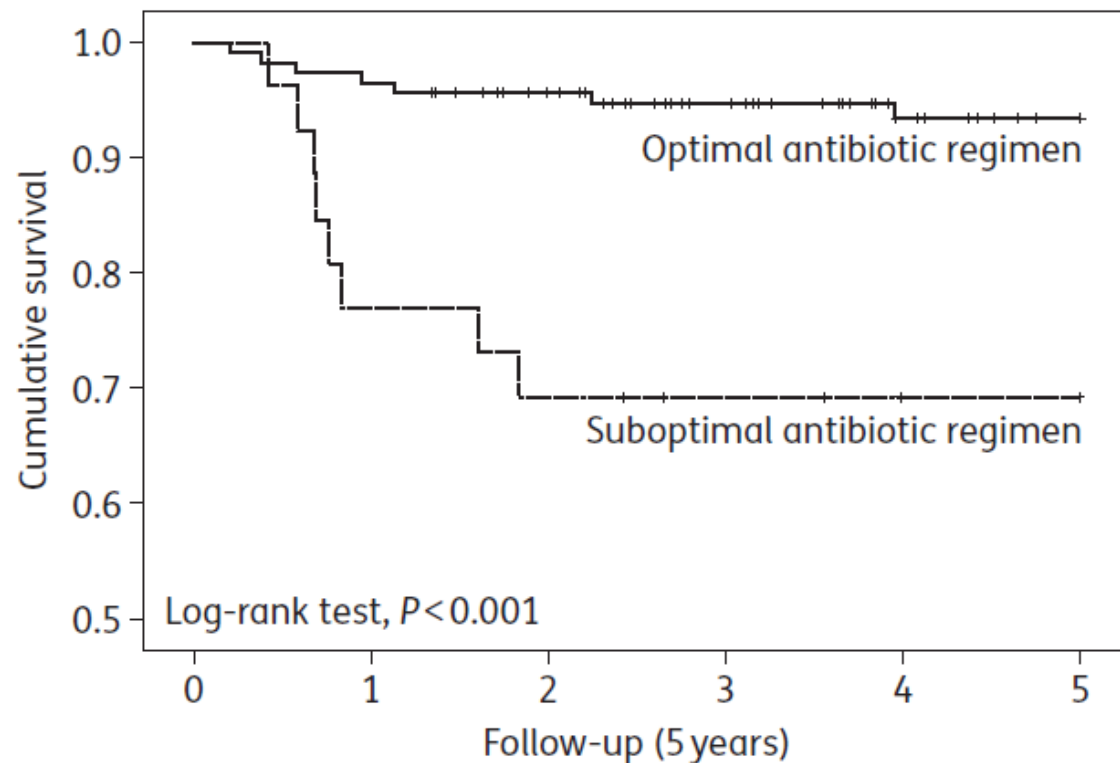
SHORT- VERSUS LONG-DURATION LEVOFLOXACIN PLUS RIFAMPICIN FOR ACUTE STAPHYLOCOCCAL PROSTHETIC JOINT INFECTION MANAGED WITH IMPLANT RETENTION: A RANDOMISED CLINICAL TRIAL



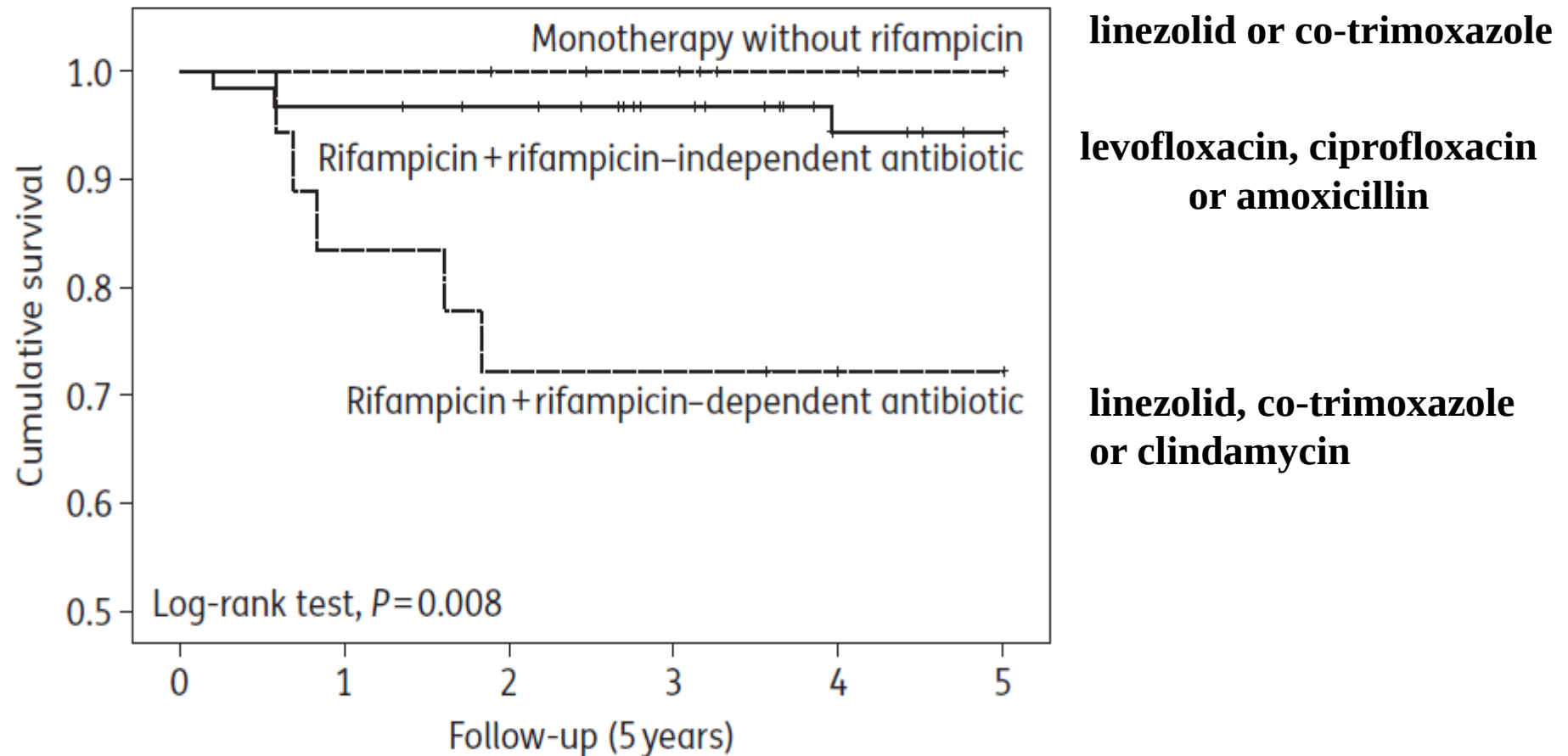
Many retrospective studies suggest that
**rifampin combinations may increase
remission rates for staphylococcal PJI**

- Aboltins C et al.: Current concepts in the management of prosthetic joint infection. Intern Med J 2014;44:834–40.
- Berdal JE et al.: Use of rifampicin and ciprofloxacin combination therapy after surgical debridement in the treatment of early manifestation prosthetic joint infections. Clin Microbiol Infect 2005;11:843–5.
- Senneville E et al. Outcome and predictors of treatment failure in total hip/knee prosthetic joint infections due to Staphylococcus aureus. Clin Infect Dis 2011;53:334–40.
- Lora-Tamayo J, Murillo O, Iribarren JA, Soriano A et al. A large multicenter study of methicillin-susceptible and methicillin-resistant Staphylococcus aureus prosthetic joint infections managed with implant retention. Clin Infect Dis 2013;56:182–94.
- Wieland BW et al.: A retrospective comparison of ceftriaxone versus oxacillin for osteoarticular infections due to methicillin-susceptible Staphylococcus aureus. Clin Infect Dis 2012;54:585–90.
- San Juan R et al.: Safety and efficacy of moxifloxacin monotherapy for treatment of orthopedic implant-related staphylococcal infections. Antimicrob Agents Chemother 2010;54:5161–6.

Importance of selection and duration of antibiotic regimen in prosthetic joint infections treated with debridement and implant retention



Cumulative 5 year survival function of PJI due to **Gram-positive** microorganisms according to the type of treatment:



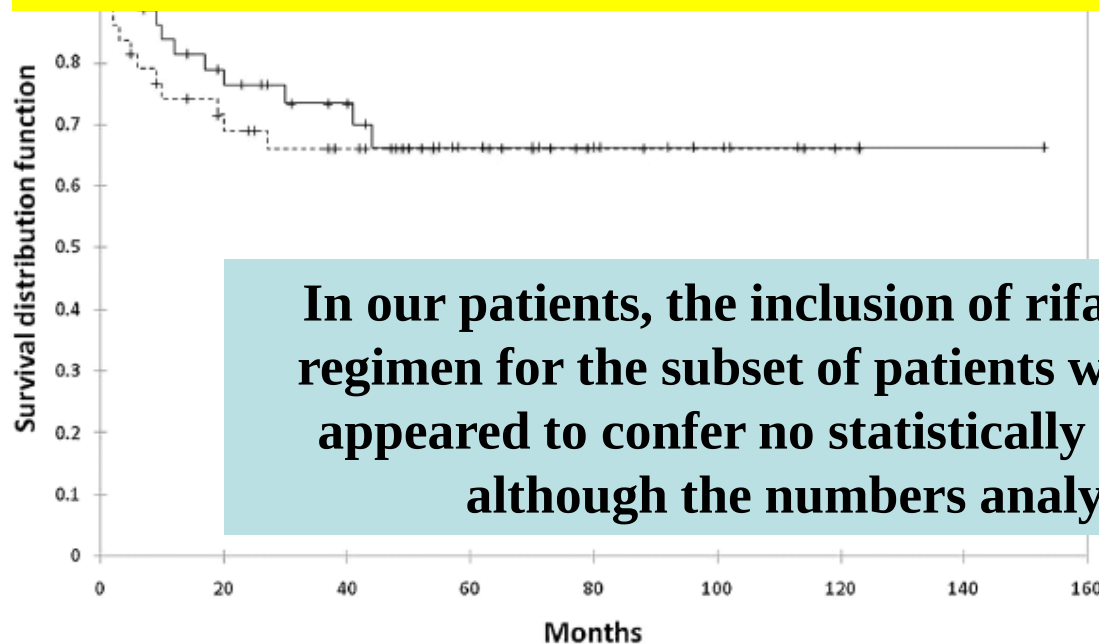
Outcome (failure or relapse) of PJIs due to **Gram-negative** microorganisms, according to the pattern of susceptibility and antibiotic treatment received

	Number (%) of patients, remission (N=18)	Number (%) of patients, failure (N=3)	P
Type of antibiotic treatment			
ciprofloxacin	13 (72.2)	1 (33.3)	0.247
levofloxacin	3 (16.7)	0 (0)	1.000
ciprofloxacin + carbapenem	2 (11.1)	0 (0)	1.000
co-trimoxazole	0 (0)	2 (2)	0.014
Type of treatment categorized			
treatment with fluoroquinolones	18 (100)	1 (33.3)	
treatment without fluoroquinolones	0 (0)	2 (66.7)	0.014

0.004^a

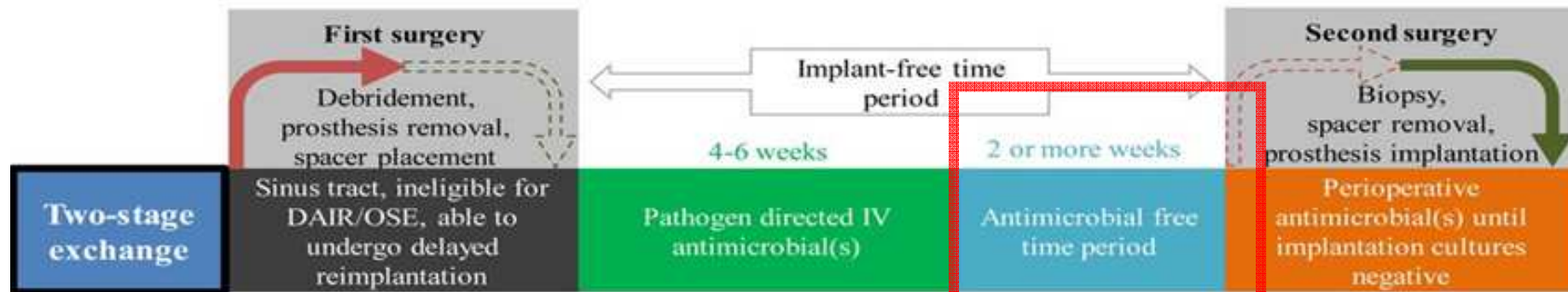
87 patients
debridements were performed within
3 weeks of symptom

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, $p = 0.02$).



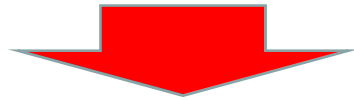
In our patients, the inclusion of rifampin in the antibiotic regimen for the subset of patients with *S. aureus* infection appeared to confer no statistically significant advantage although the numbers analysed were small

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



?

- Culture-negative infection was common among these chronic infections treated by two-stage revision, but was not associated with a worse outcome.
- **Cultures taken at reimplantation following an antibiotic-free period did not predict outcome and clinical failure of treatment was more often identified during antibiotic treatment than after antibiotics were stopped.**



Reimplantation may be considered without an antibiotic-free period, with additional antibiotic prophylaxis before reimplantation.

Where multiple reimplantation cultures are positive in the absence of clinical indicators of ongoing infection, a limited course of oral antibiotics may be appropriate.

Beion P. et al., **Two-stage revision for prosthetic joint infection: predictors of outcome and the role of reimplantation microbiology** J Antimicrob Chemother. 2010 Mar; 65(3): 569–575.

Two-stage revision of prosthetic hip joint infections using antibiotic-loaded cement spacers: When is the best time to perform the second stage?

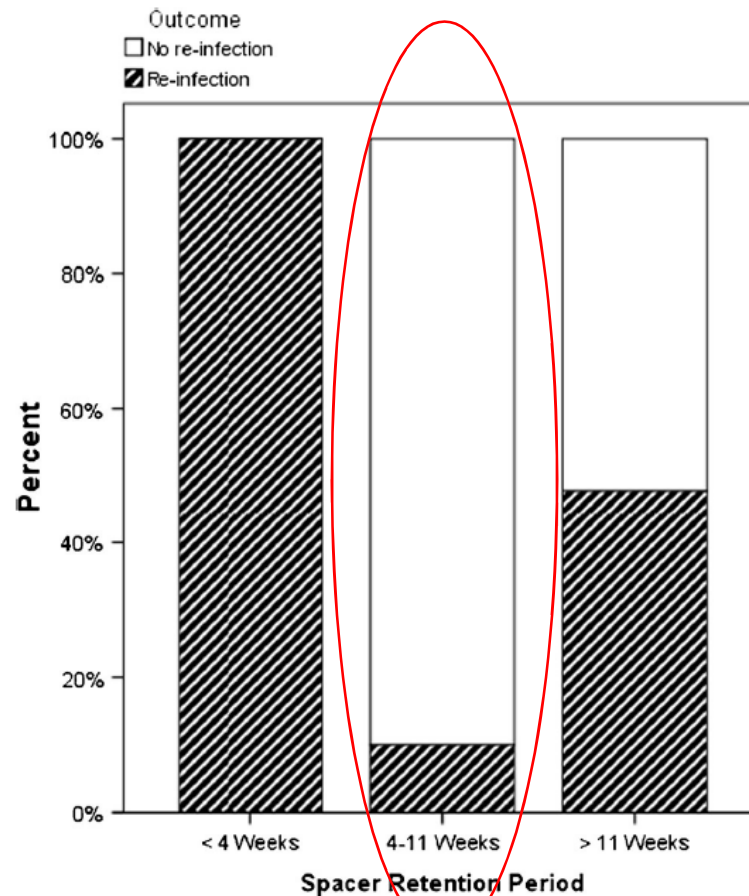


Fig. 1 Reinfection-rates depending on time of spacer-retention in patients who have undergone two-stage revision arthroplasty

TERAPIA ANTIBIOTICA CONSERVATIVA CRONICA

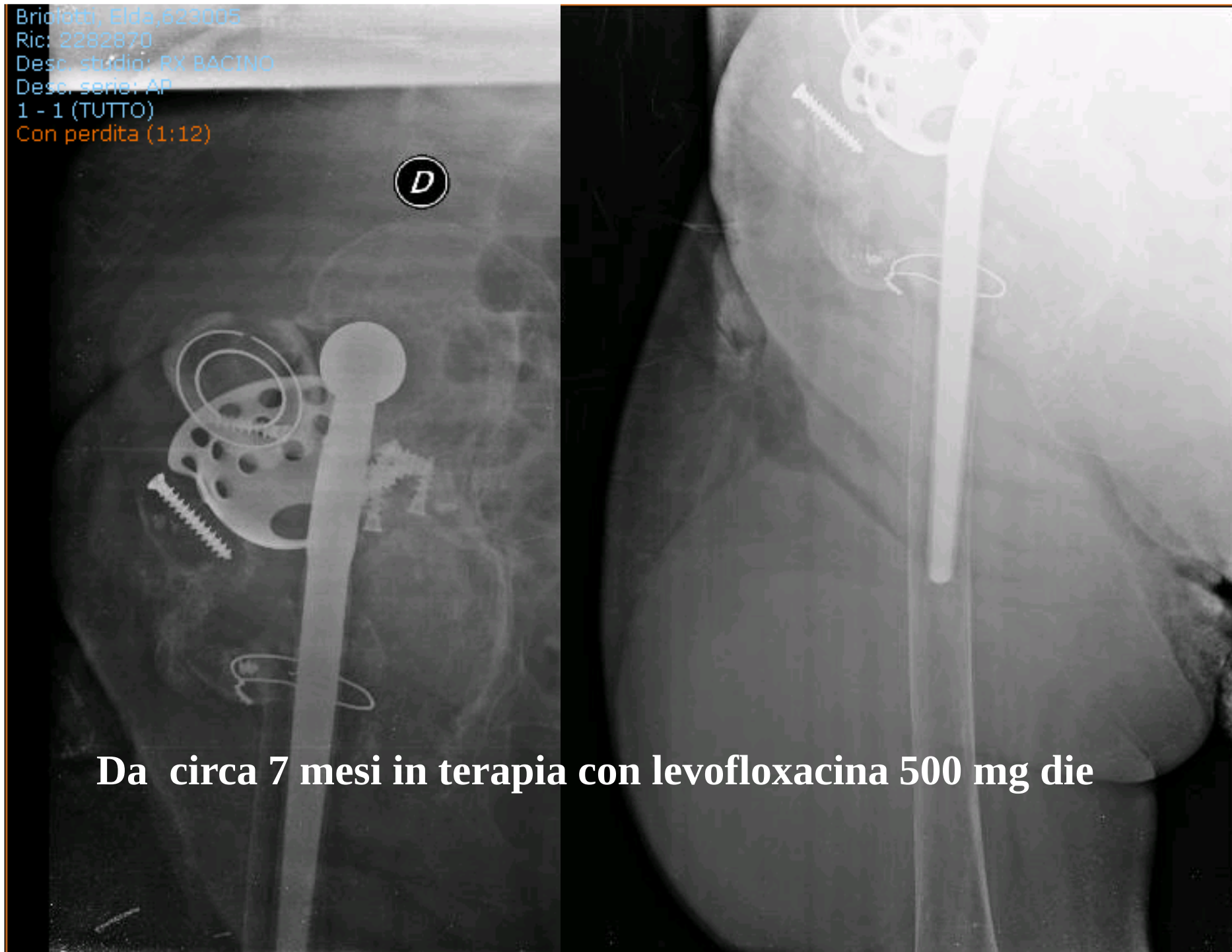
- **Controindicazioni all'intervento / rifiuto del Pz**
- **Elevata sensibilità del patogeno ad antibiotici orali**
- **Buona tollerabilità parenchimi / paziente alla terapia prescelta**
- **Protesi stabile**

**MONITORAGGIO BIOCHIMICO/MICROBIOLOGICO /
RADIOLOGICO**

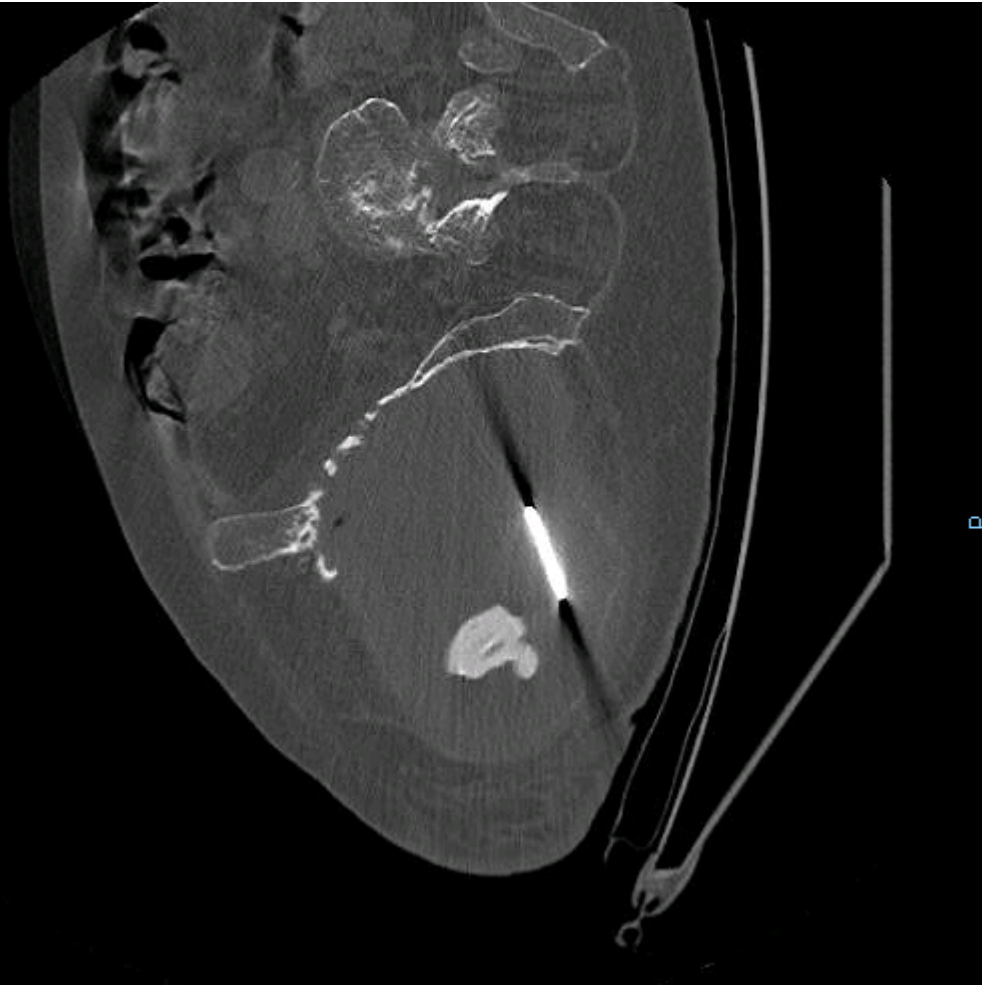
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Ric: 2282870
Desc. studio: RX BACINO
Desc. serie: AP
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Con perdita (1:12)

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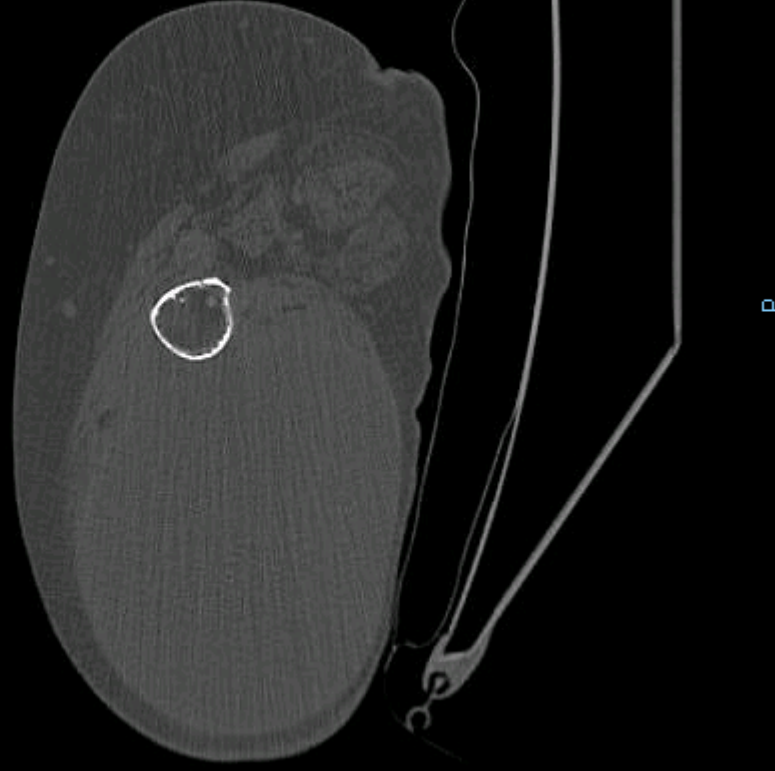
Da circa 7 mesi in terapia con levofloxacin 500 mg die



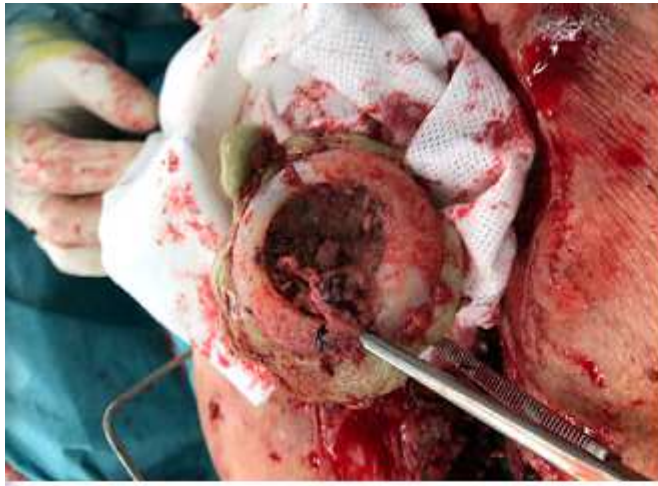
U47) Osp. S.
C (CON APPARECCHIATURA SPIRALE, MULTISTRATO) ULTERIORE DISTRETTO



C (CON APPARECCHIATURA SPIRALE, MULTISTRATO) ULTERIORE







Altro Provenienza: 1° campione
Esame culturale

(Culturale)

Positivo/a
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
Meropenem	S	<=0.5	I	8
Piperacillina	R	>16	R	>16
Piperacillina-tazobattam	S	<=4/4	R	>16/4
Tigeciclina	R		R	>2
Tobramicina	R	>4	R	>4
Trimetoprima-sulfametoxazolo	R	>4/76	R	>4/76
Imipenem			I	8

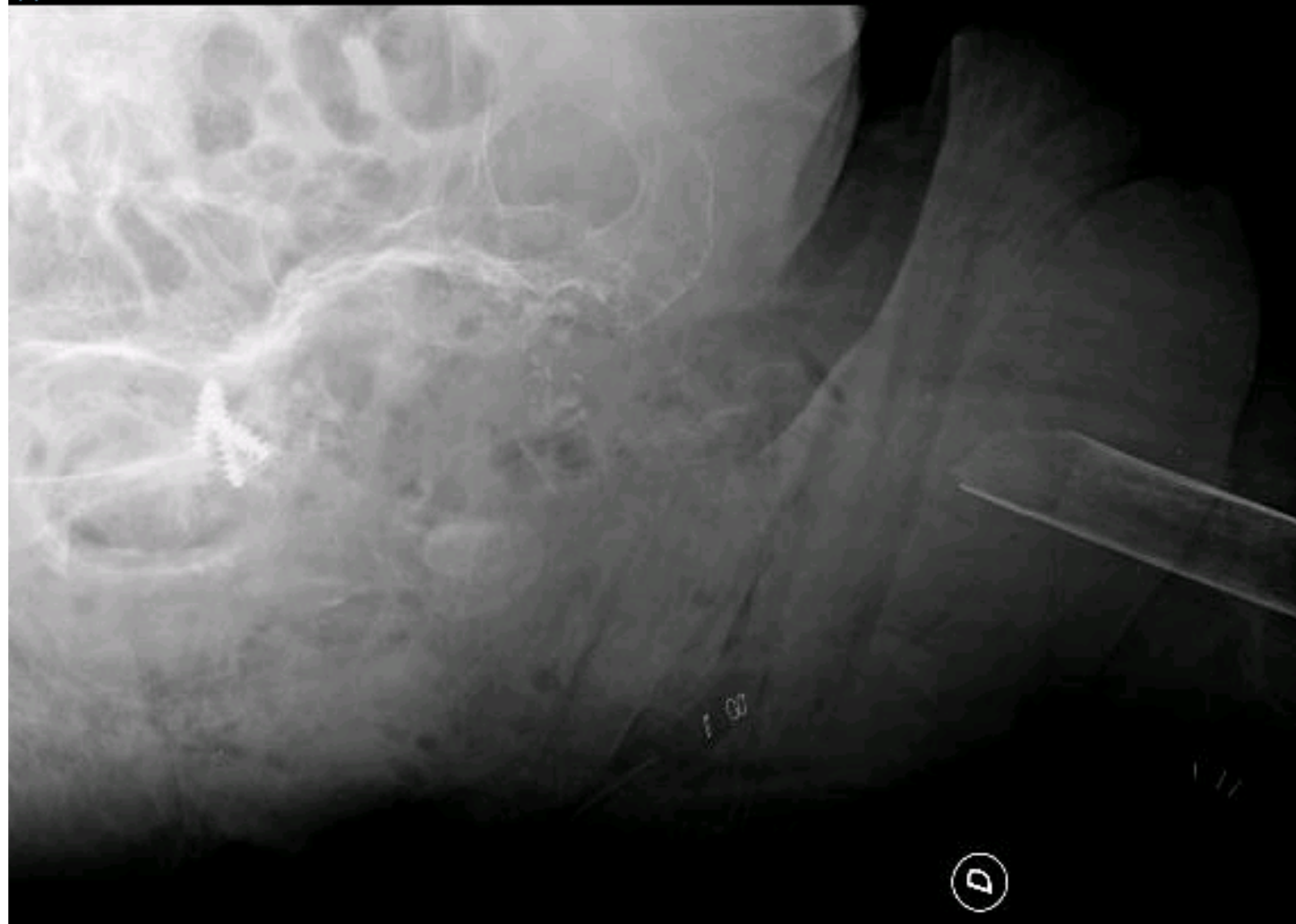
S= Sensibile, R= Resistente, I= Intermedio

Altro
Test screening carbapenemasi

Positivo/a



11/09/2017 12:14:09
ASL VC
C:2128 L:3295
Zoom 23%





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www.em-consulte.com

Médecine et
maladies infectieuses

Médecine et maladies infectieuses xxx (2017) xxx–xxx

Original article

Proposal for shorter antibiotic therapies

Propositions pour des antibiothérapies plus courtes

C. Wintenberger^a, B. Guery^b, E. Bonnet^c, B. Castan^d, R. Cohen^e, S. Diamantis^f, P. Lesprit^g,
L. Maulin^h, Y. Péanⁱ, E. Peju^j, L. Piroth^j, J.P. Stahl^k, C. Strady^l, E. Varon^m, F. Vuotto^b,
R. Gauzit^{n,*}, Recommendation Group of the SPILF

review of current guidelines issued by the main sci-entific societies (IDSA, BSAC, SPILF, ESCMID) and literature analysis on PubMed (analysis of articles published over the past Suggested treatment duration:• 6 weeks:° prosthetic joint infections (the managementof complex case patients must be discussedwith the reference center for complex bone and joint infections),° spondylodiscitis (except for osteosynthesis device),° diabetic foot osteomyelitis without surgery.20 years) using the following search terms: “prosthetic jointinfection”, “orthopedic implant-related infection”, “prosthetichip or knee associated infections”, “septic arthritis”, “infectiousspondylodiscitis”, “diabetic foot osteomyelitis”, “osteomyeli-tis”, “antibiotic therapy”, “antimicrobial agent”, “short versuslong-term”, “weeks”, “months”, and “duration”. We also ana-lyzed the abstracts of the last two years’ Interscience Conferenceon Antimicrobial Agents and Chemotherapy (ICAAC) and European Congress of Clinical Microbiology and InfectiousDiseases (ECCMID).

References – bone and joint infections, except for device-related infections.

Type of surgical treatment	Antibiotic therapy duration (including IV route)	Number of patients	Microorganisms	Success rate Short/long	Study type/Evidence required	References
<i>Spondylodiscitis</i>						
If required	6 weeks (2 weeks) vs. 12 weeks (2 weeks)	351	<i>S. aureus</i> 145 (41%); CoNS 61 (17%); <i>Streptococci</i> 32 (18%)	90.9% vs. 90.9%	Randomized double-blind prospective multicenter study	Bernard et al., 2015 [197]
	6 weeks (3 weeks) vs. 6 weeks (4 weeks)	120		34 (94) vs. 75 (89)	Retrospective multicenter study	Roblot et al. 2007 [196]
<i>Septic arthritis</i>						
	3–4 weeks	32	<i>Streptococci</i> 32 (18%)	80%	Retrospective monocentric study	Nolla et al. 2015 [193]
	4–6 weeks	145	<i>S. aureus</i> 145 (41%)		Retrospective monocentric study	Nolla et al. 2015 [193]
	6 weeks	43	<i>Staphylococci</i> 60/118; <i>Streptococci</i> 16/118	91.5%	Prospective monocentric study	Fahrad et al., 2010 [173]
<i>Diabetic foot osteomyelitis</i>						
Drainage	2 weeks (1 week) vs. > 4 weeks	169	<i>Staphylococci</i> 98 (52%)	NS*	Retrospective monocentric study	Uckay et al. 2011 [194]
Absence	6 weeks (2 weeks) vs. 12 weeks (2 weeks)	40	<i>Staphylococci</i> 20 (34%) Polymicrobial infection 18/40 (45%)	12/20 vs. 14/20 (65%)	Randomized prospective multicenter study	Tone et al. 2015 [188]



Journal of Bone and Joint Infection

2017; 2(4): 184-193. doi: 10.7150/jbji.21692

Research Paper

Osteomyelitis of the Pelvic Bones: A Multidisciplinary Approach to Treatment

Maria Dudareva, Jamie Ferguson[✉], Nicholas Riley, David Stubbs, Bridget Atkins, Martin McNally

The Bone Infection Unit, Nuffield Orthopaedic Centre, Oxford University Hospitals, Oxford, OX3 7LD, United Kingdom

✉ Corresponding author: Jamie Ferguson MB ChB, FRCS (Tr & Orth), MEd., Orthopaedic Fellow, Nuffield Orthopaedic Centre, Oxford, OX3 7LD, United Kingdom, jamie.ferguson@ouh.nhs.uk

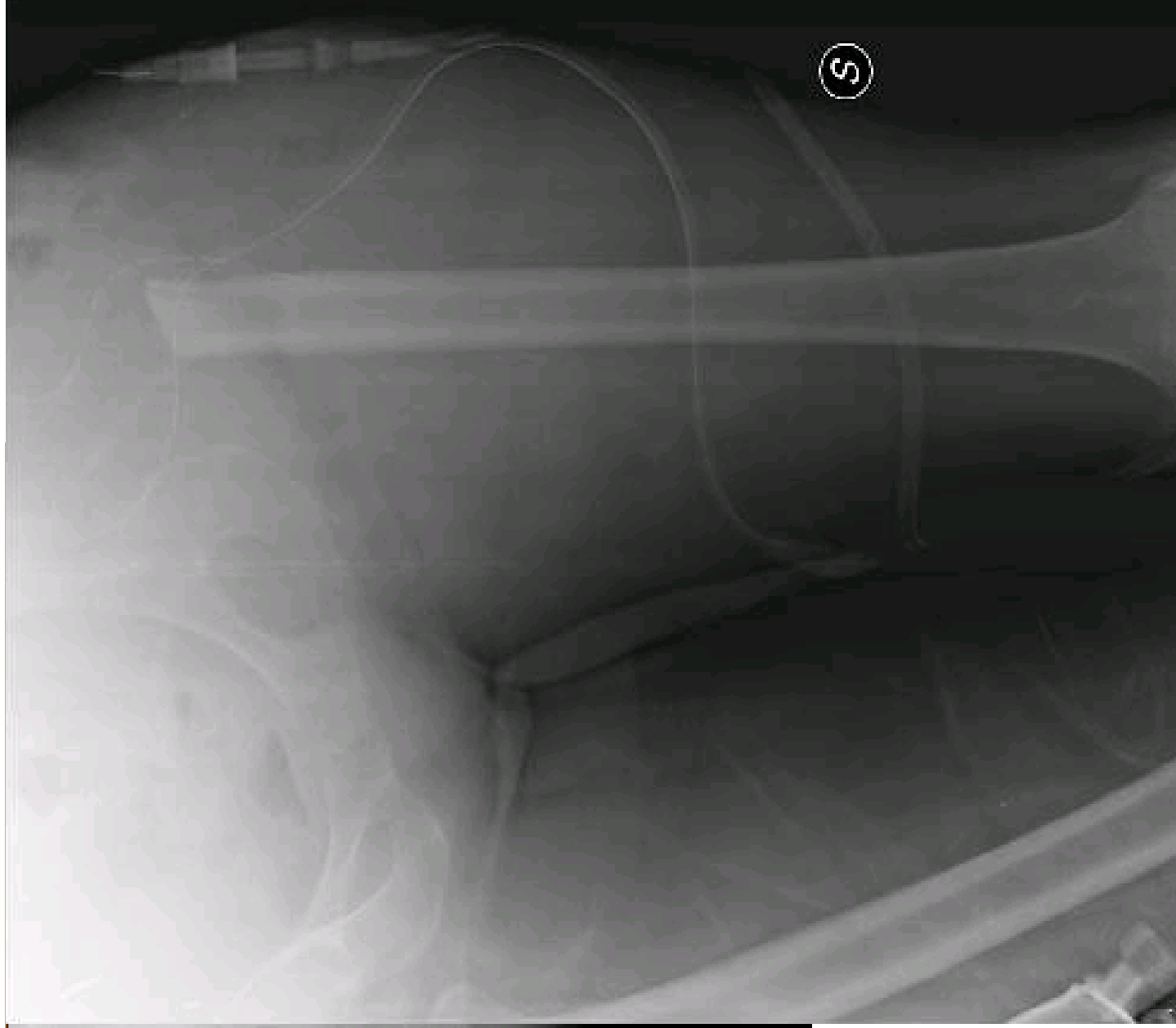
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Received: 2017.06.29; Accepted: 2017.08.16; Published: 2017.10.09

**Pressure Ulcer-Related Pelvic Osteomyelitis:
A Neglected Disease?**

15/02/2018

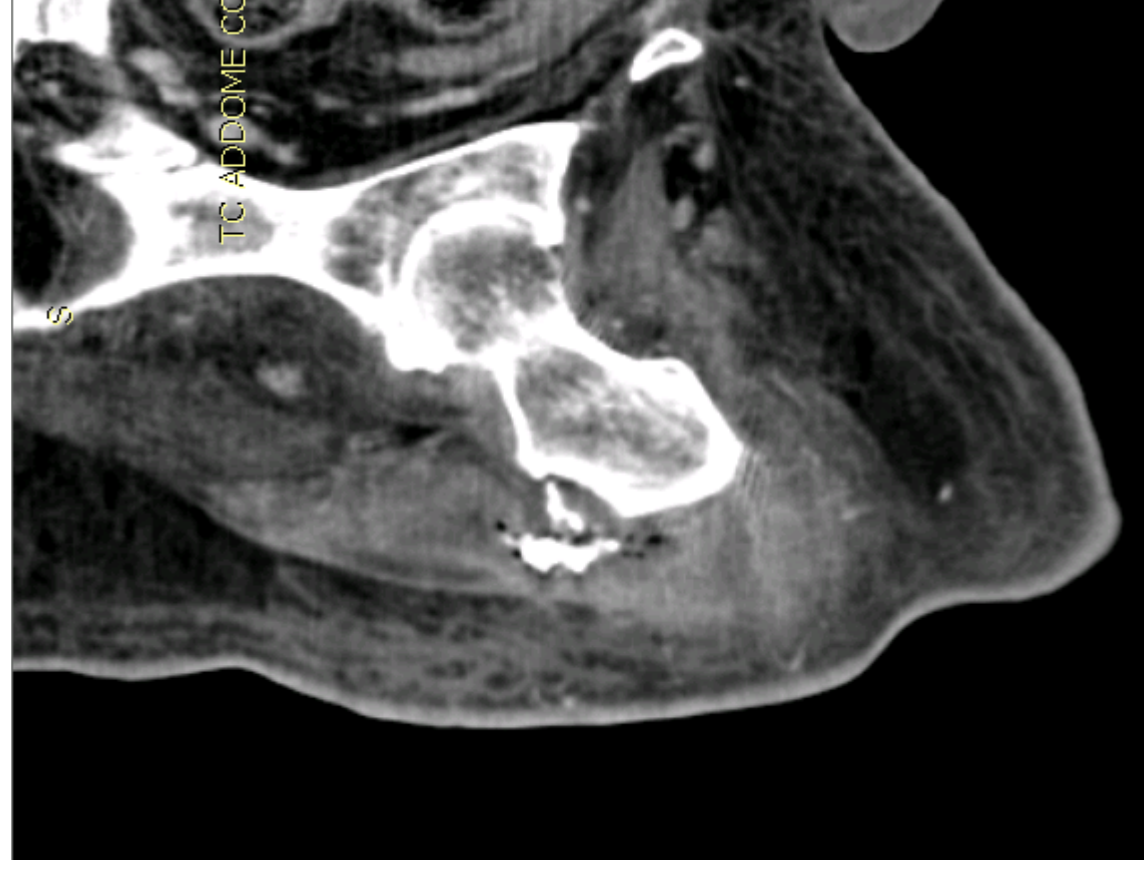
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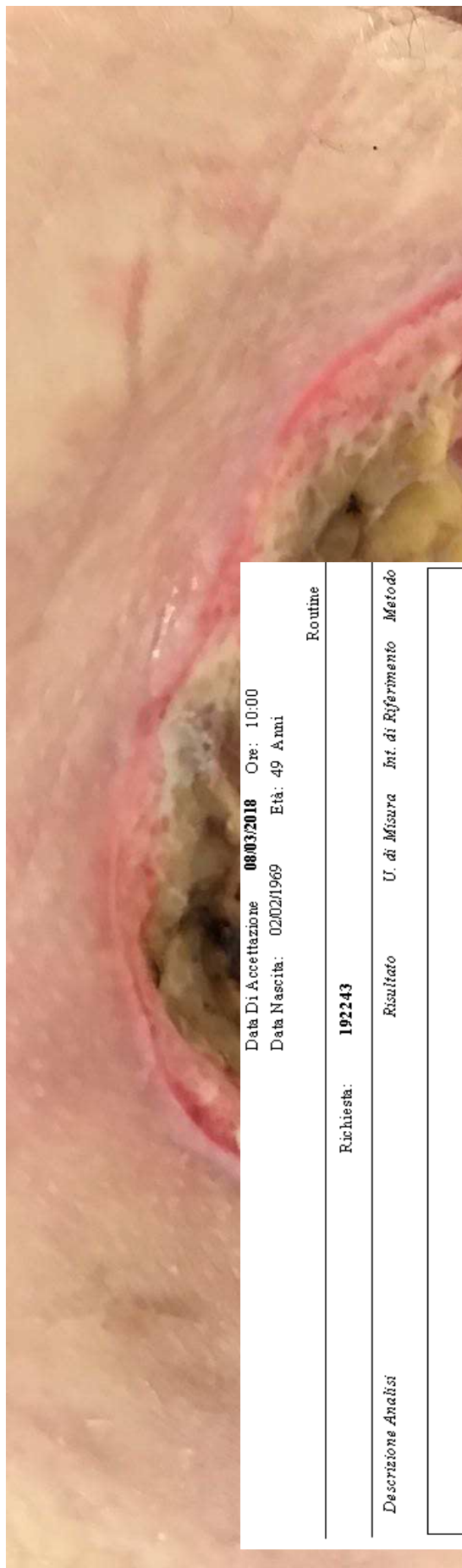


ANTIBIOTICI		1	MIC	2	MIC
Amikacina		R	>32	I	16
Cefepime		R	>32		
Cefotaxime		R	>32	R	>32
Ceftazidime		R	>32		
Ciprofloxacina		R	>2	R	>2
Colistina		S	≤0.5	S	≤0.5
Ertapenem		R	>4	R	>4
Fosfomicina		R	32	R	>128
Gentamicina		R	>8	R	8
Imipenem		R	>8	R	>8
Meropenem		R	>8	R	>8
Piperacillina/Tazobactam		R	>64	IE	>64
Tigeciclina		R	>4	IE	2
Trimetoprim/Sulfametoxazolo		R	>160	R	>160
Nitrofurantoina				R	>256

S= Sensible, R= Resistente, I= Intermedio





Data Di Accettazione **08/03/2018** Ore: 10:00

Data Nascita: 02/02/1969 Età: 49 Anni

Routine

Richiesta: 192243

Descrizione Analisi

Risultato

U. di Misura Int. di Riferimento Metodo

Liquido Provenienza:
Ricerca areobii/miceti

Altro Provenienza: 3° campione
Esame culturale

Positivo/a

Arithmogam na

Arthropodan

ANTIBIOTICI	I	MTC
Amikacina	\$	<=2
Amoxicilina/Acido Clavulánico	\$	<=2
Cefepime	\$	<=1
Cefotaxime	\$	<=1
Cefazidime	\$	<=1
Ciprofloxacina	R	>2
Ertapenem	\$	<=0.5
Fosfomicina	\$	<=16
Gentamicina	\$	<=1
Imipenem	\$	<=0.25
Meropenem	\$	<=0.25
Piperacilina/Tazobactam	\$	8
Tigeciclina	\$	<=0.5
Eb1	-	Neg
Trimetoprim/Sulfametoxazol	\$	<=20

S = Servable, *R* = Reversible, *I* = Interchangeable

S = Servable, *R* = Resister, *I* = Intermediary

Positivo/a

1 *Proteus mirabilis*

ANTIBIOTIC	1	MIC
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Amikacina	S	<=2
Amoxicilina/Acido Clavulanico	R	16
Cefepime	I	4
Cefotaxime	R	>32
Ceftazidime	I	4
Ciprofloxacin	R	>2
Colistina	R	>8
Ertapenem	S	<=0.5
Fosfomicina	S	<=16
Gentamicina	R	>8
Imipenem	S	2
Meropenem	S	<=0.25
Piperacilina/Tazobactam	S	<=4
Tigeciclina	R	4
Trimetoprim/Sulfametoxazolo	R	>160

Referto Ambulatoriale

Redatto dal Dottor

in data 09/02/2018 13:10

Cognome e Nome:

Sesso: F

Data di nascita:

~~esito Diagnostico.~~

OSTEOMIELETTA GIÀ 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 ancora positivo.**

Dal 29/12/2016 al 16/01/2017 ricovero in Malattie Infettive per neutropenia da sovradosaggio di teicoplanina (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 scintigrafia 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.

Compilata oggi DEM per Rx tibia sin.

Si rimane a disposizione per ogni chiarimento.

Cordiali saluti

◀ 9 scintigrafie con LEU +

Per fare fronte alla complessità clinica e dare una risposta valida
al Paziente con costi sostenibili (diretti e indiretti)
implementando un **approccio multidisciplinare atto a
definire diagnostica e terapia appropriata**
va ritenuta **anacronistica la parcellizzazione** con conseguenti
richieste di multipli accertamenti ad alto costo da parte di
diverse strutture,
ininfluenti ai fini diagnostici e prognostici,
con **terapia antibiotiche ** protratte e inconcludenti,**
interventi chirurgici parziali, reiterati e non congrui

***** La durata della terapia antibiotica non dovrebbe superare le 6-8 settimane dall'ultimo intervento: la persistenza di segni locali di infezione devono far considerare ulteriore approccio chirurgico***