

Approccio al Piede Infetto

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Guidelines on the
diagnosis and
treatment of foot
infection in persons
with diabetes

IWGDF/IDSA 2023

60% ulcere sono infette
20% osteomielite

- Le infezioni del piede sono tra le principali cause di ospedalizzazione
- Il 20% delle DFI moderate e severe va incontro all'amputazione
- Le infezioni del piede si associano ad un aumentato rischio di mortalità.



ARTICLE

High prevalence of ischaemia, infection and serious comorbidity in patients with diabetic foot disease in Europe. Baseline results from the Eurodiale study

L. Prompers • M. Huijberts • J. Apelqvist • E. Jude • A. Piaggese • K. Bakker • M. Edmonds • P. Holstein • A. Jirkovska • D. Mauricio • G. Ragnarson Tennvall • H. Reike • M. Spraul • L. Uccioli • V. Urbancic • K. Van Acker • J. van Baal • F. van Merode • N. Schaper

Table 1 Classification of foot disease

Stage	Definition	Number of patients	Percentage of study population
A	PAD −, infection −	270	24
B	PAD −, infection +	305	27
C	PAD +, infection −	205	18
D	PAD +, infection +	347	31

il 58% erano infette

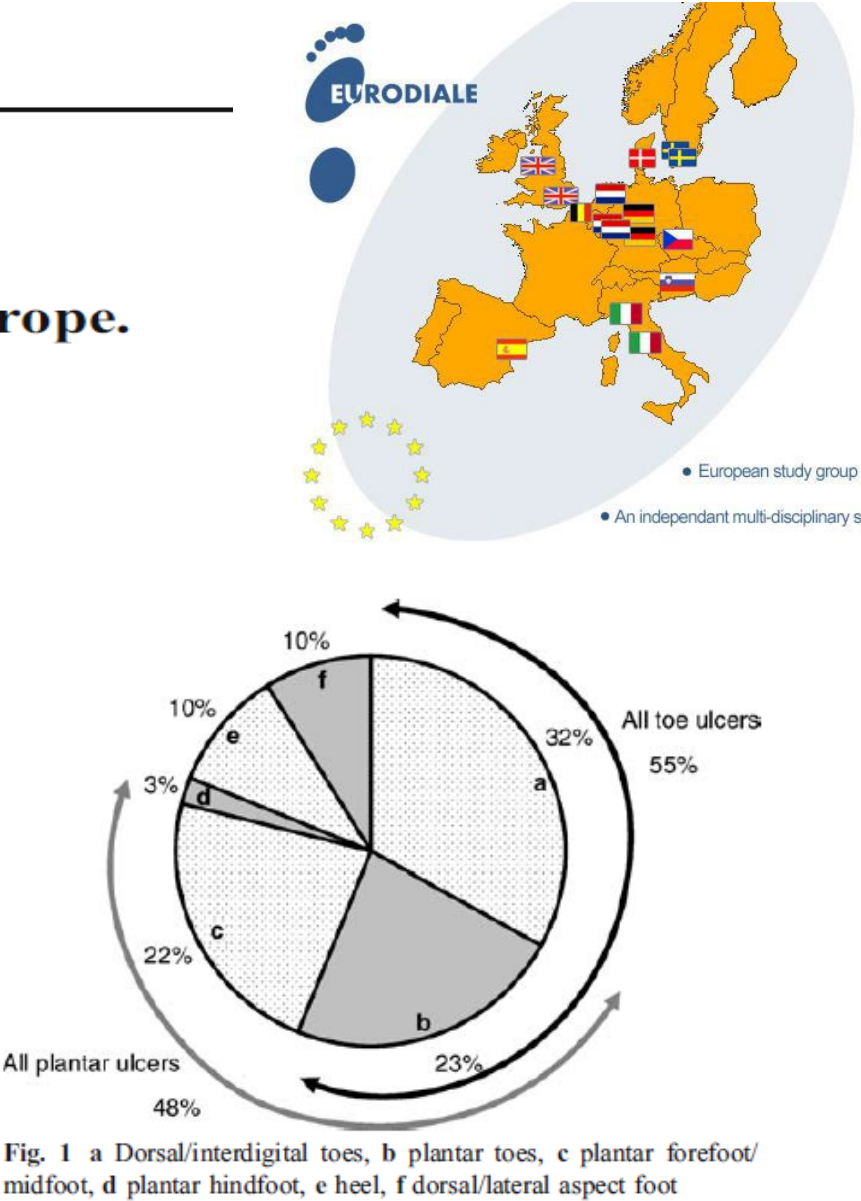


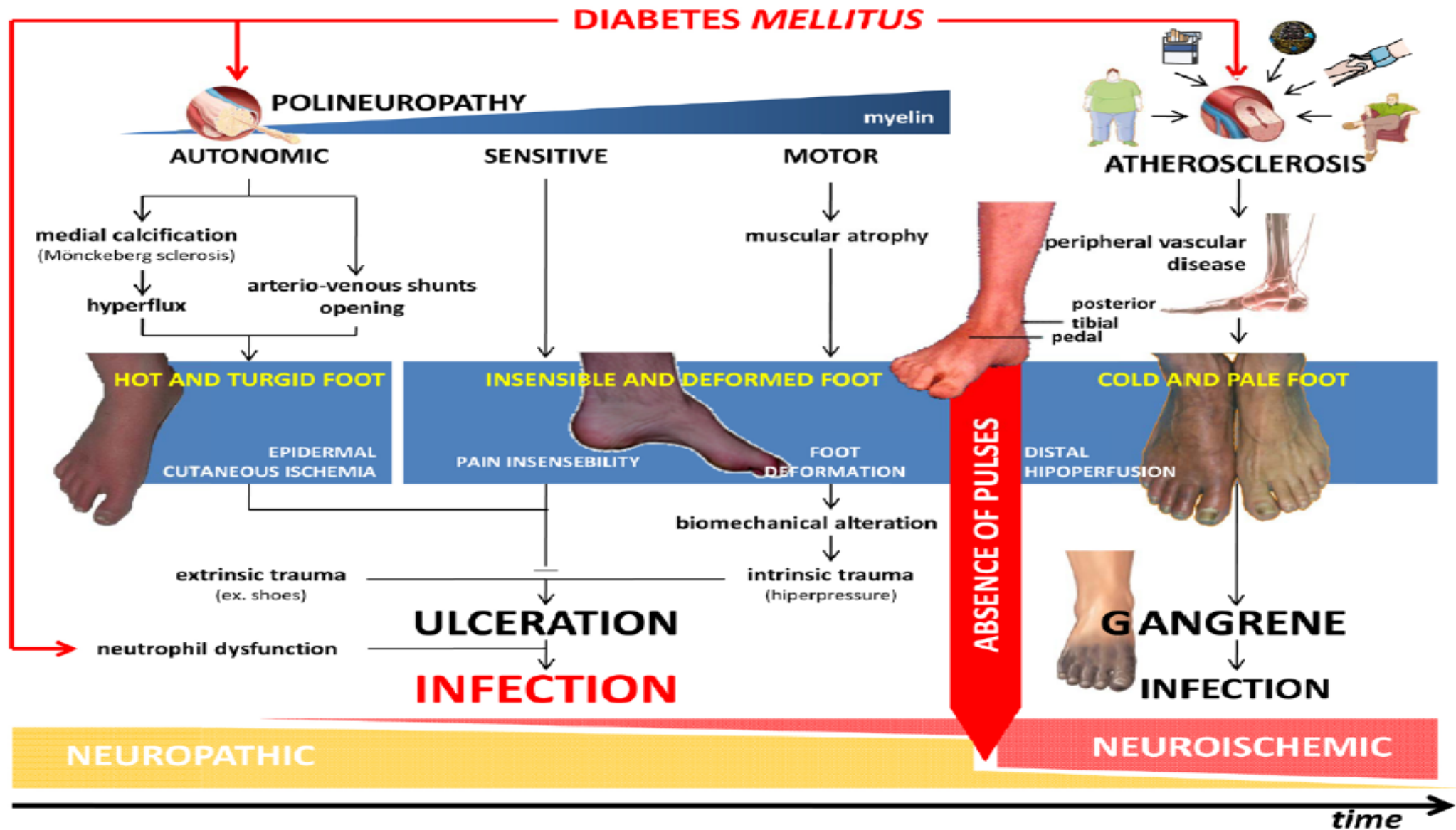
Fig. 1 a Dorsal/interdigital toes, b plantar toes, c plantar forefoot/midfoot, d plantar hindfoot, e heel, f dorsal/lateral aspect foot

Sistema immunitario

- Alterazioni dei normali processi dell'immunità cellulare
- Anomalie della chemiotassi e fagocitosi a carico dei PMN e monociti.
- Alterata aderenza dei PMN e monociti ai microrganismi.
- Riduzione della loro attività battericida

Tali meccanismi di difesa sono associati al grado di compenso metabolico.





La vasculopatia periferica

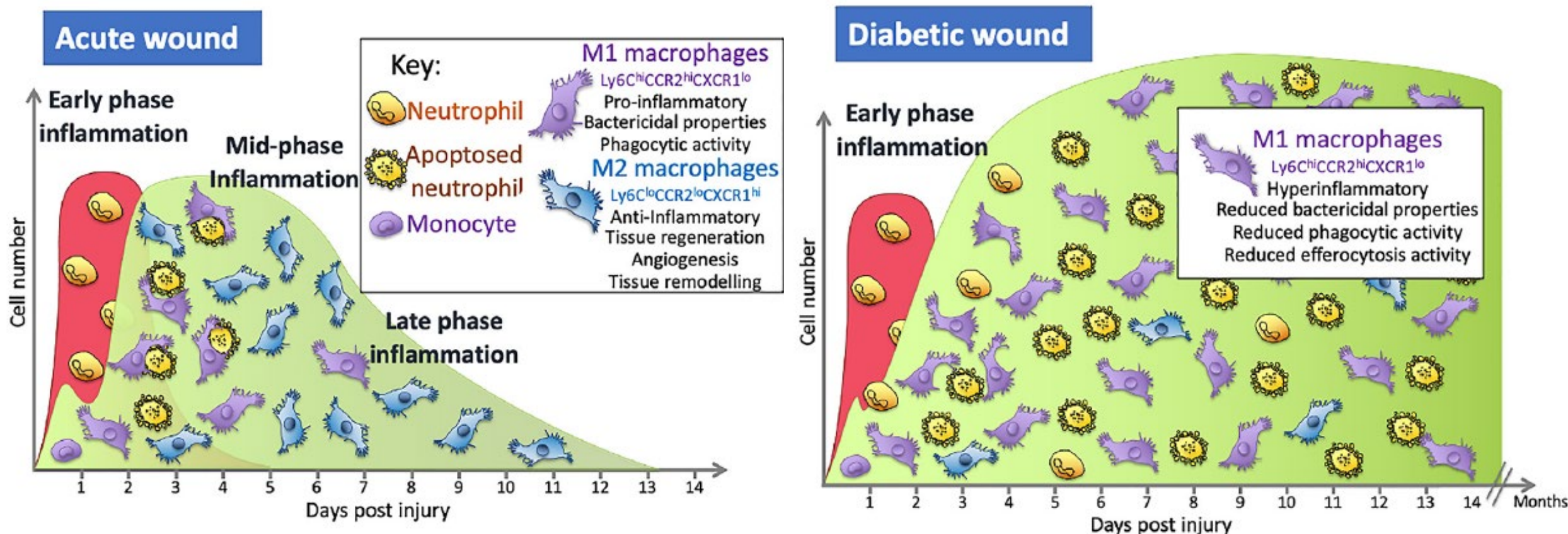
- L'infezione è un fattore ischemizzante.
- L'ischemia è molto comune nei pazienti con infezione.
- L'ischemia in presenza di un processo infettivo condiziona negativamente l'evoluzione del quadro clinico.
- Maggiore presenza di batteri MDRO.



Review

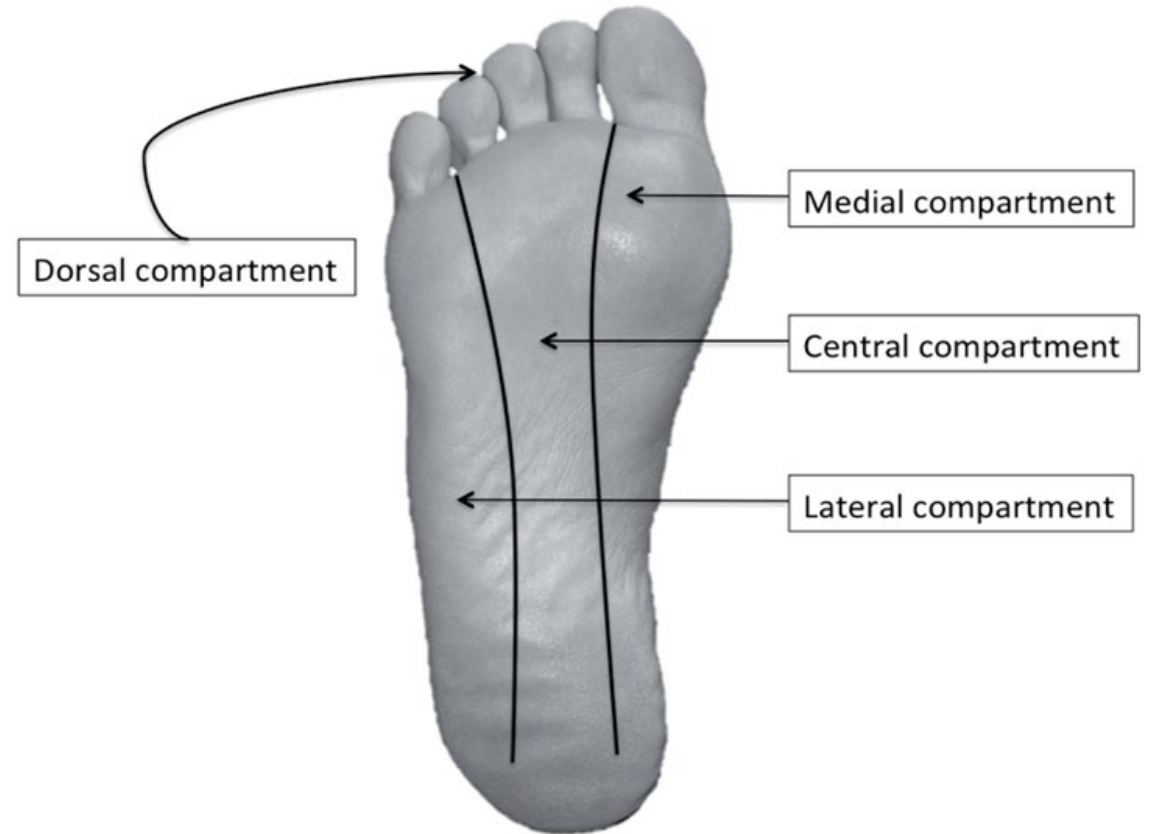
Skin Wound Healing: Normal Macrophage Function and Macrophage Dysfunction in Diabetic Wounds

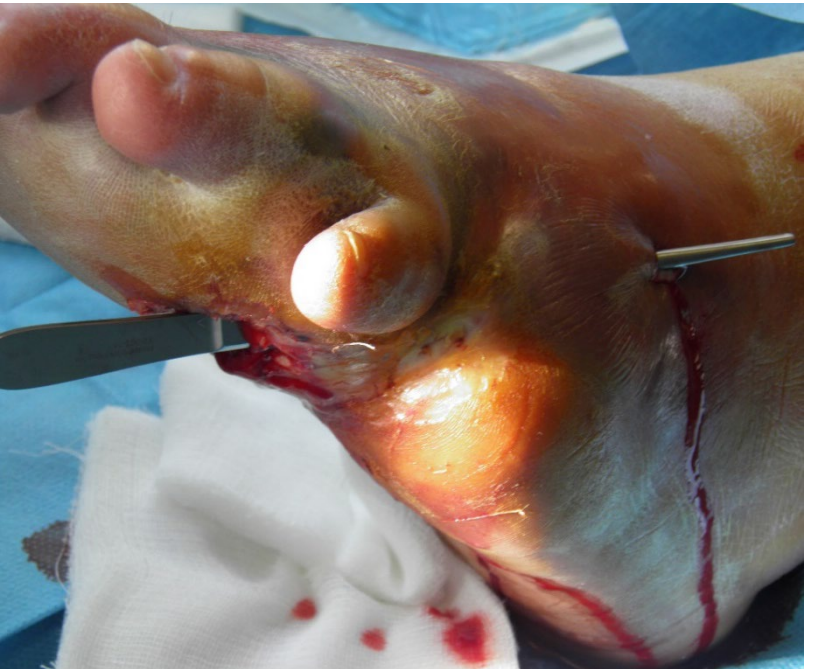
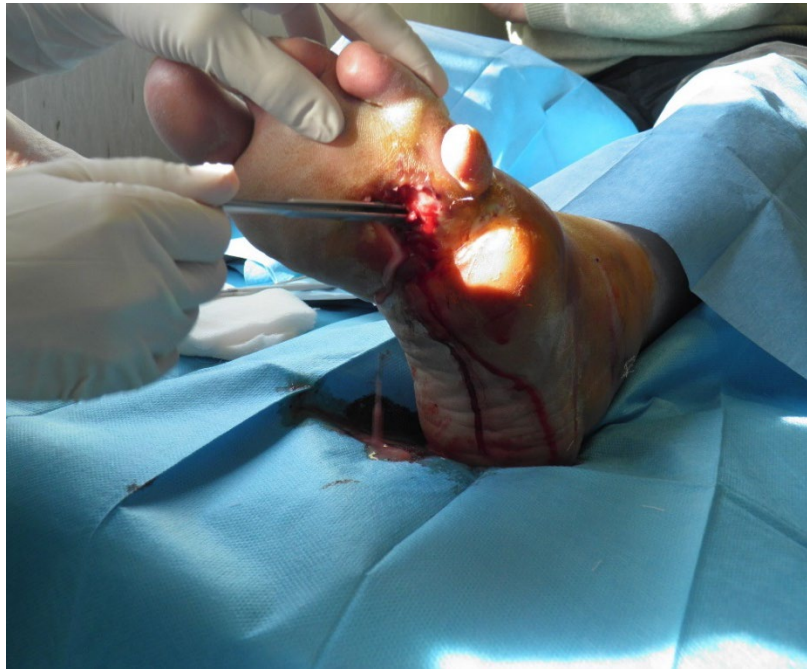
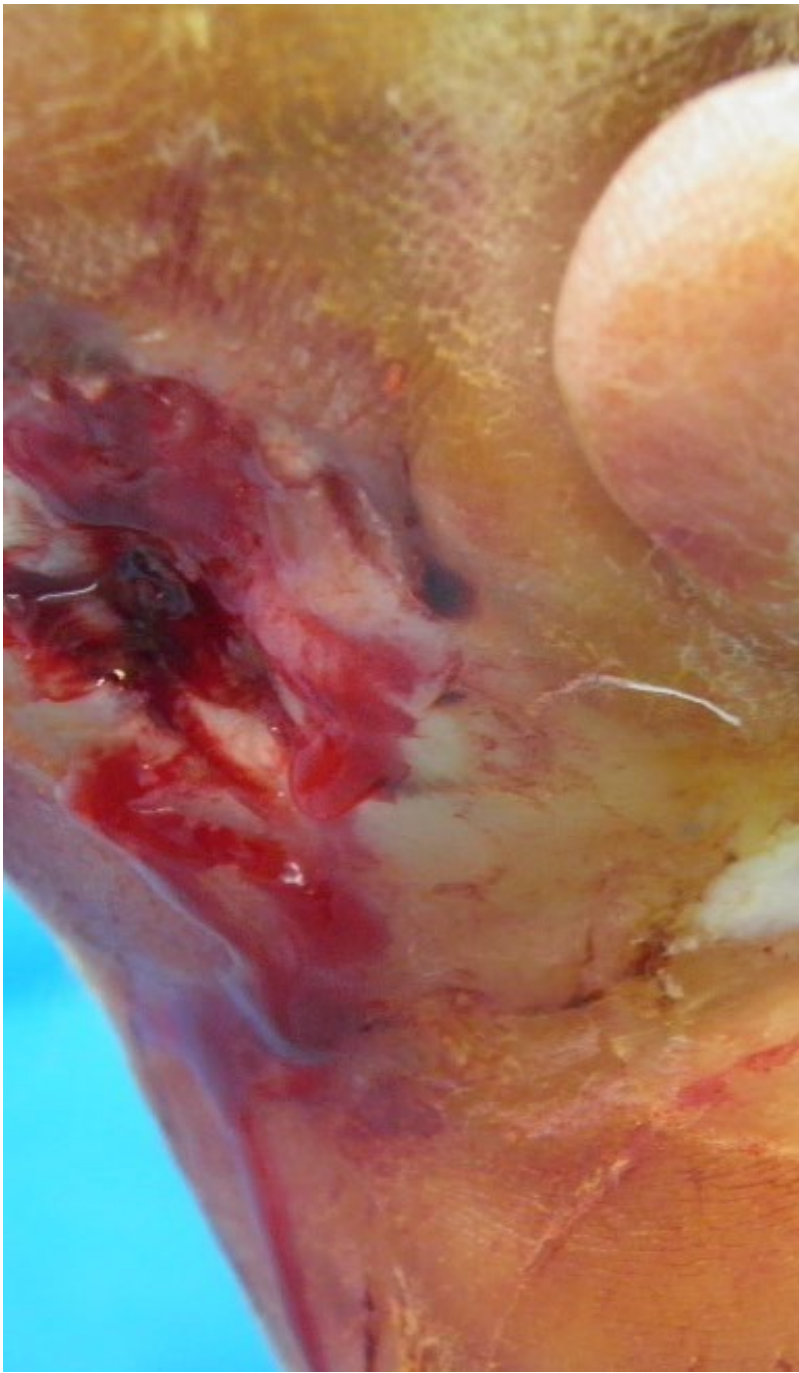
Savannah M. Aitcheson ¹ , Francesca D. Frentiu ¹ , Sheree E. Hurn ², Katie Edwards ³ and Rachael Z. Murray ^{1,*} 



Compartimenti del piede

- La stessa struttura anatomica del piede può favorire la progressione dell'infezione.
- Infatti la presenza di compartimenti consente all'infezione di propagarsi prossimalmente lungo le guaine tendinee e le fasce con estrema facilità.





La microbiologia dell'ulcera ...

Pathogenesis of Open Wound Infections

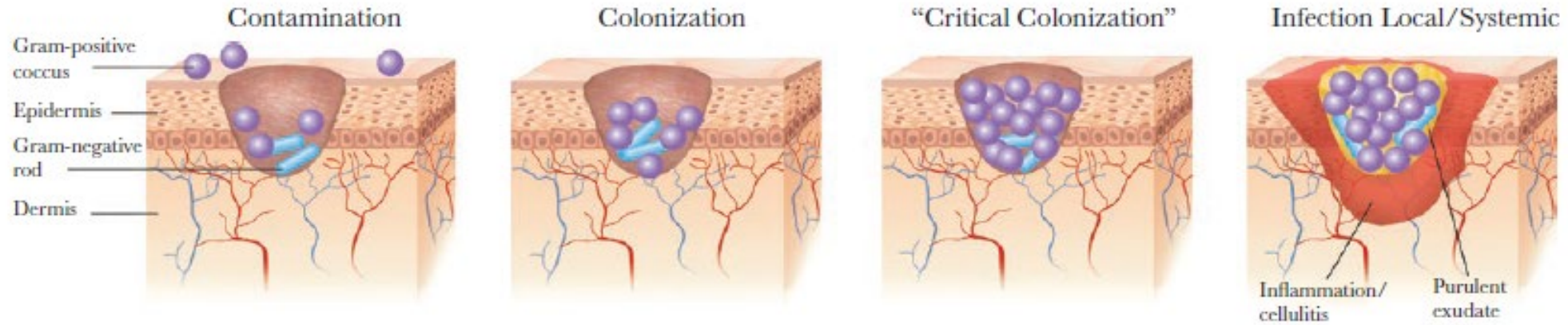
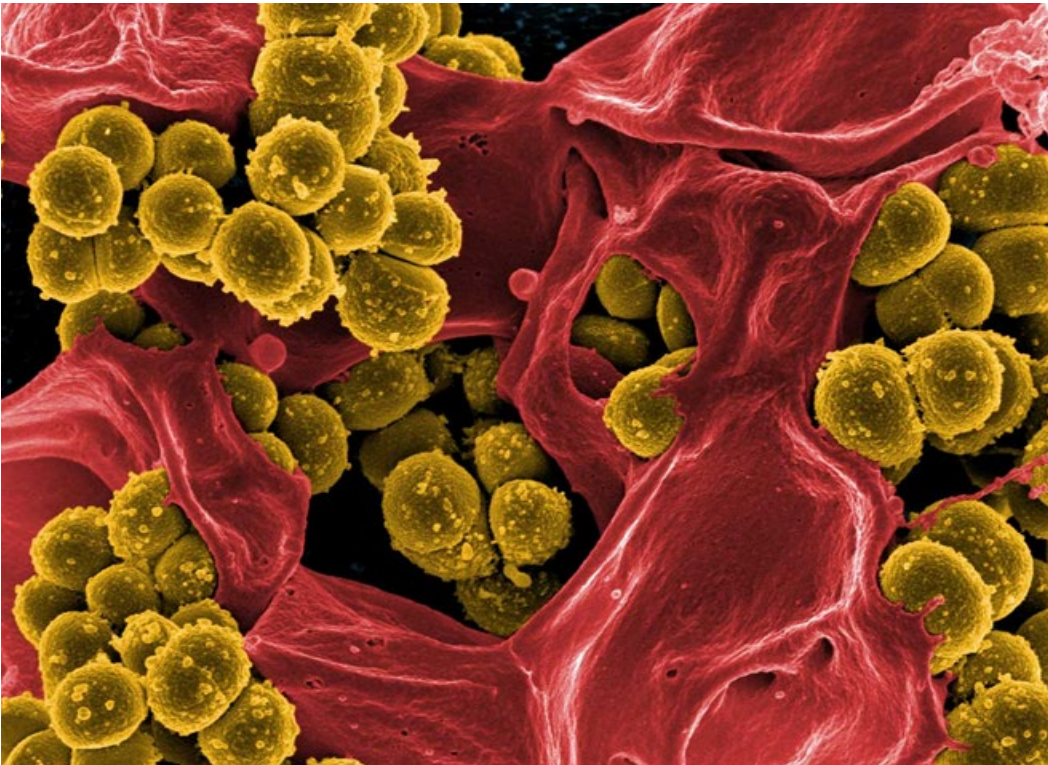


Figure 1. The typical evolution of a superficial wound infection. The growth of microorganisms in a wound and the host response determine how far along in this spectrum the process goes.

- Contaminazione: batteri senza proliferazione
- Colonizzazione: proliferazione batterica senza risposta da parte dell'ospite
- Infezione: proliferazione batterica, invasione attiva, e risposta da parte dell'ospite significativa o severa

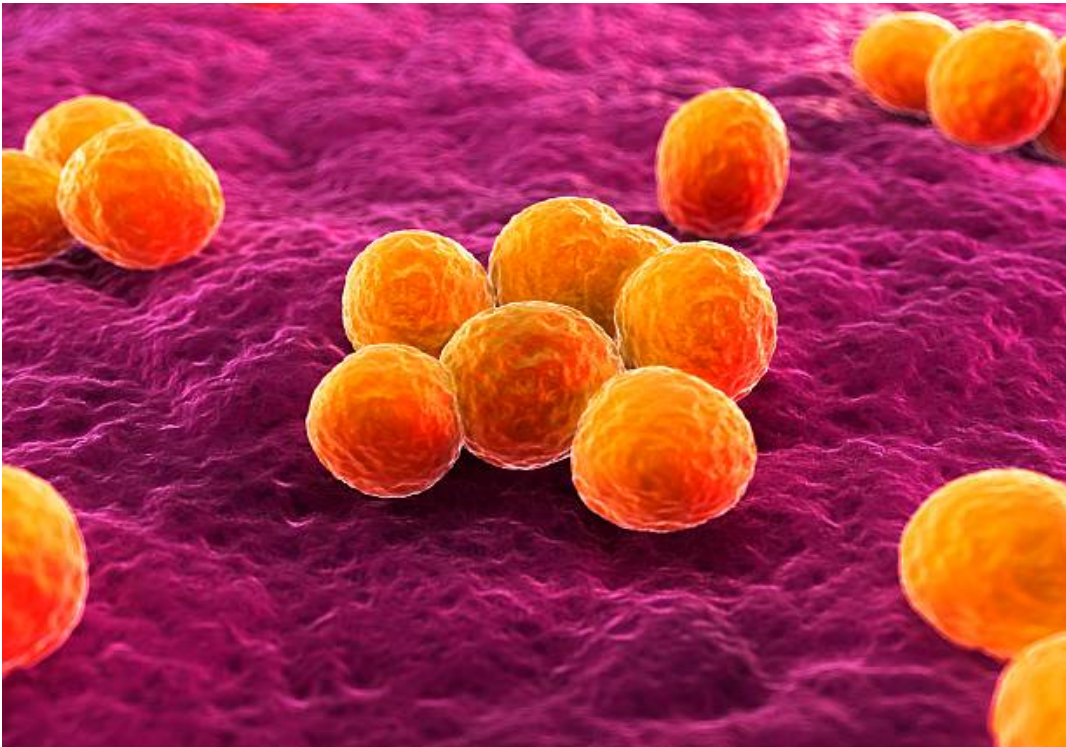
“ The germ is nothing. It is the terrain in which it is found that is everything.”

Pasteur, L. (1880)



- Tutte le ferite croniche sono contaminate da batteri
- La guarigione della ferita avviene anche in presenza di batteri.
- Non la presenza di microrganismi, ma la loro interazione con il paziente influenza la guarigione della ferita.

Ruolo dei batteri: colonizzazione vs infezione



- Batteri commensali Staphylococcus CoN – Corynebacterium – Streptococcus si trasformano in patogeni
- Specie non patogene possono interagire tra loro e creare «functionally equivalent pathogroup»
- L'interazione tra i germi è responsabile della maggiore resistenza del biofilm e della persistenza dell'infezione



monomicrobial



polymicrobial

species number



RESISTANCE



strict anaerobes



anaerobes

Enterobacteriaceae

Pseudomonas spp.

non-fermentating Gram-negative bacilli

Gram-negative aerobic bacilli

β-hemolytic streptococci

Staphylococcus aureus

coagulase-negative staphylococci

Enterococcus spp.

Gram-positive aerobic cocci

NEUROPATHIC

NEUROISCHEMIC

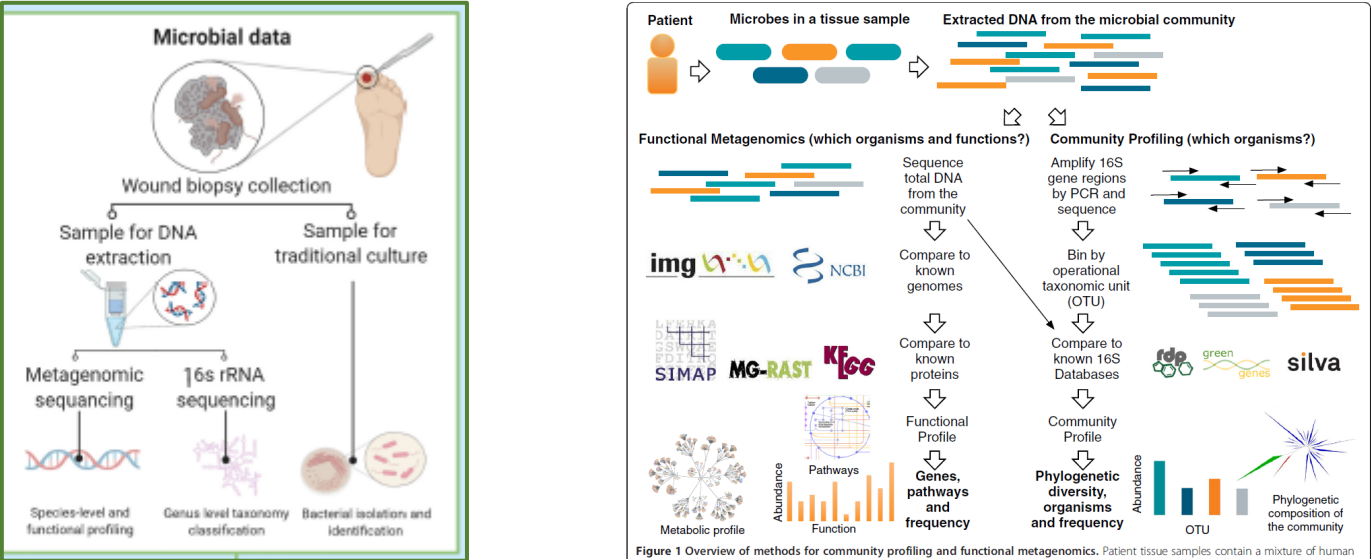
time

REVIEW

Open Access

Microbiology of diabetic foot infections: from Louis Pasteur to ‘crime scene investigation’

Anne Spichler¹, Bonnie L Hurwitz², David G Armstrong³ and Benjamin A Lipsky^{4,5*}





Contents lists available at ScienceDirect

Human Microbiome Journal

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



The diabetic foot microbiota: A review

J. Jneid^a, J.P. Lavigne^{b,c,*}, B. La Scola^a, N. Cassir^{a,*}



- Le tecniche molecolari hanno dimostrato di isolare una flora diversa e più numerosa di quella isolata dalle colture convenzionali
- DFUs presentano un microbiota più spesso polimicrobico e con maggior numero di anaerobi se confrontato con altre tipologie di ulcere
- Il microbiota di tessuti profondi dell'ulcera è differente e più complesso di quello dei tessuti più superficiali
- Vi è una predominanza di batteri patogeni localizzati nei tessuti più profondi.
- Mappa genetica dei germi e delle loro resistenze.

IWGDF Infection Guideline



Recommendation 6: Use conventional, rather than molecular, microbiology techniques for the first-line identification of pathogens from soft tissue or bone samples in a patient with a diabetes-related foot infection (Strong; Moderate)

Definizione di Infezione

- Ulcera infetta: stato patologico causato dall'invasione e moltiplicazione di batteri nei tessuti che produce una risposta infiammatoria da parte dell'ospite
-
- Piede diabetico infetto: manifestazione clinica di un processo infiammatorio che coinvolge un ulcera del piede localizzata al di sotto dei malleoli.



microorganisms



Review

Biofilms in Diabetic Foot Ulcers: Significance and Clinical Relevance

Cassandra Pouget ¹, Catherine Dunyach-Remy ², Alix Pantel ², Sophie Schuldiner ³,
Albert Sotto ⁴ and Jean-Philippe Lavigne ^{2,*} 

80% delle amputazioni presentano biofilm di ulcere infette.

60% - 80% delle ulcere croniche presentano il biofilm vs il 20% di quelle acute

Produzione del Biofilm



Un biofilm è un aggregato di cellule microbiche associate ad una superficie incluse in una matrice polimerica extracellulare da esse prodotta.

Batteri patogeni e commensali co-aggregati simbioticamente



Review

Biofilms in Diabetic Foot Ulcers: Significance and Clinical Relevance

Cassandra Pouget ¹, Catherine Dunyach-Remy ², Alix Pantel ², Sophie Schuldiner ³, Albert Sotto ⁴ and Jean-Philippe Lavigne ^{2,*} 

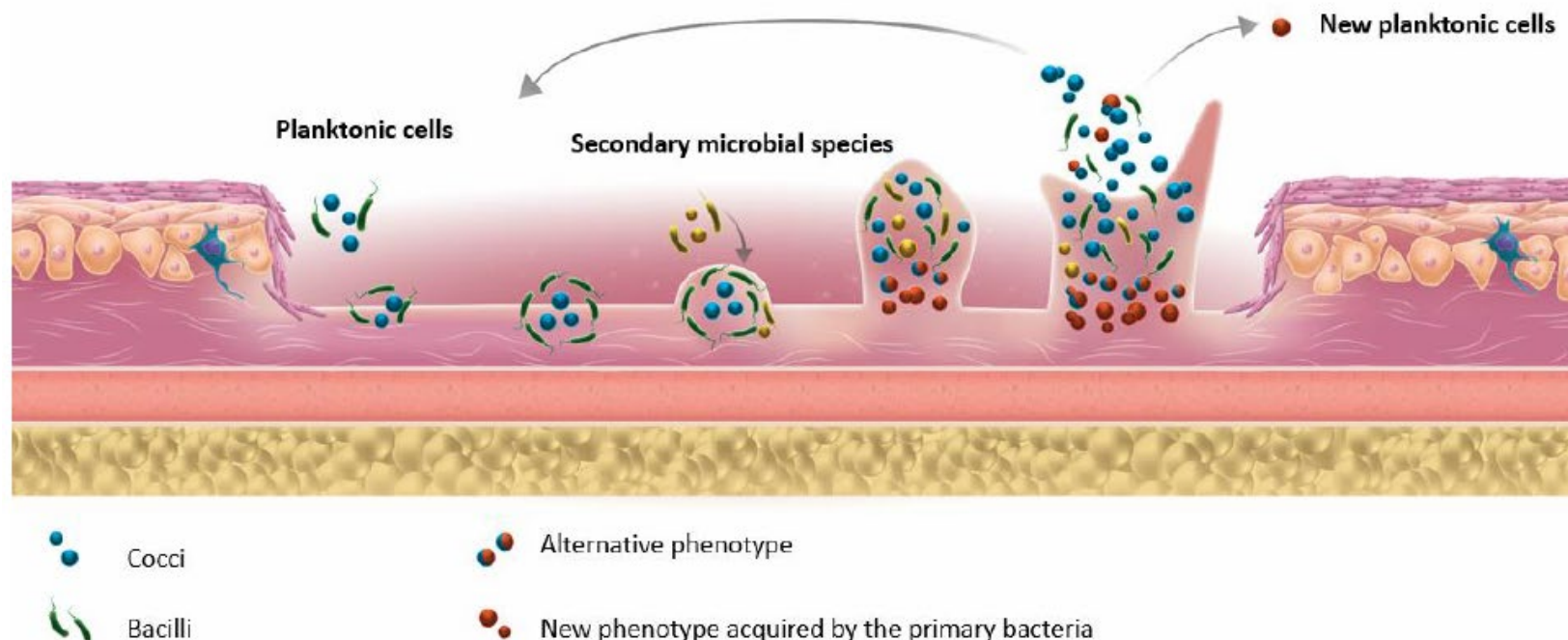


Figure 1. Different bacterial steps of biofilm formation.

Azioni del Biofilm

Antibiotico-resistenza

- Inabilità dei farmaci a penetrare attraverso la matrice
- Mancanza di accumulo di antibiotici a causa dell'impermeabilità
- Presenza di batteri in forma sessile, che sono metabolicamente inattivi e quindi tollerano meglio l'azione dell'antibiotico
- Trasferimento di geni di resistenza- antibiotica tra i batteri

Risposta immune

- I batteri all'interno del biofilm evadono le naturali difese dell'ospite
- Limitata penetrazione dei leucociti e della loro produzione all'interno del biofilm
- Ridotta fagocitosi delle cellule dell'ospite e soppressione dei leucociti
- Modifiche genetiche che incrementano la resistenza dei batteri

ORIGINAL PAPER

WILEY THE INTERNATIONAL JOURNAL OF
CLINICAL PRACTICE

Association between biofilm and multi/extensive drug resistance in diabetic foot infection

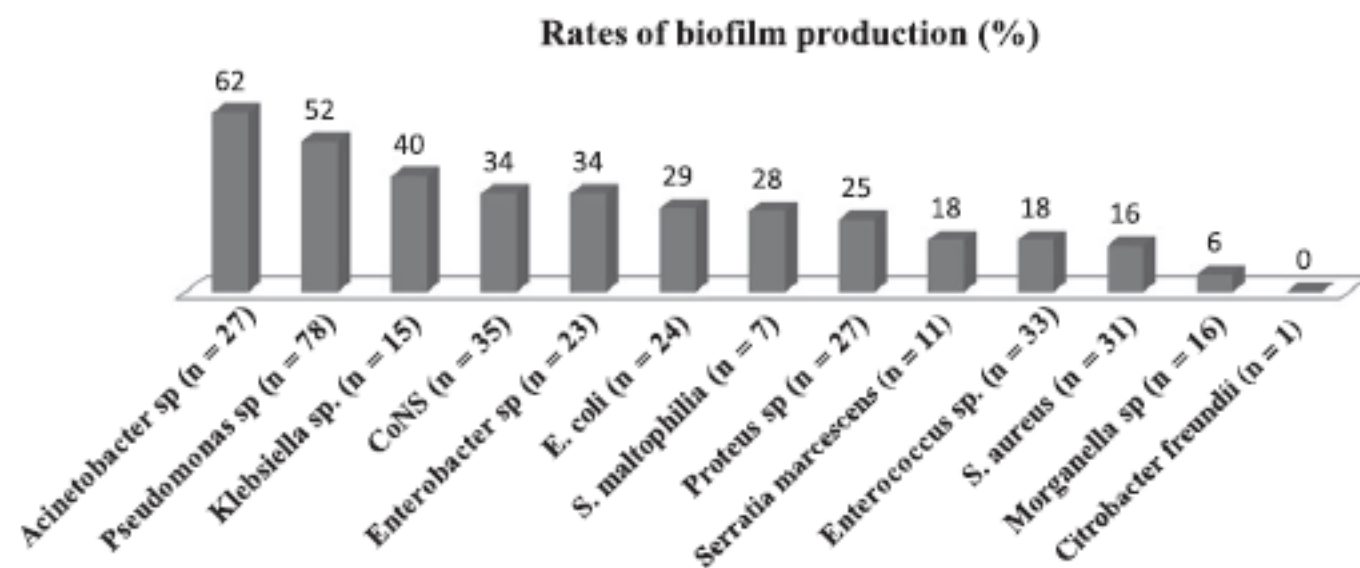
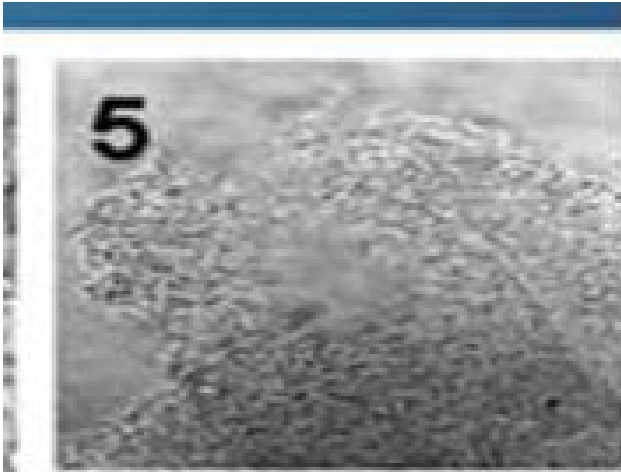
Aslı Vatan¹ | Nese Saltoglu¹  | Mucahit Yemisen¹ | Ilker Inanc Balkan¹ | Serkan Surme¹ |

FIGURE 2 Biofilm-producing microorganisms in patients with diabetic foot infection (CoNS = coagulase-negative Staphylococci)

ORIGINAL PAPER

Association between biofilm and multi/extensive drug resistance in diabetic foot infection

Aslı Vatan¹ | Nese Saltoglu¹  | Mucahit Yemisen¹ | Ilker Inanc Balkan¹ | Serkan Surme¹ | Tayfur Demiray³ | Birgul Mete¹ | Fehmi Tabak¹ | Study Group, Cerrahpasa Diabetic Foot²



	Univariate analysis			Multivariate analysis		
	OR	95% CI	P	OR	95% CI	P
Amputation history	2.20	1.14-4.24	.01	1.00	0.43-2.3	.98
Antibiotic exposure within last 3 months	2.94	1.5-5.75	.002	0.37	0.09-1.3	.14
Recurrent foot infection within last 6 months	2.35	1.23-4.53	.01	0.94	0.25-3.5	.93
Rehospitalization due to infection in the same foot within last 3 months	2.44	1.06-5.58	.03	0.47	0.18-1.2	.12
MDR	7.76	4.53-13.35	.001	3.63	1.58-8.33	.002
XDR	11.33	4.97-26.55	.001	4.06	1.25-13.1	.01

- Uso di antibiotici negli ultimi 3 mesi
- DFI ricorrenti negli ultimi 6 mesi
- Ospedalizzazione negli ultimi 3 mesi
- Storia di pregressa amputazione
- Germi MDR-XDR

The Impact of Multidrug-Resistant Organisms on Outcomes in Patients With Diabetic Foot Infections

Oryan Henig,^{1,2,a} Jason M. Pogue,^{3,4} Emily Martin,⁵ Umar Hayat,⁶ Mahmoud Ja'ara,⁶ Paul E. Kilgore,⁷ Raymond Cha,⁷ Sorab Dhar,⁸ and Keith S. Kaye¹

Table 1. Description of the Cohort and Outcomes of Patients With DFI-MDRO Compared With Patients With DFI-Non-MDRO

	DFI-MDRO (n = 364)	DFI-Non-MDRO (n = 284)	Crude OR (95% CI) ^a	Adjusted OR (95% CI)
Outcomes (within 1 y)				
Recurrent DFI, No. (%)	90 (24.7)	35 (12.3)	2.34 (1.53–3.58)	2.1 (1.38–3.21)
LEA, No. (%)	59 (16.2)	29 (10.2)	1.70 (1.06–2.73)	1.25 (0.74–2.13)
Less extensive amputation, No. (%)	170 (46.7)	145 (51.1)	0.84 (0.62–1.15)	0.79 (0.96–1.35)
Length of stay, median (IQR), d	9 (6 to 13)	7 (5 to 11)	$P < .001$	
Readmissions, No. (%)	234 (64.3)	157 (55.3)	1.46 (1.06–2.0)	1.13 (0.80–1.61)
Mortality, No. (%)	23 (7.6)	13 (5.6)	1.38 (0.68–2.78)	0.95 (0.43–2.09)



Review

The Influence of Multidrug-Resistant Bacteria on Clinical Outcomes of Diabetic Foot Ulcers: A Systematic Review

Gianmarco Matta-Gutiérrez , Esther García-Morales *, Yolanda García-Álvarez ,
Francisco Javier Álvaro-Afonso , Raúl Juan Molines-Barroso and José Luis Lázaro-Martínez 



- MDRO nel 53% dei casi di DFI; MRSA con prevalenza del 15-30%
- MDRO vs non MDRO: maggiore tempo di guarigione
- DFI da *Pseudomonas aeruginosa multiresistente* associata a tempi di terapia antibiotica più lunghi
- La presenza di ischemia, profondità maggiore e grado di infezione i principali fattori prognostici sfavorevoli

Infezione dei tessuti molli

Infezione dell'osso – osteomielite



The background of the top half of the slide is a composite image. On the left, there is a grayscale scanning electron micrograph showing several rod-shaped bacteria. On the right, there is a green-tinted version of the same micrograph. The text is overlaid on the green-tinted portion.

Guidelines on the diagnosis and treatment of foot infection in persons with diabetes

IWGDF/IDSA 2023



Part of the 2023 IWGDF Guidelines on
the prevention and management of
diabetes-related foot disease

IWGDF Infection Guideline



Recommendation 1:

- a. Diagnose a soft tissue diabetes-related infection clinically, based on the presence of local or systemic signs and symptoms of inflammation. (Strong; Low)
- b. Assess the severity of any diabetes-related foot infection using the IWGDF/IDSA classification scheme. (Strong; Low)



Segni di allarme

- Cellulite – iperemia
- Edema
- Calore localizzato
- A volte dolore



- Secrezione purulenta
- Secrezione verdastra (Ps. Aeruginosa-Acinetobacter)
- Odore sgradevole
- Necrosi superficiale o profonda



Segni secondari:

- Alterazione del tessuto di granulazione.
- Ritardata guarigione della lesione

Classificazione clinica

Infezione superficiale

quando interessa esclusivamente i tessuti cutanei molli esterni alla fascia (cute e sottocutaneo adiposo).



Classificazione clinica

Infezione profonda

quando interessa: la fascia, i muscoli, tendini, le articolazioni e/o l'osso





Clinical classification of infection, with definitions	IWGDF classification
Uninfected	
No systemic or local symptoms or signs of infection	1 (uninfected)
Infected	
At least two of these items are present: - Local swelling or induration - Erythema >0.5 cm* around the wound - Local tenderness or pain - Local increased warmth - Purulent discharge And no other cause(s) of an inflammatory response of the skin (e.g. trauma, gout, acute Charcot neuro-osteoarthropathy, fracture, thrombosis or venous stasis)	
Infection with no systemic manifestations (see below) involving - only the skin or subcutaneous tissue (not any deeper tissues), and - any erythema present does not extend >2 cm** around the wound	2 (mild infection)
Infection with no systemic manifestations, and involving: - erythema extending ≥ 2 cm* from the wound margin, and/or - tissue deeper than skin and subcutaneous tissues (e.g. tendon, muscle, joint, bone,)	3 (moderate infection)

IWGDF Infection Guideline



Clinical classification of infection, with definitions	IWGDF classification
Uninfected	
Any foot infection with associated systemic manifestations (of the systemic inflammatory response syndrome [SIRS]), as manifested by ≥ 2 of the following: ▪ Temperature $>38^{\circ}\text{C}$ or $<36^{\circ}\text{C}$ ▪ Heart rate >90 beats/minute ▪ Respiratory rate >20 breaths/minute or $\text{PaCO}_2 <4.3$ kPa (32 mmHg) ▪ White blood cell count $>12,000/\text{mm}^3$, or $<4,000/\text{mm}^3$, or $>10\%$ immature (band) forms	4 (severe infection)
Infection involving bone (osteomyelitis)	Add “(O)” after 3 or 4***

Note: * Infection refers to any part of the foot, not just of a wound or an ulcer; ** In any direction, from the rim of the wound. The presence of clinically significant foot ischemia makes both diagnosis and treatment of infection considerably more difficult; *** If osteomyelitis is demonstrated in the absence of ≥ 2 signs/symptoms of local or systemic inflammation, classify the foot as either grade 3(O) (if <2 SIRS criteria) or grade 4(O) if ≥ 2 SIRS criteria) (see text).

The Infected Diabetic Foot: Re-evaluating the Infectious Diseases Society of America Diabetic Foot Infection Classification

Lawrence A. Lavery,^{1,✉} Easton C. Ryan,² Junho Ahn,² Peter A. Crisologo,¹ Orhan K. Oz,³ Javier La Fontaine,¹ and Dane K. Wukich²

Departments of ¹Plastic Surgery, ²Orthopedic Surgery, and ³Radiology, University of Texas Southwestern Medical Center, Dallas

Results. Osteomyelitis patients had greater antibiotic duration (32.5 ± 46.8 vs 63.8 ± 55.1 days; $P < .01$), surgery frequency (55.5% vs 99.4%; $P < .01$), number of surgeries (2.1 ± 1.3 vs 3.3 ± 2.3 ; $P < .01$), amputations (26.3% vs 83.4%; $P < .01$), reinfection (38.0% vs 56.7%; $P < .01$), and length of stay (14.5 ± 14.9 vs 22.6 ± 19.0 days; $P < .01$). There were no differences in moderate and severe STI outcomes except for infection readmissions (46.2% vs 25.0%; $P = .02$), and acute kidney injury (31.2% vs 50.0%; $P = .03$). There were no differences in moderate and severe osteomyelitis except the number of surgeries (2.8 ± 2.1 vs 4.1 ± 2.5 ; $P < .01$) and length of stay (18.6 ± 17.5 vs 28.2 ± 17.7 ; $P < .01$).

SOCIETY FOR VASCULAR SURGERY[®] DOCUMENT

The Society for Vascular Surgery Lower Extremity Threatened Limb Classification System: Risk stratification based on Wound, Ischemia, and foot Infection (WIfI)

Joseph L. Mills, Sr, MD,^a Michael S. Conte, MD,^b David G. Armstrong, DPM, MD, PhD,^a Frank B. Pomposelli, MD,^c Andres Schanzer, MD,^d Anton N. Sidawy, MD, MPH,^e and George Andros, MD,^f on behalf of the Society for Vascular Surgery Lower Extremity Guidelines Committee, *Tucson, Ariz; San Francisco and Van Nuys, Calif; Brighton and Worcester, Mass; and Washington, D.C.*

Table II. Society for Vascular Surgery Lower Extremity Threatened Limb (SVS WIfI) classification system

I. Wound
II. Ischemia
III. foot Infection
W I fI score

Severe diabetic foot infections without systemic inflammatory response syndrome: Prospective validation of a new category

Javier Aragón-Sánchez MD, PhD¹  | Gerardo Viquez-Molina MD²  |
 María Eugenia López-Valverde MD³  | José María Rojas-Bonilla MD² 

Score calculation

Albumin <2.8 g/dl	1
Erythrocyte sedimentation rate > 94 mm/h	1.5
Neutrophil-to-lymphocyte ratio > 4.52	2
Skin necrosis	4

TABLE 1 Modified IDSA/IWGDF severity classification after subclassifying moderate infections into two types

	Moderate (n = 73, 36.5)	Moderate/severe (n = 38, 19%)	Severe (n = 89, 44.5%)	p-value (effect size) [moderate vs. moderate/severe]	p-value (moderate/ severe vs. severe)
Any amputation, n (%)	15 (20.5)	20 (52.6)	48 (53.9)	<0.001 (0.33)	0.89
Major amputation, n (%)	1 (1.4)	4 (10.5)	9 (10.1)	0.04 (0.24)	0.94
Hospitalisation, n (%)	23 (31.5)	28 (73.7)	78 (87.6)	<0.001 (0.44)	0.05
Length of hospital stay in days, median (IQR)	12 (10.5)	12.5 (15.8)	16.5 (12.8)	1.0	0.10
Treated without antibiotics, n (%)	41 (56.2)	6 (15.8)	8 (9)	<0.001 (0.47)	0.35
Length of antibiotic therapy in days, median (IQR)	9.5 (13.5)	16 (19.3)	16 (21)	0.32	0.30
Reinfection, n (%)	8 (11.0)	3 (7.9)	10 (11.2)	0.74	0.75
Infection-related mortality, n (%)	3 (4.1)	2 (5.3)	8 (9.0)	1.0	0.72
Healing time in days, median (IQR)	69 (69.3)	108 (118)	107 (85.5)	0.2	0.9

Abbreviations: IDSA/IWGDF, Infectious Diseases Society of America/International Working Group on Diabetic Foot; IQR, interquartile range.

IWGDF Infection Guideline



Recommendation 2: Consider hospitalizing all persons with diabetes and a severe foot infection, and those with a moderate infection that is complex or associated with key relevant morbidities. (Strong; Low)

B. Factors that should lead to considering hospitalisation

Severe infection (see findings suggesting a more serious diabetes-related foot infection above)

Metabolic or haemodynamic instability

Intravenous therapy needed (and not available/appropriate as an outpatient)

Diagnostic tests needed that are not available as an outpatient

Severe foot ischaemia is present

Surgical procedures (more than minor) required

Failure of outpatient management

Need for more complex dressing changes than patient/caregivers can provide

Need for careful, continuous observation

Gestione clinica dell'infezione



- «Time is Tissue»



The Diabetic Foot Attack: “Tis Too Late to Retreat!”

**Prashanth R. J. Vas¹, Michael Edmonds¹, Venu Kavarthapu¹,
Hisham Rashid¹, Raju Ahluwalia¹, Christian Pankhurst²,
and Nikolaos Papanas³**

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L’infezione nel piede diabetico costituisce una minaccia per l’arto inferiore

- Valutazione clinica della severità
- Valutazione quadro vascolare
- Valutazione stato generale del paziente e del suo quadro metabolico
- Comorbidità associate

Piede Diabetico Acuto



- Presenza di lesione
 - Edema
 - Eritema
 - Cellulite
 - Calore

Piede Diabetico Acuto



- Zone fluttuanti
 - Crepitii
 - Marezzature
- Raccolta profonda

L'osteomielite: frequente complicanza del piede diabetico (10-15% infezioni moderate; 50% infezioni severe)

- Nel 50-60% dei pz ricoverati; nel 10-20% dei pz ambulatoriali.
- La sede più frequente di osteomielite è l'avampiede (90%), seguita dal mesopiede (5%) e retropiede (5%)
- spesso sottovalutata e misconosciuta
- difficile approccio diagnostico
- approccio terapeutico non univoco

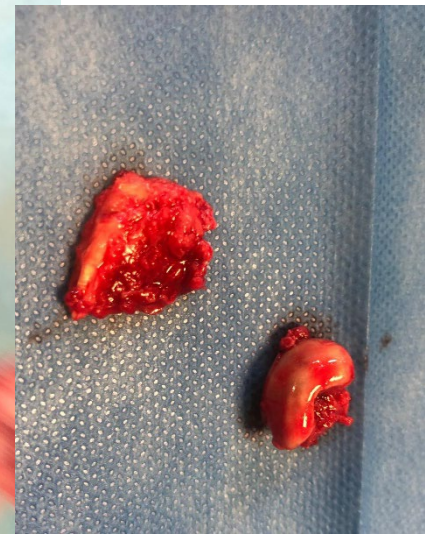


Diagnosi tardiva

- Il quadro più frequente di infezione cronica è l'osteomielite
- L'osteomielite è conseguenza di ulcere in cui l'infezione diventa profonda fino ad arrivare all'osso
- L'osteomielite è la causa di mancata guarigione dell'ulcera



L'osteomielite cronica è una delle principali cause di amputazione



Osteomyelitis in diabetic foot: A comprehensive overview

Laura Giurato, Marco Meloni, Valentina Izzo, Luigi Uccioli



Ulcera cronica da almeno sei settimane
con scarsa tendenza alla guarigione

Diametro maggiore di 2 cm



sensibilità del 56% - specificità del 92%

Profondità maggiore di 3 mm



rischio del 82% di osteomielite
vs 33% un'ulcera più superficiale

IWGDF 2015



Diabet. Med. 17, 74–77 (2000)

'Sausage toe': a reliable sign of underlying osteomyelitis

S. M. Rajbhandari*, M. Sutton*, C. Daviest†, S. Tesfaye* and J. D. Ward*

Conclusions The appearance of a 'sausage toe' should alert the physician of the possibility of underlying osteomyelitis in diabetic foot, so that prompt treatment can be commenced with antibiotics.



Tale classificazione definisce la capacità dell'infezione di esporre il pz a rischio di perdere l'arto o la vita per shock settico.

non limb-threatening

limb-threatening

life-threatening



La cellulite semplice



- E' un'infezione della cute e del sottocutaneo
- L'eziologia è prevalentemente monomicrobica *B-hemolytic streptococcus*
- Si manifesta con iperemia, edema, calore, a volte piccola secrezione purulenta dal fondo dell'ulcera e dolore.

La cellulite semplice



- Non si associa a manifestazioni sistemiche
- Gestione in ambiente ambulatoriale in assenza di associata ischemia
- Si tratta con antibiotici mirati su batteri Gram positivi (specialmente streptococchi), somministrata per via orale

Limb-threatening lesion: ascesso-flemmone



- Riconosce tipicamente una flora batterica polimicrobica
- E' sempre necessario fare dei prelievi colturali raccolti in profondità

Limb-threatening lesion: ascesso-flemmone



- Valutazione dell'area da trattare; Incisione dell'area sospetta
- Incisioni ampie e profonde a volte combinate plantari e dorsali
- Valutazione eventuale coinvolgimento dell'osso.

Trattamento chirurgico

The Role of Early Surgical Debridement and Revascularization in Patients With Diabetes and Deep Foot Space Abscess: Retrospective Review of 106 Patients With Diabetes

Ezio Faglia, MD,¹ Giacomo Clerici, MD,² Maurizio Caminiti, MD,³
Antonella Quarantiello, MD,⁴ Michela Gino, MD,⁵ and Alberto Morabito, PhD⁶

TABLE 4 Final outcome of surgical treatment of patients directly hospitalized (group A) and referred from other hospitals (group B)

Surgical Intervention	Group A	Group B	
Drainage without amputation	9	4	
One or more ray amputation	21	21	$\chi^2 = 24.4$
Transmetatarsal amputation	12	10	$P < .001$
Chopart amputation	1	23	
Above-the-ankle amputation	—	5	

Livello di amputazione più prossimale nei pazienti con ritardato drenaggio dell'infezione

Limb-threatening lesion: cellulite necrotizzante



E' un'infezione che coinvolge i tessuti sottocutanei fino alla fascia con associata necrosi della cute

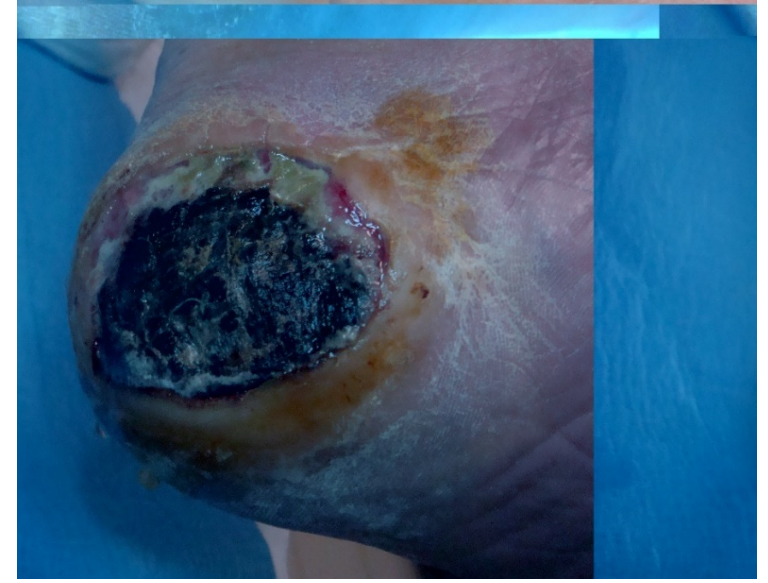
Limb-threatening lesion: gangrena



Si associa ad una condizione di ischemia locale. Necrosi umida in rapida evoluzione
Rapida estensione ai tessuti più profondi ed osso. Trombosi dei vasi per liberazione di tossine

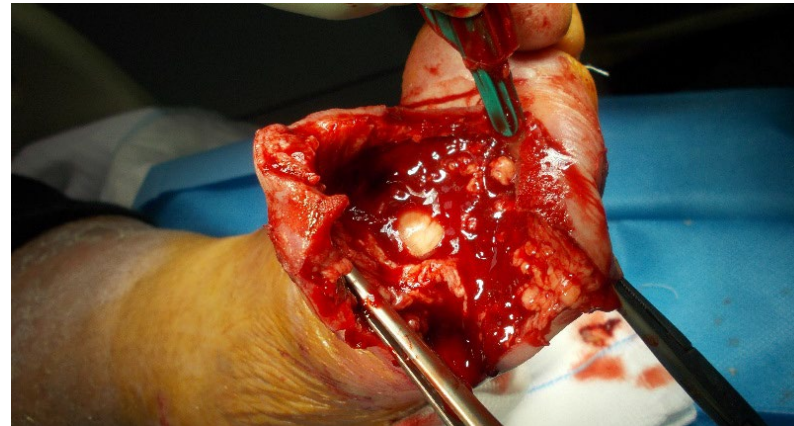
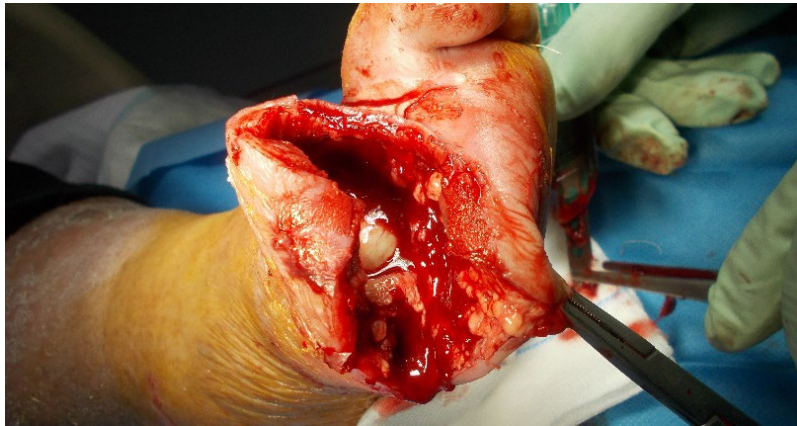
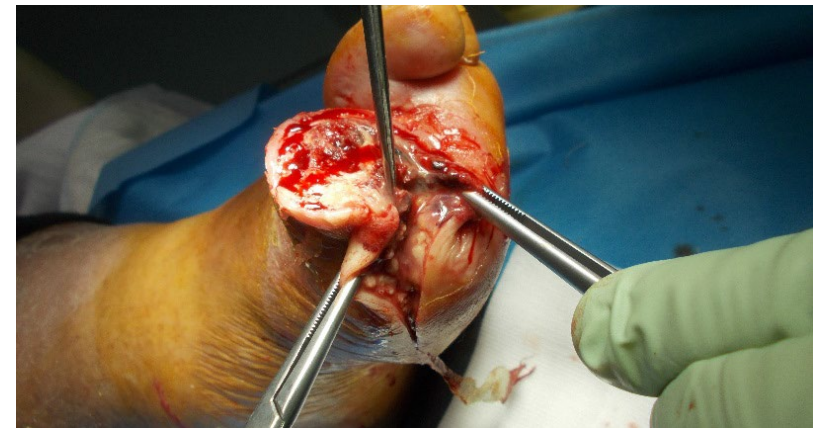
Necessita di approccio tempestivo

Limb-threatening lesion: gangrena



- Si manifesta con tumefazione della cute, cianosi iniziale ,successivo colore bronzino
- flittene a contenuto sieroso-emorragico-purulento di odore nauseante
- estese necrosi dei tessuti e di parti del piede

Necessita di approccio tempestivo



Terapia chirurgica



Life-threatening lesion: fascite necrotizzante



Rapida evoluzione del processo infettivo in 24-72 ore con coinvolgimento dei tessuti sotto fasciali con necrosi estesa in assenza di coinvolgimento muscolare

Life-threatening lesion: cellulite crepitante



- Si caratterizzata per la formazione di gas nei tessuti e di una secrezione scura e di odore fetido (gangrena gassosa).
- Riconosce un'eziologia polimicrobica con la presenza contemporanea di aerobi ed anaerobi facoltativi
- Necessita di un approccio terapeutico tempestivo. Altissimo rischio per la vita

IWGDF Infection Guideline



Recommendation 3: Assess inflammatory serum biomarkers such as C-reactive protein, erythrocyte sedimentation rate, or procalcitonin in a person with diabetes and a possible infected foot ulcer for whom the clinical examination is diagnostically equivocal or uninterpretable. (Best Practice Statement)

Recommendation 5: In a person with suspected soft tissue diabetes-related foot infection, consider a sample for culture to determine the causative microorganisms, preferably by aseptically collecting a tissue specimen (by curettage or biopsy) from the wound. (Conditional; Moderate)

Biopsia di tessuto profondo o di osso (Riferimento standard)

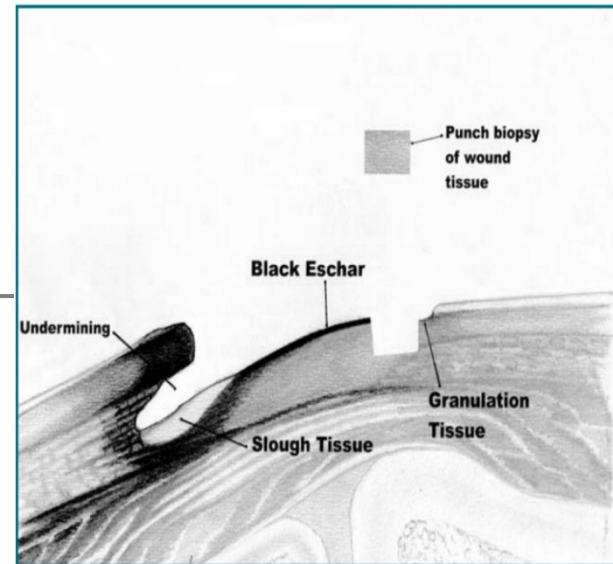
Table 5. Recommendations for Collection of Specimens for Culture From Diabetic Foot Wounds

Do

- Obtain an appropriate specimen for culture from almost all infected wounds
- Cleanse and debride the wound before obtaining specimen(s) for culture
- Obtain a tissue specimen for culture by scraping with a sterile scalpel or dermal curette (curettage) or biopsy from the base of a debrided ulcer
- Aspirate any purulent secretions using a sterile needle and syringe
- Promptly send specimens, in a sterile container or appropriate transport media, for aerobic and anaerobic culture (and Gram stain, if possible)

Do not

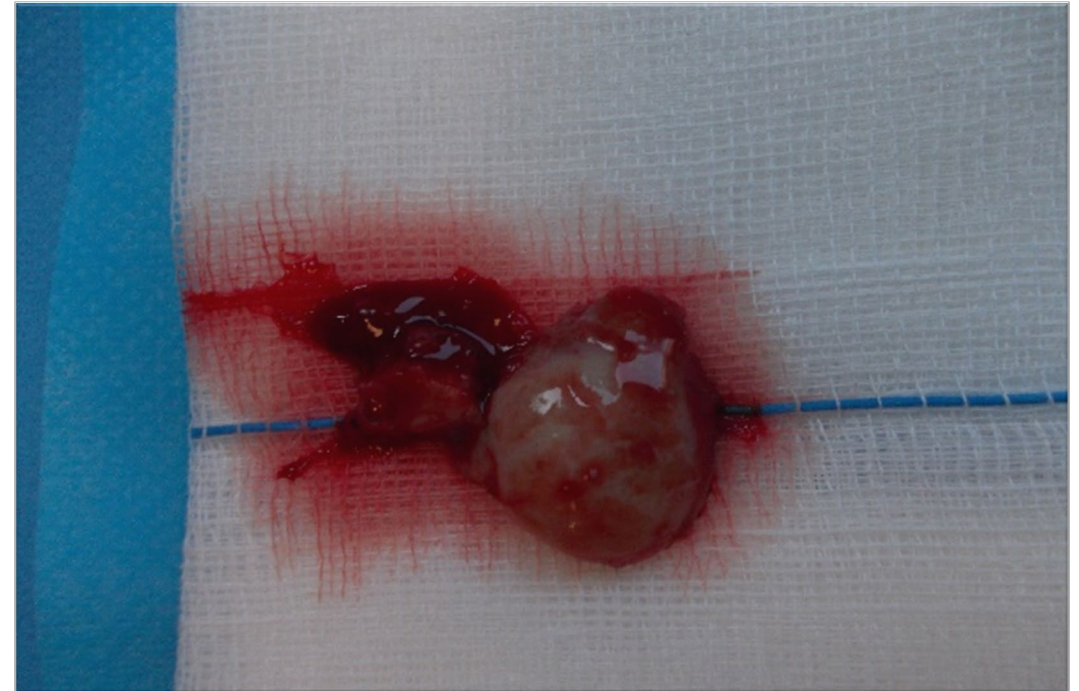
- Culture a clinically uninfected lesion, unless for specific epidemiological purposes
- Obtain a specimen for culture without first cleansing or debriding the wound
- Obtain a specimen for culture by swabbing the wound or wound drainage



Le informazioni più accurate sullo stato dell'ulcera le fornisce la biopsia tissutale.

Recommendation 10: In a person for whom there is suspicion of osteomyelitis of the foot (before or after treatment), consider obtaining bone (rather than soft tissue) samples for culture, either intraoperatively or percutaneously. (Conditional; Moderate)

- Ottenuto in maniera asettica
- Meglio se in assenza di tp antibiotica
- Analisi microbiologica ed istologica
- Non sempre effettuabile





Deep wound cultures correlate well with bone biopsy culture in diabetic foot osteomyelitis

M. Malone^{1,2*}

F. L. Bowling³

A. Gannass²

E. B. Jude⁴

A. J. M. Boulton³

**Identificazione patogeni:
74% vs 82% (biopsia ossea)**

Abstract

Conclusions Deep wound cultures correlate well with osseous cultures and provide a sensitive method in assessing and targeting likely pathogens that cause osseous infections. This will help aid the clinician in guiding antibiotic therapy in centers where bone biopsies may not be readily available. Copyright

Role of Inflammatory Markers in Diagnosing Diabetic Foot Infection

A Meta-Analysis

Aneela Majeed, MD, FACP, Adeela Mushtaq, MD,† Ahmad Iftikhar, MD,‡ Umar Zahid, MD, MPH,§ Mustafa Nadeem Malik, MD,|| Faryal Razzaq, MBBS,‡ and Mayar Al Mohajer, MD, FACP¶*

- VES-PCR-PCT hanno la capacità di differenziare grado 1 (non infezione) dal grado 2 (infezione).
- La PCR è significativamente associata con la severità della malattia.
- La PCT è predittiva di infezione sistemica e di complicazioni come batteriemia, shock settico.
- La **VES** differenzia infezione di grado 2 da infezione di grado 3 (osteomielite).
- Una **VES di 39 mm/h** è diagnostica per infezione di grado 2 (AUC valore di 0.91).
- Una **VES di 70 mm/h** è indicativa della presenza di osteomielite (AUC valore di 0.84).

The efficacy of inflammatory markers in diagnosing infected diabetic foot ulcers and diabetic foot osteomyelitis: Systematic review and meta-analysis

Harman Sharma^{1*}, Sandhli Sharma², Anirudh Krishnan^{1‡}, Daniel Yuan^{1‡}, Venkat N. Vangaveti^{1,3}, Usman H. Malabu^{1,3}, Nagaraja Haleagrahara¹

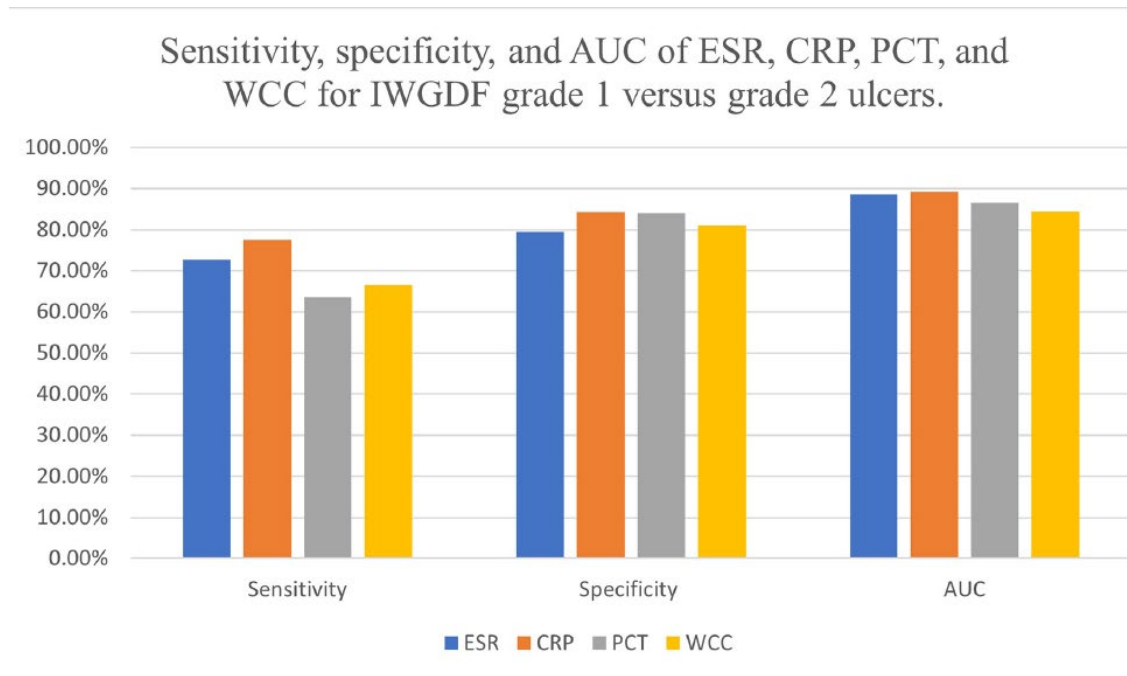


Fig 10. Bar graph of sensitivity, specificity, and AUC of ESR, CRP, PCT and WCC for IWGDF grade 1 versus grade 2 ulcers.

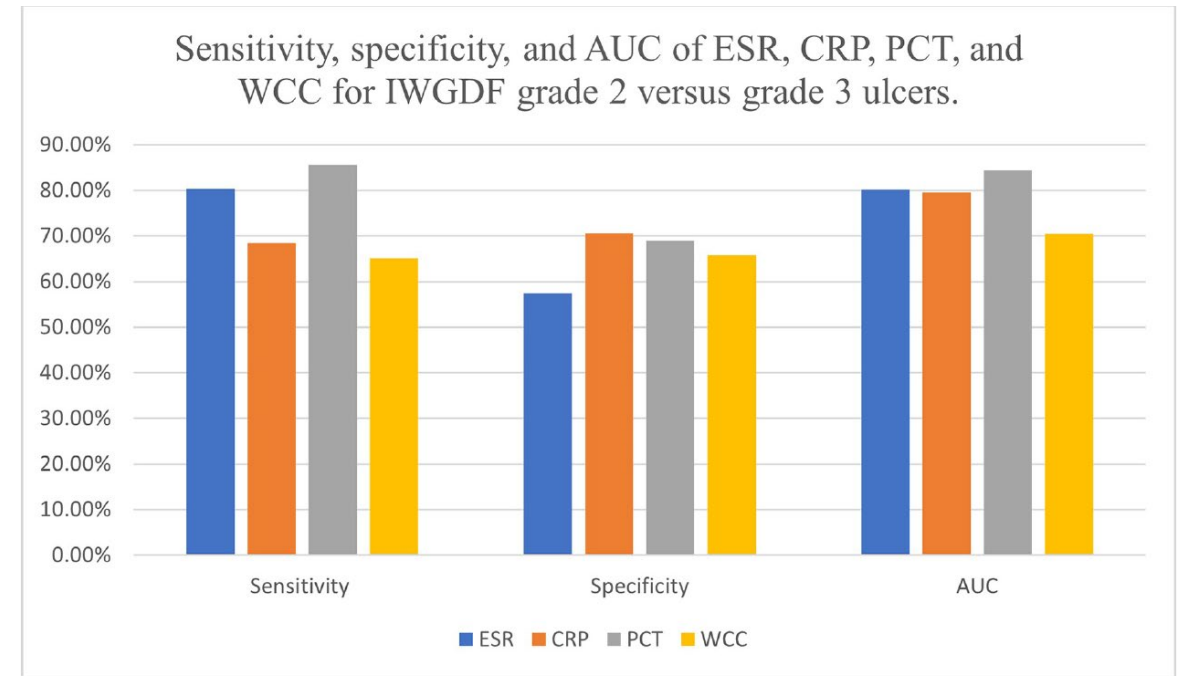


Fig 11. Bar graph of sensitivity, specificity, and AUC of ESR, CRP, PCT and WCC for IWGDF grade 2 versus grade 3 ulcers.

Research Article

Procalcitonin Is a Prognostic Marker of Hospital Outcomes in Patients with Critical Limb Ischemia and Diabetic Foot Infection

Marco Meloni¹, Valentina Izzo¹, Laura Giurato¹, Enrico Brocco², Michele Ferrannini³, Roberto Gandini⁴ and Luigi Uccioli^{1,2}

TABLE 2: Positivity of procalcitonin according to the degree of infection and comorbidities.

Variables	Positive procalcitonin	Normal procalcitonin	<i>p</i> values
Moderate infection	15/23 (65.2%)	—	
Severe infection	8/23 (34.8%)	—	
ESRD	13/23 (56.5%)	19/63 (30.1%)	0.0002
IHD	17/23 (73.9%)	45/63 (71.4%)	0.2
Heart failure	12/23 (52.2%)	12/63 (19%)	0.0001

ESRD: End-stage renal disease; IHD: ischemic heart disease.

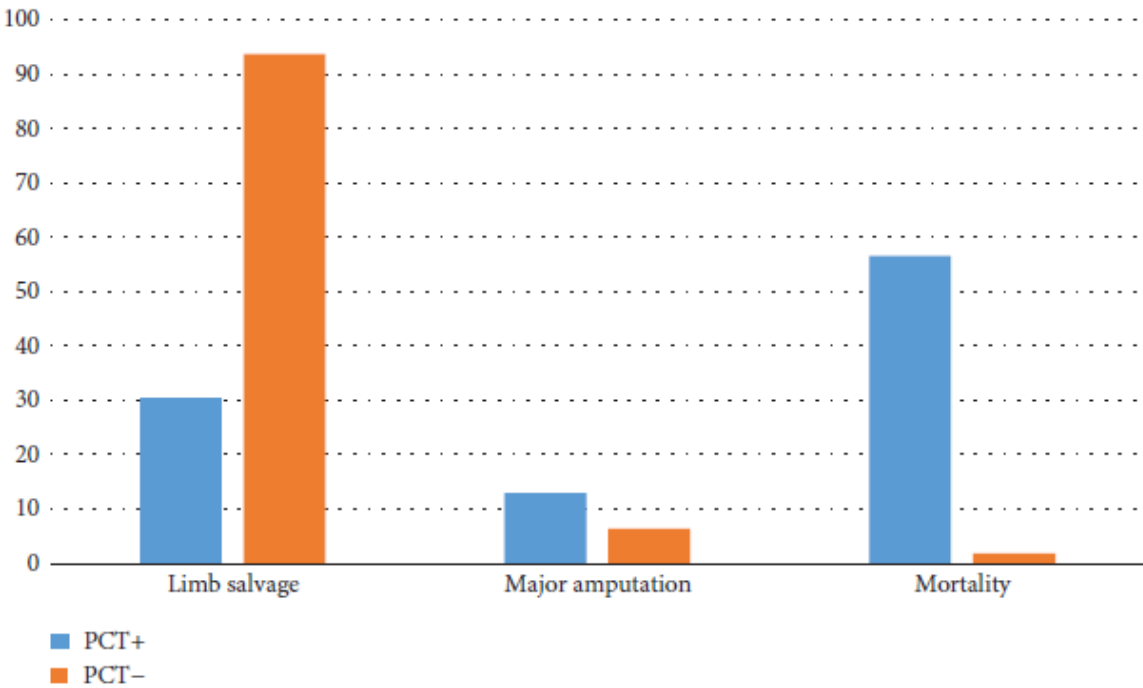


FIGURE 1: Hospital outcomes in patients with or without positive values of PCT. PCT: procalcitonin.

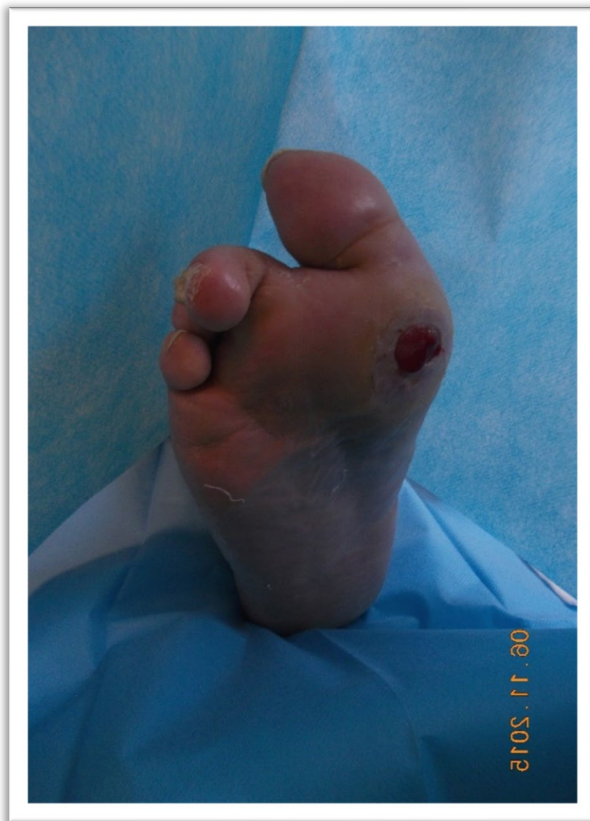
IWGDF Infection Guideline



Recommendation 7: In a person with diabetes, consider using a combination of probe-to-bone test, plain X-rays, and erythrocyte sedimentation rate, or C-reactive protein, or procalcitonin as the initial studies to diagnose osteomyelitis of the foot. (Conditional; Low)

Recommendation 8: Perform magnetic resonance imaging when the diagnosis of diabetes-related osteomyelitis of the foot remains in doubt despite clinical, plain X-rays and laboratory findings. (Strong; Moderate)

Recommendation 9: Consider using positron emission tomography, leukocyte scintigraphy or single photon emission computed tomography as an alternative to magnetic resonance imaging for the diagnosis of diabetes-related osteomyelitis of the foot. (Conditional; Low)



Lesione cronica I testa MT



sensibilità 97%-specificità 91%

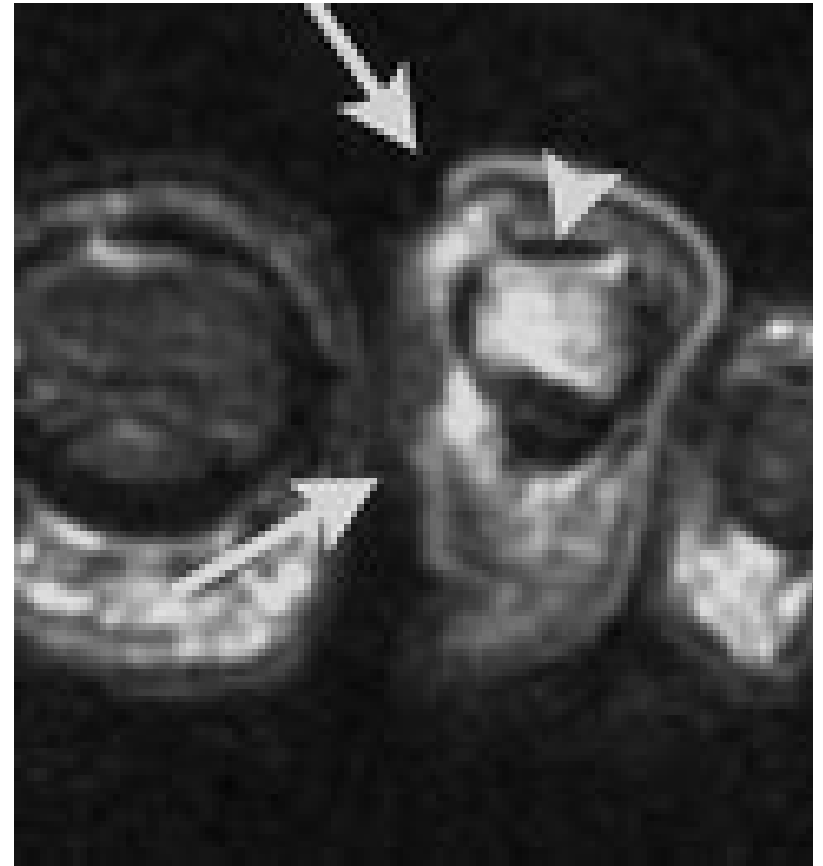
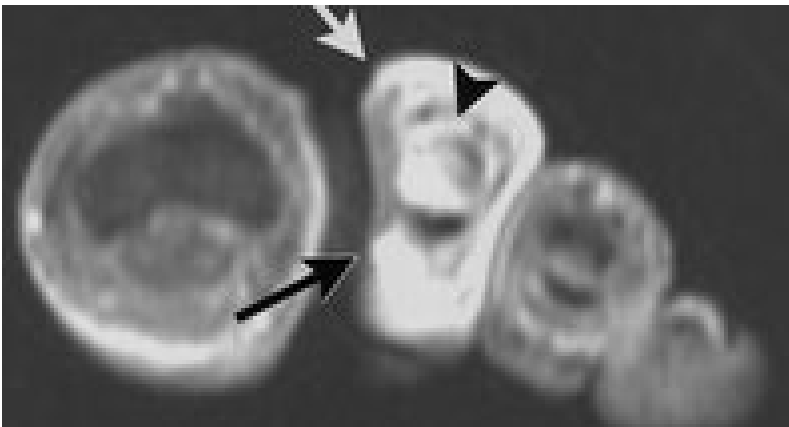
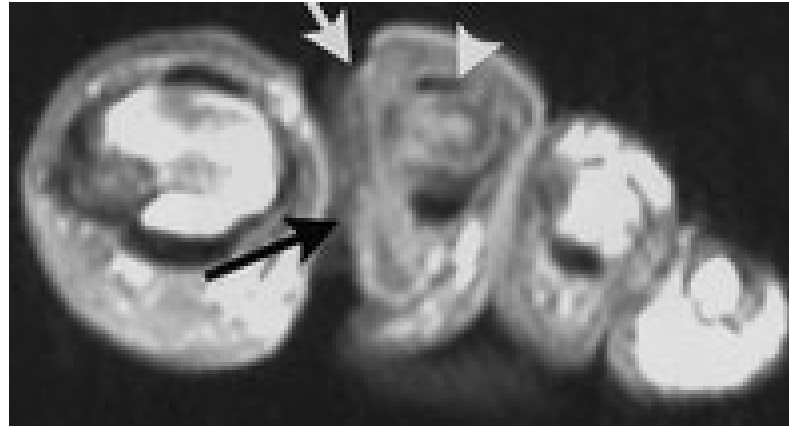


RX: alterazioni radiografiche di osteomielite

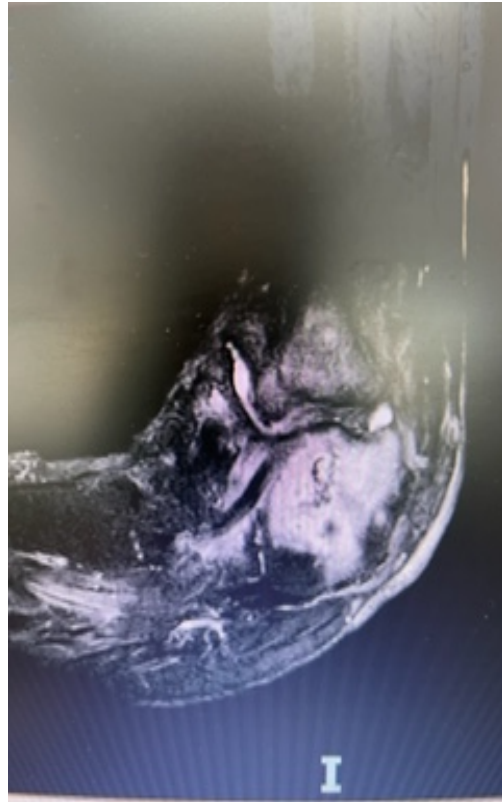


erosione della corticale - lisi della corticale - lisi dell'osso - sequestro osseo
edema dei tessuti molli circostanti





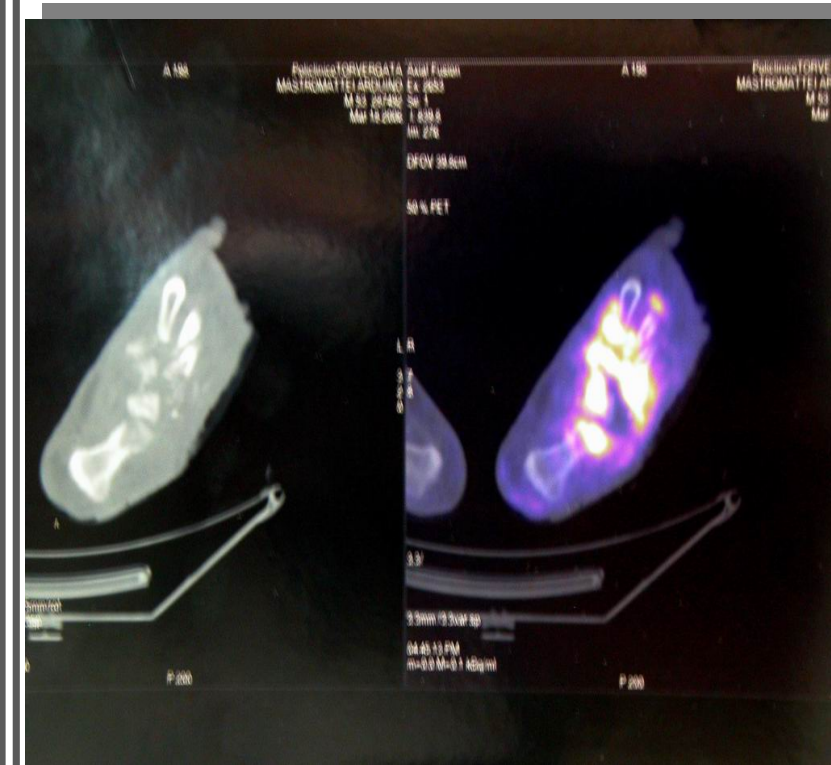
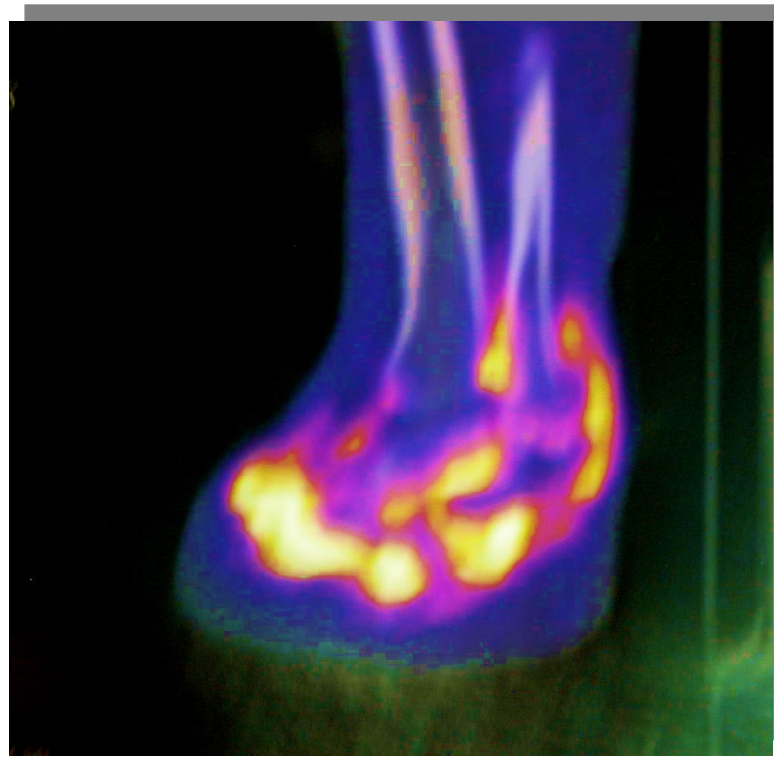
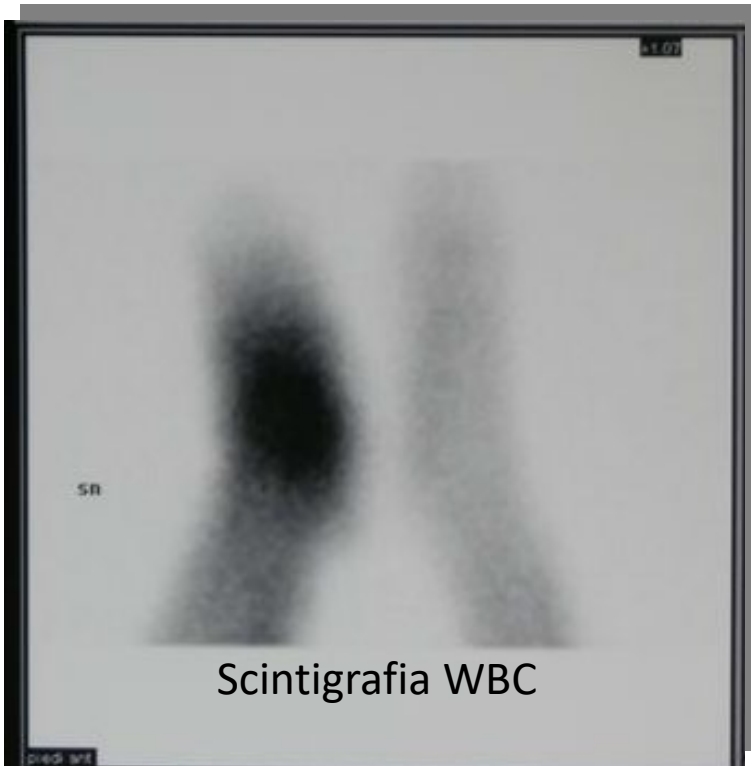
RM nell'osteomielite



RM nell'osteomielite



RM nell'infezione tessuti molli



Metodiche scintigrafiche (SPECT/TC)

RX nel follow-up dell'osteomielite



26/06/2013

07/09/2013

Recommendation 13: Select an antibiotic agent for treating a diabetes-related foot infection based on: the likely or proven causative pathogen(s) and their antibiotic susceptibilities; the clinical severity of the infection; published evidence of the efficacy of the agent for infections of the diabetes-related foot; risk of adverse events including collateral damage to the commensal flora; the likelihood of drug interactions; agent availability and, costs. Best Practice Statement

La terapia antibiotica ideale: spettro ristretto, alta dose e breve durata

La scelta della terapia antibiotica empirica



- Gravità della lesione
- Vascolarizzazione
- Durata della lesione
- Precedente uso di antibiotici
- Ricorrenza
- Epidemiologia locale
- Comorbidità (dialisi)

La scelta della terapia antibiotica mirata



ISTITUTO SANITARIO REGIONALE
ASL ROMA 2

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Cognome / Nome
GHIGI ROLANDO
Sesso: M Data Nascita: 28/ 04/ 1941 Età: 81 Anni
Codice Fiscale
GHGRND41D28H501F

Provenienza: routine
AMB. ENDOCR. - SE

Esame Esito U.M. Valori di Riferimento Metodica

BATTERIOLOGIA MICOLOGIA PARASSITOLOGIA

Materiale: Tampone ferita
CULTURA LIQUIDI/SECREZIONI (semina diretta)

Esame Culturale Positivo

Isolato 1 **Klebsiella pneumoniae**
Pseudomonas aeruginosa è intrinsecamente resistente ad ampicillina, amoxicillina-acido clavulanico, ampicillina-sulbactam, cefazolina, cefalotina, cefalexina, cefadroxil, cefotaxime, ceftriaxone, ertapenem, cloramfenicolo, trimetoprim, tetraciclina e tigeciclina. (AM, CN, CRO, CTX, AXC, ETP, TGC). Enterococcus resistente alla vancomicina. Resistente alla gentamicina ad alto livello. Resistente alla kanamicina ad alto livello. Enterococcus resistente al test con teicoplanina

Isolato 2 **Pseudomonas aeruginosa**
Pseudomonas aeruginosa è intrinsecamente resistente ad ampicillina, amoxicillina-acido clavulanico, ampicillina-sulbactam, cefazolina, cefalotina, cefalexina, cefadroxil, cefotaxime, ceftriaxone, ertapenem, cloramfenicolo, trimetoprim, tetraciclina e tigeciclina. (AM, CN, CRO, CTX, AXC, ETP, TGC). Enterococcus resistente alla vancomicina. Resistente alla gentamicina ad alto livello. Resistente alla kanamicina ad alto livello. Enterococcus resistente al test con teicoplanina

Isolato 3 **Enterococcus faecium**
Pseudomonas aeruginosa è intrinsecamente resistente ad ampicillina, amoxicillina-acido clavulanico, ampicillina-sulbactam, cefazolina, cefalotina, cefalexina, cefadroxil, cefotaxime, ceftriaxone, ertapenem, cloramfenicolo, trimetoprim, tetraciclina e tigeciclina. (AM, CN, CRO, CTX, AXC, ETP, TGC). Enterococcus resistente alla vancomicina. Resistente alla gentamicina ad alto livello. Resistente alla kanamicina ad alto livello. Enterococcus resistente al test con teicoplanina

Isolato 4 **Candida albicans**
Pseudomonas aeruginosa è intrinsecamente resistente ad ampicillina, amoxicillina-acido clavulanico, ampicillina-sulbactam, cefazolina, cefalotina, cefalexina, cefadroxil, cefotaxime, ceftriaxone, ertapenem, cloramfenicolo, trimetoprim, tetraciclina e tigeciclina. (AM, CN, CRO, CTX, AXC, ETP, TGC). Enterococcus resistente alla vancomicina. Resistente alla gentamicina ad alto livello. Resistente alla kanamicina ad alto livello. Enterococcus resistente al test con teicoplanina

Isolato 5 **Candida tropicalis**
Pseudomonas aeruginosa è intrinsecamente resistente ad ampicillina, amoxicillina-acido clavulanico, ampicillina-sulbactam, cefazolina, cefalotina, cefalexina, cefadroxil, cefotaxime, ceftriaxone, ertapenem, cloramfenicolo, trimetoprim, tetraciclina e tigeciclina. (AM, CN, CRO, CTX, AXC, ETP, TGC). Enterococcus resistente alla vancomicina. Resistente alla gentamicina ad alto livello. Resistente alla kanamicina ad alto livello. Enterococcus resistente al test con teicoplanina

Antibiotici Saggiali	Isolato 1	Isolato 2	Isolato 3	Isolato 4	Isolato 5																
MIC	S	R	MBP	MIC	S	R	MBP	MIC	S	R	MBP	MIC	S	R	MBP	MIC	S	R	MBP	MIC	
Amoxicillina																					
Amikacina																					
Aztreonam																					
Amoxicillina/clavulanato (f)																					
Ceftazidima																					
Ciprofloxacina																					
Ceftriaxone																					
Ceftolozan-tazobactam																					
Cefuroxime sodico																					
Ceftazidime/avibactam																					
Ertapenem																					
Cefepime																					
Fosfomicina c/G6P																					
Gentamicina																					
Imipenem																					
Levofloxacina																					
Meropenem																					
Meropenem-vaborbactam																					
Tobramicina																					
Trimetoprima/sulfametossazolo																					
Temocillina																					
Piperacillina/tazobactam																					
Cefalexina																					
Cefotaxima																					
Cefixima																					
Gentamicina-Sin																					
Linezolid																					
Quinupristin-dalfopristin																					
Teicoplanina																					
Vancomicina																					

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BATTERIOLOGIA MICOLOGIA PARASSITOLOGIA

Materiale: Tampone ferita
CULTURA LIQUIDI/SECREZIONI (semina diretta)

Esame Culturale Assenza di crescita batterica

Il Dirigente: Graziela Sivilla

Referto Completo

Antibiotici Saggiali	Isolato 1	Isolato 2	Isolato 3	Isolato 4	Isolato 5																
MIC	S	R	MBP	MIC	S	R	MBP	MIC	S	R	MBP	MIC	S	R	MBP	MIC	S	R	MBP	MIC	
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Cefalexina																					
Cefotaxima																					
Cefixima																					
Gentamicina-Sin																					
Linezolid																					
Quinupristin-dalfopristin																					
Teicoplanina																					
Vancomicina																					

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Sesso: M Data Nascita: 28/ 04/ 1941 Età: 81 Anni
Codice Fiscale
GHGRND41D28H501F

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AMB. ENDOCR. - SE

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Antibiotici Saggiali	Isolato 1	Isolato 2	Isolato 3	Isolato 4	Isolato 5																
MIC	S	R	MBP	MIC	S	R	MBP	MIC	S	R	MBP	MIC	S	R	MBP	MIC	S	R	MBP	MIC	
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Cefixima																					
Gentamicina-Sin																					
Linezolid																					
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Teicoplanina																					
Vancomicina																					

Data di Produzione: 02/ 05/ 2023 Ore: 13: 50 Pagina: 1/ 1

IWGDF Infection Guideline



Table 5: Duration of antibiotic therapy according to the clinical situation

Infection severity (skin and soft tissues)	Route	Duration
Class 2: mild	oral	1-2 weeks*
Class 3 / 4: moderate / severe	oral/initially iv	2-4 weeks
Bone/joint	Route	Duration
Resected	oral/initially iv	2-5 days
Debrided (soft tissue infection)	oral/initially iv	1-2 weeks
Positive culture or histology of bone margins after bone resection	oral/initially iv oral/initially iv	3 weeks 6 weeks
No surgery or dead bone		

*: 10 days following surgical debridement

Terapia chirurgica conservativa



procedura in cui solo l'osso infetto ed il tessuto molle non vitale sono rimossi senza amputazione di altre parti del piede .



Recommendation 21: Consider performing surgical resection of infected bone combined with systemic antibiotics in a person with diabetes-related osteomyelitis of the foot. (Conditional; Low)

Recommendation 22: Consider antibiotic treatment without surgery in case of (i) forefoot osteomyelitis without an immediate need for incision and drainage to control infection, and (ii) without peripheral artery disease, and (iii) without exposed bone. (Conditional; Low)

Recommendation 17: Use the outcome at a minimum follow-up duration of 6 months after the end of the antibiotic therapy to diagnose remission of diabetes-related osteomyelitis of the foot. Best Practice Statement

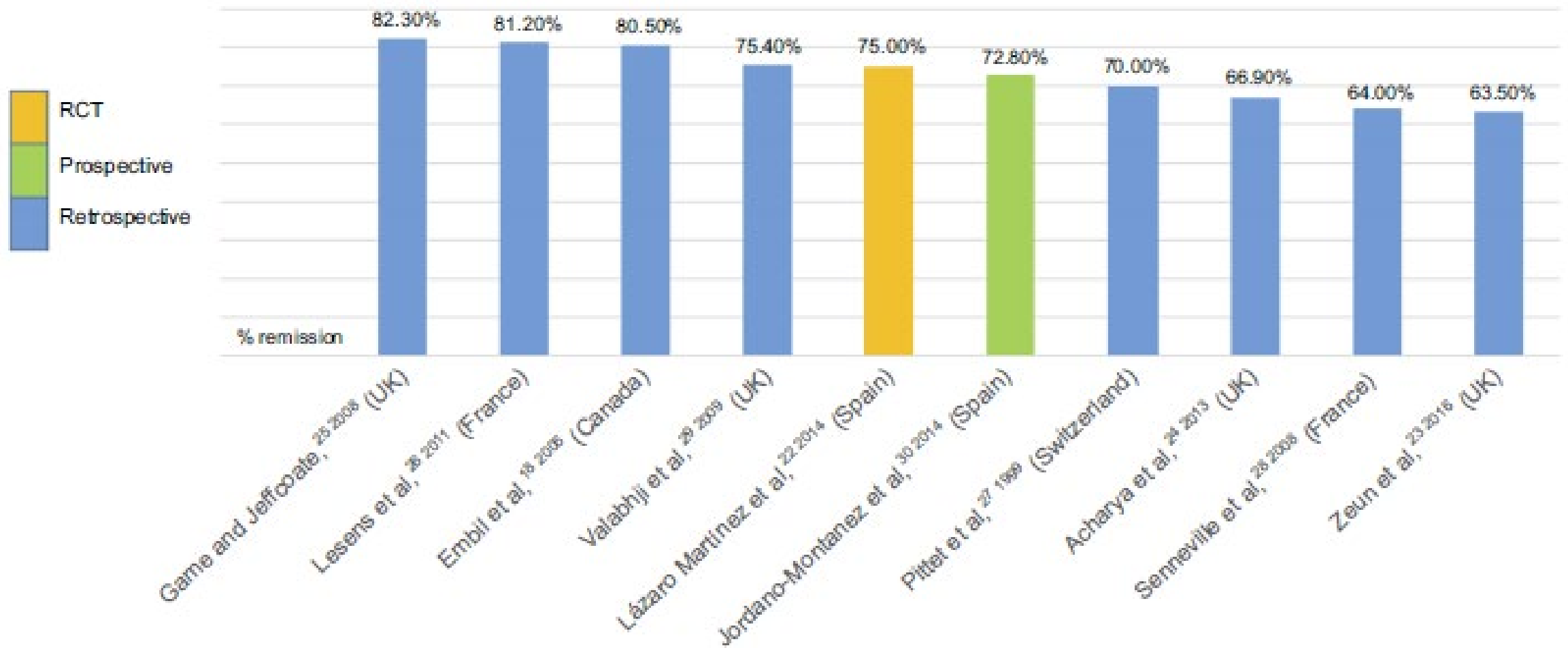
Optimal management of diabetic foot osteomyelitis: challenges and solutions

This article was published in the following Dove Press journal:
Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy

José Luis Lázaró Martínez 
Yolanda García Álvarez 
Aroa Tardáguila-García 
Esther García Morales 

Instituto de Investigación Sanitaria del
Hospital Clínico San Carlos, Universidad
Complutense de Madrid, Madrid 28040,
Spain

Purpose: Diabetic foot osteomyelitis (DFO) is the most frequent infection associated with diabetic foot ulcers, occurs in >20% of moderate infections and 50%–60% of severe infections, and is associated with high rates of amputation. DFO represents a challenge in both diagnosis and therapy, and many consequences of its condition are related to late diagnosis, delayed referral, or ill-indicated treatment. This review aimed to analyze the current evidence on DFO management and to discuss advantages and disadvantages of different treatment options.



Distribution of rates of remission of diabetic foot osteomyelitis with antibiotic treatment.



Antibiotics Versus Conservative Surgery for Treating Diabetic Foot Osteomyelitis: A Randomized Comparative Trial

José Luis Lázaro-Martínez,¹ Javier Aragón-Sánchez,² and Esther García-Morales¹

Six-Week Versus Twelve-Week Antibiotic Therapy for Nonsurgically Treated Diabetic Foot Osteomyelitis: A Multicenter Open-Label Controlled Randomized Study

Alina Tone,¹ Sophie Nguyen,¹
Fabrice Devemy,² Hélène Topolinski,³
Michel Valette,¹ Marie Cazaubiel,⁴
Armelle Fayard,⁵ Éric Beltrand,⁶
Christine Lemaire,³ and Éric Senneville¹

Three Weeks Versus Six Weeks of Antibiotic Therapy for Diabetic Foot Osteomyelitis: A Prospective, Randomized, Noninferiority Pilot Trial

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Table 2. Characteristics of Cases in Which There Was a Clinical Remission Versus a Clinical Failure (Intention-to-Treat Population) (n = 93)

Characteristic	Clinical Failure (n = 20)	Clinical Remission (n = 73)	P Value ^a
Female sex	2 (10)	15 (21)	.28
Median age	62 years	68 years	.02 ^b
Osteomyelitis involving toe (vs another anatomic site)	12 (60)	41 (56)	.76
Lower extremity angioplasty performed	0 (0)	8 (11)	.12
Osteomyelitis due to <i>Staphylococcus aureus</i>	12 (60)	32 (44)	.10
No. of surgical debridements, median	1 intervention	1 intervention	.83
Partial amputations	9 (45)	25 (34)	.38
3-week course of antibiotic therapy	7 (35)	37 (51)	.21
Estimated episodes with adequate adherence by nurses/clinicians	18 (90)	59 (81)	.34
Length of hospital stay, median	13 days	10 days	.87

Data are presented as No. (%) unless otherwise indicated.

^aPearson χ^2 test or Wilcoxon rank-sum test.

^bStatistically significant ($P < .05$).

Table 1. Characteristics and Outcomes of Subjects With a Diabetic Foot Osteomyelitis Episode, by Duration of Treatment With Systemic Antibiotic Therapy After Debridement (Intention-to-Treat Population) (n = 93)

Characteristic	Duration of Antibiotic Therapy		<i>P</i> Value ^a
	3 Weeks (n = 44)	6 Weeks (n = 49)	
Clinical			
Female sex	6 (14)	11 (22)	.27
Median age	70 years	65 years	.23
Median body mass index	27 kg/m ²	28 kg/m ²	.89
Osteomyelitis involving toe	22 (50)	31 (63)	.20
Charcot midfoot deformities	6 (14)	6 (12)	.84
Clinical peripheral arterial disease	27 (61)	26 (53)	.42
Transcutaneous oxygen tension (dorsal foot), median	36 mm Hg	41 mm Hg	.58
Successful angioplasty performed	4 (9)	4 (8)	.87
Wound score at admission, median	16 points	17 points	.56
Pathogens			
<i>Staphylococcus aureus</i>	21 (48)	23 (47)	.94
Gram-negative bacteria	11 (25)	17 (35)	.31
Polymicrobial infection	20 (45)	28 (57)	.26
Therapy			
No. of surgical debridements, median	1 intervention	1 intervention	.27
Partial amputation	16 (36)	18 (36)	.97
Hyperbaric oxygen therapy	6 (14)	5 (10)	.61
Duration of intravenous therapy, median	1 day	3 days	.37
Outcome			
Complete remission	37 (84)	36 (73)	.21
Microbiological recurrence only	3 (7)	5 (10)	.56
Adverse events	17 (39)	16 (33)	.54
Serious adverse events	5 (11)	9 (18)	.35
Antibiotic-related adverse events	4 (9)	7 (14)	.44
Complete wound healing after therapy	28 (64)	29 (59)	.67

Data are presented as No. (%) unless otherwise indicated.

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IWGDF Infection Guideline



Recommendation 19: Consider performing early (within 24-48 hours) surgery combined with antibiotics for moderate and severe diabetes-related foot infections to remove infected and necrotic tissue. (Conditional; Low)

Recommendation 18: Urgent surgical consultation should be obtained in cases of severe infection or moderate diabetes-related foot infection complicated by extensive gangrene, necrotizing infection, signs suggesting deep (below the fascia) abscess, compartment syndrome, or severe lower limb ischaemia. Best Practice Recommendation

Recommendation 20: In people with diabetes, peripheral artery disease and a foot ulcer or gangrene with infection involving any portion of the foot, obtain an urgent consultation by a surgical specialist as well as a vascular specialist in order to determine the indications and timings of a drainage procedure and/or revascularisation procedure. Best Practice Statement



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