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PIEDE DIABETICO
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*Focus sul piede nella
gestione del diabete*

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EVOLUZIONE DELLA VASCULOPATIA PERIFERICA: UNA MALATTIA CON MULTIPLI ASPETTI

Marco Meloni

Centro Piede Diabetico

UOC di Endocrinologia e Diabetologia
Policlinico Universitario Roma Tor Vergata



TOR VERGATA
UNIVERSITÀ DEGLI STUDI DI ROMA

From a Spark to a Flame: The Evolution of Diabetic Foot Disease in the Last Two Decades

Marco Meloni, MD^{1,2} , Alberto Piaggese, MD³ ,
and Luigi Uccioli, MD^{1,2}

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Extremity Wounds
1–5

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Nonostante i numerosi progressi compiuti, la sindrome del **piede diabetico rappresenta attualmente una condizione invalidante** che comporta ricoveri ospedalieri, amputazioni e decessi. **Il fenotipo dei pazienti affetti da piede diabetico è cambiato** significativamente negli ultimi due decenni, passando **da una forma neuropatica a una vascolare**, con un quadro clinico più **aggressivo e progressivo**, associato a una complessa serie di **comorbidità** che caratterizzano un gruppo di pazienti particolarmente difficili da trattare.

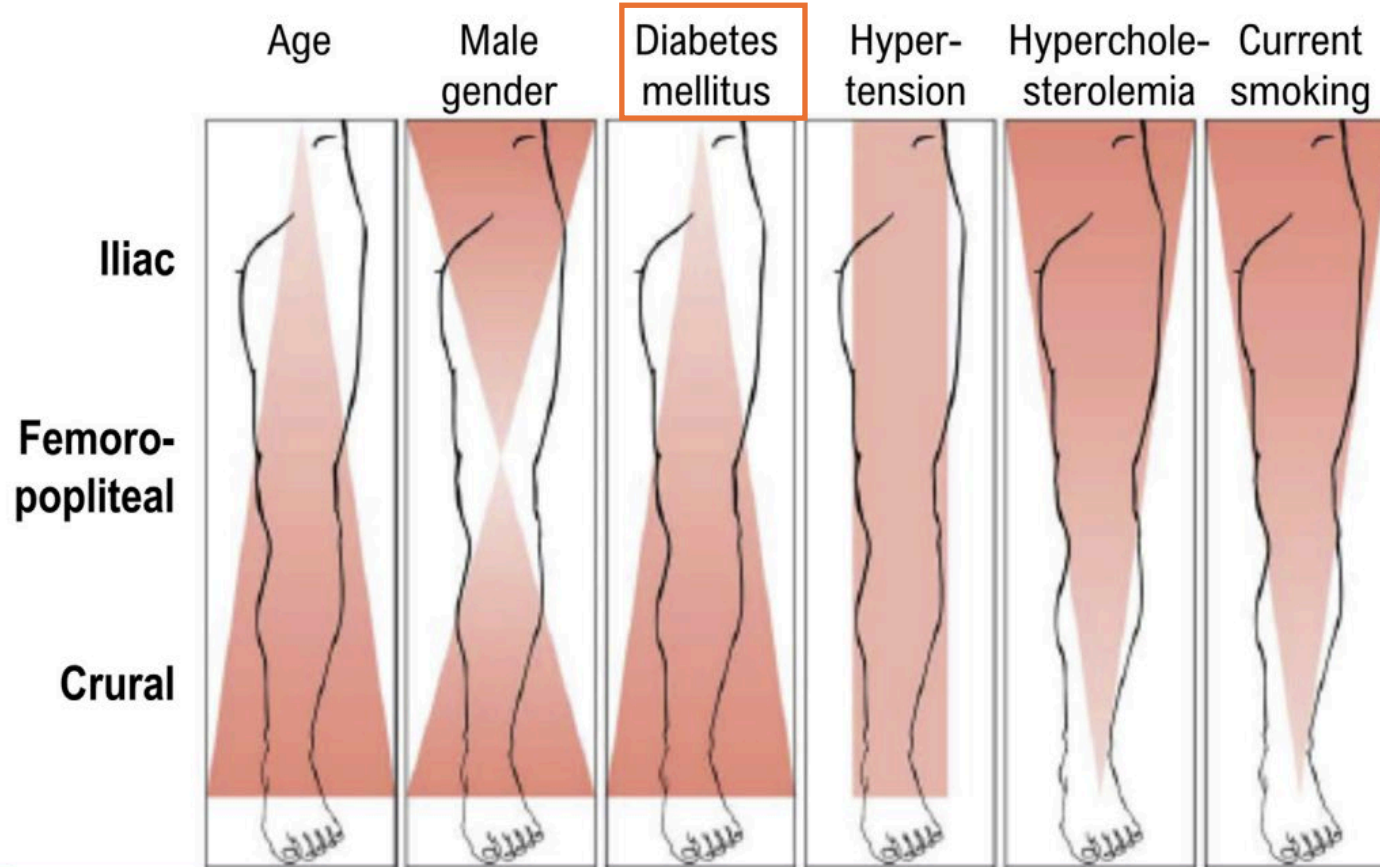
Il Piede Diabetico nelle ultime due decadi

Table 1. Evolution of Characteristics and Treatment of Diabetic Foot Disease Before and After 2010.

Characteristics of DFUs before 2010¹² Neuropathic ulcers 52.5% Ischaemic/neuro-ischaemic ulcers 47.5%	Characteristics of DFUs after 2010¹⁴ Neuropathic ulcers 32.2% Ischaemic/neuro-ischaemic ulcers 67.8%
Main cardiovascular co-morbidities in patients with DFUs before 2010¹² Heart failure 10.9% ESRD 5.8%	Main cardiovascular co-morbidities in patients with DFUs after 2010¹⁴ Heart failure 22.4% ESRD 20%
Characteristics of PAD before 2010^{15,26} Involvement of infra-popliteal arteries	Characteristics of PAD after 2010^{17,18,25,26} Involvement of foot arteries
Treatment of PAD before 2010¹⁶ Management of main cardiovascular risk factors (diabetes, dyslipidemia, hypertension, smoke cessation) Revascularisation (open surgery and endovascular) Antiplatelet therapy	Treatment of PAD after 2010^{19,32-38} Management of main cardiovascular risk factors (diabetes, dyslipidemia, hypertension, smoke cessation) Revascularisation (open surgery and endovascular) Antiplatelet therapy plus anti-thrombotic therapy (Rivaroxaban) Peripheral Blood Mononuclear Cells Therapy

Abbreviations: DFUs, diabetic foot ulcers; ESRD, end-stage-renal-disease; PAD, peripheral arterial disease.

Associazione dei fattori di rischio con i modelli di patologia aterosclerotica



Multisegmentale e bilaterale

Distale (arterie di gamba)

Fig 2.3. Association of risk factors with the level of atherosclerotic target lesions. The red overlay on the anatomic cartoon illustrates the association of risk factor with patterns of atherosclerotic disease.²¹⁷ (Reprinted from Diehm N, Shang A, Silvestro A, Do DD, Dick F, Schmidli J, et al. Association of cardiovascular risk factors with pattern of lower limb atherosclerosis in 2659 patients undergoing angioplasty. Eur J Vasc Endovasc Surg 2006;31:59-63.)

Peripheral Arterial Disease in Diabetic and Nondiabetic Patients

Jude et al,
Diabetes Care 2001

A comparison of severity and outcome

EDWARD B. JUDE MD, MRCP
SAMSON O. OYIBO, MRCP

NICHOLAS CHALMERS, FRCR
ANDREW J.M. BOULTON, MD, FRCP

Table 2—Differences in median arterial occlusion score between diabetic and nondiabetic patients

Arterial segment†	Median interquartile range additive occlusion score		P value
	Diabetic patients	Nondiabetic patients	
Aorta	3 (3–4)	3 (3–3.5)	0.50
Common iliac	3 (2–3)	3 (2–3)	0.76
External iliac	2 (0–3)	3 (2–3)	0.15
Internal iliac	3 (0–6)	3 (0–4)	0.51
Profunda femoris	3 (0–5)	0 (0–2)	0.02
Superficial femoral	8 (4–13)	7 (2–9)	0.10
Popliteal	7 (3–10)	3 (0–4)	0.02
Anterior tibial	13 (4–15)	3 (0–13)	0.002
Peroneal	5 (0–15)	0 (0–6)	0.001
Posterior tibial	15 (0–15)	4 (0–14)	0.001

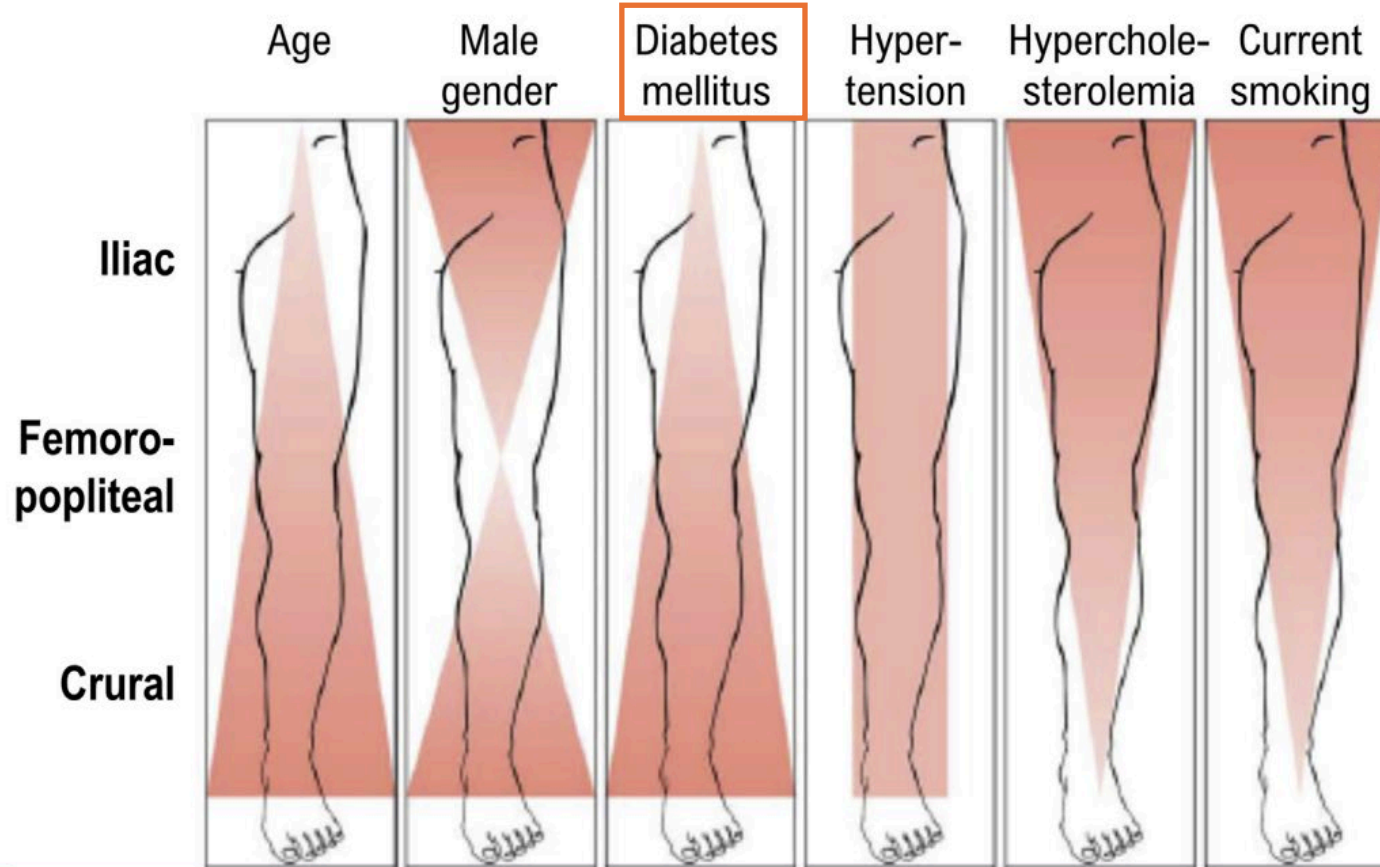
Data are n (interquartile range). †Because arterial segment disease was bilaterally similar, only one side (left) is used for analysis.

Nei pazienti diabetici **il coinvolgimento delle arterie sotto il ginocchio** era maggiore rispetto ai non diabetici, e la malattia infra-poplitea era correlata a **un rischio maggiore di amputazione.**

When is a technically successful peripheral angioplasty effective in preventing above-the-ankle amputation in diabetic patients with critical limb ischaemia?

*«In patients with diabetes, PTA is effective in avoiding major amputation, provided **recanalization occurs in at least one tibial artery down to the foot...**»*

Associazione dei fattori di rischio con i modelli di patologia aterosclerotica



Foot artery disease?

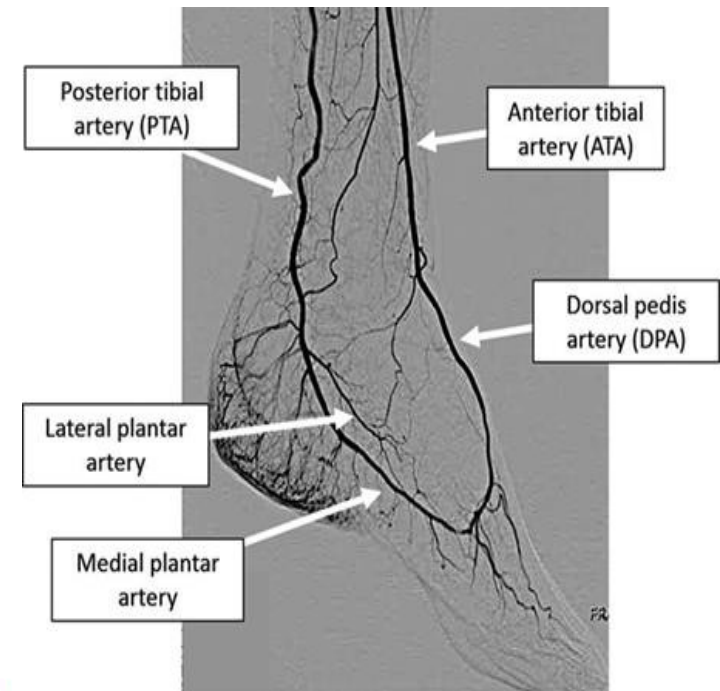
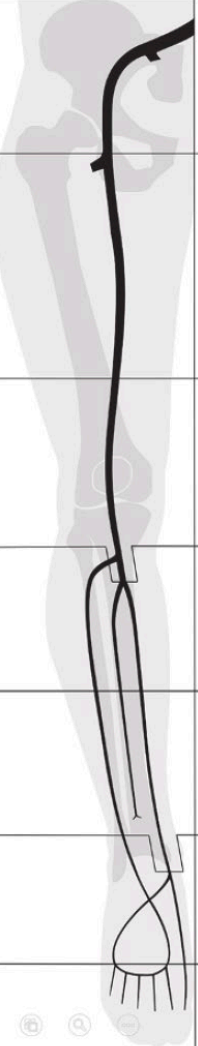


Fig 2.3. Association of risk factors with the level of atherosclerotic target lesions. The red overlay on the anatomic cartoon illustrates the association of risk factor with patterns of atherosclerotic disease.²¹⁷ (Reprinted from Diehm N, Shang A, Silvestro A, Do DD, Dick F, Schmidli J, et al. Association of cardiovascular risk factors with pattern of lower limb atherosclerosis in 2659 patients undergoing angioplasty. Eur J Vasc Endovasc Surg 2006;31:59-63.)

Arterie del piede: attori protagonisti o spettatori?

Aggregated segments		Prevalence of disease (%)	Risk factors for CLI Odds Ratio (95% CI)
ATG		9.8	0.53 (0.26-1.1)
SFA		45.5	0.51 (0.29-0.89)
P-TPT		46.3	1.17 (0.68-2.01)
Prox BTK vessels		0 artery 14.3 1 artery 24.3 2 arteries 37.7 3 arteries 23.7	0 artery ref. 1 artery 1.7 (0.76-3.83) 2 arteries 1.86 (0.72-4.83) 3 arteries 4.84 (1.12-20.88)
Dist BTK vessels		0 artery 13.2 1 artery 25.5 2 arteries 44.9 3 arteries 16.4	0 artery ref. 1 artery 1.69 (0.74-3.87) 2 arteries 5.81 (1.91-17.62) 3 arteries 5.71 (1.03-31.78)
Big FAD		0 artery 27.9 1 artery 20.2 2 arteries 31.5 3 arteries 20.4	Any of Plantars, Dorsalis Pedis and SAD 13.25 (1.69-104.16)
SAD		25.1	



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ORIGINAL ARTICLE

RECENT DEVELOPMENTS IN THE MANAGEMENT OF THE DIABETIC FOOT

BAD transmission and SAD distribution: a new scenario for critical limb ischemia

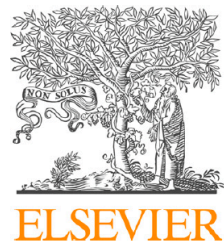
Roberto FERRARESI ¹ *, Giovanni MAURI ², Fabrizio LOSURDO ³, Nicola TROISI ⁴,
Diego BRANCACCIO ⁵, Carlo CARAVAGGI ⁶, Luca NERI ⁷

1915 angiogrammi

- 80% *foot artery disease*
- La «*foot artery disease*» era associata a un modello più severo di ischemia critica d'arto (RR 13.25)
- Diabete e dialisi risultavano associati alla *foot artery disease*

Arterie del piede*: attori protagonisti nelle ulcere diabetiche ischemiche

DIABETES RESEARCH AND CLINICAL PRACTICE 152 (2019) 9–15



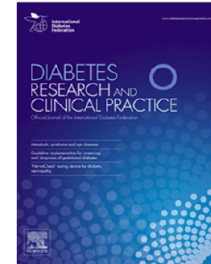
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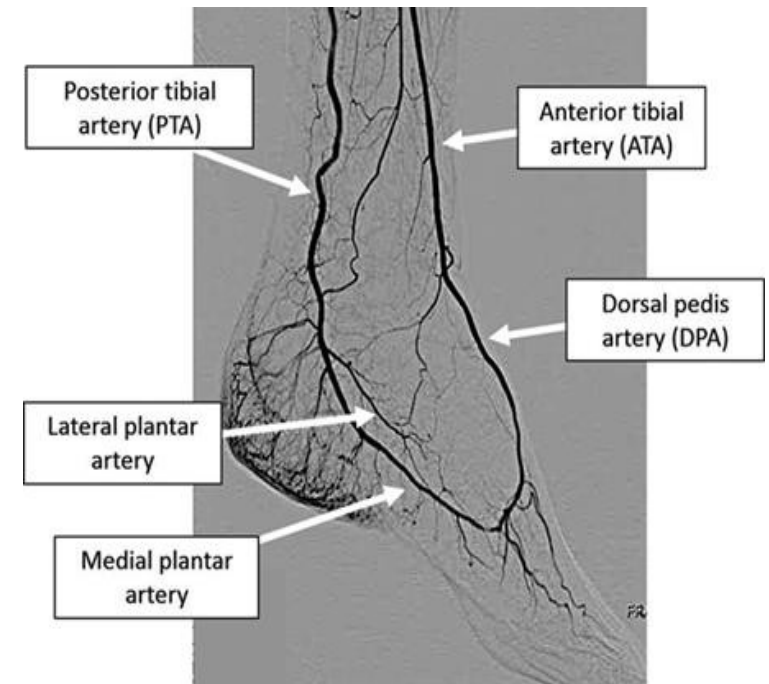


International
Diabetes
Federation



Below-the-ankle arterial disease severely impairs the outcomes of diabetic patients with ischemic foot ulcers

Marco Meloni^{a,*}, Valentina Izzo^a, Laura Giurato^a, Roberto Gandini^b, Luigi Uccioli^a



*arteria pedidia, arterie plantari (laterale e mediali)

Arterie del piede*: attori protagonisti nelle ulcere diabetiche ischemiche

- La **patologia vascolare sotto la caviglia (BTA)** è stata riscontrata nel **44%** dei pazienti
- Il **50%** dei pazienti presentava insufficienza renale terminale (**dialisi**)
- La malattia arteriosa sotto la caviglia (BTA) comporta un tasso **più elevato di amputazioni maggiori** (18,3% contro 6,6%) e di **mortalità** (16,7% contro 10,5%) rispetto alla malattia arteriosa sopra la caviglia
- La malattia arteriosa sotto la caviglia (BTA) è risultata un **fattore predittivo** indipendente di **mancata guarigione e amputazione**

Campione : 272 pazienti

Meloni M et al. Below-the-ankle arterial disease severely impairs the outcomes of diabetic patients with ischemic foot ulcers. Diabetes Res Clin Pract. 2019

TRATTAMENTO DELLA FOOT ARTERY DISEASE



Journal of
Clinical Medicine



Article

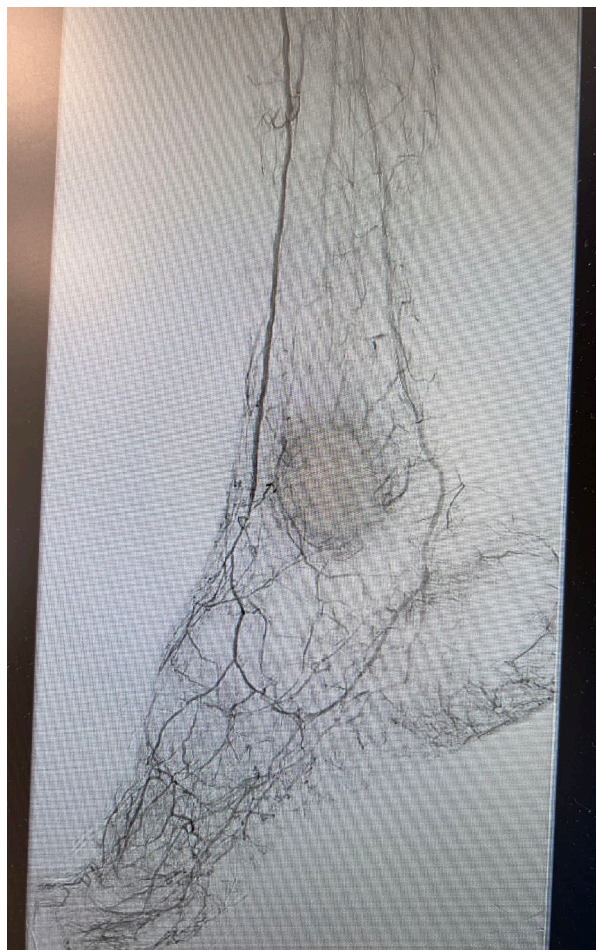
Foot Revascularization Avoids Major Amputation in Persons with Diabetes and Ischaemic Foot Ulcers

Marco Meloni ^{1,*}, Daniele Morosetti ², Laura Giurato ¹, Matteo Stefanini ³, Giorgio Loreni ^{4,5}, Marco Doddi ⁴, Andrea Panunzi ¹, Alfonso Bellia ¹, Roberto Gandini ², Enrico Brocco ⁵, José Luis Lazaro-Martinez ⁶, Davide Lauro ¹ and Luigi Uccioli ¹

- Quale approccio è più indicato per la malattia vascolare sotto la caviglia?
- È utile la ricanalizzazione dell'arteria del piede?

TRATTAMENTO DELLA FOOT ARTERY DISEASE

**SUCCESSO DELLA
RIVASCOLARIZZAZIONE**

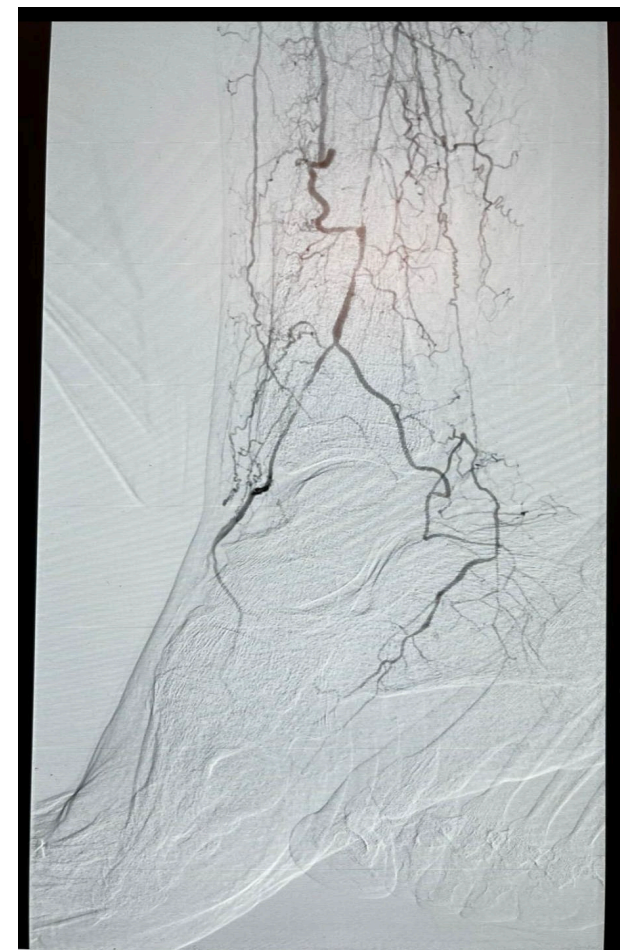


VS

**SUCCESSO PARZIALE DELLA
RIVASCOLARIZZAZIONE**



**FALLIMENTO DELLA
RIVASCOLARIZZAZIONE**



TRATTAMENTO DELLA FOOT ARTERY DISEASE



Journal of
Clinical Medicine



Article

Foot Revascularization Avoids Major Amputation in Persons with Diabetes and Ischaemic Foot Ulcers

Marco Meloni ^{1,*}, Daniele Morosetti ², Laura Giurato ¹, Matteo Stefanini ³, Giorgio Loreni ^{4,5}, Marco Doddi ⁴, Andrea Panunzi ¹, Alfonso Bellia ¹, Roberto Gandini ², Enrico Brocco ⁵, José Luis Lazaro-Martinez ⁶, Davide Lauro ¹ and Luigi Uccioli ¹

Esiti della rivascolarizzazione delle arterie del piede, sia in caso di successo che di insuccesso, in pazienti con arteriopatia sotto la caviglia:

- **GUARIGIONE** (89.3 vs. 9.1%, $p < 0.0001$)
- **AMPUTAZIONE MAGGIORE** (2.1 vs. 36.3%, $p < 0.0001$)



Article

Foot Revascularization Avoids Major Amputation in Persons with Diabetes and Ischaemic Foot Ulcers

Marco Meloni ^{1,*}, Daniele Morosetti ², Laura Giurato ¹, Matteo Stefanini ³, Giorgio Loreni ^{4,5}, Marco Doddi ⁴, Andrea Panunzi ¹, Alfonso Bellia ¹, Roberto Gandini ², Enrico Brocco ⁵, José Luis Lazaro-Martinez ⁶, Davide Lauro ¹ and Luigi Uccioli ¹

«Il **fallimento della rivascolarizzazione delle arterie del piede** si è rivelato un fattore predittivo indipendente di **mancata guarigione, amputazione minore e amputazione maggiore.**»

Dalla patologia vascolare sotto il ginocchio alla patologia vascolare sotto la caviglia

2007

«In patients with diabetes, PTA is effective in avoiding major amputation, provided recanalization occurs in at least one tibial artery down to the foot...»

2021

«Foot revascularization is mandatory to achieve healing and avoid major amputation in persons with ischaemic DFU and BTA arterial disease»

ORIGINAL ARTICLE

RECENT DEVELOPMENTS IN THE MANAGEMENT OF THE DIABETIC FOOT

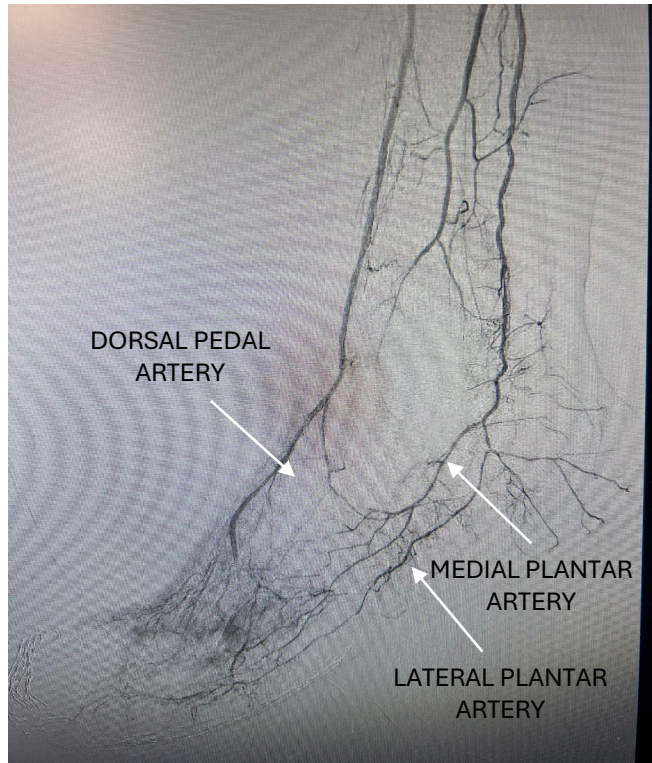
BAD transmission and SAD distribution: a new scenario for critical limb ischemia

Roberto FERRARESI ^{1 *}, Giovanni MAURI ², Fabrizio LOSURDO ³, Nicola TROISI ⁴,
Diego BRANCACCIO ⁵, Carlo CARAVAGGI ⁶, Luca NERI ⁷

Nei soggetti affetti da ischemia critica degli arti inferiori, è importante riconoscere **due diversi modelli** patologici: **la malattia delle grandi arterie (Big Artery Disease, BAD)** e la malattia delle **piccole arterie (Small Artery Disease, SAD)**, che contribuiscono al network vascolare del piede.

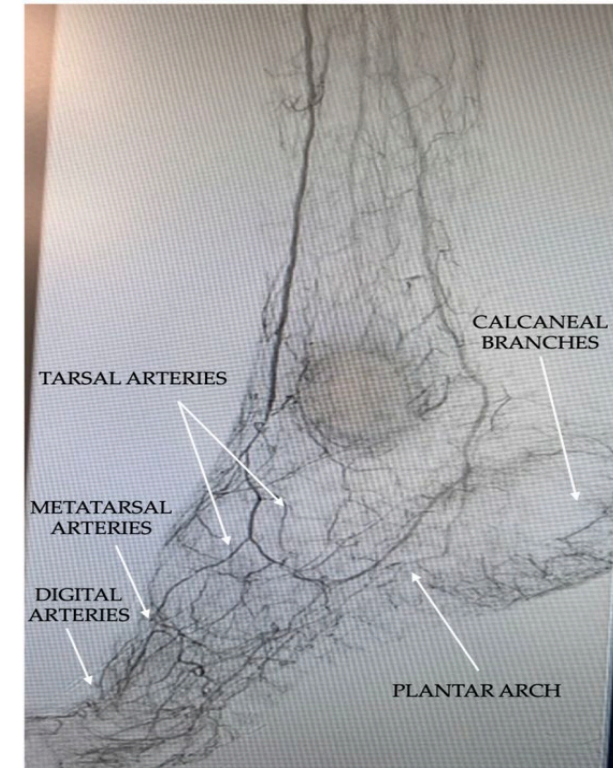
NETWORK VASCOLARE DEL PIEDE

«BIG ARTERIES»



**RESPONSABILI DELLA TRASMISSIONE DEL
FLUSSO SANGUIGNO**

«SMALL ARTERIES»



**RESPONSABILI DELLA DISTRIBUZIONE DEL
FLUSSO SANGUIGNO**

SMALL ARTERY DISEASE

- Malattia misteriosa (non macrovascolare, non microvascolare), dati scarsi
- Prevalenza stimata del 25% nelle persone con arteriopatia periferica
- Associazione con diabete e insufficienza renale terminale (ESRD)
- «Undruggable disease»



Small Artery Disease in Persons with Diabetic Foot Ulcers: Incidence, Characteristics, and Outcomes

The International Journal of Lower
Extremity Wounds
1-8

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MaryAnn Liebert

A Part of Sage

Valutare l'impatto della “Small Artery Disease” nei
pazienti con piede diabetico ischemico

ASSENZA DI SMALL ARTERIES



GRUPPO DI STUDIO

Meloni M, Morosetti D, Uccioli L et al, 2026 IJLEW

PRESENZA DI SMALL ARTERIES



GRUPPO DI CONTROLLO

RISULTATI (dati generali)

- **Popolazione:** 128 pazienti, 80 (62.5%) con SAD e 48 (37.5%) senza
- **Età media:** 70.3 ± 11.1 anni
- **Sesso:** 71.8% uomini
- **Tipo di diabete (2):** 81.1%
- **Durata media del diabete:** 24.3 ± 12.4 anni

RISULTATI (dati baseline)

Table 2. Baseline Characteristics of the Whole Population, Study and Control Group.

Variables	Whole population (n = 128)	SAD group (n = 80)	Not SAD group (n = 48)	P value
Age (years)	70.3 ± 11.1	72.4 ± 9.5	66.1 ± 13	.03
Sex (male)	92 (71.8)	57 (71.2)	35 (72.9)	.4
Diabetes (type 2), n (%)	104 (81.5)	67 (83.7)	35 (72.9)	.07
Diabetes duration (years)	24.3 ± 12.4	25.8 ± 13	21.8 ± 11.4	.06
Hypertension, n (%)	119 (92.9)	75 (93.7)	44 (91.7)	.4
Dyslipidemia, n (%)	107 (83.6)	68 (85)	39 (81.3)	.3
Active smoke, n (%)	13 (10.1)	9 (11.2)	4 (8.3)	.2
Dialysis, n (%)	34 (26.6)	24 (30)	10 (20.8)	.02
IHD, n (%)	83 (64.8)	64 (80)	19 (40)	.0002
Ulcer size (<5 cm ²), n (%)	114 (89.1)	71 (88.7)	43 (89.5)	.2
Infection, n (%)	89 (69.5)	55 (68.7)	34 (70.8)	.5
Deep to the bone, n (%)	75 (58.6)	47 (58.7)	28 (58.3)	.1
Gangrene	91 (71.1)	64 (80)	27 (56.2)	.001
BTK arterial disease	128 (100)	80 (100)	48 (100)	NS
BTA arterial disease (pedal and/or plantar arteries)	110 (85.9)	72 (90)	38 (79.2)	.08
TcPO2 (baseline)	20 ± 10	16 ± 9	27 ± 11	.03
TcPO2 (after revascularization)	39 ± 9	34 ± 8	48 ± 10	.02

Abbreviations: SAD, small artery disease; IHD, ischaemic heart disease; BTK, below-the-knee; BTA, below-the-ankle; TcPO2, transcutaneous pressure of oxygen.

RISULTATI (esiti a 1 anno)

Table 3. Outcomes of the Whole Population, Study Group and Control Group.

Outcomes	Whole population N= 128	SAD yes N= 80	SAD no N= 48	P value
Healing (%)	70.3	57.1	90.9	<.0001
Minor amputation (%)	67.2	80	45.4	<.0001
Major amputation (%)	9.3	10	4.1	.02
Mortality (%)	9.4	15	0	.003

Abbreviations: SAD, small artery disease.

RISULTATI (analisi multivariata)

ASSENZA DI GUARIGIONE

- SAD [OR 5.6, CI95%(2.4-13.3),p=0.0001]
- End-stage-renal-disease [OR 3.1, CI95%(1.5-8.7),p=0.002]

AMPUTAZIONE MAGGIORE

- SAD [OR 2.8, CI95%(1.6-8.5),p=0.003]
- Revascularization failure [OR 2.2, CI95%(1.5-6.8),p=0.003]

SMALL ARTERY DISEASE

Original Article

Small Artery Disease as a Predictor of Wound Healing in Patients with Diabetic Foot After Revascularization

The International Journal of Lower
Extremity Wounds
2025, Vol. 24(3) 621–629
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The presence of **SAD** was significantly associated with long-term **unhealed DFUs** and the risk of lower limb **amputations**.



Review

Peripheral Arterial Disease in Diabetic Foot: One Disease with Multiple Patterns

Marco Meloni ^{1,2,*}  and Prashanth R. J. Vas ^{3,4,5}

Una caratterizzazione più precisa della vasculopatia periferica nel diabete è fondamentale per sviluppare **strategie di trattamento efficaci e personalizzate**, migliorando in definitiva gli esiti per i pazienti e riducendo il peso delle complicanze del piede diabetico.

Alla luce di queste complessità, **non è sufficiente un unico termine**, "arteriopatia periferica", per descrivere una gamma così diversificata di quadri patologici.

Questa eccessiva semplificazione può essere pericolosa, in quanto **può portare ad approcci terapeutici inadeguati** e a un'assistenza al paziente non ottimale.



Review

Peripheral Arterial Disease in Diabetic Foot: One Disease with Multiple Patterns

Marco Meloni ^{1,2,*}  and Prashanth R. J. Vas ^{3,4,5}

Table 1. Pattern of peripheral arterial disease in patients with ischaemic diabetic foot ulcers.

Pattern 1	Pattern 2	Pattern 3
• Presence of below-the-knee arterial disease (anterior tibial artery, posterior tibial artery, and peroneal artery) • Presence or absence of above-the-knee arterial disease (iliac arteries, femoral arteries, popliteal artery, and tibio-peroneal trunk) • Absence of below-the-ankle arterial disease	• Presence of below-the-ankle arterial disease (pedal artery, medial plantar artery, and lateral plantar artery) • Presence or absence of below-the-knee and above-the-knee arterial disease • Absence of small arterial disease	• Presence of small artery disease (plantar arch, digital, metatarsal, tarsal, and calcaneal branches) • Presence or absence of below-the-ankle and below-the-knee arterial disease

Pattern 1

- Presence of below-the-knee arterial disease (anterior tibial artery, posterior tibial artery, and peroneal artery)
- Presence or absence of above-the-knee arterial disease (iliac arteries, femoral arteries, popliteal artery, and tibio-peroneal trunk)
- Absence of below-the-ankle arterial disease

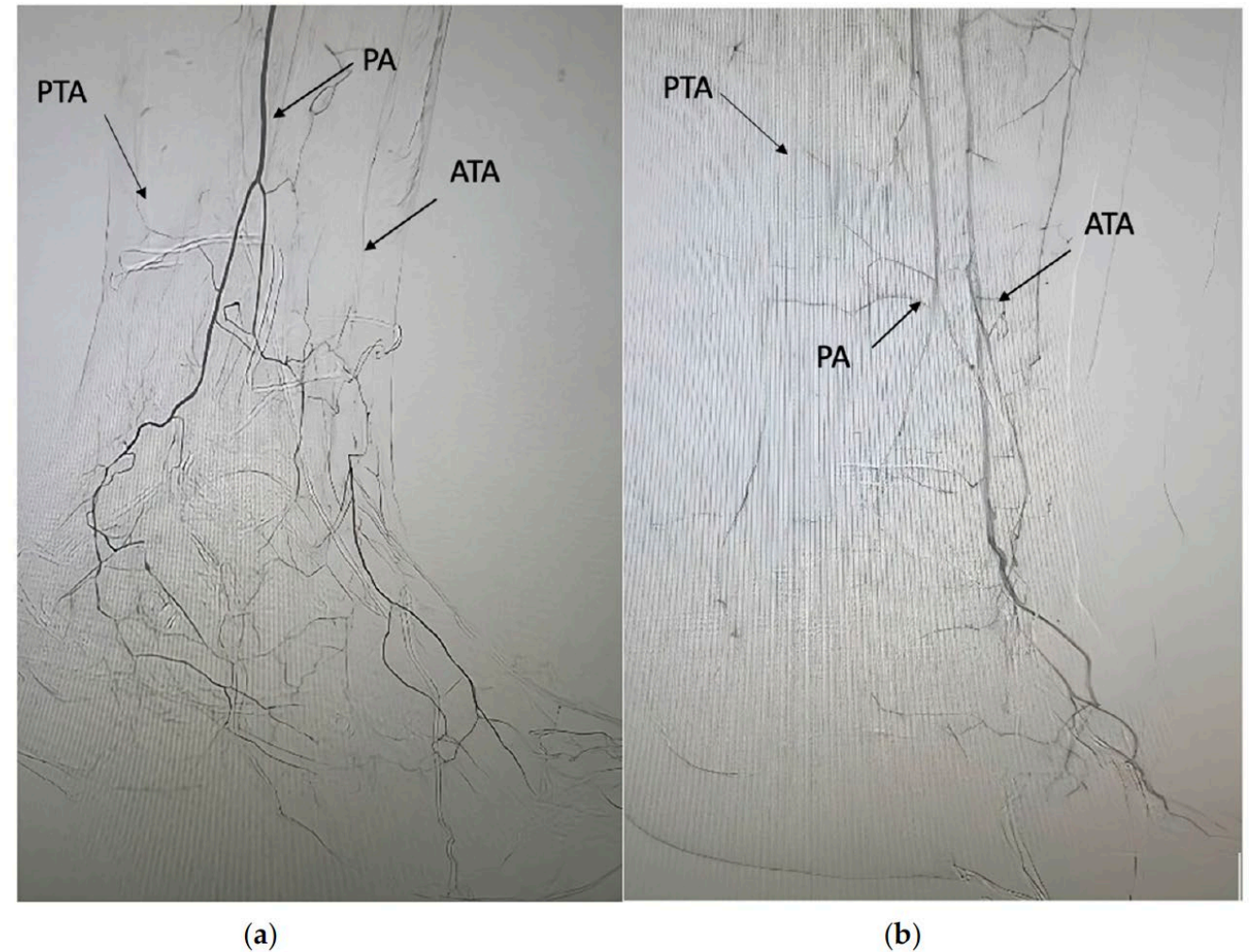


Figure 2. (a). Arterial disease with occlusion of anterior tibial (ATA) and posterior tibial artery (PTA). Foot perfusion is partially ensured by the peroneal artery (PA). (b). Arterial disease with occlusion of the posterior tibial artery (PTA) and stenosis of the distal part of the peroneal artery (PA). Foot perfusion is partially ensured by the anterior tibial artery (ATA) presenting some distal stenosis.

Pattern 2

- Presence of below-the-ankle arterial disease (pedal artery, medial plantar artery, and lateral plantar artery)
 - Presence or absence of below-the-knee and above-the-knee arterial disease
 - Absence of small arterial disease
-

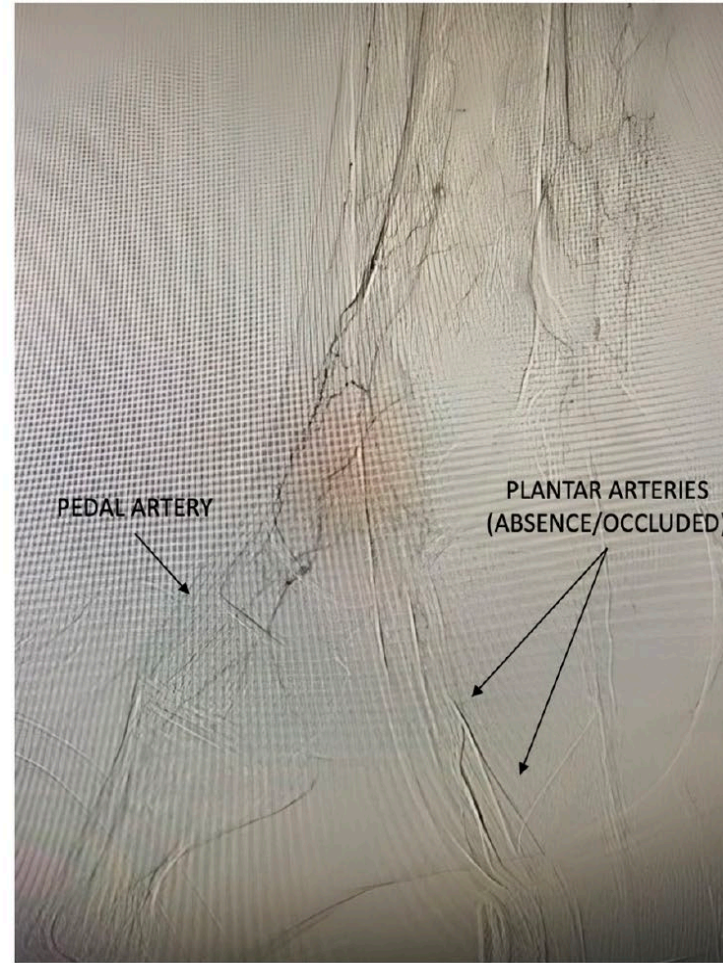


Figure 3. Below-the-ankle arterial disease with the absence/occlusion of the pedal and plantar arteries in a patient presenting an open tibial artery.

Pattern 3

- Presence of small artery disease (plantar arch, digital, metatarsal, tarsal, and calcaneal branches)
 - Presence or absence of below-the-ankle and below-the-knee arterial disease
-



Figure 5. (a) Gangrene of forefoot in a patient with small artery disease (grade 3) with preserved major foot arteries after revascularisation procedure (b). Despite revascularisation, there is an absence of visible flow into the digital and metatarsal arteries. (b).

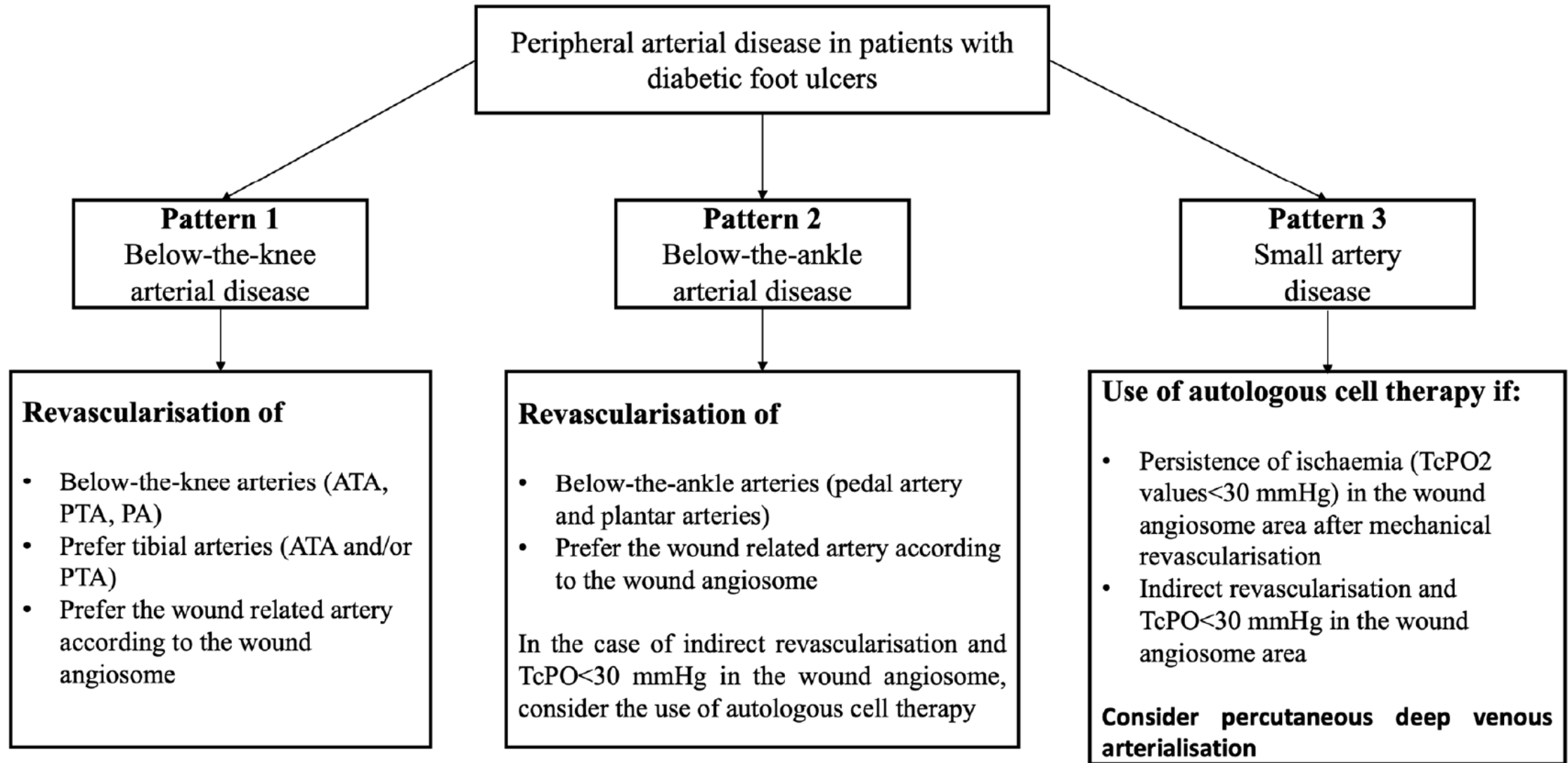


Figure 7. Suggested algorithm of treatment according to the different patterns of PAD.



Incidence and causes of major amputation in patients with diabetic foot ulcers: data from a retrospective study

Table 2 Causes of major amputation

Variable	Values (N= 30)
Untreatable CLTI (revascularization failure) n (%)	17 (56.7)
Calcaneus osteomyelitis n (%)	5 (16.7)
Necrotizing fasciitis n (%)	5 (16.7)
Tarsal osteomyelitis n (%)	3 (10)

- Sample: 1226 patients
- Major amputation rate: 2.4%

Critical limb ischaemia with mechanical failure of revascularization was the main cause of major amputation

VASCULOPATIA PERIFERICA NEGLI AMPUTATI



Patterns of Arterial Obstruction in Chronic Limb-Threatening Ischemia: A Comprehensive Histopathological Analysis of Amputated Limbs

Questo studio ha indagato i **modelli isto-patologici di ostruzione vascolare** nei pazienti con CLTI sottoposti ad **amputazione maggiore per malattia vascolare non trattabile**

Ucci A, Massoni CB, Perini P et al. Patterns of Arterial Obstruction in Chronic Limb-Threatening Ischemia: A Comprehensive Histopathological Analysis of Amputated Limbs. Ann Vasc Surg. 2026

VASCULOPATIA PERIFERICA NEGLI AMPUTATI (pattern istologico)

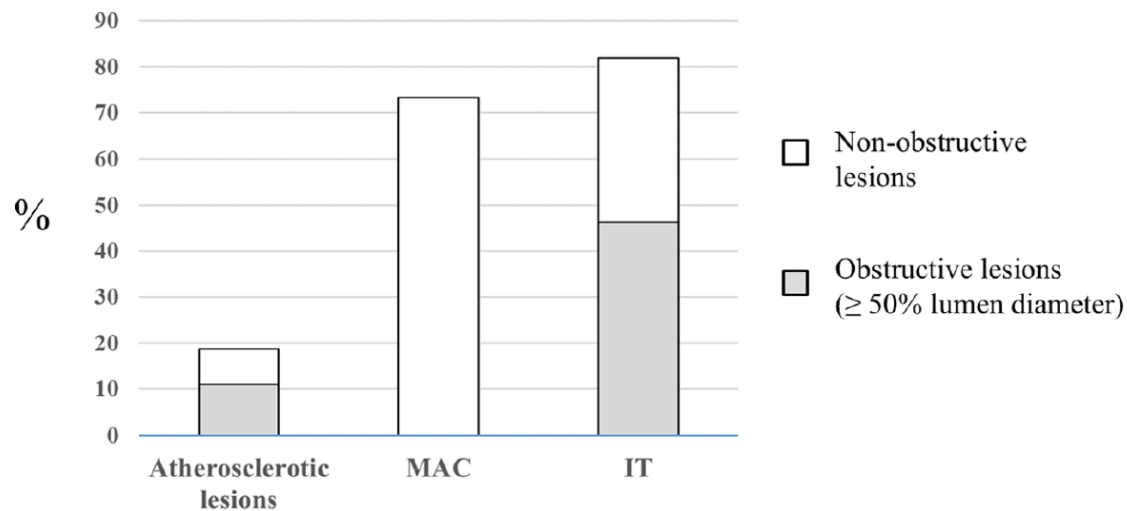
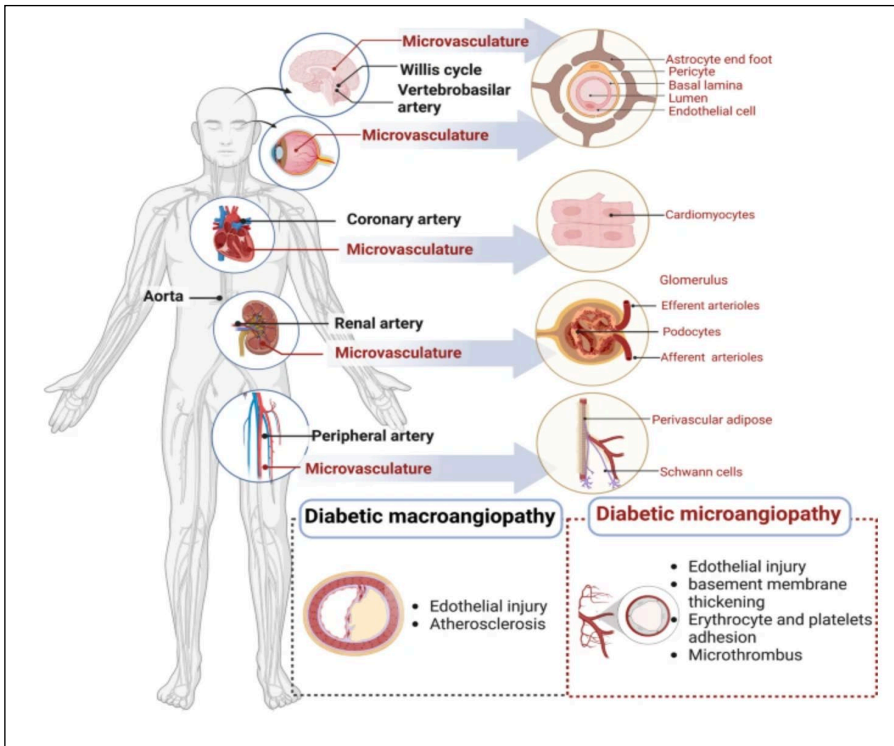


Fig. 1. Prevalence of lesion patterns in 310 arterial segments.

- **Atherosclerosis was present in 18.7%** of the segment, medial arterial calcification (**MAC**) in **73.2%**, and **intimale thickening (IT)** in **81.9%**.
- Arterial obstruction in CLTI results from both, atherosclerosis and MAC-IT, with MAC-IT predominating in distal arteries
- Our findings **challenge the traditional atherocentric view of PAD**, confirming that **MAC-IT is a dominant contributor to perfusion failure** in CLTI

VASCULOPATIA PERIFERICA NEGLI AMPUTATI (pattern clinico-anatomico)



AMPUTATI VS NON AMPUTATI

- N° vasi affetti (6.3 ± 1.8 vs 4.1 ± 1.5 $p=0.002$)
- Vasi di gamba (100 vs 77.8%, $p=0.0001$)
- Vasi del piede (big arteries) (95 vs 35%, $p<0.0001$)
- Small artery disease (70 vs 47.8%, $p=0.0001$)

Il quadro vascolare mostra pertanto nei pazienti amputati una distribuzione **multi-segmentale**, risultando **più aggressivo sia a livello macrovascolare che microvascolare** (*Panvasculopathy* *Diabetic Foot Disease, PDFD*).

CONCLUSIONI

- Evoluzione del piede diabetico negli ultimi 20 anni con **prevalenza del pattern vascolare**
- Evoluzione dell'arteriopatia periferica con un coinvolgimento **ultra-distale**
- La vasculopatia periferica nel paziente con piede diabetico ischemico è una **panvasculopatia** con interessamento diffuso di macro e microvasi
- Il trattamento dell'arteriopatia periferica è definito dal pattern di presentazione della stessa