

L'inquadramento diagnostico e la terapia conservativa del Piede di Charcot

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IRCCS MULTIMEDICA

Sesto San Giovanni (MI)



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2023



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**Congresso
Nazionale
PIEDE DIABETICO
GDS SID-AMD**



La **S**indrome
del **piede diabetico**:
competenze
in azione
con uno sguardo
al futuro



Dichiaro che negli ultimi due anni ho avuto rapporti di consulenza scientifica con:

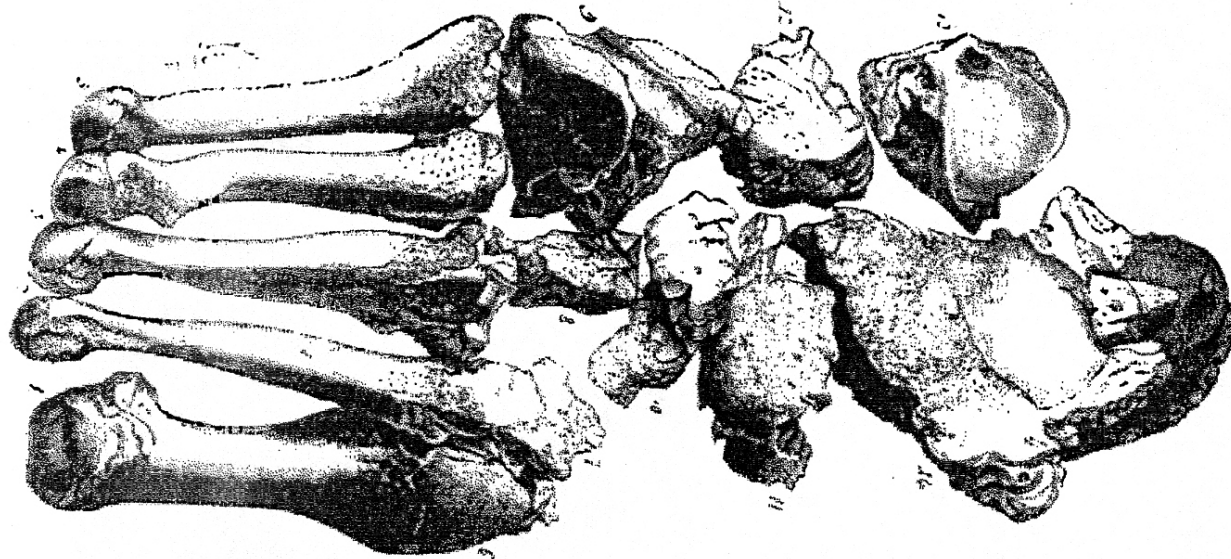
- Molteni
- Bonesupport
- Cybion

La neuroartropatia di Charcot (NAC) del piede e della caviglia è un processo clinico ad evoluzione deformante e distruttiva che può indurre marcata instabilità, lesioni ricorrenti e recidivanti, amputazioni minori e maggiori.

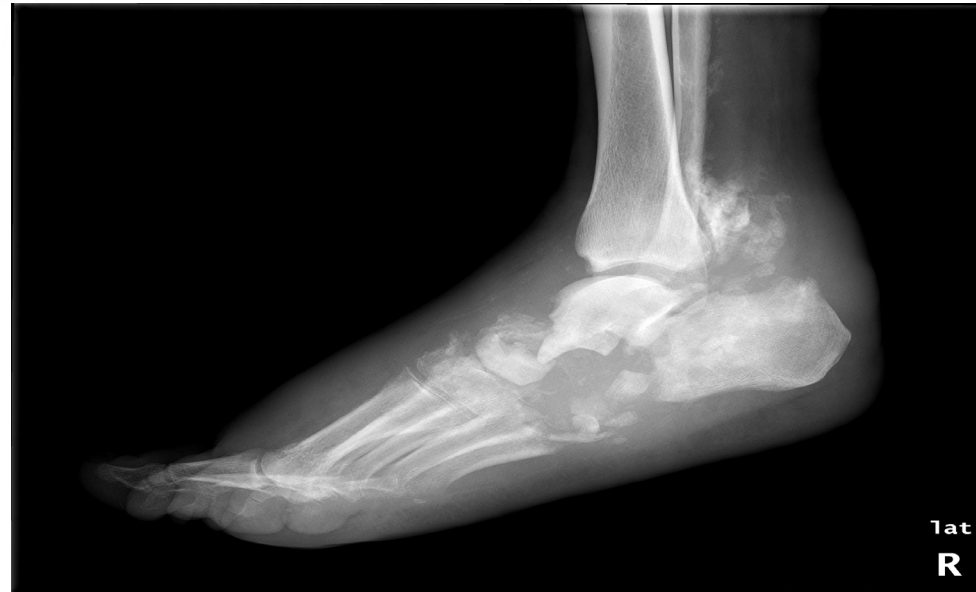
Già descritta come “artrite neuropatica” nel 1703 da Musgrave, ma definitivamente classificata da Charcot nel 1868, essa è stata associata con numerose patologie inducenti neuropatia (Lebbra, Siringomielia, esposizione a tossici, artrite reumatoide, sclerosi multipla). Tuttavia le due cause più frequentemente riconosciute alla base della NAC in **negli ultimi 50-60 anni** sono state il **diabete mellito e l'esotossicosi alcolica**.

Armstrong et al 2002; Frykberg 2006; Sanders and Frykberg 2007





Squelette d'un pied ataxique : 1, 2, 3, 4, 5, métatarsiens ; 6, 7, premier et deuxième cunéiformes soudés aux métatarsiens correspondants ; 8, fragment osseux paraissant être le troisième cunéiforme ; 9, cuboïde ; 10, 11, deux fragments du scaphoïde ; 12, 13, b. b. et corps de l'astragale ; 14, calcaneum.

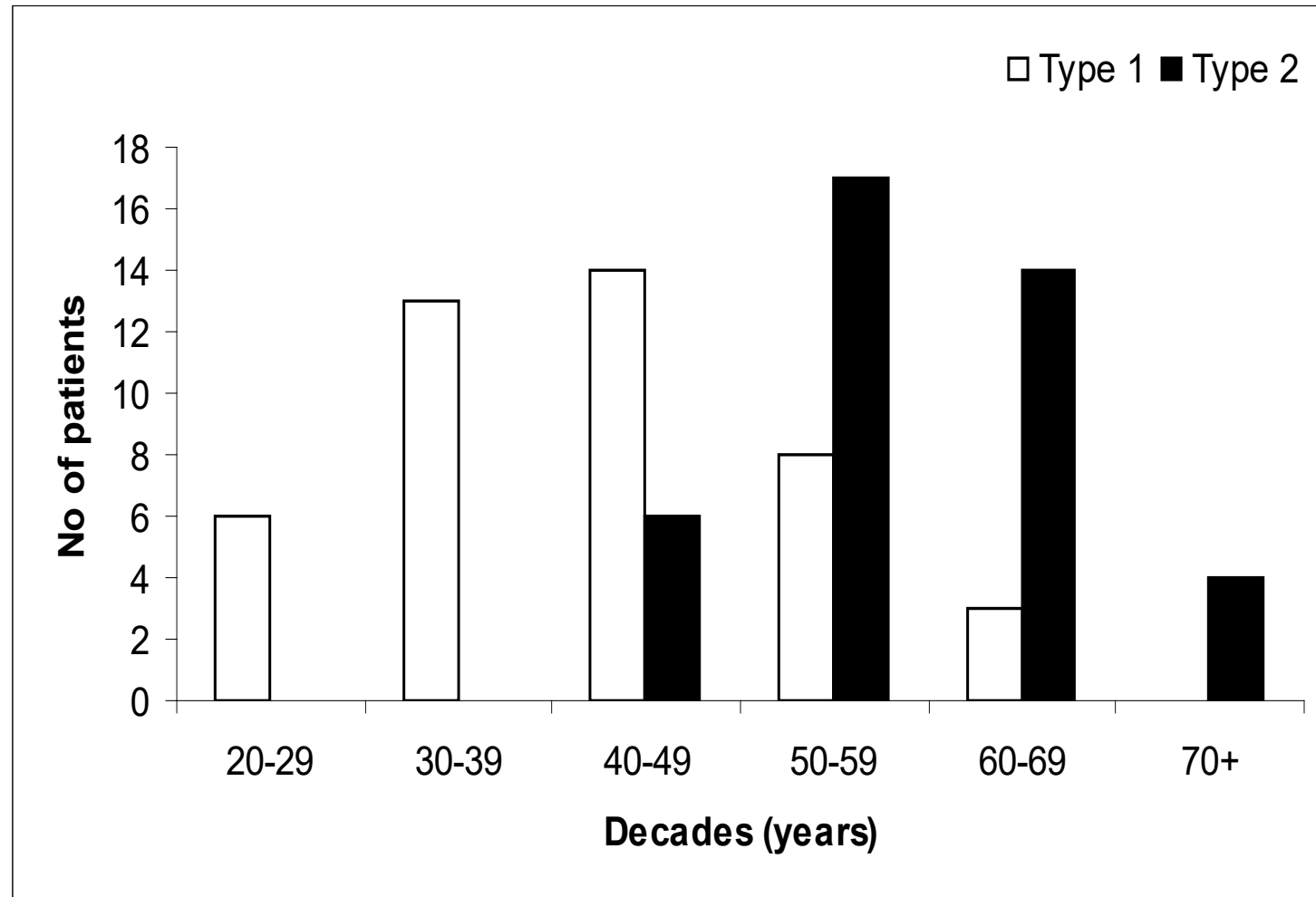


EPIDEMIOLOGIA

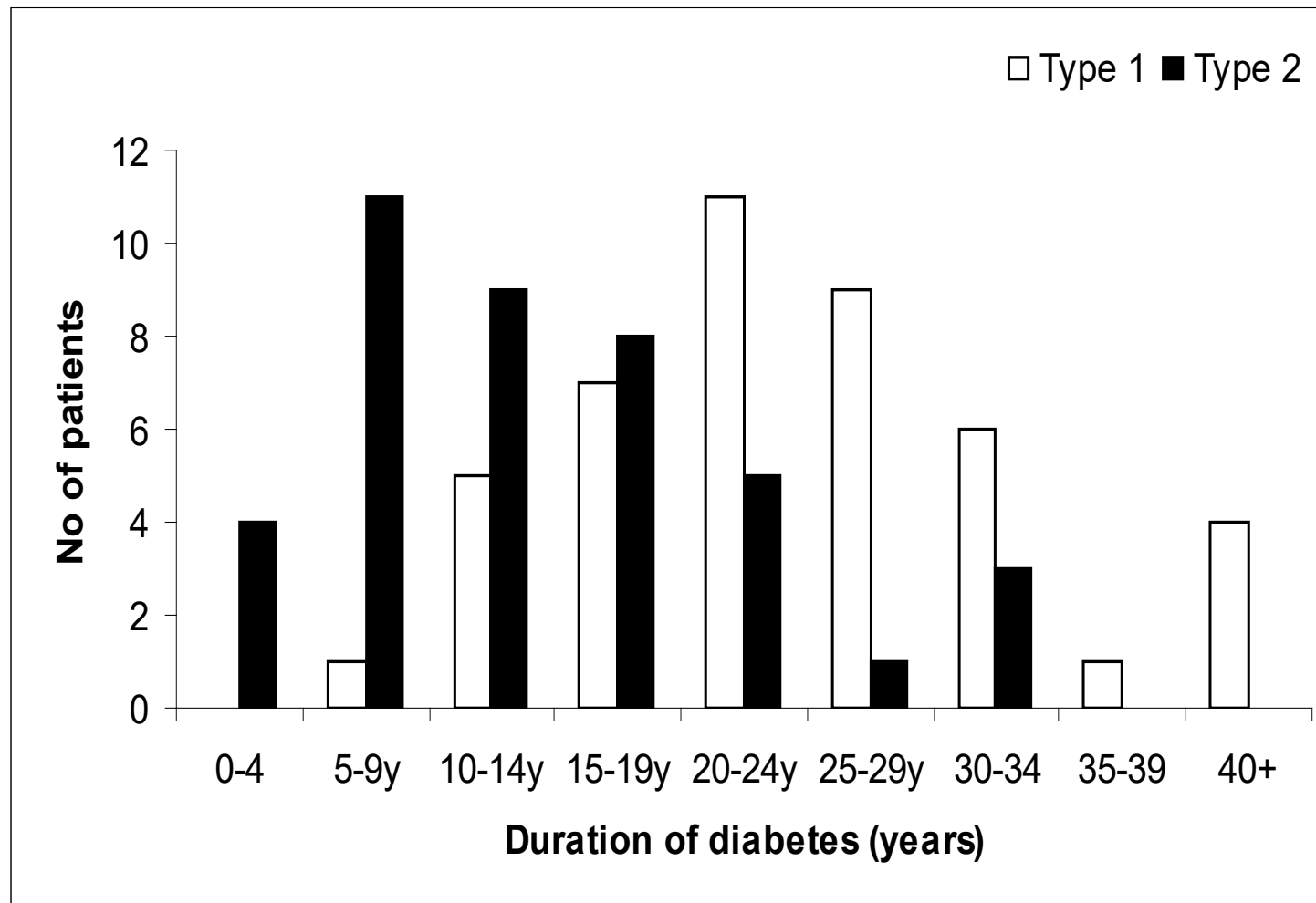
La stima di prevalenza della NAC è molto ampia, variando dallo 0,08 % al 13 % a seconda che venga considerata una popolazione diabetica generale o una popolazione afferente a Centri qualificati per la diagnosi.

Leggera prevalenza nel DMT1 rispetto al DMT2
Molto spesso da occhi non esperti la NAC può essere confusa con osteomielite, infezione acuta dei tessuti molli, gotta, artrite, frattura, neoplasia o trombosi venosa.

Age



Duration of diabetes



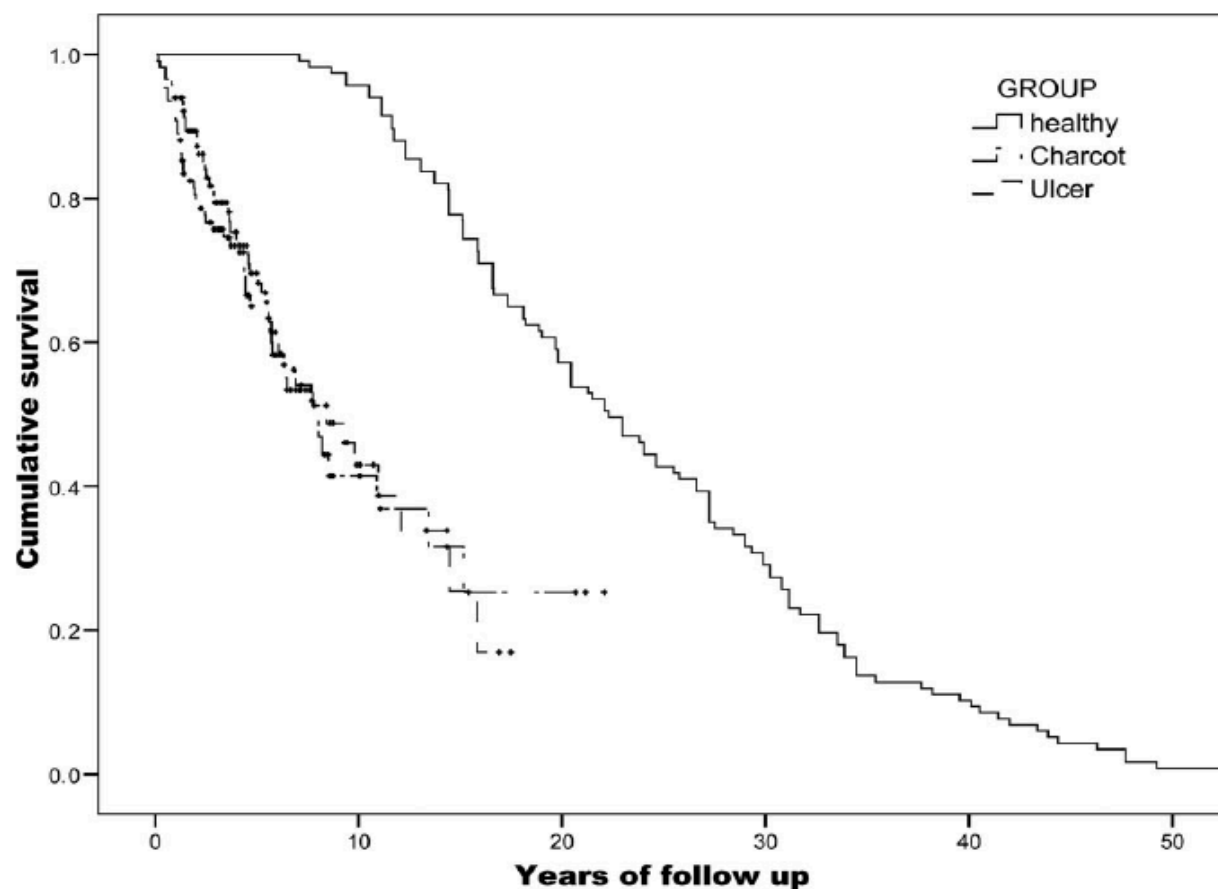
Mortality Associated With Acute Charcot Foot and Neuropathic Foot Ulceration

JULIETTE VAN BAAL, MSC^{1,2}
RICHARD HUBBARD, MD³

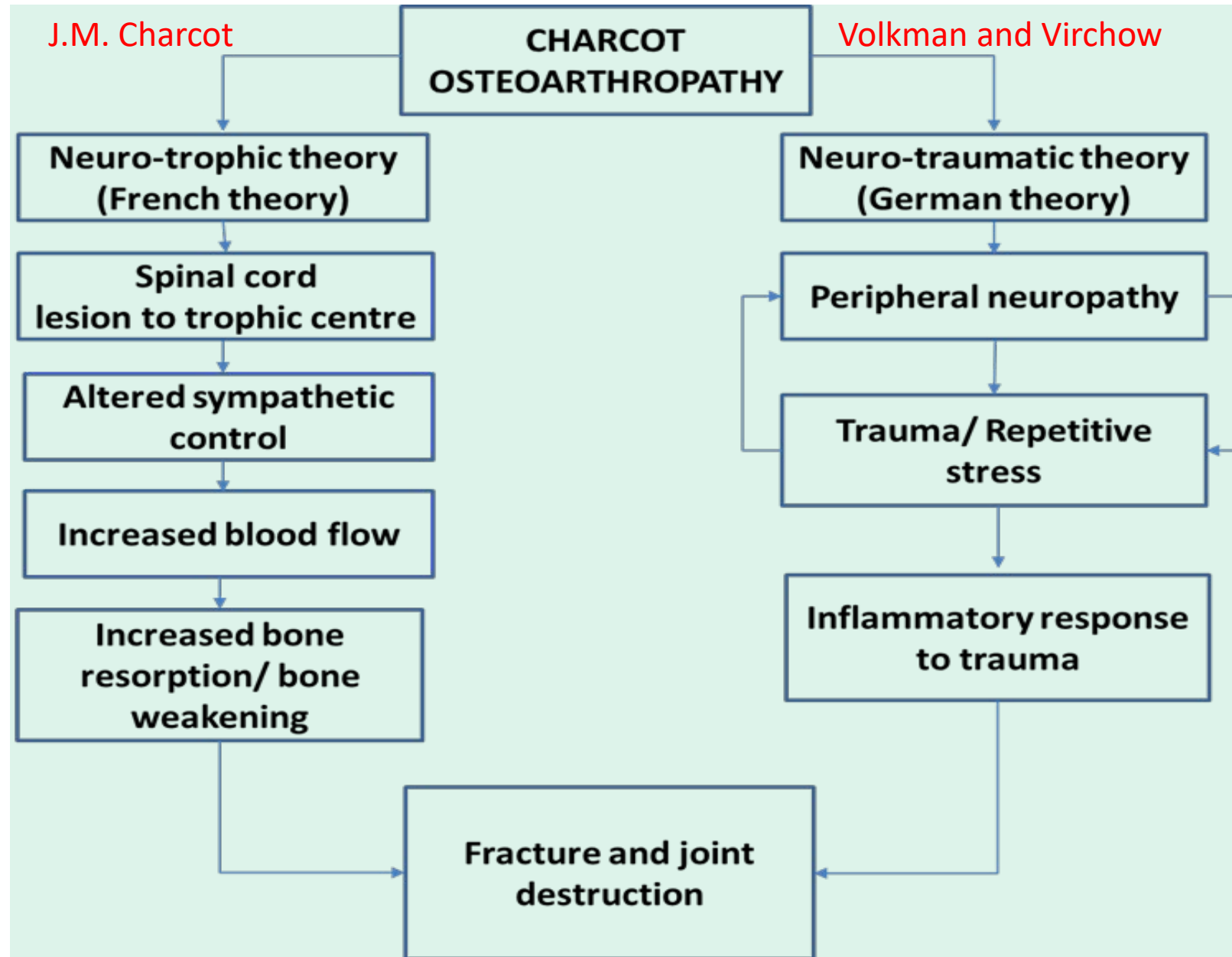
FRAN GAME, FRCP¹
WILLIAM JEFFCOATE, MRCP¹

Diabetes Care 33:1086–1089, 2010

Charcot foot and neuropathic foot ulceration



Kaplan-Meier survival curve cohort 1980–2007 versus an age- and sex-matched British population.



Therapeutics of Charcot neuroarthropathy and pharmacological mechanisms: A bone metabolism perspective

Liang Liu¹, Qiong Wang¹, Yan Zhang, Jingqi Liang, Peilong Liu and Hongmou Zhao*

Department of Foot and Ankle Surgery, Honghui Hospital of Xi'an Jiaotong University, Xi'an, China

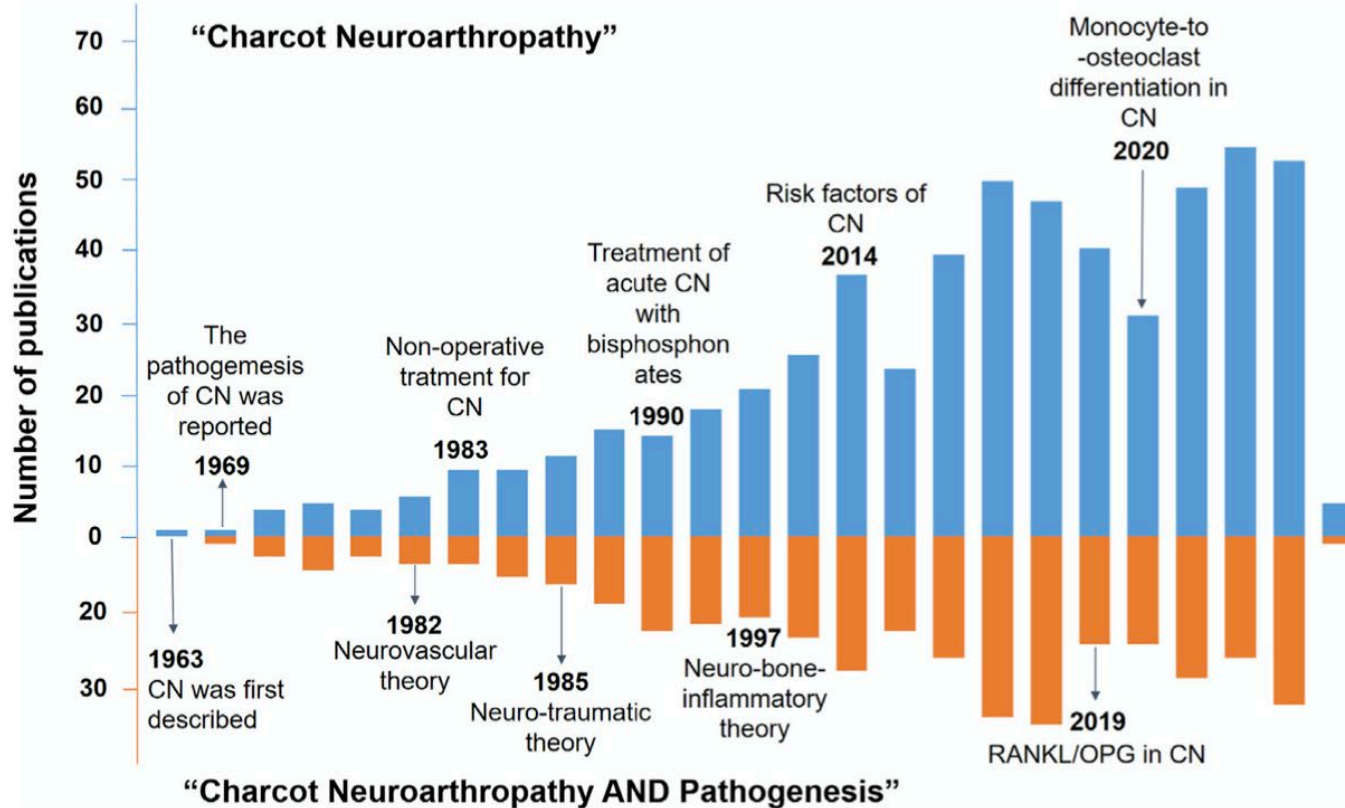
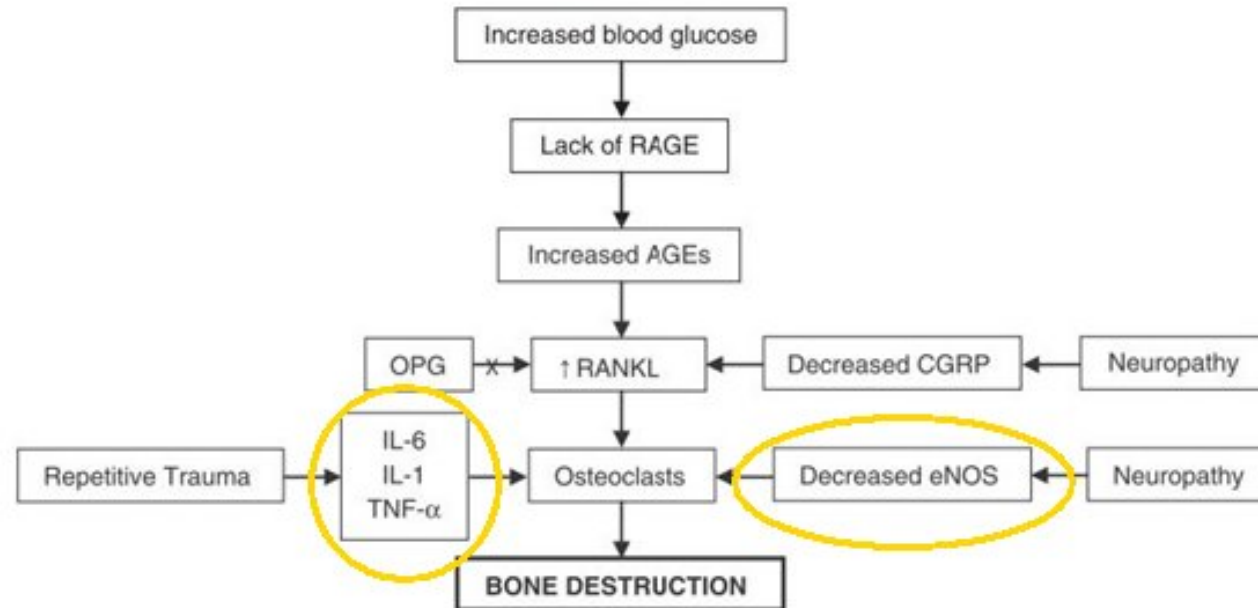


FIGURE 1
Timeline of the key development events in the knowledge (blue histogram) and pathogenesis of CN (orange histogram).

The pathogenesis of Charcot neuroarthropathy: current concepts



Novel Biomarkers Predictive of Diabetic Charcot Foot—An Overview of the Literature

Anca Bobircă ^{1,2,†}, Anca Emanuela Musetescu ^{3,†}, Anca Bordanu ^{4,*}, Anca Pantea Stoian ^{5,†}, Teodor Salmen ^{6,*}, Dan-Cristian Marinescu ⁷, Cristina Alexandru ^{1,2}, Alesandra Florescu ³, Raluca Radu ⁸, Sebastian Isac ⁹, Traian Patrascu ^{10,11}, Dragos Serban ^{11,12} and Florin Bobircă ^{10,11}

Life 2022, 12, 1944. <https://doi.org/10.3390/life12111944>

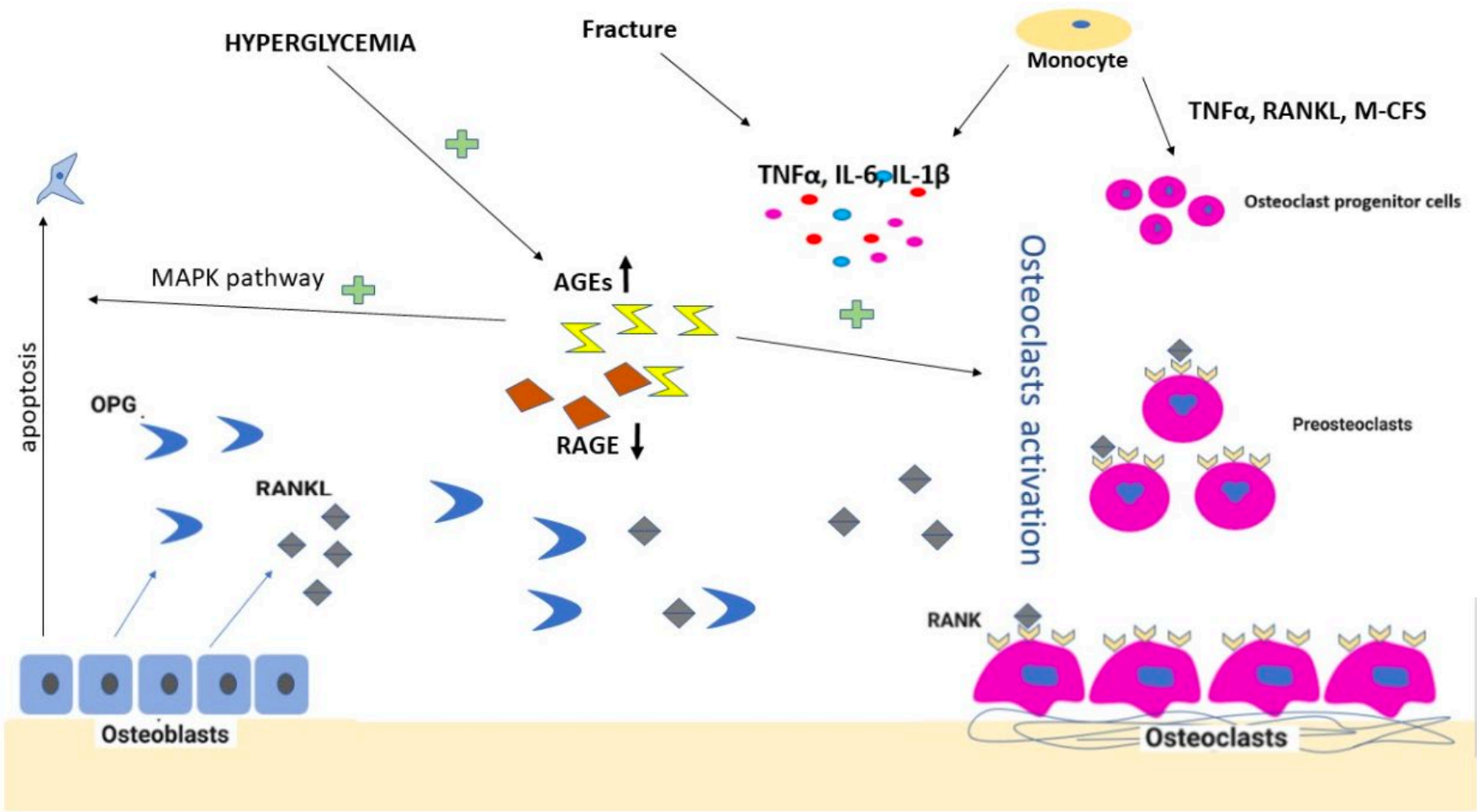


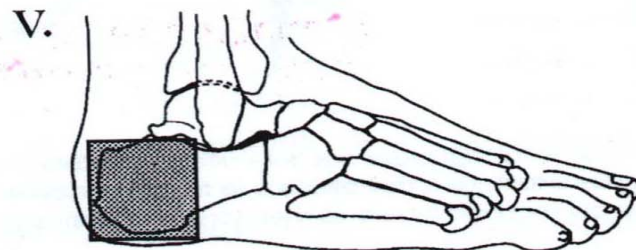
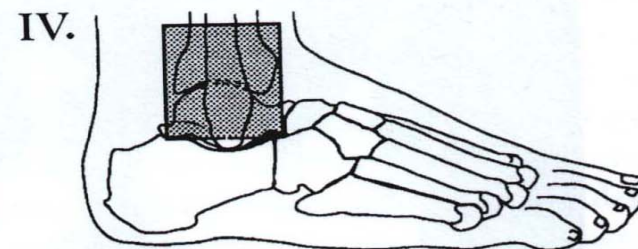
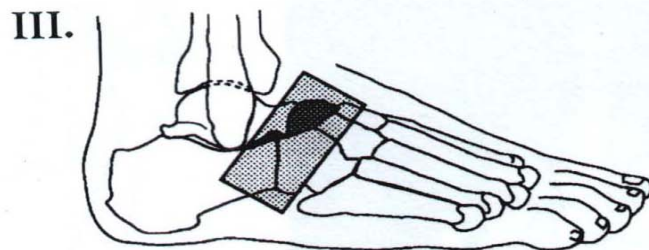
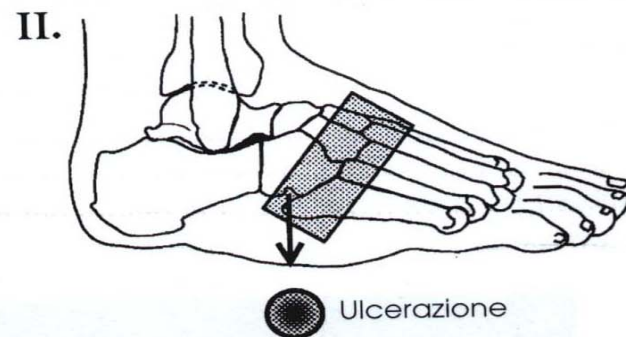
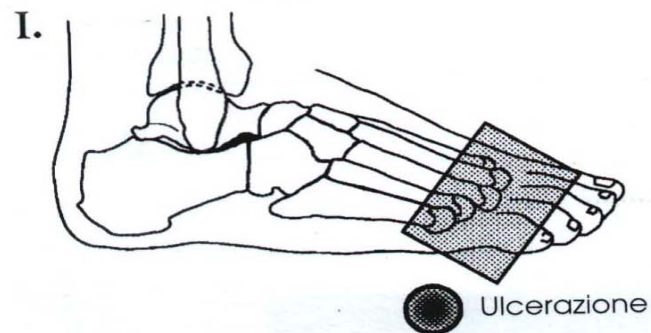
Table 4. The summarization of the biomarkers known for Charcot’s foot. C-RP = C-reactive protein; ESR = erythrocyte sedimentation rate; WCC = white blood cell count; IL-1 β = interleukin 1 beta; IL-6 = interleukin 6; TNF- α = tumor necrosis factor alpha; RANKL = receptor activator of nuclear factor kappa-B ligand; OPG = osteoprotegerin; AGE = advanced glycation end products; fsRANKL = free soluble receptor activator of nuclear factor- κ B; sRAGE = soluble receptors of advanced glycation end products; b-ALP = bone alkaline phosphatase; Dkk-1 = Dickkopf-related

s/integrated family member 1; Wif-1 = Wnt inhibitory factor 1;

	X	Osteocalcin	C-Terminal Telopeptide	b-ALP	Tartrate-Resistant Acid Phosphatase			
Petrova et al. [16]			0.24 vs. 0.12 vs. 0.15 µg/L, <i>p</i> = 0.004	16.4 vs. 13.6 vs. 10.1 µg/L, <i>p</i> = 0.006	3.9 vs. 3.9 vs. 2.7 UI/L, <i>p</i> = 0.126			
Jansen et al. [37]	387 ± 136 vs. 95 ± 83 ng/L, <i>p</i> < 0.001	16.9 ± 5.7 vs. 14.7 ± 11.5 µg/L, <i>p</i> = 0.153						
Jirkovská et al. [47]	↓, <i>p</i> < 0.03							
	Total Hip BMD	L2-L4 BMD	Calcaneal BMD	Femoral Neck BMD	Sclerostin	Dkk-1	Wnt-1	Wif-1
Folestad et al. [20]					↑	↑	↑	↑
Jansen et al. [37]	↔, <i>p</i> = 0.294	+0.036 g/cm ² (+2.9%) vs. +0.125 g/cm ² (+10.1%)						
Jirkovská et al. [47]		−0.57 ± 1.28 vs. −0.91 ± 0.84, <i>p</i> > 0.05	−3.00 ± 1.39 vs ±2.36 ± 1.12; <i>p</i> < 0.01	−1.58 ± 1.24 vs. −0.76 ± 0.98, <i>p</i> < 0.05				
Christensen et al. [48]			↓, <i>p</i> < 0.01					

Markers	Novel Biomarkers
[44]	RANKL [20,35,40,41]
[4]	OPG [20,35]
[1]	AGE [3,15,37]
[38]	fsRANKL [15,16,37]
[7,38]	sRAGE [15,37]
[8,39]	Osteocalcin [15,37]
	C-terminal telopeptide [16]
	b-ALP [16,44,47]
	Tartrate-resistant acid phosphatase [16]
	Sclerostin [20–23]
	Dkk-1 [20–23]
	Wnt-1 [20–23]
	Wif-1 [20–23]
	Total hip BMD [37,45]
	L2-L4 BMD [37,47]
	Calcaneal BMD [37,38,47,48]
	Femoral neck BMD [47–49]
No difference	No difference

CLASSIFICAZIONE CLINICA



- I. = Articolazioni interfalangee e falangi; articolazioni metatarso-falangee e ossa metatarsali
II. = Articolazioni tarso-metatarsali
III. = Articolazioni navicolo-cuneiforme, talonavicolare e calcaneocuboide
IV. = Articolazione della caviglia
V. = Calcagno.

LJS '90

STADI DELLA NEUROARTROPATIA DI CHARCOT sec. Eichenholz/Shibata

Modified Eichenholtz stages ^a

Stage	Phase	Description
0	Inflammatory	Localized warmth, swelling, and redness; minimal to no radiographic abnormalities; MRI may show nondisplaced pathologic fracture(s) and increased marrow edema to the foot and/or ankle
1	Development	Localized warmth, marked swelling, and redness; radiographic presence of bony debris, fragmentation of subchondral bone, periarticular fracture, subluxation, and/or dislocation
2	Coalescence	Continued but decreased warmth, swelling, and redness; radiographic presence of absorption of fine debris, new bone formation, coalescence of fragments, fusion of joints (ankylosis), and/or sclerosis of bone ends
3	Remodeling	Marked decrease or absence of warmth, swelling, and redness; physically enlarged fixed (“healing”) deformity; radiographic appearance of remodeled and new bone formation, decreased sclerosis, and/or possible gross residual deformity

Eichenholz SN. Charcot joints, 1966
Shibata T et al. JBJS 1990; 72, 749-56

RESEARCH ARTICLE

**Diagnosis and treatment of active charcot neuro-
osteoarthropathy in persons with diabetes mellitus:
A systematic review**

Katherine M. Raspovic¹  | Nicolaas C. Schaper² | Catherine Gooday³  |
Arun Bal⁴ | Robert Bem⁵ | Avneesh Chhabra⁶ | Mary Hastings⁷ |
Crystal Holmes⁸ | Nina L. Petrova⁹ | Maria Gala Santini Araujo¹⁰  |
Eric Senneville¹¹  | Dane K. Wukich¹



- ARROSSAMENTO;
- EDEMA;
- GRADIENTE TERMICO $>2^{\circ}\text{C}$
- EDEMA MIDOLLARE, FRATTURE ANCHE MICROSCOPICHE



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Diabetes Metab Res Rev. 2023;e3653.

DIAGNOSI

TEMPERATURA CUTANEA: Armstrong DG et al. 1997 hanno evidenziato una differenza statisticamente significativa della temperatura cutanea nel piede affetto da Charcot rispetto al controlaterale di circa 4,6 °C. L'elevata temperatura cutanea appare essere compatibile con diagnosi di Charcot, ma non vi sono attualmente studi che ne confermino l'accuratezza e l'affidabilità diagnostica.



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DIAGNOSTICA PER
IMMAGINI

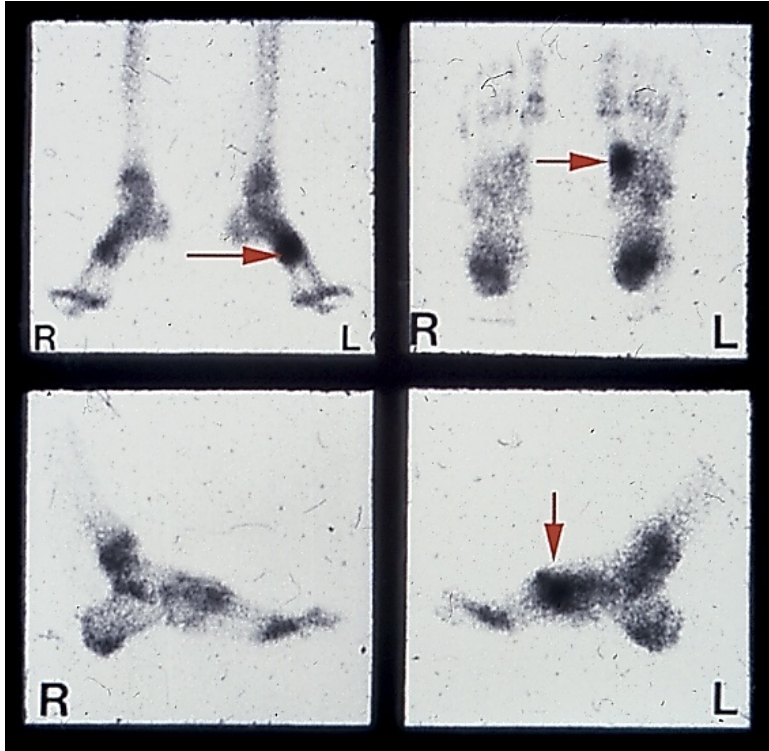
DIAGNOSI STRUMENTALE



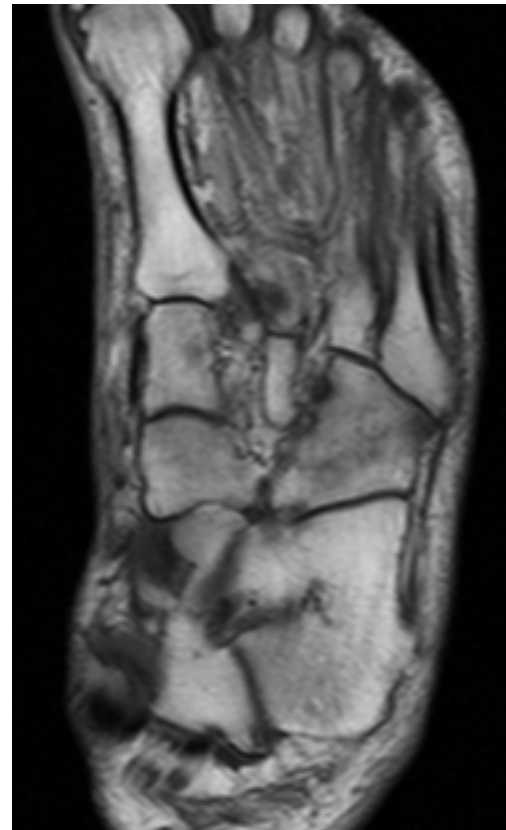
DIAGNOSI STRUMENTALE



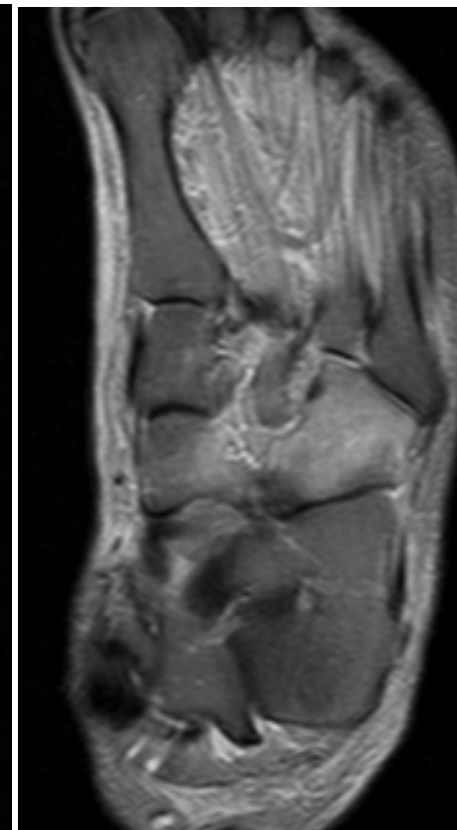
DIAGNOSI STRUMENTALE



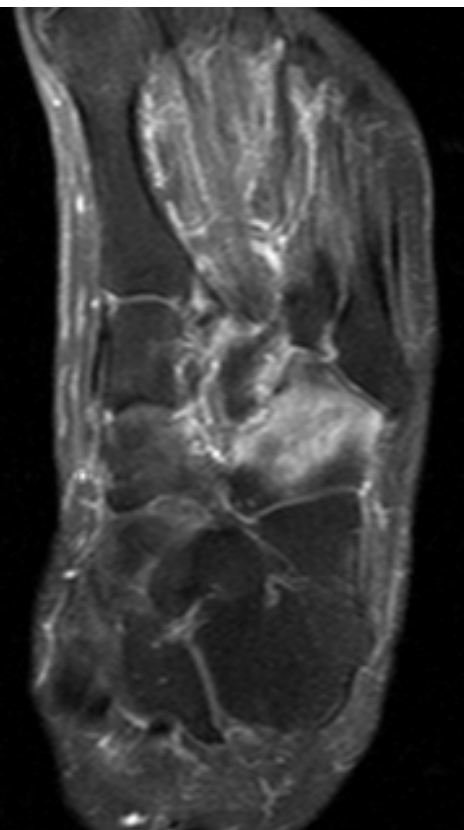
T1



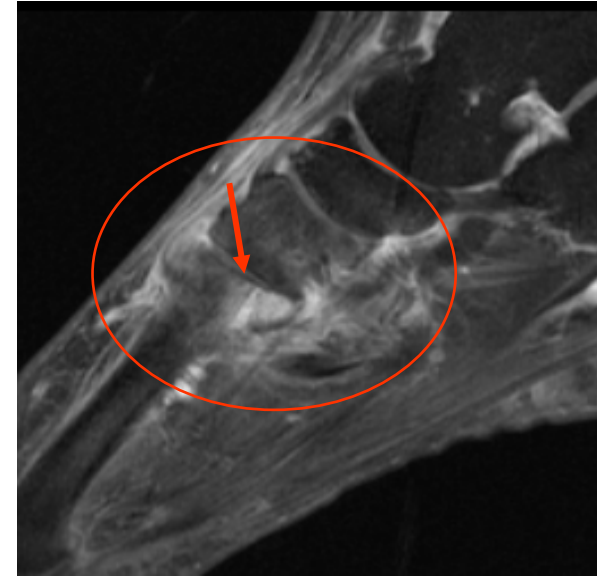
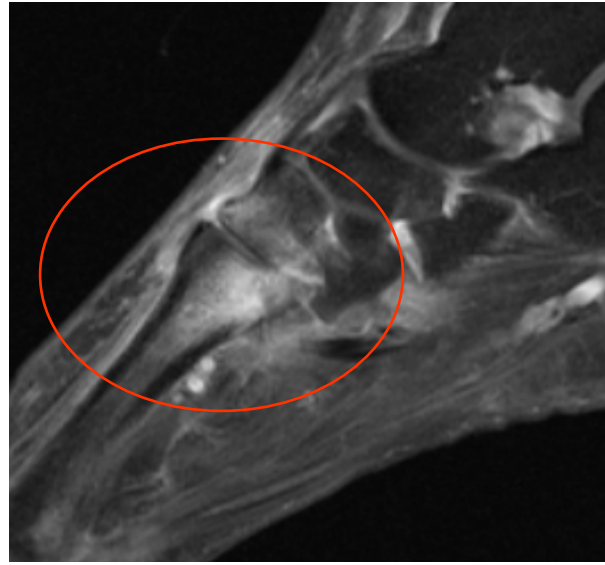
STIR



GAD



Bone marrow oedema + Fracture



RESEARCH

Open Access



A randomised feasibility study of serial magnetic resonance imaging to reduce treatment times in Charcot neuroarthropathy in people with diabetes (CADOM)

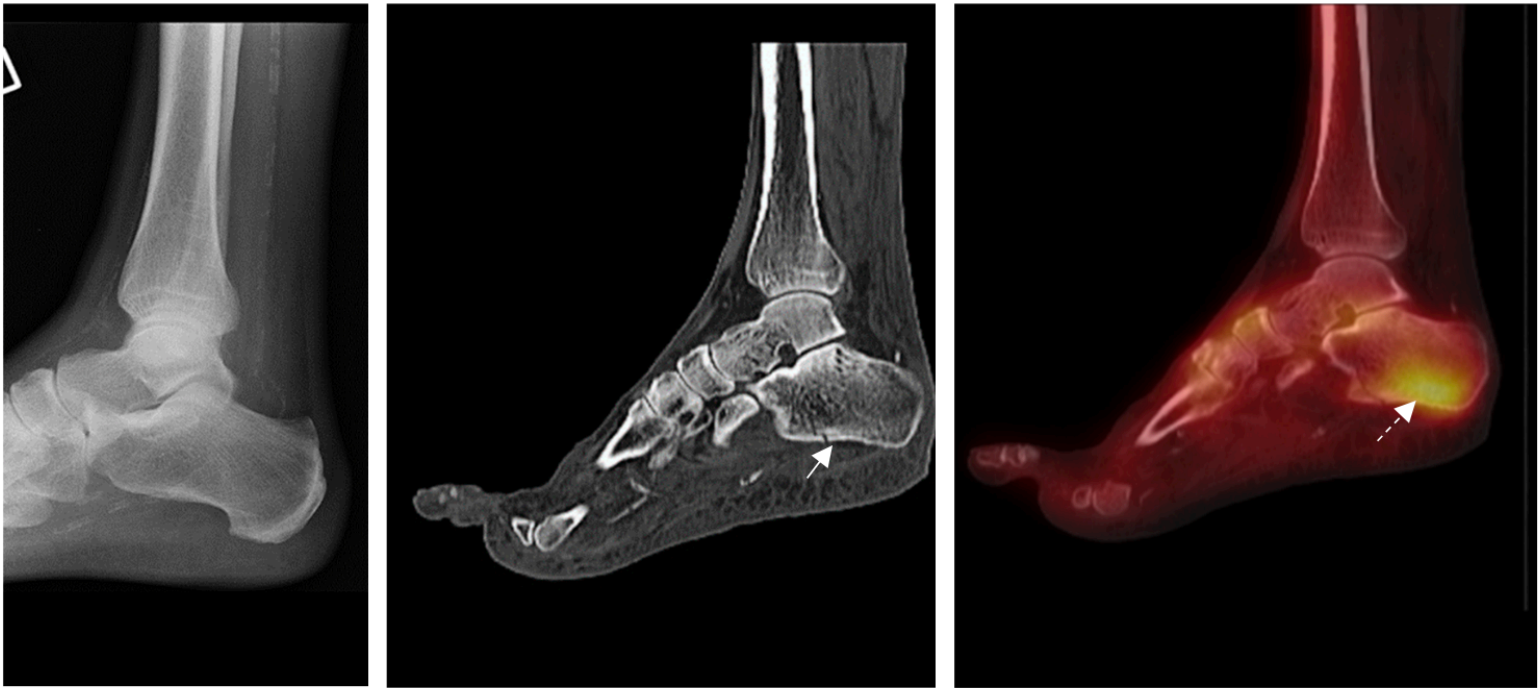
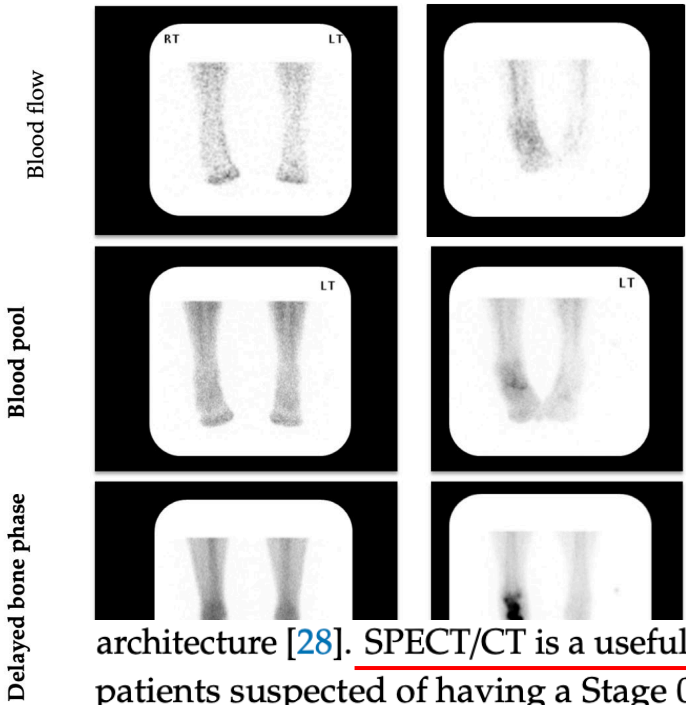
Catherine Gooday^{1,2*} , Frances Game³, Jim Woodburn⁴, Fiona Poland⁵, Erika Sims⁶, Ketan Dhatariya^{2,7}, Lee Shepstone⁷, Garry Barton⁷ and Wendy Hardeman⁸

- E' possibile, e scevro da complicanze, eseguire il follow-up della fase acuta del piede di Charcot mediante serie di RMN oltre che con misurazioni seriate della temperatura cutanea sopra l'articolazione coinvolta
- La differenza di durata media del trattamento di immobilizzazione non è risultata statisticamente significativa tra i due gruppi (A: gruppo in follow-up clinico VS B: gruppo in follow-up clinico+RMN), con durata media più lunga nel gruppo che eseguiva anche RMN (A 235 $\pm$ 108,3 VS B 292 $\pm$ 177,4 giorni)
- I soggetti trattati con dispositivo di scarico non rimovibile hanno raggiunto più velocemente la remissione della fase acuta rispetto a quelli trattati con dispositivo rimovibile.

The Role of Bone Scintigraphy with SPECT/CT in the Characterization and Early Diagnosis of Stage 0 Charcot Neuroarthropathy

Raju Ahluwalia ^{1,2,*}, Ahmad Bilal ¹, Nina Petrova ^{2,3}, Krishna Boddhu ¹, Chris Manu ², Prashanth Vas ^{2,3}, Maureen Bates ², Ben Corcoran ⁴, Ines Reichert ^{1,2}, Nicola Mulholland ⁴, Venu Kavarthapu ^{1,2}, Gill Vivian ^{4,†} and Michael Edmonds ^{2,3,†}

J. Clin. Med. 2020, 9, 4123; doi:10.3390/jcm9124123



architecture [28]. SPECT/CT is a useful functional and structural imaging modality in the evaluation of patients suspected of having a Stage 0 Charcot foot. It has identified increased blood flow and bony changes that may be the initial events in Charcot pathophysiology and also aids the early diagnosis of CN in patients presenting with a hot swollen foot. SPECT/CT demonstrates that, even in Stage 0 Charcot foot, there is distinct bone pathology, predominantly fracture, which demands appropriate urgent treatment. If SPECT/CT is not easily available, then CT alone could be carried out as it may identify 59% of the bony lesions.

(c)
of a patient presenting with a unilateral hot foot Neuroarthropathy (CN). (a) Lateral foot/CT showing of vascular calcification); (b) CT shows fracture; (c) increased uptake within the calcaneum correlation between Single Photon Emission Computed Tomography (SPECT) and CT (SPECT/CT fusion imaging).

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Diabetes Metab Res Rev. 2023;e3653.

DIAGNOSTICA DI
LABORATORIO

	DM + CN	DM - CN	CONTROLLI NO DM
PCR		p=0,045	p=0,005
Fosfatasi Alcalina	==	==	p=0,006

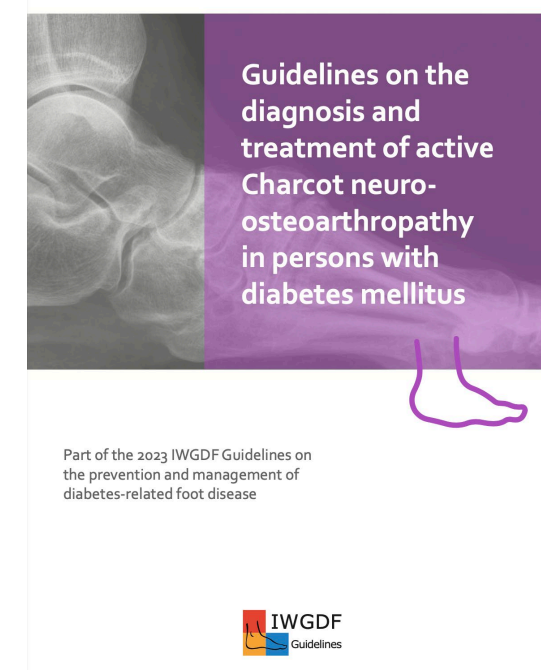
Petrova, 2005

	DM + CN	DM + NEUROPATIA	CONTROLLI NO DM
PCR		p=0,044	p=0,012
VES		p=0,001	p=0,001

Folestad, 2015

Non è stata identificata una evidenza riguardo all’accuratezza diagnostica di PCR, VES e fosfatasi alcalina osso-specifica quando sono state confrontate con diagnostiche di imaging in soggetti con piede di Charcot acuto.

I dati disponibili suggeriscono che tali test di laboratorio hanno scarso valore aggiuntivo nel diagnosticare o escludere il piede di Charcot acuto.



Clinical Question: Which blood tests have sufficient accuracy to make the diagnosis of active Charcot neuro-osteoarthropathy more likely in a person with diabetes mellitus and intact skin?

Recommendation 10: We suggest not using C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), white blood count, alkaline phosphatase, or other blood tests in a person with diabetes mellitus and suspected active Charcot neuro-osteoarthropathy with intact skin to diagnose or exclude the disease. (Conditional; Low)

CASE REPORT

Ischemic Charcot foot: different disease
with different treatment?L. M. PALENA¹, E. BROCCO², S. NINKOVIC², A. VOLPE³, M. MANZI¹

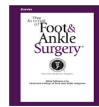
The Journal of Foot & Ankle Surgery 55 (2016) 727–731



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The Journal of Foot & Ankle Surgery 000 (2021) 1–6

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journal homepage: www.jfas.org



hospitalized patients were considered. Even
PAD could be as high as 40% in this group
66% [14]. These differences may represent the l

Article

The Neuro-Ischaemic Charcot Foot: Prevalence, C and Severity of Peripheral Arterial Disease in Ac Charcot Neuro-Arthropathy

Marco Meloni^{1,2,*}, Raju Ahluwalia³, Alfonso Bellia^{1,2}, Enrico Brocco⁴, Michela L
Aikaterini Andreadi^{1,2}, Laura Giurato^{1,2}, Valeria Ruotolo^{1,2}, Nicola Di Daniele^{1,6}, J
and Luigi Uccioli⁷

J. Clin. Med. 2022, 11, 6230. <https://doi.org/10.3390/jcm11216230>

Critical Limb Ischemia in Association with Charcot Neuroarthropathy: Complex Endovascular Therapy for Limb Salvage

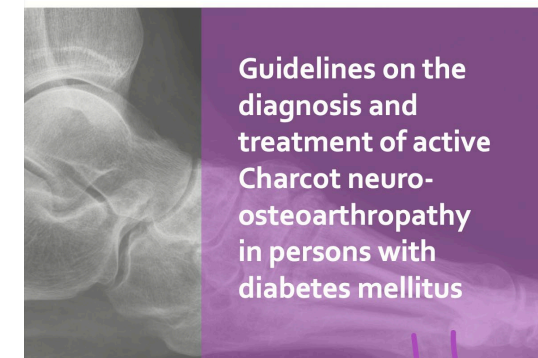
Luis Mariano Palena · Enrico Brocco ·
Marco Manzi

Table 5. Characteristics of PAD in patients with CN and PAD.

Variable	Values (N and %)
Vessels affected	2.9 (min 1–max 6)
Femoral-popliteal axis	19/24 (79.2%)
Iliac artery	0/24 (0%)
Common femoral artery	0/24 (0%)
Superficial femoral artery	19/24 (79.2%)
Popliteal artery	8/24 (33.3%)
BTK arteries	18/24 (75%)
Anterior tibial artery	14/24 (58.3%)
Posterior tibial artery	12/24 (50%)
Peroneal artery	7/24 (29.2%)
BTA arteries	4/24 (16.7%)
Baseline TcPO2 (mmHg)	33 ± 5
Revascularization for healing ulceration (yes)	14/24 (58.3%)

BTK: below-the-knee; BTA: below-the-ankle.

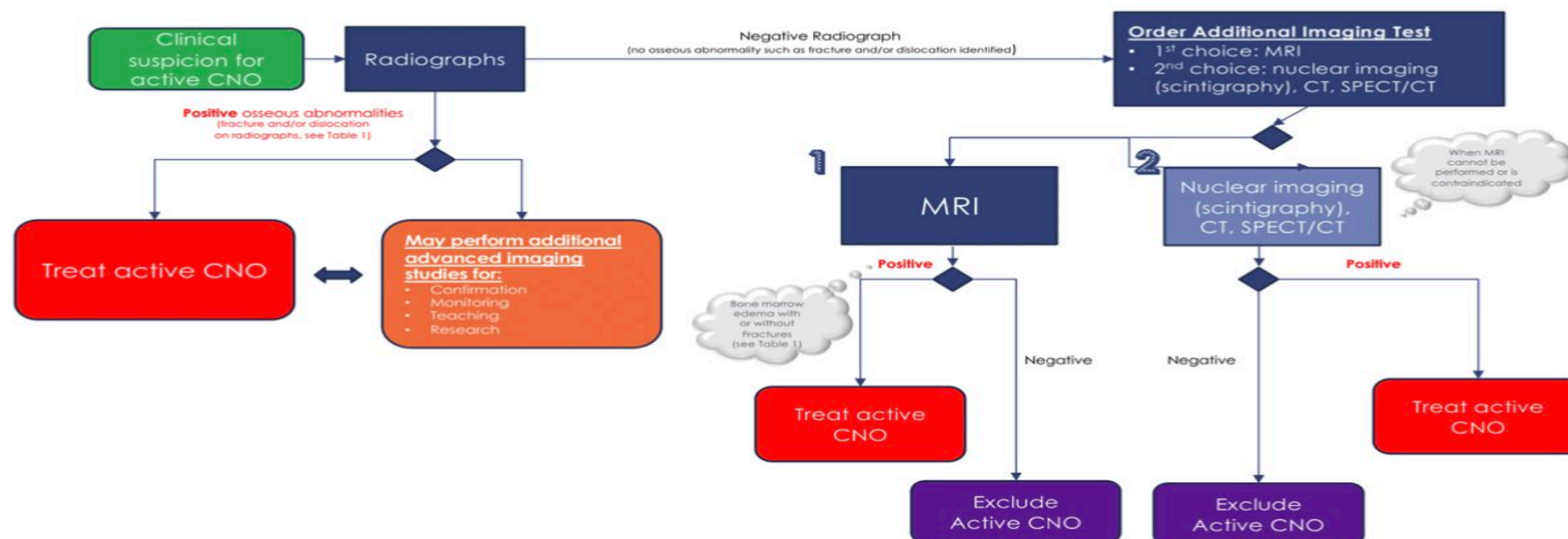
a mean duration of 16 ± 6 years (see Table 2). In total, 24 patients (31.6%) had a diagnosis
of PAD and were considered neuro-ischaemic CN patients; they were observed to be older



Guidelines on the diagnosis and treatment of active Charcot neuro-osteoarthropathy in persons with diabetes mellitus



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

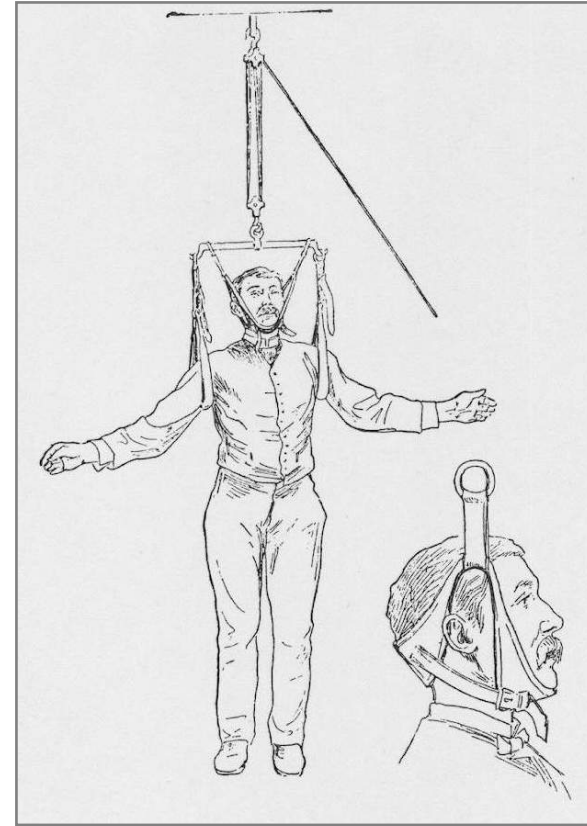


RESEARCH ARTICLE

Diagnosis and **treatment** of active charcot neuro-osteopathy in persons with diabetes mellitus: A systematic review

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Eric Senneville¹¹  | Dane K. Wukich¹

Trattamento dello Charcot in fase acuta

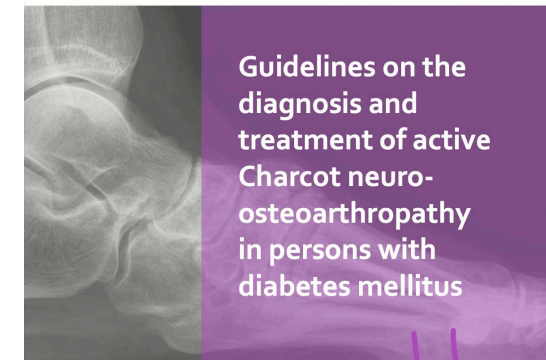


Off-Loading

Recommendation 15: Use a non-removable knee-high device to immobilise and offload the foot to promote remission of the disease, and prevention or progression of deformity in a person with active Charcot neuro-osteoarthropathy and intact skin. (Strong; Low)

Recommendation 19: Treatment with a knee-high offloading device should be considered as soon as possible once the diagnosis of active Charcot neuro-osteoarthropathy is considered. (Strong; Low)

Recommendation 20: In a person with active Charcot neuro-osteoarthropathy who is being treated with a knee-high device, we suggest using assistive devices to reduce weight-bearing on the affected limb. (Conditional; Low)



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



Short communication

**Response of Charcot's arthropathy to contact casting:
assessment by quantitative techniques**

M. McGill¹, L. Molyneaux², T. Bolton², K. Ioannou³, R. Uren³, D. K. Yue¹

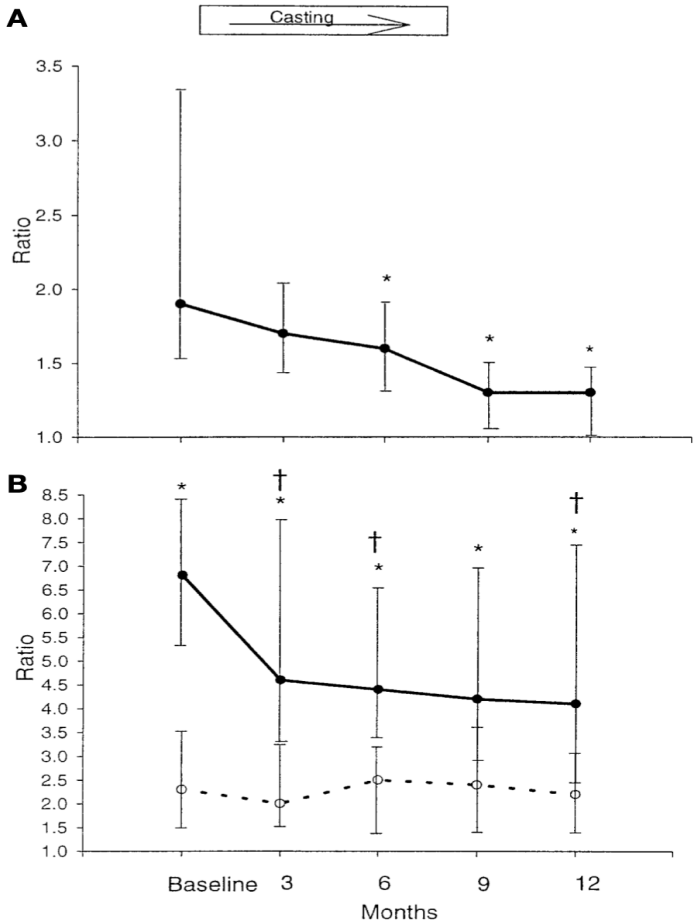


Fig. 1A, B. The ratio of bone isotope uptake between **A** the affected and unaffected feet in the bilateral scan method (* different to baseline $p < 0.05$ and **B** the affected foot and tibia in the unilateral scan method (* different to normal $p < 0.005$, + different to baseline $p < 0.04$; tibia:foot ratio for affected foot; - - - tibia:foot ratio for unaffected foot

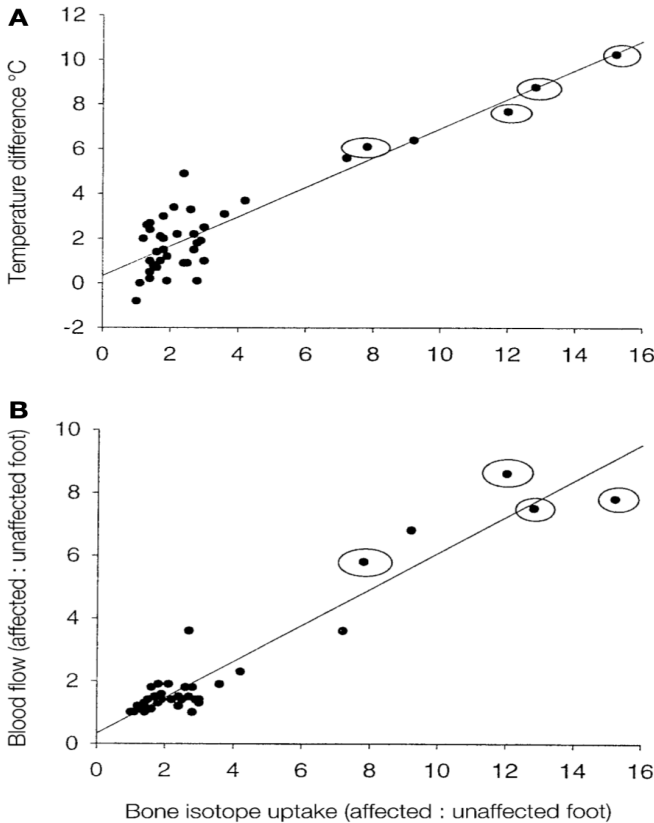


Fig. 2A, B. The relation between **A** temperature difference and the ratio of bone isotope uptake between affected and unaffected feet ($r = 0.90$) and **B** isotopic activities in the blood flow phase and bone uptake phase ($r = 0.92$) ○ data from patient M, $p = 0.0001$

The perils of procrastination: effects of early vs. delayed detection and treatment of incipient Charcot fracture

[E Chantelau](#)¹

Abstract

Background: At the onset of acute diabetic Charcot foot, therapeutic intervention may be delayed because plain X-rays may not show fractures.

Aim of the study: To assess the clinical course of acute Charcot foot in 24 patients without evidence of definite fractures on the first X-ray after onset of symptoms, who were referred to the foot clinic for diagnosis and treatment either early or delayed, i.e. before or after definite fractures were detectable on repeat X-rays.

Patients and methods: Eleven patients were referred early (incipient Charcot foot, case group), and 13 patients were referred delayed (overt Charcot foot, control group). In the foot clinic, both groups were immediately treated with off-loading and subsequent surgery. **Progression to Fractures: 1 (9%) vs 13 (100%)** of fractures and subsequent surgery.

Results: Based on X-rays at the onset of symptoms, in 19 of the 24 patients the condition had been misdiagnosed prior to referral (in 11 patients as sprain injury). Additional imaging techniques (MRI, CT scan or bone scintigraphy) had been performed in 10 patients prior to referral. While these techniques had been used more frequently in the cases vs. the controls ($P=0.012$), misdiagnosis was less frequent in the cases vs. the controls ($P=0.013$). Only one out of 11 case patients developed extended foot fractures and severe deformity, vs. 12 out of 13 control patients ($P<0.001$).

Conclusion: Early detection of incipient Charcot foot is facilitated by imaging techniques other than plain X-rays. Immediate off-loading of incipient Charcot foot appears to minimize fractures and incapacitating deformities.

Exp Clin Endocrinol Diabetes. 2007 Jun;115(6):360-4.

Weight-bearing intensity produces charcot deformity in injured neuropathic feet in diabetes

[R Kimmerle¹](#), [E Chantelau](#)

Abstract

The purpose of the study was to investigate the relationship between the intensity of unrestrained weight bearing after a non-fracture injury (e.g. sprain), and the development of osteoarthropathic deformities of the foot (Charcot foot) in patients with diabetic neuropathy.

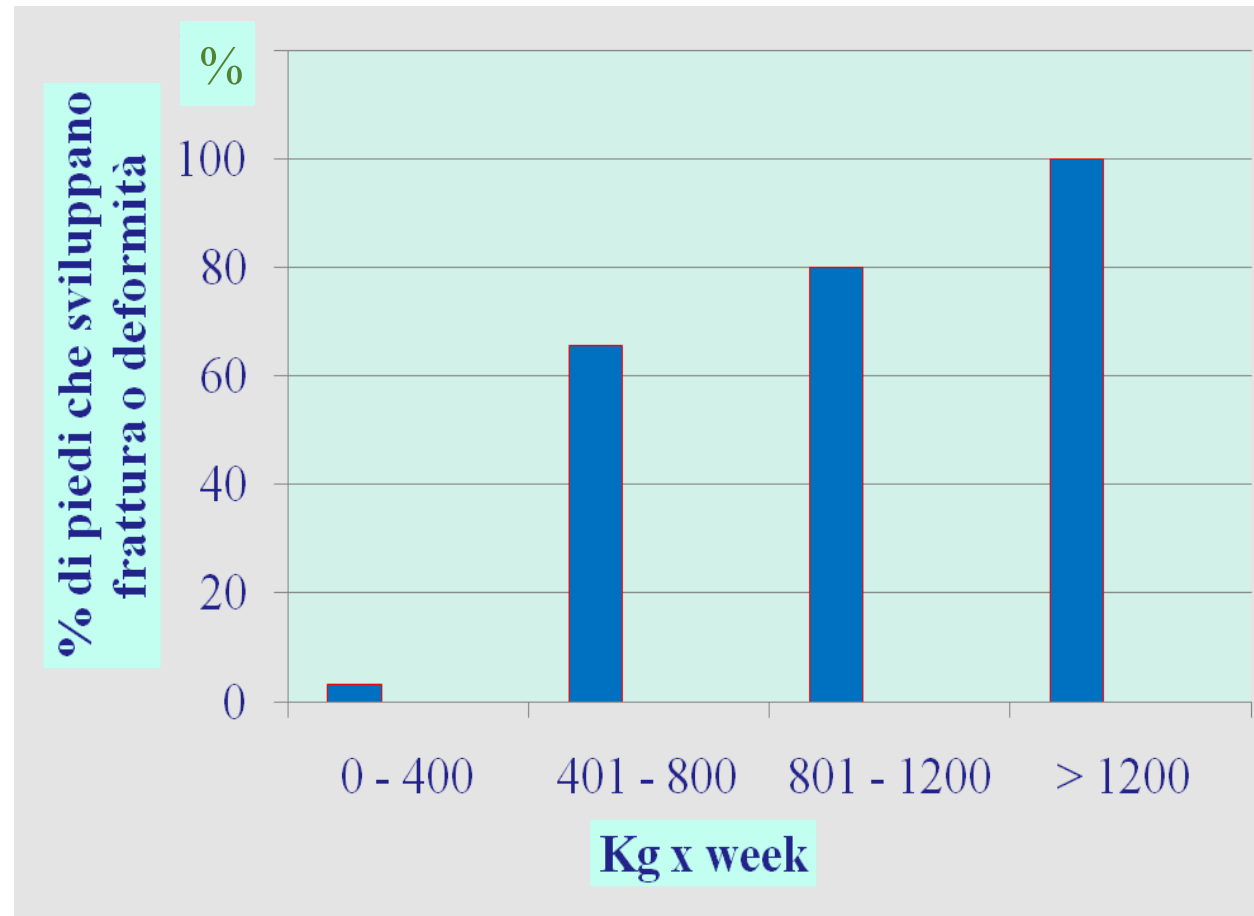
Methods: 34 diabetic patients (14 Type 1, 20 Type 2) with foot bone injuries were studied in retrospect. At onset of injury symptoms (e.g. foot swelling), 32 of 34 feet displayed unremarkable X-ray, but pathologic MR imaging (e.g. bone marrow edema along the Lisfranc and/or the Chopart joint). Cumulative load forces after the onset of symptoms until treatment by total contact cast (TCC) were estimated using the product of body weight and number of weeks of ambulation (kg x week) as a surrogate. Feet were classified in 3 groups according to the degree of foot deformities found at the start of treatment with TCC: Feet without deformities (group A, n=16), feet with minor deformities (partially reduced plantar arch (group B, n=6) and feet with major deformities (collapsed plantar arch, group C, n=12)

Results: Feet in group A had been exposed to 262 (95% CI 135-390) kg x week, compared to 974 (95% CI 342-1606) in group B, and to 2348 (95% CI 1265-3430) kg x week in group C ($p<0.05$ between groups), indicative of a dose-response relationship between weight-bearing and progressive foot deformities. Destruction along the Lisfranc joint was observed in 2/16 feet in group A, versus 18/18 feet in group B and C combined ($p<0.001$). In group A, the undeformed feet were healed without major deformities (except for 2 non-compliant patients), whereas in group B and C feet remained as deformed as they were at TCC application.

Conclusion: Unrestrained weight-bearing of injured foot bones and joints of more than 400 kg x week (equivalent to 8 weeks of normal walking by a person of 50 kg body weight) prompts Charcot deformities, with disintegration of the Lisfranc joint. Early off-loading by TCC treatment allows healing without deformities.

Weight-Bearing Intensity Produces Charcot Deformity in Injured Neuropathic Feet in Diabetes

Kimmerle, Chantelau, Exp Clin Endocrinol Diabetes, 2007



REVIEW

Open Access

Factors impacting the evidence-based assessment, diagnosis and management of Acute Charcot Neuroarthropathy: a systematic review



D. Diacogiorgis^{1,2}, B. M. Perrin^{2,3*} and M. I. C. Kingsley^{3,4}

FATTORI LEGATI ALL'ORGANIZZAZIONE DEL SISTEMA SANITARIO E AMBIENTALI

- Spesso il Sistema Sanitario non è organizzato in termini di conoscenze e capacità, per riconoscere diagnosticare e trattare il piede di Charcot acuto
- Difficile accesso a diagnostica tipo RMN

FATTORI LEGATI ALL'INDIVIDUO

- Incapacità di identificare un episodio potenzialmente precipitante
- Scarsa consapevolezza dello stato di salute dei piedi

FATTORI LEGATI AI PROFESSIONISTI DELLA SALUTE

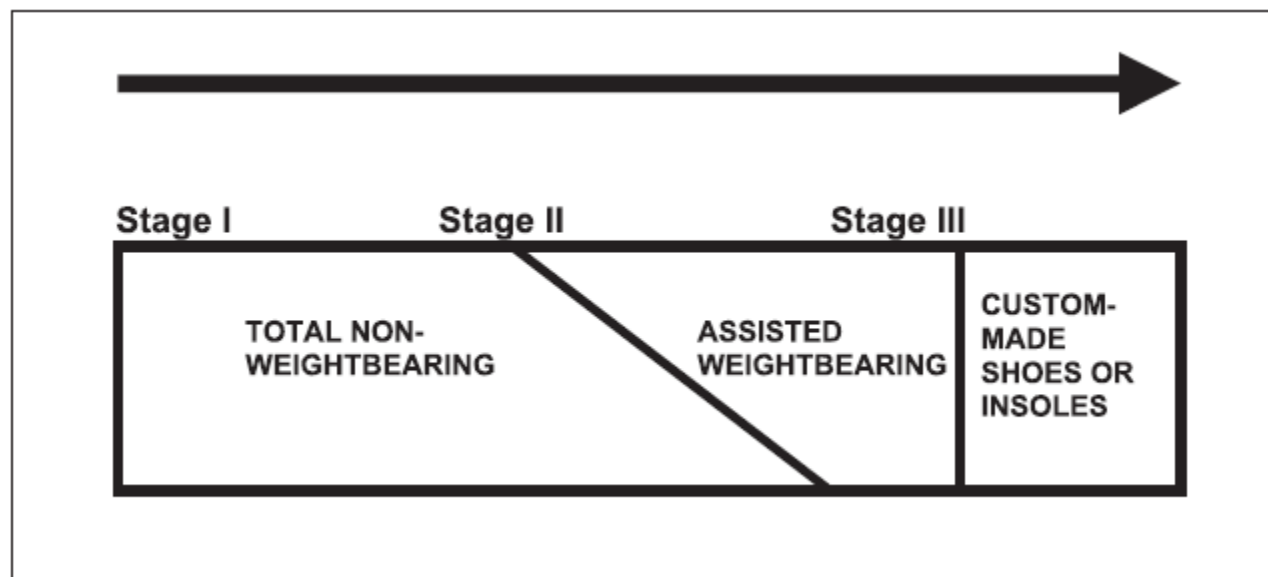
- Difficoltà nel riconoscere il piede di Charcot, frequente errore di diagnosi differenziale
- Carente consapevolezza della patologia, carente attitudine a sospettare la patologia
- Estrema variabilità di consapevolezza di indicazioni ed utilizzo del TCC



TARDIVO INVIO E PRESA IN CARICO DA PARTE DI SPECIALISTI/TEAM SPECIALISTICI

Modified Eichenholtz stages^a

Stage	Phase	Description
0	Inflammatory	Localized warmth, swelling, and redness; minimal to no radiographic abnormalities; MRI may show nondisplaced pathologic fracture(s) and increased marrow edema to the foot and/or ankle
1	Development	Localized warmth, marked swelling, and redness; radiographic presence of bony debris, fragmentation of subchondral bone, periarticular fracture, subluxation, and/or dislocation
2	Coalescence	Continued but decreased warmth, swelling, and redness; radiographic presence of absorption of fine debris, new bone formation, coalescence of fragments, fusion of joints (ankylosis), and/or sclerosis of bone ends
3	Remodeling	Marked decrease or absence of warmth, swelling, and redness; physically enlarged fixed (“healing”) deformity; radiographic appearance of remodeled and new bone formation, decreased sclerosis, and/or possible gross residual deformity



RESEARCH

Open Access



Duration of total contact casting for resolution of acute Charcot foot: a retrospective cohort study

Danielle A. Griffiths¹ and Michelle R. Kaminski^{2,3*} 

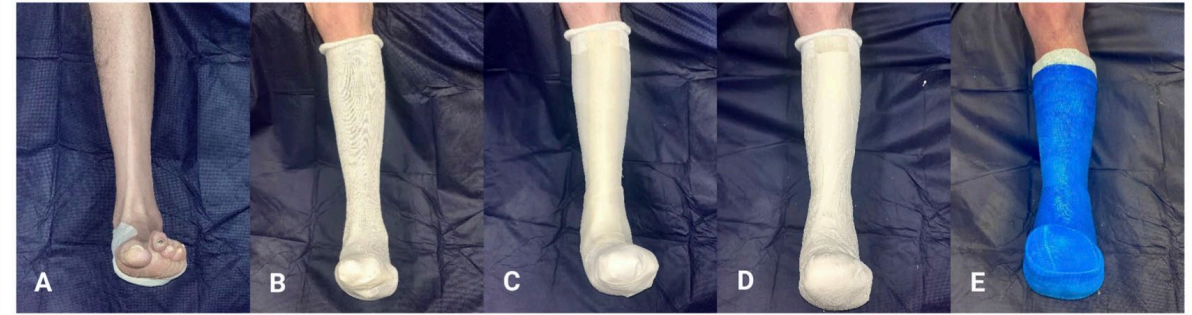


Fig. 1 Application of total contact cast. (A) Felt padding ('D-filler') is placed under medial longitudinal arch (except in cases of severe 'rockerbottom' deformity). (B) Cotton tube bandage is applied to protect lower limb and foot. (C) Silicone strips are applied over bony prominences. (D) Plaster of paris inner layer is applied. (E) Fibreglass outer layer is applied. Participant photographs printed with permission

La durata del trattamento TCC è stata valutata in alcuni studi, con risultati eterogenei:

- United Kingdom: 9 – 12 mesi
- US, Europa, Asia-Pacific Countries: 3-9 mesi

Questo studio australiano ha valutato retrospettivamente (2012-2015) la durata del trattamento TCC nell'area metropolitana di Melbourne in 27 soggetti con diagnosi di Charcot stadio 0-1 di Eickenholtz-Shibata, osservando una durata mediana di **4,3 mesi (2,7 – 7,8)**, considerando come durata il numero di giorni compresi tra la prima applicazione di TCC e la sospensione del trattamento per guarigione dello stato acuto.

Purtroppo, anche in questo studio si segnala una errata diagnosi iniziale nel 63% dei soggetti.

Diagnosis and treatment of active charcot neuro-osteoarthropathy in persons with diabetes mellitus: A systematic review

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Diabetes Metab Res Rev. 2023;e3653.

TERAPIA FARMACOLOGICA

Opinion

RANKL-RANK-OPG Pathway in Charcot Diabetic Foot: Pathophysiology and Clinical-Therapeutic Implications

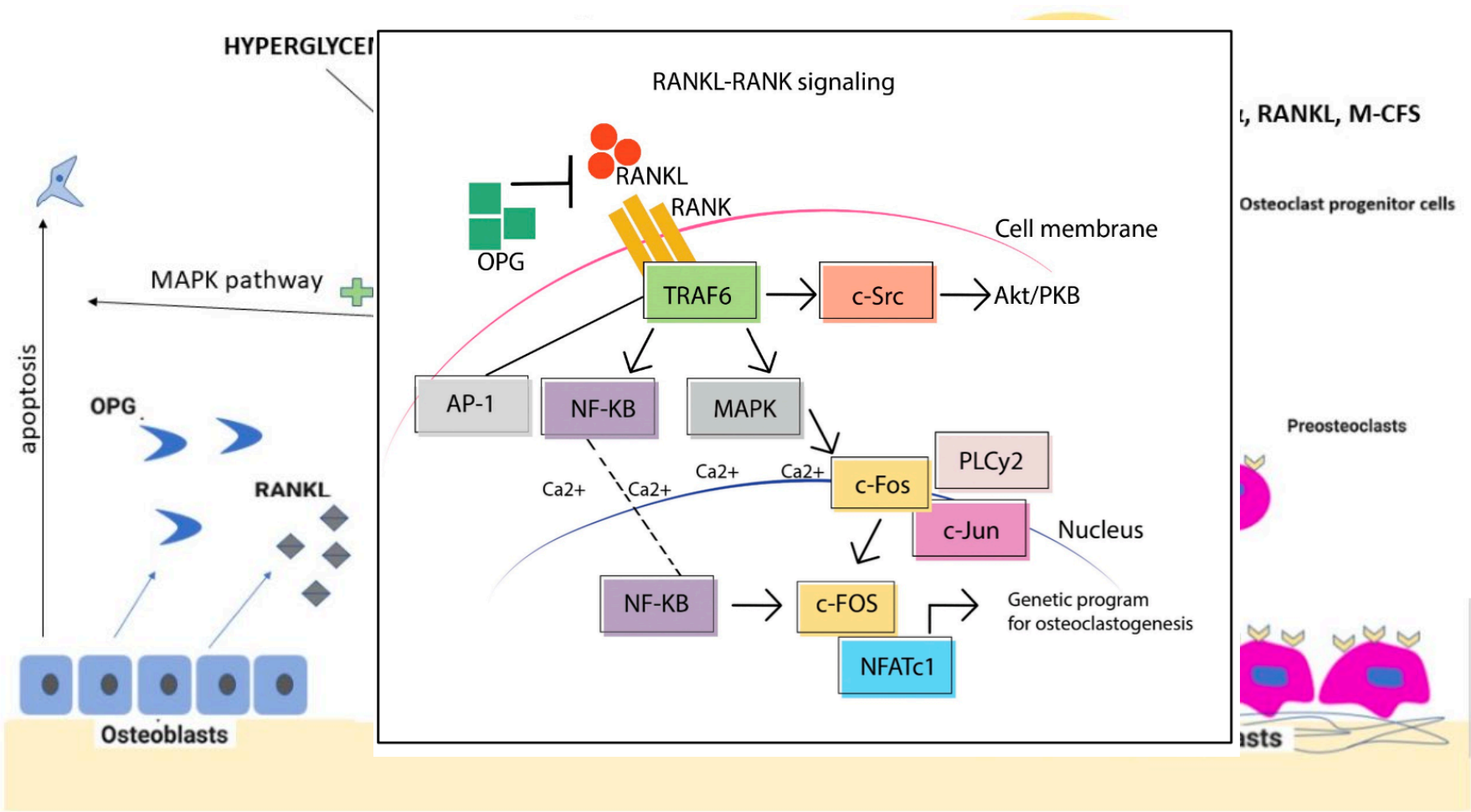
Tommaso Greco^{1,*,+} , Antonio Mascio^{1,+}, Chiara Comisi¹, Chiara Polichetti¹ , Silvio Caravelli² , Massimiliano Mosca², Nicola Mondanelli³ , Elisa Troiano³ , Giulio Maccauro¹ and Carlo Perisano¹

Int. J. Mol. Sci. **2023**, *24*, 3014. .

Novel Biomarkers Predictive of Diabetic Charcot Foot—An Overview of the Literature

Anca Bobircă ^{1,2,†}, Anca Emanuela Musetescu ^{3,†}, Anca Bordanu ^{4,*}, Anca Pantea Stoian ^{5,†}, Teodor Salmen ^{6,*}, Dan-Cristian Marinescu ⁷, Cristina Alexandru ^{1,2}, Alesandra Florescu ³, Raluca Radu ⁸, Sebastian Isac ⁹, Traian Patrascu ^{10,11}, Dragos Serban ^{11,12} and Florin Bobircă ^{10,11}

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RANKL-RANK-OPG Pathway in Charcot Diabetic Foot: Pathophysiology and Clinical-Therapeutic Implications

Tommaso Greco ^{1,*†} , Antonio Mascio ^{1,†}, Chiara Comisi ¹, Chiara Polichetti ¹ , Silvio Caravelli ² ,
Massimiliano Mosca ², Nicola Mondanelli ³ , Elisa Troiano ³ , Giulio Maccauro ¹ and Carlo Perisano ¹

Int. J. Mol. Sci. **2023**, *24*, 3014. 

TERAPIA FARMACOLOGICA

Il trattamento del piede di Charcot in fase acuta è basato su terapie non chirurgiche mirate a ridurre il carico e l'edema del piede coinvolto.

Il gold standard del trattamento conservativo non farmacologico è il Total Contact Cast, che assicura l'immobilizzazione di piede e caviglia e lo scarico totale.

Negli ultimi anni sono state studiate alcune possibili terapie farmacologiche che potrebbero interagire con la cascata di segnale RANKL-RANK-OPG e il processo di sviluppo degli osteoclasti:

- Bifosfonati
- Calcitonina
- Anticorpi umani monoclonali anti-RANKL (Denosumab)

BIFOSFONATI

Classe di farmaci con azione anti-osteoclastica, inibiscono la proliferazione degli osteoclasti e ne riducono l'emivita. Hanno dimostrato moderata efficacia nel ridurre il turn over osseo e la temperatura cutanea.

Il loro uso è stato limitato a causa degli effetti collaterali riportati in letteratura, quali deterioramento della funzionalità renale (particolarmente importante nei diabetici neuropatici) e osteonecrosi mascellare.

BIFOSFONATI

Table 2. Studies on the treatment of CF with Bisphosphonates.

Author, Year	Participants	Treatment	Results
Jude et al., 2001 [65]	39	Pamidronate 90 mg (single dose) vs. Placebo	Reduction of symptoms related to diabetic neuropathy in treatment group
Pakarinen et al., 2002 [66]	32	Pamidronate 30–60 mg (i.v., once a week for 6 weeks)	No differences between the two groups
Pitocco et al., 2005 [67]	20	- All patients received a TCC boot for the first 2 months and pneumatic walker for the other 4 months - 11 patients treated with Alendronate 70 mg orally once a week (test group)	At 6 months, significant reduction of bone reabsorption markers with increased foot bone density compared with the control group (more evident in the distal phalanxes than in the midfoot)
Moreno et al., 2007 [68]	7	Pamidronate 90 mg (i.v., 3 doses at 2 months-interval)	Rapid resolution of symptoms, marked reduction of bone remodeling and radiological healing at final follow-up
Naqvi et al., 2008 [69]	3	Pamidronate 90 mg (i.v., doses at 2 months-interval)	- Improvement in swelling, pain, erythema and warmth - Patients able to bear weight on their foot and no longer required the use of a walking aid
Pakarinen et al., 2011 [70]	35	Zolendronate 4 mg (i.v., 3 doses in 3 months) and foot immobilization vs. placebo	- No significative difference in the two groups - The treatment group required more days of immobilization.
Das et al., 2019 [71]	36	Methylprednisone vs. zolendronate vs. placebo	- No benefit was observed in treatment with zoledronate for remission of CN - Methylprednisone group had a worse prognosis

(mg: milligrams; i.v.: intravenous; TCC: Total Contact Cast).

CALCITONINA

La Calcitonina, polipeptide secreto dalle cellule C parafollicolari della tiroide, agisce direttamente sugli osteoclasti inibendone l’attività di riassorbimento osseo.

Table 3. Studies on the treatment of CF with calcitonin.

Author, Year	Partecipants	Treatment	Results
Bem et al., 2006 [73]	32	Calcitonin spray 200 IU + calcium vs. calcium alone	- Reduced bone turnover at 3 months - No significative difference between the two groups in foot-temperature reduction

(IU: International Units).

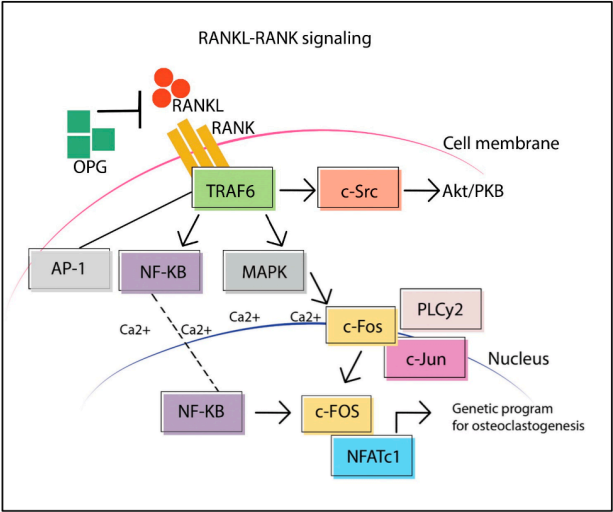
DENOSUMAB

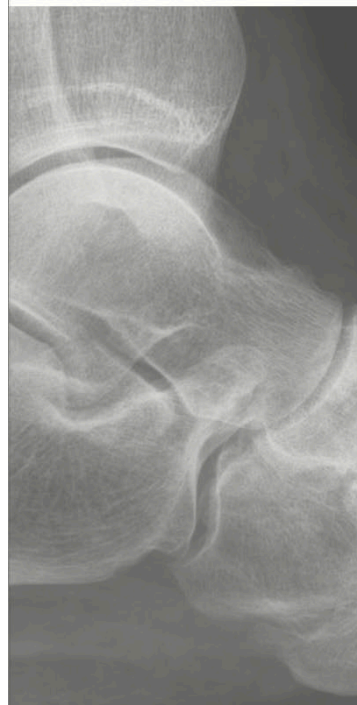
Anticorpo monoclonale umano che si lega selettivamente con alta affinità al RANKL, impedendo l’attivazione del recettore RANK sulla superficie degli osteoclasti, con conseguenti inibizione di ogni attività osteoclastica e riduzione del riassorbimento osseo.

Table 1. Studies on the treatment of CF with Denosumab.

Author, Year	Participants	Treatment	Results
Busch-Westbroek et al., 2017 [58]	22	Denosumab 60 mg (single subcutaneous dose) and TCC protocol	Fracture resolution and shorter TCC treatment time
Shofler et al., 2021 [59]	7	Denosumab 60 mg (single subcutaneous dose) in the CF acute phase	Exit from the acute phase in an average of 52.00 ± 17.89 days after injection
Carvés et al., 2021 [57]	7	Denosumab 60 mg (single subcutaneous dose) in refractory stage	- All patients clinically improved - 5 patients showed stability of structural damage (radiography) - 4 patients with significant decrease of metabolic activity (PET-CT) - No adverse event or hypocalcemia was observed.

(mg: milligrams; TCC: Total Contact Cast).





Guidelines on the diagnosis and treatment of active Charcot neuro-osteoarthropathy in persons with diabetes mellitus



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

DIAGNOSIS

Clinical Question: In a person with diabetes mellitus and intact skin, in whom active Charcot neuro-osteoarthropathy (CNO) is considered, what is the accuracy of clinical findings to diagnose active CNO?

Recommendation 1: Always consider active Charcot neuro-osteoarthropathy in a person with diabetes mellitus, neuropathy and intact skin when there are clinical findings of an increase in temperature, oedema, and/or redness of the foot, compared to the contralateral foot. Best Practice Statement.

Recommendation 2: Consider using infrared thermometry to measure skin temperature of the feet in a person with diabetes mellitus and suspected Charcot neuro-osteoarthropathy with intact skin, using a standardised approach to the measurement of temperatures to allow for more accurate comparison over time. (Conditional; Low)

Recommendation 3: When using infrared thermometry to measure skin temperature of the feet in a person with diabetes mellitus and suspected active Charcot neuro-osteoarthropathy with intact skin, consider calculating temperature difference between both legs, using the highest temperature on the affected foot or ankle in comparison with the same anatomic point on the contralateral extremity. (Conditional; Low)

Recommendation 4: In a person with diabetes mellitus with bilateral active Charcot neuro-osteoarthropathy (CNO) and intact skin or with unilateral CNO and intact skin in the absence of the contralateral limb, ascending temperature gradients (toe-knee) may be useful for comparison over time. Best Practice Statement

Recommendation 5: Initiate knee high immobilization/offloading promptly while further diagnostic studies are performed to confirm or rule out active Charcot neuro-osteoarthropathy (CNO), when active CNO is suspected in a person with diabetes mellitus and intact skin. (Strong; Low)

Clinical Question: Which imaging modalities have sufficient accuracy to render the diagnosis of active Charcot neuro-osteoarthropathy (CNO) more likely in a person with diabetes mellitus and intact skin in whom the diagnosis of active CNO is considered?

Recommendation 6: Perform plain X-ray of the foot and ankle in a person with diabetes mellitus and suspected active Charcot neuro-osteoarthropathy. Ideally, bilateral plain X-rays should be performed, if possible, for comparison purposes. Best Practice Statement.

Recommendation 7: Perform X-rays that include the anteroposterior (AP), medial oblique, and lateral projections in a person with diabetes mellitus and suspected active Charcot neuro-osteoarthropathy. The ankle and foot views should include the AP, mortise, and lateral projections. Ideally, standing (also known as “weight-bearing”) radiographs should be performed. If a patient is not able to bear weight on their feet, non-weight-bearing radiographs are an alternative, but may not demonstrate malalignments that are more apparent in the standing position. Best Practice Statement.

Recommendation 8: Perform Magnetic Resonance Imaging in a person with diabetes mellitus and suspected active Charcot neuro-osteoarthropathy with normal appearance of the plain X-rays to diagnose or exclude the disease and its activity. (Strong; Moderate)

Recommendation 9: If Magnetic Resonance Imaging is unavailable or is contraindicated in a person with diabetes mellitus and suspected active Charcot neuro-osteoarthropathy, consider a nuclear imaging scan (scintigraphy), CT (computed tomography) scan, or SPECT-CT (Single Photon Emission Computed Tomography) to support the diagnosis of active Charcot neuro-osteoarthropathy. (Conditional; Low)

Clinical Question: Which blood tests have sufficient accuracy to make the diagnosis of active Charcot neuro-osteoarthropathy more likely in a person with diabetes mellitus and intact skin?

Recommendation 10: We suggest not using C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), white blood count, alkaline phosphatase, or other blood tests in a person with diabetes mellitus and suspected active Charcot neuro-osteoarthropathy with intact skin to diagnose or exclude the disease. (Conditional; Low)

IDENTIFICATION OF REMISSION

Clinical Question: Which clinical examinations and imaging techniques can be used to ascertain remission of Charcot neuro-osteoarthropathy in a person with diabetes mellitus and intact skin who has been treated for the disease?

Recommendation 11: Consider measurement of skin temperature of the affected and unaffected limb with serial examinations to monitor disease activity in a person with diabetes mellitus and active Charcot neuro-osteoarthropathy with intact skin. (Conditional, Low)

Recommendation 12: We suggest not using soft tissue oedema alone to determine when active Charcot neuro-osteoarthropathy is in remission. (Conditional; Low)

Recommendation 13: We suggest that the findings of temperature measurement, clinical oedema, and imaging should all be considered when concluding that active Charcot neuro-osteoarthropathy is in remission. (Conditional; Low)

Recommendation 14: We suggest that frequency of appointments for assessing disease activity in active Charcot neuro-osteoarthropathy should depend on specific factors such as fluctuation in oedema volume, co-morbidities, the risks associated with treatment and recovery, access to assistance with home treatment needs, and a person's progress and recovery. (Conditional; Low)

TREATMENT

Clinical Question: Which type of offloading device should be advised to a person with diabetes mellitus and active Charcot neuro-osteoarthropathy with intact skin and should this be accompanied with non-weight bearing advice?

Recommendation 15: Use a non-removable knee-high device to immobilise and offload the foot to promote remission of the disease, and prevention or progression of deformity in a person with active Charcot neuro-osteoarthropathy and intact skin. (Strong; Low)

Recommendation 16: Consider using a total contact cast in the treatment of active Charcot neuro-osteoarthropathy with intact skin in a person with diabetes mellitus. A knee-high walker rendered non-removable can be considered as a second choice in order to immobilise and offload the foot. (Conditional; Low)

Recommendation 17: A removable knee-high device worn at all times can be considered as the third treatment choice in a person with diabetes mellitus, active Charcot neuro-osteoarthropathy and intact skin of the foot for whom a non-removable knee-high offloading device is contraindicated or not tolerated. (Conditional; Low)

Recommendation 18: We suggest not to use a below the ankle offloading device (e.g. surgical shoe, postoperative sandal, custom moulded shoe, or slipper cast) in the treatment of active Charcot neuro-osteoarthropathy and intact skin, given the inadequate immobilisation of the diseased bone and joints, and limited off-loading capacity. (Conditional; Low)

Recommendation 19: Treatment with a knee-high offloading device should be considered as soon as possible once the diagnosis of active Charcot neuro-osteoarthropathy is considered. (Strong; Low)

Recommendation 20: In a person with active Charcot neuro-osteoarthropathy who is being treated with a knee-high device, we suggest using assistive devices to reduce weight-bearing on the affected limb. (Conditional; Low)

Clinical Question: Can medical therapy in a person with diabetes mellitus and active CNO with intact skin result in shorter time to remission and prevent complications?

Recommendation 21: Do not use alendronate, pamidronate, zoledronate, calcitonin, parathyroid hormone, or methylprednisolone as treatment for active Charcot neuro-osteoarthropathy in a person with diabetes mellitus and intact skin. (Strong; Moderate)

Recommendation 22: We suggest not to use denosumab as treatment for active Charcot neuro-osteoarthropathy in a person with diabetes mellitus and intact skin. (Conditional; Low)

Recommendation 23: We suggest to evaluate the need for vitamin D and calcium supplementation in a person with diabetes mellitus and active Charcot neuro-osteoarthropathy with intact skin during the phase of fracture healing, in doses according to (inter)national guidelines on supplementation in persons at risk for vitamin D deficiency and/or those with insufficient calcium intake. (Conditional, Low)

Clinical Question: In a person with diabetes mellitus and active Charcot neuro-osteoarthropathy with intact skin, is reconstructive surgery associated with shorter time to remission, prevention of deformity development, and prevention of deformity progression compared to no surgery?

Recommendation 24: In a person with active Charcot neuro-osteoarthropathy and intact skin, and with instability of foot and ankle joints, and/or deformity with a high-risk of developing ulcer in the offloading device, or pain that cannot be sufficiently stabilized in a Total Contact Cast or a non-removable knee-high device, we suggest that surgical intervention should be considered (Conditional; Low)

PREVENTION OF RE-ACTIVATION

Clinical Question: In persons with diabetes mellitus and active Charcot neuro-osteoarthropathy with intact skin who have been treated and are in remission, is therapeutic footwear preferred to conventional footwear to prevent re-activation of the disease?

Recommendation 25: Footwear and/or orthoses that best accommodate and support the shape of the foot/feet and ankle to help prevent re-activation of Charcot neuro-osteoarthropathy (CNO) are recommended in a person with diabetes mellitus, intact skin, treated for active CNO with an off-loading device and who is now in remission. (Strong; Moderate)

Recommendation 26: When deformity and/or joint instability is present, in order to optimise plantar pressure distribution, below the knee customized devices should be used for additional protection in a person with diabetes mellitus, intact skin, treated for active Charcot neuro-osteoarthropathy who is now in remission. (Strong; Moderate)

Grazie per l'attenzione



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