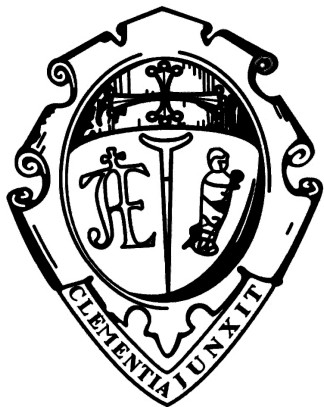




L'arteriopatia periferica: molto associata al rischio di eventi vascolari, poco studiata nei CVOTs

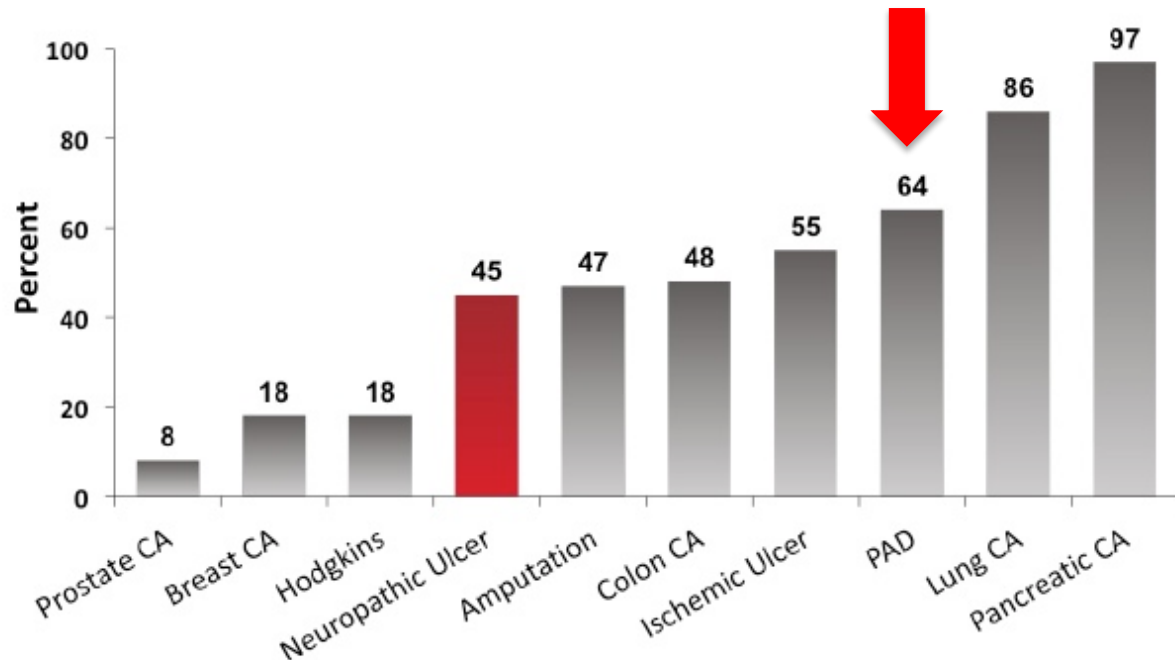
Alberto Piaggese

SD Piede Diabetico - Dipartimento Medicine Specialistiche
Azienda Ospedaliero-Universitaria Pisana

Nessun Conflitto di Interessi



5-Year Mortality Rates



Armstrong DG, Wrobel J, Robbins JM. Guest Editorial: are diabetes-related wounds and amputations worse than cancer? *Int Wound J.* 2007;4(4):286-287

Review Article

Diabetic Foot Syndrome as a Possible Cardiovascular Marker in Diabetic Patients

Antonino Tuttolomondo, Carlo Maida, and Antonio Pinto

*Dipartimento Biomedico di Medicina Interna e Specialistica, U.O.C di Medicina Interna e Cardioangiologia,
Università degli Studi di Palermo, Piazza delle Cliniche, No. 2, 90127 Palermo, Italy*

Correspondence should be addressed to Antonino Tuttolomondo; bruno.tuttolomondo@unipa.it

Received 10 December 2014; Accepted 18 March 2015

Academic Editor: Shi Fang Yan

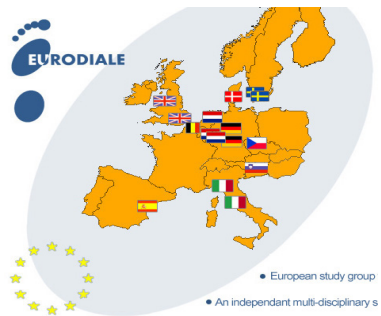
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LIPID AND METABOLIC EFFECTS OF GASTROINTESTINAL SURGERY (R. COHEN, SECTION EDITOR)

The Diabetic Foot as a Proxy for Cardiovascular Events and Mortality Review

**Isa Dietrich^{1,2} • Gustavo Arruda Braga² • Fernanda Gomes de Melo² •
Ana Carolina Calmon da Costa Silva Silva²**



24%



49%

England and Wales

01 April 2015 to 31 March 2018



National Diabetes Foot Care Audit Fourth Annual Report

V1.0

9 May 2019

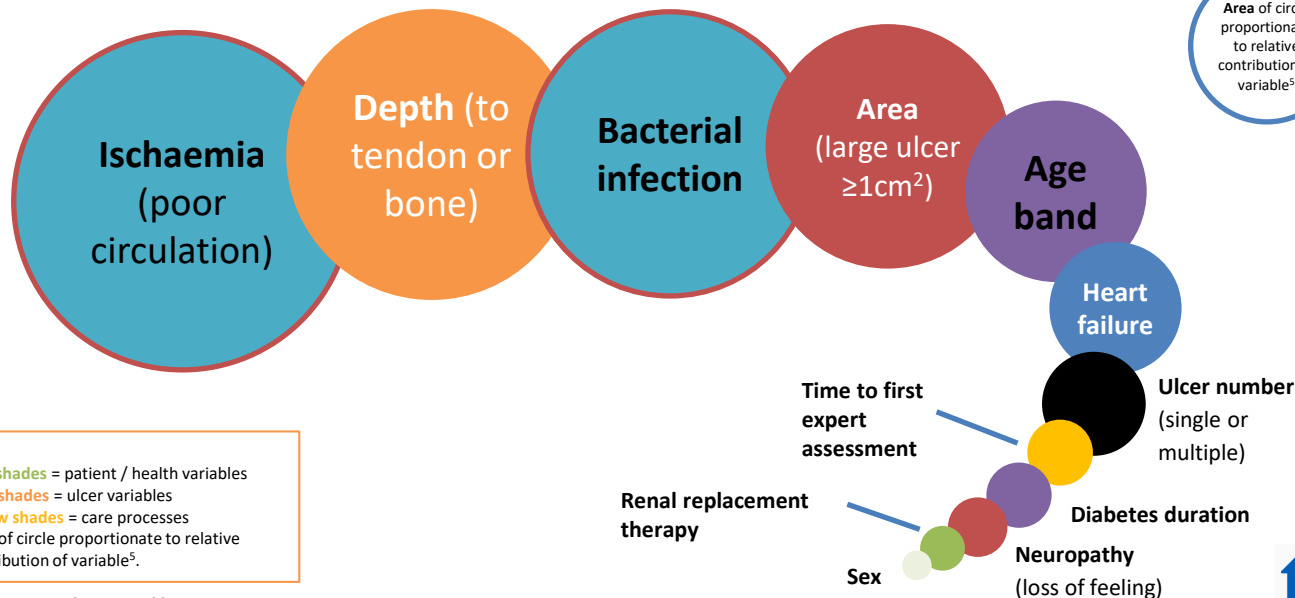
Information and technology
for better health and care

Appendix: Modelling

Foot disease admission: Variable strength



Area of circle proportionate to relative contribution of variable⁵

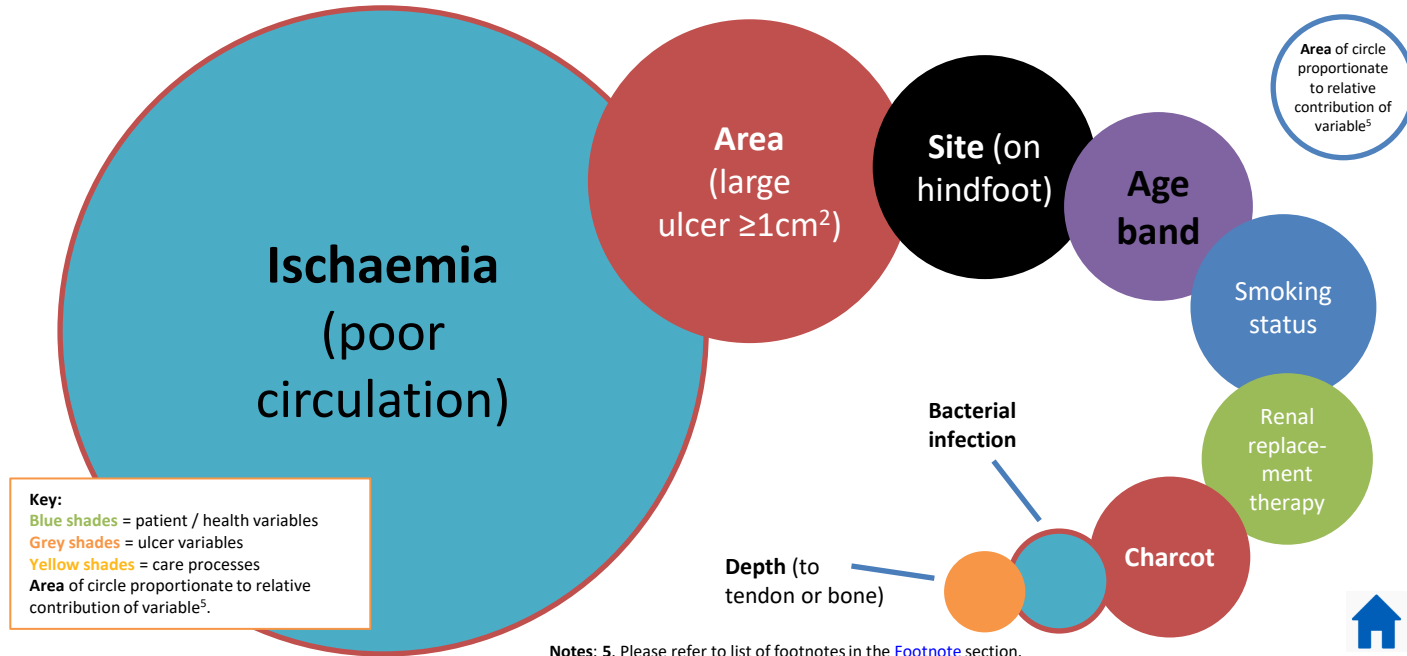


Notes: 5. Please refer to list of footnotes in the [Footnote](#) section.



Appendix: Modelling

Major amputation: Variable strength



A satellite map of the Mediterranean Sea and surrounding landmasses. The sea is a deep blue, while the land is green with some brownish areas indicating arid regions. The Italian Peninsula is prominent in the center-right. Overlaid on the map are white text labels and small square markers.

60 M inhabitants

■ 3 M DM

■ 300.000 DF

■ 3.382 LEA

Screening for peripheral arterial disease by means of the ankle-brachial index in newly diagnosed Type 2 diabetic patients

E. Faglia, C. Caravaggi*, R. Marchetti†, R. Mingardi‡, A. Morabito§, A. Piaggese¶, L. Uccioli** and A. Cieriello†† (Coordinator) for the SCAR (SCreening for ARterioopathy) study group

Internal Medicine Unit, Diabetology Centre, Policlinico Multimedica, Sesto S. Giovanni, *Centre for the Study and Treatment of Diabetic Foot Pathology, Abbiategrasso Hospital, †Teseo Ricerche C.R.O., Pisa, ‡Diabetic Foot and Vascular Medicine, Villa Berica Hospital, Vicenza, §Medical Statistics Unit, University of Milan, ¶Department of Endocrinology and Metabolism, Diabetology Section, University of Pisa, **Department of Internal Medicine, University of Roma Tor Vergata, and ††Department of Pathology and Experimental and Clinical Medicine, University of Udine, Italy

Accepted 22 October 2004

Abstract

Aim To evaluate the prevalence of peripheral arterial disease (PAD) with the ankle-brachial index (ABI) in newly diagnosed Type 2 diabetic subjects.

Methods Between autumn 2002 and spring 2003, 2559 newly diagnosed Type 2 diabetic subjects (about 15% of the cases/year in Italy) were enrolled in 265 diabetology centres. Family history of diabetes, smoking, height, weight, waistline, fasting glycaemia, glycosylated haemoglobin, total and HDL-cholesterol and triglyceride values were collected. Claudication, cyanosis, cold foot, foot hair anomalies, skin thinning and femoral, popliteal, posterior tibial and dorsalis pedis pulses were assessed. The ABI was measured with a portable Doppler continuous-wave instrument.

Results An ABI < 0.9 was found in 539 (21.1%) patients. Claudication was present in 187 (7.3%). Femoral pulse was absent in 218 (8.5%), popliteal in 316 (12.3%), tibial in 563 (22.0%) and dorsalis pedis in 578 (22.6%). Foot cyanosis was observed in 88 (3.4%), cold foot in 359 (13.9%), skin thinning in 468 (18.3%) and hair anomalies in 857 (33.5%). Multivariate analysis of the variables associated with ABI < 0.9 in the univariate analysis confirmed the independent role of age [relative risk (RR) 1.02, $P < 0.001$, confidence interval (CI) 1.01, 1.04], claudication (RR 4.53, $P < 0.001$, CI 2.97, 6.93), absence of tibial pulse (RR 3.45, $P \leq 0.001$, CI 2.54, 4.68) and pedis pulse (RR 1.96, $P \leq 0.001$, CI 1.4, 2.68).

Conclusions PAD, as represented by ABI < 0.9, is common in newly diagnosed Type 2 diabetic patients.

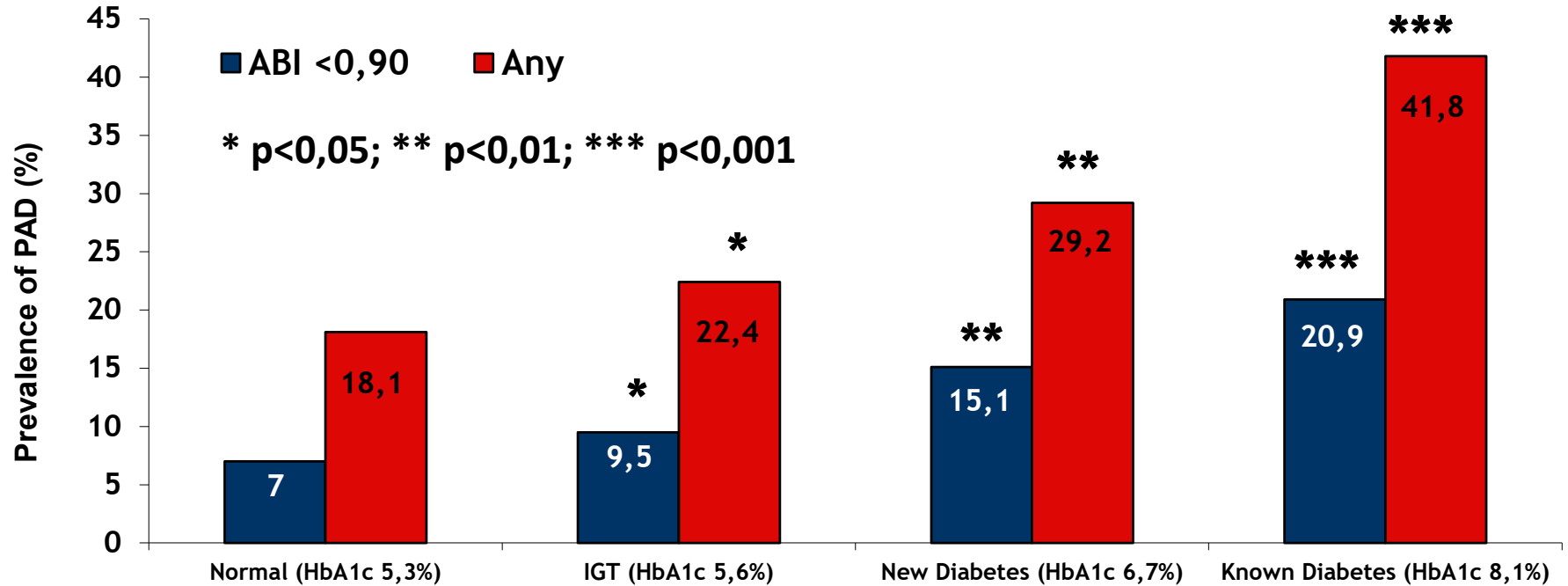
Diabet. Med. 22, 1310–1314 (2005)

Keywords ankle-brachial index, claudication, clinical foot examination, newly diagnosed type 2 diabetes, peripheral arterial disease, peripheral pulses

Abbreviations ABI, ankle-brachial index; BMI, body mass index; PAD, peripheral arterial disease; ROC, receiver–operating characteristic

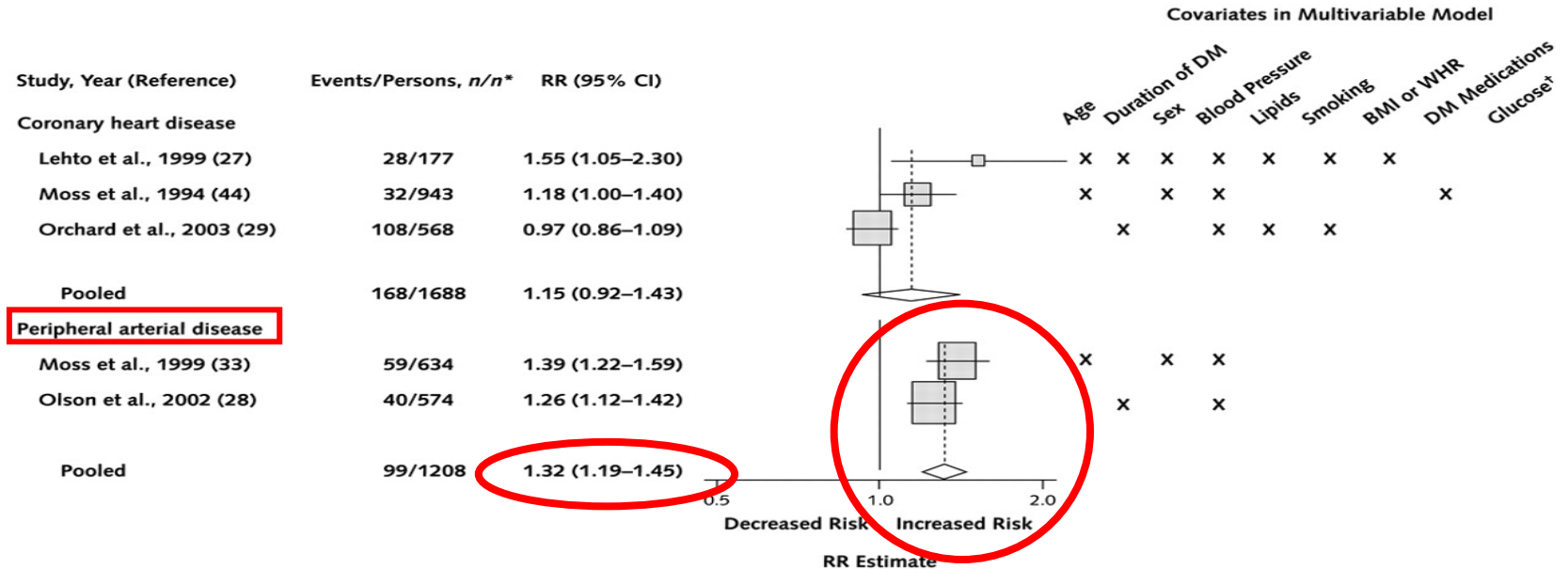
21.1%

PREVALENCE OF PAD

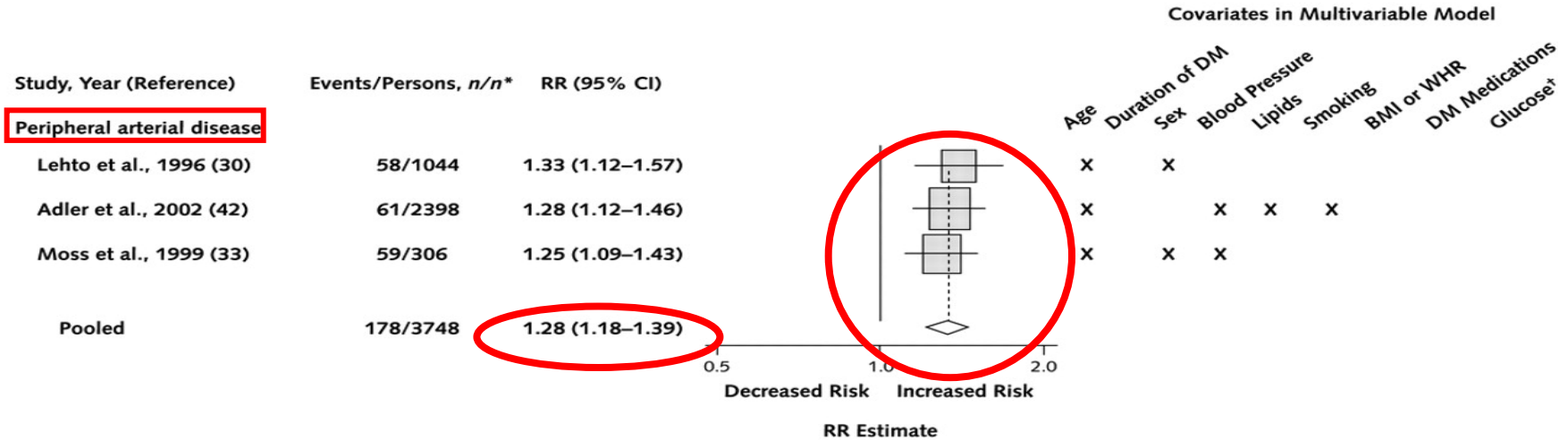


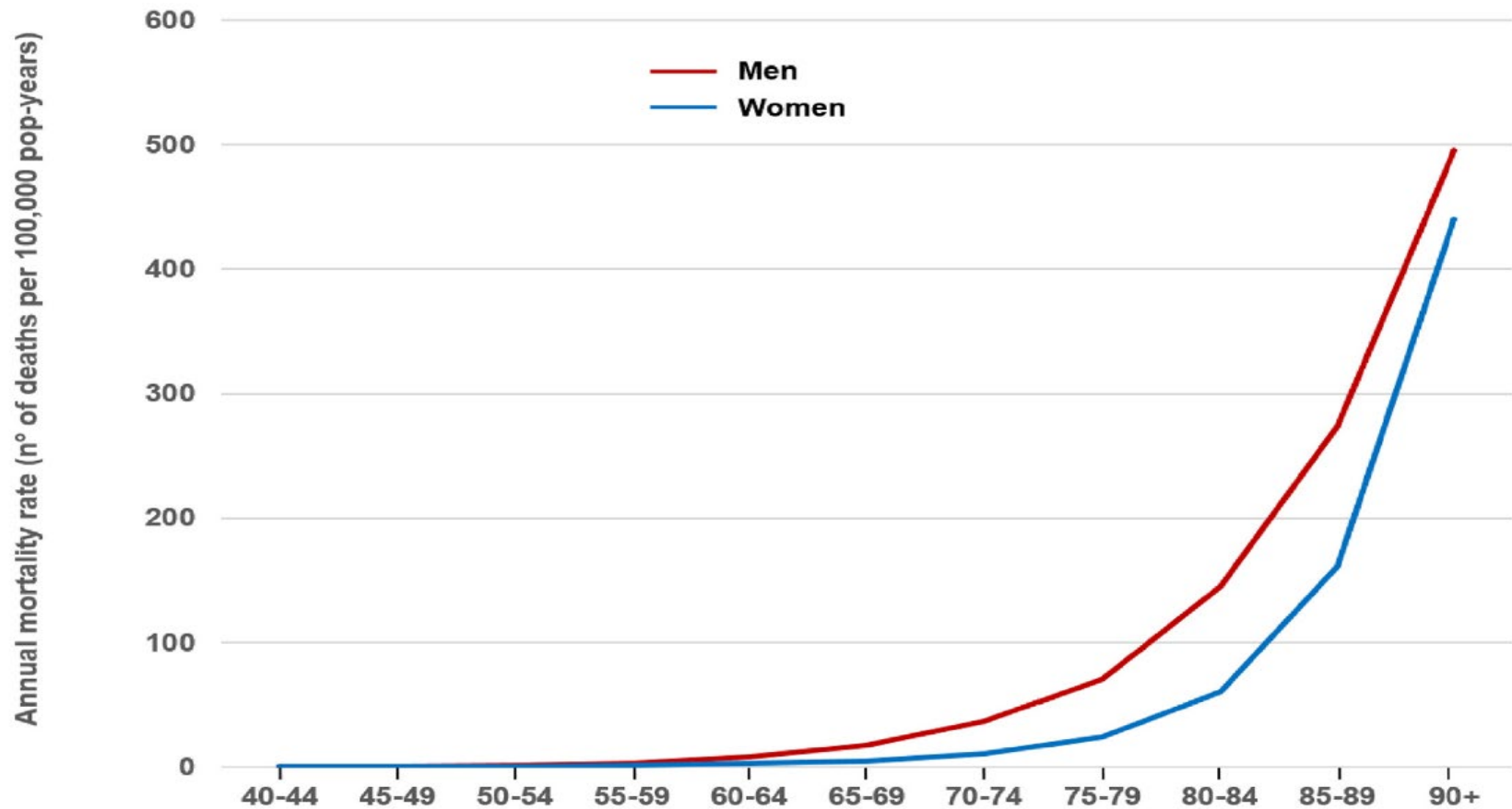
[Beks PJ. The Hoorn Study. Diabetologia 1995]

Relative risk (RR) estimates and 95% CIs for HbA1c (per 1% increase) and incident coronary heart disease and peripheral arterial disease in persons with type 1 diabetes



Relative risk (RR) estimates and 95% CIs for HbA1c (per 1% increase) and incident peripheral arterial disease in persons with type 2 diabetes

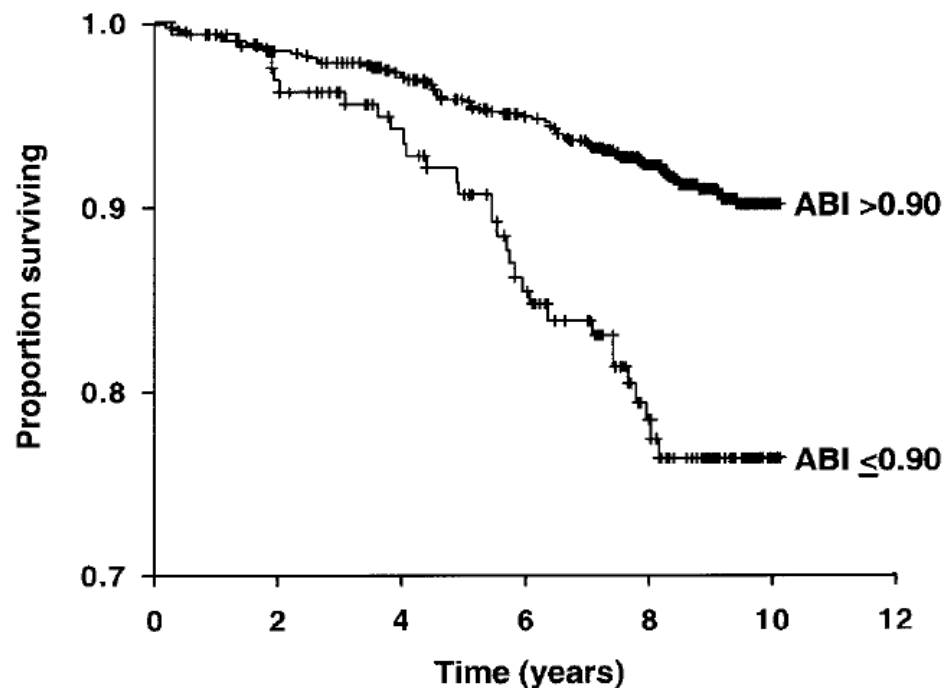


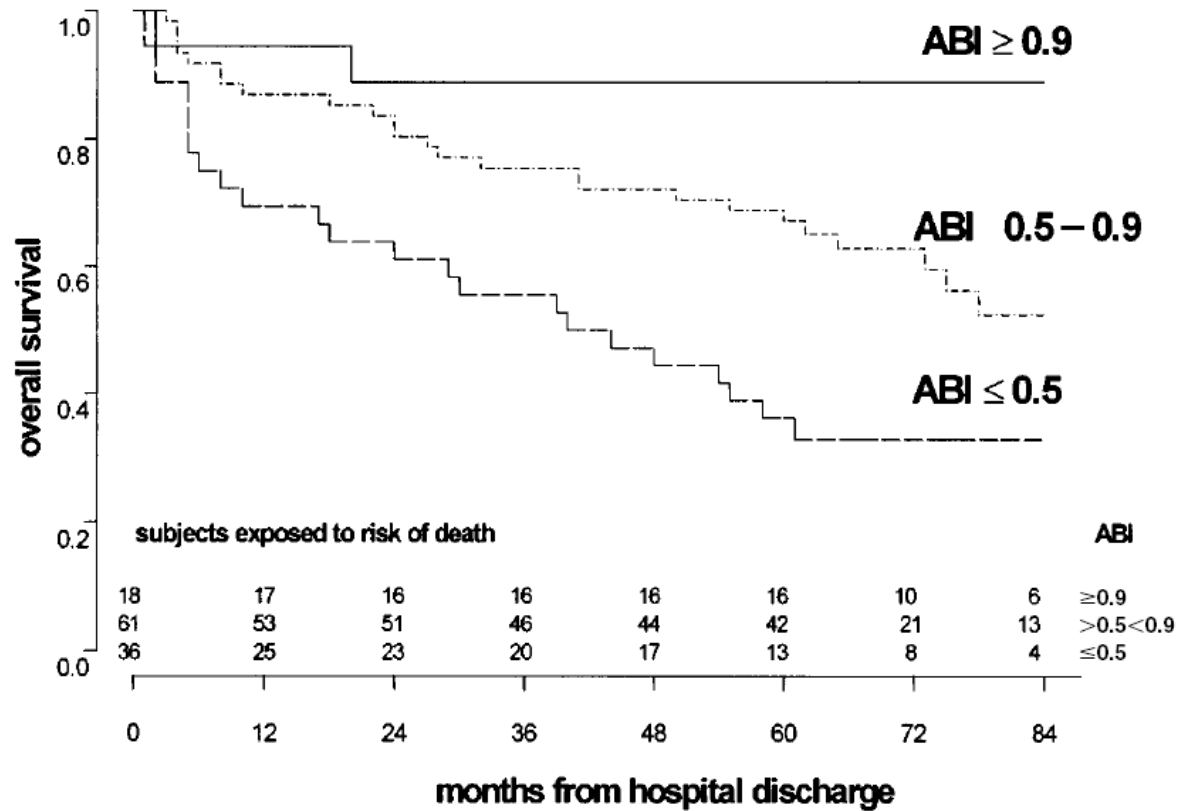


[Voci et al. *Nutr Met Cardiovasc Dis*, 2022]

Peripheral Arterial Disease and Risk of Cardiac Death in Type 2 Diabetes

The Fremantle Diabetes Study





[Faglia et al, Diabetes Care 2001]

PERIPHERAL ARTERIOPATHY FEATURES

DIABETIC

- 40 – 50 yrs
- No gender predominance
- Polidistrictual
- Distal
- No collaterals
- Bilateral
- Painless

NON DIABETIC

- 60 – 70 yrs
- Male predominance
- Smoke
- Proximal
- Collaterals
- Monolateral
- Painful

PERIPHERAL ARTERIOPATHY FEATURES

DIABETIC

- 40 – 50 yrs
- No gender predominance
- Polidistrictual
- Distal
- No collaterals
- Bilateral
- Painless

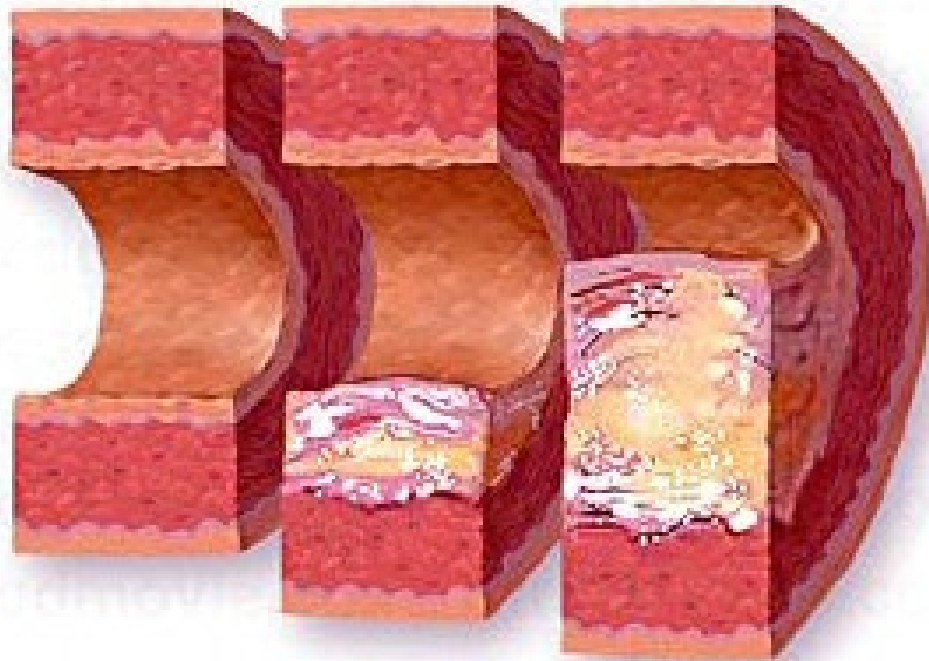
NON DIABETIC

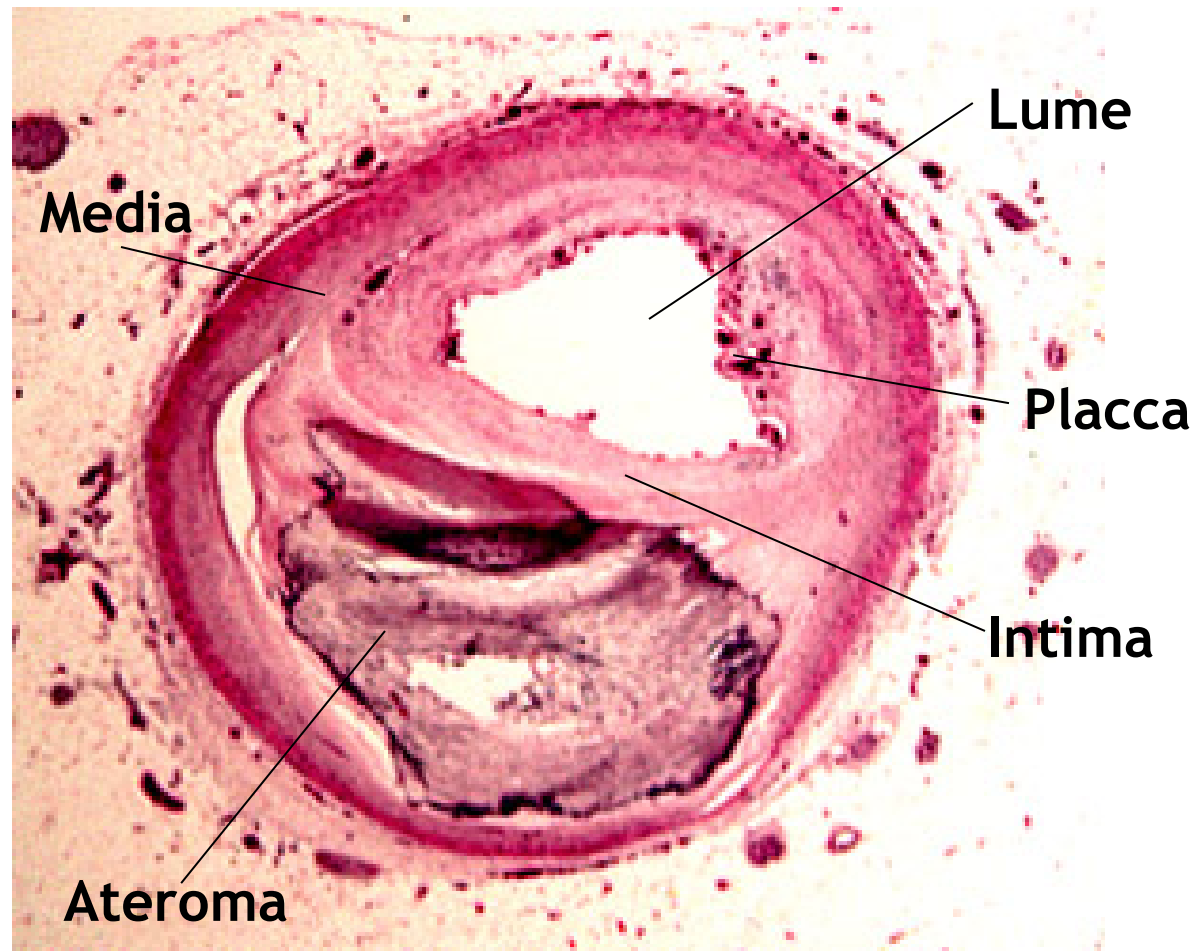
- 60 – 70 yrs
- Male predominance
- Smoke
- Proximal
- Collaterals
- Monolateral
- Painful

Diagnostic Parameters

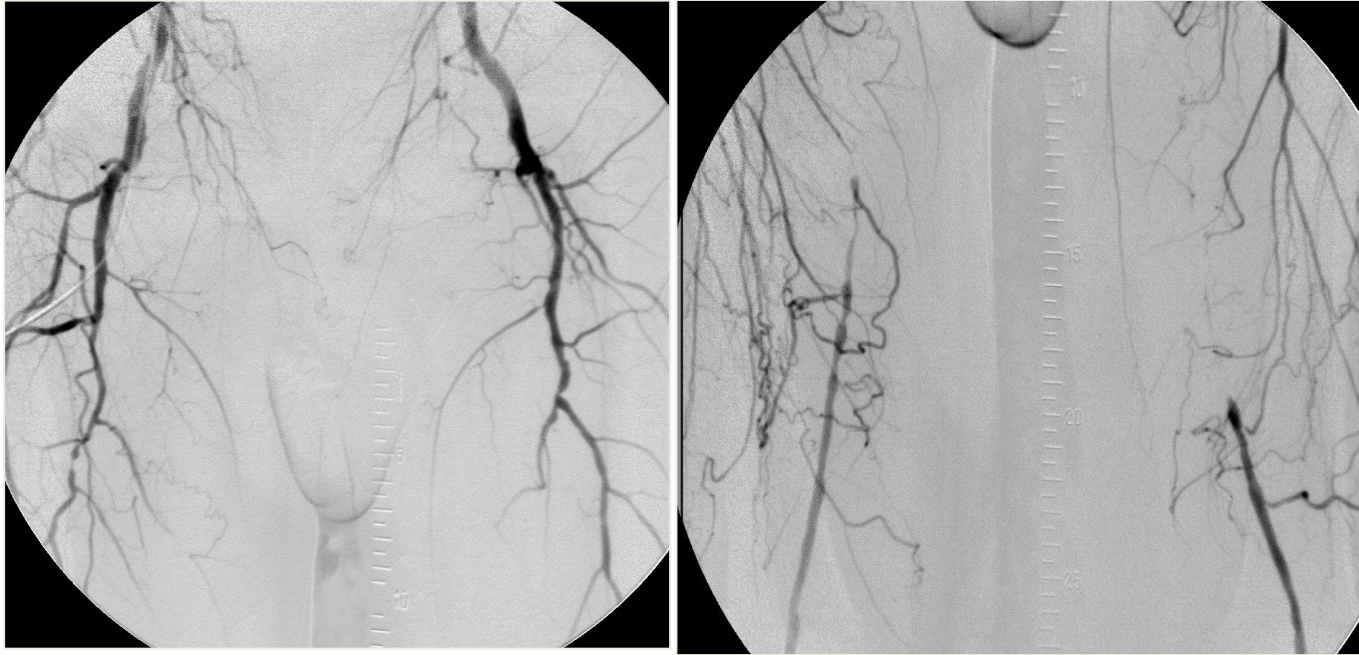
	Normal	PAD	Critical Ischemia
Ankle pressure (mmHg)	> 100	100 - 50	< 50
Allux pressure (mmHg)	> 50	50 - 30	< 30
ABPI (ratio)	> 0.9*	0.9 – 0.5	< 0.5
TcPO₂ (mmHg)	> 60	60 - 40	< 40

***If > 1.3 consider Monckeberg's sclerosis**

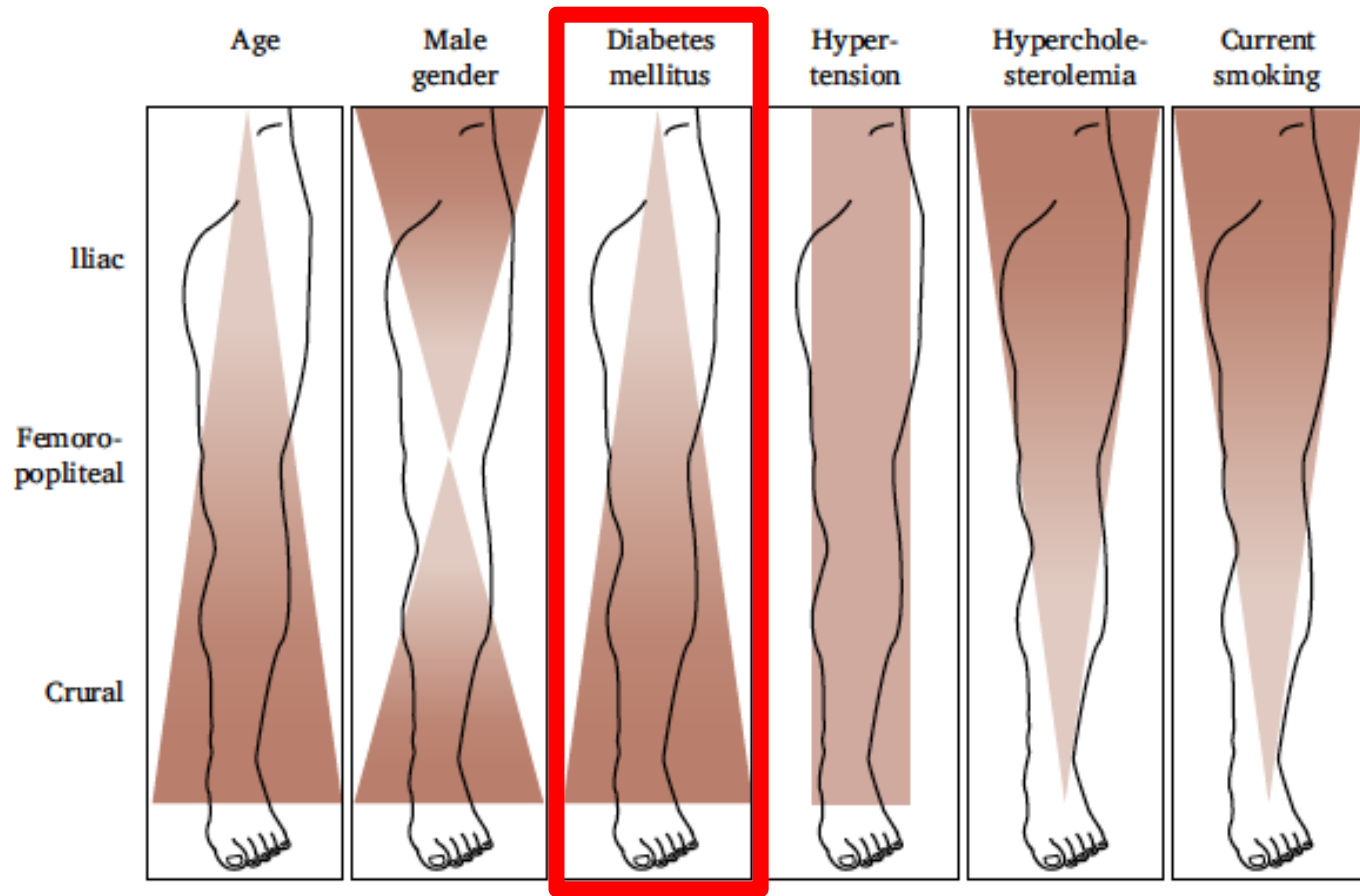




PAD IN THE ILIAC AND FEMORAL ARTERIES







[Diehm et al. Eur J Vasc Endovasc Surg, 2006]

ORIGINAL ARTICLE

RECENT DEVELOPMENTS IN THE MANAGEMENT OF THE DIABETIC FOOT

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

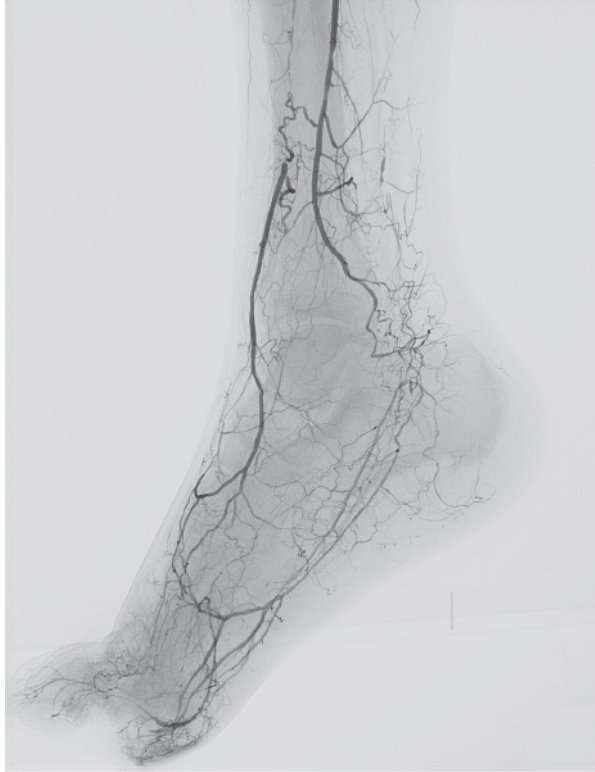
Roberto FERRARESI ¹ *, Giovanni MAURI ², Fabrizio LOSURDO ³, Nicola TROISI ⁴,
Diego BRANCACCIO ⁵, Carlo CARAVAGGI ⁶, Luca NERI ⁷

¹Peripheral Interventional Unit, Humanitas Gavazzeni Hospital, Bergamo, Italy; ²Department of Interventional Radiology, European Institute of Oncology, Milan, Italy; ³Diabetic Foot Clinic, Humanitas Gavazzeni Hospital, Bergamo, Italy; ⁴Department of Vascular and Endovascular Surgery, San Giovanni di Dio Hospital, Florence, Italy; ⁵University of Milan, Milan, Italy; ⁶Diabetic Foot Clinic, Multimedica Institute for Research and Care, Milan, Italy; ⁷Department of Clinical and Community Sciences, University of Milan, Milan, Italy

*Corresponding author: Roberto Ferraresi, Peripheral Interventional Unit, Humanitas Gavazzeni, Bergamo, Italy. E-mail: ferraresi.md@gmail.com

BAD vs

SAD



[Ferraresi et al. J Cardiovasc Surg, 2018]



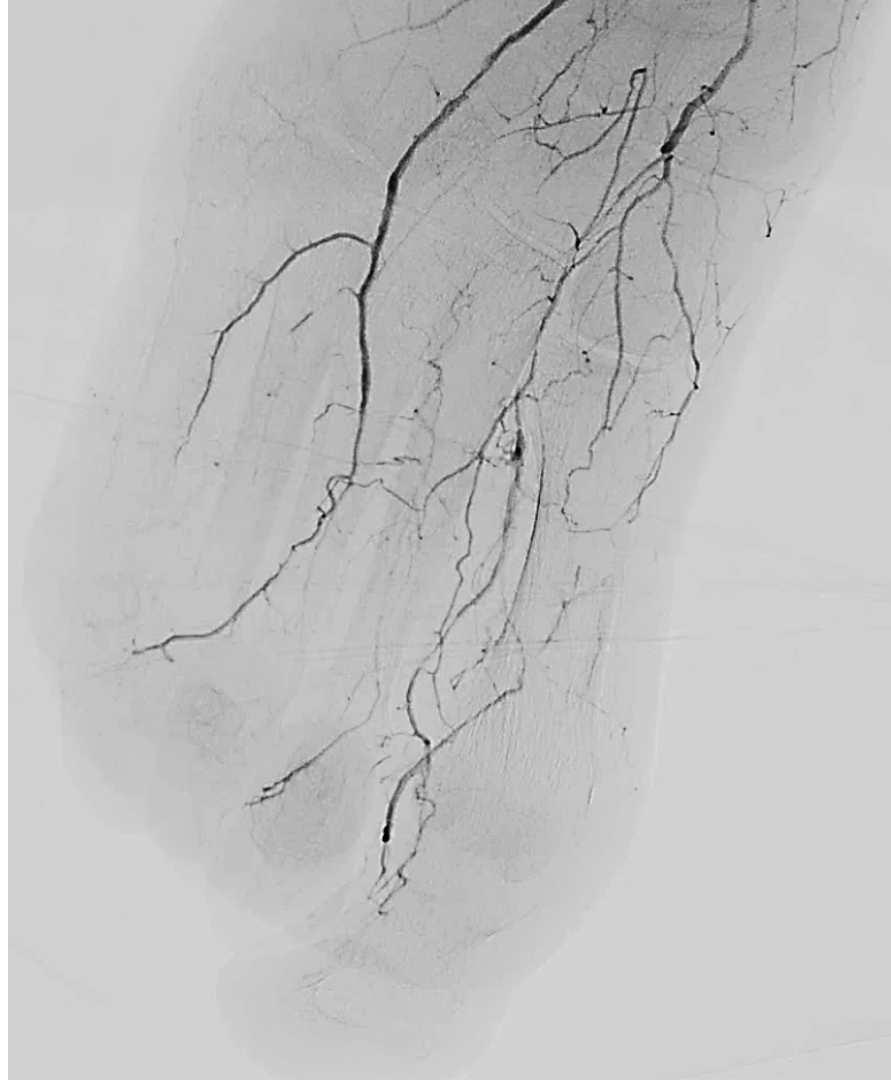
VÄI.
**Über die reine Mediaverkalkung der
Extremitätenarterien und ihr Verhalten zur
Arteriosklerose.**

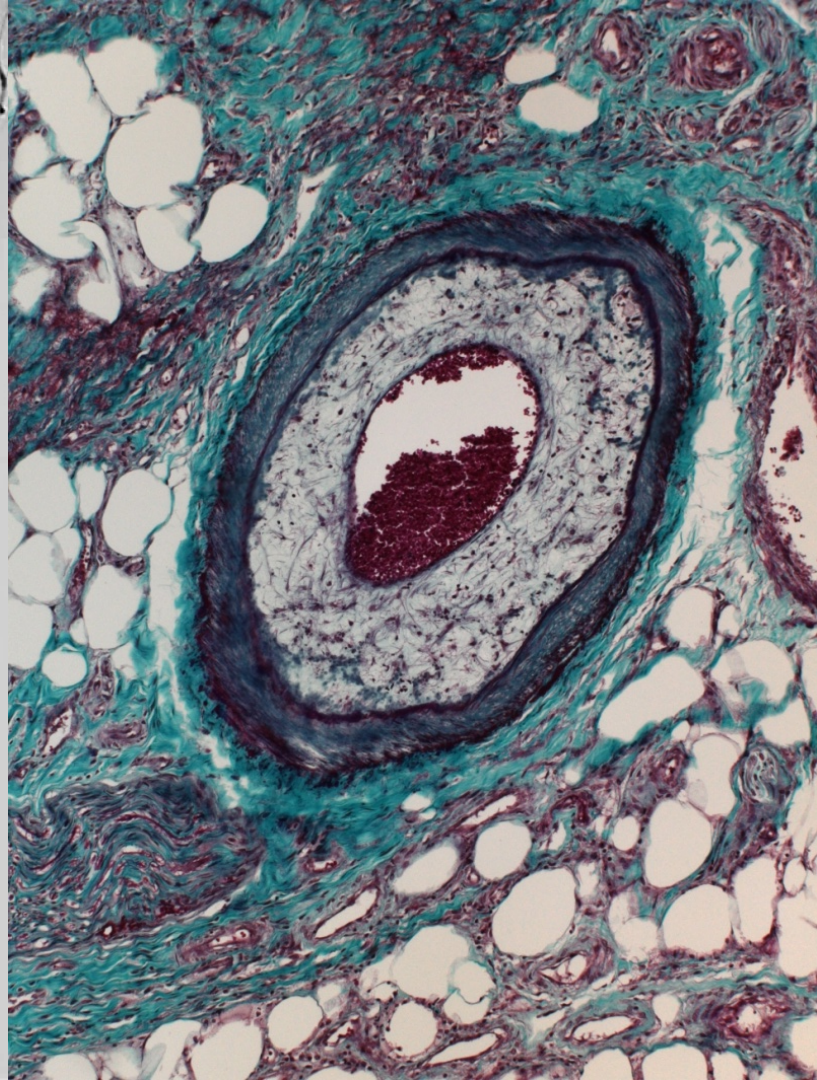
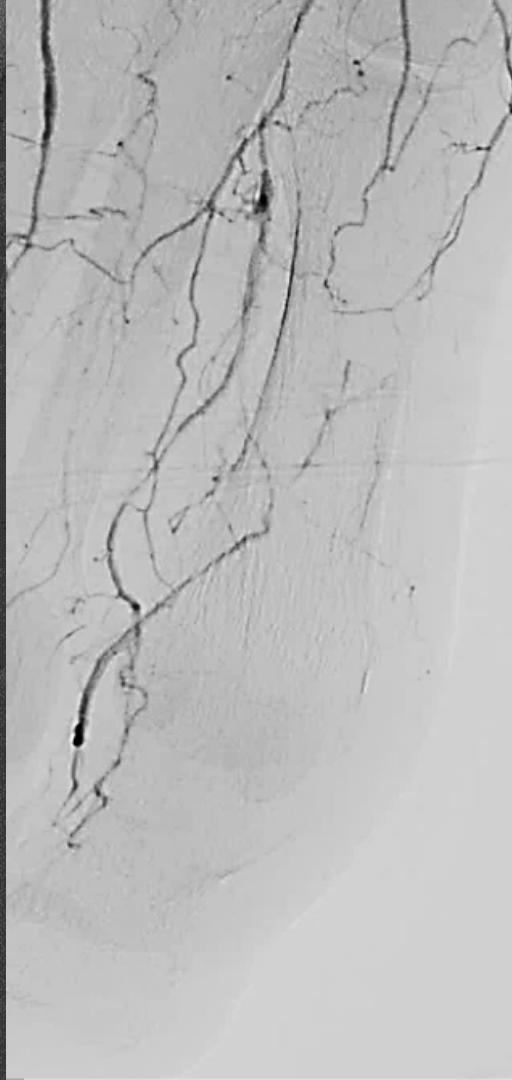
(Aus dem Pathologisch- anatomischen Institut des Allgem. Krankenhauses
Harburg-Eppendorf.)

Von
Dr. J. G. Monckeberg.

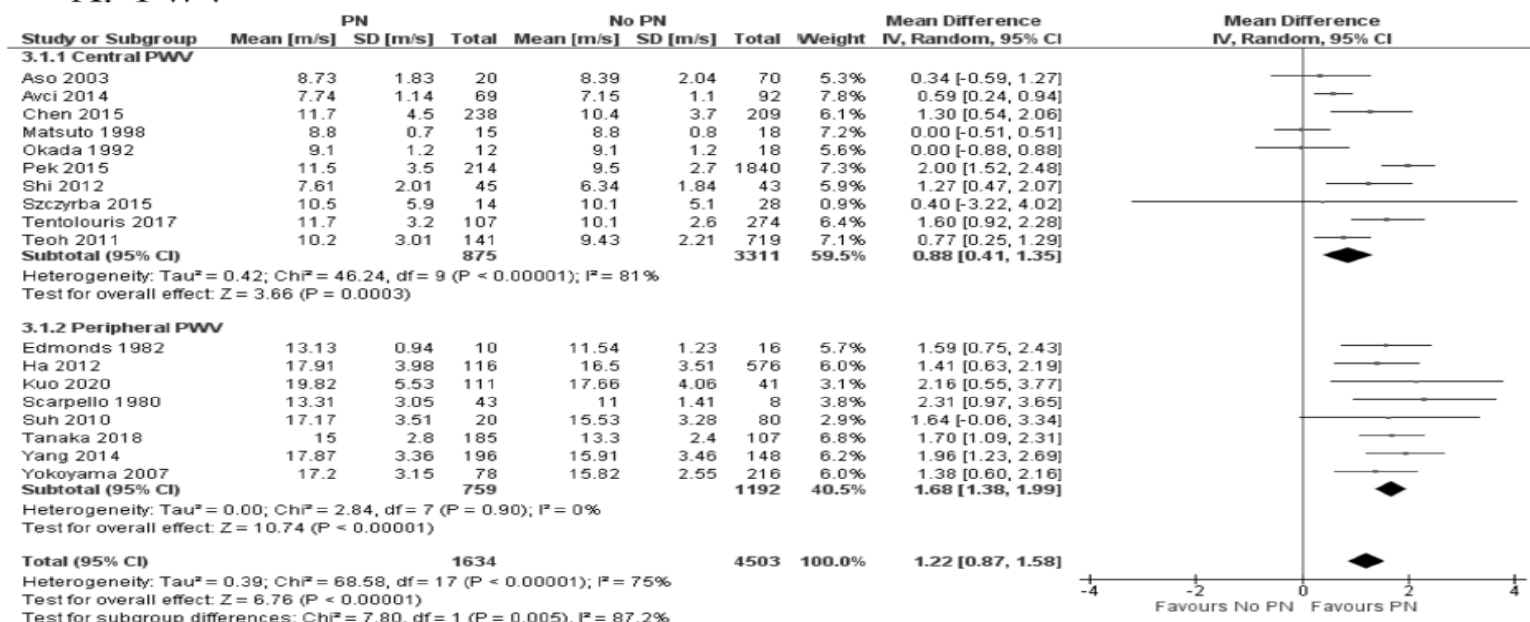
Monckeberg, 1903

- A relevant decrease in the thickness of the media occurs; this **apparent reduction** is due to the fact that the calcification takes place on **degenerated muscle fibers that are no longer contractible and slack**
- In the highest degrees of MAC, the artery is transformed into a rigid tube..., **on such vessels there is usually a diffuse intimal overgrowth**
- I am unable to prove whether the secondary intimal growth in pure MAC can lead to obliteration of the vessel; **but some of my cases make it likely**

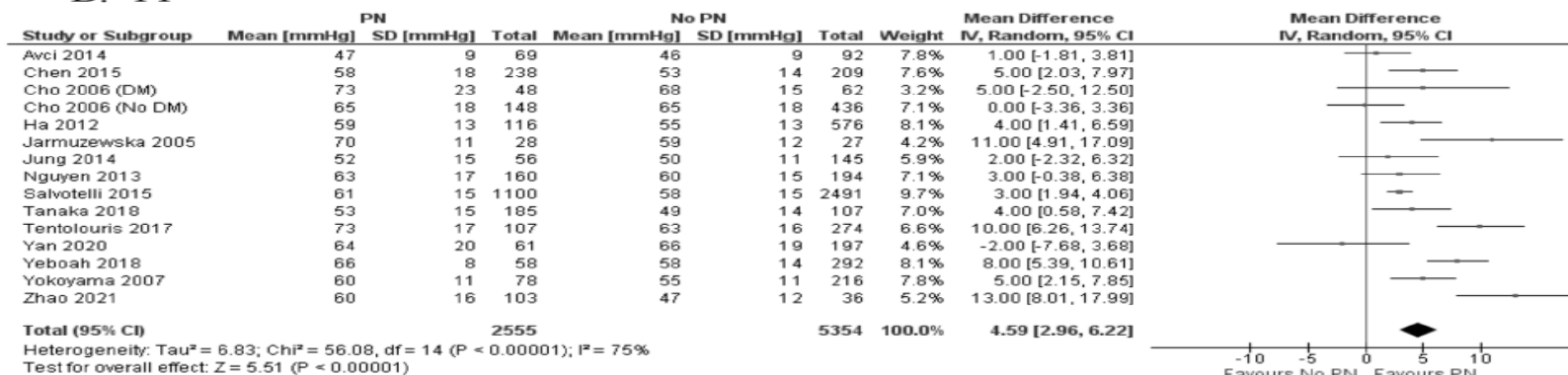




A. PWV



B. PP



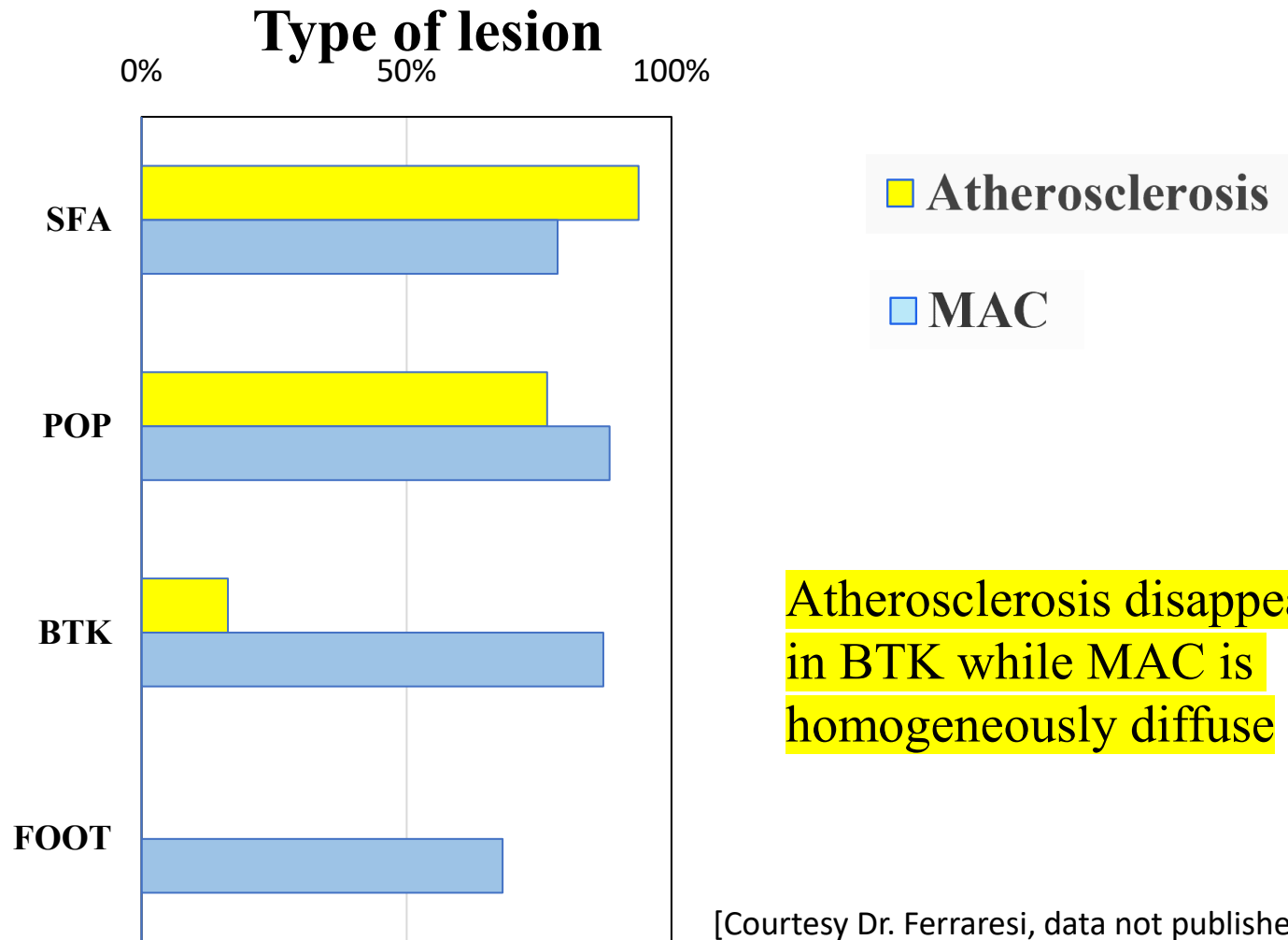
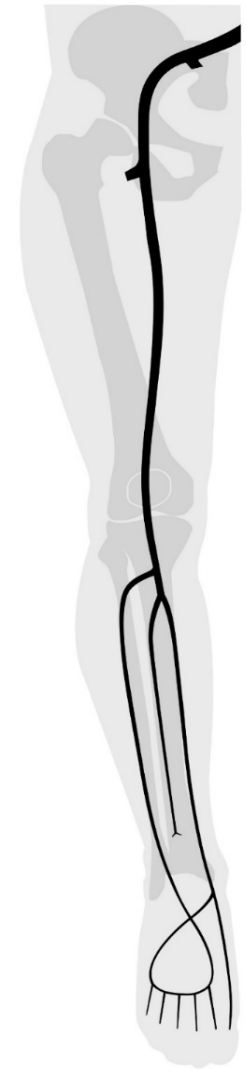
Prevalence of Nonatheromatous Lesions in Peripheral Arterial Disease

W. Charles O'Neill, Kum Hyun Han, Thomas M. Schneider, Randolph A. Hennigar

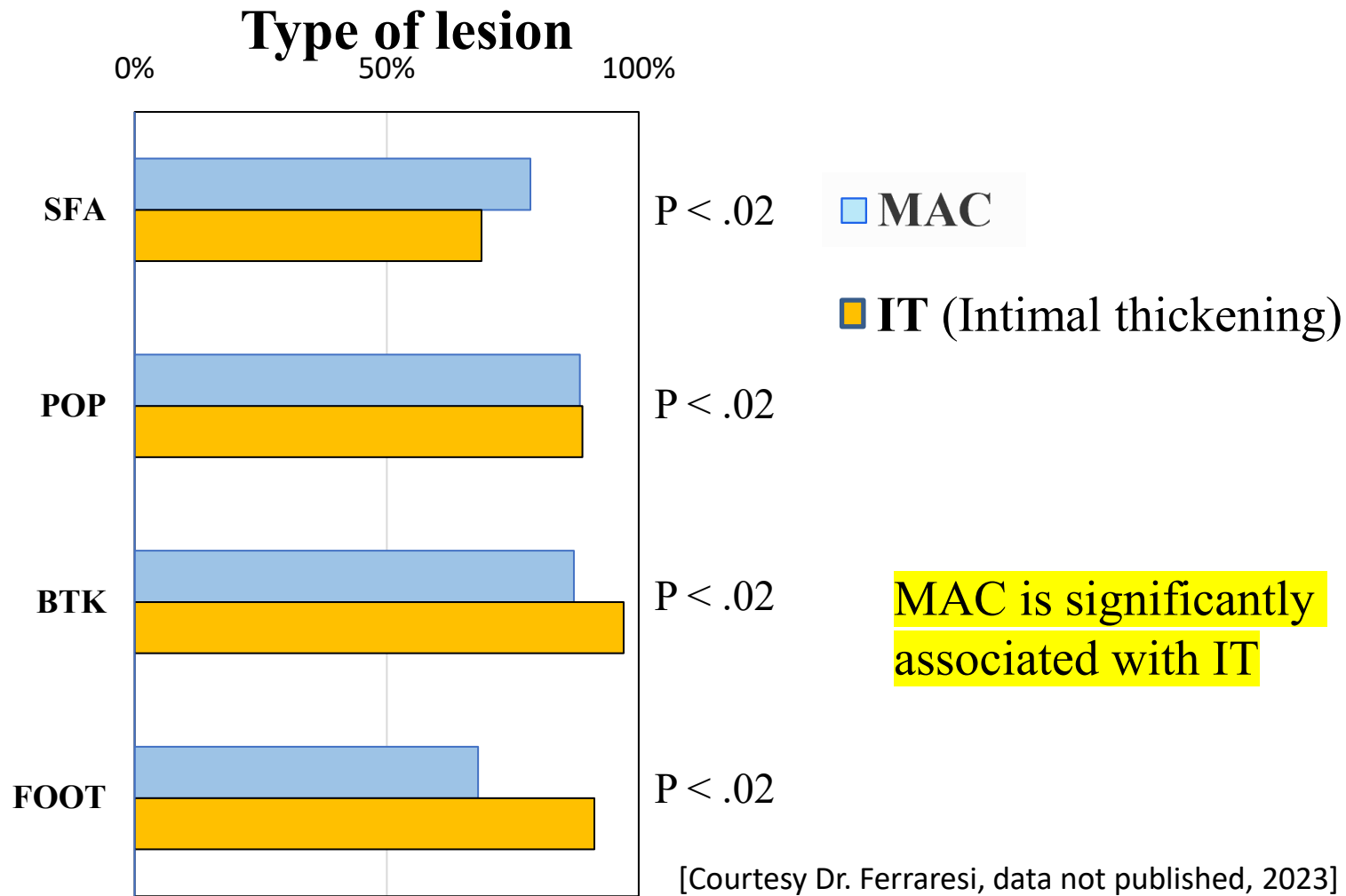
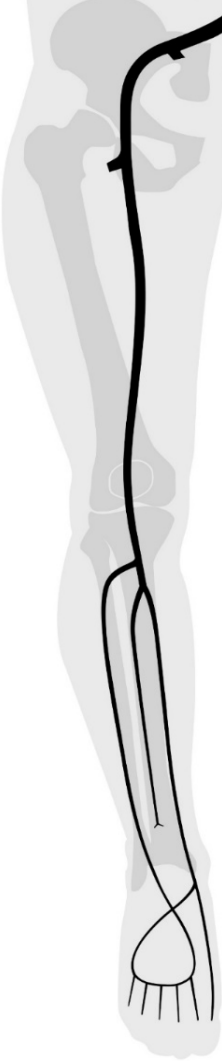
Arterioscler Thromb Vasc Biol. 2015;35:439-447

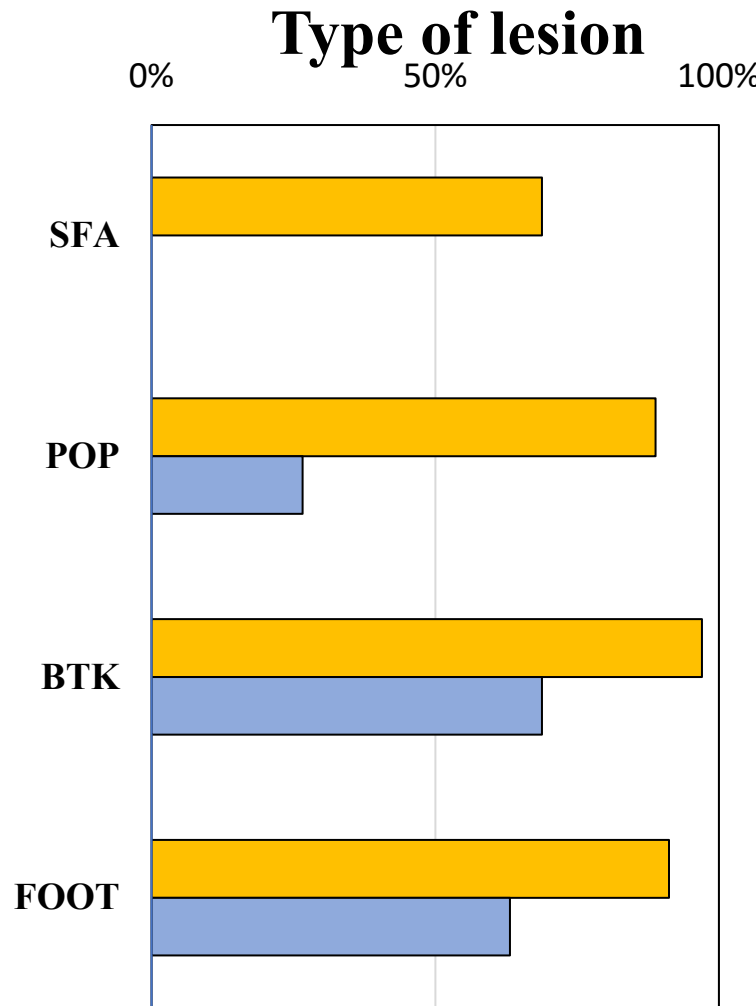
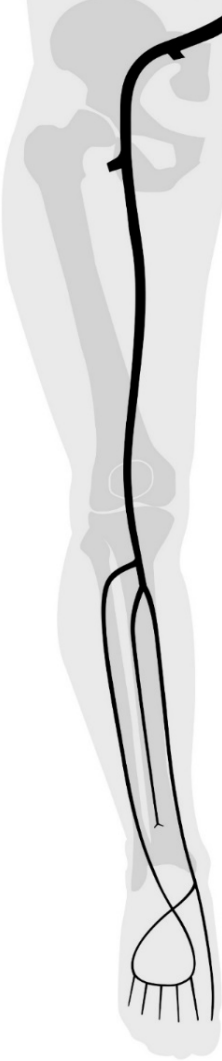
- 176 upper and lower leg arteries
- 60 pts with PAD (58% DM, 35% ESRD)

- The most common findings were calcification of the media (72% of arteries) and intimal thickening without lipid (68% of arteries), with the presence of atheromas in only 23% of arteries. Intimal calcification occurred in 43% and was generally much less extensive than medial calcification. Nonatheromatous intimal thickening was frequently severe, resulting in complete occlusion in some vessels.
- The majority of arteries in patients with PAD have a vascular lesion that is distinct from atherosclerosis, suggesting a different pathogenesis. The bulk of vascular calcification in the lower extremities is medial rather than intimal



[Courtesy Dr. Ferraresi, data not published, 2023]





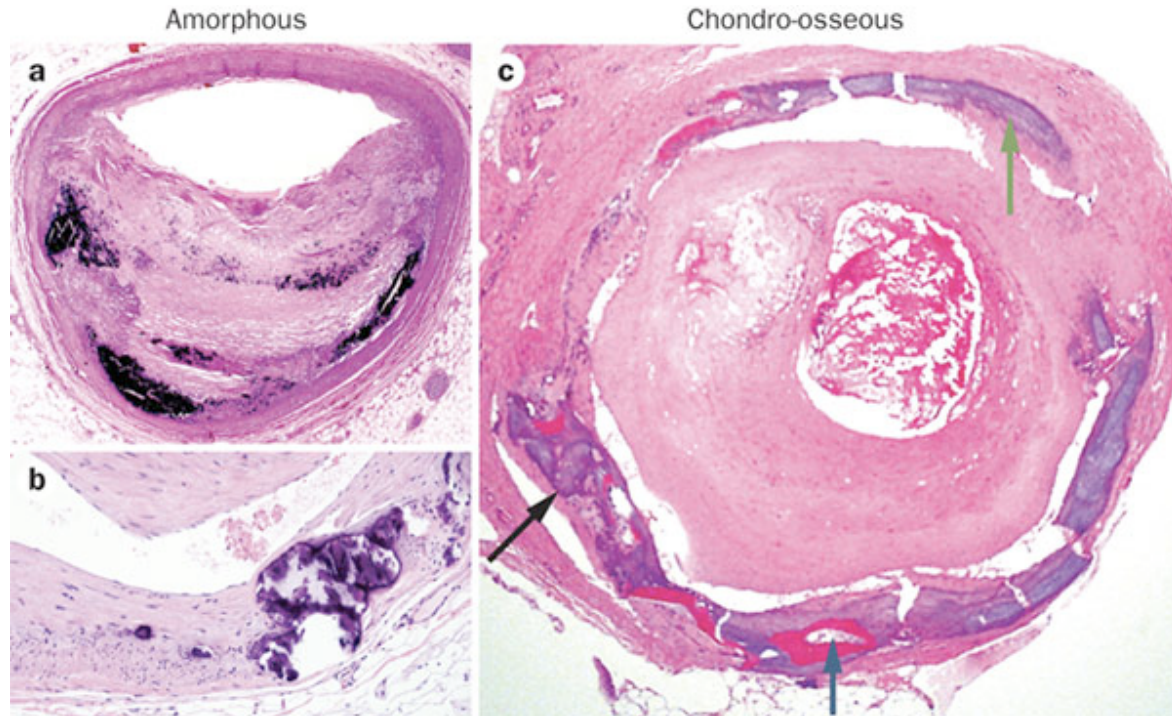
■ IT (Intimal thickening)

■ Obstructive IT
($\geq 50\%$ lumen)

IT is non-obstructive in
SFA-POP, highly
obstructive in BTK &
FOOT

[Courtesy Dr. Ferraresi, data not published, 2023]

MECHANISMS OF ARTERIAL CALCIFICATION



ORIGINAL ARTICLE



Below-the-ankle arterial disease: a new marker of coronary artery disease in patients with diabetes and foot ulcers

Marco Meloni^{1,2} · Alfonso Bellia^{1,2} · Laura Giurato^{1,2} · Davide Lauro^{1,2} · Luigi Uccioli³

Received: 30 April 2022 / Accepted: 29 June 2022

© Springer-Verlag Italia S.r.l., part of Springer Nature 2022

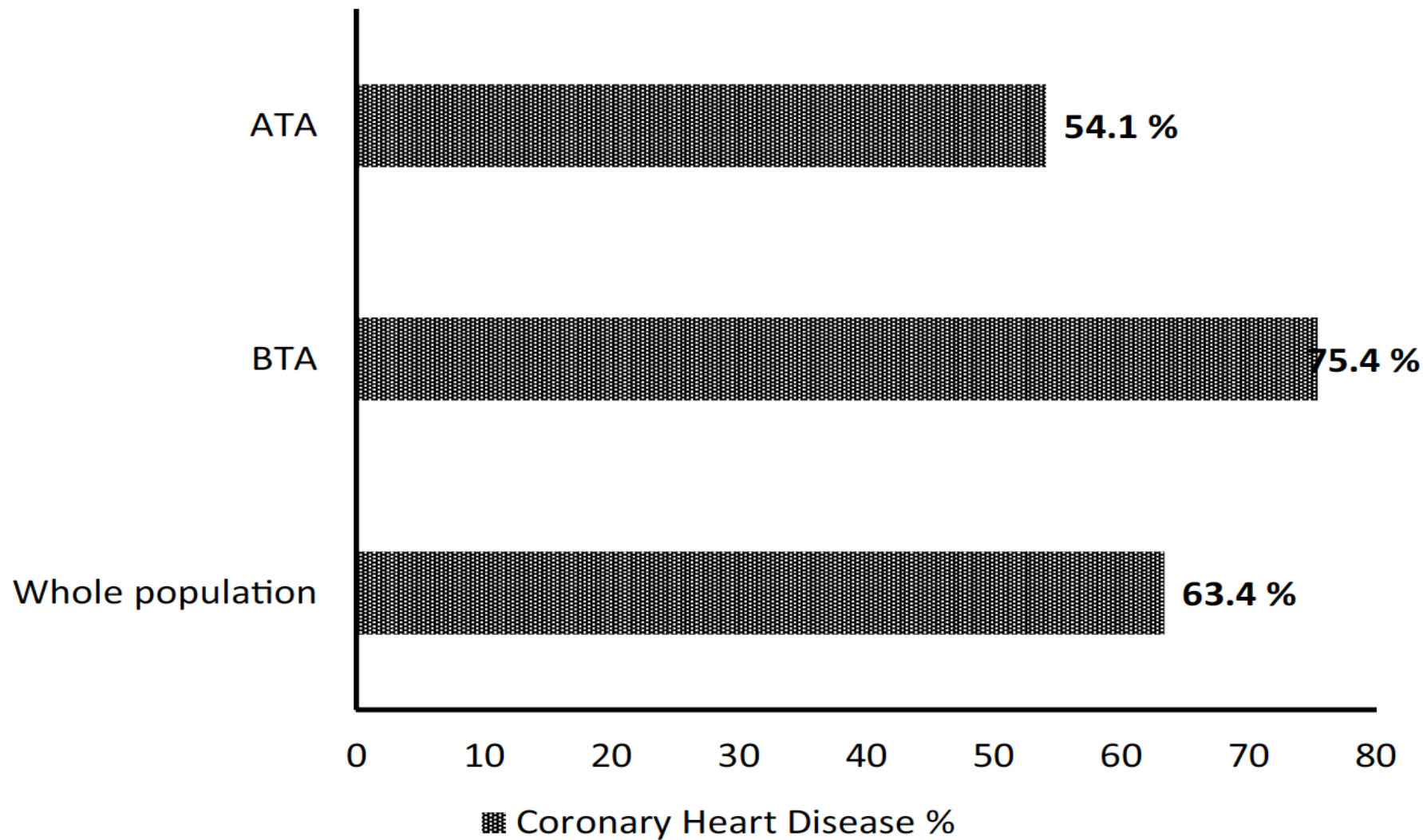
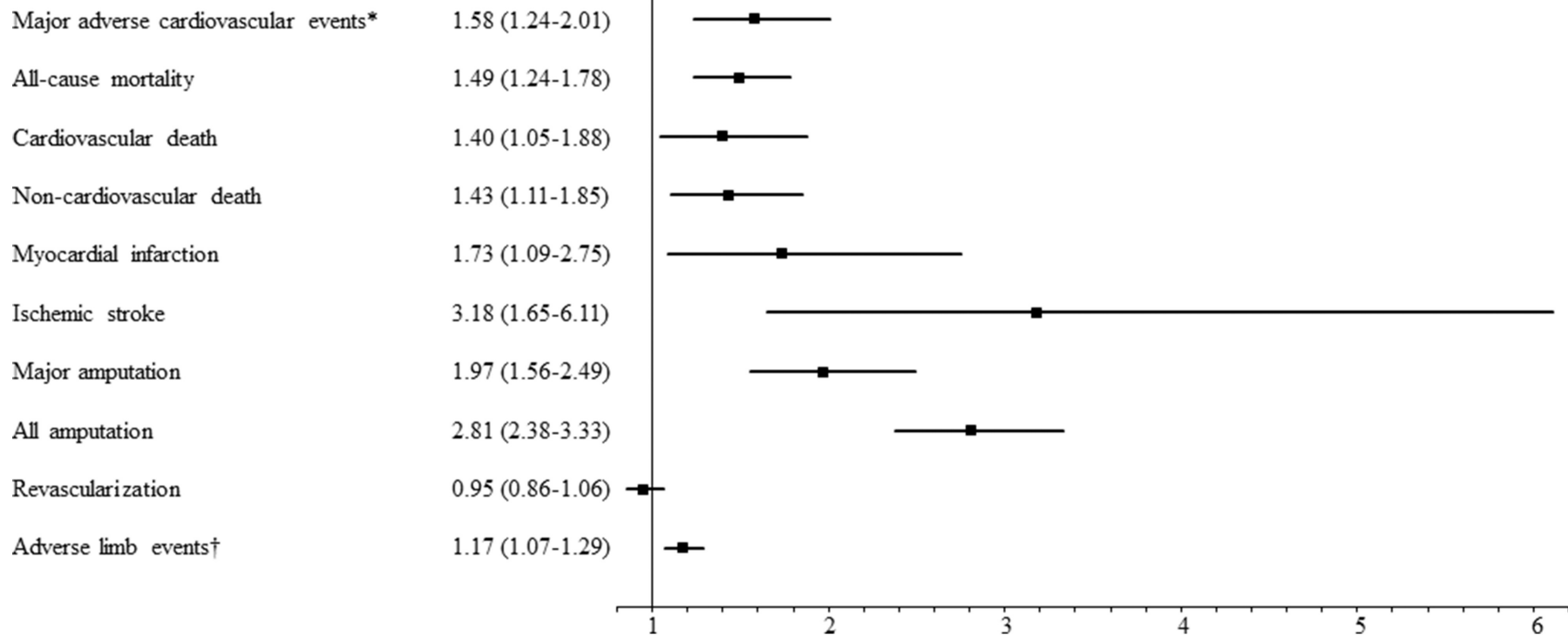


Table 4 Multivariate analysis of factors associated with coronary artery disease (CAD)

	OR	95%	<i>p</i> value*
Age, per 10 years	1.1	0.7–1.4	0.06
Diabetes duration > 10 vs < 10 years	0.9	0.8–1.7	0.4
ESRD	1.5	1.1–2.2	0.001
BTA vs ATA arterial disease	1.9	1.3–4.5	0.0001
TcPO ₂ (< 25 mmHg)	1.2	0.9–1.7	0.08

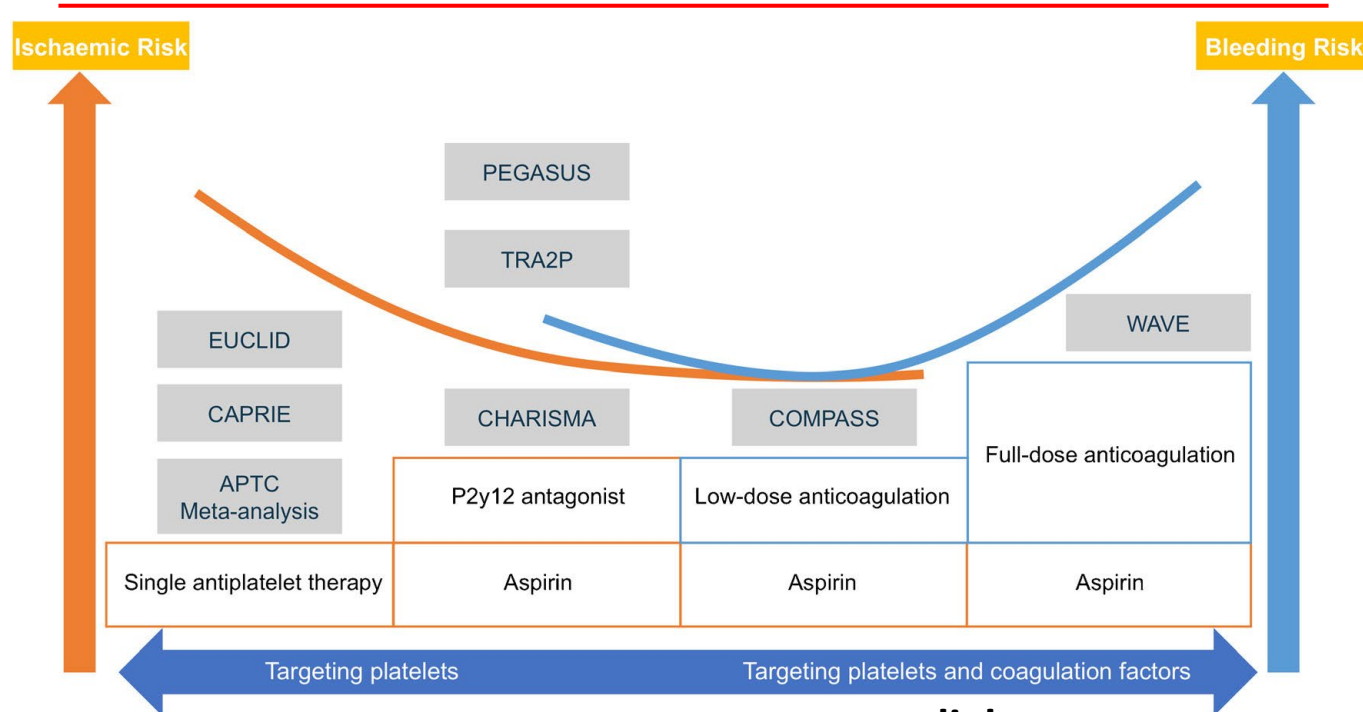
Diabetic vs. non-diabetic patients

Hazard Ratio (95%CI)



COMPASS TRIAL

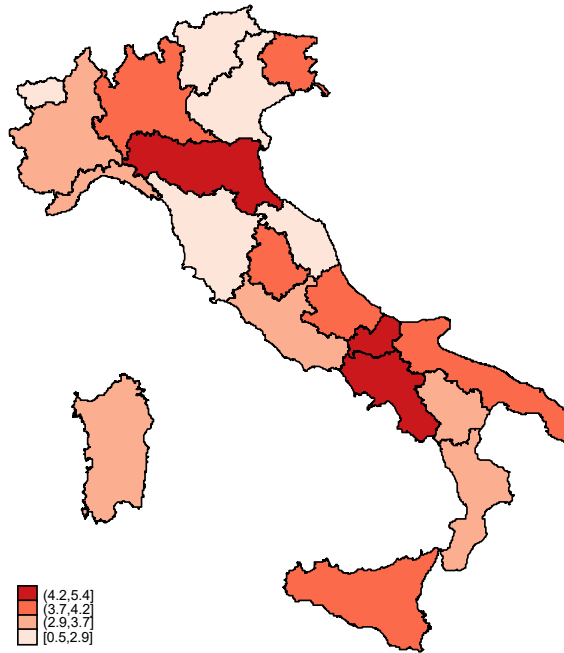
rivaroxaban 2.5 mg BID + ASA daily



PAD patients + polyvascular disease/history of heart failure/ **diabetes**, or renal insufficiency are particularly susceptible to major vascular events and have greater absolute risk reduction in adding rivaroxaban 2.5 mg BID to aspirin as compared to aspirin alone.

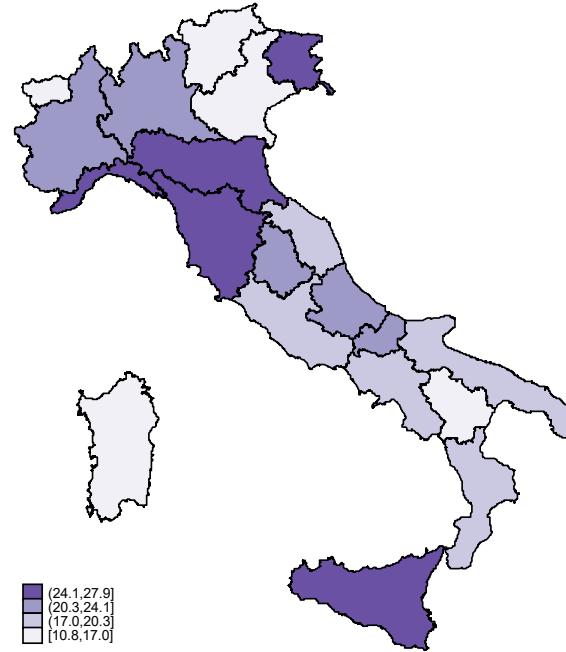
Amputations and Revascularization Rates in DM

Major Amputations



per 100.000 inhabitants

Revascularizations



per 100.000 inhabitants

[Courtesy Dr. Maggini, ISS]

Lower Extremity Amputations in Persons with and without Diabetes in Italy: 2001–2010

Flavia L. Lombardo¹, Marina Maggini¹, Alessandra De Bellis², Giuseppe Seghieri², Roberto Anichini^{2*}

1 National Centre for Epidemiology, Surveillance and Health Promotion, National Institute of Health, Roma, Italy, **2** Diabetes Unit and Diabetic Foot Unit, Department of Internal Medicine General Hospital Pistoia, Pistoia, Italy

Abstract

Objective: To analyze hospitalization for lower extremity amputations (LEAs) and amputee rates in persons with and without diabetes in Italy.

Research Design and Methods: All patients with LEAs in the period 2001–2010 were identified analyzing the National Hospital Discharge Record database. For each year, amputee and hospitalization rates for LEAs were calculated either for persons with diabetes or without. Time trend for major and minor amputations were analysed.

Results: From 2001 to 2010 a mean annual number of 11,639 individuals underwent a lower extremity amputation: 58.6% had diabetes accounting for 60.7% of total hospitalizations. In 2010, the crude amputee rate for LEAs was 20.4 per 100,000 inhabitants: 247.2 for 100,000 persons with diabetes, and 8.6 for those without diabetes. Having diabetes was associated to an increased risk of amputation (Poisson estimated RR 10.9, 95%CI 9.4–12.8). Over the whole period, a progressive reduction of amputee rates was observed for major amputations either among persons with diabetes (–30.7%) or without diabetes (–12.5%), while the rates of minor amputations increased progressively (+22.4%) among people without diabetes and were nearly stable in people with diabetes (–4.6%). A greater number of minor amputations were performed among persons with than without diabetes: in 2010, the minor-to-major ratio among persons with diabetes (2.5) was more than twice than in those without diabetes (1.0).

Conclusions: The nationwide analyses confirm a progressive reduction of hospitalization and amputee rates for major LEAs, suggesting an earlier and more diffuse approach aimed at limb salvage.

Citation: Lombardo FL, Maggini M, De Bellis A, Seghieri G, Anichini R (2014) Lower Extremity Amputations in Persons with and without Diabetes in Italy: 2001–2010. PLoS ONE 9(1): e86405. doi:10.1371/journal.pone.0086405

Editor: Christian Herder, German Diabetes Center, Leibniz Center for Diabetes Research at Heinrich Heine University Dusseldorf, Germany

Received: April 30, 2013; **Accepted:** December 13, 2013; **Published:** January 28, 2014

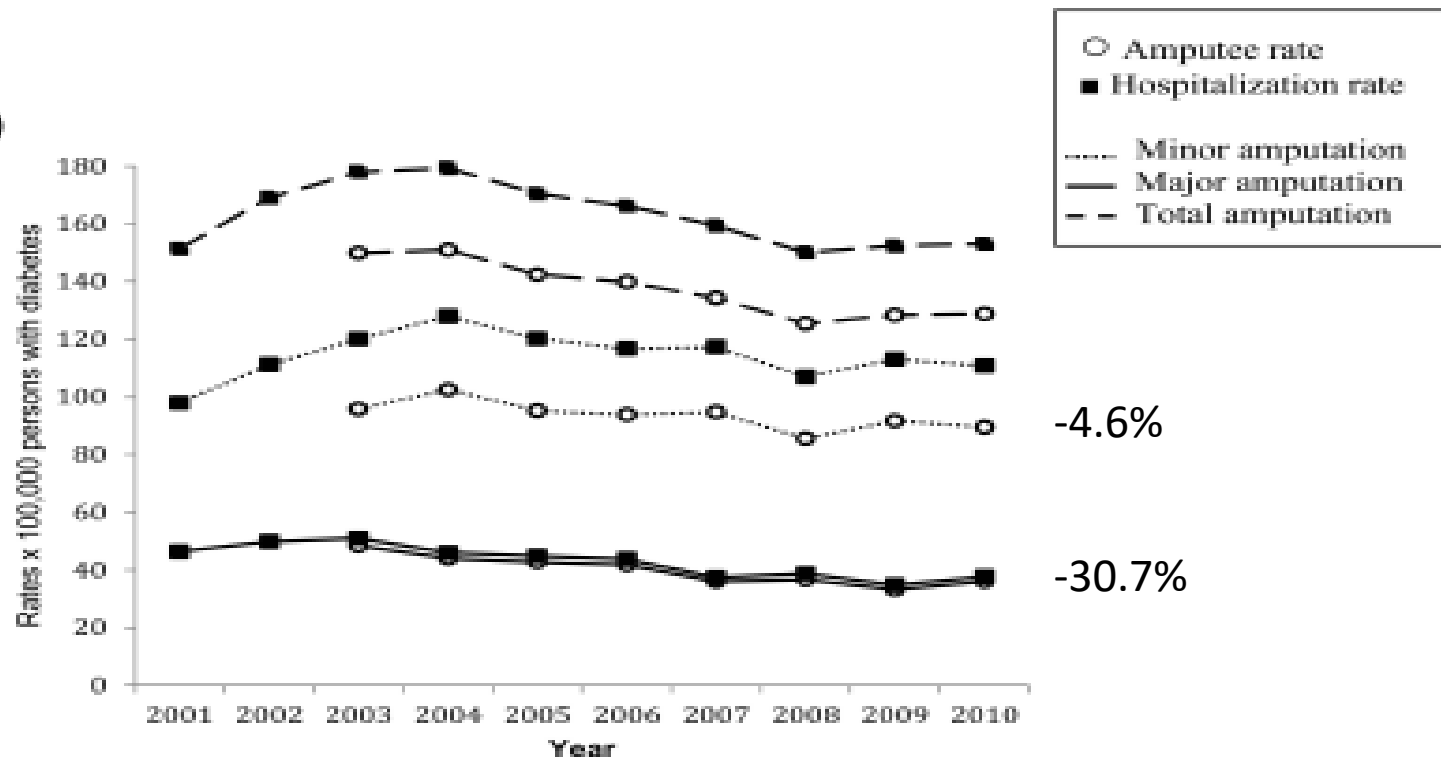
Copyright: © 2014 Lombardo et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Funding: The authors have no support or funding to report.

Competing Interests: The authors have declared that no competing interests exist.

* E-mail: ranichini@usbtoscana.it

a)



[Lombardo et al. Plos One, 2014]

ORIGINAL ARTICLE

Changes in Diabetes-Related Complications in the United States, 1990–2010

Edward W. Gregg, Ph.D., Yanfeng Li, M.D., Jing Wang, M.D.,
Nilka Rios Burrows, M.P.H., Mohammed K. Ali, M.B., Ch.B., Deborah Rolka, M.S.,
Desmond E. Williams, M.D., Ph.D., and Linda Geiss, M.A.

LOWER LIMB AMPUTATIONS X 10.000 DIABETIC PATIENTS

	USA	ITALY
2001	48.7	14.9
2010	28.4	12.9
DELTA %	-51.4	-16.7

Natural History of Diabetic Peripheral Vascular Disease

25% → 35% → 15%

The diagram illustrates the progression of Diabetic Peripheral Vascular Disease (PAD) through three stages: Normal (25%), PAD (35%), and Critical Ischemia (15%). A red arrow points from 25% to 35%, and another from 35% to 15%. A red box highlights the PAD and Critical Ischemia columns of the table below.

	Normal	PAD	Critical Ischemia
Ankle Pressure (mmHg)	> 100	100 - 50	< 50
Toe pressure (mmHg)	> 50	50 - 30	< 30
ABPI (ratio)	> 0.9*	0.9 – 0.5	< 0.5
TcPO₂ (mmHg)	> 60	60 - 40	< 40

*If > 1.3 consider Monckeberg's sclerosis



Article

Autologous Peripheral Blood Mononuclear Cells for Limb Salvage in Diabetic Foot Patients with No-Option Critical Limb Ischemia

Alessia Scatena ^{1,*} , Pasquale Petruzzi ², Filippo Maioli ³ , Francesca Lucaroni ⁴, Cristina Ambrosone ⁴, Giorgio Ventoruzzo ³, Francesco Liistro ⁵, Danilo Tacconi ⁶, Marianna Di Filippi ¹, Nico Attempati ², Leonardo Palombi ⁴, Leonardo Ercolini ³ and Leonardo Bolognese ⁵



check for
updates

Citation: Scatena, A.; Petruzzi, P.; Maioli, F.; Lucaroni, F.; Ambrosone, C.; Ventoruzzo, G.; Liistro, F.; Tacconi, D.; Di Filippi, M.; Attempati, N.; et al.

- ¹ Diabetology Unit, San Donato Hospital Arezzo, Local Health Authorities South East Tuscany, 52100 Arezzo, Italy; marianna.difilippi@uslsudest.toscana.it
 - ² Interventional Radiology Unit, San Donato Hospital Arezzo, Local Health Authorities South East Tuscany, 52100 Arezzo, Italy; pasquale.petruzzi@uslsudest.toscana.it (P.P.); nico.attempati@uslsudest.toscana.it (N.A.)
 - ³ Vascular Surgery Unit, San Donato Hospital Arezzo, Local Health Authorities South East Tuscany, 52100 Arezzo, Italy; filippo.maioli@gmail.com (F.M.); giorgio.ventoruzzo@uslsudest.toscana.it (G.V.); leonardo.ercolini@uslsudest.toscana.it (L.E.)
 - ⁴ Department of Biomedicine and Prevention, University of Rome Tor Vergata, 00133 Roma, Italy; f.lucaroni@gmail.com (F.L.); cristinambrosone@gmail.com (C.A.); leonardo.palombi@gmail.com (L.P.)
 - ⁵ Interventional Cardiology Unit, San Donato Hospital Arezzo, Local Health Authorities South East Tuscany, 52100 Arezzo, Italy; francesco.liistro@uslsudest.toscana.it (F.L.); leonardo.bolognese@uslsudest.toscana.it (L.B.)
 - ⁶ Infectious Disease Unit, San Donato Hospital Arezzo, Local Health Authorities South East Tuscany, 52100 Arezzo, Italy; danilo.tacconi@uslsudest.toscana.it
- * Correspondence: alessia.scatena@uslsudest.toscana.it; Tel.: +39-05-7525-5408

■ 3,75 M inhabitants

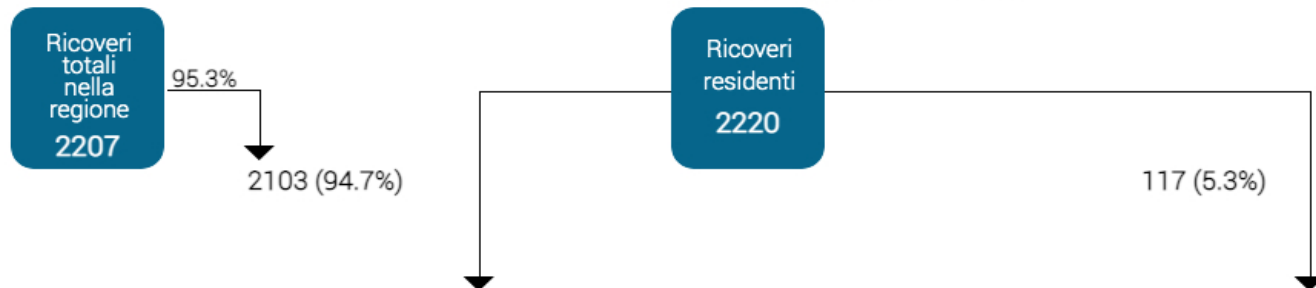
■ 250.000 DM

■ 12.500 DF

■ 153 LEA

Rivascolarizzazione arti inferiori

Toscana -01/01/2021 - -31/12/2021



Ricoveri in strutture della stessa regione

Struttura di Ricovero	Comune	Ricoveri	% Ricoveri	Volume*
Altre Strutture		431	19.4	0
Osp. S. Giovanni Di Dio Torregalli	Firenze	277	12.5	281
Azienda Ospedaliera Universitaria Senese	Siena	255	11.5	279
Ospedale Area Aretina Nord	Arezzo	251	11.3	264
Azienda Ospedaliero-Universitaria Pisana	Pisa	248	11.2	276
Az. Ospedaliero - Universitaria Careggi	Firenze	248	11.2	257
Ospedale Delle Apuane	Massa	226	10.2	237
Ospedale Livorno	Livorno	167	7.5	167

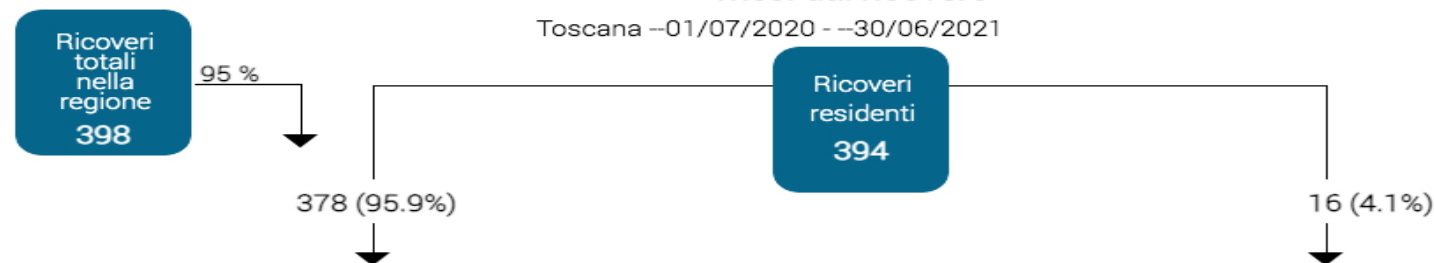
Ricoveri in strutture di altre regioni

Struttura di Ricovero	Comune	Ricoveri	% Ricoveri	Volume*
Altre Strutture		117	5.3	0

*Volume totale di ricoveri nella struttura per l'indicatore in studio

Arteriopatia degli arti inferiori III e IV stadio: amputazione degli arti inferiori entro 6 mesi dal ricovero

Toscana --01/07/2020 --30/06/2021



Ricoveri in strutture della stessa regione

Struttura di Ricovero	Comune	Ricoveri	% Ricoveri	% ADJ*
Altre Strutture		66	16.8	-
Azienda Ospedaliera Universitaria Senese	Siena	60	15.2	1.38
Ospedale Area Aretina Nord	Arezzo	53	13.5	-
Osp. S. Giovanni Di Dio Torregalli	Firenze	49	12.4	1.69
Az. Ospedaliero - Universitaria Careggi	Firenze	36	9.1	-
Azienda Ospedaliero-Universitaria Pisana	Pisa	33	8.4	-
Ospedale Delle Apuane	Massa	30	7.6	16.52
Ospedale Della Misericordia	Grosseto	28	7.1	-
Nuovo Ospedale Di Prato S.Stefano	Prato	23	5.8	-

Ricoveri in strutture di altre regioni

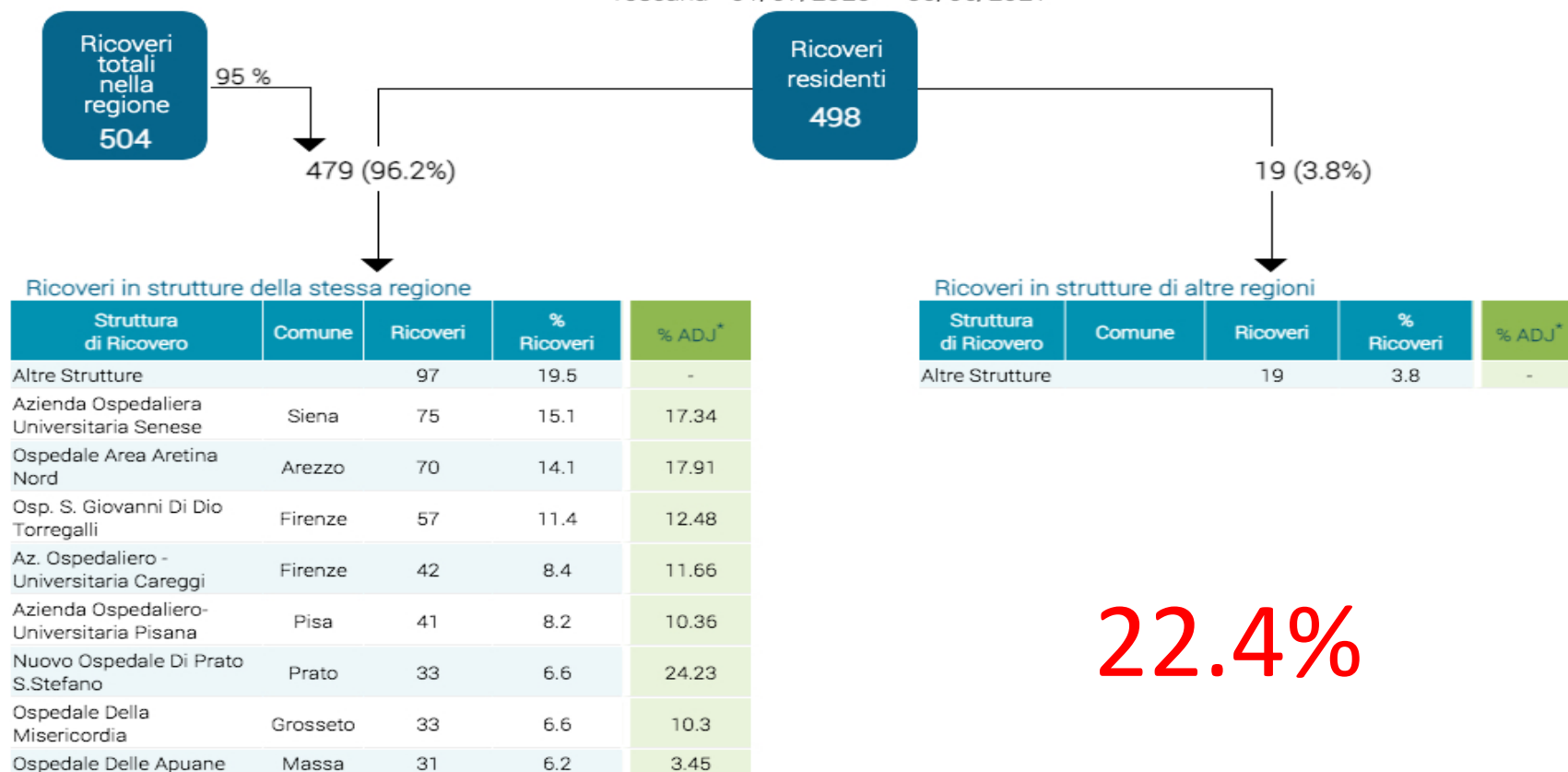
Struttura di Ricovero	Comune	Ricoveri	% Ricoveri	% ADJ*
Altre Strutture		16	4.1	-

17.7%

*Rischio aggiustato calcolato su tutti i ricoveri della struttura per l'indicatore in studio

Arteriopatia degli arti inferiori III e IV stadio: mortalità entro 6 mesi dal ricovero

Toscana -01/07/2020 - -30/06/2021



*Rischio aggiustato calcolato su tutti i ricoveri della struttura per l'indicatore in studio

Firenze, 15 Aprile 2023



CONCLUSIONI

- La Arteriopatia Periferica è una complicanza frequente, grave e progressiva del diabete
- La sua elevata morbilità e mortalità la caratterizzano come una delle patologie a più alta complessità tra quelle associate al diabete.
- La sua patogenesi ed evoluzione clinica sono ancora oggetto di studio ma sempre di più emergono correlazioni dirette con il controllo metabolico e le altre complicanze, in particolare la neuropatia.
- Uno screening proattivo precoce ed un approccio terapeutico multifattoriale terapia sono essenziali per ridurre la progressione e contenere