Con il Patrocinio di

GISE
Società Italiana di Cardiologia Interventistica

Malattia coronarica cronica in paziente già sottoposto a PCI: dallo studio Compass alla pratica clinica

Strategie vincenti nella gestione della terapia antitrombotica nel paziente con cardiopatia ischemica cronica

CASO CLINICO 3:
Pz con vasculopatia periferica e storia di PCI

SIMONA PIERINI

Sistema Socio Sanitario
Ospedale Edoardo Bassini
Regione Lombardia
ASST Nord Milano

Uomo di 69 anni

- Nato e vissuto in Camerun fino al 2013
- Storia di DIABETE MELLITO di lunga data, in terapia con metformina

COMPLICANZE PLURIME DI MALATTIA:

- Nefropatia → IRC moderata (eGFR 45 ml/min sec CKD-EPI)
- Neuropatia periferica
- Arteriopatia periferica → esiti di amputazione ultime falangi del piede dx nel 2013

2014: RICOVERO IN NEFROLOGIA

- In seguito ad addominalgie presentazione in PS, con riscontro di **IRA su IRC** (*creatinina 3.5 mg/dl; eGFR 20 ml/min sec CKD-EPI*) → alla biopsia quadro compatibile con glomerulosclerosi diabetica avanzata.
- EMG: neuropatia sensitivo-motoria degli arti inferiori di grado avanzato.
- Anemia microcitica ipocromica.
- OSAS di grado moderato.
- ECOCG: Ipertrofia concentrica severa (non storia nota di IA)

2015: RICOVERO c/o altro Ospedale

- In seguito a perdita di coscienza con rilascio sfinterico con riscontro di numerosi **episodi di tachicardia SV** → impostata terapia beta-bloccante.
- Eseguita coronarografia per dubbie alterazioni all'ECG con contestuale incremento di troponina → escluse patologie coronariche di tipo ostruttivo.

2017: RICOVERO IN NEFROLOGIA

- Rientra da un soggiorno in Camerun con un flemmone del I dito del piede sin (post-traumatico) → ***angiografia arto inferiore sin***.

ANGIOGRAFIA e PTA AI SIN (20/1/2017)

- Arteria femorale superficiale e poplitea con estese calcificazioni parietalie, prive di stenosi significative e con buon flusso.
- Ateromasia non significativa del tronco tibio-peroniero.
- **Severa ateromasia di arteria tibiale anteriore con stenosi subocclusive al terzo prossimale e distale.**
- Arteria tibiale posteriore ed interossea occluse al terzo medio di sviluppo.

➢ ***Predilatazione di tutto vaso con pallone 2.0 x 80 mm. Dilatazione finale con DEB 2.5 x 150 mm con buon risultato angiografico finale e flusso diretto al piede tramite arteria dorsale.***

2017: RICOVERO IN NEFROLOGIA

- Viene successivamente sottoposto a bonifica chirurgica piede sin. e amputazione I raggio al terzo prossimale del metatarso.

- Dopo qualche mese ricovero in urgenza in presenza di flemmone plantare piede sinistro → *amputazione TMT sinistra con innesto di sostituto dermico plantare*.

30/12/2017: RICOVERO IN NEFROLOGIA

- **POLMONITE A FOCOLAI MULTIPLI**

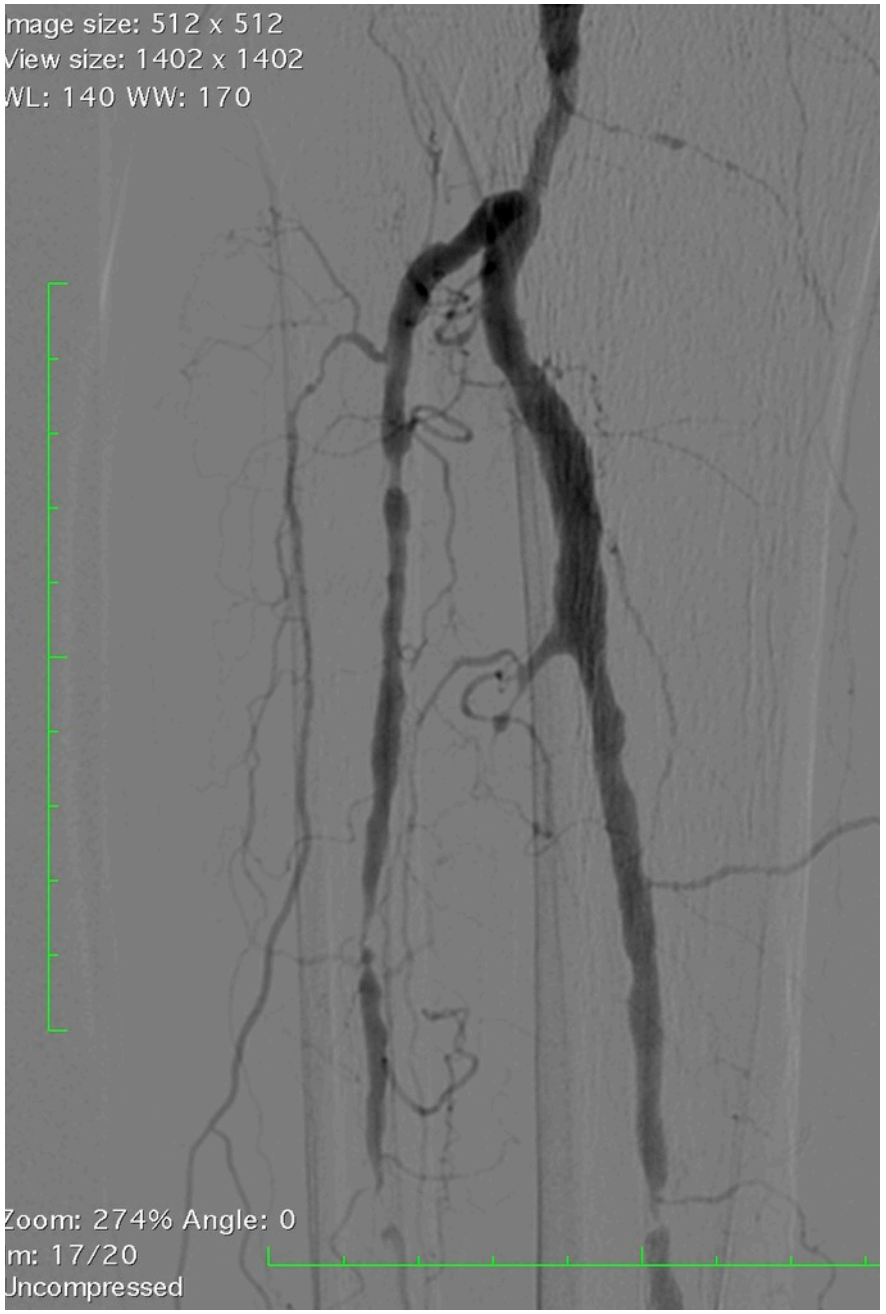
- Presenza di **LESIONE TROFICA PIEDE DX** con tampone del pos per Klebsiella e St chromogenes → avviata terapia con piperacillina e tazobactam.

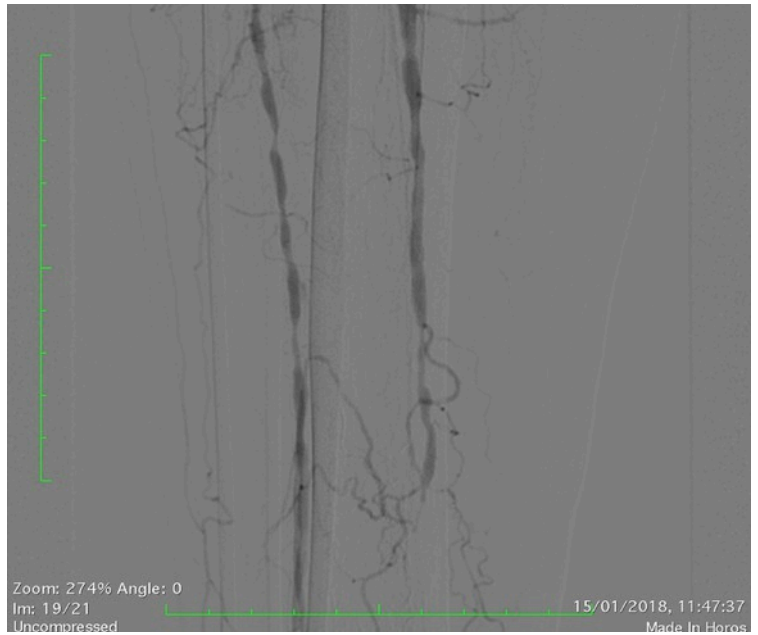
➢ *INDICAZIONE AD ANGIOGRAFIA ARTO INFERIORE DX*

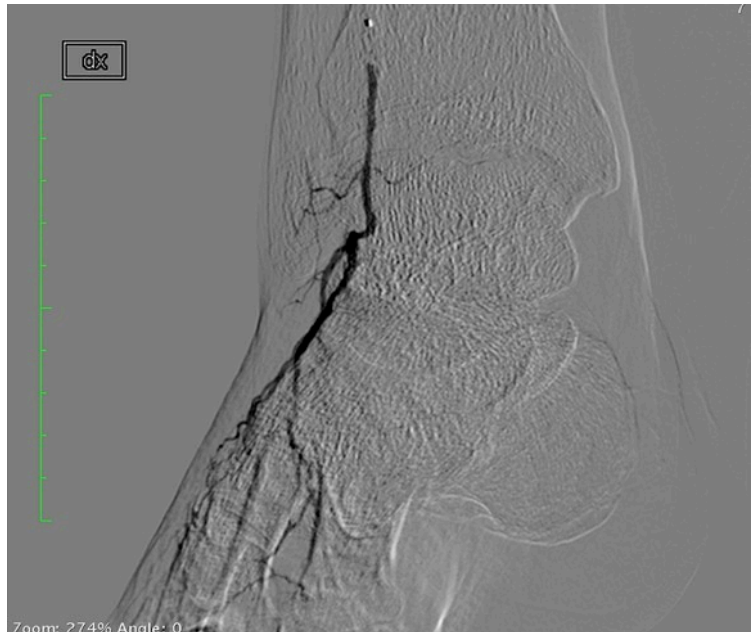
ANGIOGRAFIA e PTA AI DX (15/1/2018)

- Ateromasia calcifica non critica della SFA, malattia non critica della poplitea
- BTK: occlusione della peroniera al tratto ostio prox; severa malattia ateromasica della TP con occlusione del vaso sopra la caviglia; TA con multiple lesioni subocclusive in serie.

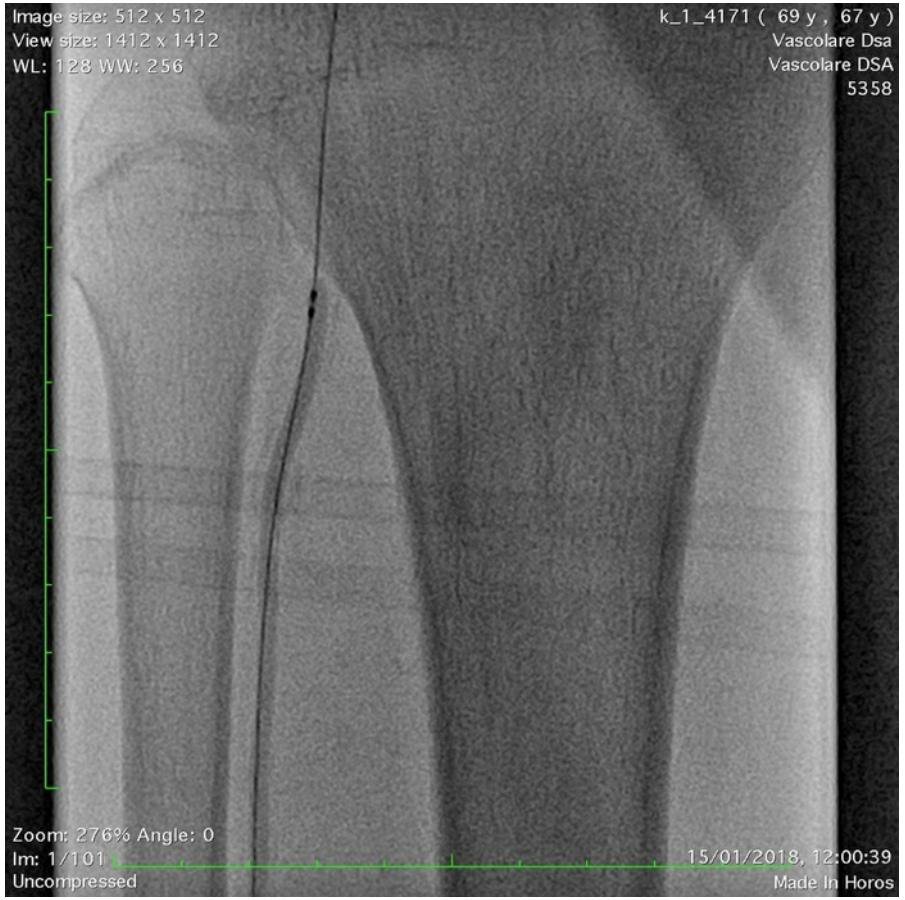
➢ *Viene eseguita PTA TA dx e trattamento con DEB con ottimo risultato finale.*

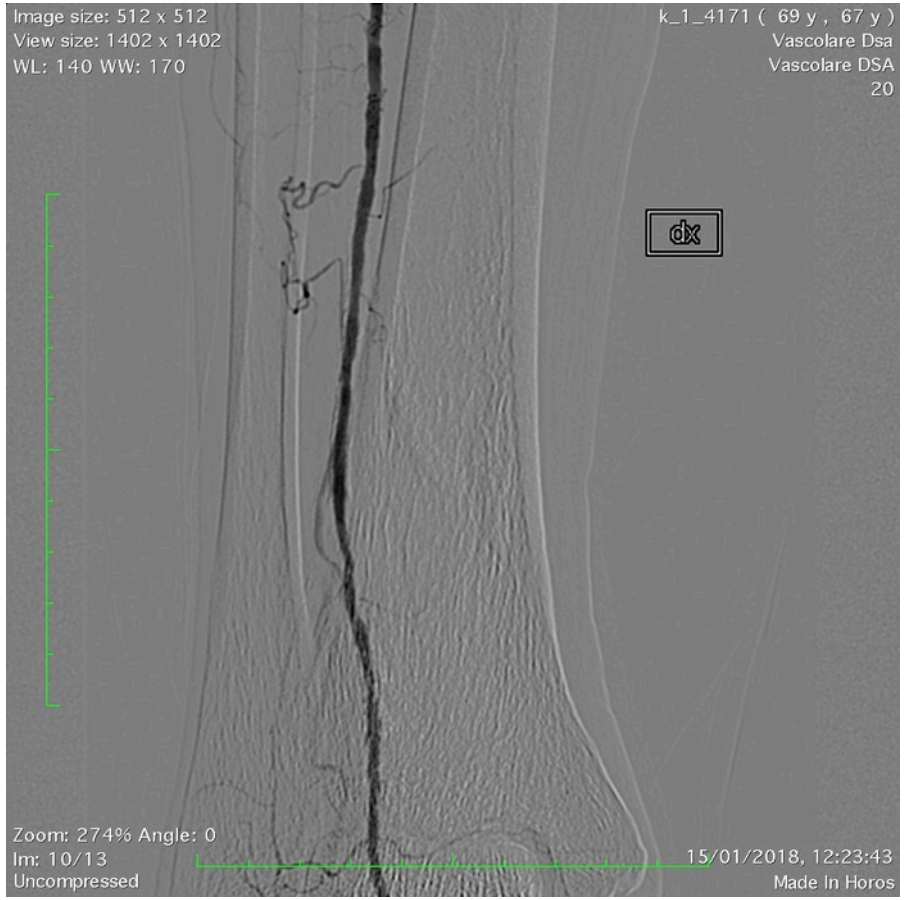






ANGIOGRAFIA AI DX (15/1/2018)





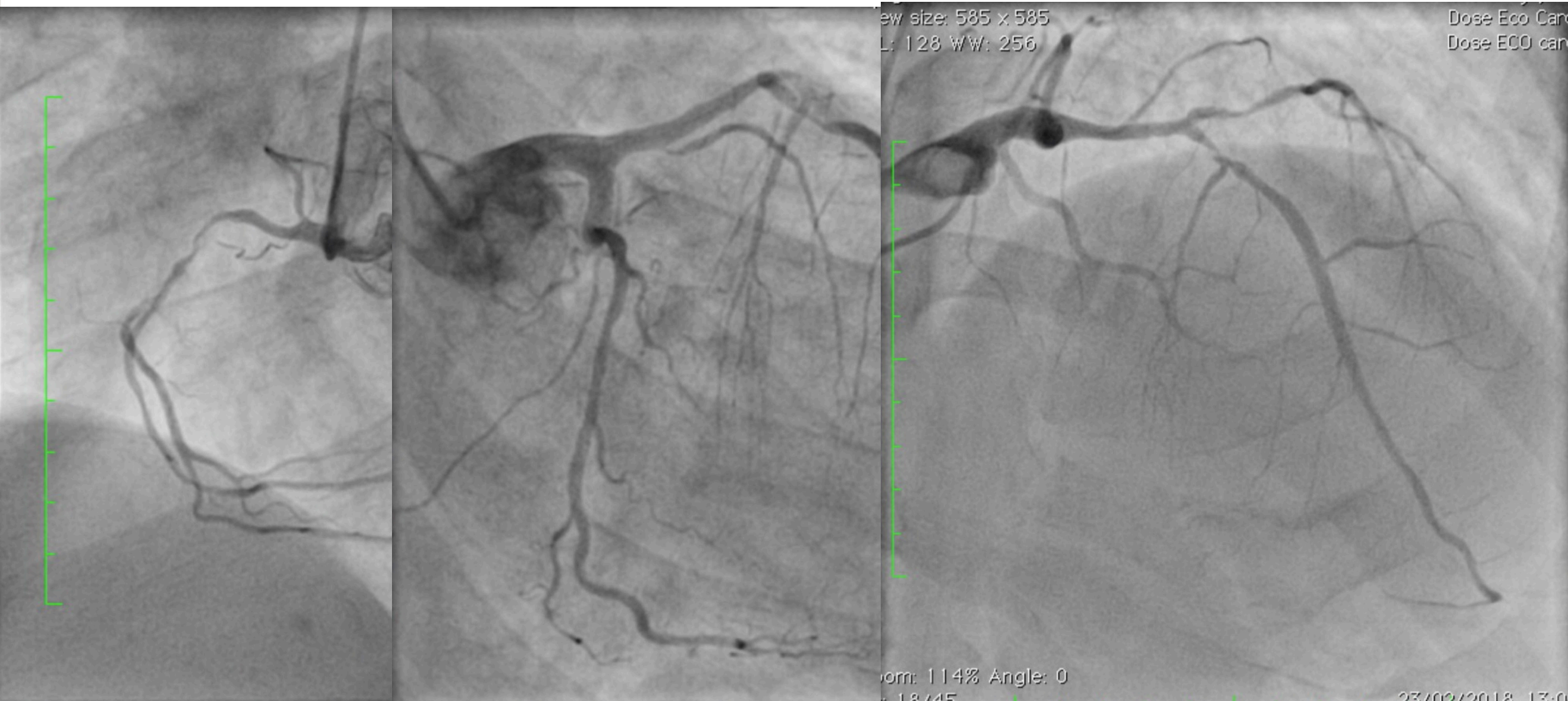
PTA AI DX (15/1/2018)

15 febbraio 2018

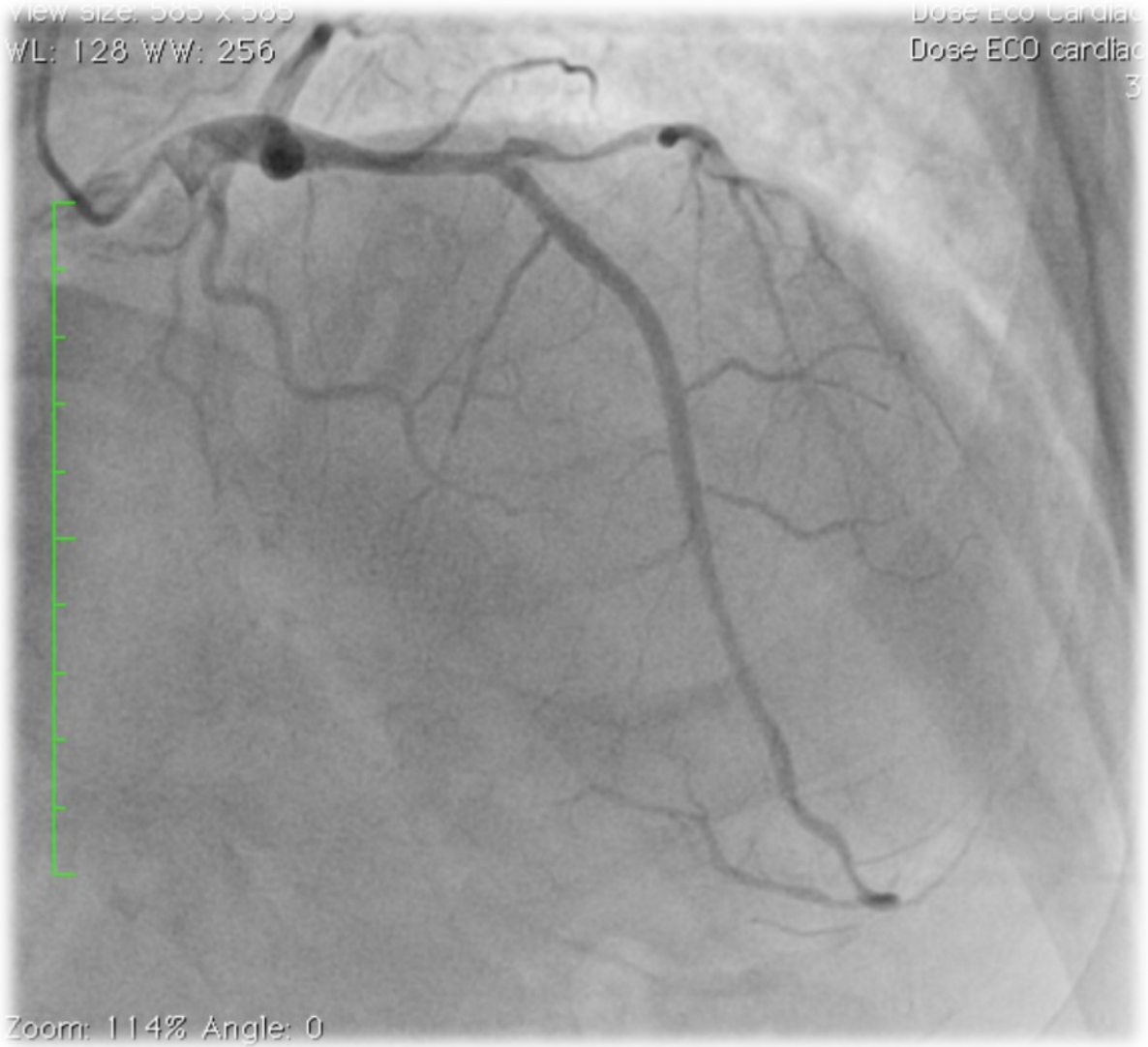
- Ricovero in UTIC per **SCA complicata da EPA** → risoluzione del quadro mediante cicli di CPAP e terapia diuretica infusionale.

- Dopo stabilizzazione clinica, previa profilassi di prevenzione CIN (GFR = 35 ml/min sec CKD-EPI), in data 23/2, viene sottoposto a **CORONAROGRAFIA**.

23/2/2018 CORONAROGRAFIA

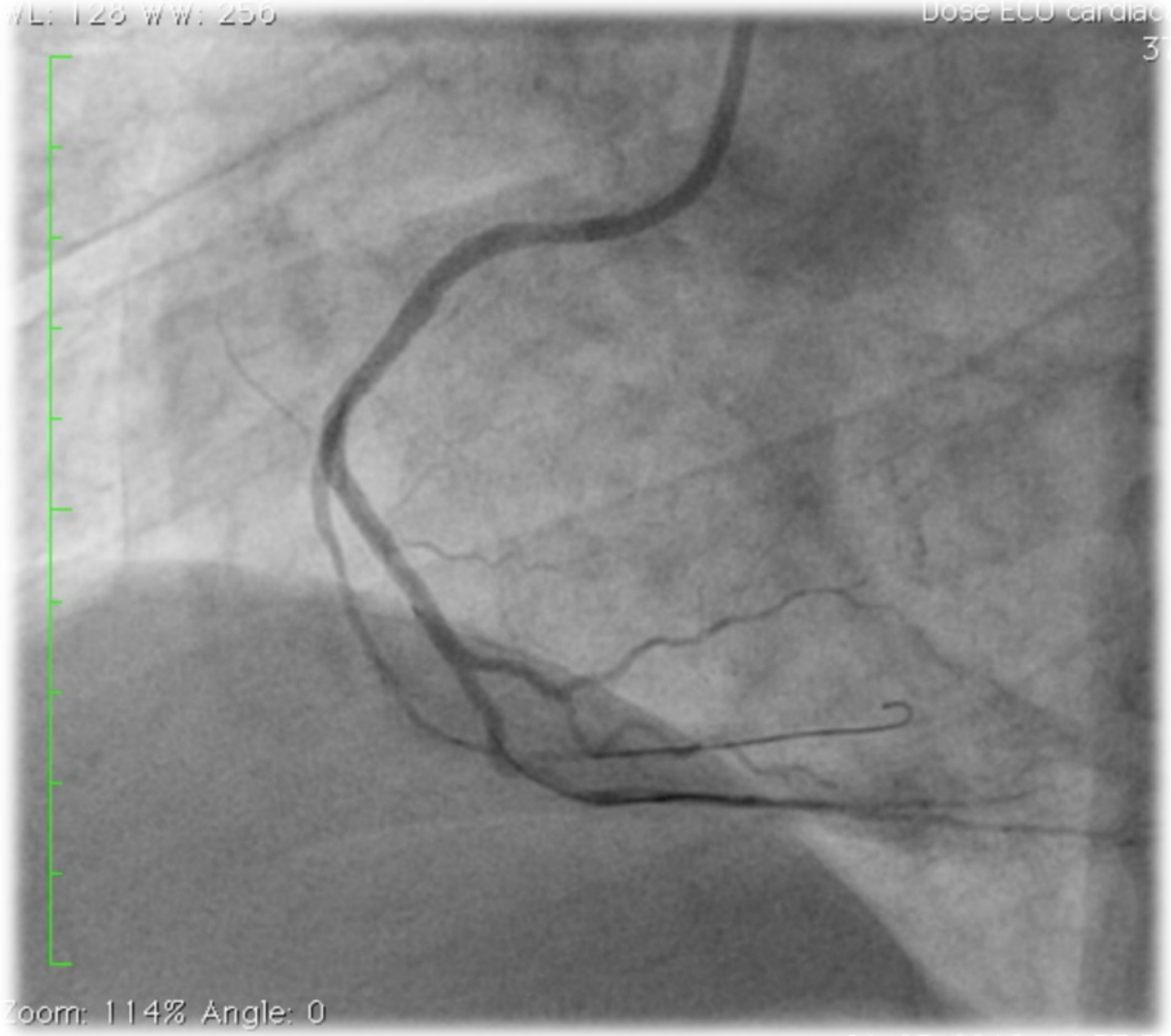


PCI IVA



EES 3.0 x 20 mm, postdilatato con pallone NC 3.25 mm

PCI CD (1/3/2018)



EES 2.5 x 38 mm, postdilatato con pallone NC 2.75 mm

DECORSO SUCCESSIVO

- Asintomatico per angor, buon compenso c-c
- **ECOCG:** severa ipertrofia concentrica del VS, FE conservata, alterazioni segmentarie dell'apice e della parete inferiore; atrii di dimensioni ai limiti superiori. Ectasia della radice aortica, placche fibrotiche all'aorta ascendente. VD normale.

- Episodi ricorrenti di TPSV non efficacemente prevenuti dalla terapia farmacologica con verapamil/beta-bloccante → ATC

TERAPIA ALLA DIMISSIONE:

- **DAPT (ASA + TICAGRELOR) per 12 mesi**

- PANTOPRAZOLO 40 mg
- NEBIVOLOLO 5 mg
- AMLODIPINA 5 mg
- ATORVASTATINA 80 mg

- Nel maggio-giugno 2018 comparsa di LESIONE TALLONE DX con tampone pos. per Pseudomonas Aeruginosa multiresistente, con segni rx di possibile iniziale erosione ossea → avviata terapia antibiotica dapprima con gentamicina + cefalosporina, successivamente con teicoplanina.

- A luglio 2018 esegue **Tc pO_2 AI**: a destra TP = 74 mmHg,TA = 60 mmHg; a sinistra TP = 66 mmHg, distretto a carico tibiale anteriore sottoposto ad amputazione.

- Dal luglio all'ottobre 2018 periodo di soggiorno all'estero (Germania).

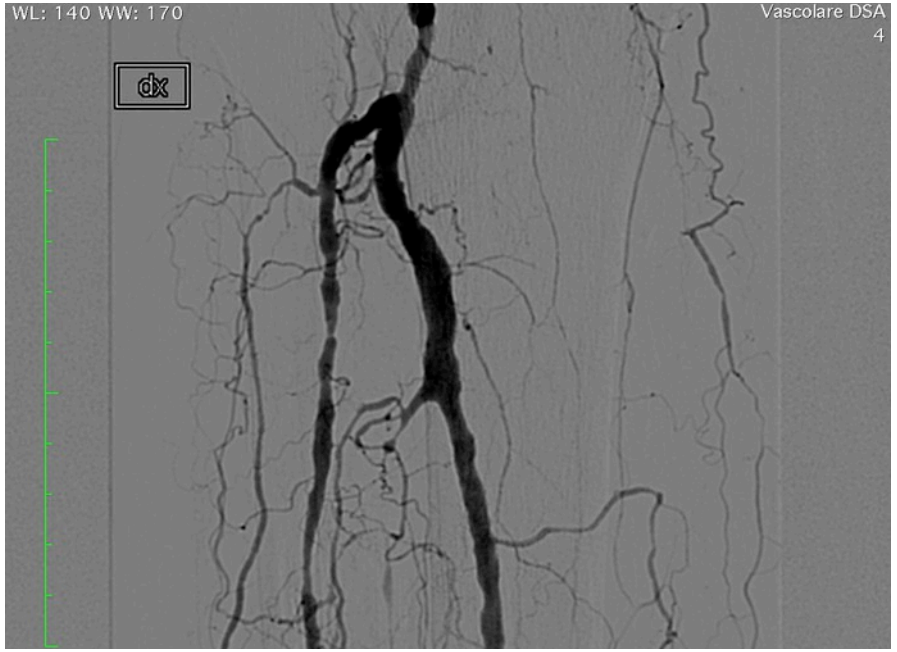
- Rientra in Italia il 25/9/2018: peggioramento lesione tallone destro, sanguinante, maleodorante, con *esposizione ossea*) → Tc pO_2 dorso piede destro = 42 mmHg. In data 8/10 intervento di curettage, calcanectomia, innesto HMPA + biopsia ossea (neg.)

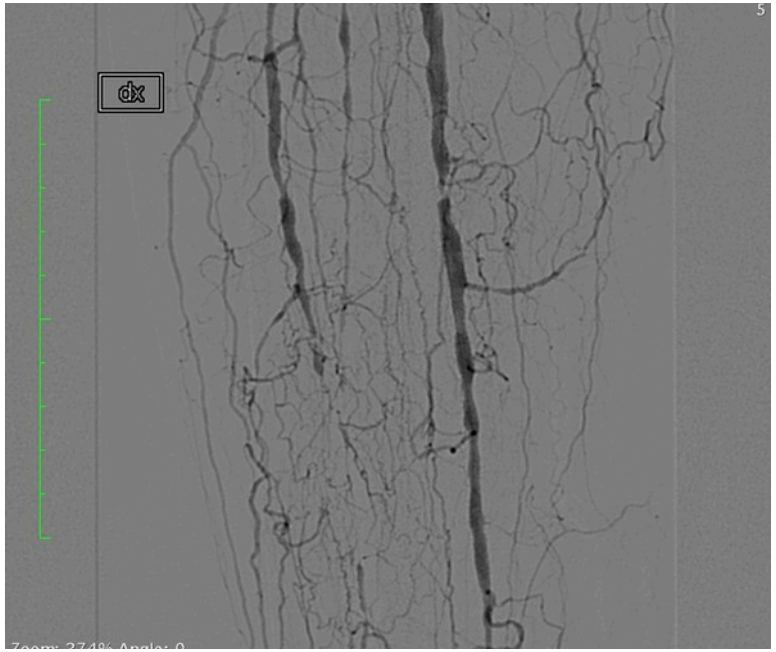
-

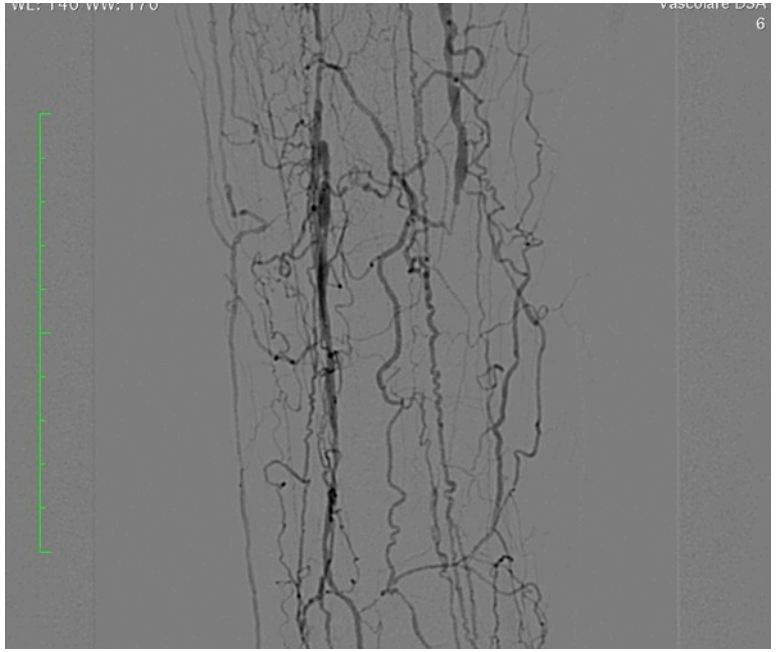
- Da gennaio 2019 comparsa di lesione laterale piede destro molto dolente → terapia con gentamicina.

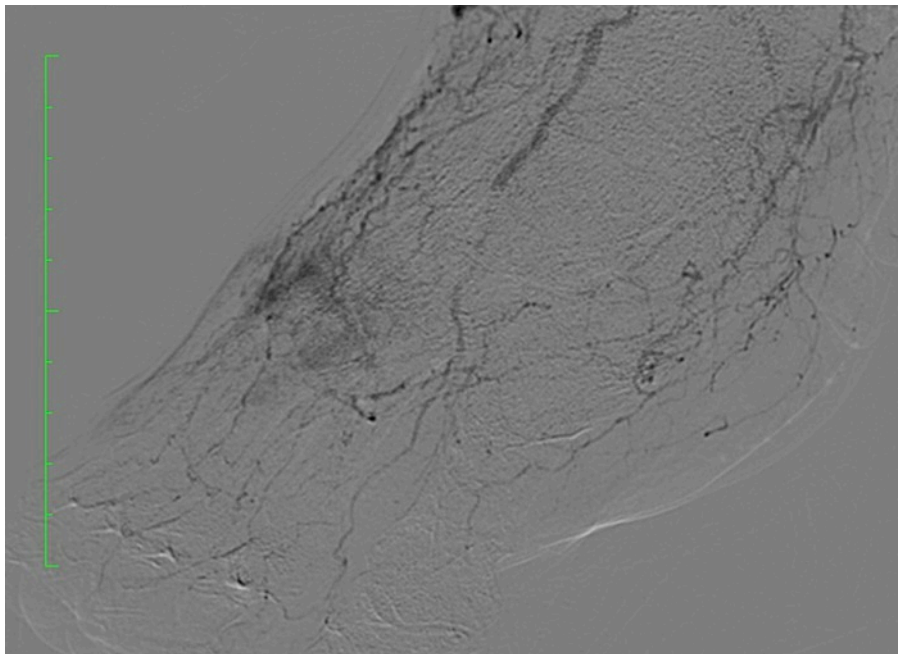
- 21/2/2019 **TcpO2 TA dx** = 10 mmHg –> INDICAZIONE AD ANGIOGRAFIA prima di revisione chirurgica piede.

- Ricovero elettivo in Nefrologia in data 19/3/2019 per angiografia AI dx.

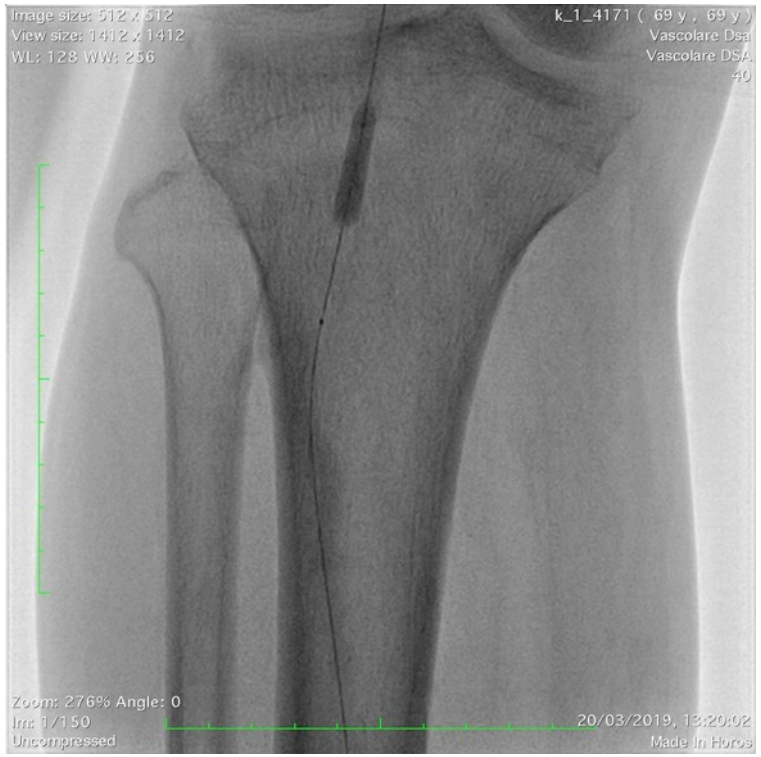


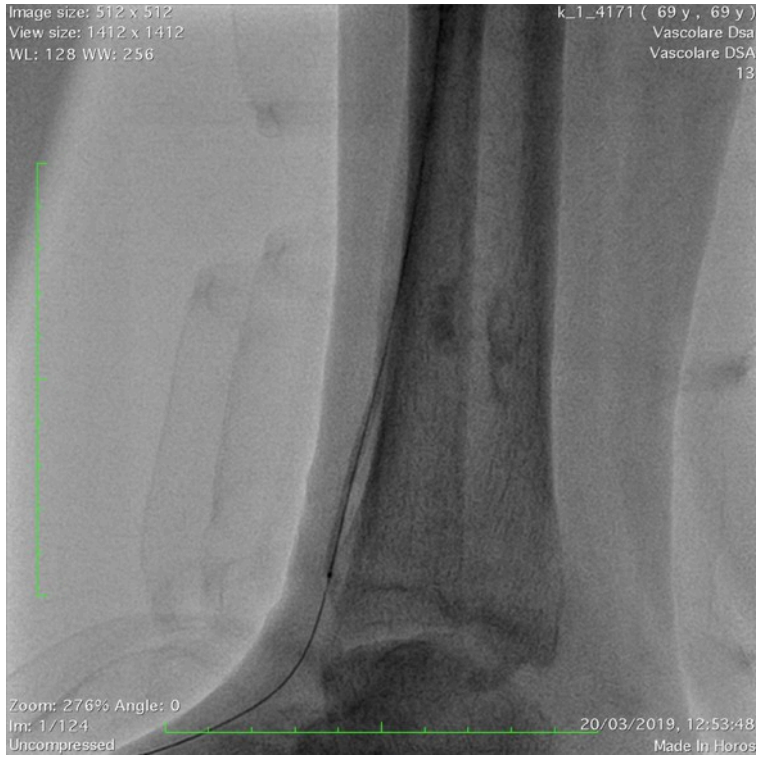


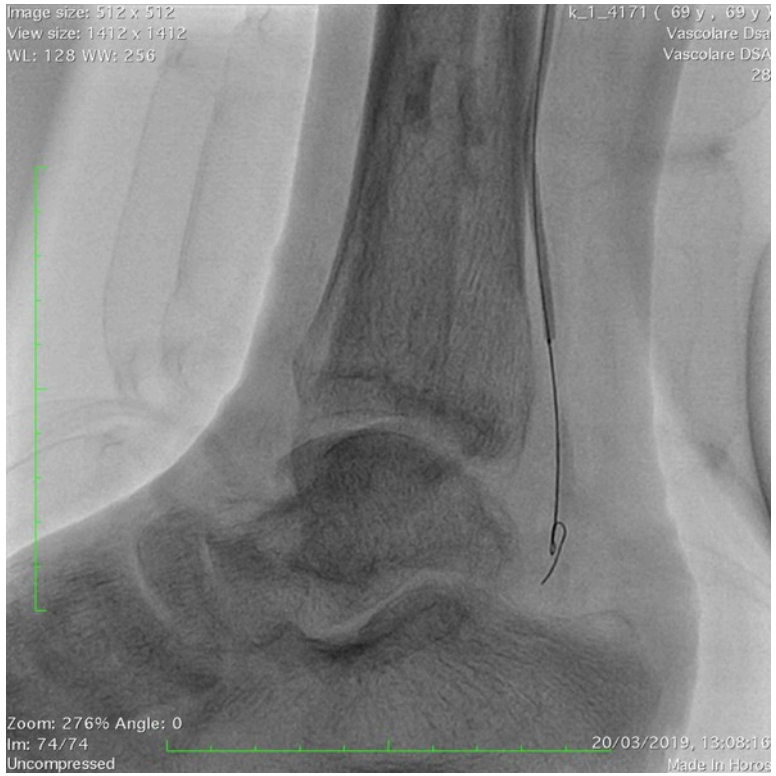




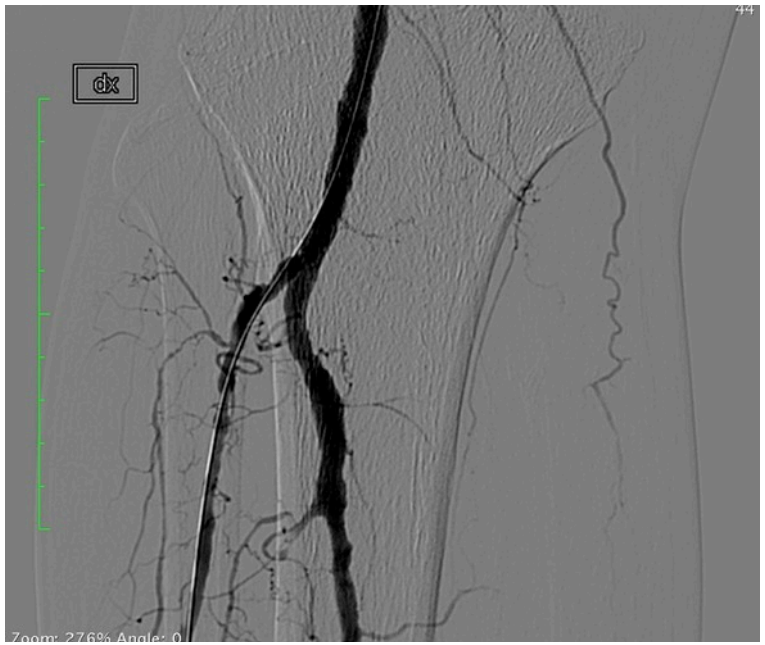
ANGIOGRAFIA ARTO INF. DX (20/3/2019)

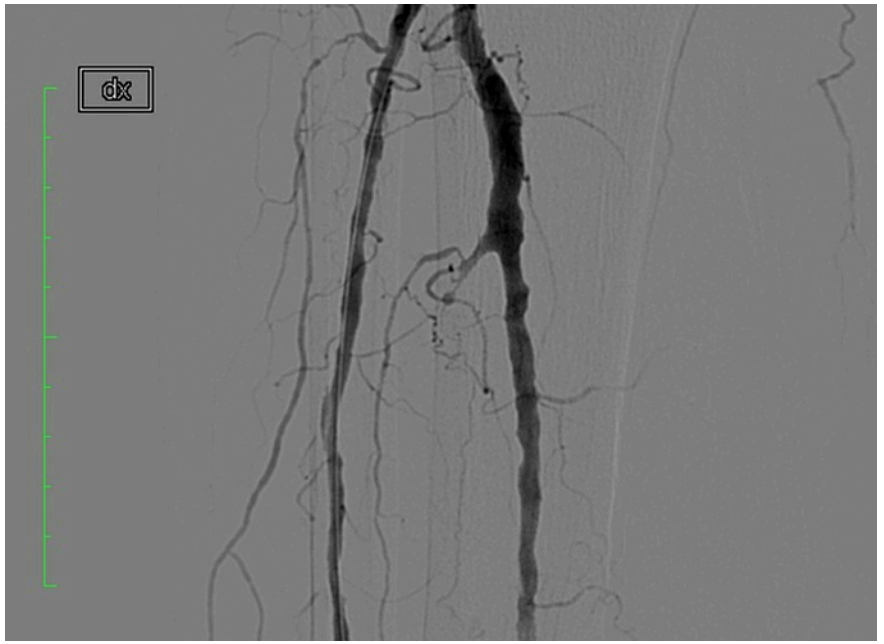


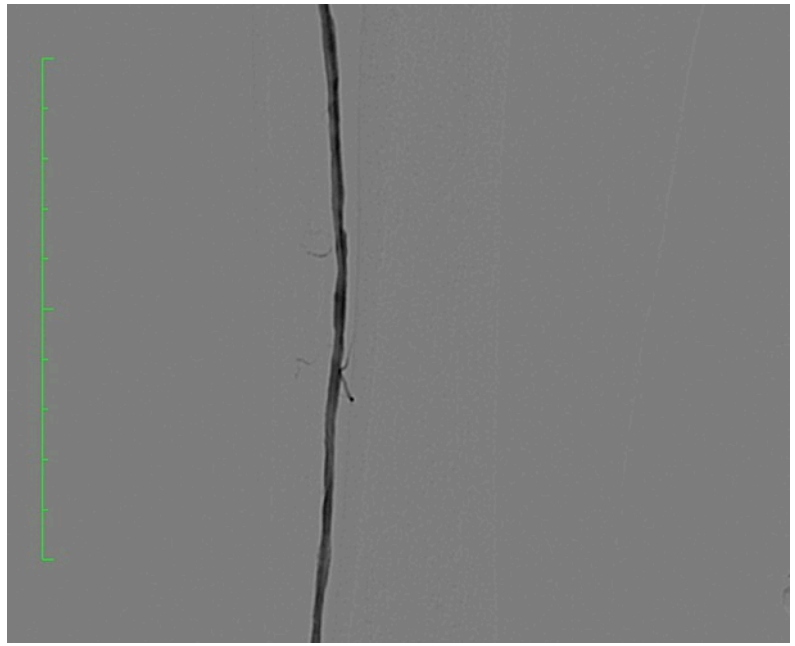


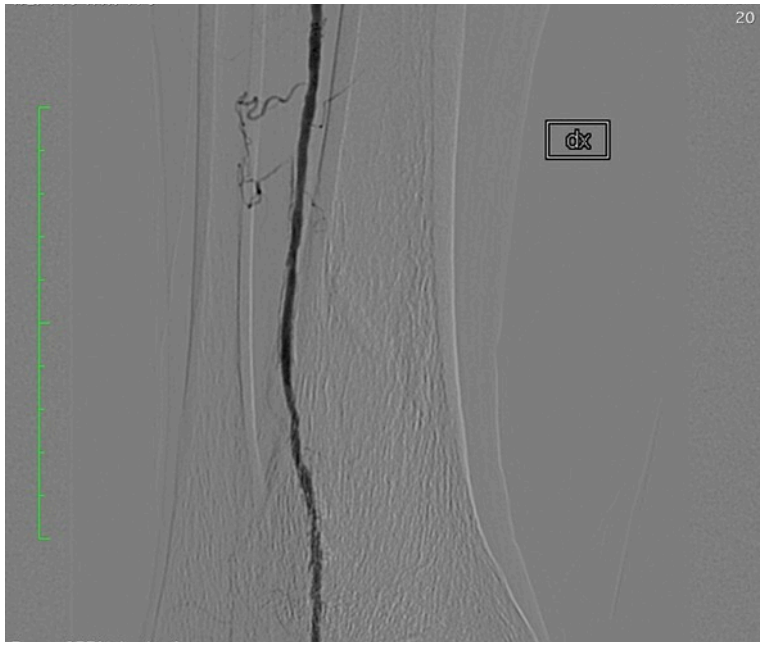


PTA AI DX (20/3/2019)









PTA AI DX (20/3/2019)

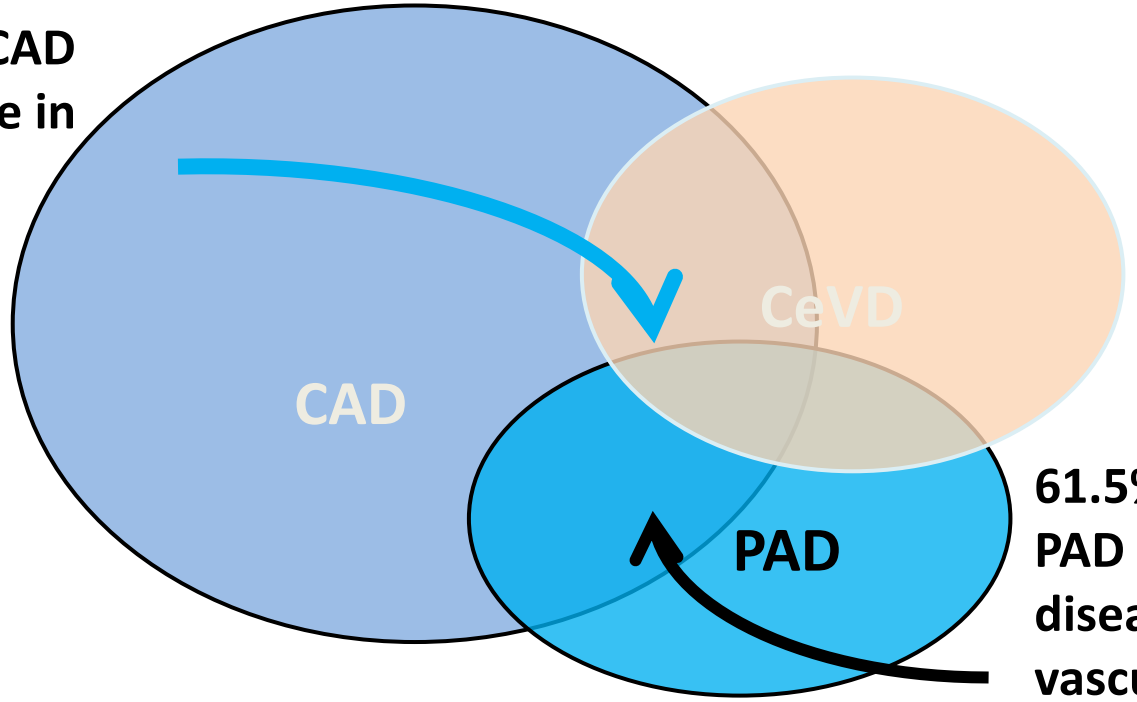
DIMESSO in data 21/3/2019

- **Proseguire DAPT (ASA + CLOPIDOGREL) per 3 mesi**
- PANTOPRAZOLO 40 mg
- NEBIVOLOLO 5 mg
- ATORVASTATINA 40 mg
- AMLODIPINA 5 mg

PZ CANDIDABILE a RIVAROXABAN a basse dosi + ASA ?

ATHEROTHROMBOSIS IS A POLYVASCULAR DISEASE WITH SUBSTANTIAL PATIENT OVERLAP BETWEEN CAD AND PAD

24.7% of patients with CAD had concomitant disease in other vascular beds



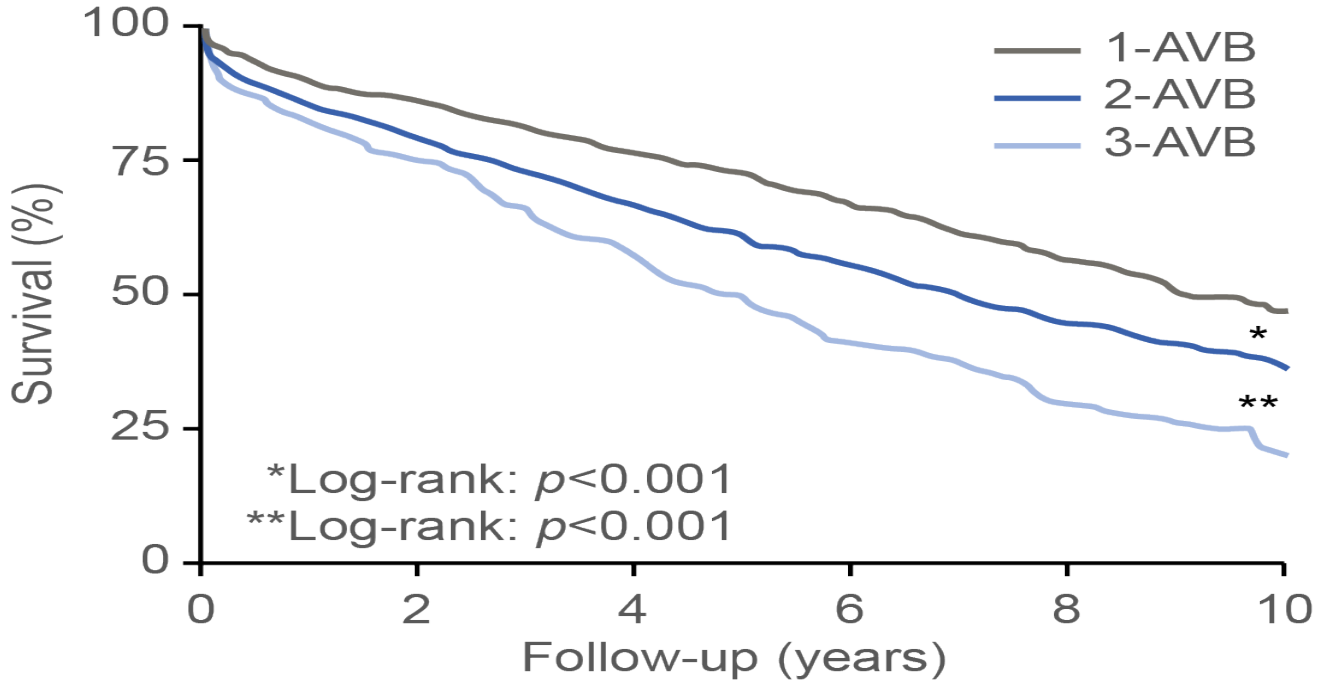
61.5% of patients with PAD had concomitant disease in other vascular beds

CeVD, cerebrovascular disease
*Note: definitions of CAD and PAD in REACH are not identical with COMPASS
Bhatt DL *et al*, *J Am Med Assoc* 2006;295:180–189

REACH registry: enrolled 40,258 patients with established CAD, 8273 patients with established PAD, and 18,843 patients with established cerebrovascular disease from 44 countries*

Patients with polyvascular disease have even higher risk of morbidity and mortality

Long-term all cause mortality in patients with PAD stratified according to number of affected vascular beds (AVB)[2]



Patients with PAD or CAD often have polyvascular disease[1,2,4]

Polyvascular disease is associated with an increased risk of morbidity and mortality[2–4]

1. Bhatt DL *et al*, *JAMA* 2006;295:180–189; 2. van Kuijk P *et al*, *Eur Heart J* 2010;32:992–999; 3. Alberts MJ *et al*, *Eur Heart J* 2009;30:2318–2326; 4. Steg P *et al*, *JAMA* 2007;297:1197–1206

COMPASS: STUDY POPULATION

Definition of CAD

- Previous MI

OR

- Stable angina or unstable angina with documented multi-vessel CAD, >50% stenosis in at least 2 major coronary arteries on coronary angiography, or positive stress test (electrocardiogram) or nuclear perfusion scintigram

OR

- Multi-vessel percutaneous coronary intervention

OR

- Multi-vessel coronary artery bypass grafting surgery within 1 week or at least 4 years ago or with recurrent angina or ischaemia at any time following surgery

Definition of PAD

- Previous aorto-femoral bypass surgery, limb bypass surgery or percutaneous transluminal angioplasty of the iliac or infrainguinal arteries

OR

- Previous limb or foot amputation for arterial vascular disease*

OR

- History of intermittent claudication and either an ankle/arm blood pressure ratio ≤0.90 or significant peripheral artery stenosis (>50%) documented by angiography or non-invasive testing by duplex ultrasound

OR

- Asymptomatic carotid artery stenosis[#] >50% as diagnosed by duplex ultrasound or angiography

*i.e. excludes trauma; [#]i.e. no ipsilateral stroke or transient ischaemic attack within 6 months

Clinical study protocol BAY 59-7939/15786

BASELINE CHARACTERISTICS

COMPASS

	Rivaroxaban + aspirin N=9,152	Rivaroxaban N=9,117	Aspirin N=9,126
Age, yr*	68	68	68
Female	22%	22%	22%
SBP/DBP, mmHg*	136/77	136/78	136/78
Cholesterol, mmol/L*	4.2	4.2	4.2
CAD	91%	90%	90%
PAD	27%	27%	27%
Diabetes	38%	38%	38%
Lipid-lowering	90%	90%	89%
ACE-I/ARB	71%	72%	71%

*Mean

Eikelboom JW et al. N Engl J Med 2017; DOI: 10.1056/NEJMoa1709118;

COMPASS included over 7000 patients with symptomatic PAD or concomitant CAD and PAD

	Number of patients
All patients with PAD	7470
Symptomatic lower-extremity PAD	4129
Carotid disease	1919
CAD + asymptomatic PAD (ABI <0.90)	1422

- PAD was defined according to patient presentation at enrolment
- In addition, a patient could be defined as a PAD patient based on medical history and/or measurement of ABI at baseline visit
  - The latter category added patients with CAD and asymptomatic PAD patients into the overall PAD subgroup
- Median follow-up: 21 months

Anand SS et al, Lancet 2017: doi:10.1016/S0140-6736(17)32757-5

BASELINE CHARACTERISTICS

COMPASS

	Rivaroxaban + aspirin N=9,152	Rivaroxaban N=9,117	Aspirin N=9,126
Estimated GFR %			
• < 30 ml/min	0.8	0.9	0.9
• 30 to < 60 ml/min	21.6	22.2	22.2
• ≧ 60 ml/min	77.5	76.8	76.8
Race %			
• White	62	62.2	62.3
• Black	0.8	1.0	1.0
• Asian	15.9	15.6	15.3
• Other	21.3	21.2	21.4

Eikelboom JW et al. N Engl J Med 2017; DOI: 10.1056/NEJMoa1709118;

COMPASS PAD

Articles

Rivaroxaban with or without aspirin in patients with stable peripheral or carotid artery disease: an international, randomised, double-blind, placebo-controlled trial

*Sonia S Anand, Jackie Bosch, John W Eikelboom, Stuart J Connolly, Rafael Diaz, Peter Widimsky, Victor Aboyans, Marco Alings, Ajay K Kakkar, Katalin Keltai, Aldo P Maggioni , Basil S Lewis, Stefan Störk, Jun Zhu, Patricio Lopez-Jaramillo, Martin O'Donnell, Patrick J Commerford, Dragos Vinereanu, Nana Pogosova, Lars Ryden, Keith A A Fox, Deepak L Bhatt, Frank Misselwitz, John D Varigos, Thomas Vanassche, Alvaro A Avezum, Edmond Chen, Kelley Branch, Darryl P Leong, Shrikant I Bangdiwala, Robert G Hart, Salim Yusuf; on behalf of the COMPASS Investigators**

www.thelancet.com Published online November 10, 2017
http://dx.doi.org/10.1016/S0140-6736(17)32409-1

COMPASS: ELIGIBILITY PAD

- Peripheral artery revascularization
- Limb or foot amputation for arterial vascular disease
- Intermittent claudication plus:
  - ✓ Low ABI (<0.90), or
  - ✓ Significant peripheral artery stenosis (≥50%)
- Previous carotid revascularization, asymptomatic carotid artery stenosis ≥50%
- CAD + low ABI (<0.90)

www.thelancet.com Published online November 10, 2017

COMPASS

PAD: PRIMARY OUTCOME & COMPONENTS

Outcome	R + A N=2,492	R N=2,474	A N=2,504	Riva + aspirin vs. aspirin		Riva vs. aspirin	
	N (%)	N (%)	N (%)	HR (95% CI)	p	HR (95% CI)	p
MACE	126 (5.1)	149 (6.0)	174 (6.9)	0.72 (0.57-0.90)	0.005	0.86 (0.69-1.08)	0.19
MI	51 (2.0)	56 (2.3)	67 (2.7)	0.76 (0.53-1.09)	-	0.84 (0.59-1.20)	-
Stroke	25 (1.0)	43 (1.7)	47 (1.9)	0.54 (0.33-0.87)	0.001	0.93 (0.61-1.40)	-
CV Death	64 (2.6)	66 (2.7)	78 (3.1)	0.82 (0.59-1.14)	-	0.86 (0.62-1.19)	-

www.thelancet.com Published online November 10, 2017

COMPASS

PAD: LIMB OUTCOMES

Outcome	R + A N=2,492	R N=2,474	A N=2,504	Riva + aspirin vs. aspirin		Riva vs. aspirin	
	N (%)	N (%)	N (%)	HR (95% CI)	p	HR (95% CI)	p
MALE	30 (1.2)	35 (1.4)	56 (2.2)	0.54 (0.35-0.84)	0.005	0.63 (0.41-0.96)	0.03
Major amputation	5 (0.2)	8 (0.3)	17 (0.7)	0.30 (0.11-0.80)	0.01	0.46 (0.20-1.08)	0.07

www.thelancet.com Published online November 10, 2017

PAD: KEY COMPOSITE OUTCOME

Outcome	R + A N=2,492	R N=2,474	A N=2,504	Riva + aspirin vs. aspirin		Riva vs. aspirin	
	N (%)	N (%)	N (%)	HR (95% CI)	p	HR (95% CI)	p
MACE, MALE or Major amputation	157 (6.3)	188 (7.6)	225 (9.0)	0.69 (0.56-0.85)	0.0003	0.84 (0.69-1.02)	0.08

NNT 37

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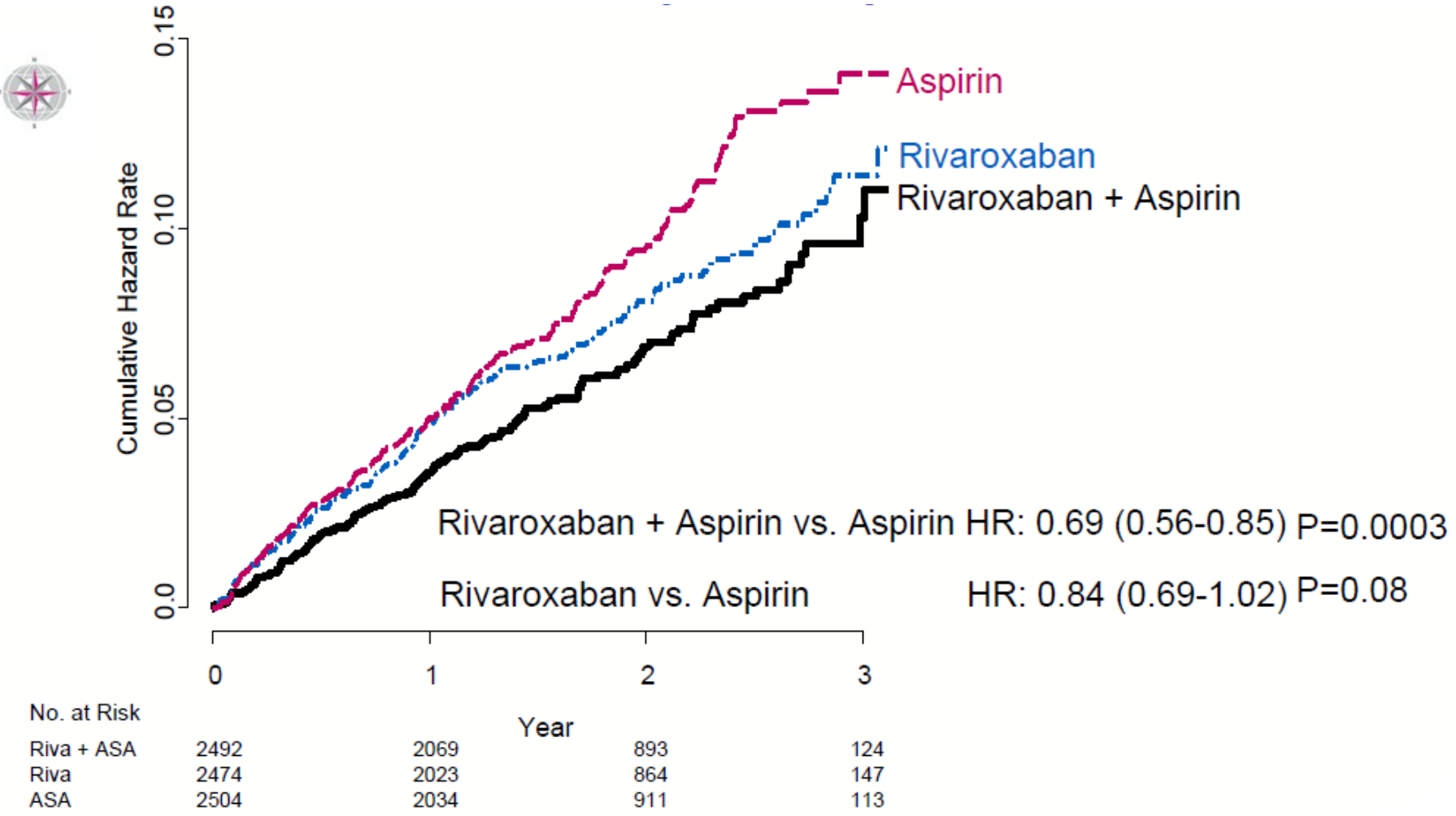
PAD: MACE OR MALE OR MAJOR AMPUTATION



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COMPASS

PAD: KEY COMPOSITE OUTCOME

Outcome	R + A N=2,492	R N=2,474	A N=2,504	Riva + aspirin vs. aspirin		Riva vs. aspirin	
	N (%)	N (%)	N (%)	HR (95% CI)	p	HR (95% CI)	p
Major Bleeding	77 (3.1)	79 (3.2)	48 (1.9)	1.61 (1.12-2.31)	0.009	1.68 (1.17-2.40)	0.004
Fatal	4 (0.2)	5 (0.2)	3 (0.1)	-	-	-	-
Non-Fatal ICH	4 (0.2)	3 (0.1)	8 (0.3)	-	-	-	-
Non-fatal other critical organ*	13 (0.5)	18 (0.7)	8 (0.3)	1.55 (0.64-3.74)	0.33	2.15 (0.94-4.96)	0.06

* symptomatic

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COMPASS

NET CLINICAL BENEFIT IN PAD

Outcome	R + A N=2,492	R N=2,474	A N=2,504	Riva + aspirin vs. aspirin		Riva vs. aspirin	
	N (%)	N (%)	N (%)	HR (95% CI)	p	HR (95% CI)	p
Net Clinical Benefit	169 (6.8)	207 (8.4)	234 (9.3)	0.72 (0.59-0.87)	0.0008	0.89 (0.74-1.07)	0.23

ARR -2,5%; RRR -28%

NNT 40

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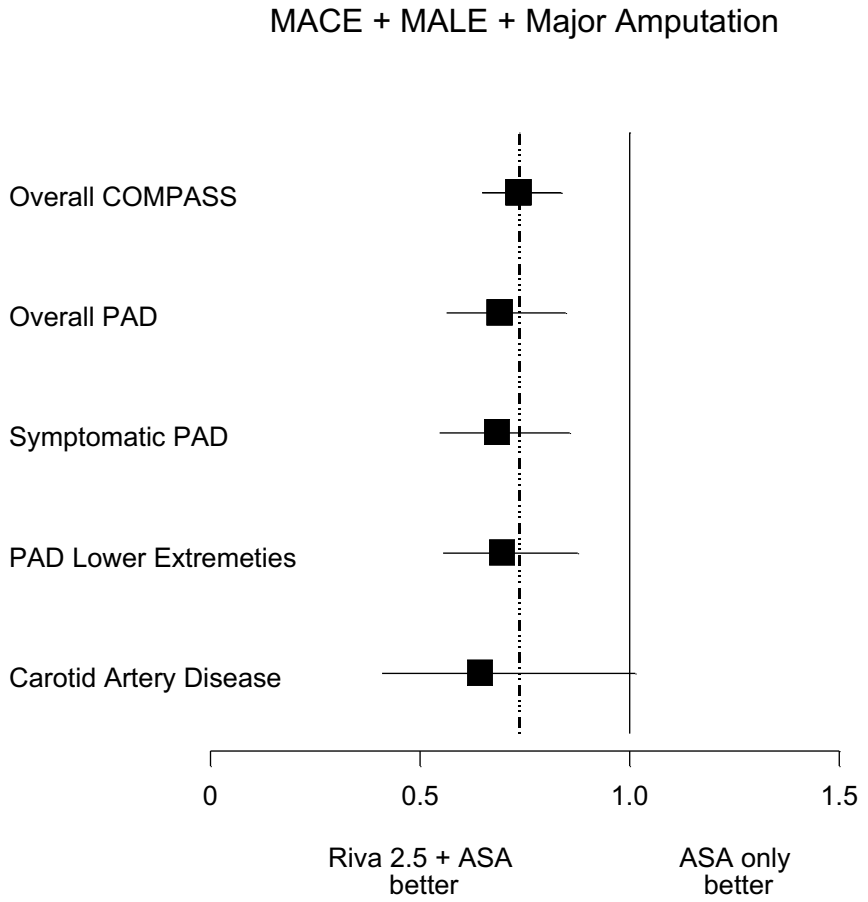
PAD SUBSETS



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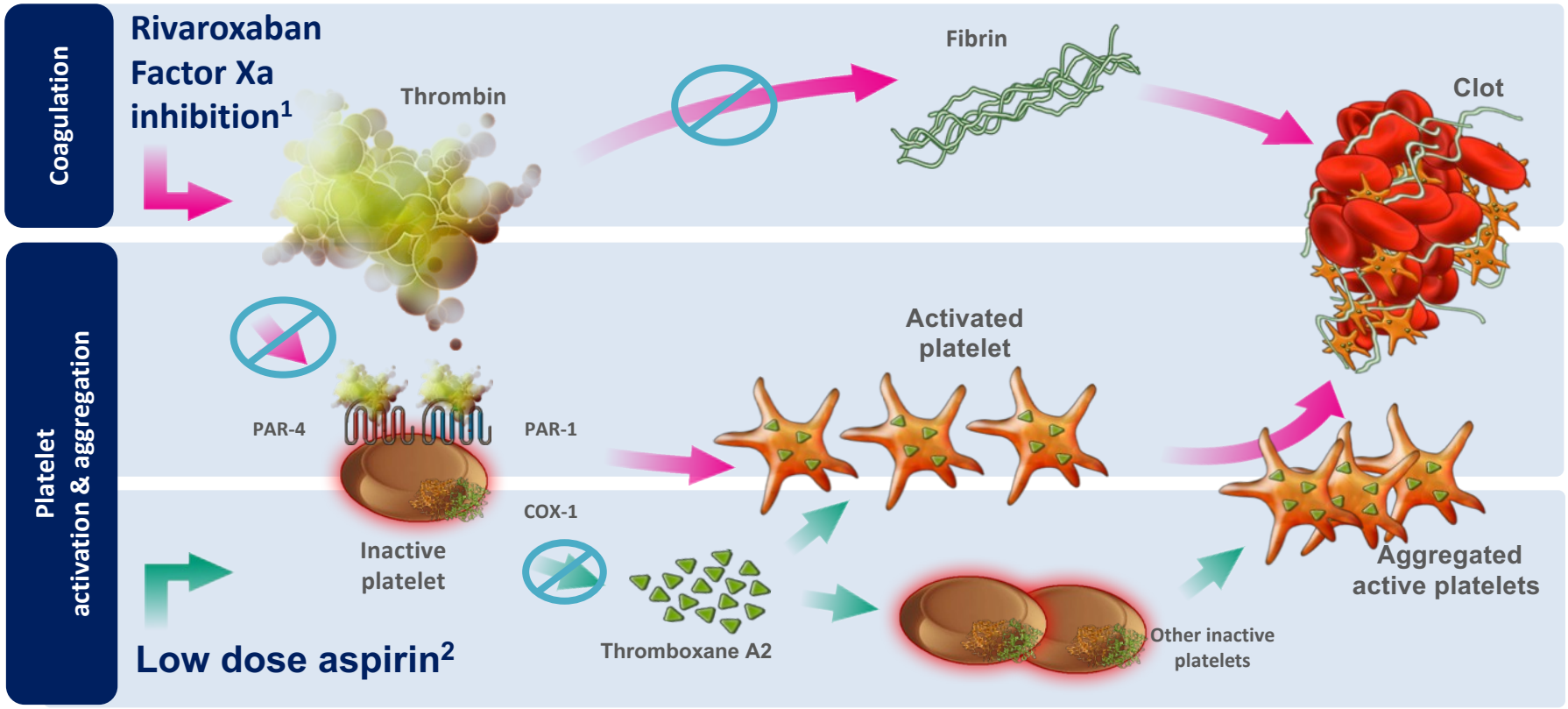
Rivaroxaban and aspirin synergistically target essential components of atherothrombosis



Rivaroxaban impacts not only fibrin formation, but also platelet activation

1. Adapted from Angiolillo DJ et al. Eur Heart J 2010;31:17–28; 2. Adapted from Mitchell JRA. BMJ 1981;282:590–594

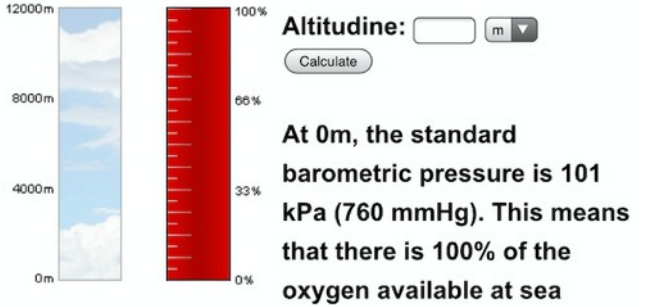
CONCLUSIONS:

COMPASS

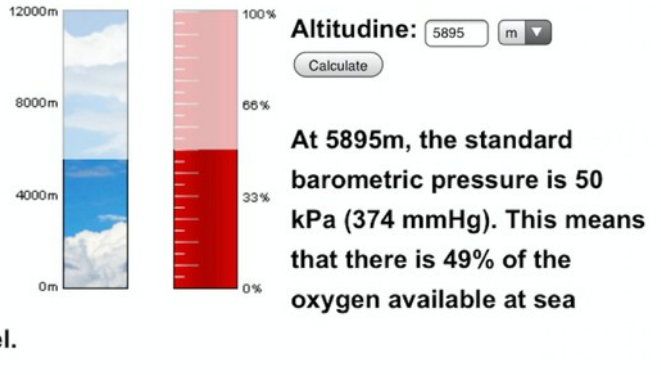
VASCULAR DOSE RIVAROXABAN SHOWED IMPROVED OUTCOMES FOR PAD PATIENTS WITH A NEED FOR INCREASED VASCULAR PROTECTION

- Rivaroxaban vascular dose 2.5 mg bid plus aspirin reduced the composite endpoint of stroke, MI or CV death by 28%
  - MALE by 46%
  - Major amputations by 70%
- Despite an expected increase in major bleeding events with rivaroxaban 2.5 mg bid plus aspirin, no significant increase was observed in fatal or critical organ bleeding
- **This dual pathway inhibition of rivaroxaban vascular dose and aspirin represents a major advance in the management of PAD and is the only available therapeutic option to significantly reduce both MACE and MALE**

Grazie per l'attenzione



Sea level



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Kilimanjaro, agosto 2018