

Is non-functional microcirculation the same as flow- independent ischemia?

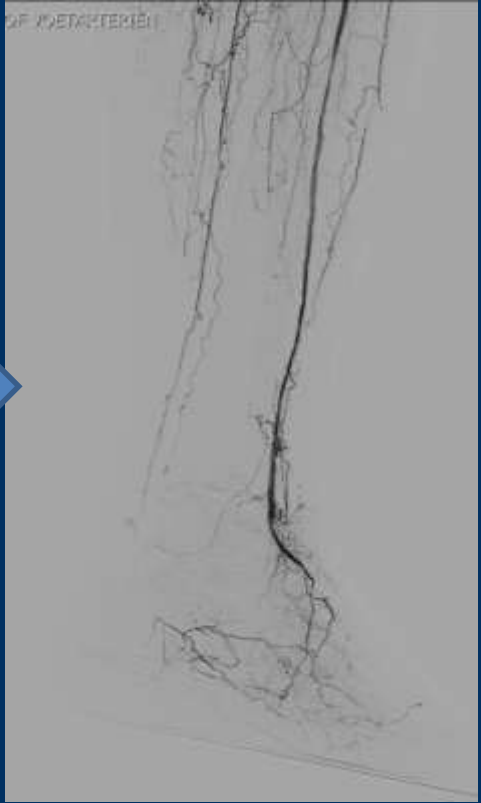
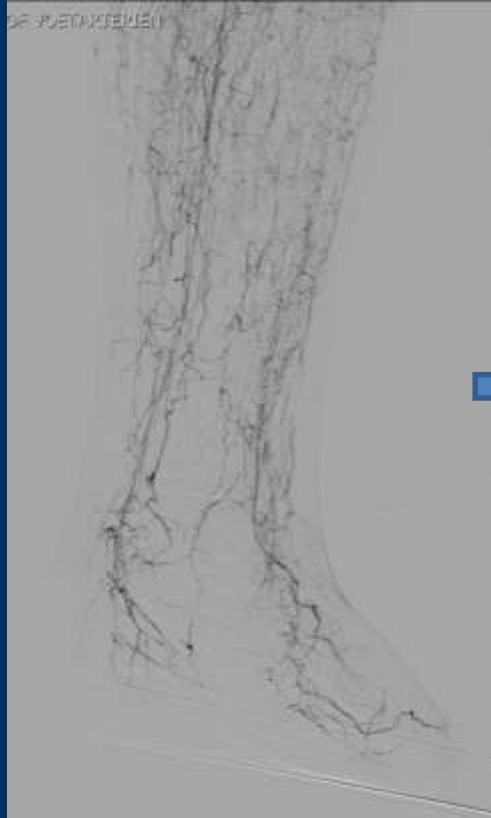
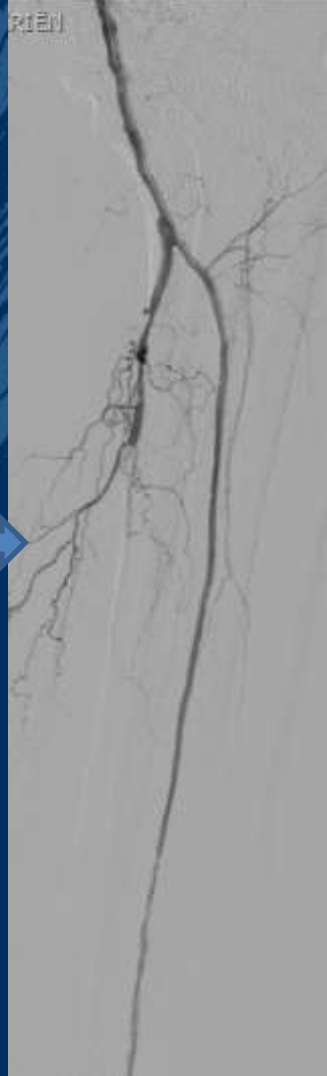
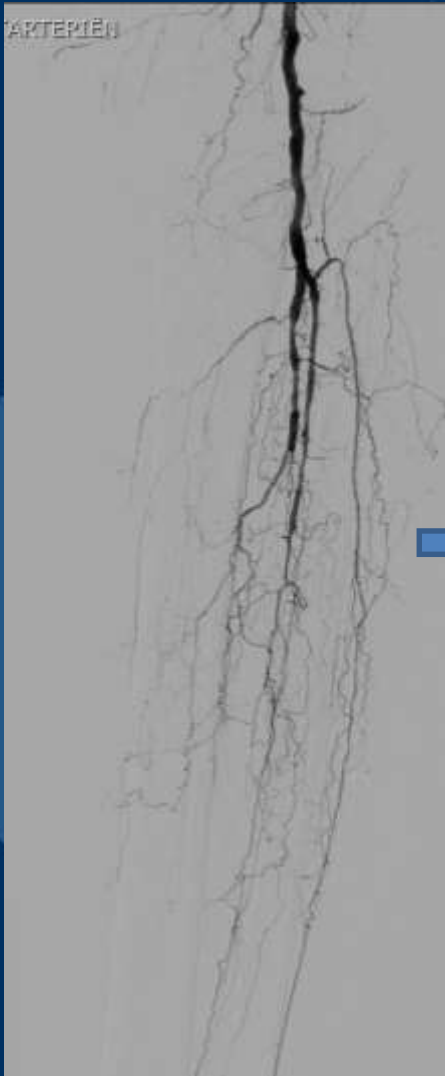
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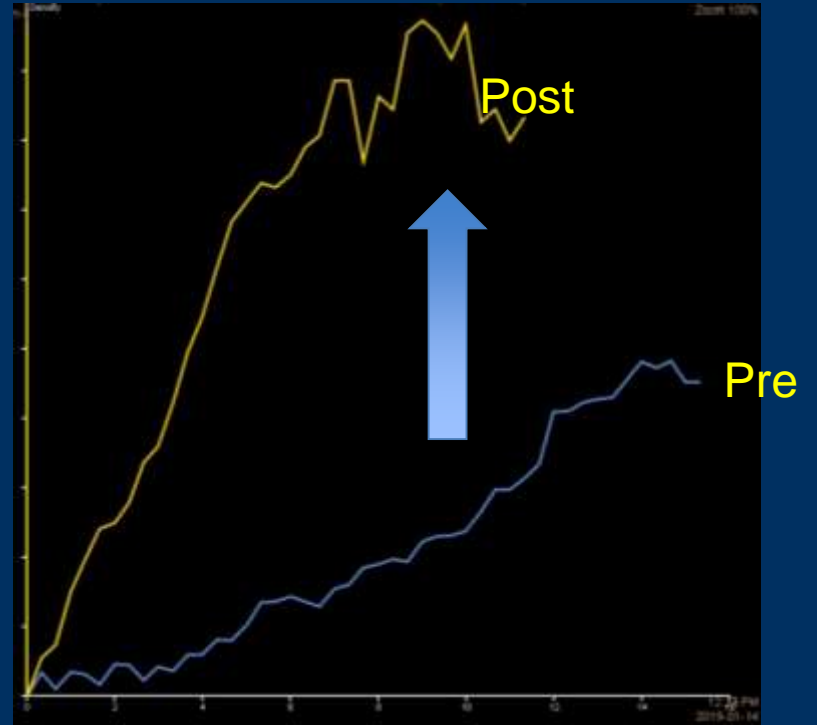
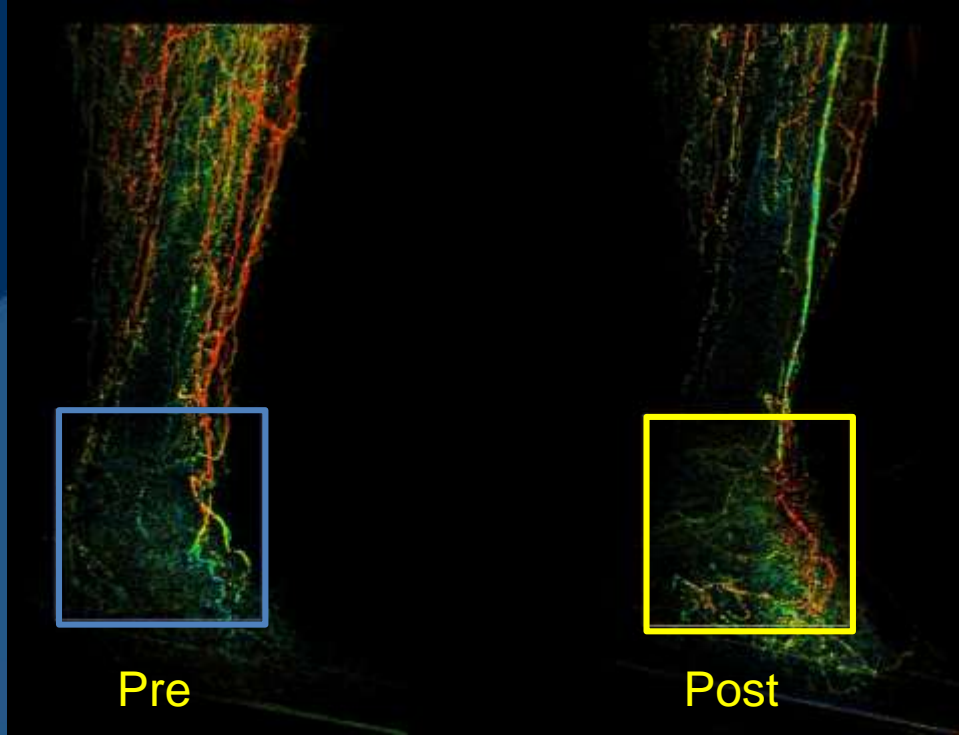
Disclosure

- Institution research grant from philips.

case

- Female 84 years old.
- Diabetes type 2
- Non- healing ulcer at left forefoot stump
- Earlier lower limb amputation right leg.
- Low grade infection in ulcer.
- Polyneuropathy





Follow-up

- ABI from not measurable to 0.7

4 months:

- Amputation due to progressive infection
- ATA patent on duplex.

(New) definition of Critical limb ischemia (CLI)

Shortage of oxygen in the tissue = CLI

- Inflow problem
- **Microcirculation problem**

Inflow problem

- **Occlusive disease.**

This can be treated with revascularization and >90% **good** outcome.

Microcirculation problem + occlusive disease.

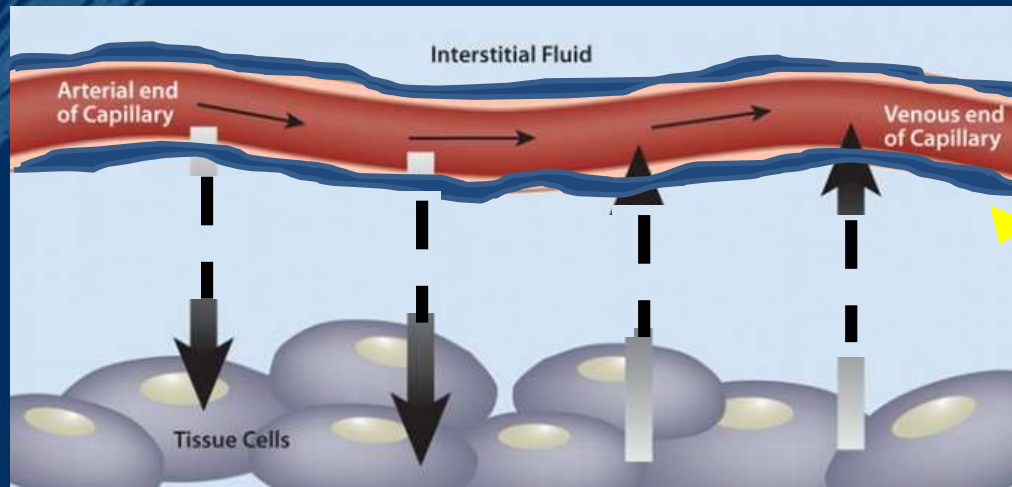
- **Microcirculation.**

~20%

The occlusion can be treated with
revascularization but with >90% **poor** outcome.

Microangiopathy:

Etiology: Genetic diabetes mellitus,
High capillary pressure



Damaged capillaries leakage deposits of hyaline thickening of the capillary basement membrane



Testing the sympathetic nervous system of the foot has a high predictive value for early amputation in patients with diabetes with a neuroischemic ulcer

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ABSTRACT

Objective: There is evidence from the literature that dysfunctionality of the sympathetic nervous system of the foot with subsequent loss of local autoregulation could be a predictor of early amputation in patients with diabetes with a neuroischemic ulcer. To confirm this we tested the functionality of the sympathetic nervous system in the foot in a consecutive group of 27 patients with diabetes with critical limb ischemia and non-healing neuroischemic ulcer.

Research design and methods: Prospective cohort with retrospective analysis after 12 months of routinely acquired clinical data. All patients in the study group underwent angiography of the foot as part of a routine angioplasty procedure. Primary study endpoint was lower extremity amputation-free survival at 12 months. Because of the study design no other endpoints could be analysed. The functionality of the sympathetic nervous system was tested with perfusion angiography.

Results: Thirty-one patients were followed for 12 months. The Capillary Resistance Index (CRI) was used to measure the response of the sympathetic nervous system. CRI<0.9 is the cut-off point for a non-regenerative sympathetic nervous system. All patients (n=11) with a CRI<0.9 underwent a major amputation before 12 months. Of all patients with a CRI only 12% underwent major amputation. The positive predictive value for major amputation before 12 months for patients with a CRI < 0.9 was 100%.

Conclusions: A non-regenerative sympathetic nervous system of the foot is a strong predictor of early major amputation (log rank $p<0.001$, HR 14.22, 95% CI 3.84 to 55.35).

INTRODUCTION

Diabetes-related foot complications are the major cause of lower limb amputation. The presence of peripheral arterial disease (PAD) in particular is associated with an increased risk of ulceration, failure of ulcer to heal and amputation.¹ Many parameters have been identified as possible predictors for poor outcome in patients with diabetic foot disease, for example, renal failure, dialysis, infection, gangrene and PAD.^{2,3} Prediction models for early amputation such as the

Significance of this study

What is already known about this subject?

Over the past 20 years some publications have suggested that a dysfunctional sympathetic nervous system of the foot could be a predictor for poor outcome of neuroischemic ulcer in patients with diabetes. These papers have never attracted much attention.

What are the new findings?

The inability to reduce the peripheral resistance in the foot with a local alpha-blocker is a predictor for a foot dysfunction sympathetic nervous system of the foot and amputation before 12 months. Perfusion angiography offers a very simple test to evaluate the functionality of the sympathetic nervous system by measuring change in total blood flow through the foot.

How might these results change the focus of research or clinical practice?

The initial clinical impact of our findings could be that in patients with diabetes with a Capillary Resistance Index (CRI)<0.9 and a remaining or worsening non-healing ulcer after revascularisation, a second intervention is probably in vain. Whereas in patients with a CRI<0.9 a revascularisation might be useful. This might be a cost-effective strategy, especially because this test does not add to the cost of the intervention.

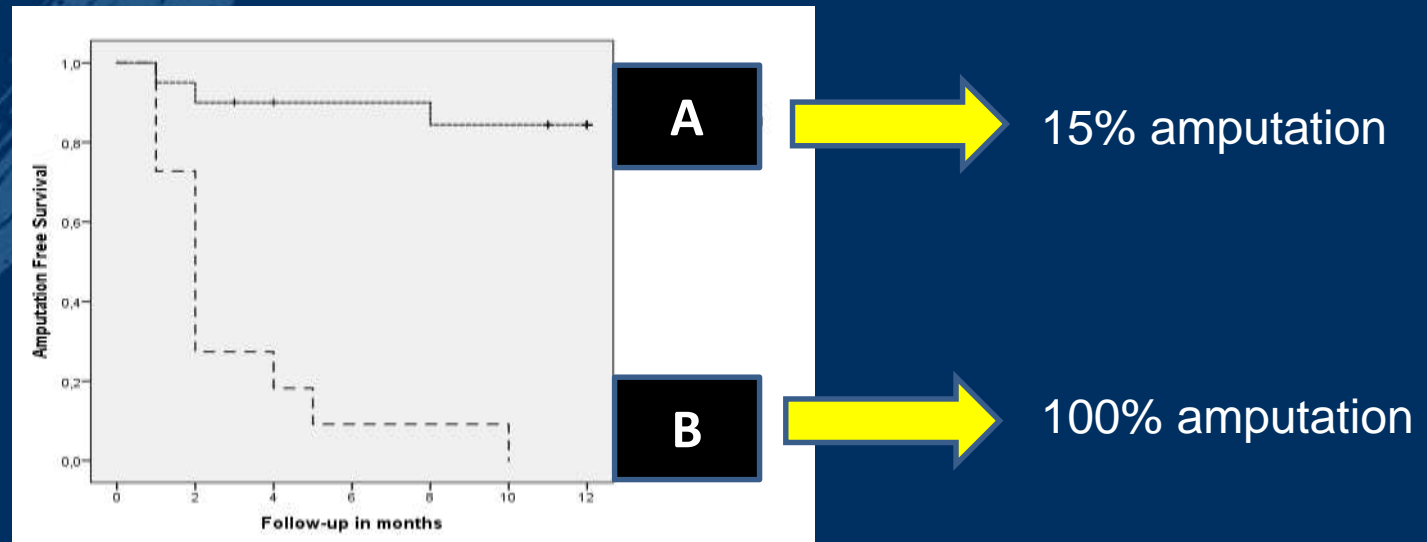
Wound, Ischemia, and foot Infection classification have been introduced.⁴ Of all patients with diabetes who undergo successful endovascular or bypass revascularisation, >20% will still undergo major amputation within 12 months.^{5,6} In >60% off all amputations the revascularisation is still patent at the time of amputation.⁵ This percentage has not decreased over the past decade, despite major advances in percutaneous revascularisation technologies.^{7,8} As well as PAD, microangiopathy has been recognised as an

Dysfunctional sympathetic nervous system in the foot is a strong predictor for early amputation.(<12 M)

Dysfunctional sympathetic nervous system is related to microangiopathy

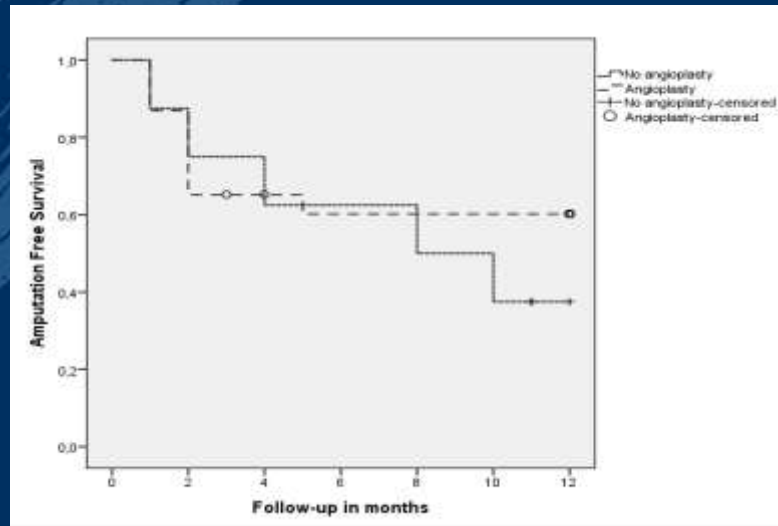
A: patients with functional sympathetic nervous system
(N=20)

B: patients with dysfunctional sympathetic nervous system
(N=11)



*Kaplan-Meier curves for amputation-free survival at 12 months
(log rank $p < 0.001$; HR 14.22 95%CI: 3.64-55.51).*

*23 patients did undergo angioplasty.
8 patients did not undergo angioplasty*



Kaplan-Meier curves of amputation-free survival in patients who did undergo angioplasty and in patients who did not undergo angioplasty (log rank $p = 0.407$; HR 0.65 95%CI: 0.22-1.94).

Conclusion

- Non-functional sympathetic nervous system in the foot, measured with perfusion angiography, in patients with a neuropathic diabetic ulcer is a parameter for **microangiopathy**.
- Successful revascularization with improvement of inflow to the foot, in patients with non-functional sympathetic nervous system, does **not** improve the (poor) outcome.

Therefore:

Microangiopathy is the same as flow-independent ischemia

Is non-functional microcirculation the same as flow- independent ischemia?

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