

Lower limb intermittent negative pressure increases foot circulation and improves wound healing in patients with diabetes and hard-to-heal leg ulcers - a case report

Øyvind H. Sundby, M.Sc.^{1,2,4}; Iacob Mathiesen, PhD.²; Aud-Eldrid Stenehjelm, MD, PhD³; Lars Øivind Høiseith, MD, PhD⁴, Jon O. Sundhagen, MD¹; Jonny Hisdal, Ph.d.¹

¹: Department of Vascular Diseases, Division of Cardiovascular and Pulmonary Diseases, Oslo University Hospital, Aker, Oslo, Norway; ²: Otivio AS, Oslo; ; ³: Department of Nephrology; ⁴: Department of of Anesthesiology, Oslo University Hospital, Ullevål, Oslo, Norway; ⁴: University of Oslo, Faculty of Medicine, Oslo, Norway

Introduction

- Peripheral arterial blood flow and microcirculation are reduced in patients with lower extremity peripheral arterial disease (PAD), renal disease, and diabetes.
- Later stages are characterized by severely diminished circulation, ischemic pain, ulceration, tissue loss and/or gangrene.
- Intermittent negative pressure (INP) applied to the lower leg and foot has shown to increase femoral artery and calf blood flow, and improve walking distance in patients with PAD [1].
- INP increases foot macro- and microcirculation in patients with PAD [2] and may improve wound healing in patients with critical limb ischemia [3]
- There are currently few alternative treatments to improve wound healing other than standard wound care.

Aim

- To explore if INP applied the lower leg and foot improves peripheral blood flow in patients with PAD and diabetes
- To explore if repeated use of INP would improve wound healing in a dialysis patient with diabetes and two chronic leg ulcers

Methods

This experimental and clinical study was conducted at the vascular laboratory at Oslo University Hospital and at the Department of Department of Nephrology.

Four male patients (n=4) diagnosed with PAD and diabetes mellitus (DM) type-II were recruited [median age: 74years (range: 70-77)]; Weight: 78kg (73-92), Height: 172cm (166-179); Body mass index (BMI): 26kg/m² (24-33), Ankle-Brachial Index (ABI): 0.47 (0.42-0.87), pain-free walking distance 140m (80-1067).

Furthermore, a dialysis patient with insulin-dependent DM, PAD and a 7 year old ulcer (Age: 44years; Weight: 89kg, Height: 186cm, BMI: 26kg/m²) evaluated the FlowOx[™] system, one hour three times per week (during dialysis) for 2 months, then later 2 hours per day at home for an additional 4 months.

Intermittent negative pressure application:

- Patients lower leg and foot was placed in a rigid polyethylene subatmospheric pressure chamber with internal padding to prevent pressure points was used to apply INP (Figure 1).
- A thermoplastic elastomer sleeve seals the device and allows for application of INP.

Methods

- Arterial blood flow velocity was measured using a bidirectional ultrasound Doppler velocimeter (SD-50, GE Vingmed Ultrasound, Horten, Norway) in pulsed mode at 10 MHz with a transducer attached to the skin with tape.
- A laser Doppler probe was attached on the pulp of the first toes on each patient.
- Arterial blood flow velocity in dorsalis pedis and skin blood flow on the first toes were measured 5 min before (atmospheric pressure), and during application of 10 min of INP. Mean arterial blood flow velocity measured during 5-min before onset of INP was used as baseline.
- The time when the INP was turned on was marked. Blood flow velocity and laser Doppler flux were sampled for the ten subsequent heartbeats after onset of INP.
- Non-parametric statistics was used to test for difference in blood flow velocity during INP compared to baseline.

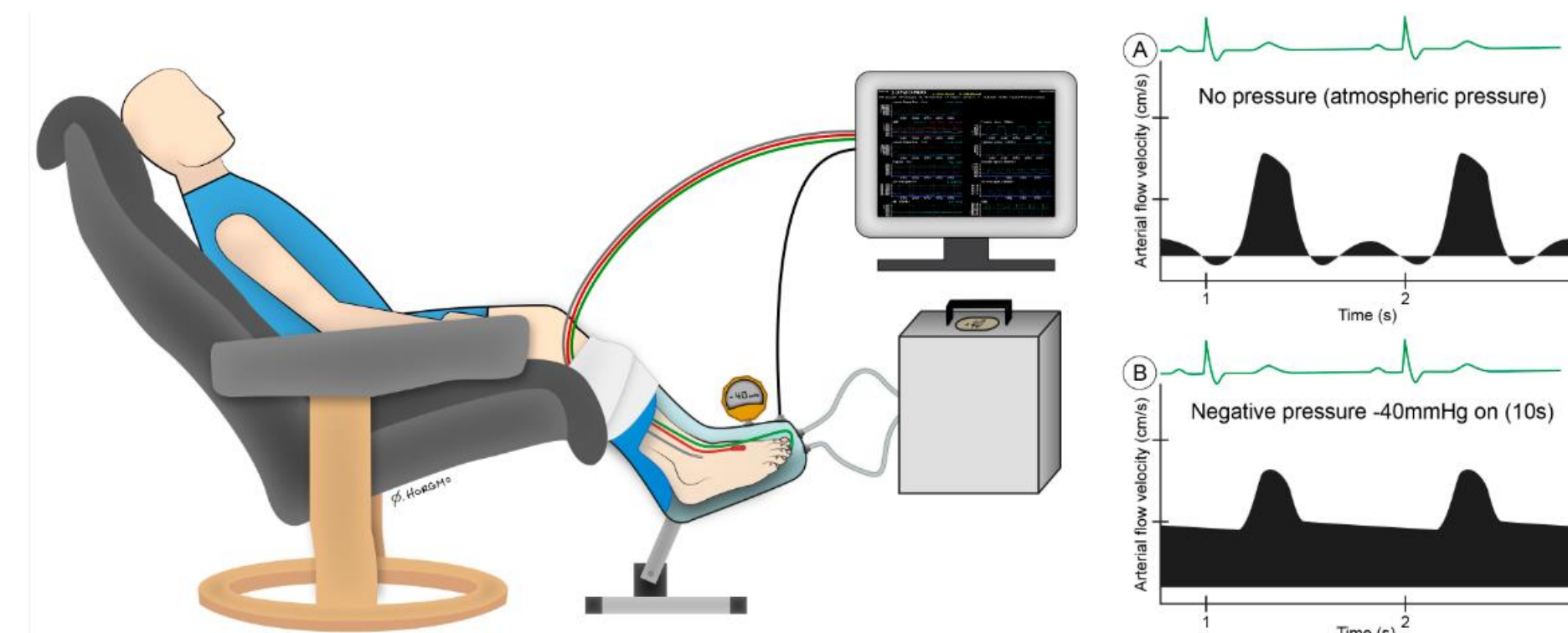


Figure 1. Illustration of the patients' legs placed in the subatmospheric pressure chamber interfaced with the pressure control system (FlowOx[™], Oslo, Norway). The pressure chamber is sealed around the patient's leg below the knee.

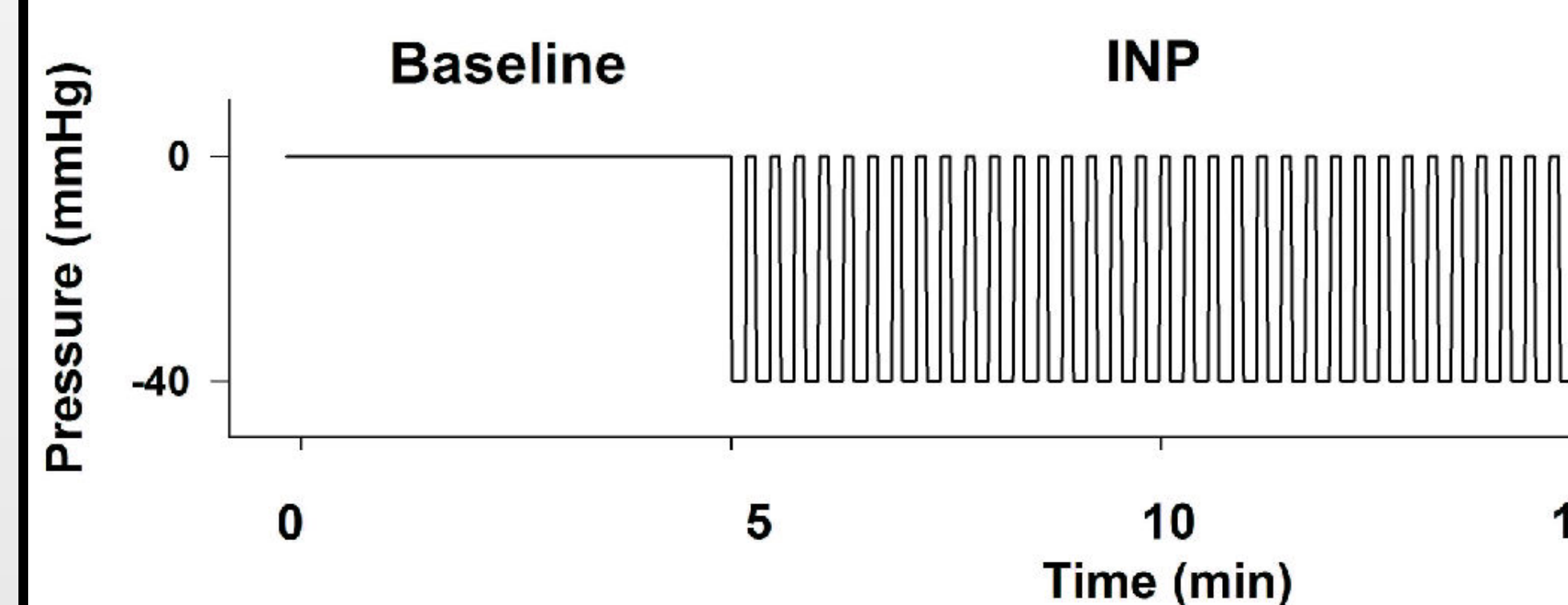


Figure 2. Illustration of how the experimental protocol. A 5-min resting flow (baseline) was sampled before 10 min INP. The INP consisted of a pressure of -40 mmHg for 10 seconds, followed by 7 seconds of atmospheric pressure (760 mmHg) three times per minute

Results

- Average maximal blood flow was observed at the 2nd heartbeat after onset of negative pressure:
- All patients had a significant increase in arterial blood flow velocity at onset of negative pressure during individual heartbeats compared to 5 min baseline (p<0.001).
- The maximal increase in blood flow velocity was 45% with a range of 18 to 164 %, compared to baseline (p=0.001, Wilcoxon Signed Rank Test).

Results

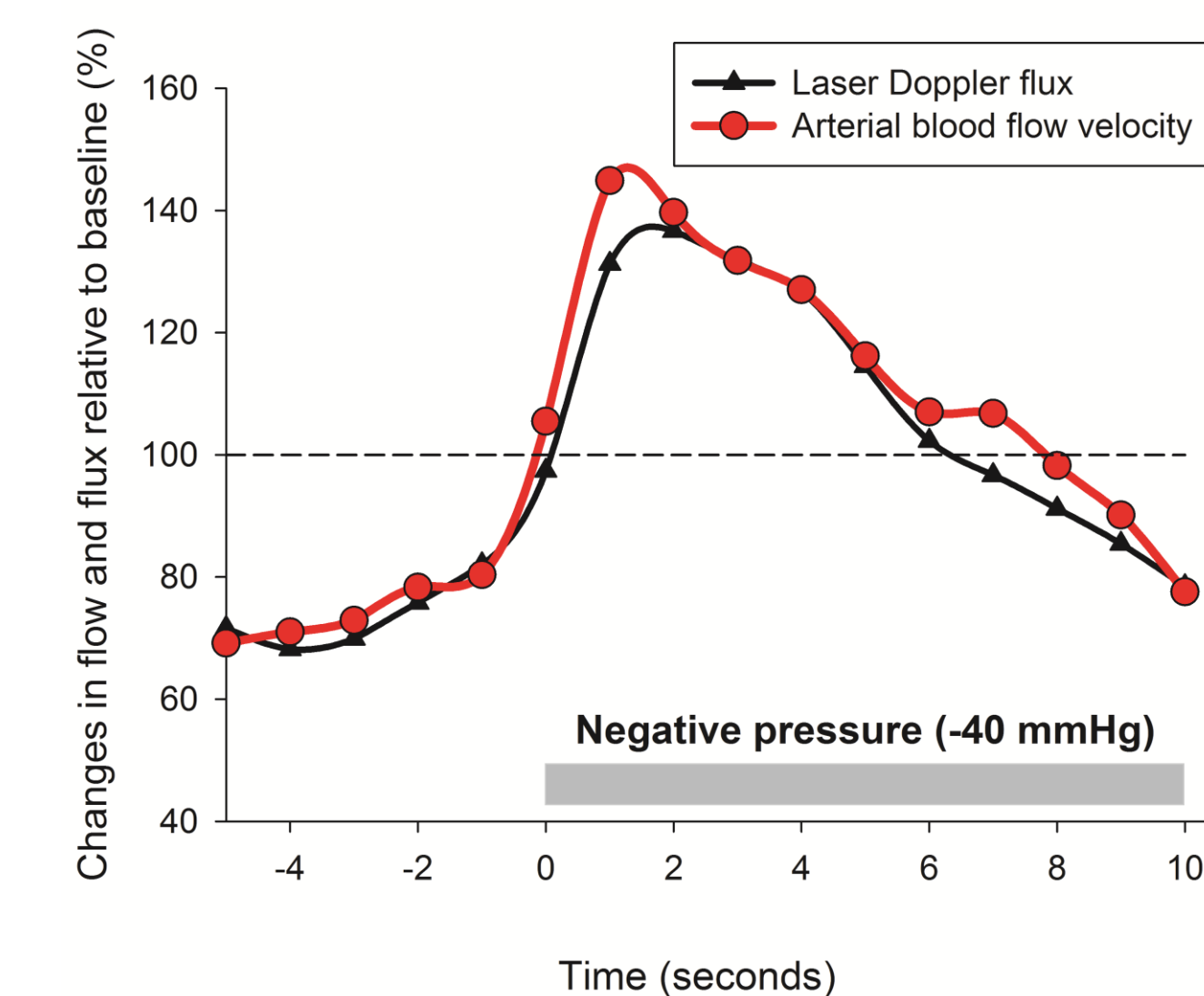


Figure 3. Relative changes in blood flow velocity (Ultrasound Doppler) and skin blood flow (lase Doppler) compared to baseline (100%) for all four patients with PAD and diabetes. The figure shows an average of 141 analyzed INP cycles recorded during 10 minutes for the four diabetic patients.

- The dialysis patient's ulcer was completely epithelized after 6 months of INP treatment. The ABI changed from 0.77 to 0.97 in the treated limb, vs. 0.61 to 0.66 in the untreated leg.
- Due to the healed ulcers, the patient is now in line for a renal transplantation.



Figure 4 Left: Dialysis patients with 7 year old ulcer before (A) and after 6 months of INP treatment (B) **Right:** The FlowOx[™] used by the patient.



Summary and Conclusion

- Mild intermittent negative pressure (FlowOx[™]) induced a significant transient increase in blood flow during onset of negative pressure compared to baseline in patients with PAD and diabetes.
- A transient increase in tissue blood flow is likely to improve oxygenation, improve removal of waste substances and potentially initiate processes leading to wound healing. Further clinical studies are warranted.

References

- [1] Smyth, C. N. (1969). Effect of suction on blood-flow in ischaemic limbs. Lancet, 2 (7622), 657-659.
- [2] [3] Sundby ØH, Høiseith LØ, Mathiesen I, Weedon-Fekjær H, Sundhagen JO, Hisdal J. The acute effects of lower limb intermittent negative pressure on foot macro- and microcirculation in patients with peripheral arterial disease. PLoS One. 2017;12(6):e0179001.
- [3] Sundby ØH, Høiseith LØ, Mathiesen I, Jorgensen JJ, Sundhagen JO, Hisdal J. The effects of intermittent negative pressure on the lower extremities' peripheral circulation and wound healing in four patients with lower limb ischemia and hard-to-heal leg ulcers: a case report. Physiological Reports. 2016;4(20).