"An injection a day may keep CLI away?"

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Welcome to another diabetic foot digest commentary. Hopefully there will be a few abstracts that may catch your interest.

The focus paper is an open-label randomised controlled study from a group in Naples, Italy. Its main objective was to investigate the effect of liraglutide, a glucagon-like peptide 1 receptor agonist (GLP-1RA), on peripheral arterial perfusion, measured as peripheral transcutaneous oxygen pressure ($TcPO_2$) in individuals with type 2 diabetes and existing mild peripheral artery disease (PAD). The authors screened 89 subjects with type 2 diabetes with an HbA_{1c} of 6.5–8% and PAD, recruiting 55 people. Inclusion criteria included GLP-1RA naïve or not taken for 3+ months, $TcPO_2$ 30–49 mmHg (foot dorsum). PAD diagnosis was determined by Doppler ultrasonography, CT angiography, or angiography within 12 months.

The authors randomised 27 subjects to target daily dose 1.8 mg of subcutaneous liraglutide titrated 0.6 mg weekly to target (LG) and 28 to control group (CG) for 6 months. Primary outcomes were a change from baseline $TcPO_2$ between groups and proportional comparison of subjects who reached 10% increase from baseline $TcPO_2$ in each group.

The mean age was 67.5 (SD ± 8.5) years; 78% (n=43) were male. The median HbA_{1c} was 6.9% (range 6.5–7.8%) and the mean $TcPO_2$ was 40.3 (± 5.7) mmHg.

The 10% increase of $TcPO_2$ occurred in 24 participants (89%) in LG and 13 (46%) in CG (relative risk 1.91; 95% CI 1.26–2.90; p<0.001). However, overall, there was a $TcPO_2$ increase at follow-up in both groups, but with a significant difference favouring the LG (difference of 11.2 mmHg; 95% CI 8.0–14.5 mmHg; p<0.001). Compared with CG, individuals in LG had a significant reduction of C-reactive protein (–0.4 mg/dl; 95% CI –0.7, –0.07; p=0.02), urinary albumin:creatinine ratio (–119.4 mg/g; 95% CI –195.0, –43.8; p=0.003), and improvement of 6-minute walking distance (25.1 m; 95% CI 21.8–28.3 m; p<0.001).

There have been several previous studies indicating that GLP-1RAs have a potentially beneficial role in reducing PAD progression (SUSTAIN-6, EXSCEL and LEADER trials), but this study is the first to measure tissue perfusion which is important because it a physiological measurement of tissue oxygen levels. Of course, there are potential confounders of $TcPO_2$, namely oedema and inflammation. There was no account of these in the study design.

There was no record of activity, which may explain the fact that both groups had an increase in $TcPO_2$ levels by developing increased collateral supply. The study had a short follow-up period of only 6 months, a longer-term follow-up would be required to see if these results were sustained or changed. Additionally, the sample size was small, and being open labelled this study could be prone to high bias. It would also perhaps have benefitted from also using other comparative assessment methods e.g. waveform analysis, digital PPG, etc.

However, this study suggests that perhaps liraglutide could be used to prevent the clinical progression of PAD in individuals with type 2 diabetes. ■

Caruso P, Maiorino MI, Longo M et al (2024)Liraglutide for lower limb perfusion in people with type 2 diabetes and peripheral artery disease: the STARDUST randomized clinical trial. *JAMA Netw Open* 4;7(3): e241545

Int J Low Extrem Wounds

Management of diabetic foot ulcer with MA-ECM using 3D bioprinting technology

Readability	✓✓✓
Applicability to practice	✓✓✓✓
WOW! Factor	✓✓✓✓

1 The authors examined the efficacy of minimally manipulated extracellular matrix (MA-ECM) prepared from autologous homologous adipose tissue by using 3D bioprinting in diabetic foot ulceration.

2 Subjects were screened and randomly divided into test (n=17) and control groups (n=16). In the test group, the customised MA-ECM was printed as a scaffold from the patient's autologous fat using a 3D bioprinter device and applied to the wound directly. The control group received standard wound care. All patients received weekly follow-up. Reduction in wound size and epithelialisation were assessed.

3 The test group patients showed complete wound closure with re-epithelialisation within 4 weeks. In comparison, the control group had delayed wound healing.

4 The authors concluded that this novel technique can be employed as a personalised therapeutic method to accelerate diabetic wound healing.

Kesavan R, Sheela Sasikumar C, Narayanamurthy VB et al (2024) Management of diabetic foot ulcer with MA-ECM (minimally manipulated autologous extracellular matrix) using 3D bioprinting technology – an innovative approach. *Int J Low Extrem Wounds* 23(1): 161–8

Gait Posture

The effects of vibrating shoe insoles on standing balance, walking, and ankle-foot muscle activity in adults with diabetic peripheral neuropathy

Readability	✓✓✓
Applicability to practice	✓✓✓✓
WOW! Factor	✓✓✓

1 Devices designed to stimulate foot sensory receptors could improve motor impairments in diabetic peripheral neuropathy (DPN). The authors examined whether wearing vibrating insoles for the first time altered measures of balance, walking and ankle-foot muscle activity in people with DPN.

2 A randomised cross-over study was conducted with 18 subjects with DPN performing tests of standing balance and level-ground walking, while wearing vibrating and non-vibrating insoles. Electromyography (EMG) was used to assess muscle activity during balance tests. Outcomes included centre of pressure (CoP) sway, EMG amplitude, spatiotemporal gait patterns, and Timed Up and Go test.

3 Wearing vibrating insoles improved CoP elliptical area compared to non-vibrating insoles and reduced the EMG amplitude.

4 The authors note these findings of small improvements with vibrating insoles had uncertain clinical meaning and further research is needed.

Hatton AL, Chatfield MD, Cattagni T, Vicenzino B (2024) The effects of vibrating shoe insoles on standing balance, walking, and ankle-foot muscle activity in adults with diabetic peripheral neuropathy. *Gait Posture* 11: 8–13

Int Wound J

A purified reconstituted bilayer matrix shows improved outcomes in treatment of non-healing diabetic foot ulcers

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! Factor	✓✓✓

1 The authors conducted a randomised controlled trial comparing a novel purified reconstituted bilayer membrane (PRBM) to the standard of care (SOC) in the treatment of non-healing diabetic foot ulcers (DFUs).

2 They randomised 105 patients to two treatment groups, PRBM (n=54) and SOC (n=51). The primary endpoint was the percentage of wounds closed after 12 weeks. Secondary outcomes included area reduction, time to healing, quality of life and cost.

3 More of the DFUs treated with PRBM healed than those treated with SOC (92% versus 67%, p=0.005). Wounds treated with PRBM healed significantly faster with a mean of 42 versus 62 days for SOC (p=0.00074); additionally they had a mean wound area reduction of 94% in 12 weeks versus 51% for SOC (p=0.0023).

4 The authors conclude that the PRBM is an effective option for the treatment of chronic DFUs.

Armstrong DG, Orgill DP, Galiano RD et al (2024) A purified reconstituted bilayer matrix shows improved outcomes in treatment of non-healing diabetic foot ulcers when compared to the standard of care: Final results and analysis of a prospective, randomized, controlled, multi-centre clinical trial. *Int Wound J* 21(4): e14882

Diabetes Metab Res Rev

Cost-effectiveness of temperature monitoring to help prevent foot ulcer recurrence in people with diabetes

Readability	✓✓✓
Applicability to practice	✓✓✓
WOW! Factor	✓✓

1 The researchers evaluated the cost-effectiveness of at-home skin temperature monitoring to help prevent diabetic foot ulcer (DFU) recurrence.

2 They randomised 304 people at high risk of DFUs to either usual foot care plus daily at-home foot skin temperature monitoring (intervention) or usual care. Primary outcome was cost-effectiveness based on foot care costs and quality-adjusted life years (QALY) during 18 months of follow-up. Incremental cost-effectiveness ratios were calculated for intervention versus usual care for willingness-to-pay/accept levels up to €100,000.

3 The intervention had a 45% probability of being cost-effective at a willingness-to-accept of €50,000 per QALY lost. This resulted from lower foot care costs in the intervention group (€6,067 versus €7,376; p=0.45) due to significantly fewer participants with ulcer recurrences (36% versus 47%; p=0.045).

4 The authors concluded that at-home skin temperature monitoring for DFU prevention compared with usual care is at best equally cost-effective.

Van Netten JJ, Aan De Stegge WB, Dijkgraaf MGW, Bus SA (2024) Cost-effectiveness of temperature monitoring to help prevent foot ulcer recurrence in people with diabetes: A multicenter randomized controlled trial. *Diabetes Metab Res Rev* 40(4): e3805

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