



“Mind the gap” ulcer offloading: International guidelines good, implementation poor.

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Welcome to this edition of Diabetes Digest. I hope you find something interesting in the selection of recent papers I've chosen.

The featured paper this issue is from Sweden. It sought to explore whether there is a gap between clinical practice and the International Working Group on the Diabetic Foot Ulcer offloading guidelines.

At the outset, I will say that this study may not be truly reflective of clinical practice universally. This paper was an observational cross-sectional study and the aims were to assess the use of different offloading interventions, factors that influence offloading choices, and gold standard offloading awareness for healing plantar neuropathic forefoot diabetic foot ulcers (DFUs).

In Sweden, prosthetic and orthotic clinics are predominately responsible for offloading DFUs. Following a pilot questionnaire of 29 questions, a final version comprising of seven closed-ended questions with a glossary list was produced.

The final survey was distributed via SurveyMonkey to the 51 prosthetic and orthotic clinics in Sweden. This was then answered by practitioners who were experienced and responsible for offloading DFUs.

The questions included: identification of the types and percentage use of 14 predefined offloading interventions, with free text for additional methods; ranked responses on a five-point Likert scale regarding consideration to practitioner, patient, intervention and wound-related factors in the provision of offloading interventions (i.e. choice preferences); and awareness regarding the gold standard for DFU offloading.

Overall, 35 (69%) clinicians responded to the questionnaire. Findings were that 86% of clinics provided modified off-the-shelf footwear with insoles (to a mean of 59% of patients); while 49% provided modified off-the-shelf footwear without insoles (to 30% of patients). Post-operative shoes were provided by 71% (to 12% of patients). Removable knee-high walkers and removable casts were provided by 49% (to 9% of patients), and 20% provided total contact casts (TCCs; to 8% of patients). None provided non-removable knee-high walkers.

When asked if they were aware that TCC was the gold standard DFU offloading intervention, 26% of practitioners were aware, 37% were unsure and 37% were unaware. The average percentage of patients provided with TCC was 2% (practitioners aware), 3% (unsure) and 0% (unaware).

Thus, in Sweden there certainly appears to be a huge gap between the recommended international evidence-based guidelines and clinical practice. In fact, this study shows a complete reverse of the guidelines.

Of course, this study has many questions regarding methodology and one cannot suggest the results are the norm. However, there is a body of evidence that the gold standard TCC is not used widely throughout the world for many identified reasons, and this study further adds to this.

Perhaps it's time to put more energy and resources into aiding guideline implementation and not further refining existing guidelines. ■

Gigante I, Sigurjónsdóttir ED, Jarl G, Hellstrand Tang U (2023) Offloading of diabetes-related neuropathic foot ulcers at Swedish prosthetic and orthotic clinics. *Diabetes Metab Res Rev* [Online ahead of print]

Inflammopharmacology

A randomized controlled trial assessing the safety and efficacy of palmitoylethanolamide for treating diabetic-related peripheral neuropathic pain

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

1 The authors investigated the use of a palmitoylethanolamide (PEA) formulation in treating diabetes-related peripheral neuropathic pain (PNP).

2 The study was a single-centre, quadruple-blinded, placebo-controlled trial with 70 participants with type 1 and type 2 diabetes and PNP. They received 600 mg of PEA or placebo daily for 8 weeks. Primary outcomes were neuropathic pain reduction. The secondary outcomes were sleep quality, mood, glucose metabolism and inflammation.

3 There was a significant reduction ($p \leq 0.001$) in total pain. Sleep significantly improved ($p \leq 0.001$). Depression significantly reduced ($p = 0.03$), but not anxiety or stress. Interleukin-6 and C-reactive protein significantly reduced in the PEA group ($p = 0.05$), with no differences in fibrinogen between groups ($p = 0.78$). The treatment was well tolerated.

4 The authors concluded that the PEA formulation reduced diabetic peripheral neuropathic pain and inflammation and improved mood and sleep. Further studies are warranted.

Pickering E, Steels EL, Steadman KJ et al (2022) A randomized controlled trial assessing the safety and efficacy of palmitoylethanolamide for treating diabetic-related peripheral neuropathic pain. *Inflammopharmacology* 30(6): 2063–77

Int Wound J

Association between vitamin D deficiency and diabetic foot ulcer wound in diabetic subjects

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

- 1 There has been an increased interest in the role of vitamin D in diabetic foot ulceration in recent years. This meta-analysis evaluated the association between vitamin D deficiency and diabetic foot ulceration.
- 2 The authors performed a systematic literature search up to March 2022 that included 7,586 people with diabetes from 12 studies in seven countries; 1,565 with foot ulcer wounds and 6,021 who were non-ulcerated. They then evaluated the influence of vitamin D deficiency in diabetic foot ulcers.
- 3 They found that people with diabetic foot ulcers had significantly lower vitamin D levels (mean difference -6.48; 95% CI -10.84 to -2.11, $p < 0.004$), a higher prevalence of vitamin D deficiency (< 50 nmol/l; OR 1.82; 95% CI 1.32–2.52, $p < 0.001$), and higher prevalence of severe vitamin D deficiency (OR 2.53; 95% CI 1.65–3.89, $p < 0.001$) compared with non-ulcerated subjects.
- 4 The authors noted that the mechanism of the relationship between serum vitamin D levels and diabetic foot ulcer wounds is still unclear, and cautioned that additional studies with large sample sizes are required to validate these findings.

Lin J, Mo X, Yang Y et al (2023) Association between vitamin D deficiency and diabetic foot ulcer wound in diabetic subjects: a meta-analysis. *Int Wound J* 20(1): 55–62

Eur J Clin Pharmacol

Coenzyme Q10 as a potential add-on treatment for patients suffering from painful diabetic neuropathy

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

- 1 The authors investigated whether the addition of coenzyme Q10 (CoQ10) to pregabalin would improve symptoms in patients with painful diabetic neuropathy.
- 2 The authors randomly allocated subjects to receive either 100 mg CoQ10 and 150 mg pregabalin ($n=57$) or placebo and pregabalin ($n=55$). CoQ10 or matched placebo was given every 8 hours for 8 weeks. The primary outcome was the change in pain intensity.
- 3 The authors found that the CoQ10 and pregabalin regimen resulted in significantly greater pain relief than the placebo and pregabalin regimen. By the end of week 2, the decrease in the mean pain score was similar in both groups. At the end of weeks 4 and 8, the decrease in the mean pain score was significantly greater in patients taking CoQ10 and pregabalin than in those taking placebo and pregabalin ($p=0.01$ and $p < 0.001$, respectively).
- 4 The authors concluded that their study supports the hypothesis that patients with painful diabetic neuropathy may benefit from using antioxidant and anti-inflammatory supplements such as CoQ10. However, further studies are required.

Amini P, Sajedi F, Mirjalili M et al (2022) Coenzyme Q10 as a potential add-on treatment for patients suffering from painful diabetic neuropathy: results of a placebo-controlled randomized trial. *Eur J Clin Pharmacol* 78(12): 1899–910

J Foot Ankle Res

Health-related quality of life and associated factors in people with diabetes at high risk of foot ulceration

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

- 1 The aim of this Dutch study was to assess health-related quality of life (HRQoL) and determine associated factors in people with diabetes at high risk of foot ulcers.
- 2 A total of 304 participants were drawn from the Diabetic Foot Temperature Trial. HRQoL was measured by the RAND 36-Item Short Form Health Survey (SF-36). Participants were mostly men (72%), mean age 64.6 (± 10.5) years, 77% type 2 diabetes and a mean diabetes duration of 20 (± 14) years.
- 3 The authors found that HRQoL was lower than Dutch population-based and general diabetes samples, but higher than in those with an ulcer. Use of a walking aid was associated with lower HRQoL across all SF-36 domains, and being of non-Caucasian ethnicity was associated with lower HRQoL in five domains. People who were not working, with higher BMI or of younger age had lower HRQoL in three domains.
- 4 The authors concluded that people at high risk of diabetic foot ulcers have reduced HRQoL, with the physical domains most affected. Assessing mobility, ethnicity, BMI and job status may be useful to identify those who might benefit from interventions targeting HRQoL.

Perrin BM, van Netten JJ, aan de Stegge WB et al (2022) Health-related quality of life and associated factors in people with diabetes at high risk of foot ulceration. *J Foot Ankle Res* 15: 83

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