



COMMENT ON FEDORKO ET AL.

Hyperbaric Oxygen Therapy Does Not Reduce Indications for Amputation in Patients With Diabetes With Nonhealing Ulcers of the Lower Limb: A Prospective, Double-Blind, Randomized Controlled Clinical Trial. *Diabetes Care* 2016;39:392–399

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Magnus Löndahl,^{1,2}
Katarina Fagher,^{1,2} and
Per Katzman^{1,2}

More than 3 years after the last study visit, the study by Fedorko et al. (1) was published in *Diabetes Care*. Several issues need to be highlighted, some of which are discussed here.

If the end point “indication for [major] amputation” is more appropriate than “major amputation” (1), only the future can tell. Amputation rate assumption of 39.39 vs. 11.54% within a 3-month period in an outpatient care setting seems odd. Accordingly, amputation rates in the trial by Faglia et al. including hospitalized patients with severe and acute infected Wagner grade 3/4 ulcers were 9 vs. 33%, and the 1-year major amputation rate in the outpatient care studies by Abidia et al. and Löndahl et al. (not published at that time) was 5% (2). Thus, the trial by Fedorko et al. (1) seems highly underpowered to reach its primary end point. How many major amputations were actually performed during the study and during the 3 poststudy years? The follow-up time was very short to fully evaluate the effects of hyperbaric oxygen therapy (HBOT) (2).

Only 61% of the HBOT group completed the 30 treatment sessions; was this considered in power calculations?

HBOT should be used only in a select group of patients with hard-to-heal

diabetic foot ulcers (2,3). Fedorko et al. (1) claim that their study population is similar to that of Löndahl et al. (4). This is not correct, as that study population was older; had a longer diabetes duration, a minimum ulcer duration of 3 months, a longer prespecified minimum prestudy period in a diabetic foot ulcer clinic; and had more comorbidities and higher rates of previous amputation (almost 50 vs. 6%) and previous vascular surgical intervention (55 vs. 12%) at baseline. Further, a mean age of 61 years is notably low (lower than the median age in European diabetic foot ulcer clinics), and there were notably many current smokers (55%).

Further, Fedorko et al. (1) report conflicting results regarding mean ulcer area; 6.1 vs. 5.1 cm², as shown on page 4, and 3.8 vs. 3.6 cm², as shown in Table 1. Which one is correct?

No data about peripheral vascular circulation were given by Fedorko et al. Transcutaneous oxygen pressure measurement (TcPO₂) is commonly used to select and evaluate patients before, during, and after HBOT (2,5).

The span in ulcer duration (28–3,650 days), combined with the 12-week–outcome end point where one-fourth of the study population was recommended

for major amputation and one-fifth was healed, suggests a heterogeneous study population and that prestudy treatment applying international treatment guidelines might have been too short to select a robust hard-to-heal study population. Are the data normally distributed?

The “bubble” theory by which Fedorko et al. (1) dismiss the previous two double-blind, randomized controlled trials seems irrelevant, and this harsh statement is of no value until its clinical relevance has been confirmed.

The International Working Group on the Diabetic Foot does not consider the trial by Duzgun et al. as justification for HBOT (3).

We agree with the authors that more studies are needed to identify patients that might benefit from HBOT, but unfortunately this study contributes little to this; worse, its conclusion is not justified by the data presented.

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¹Department of Endocrinology, Skåne University Hospital, Lund, Sweden

²Department of Clinical Sciences, Lund University, Lund, Sweden

Corresponding author: Magnus Löndahl, magnus.londahl@med.lu.se.

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