COMMENTS AND RESPONSES

Comment on: Margolis et al. Lack of Effectiveness of Hyperbaric Oxygen Therapy for the Treatment of Diabetic Foot Ulcer and the Prevention of Amputation: A Cohort Study. Diabetes Care 2013; 36:1961–1966

The retrospective study recently published by Margolis et al. (1) raises many questions. First, it appears that the excluded cohort had a lower extremity amputation (LEA) rate of 4.5% in the first 28 days. This seems high. Previous studies have shown overall amputation rates (major and minor) after 1 year of 12.5–22.6% in two smaller cohort studies of sicker patients (2,3). Given that the excluded cohort was defined as having "adequate lower extremity arterial flow" (diagnostic method unknown), these results suggest that the excluded cohort was either at inherently higher risk for an LEA or that basic wound care was poorly conducted.

Second, since the detailed selection criteria for hyperbaric oxygen therapy (HBOT) at the former National Healing Corporation were not reported, it remains unclear if they were medically appropriate. HBOT is indicated for diabetic foot ulcers (DFUs) that have failed to respond to adequate basic wound care after 4 weeks (including appropriate debridement, vascular screening for significant peripheral arterial disease, and/or local wound hypoxia, adequate offloading, and infection management). Additionally, current best practice is to assess DFUs with transcutaneous oximetry while breathing sea level air to confirm that wounds are hypoxic and thus unlikely to heal spontaneously and confirming possible benefit from HBOT with in-chamber oximetry (4). The provision of HBOT to Wagner grade 2 lesions is puzzling because prospective HBOT trials have focused on Wagner grade 3 and above, mirroring Medicare coverage policy. Since none of the advanced therapeutics currently used in wound care have been tested in DFUs above Wagner grade 2, HBOT stands alone with RCT evidence of efficacy in Wagner 3/4 grade ulcers.

Third, the method of analysis in this study has shortcomings. Although propensity scoring as a means of adjusting for the severity of wounds and patient comorbidities may be a viable approach, if conducted inappropriately it can lead to increased rather than decreased bias (5). Many other confounders can affect outcomes directly, such as renal failure, smoking, chronic heart failure, level of tissue exposed, offloading, debridement, infection severity, management of infection, ambulation, and immunosuppression (e.g., long-term steroid use/concurrent chemotherapy). Sensitivity analysis for the assumed distribution of an individual potential confounder, as reported in this article, is inadequate to account for the potential effects of such a long list of known confounders—and can make no allowance for any further confounding factors of which we are unaware.

In summary, we believe the results from this retrospective cohort study are not necessarily generalizable to other wound-care populations. We agree with Margolis et al. (1) that "it is entirely likely that HBO therapy enhances a specific aspect of wound repair and should not be used as a single agent to completely heal a wound." However, we are not confident that the retrospective analysis by Margolis et al. of practice in a single wound-care organization sheds light on the difference between efficacy and effectiveness of HBOT in DFU patients as implemented in well-designed clinical practice guidelines. Most importantly, this study should energize all organizations to rereview how HBOT is used for DFUs.

Marissa J. Carter, phd[1]
Caroline E. Fife, md[2]
Michael Bennett, md[3]

From [1]Strategic Solutions, Inc., Cody, Wyoming; [2]Intellicure, Inc., The Woodlands, Texas; and the [3]Department of Diving and Hyperbaric Medicine, Prince of Wales Hospital and the University of New South Wales, Randwick, New South Wales, Australia.

Corresponding author: Marissa J. Carter, mcarter@strategic-solutions-inc.com.

DOI: 10.2337/dc13-0566

© 2013 by the American Diabetes Association. Readers may use this article as long as the work is properly cited, the use is educational and not for profit, and the work is not altered. See http://creativecommons.org/licenses/by-nc-nd/3.0/ for details.

Acknowledgments—M.J.C. is an employee of Strategic Solutions, Inc. C.E.F. is an employee of Intellicure, Inc. No other potential conflicts of interest relevant to this article were reported.

References

1. Margolis DJ, Gupta J, Hoffstad O, et al. Lack of effectiveness of hyperbaric oxygen therapy for the treatment of diabetic foot ulcer and the prevention of amputation: a cohort study. Diabetes Care 2013;36:1961–1966
2. Beckert S, Witte M, Wicke C, Königsrainer A, Coerper S. A new wound-based severity score for diabetic foot ulcers: a prospective analysis of 1,000 patients. Diabetes Care 2006;29:988–992
3. van Battum P, Schaper N, Prompers L, et al. Differences in minor amputation rate in diabetic foot disease throughout Europe are in part explained by differences in disease severity at presentation. Diabet Med 2011; 28:199–205
4. Fife CE, Smart DR, Sheffield PJ, Hopf HW, Hawkins G, Clarke D. Transcutaneous oximetry in clinical practice: consensus statements from an expert panel based on evidence. Undersea Hyperb Med 2009;36:43–53
5. Pearl J. Remarks on the method of propensity score. Stat Med 2009;28:1415–1416; author reply 1420–1423