DOI: 10.1002/hsr2.1047

LETTER TO THE EDITOR

Health Science Reports Open Access WILEY

# Letter to the editor regarding the article by Elhage et al.: "Closed-incision negative pressure therapy at −125 mmHg significantly reduces surgical site complications following total hip and knee arthroplasties: A stratified meta-analysis of randomized controlled trials"

To the Editor,

It is with interest that I read the study entitled "Closed-incision negative pressure therapy at −125 mmHg significantly reduces surgical site complications (SSC) following total hip and knee arthroplasties: A stratified meta-analysis of randomized controlled trials" by Elhage et al.[1]

In their study, Elhage et al. compare single-use negative pressure wound therapy (sNPWT) to standard treatment for the prevention of SSC in total hip and knee arthroplasty (THA/TKA). The authors' interpretation of their findings was to recommend −125 mmHg over −80 mmHg for postoperative wound care in patients undergoing THA or TKA, although this assertion is only made in the article's abstract and is not found in the same form within the conclusions section of the main text. I believe there are several flaws with the study's methodology and that the study's results may have been misinterpreted.

At the outset, it should be noted that Elhage et al. does not compare −125 and −80 mmHg directly. Instead, the study compares −125 and −80 mmHg to conventional dressings. One should exercise caution with respect to the authors' recommendation of one setting over another based on such indirect evidence.

## 1 | USE OF COMPOSITE OUTCOMES

The study may have potentially over-emphasized the composite SSC outcome. In particular, the SSC outcome is a "composite outcome", consisting of several component outcomes including surgical site infection (SSI), seroma, and dehiscence. The problem with composite outcomes is that the composite can be overly influenced by one component outcome resulting in a statistically significant difference in the composite,[2] making it seem like the effect size applies to all outcomes included in the composite which may not necessarily be true. For example, Giannini et al.[3] and Pachowsky et al.[4] report only on a single outcome each (blistering and seroma incidence, respectively), yet these incidence rates are considered applicable to the SSC composite outcome. It is better scientific practice to present the data for each individual component outcome in cases like this, to avoid confusing readers that a beneficial treatment effect in the composite outcome is applicable to all its components.[2] Further investigation into the individual component outcomes indicates that a statistically significant treatment effect with −125 mmHg is only seen in the "persistent wound drainage" outcome. For all other outcomes investigated by the authors including SSI, dehiscence, hematoma, seroma, and blistering incidence, no statistically significant reduction in the outcome was observed with either the −125 or −80 mmHg devices. This would suggest that the persistent wound drainage outcome is contributing largely to the treatment effect observed in the SSC composite outcome.

Persistent wound drainage is an important clinical indicator regarding wound status and is often a precursor to fulminant SSI.[5] However, it is notable that only one of the −80 mmHg studies has "persistent wound drainage" as an examined outcome, perhaps skewing the comparative analysis in favor of −125 mmHg. As a result, insufficient data are presented in the present study to be able to evaluate whether −80 mmHg devices offer the same statistically significant reduction in persistent wound drainage. With further data, it is possible that the same treatment effect would be observed with −80 mmHg devices. For example, Keeney et al.[6] report a statistically significant reduction in the incidence of persistent wound drainage associated with the use of −80 mmHg versus conventional dressings, indicating a benefit in this outcome. This randomized controlled trial was not included in the present study.

## 2 | COMPARABILITY OF PATIENT COHORTS

Notably, the studies included in the stratified analysis do not compare properly matched cohorts. In the −125 mmHg analysis, 68.5% of patients were from a study by Newman et al. that specifically selected for patients having higher risk of SSC. Indeed, this study excluded over 80% of its screened patient population for not having high enough risk factors to be included in the study. In contrast, the −80 mmHg analysis did not include or exclude patients based on the presence or absence of risk factors.

It is well known that NPWT shows a greater beneficial effect in high-risk patients.[7] It is therefore not surprising that the 125 mmHg analysis (accepting a greater percentage of patients having higher risk of SSC) demonstrated greater benefit than the −80 mmHg analyses (accepting all patients irrespective of risk factors). Repeating the stratified analyses in the absence of the selected high-risk patient population within Newman et al. (i.e., performing a more "apples to apples" comparison between pressure settings) demonstrates no difference between −125 and −80 mmHg devices for the composite SSC outcome, nor any individual component outcome.

## 3 | STRATIFICATION OF SECONDARY OUTCOMES

Another noticeable limitation of the present analysis is that the authors failed to stratify their secondary endpoints by pressure setting. Stratifying the length of stay (LoS) outcome by −80 or −125 mmHg unveils a statistically significant reduction in LoS compared to standard treatment with the use of a −80 mmHg device, with no such statistically significant reduction with a −125 mmHg device. Stratifying the secondary endpoints would have provided further valuable insights than what was originally reported.

## 4 | REPLICABILITY OF FINDINGS

I was also unable to reproduce the results in the authors' literature review based on the reported search syntax. Attempting to correct this syntax and repeating the searches results in a large disparity between the article hits Elhage et al. obtained in their review and the repeated searches. This problem is compounded by the fact that at least one study reporting on a −80 mmHg device was identified when replicating the searches that should have met the authors' criteria for inclusion in their systematic literature review.[6] It is not clear from the manuscript itself why this study was excluded but it appears to meet the inclusion criteria outlined in the report. The absence of this study has implications for the current findings of Elhage et al. I encourage the authors to clarify their inclusion/exclusion criteria.

## 5 | CONCLUSIONS

In summary, I believe the publication by Elhage et al. would be improved by focusing more on the individual component outcomes reported in the included studies and by acknowledging the issues of presenting composite outcomes when the data suggest one factor is contributing heavily to the overall result. Furthermore, acknowledging the differences in patient populations between studies and performing appropriate stratifications and subanalyses to accommodate for this would provide a more accurate representation of the underlying treatment effects of the sNPWT devices. It has been established from previous systematic literature reviews and expert opinion that the optimal therapeutic benefit of NPWT is derived with a pressure level setting of between −50 and −150 mmHg.[8,9] Indeed, the evidence indicates that wound healing outcomes are broadly equivalent between −80 and −125 mmHg pressure ranges and that pressure settings should be tailored to the specific clinical situation rather than applying a default pressure.[8] Conversely, in high-risk total joint arthroplasty patient populations, statistically significant reductions in composite wound complications have been observed with −80 mmHg[6,10] indicating a clear benefit with this intervention in this patient population. I look forward to future research and publications in this field to better understand the impact of sNPWT on clinical outcomes and whether any clinically meaningful difference exists between sNPWT devices.

### AUTHOR CONTRIBUTION

**Ravi K. Bashyal**: supervision, writing – review & editing. All authors have read and approved the final version of the manuscript.

### CONFLICTS OF INTEREST

Dr. Ravi K. Bashyal is a paid consultant for Smith and Nephew and received remunerations for his work on this manuscript.

### DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available in Health Science Reports at 10.1002/hsr2.425. These data were derived from the following resources available in the public domain: Elhage, K. G., Awad, M. E., Irfan, F. B., Lumbley, J., Mostafa, G., and Saleh, K. J., 2022. Closed-incision negative pressure therapy at −125 mmHg significantly reduces surgical site complications following total hip and knee arthroplasties: A stratified meta-analysis of randomized controlled trials. Health Science Reports, 5(1), p.e425 (https://onlinelibrary.wiley.com/doi/full/10.1002/hsr2.425). Dr. Ravi K. Bashyal had full access to all of the data in this study and takes complete responsibility for the integrity of the data and the accuracy of the data analysis.

### TRANSPARENCY STATEMENT

The lead author (Ravi K. Bashyal) affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted;

and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

Ravi K. Bashyal M.D.

*NorthShore University Health System Orthopaedic and Spine Institute, Chicago, Illinois, USA*

**Correspondence**

Ravi K. Bashyal, NorthShore University Health System Orthopaedic and Spine Institute, 9650 Gross Point Road Ste. 2900, Skokie, Chicago, IL 60076, USA.

Email: ravi.bashyal@gmail.com

## REFERENCES

1. Elhage KG, Awad ME, Irfan FB, Lumbley J, Mostafa G, Saleh KJ. Closed-incision negative pressure therapy at −125 mmHg significantly reduces surgical site complications following total hip and knee arthroplasties: a stratified meta-analysis of randomized controlled trials. *Health Sci Rep*. 2022;5(1):e425. doi:10.1002/hsr2.425
2. Cordoba G, Schwartz L, Woloshin S, Bae H, Gotzsche PC. Definition, reporting, and interpretation of composite outcomes in clinical trials: systematic review. *BMJ*. 2010;341:c3920. doi:10.1136/bmj.c3920
3. Giannini S, Mazzotti A, Luciani D, et al. Postoperative wound management with negative pressure wound therapy in knee and hip surgery: a randomised control trial. *J Wound Care*. 2018;27(8):520-525. doi:10.12968/jowc.2018.27.8.520
4. Pachowsky M, Gusinde J, Klein A, et al. Negative pressure wound therapy to prevent seromas and treat surgical incisions after total hip arthroplasty. *Int Orthop*. 2012;36(4):719-722. doi:10.1007/s00264-011-1321-8
5. Wagenaar FCBM, Löwik CAM, Zahar A, Jutte PC, Gehrke T, Parvizi J. Persistent wound drainage after total joint arthroplasty: a narrative review. *J Arthroplasty*. 2019;34(1):175-182. doi:10.1016/j.arth.2018.08.034
6. Keeney JA, Cook JL, Clawson SW, Aggarwal A, Stannard JP. Incisional negative pressure wound therapy devices improve short-term wound complications, but not long-term infection rate following hip and knee arthroplasty. *J Arthroplasty*. 2019;34(4):723-728. doi:10.1016/j.arth.2018.12.008
7. WUWHS. *Closed Surgical Incision Management: understanding the Role of NPWT*. Wounds International; 2016.
8. Birke-Sorensen H, Malmsjo M, Rome P, et al. Evidence-based recommendations for negative pressure wound therapy: treatment variables (pressure levels, wound filler and contact layer)—steps towards an international consensus. *J Plastic, Reconstructive Aesthetic Surg*. 2011;64(suppl):S1-S16. doi:10.1016/j.bjps.2011.06.001
9. Apelqvist J, Willy C, Fagerdahl AM, et al. EWMA document: negative pressure wound therapy. *J Wound Care*. 2017;26(sup 3):S1-S154. doi:10.12968/jowc.2017.26.Sup3.S1
10. Helito CP, Sobrado MF, Giglio PN, et al. The use of negative-pressure wound therapy after total knee arthroplasty is effective for reducing complications and the need for reintervention. *BMC Musculoskelet Disord* 2020;21(1):490. doi:10.1186/s12891-020-03510-z