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LETTER

Hemodynamic Stability Beyond ED95 in Older Adults: Comment on Topical Airway Lidocaine Spray and Sufentanil for Tracheal Intubation [Letter]

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Dear editor

Chen et al[1] reported a randomized, double-blind, biased-coin up-and-down trial in 80 patients aged 65–80 years and found that topical airway lidocaine spray reduced the sufentanil ED95 for blunting the intubation response from 0.530 to 0.419 μg/kg. This work adds useful evidence to geriatric airway management. Still, several points deserve discussion.

The main concern lies in the primary endpoint. In the Methods section on page 3, a "positive response" was defined as MAP or heart rate remaining within 30% of baseline during the first 3 minutes after intubation, whereas a "negative response" appears to have been defined only by an increase of at least 30%. Hypotension and bradycardia were handled as adverse events rather than explicit dose-finding failures. This asymmetry is not trivial. In older adults, a blood pressure fall after induction may be as harmful as an untreated pressor response. Cohen et al[2] analyzed 4576 noncardiac procedures and found that myocardial injury risk increased once intraoperative MAP reached 65 mm Hg or lower, without evidence that this threshold depended on baseline hypertension status. Liu et al[3] studied 10,859 patients aged 60 years or older and showed that the lowest absolute MAP, rather than the largest reduction from baseline, was associated with postoperative acute kidney injury, with the lowest predicted risk near 86 mm Hg. Seen in that light, the reported ED95 is closer to the dose that suppresses hypertensive or tachycardic responses than to a dose that guarantees overall hemodynamic stability.

Besides, a related issue concerns rescue therapy. The Methods section states that nicardipine, esmolol, norepinephrine, or atropine was administered once predefined thresholds were reached. Yet the limitations paragraph states that "rescue therapy was administered only after primary outcome assessment." Both readings create difficulty. If rescue drugs were given during the 3-minute assessment window, the primary endpoint may have been altered by treatment. If rescue drugs were delayed until the window ended, clinically relevant instability may have been tolerated to preserve endpoint purity. Rescue medication is a classic intercurrent event and should be prespecified analytically, not left ambiguous.[4] The problem is more than semantic. In 38,338 adults undergoing noncardiac surgery, Saugel et al[5] found that both the burden of MAP below 65 mm Hg and cumulative norepinephrine dose were independently associated with postoperative acute kidney injury, with adjusted odds ratios of 1.55 per mm Hg·day below 65 mm Hg and 1.02 per μg/kg of norepinephrine, respectively.

Hence, we suggest that a bidirectional failure definition should include both increases and decreases beyond the prespecified range, ideally alongside an absolute MAP safety threshold. A table detailing rescue-drug timing, frequency, and group distribution would clarify whether the endpoint was observed or modified. Sensitivity analyses treating rescue therapy as failure or as a separate estimand would further improve interpretability.

Data Sharing Statement

No datasets were generated or analysed during the current study.

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Disclosure

Yuang Peng, Emily Yuqi Cheng and Jing Li are co-first authors for this communication. The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence this communication.

References

1. Chen X, Yang J, Pan K, et al. Topical airway lidocaine spray reduces the 95% effective dose of sufentanil for blunting hemodynamic response to tracheal intubation in elderly patients: a biased-coin up-and-down sequential allocation trial. *Drug Des Devel Ther*. 2026;20:1–10. doi:10.2147/DDDT.S594827
2. Cohen B, Rivas E, Yang D, et al. Intraoperative hypotension and myocardial injury after noncardiac surgery in adults with or without chronic hypertension: a retrospective cohort analysis. *Anesth Analg*. 2022;135(2):329–340. doi:10.1213/ANE.0000000000005922
3. Liu R, Chen J, Peng Y, et al. The relationship between intraoperative hypotension and acute kidney injury in elderly and super elderly patients undergoing noncardiac surgery: a retrospective cohort analysis. *BMC Geriatr*. 2025;26(1):149. doi:10.1186/s12877-025-06944-z
4. Kahan BC, Devane D. Estimands: what they are and why we should use them. *J Clin Epidemiol*. 2026;189:112054. doi:10.1016/j.jclinepi.2025.112054
5. Saugel B, Sander M, Katzer C, et al. Association of intraoperative hypotension and cumulative norepinephrine dose with postoperative acute kidney injury in patients having noncardiac surgery: a retrospective cohort analysis. *Br J Anaesth*. 2025;134(1):54–62. doi:10.1016/j.bja.2024.11.005

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