CORRESPONDENCE

In reply: Comment on “Anesthetic technique and cancer outcomes: a meta-analysis of total intravenous *versus* volatile anesthesia”

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To the Editor,

We would like to thank Chang *et al.*¹ for identifying an error in our manuscript entitled “Anesthetic technique and cancer outcomes: a meta-analysis of total intravenous *versus* volatile anesthesia”.² We have re-checked all analyses in the manuscript and can confirm that this was an isolated error due to a data transcription error relating to the Oh *et al.* study³ within our recurrence-free survival analysis. As stated by Chang *et al.*, when the reported

estimates in Oh *et al.* are corrected, the pooled hazard ratio (HR) is now 0.87; 95% confidence interval (CI), 0.66 to 1.15; $P = 0.32$ (compared with the erroneously reported HR of 0.78; 95% CI, 0.65 to 0.94; $P < 0.01$). Nonetheless, although now not statistically significant, the effect estimate still suggests that total intravenous anesthesia (TIVA) may be protective, albeit with a wider confidence interval that now includes 1.

It is important to note that the Oh *et al.* study incorporates substantial heterogeneity ($I^2 > 60\%$; $P = 0.02$), so we performed a sensitivity analysis as we did for the other outcomes reported in the manuscript. When removing the Oh *et al.* study (as an outlier), as described in our methods, the effect estimate is 0.79 (95% CI, 0.62 to 1.0; $P = 0.05$) indicating a borderline protective effect with an acceptable inconsistency score ($I^2 = 40\%$; $P = 0.16$; see attached revised forest plot).

A recent editorial⁴ related to the important question of whether anesthetic technique impacts cancer outcomes suggested that heterogeneity in magnitude of surgical procedure within study cohorts provided “context for divergent study outcomes”; with a protective effect by propofol-TIVA on cancer recurrence and survival more likely to be seen in patients having major cancer surgery. As discussed, the study by Yoo *et al.*⁵ has substantial heterogeneity in surgical magnitude. This study also contributes to the statistical heterogeneity in our meta-analysis. When this study is also removed from analysis, the pooled estimate is statistically significant (HR, 0.71; 95% CI, 0.59 to 0.86; $P < 0.01$) with no heterogeneity ($I^2 = 0\%$; $P = 0.41$), further supporting our conclusions.

A major limitation of our manuscript is that our findings are based on mostly observational studies. As stated in our conclusion, there is an imperative need for robust randomized-controlled trials in this area, which will help

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Figure Recurrence-free survival following sensitivity analysis

to strengthen the current evidence on impact (or lack thereof) of anesthetic technique on cancer outcomes.

Conflicts of interest None declared.

Editorial responsibility This submission was handled by Dr. Hilary P. Grocott, Editor-in-Chief, *Canadian Journal of Anesthesia*.

References

1. Chang CY, Chien YJ, Wu MY, Kao MC, Wang SC. Comment on “Anesthetic technique and cancer outcomes: a meta-analysis of total intravenous versus volatile anesthesia. *Can J Anesth* 2020; <https://doi.org/10.1007/s12630-019-01422-8>.
2. Yap A, Lopez-Olivo MA, Dubowitz J, Hiller J, Riedel B, Global Onco-Anesthesia Research Collaboration Group. Anesthetic technique and cancer outcomes: a meta-analysis of total intravenous versus volatile anesthesia. *Can J Anesth* 2019; 66: 546-61.
3. Oh TK, Kim K, Jheon S, et al. Long-term oncologic outcomes for patients undergoing volatile versus intravenous anesthesia for non-small cell lung cancer surgery: a retrospective propensity matching analysis. *Cancer Control* 2018; <https://doi.org/10.1177/1073274818775360>.
4. Sessler DI, Riedel B. Anesthesia and cancer recurrence: context for divergent study outcomes. *Anesthesiology* 2019; 130: 3-5.
5. Yoo S, Lee HB, Han W, et al. Total intravenous anesthesia versus inhalation anesthesia for breast cancer surgery: a retrospective cohort study. *Anesthesiology* 2019; 130: 31-40.

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