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LETTER

# Bradycardia in Ophthalmic Surgery: A Care-Bundle, Not Drug-to-Drug, Comparison [Letter]

Yu-Tung Lin[1], Wen-Ting Chang[2], Ming-Hui Hung[2]

[1]School of Medicine, Tzu Chi University, Hualien, Taiwan; [2]Department of Anesthesiology, National Taiwan University Hospital, Taipei, Taiwan

Correspondence: Ming-Hui Hung, Department of Anesthesiology, National Taiwan University Hospital, 7 Chung-Shan South Road, Taipei, 100225, Taiwan, Email hung.minghui@gmail.com



## Dear editor

Wu et al report a lower incidence of intraoperative bradycardia with rocuronium–sugammadex versus cisatracurium–neostigmine in ophthalmic surgery.[1] While the topic is clinically important, several features limit causal interpretation, and the drug-to-drug framing of the title may mislead readers.

First, the rocuronium arm was delivered as a self-pay anesthesia package that included bispectral index monitoring, with higher bispectral index use and lower volatile and opioid consumption. This represents a care bundle rather than a single pharmacologic exposure, yet the title and conclusions attribute the difference to drug choice alone. In addition, bradycardia occurred primarily during ocular manipulation, whereas reversal agents were administered only at the end of anesthesia. The primary endpoint therefore largely preceded any plausible effect of neostigmine versus sugammadex, making the drug-pair comparison misleading.

Second, sample size justification also raises concerns. The authors based their calculation on Cohen's $f^2$=0.15, which represents a medium effect size for multiple linear regression. However, $f^2$ is defined for continuous outcomes, not binary endpoints; applying it to logistic regression is inappropriate. For binary outcomes, the relevant determinant is the number of events. In reality, only 36 bradycardia events occurred, while 10 covariates were entered into the model, yielding an events-per-variable ratio of approximately 3.6, well below recommended thresholds for logistic regression stability.[2] Such overfitting risks unstable effect estimates. This concern is amplified by internal inconsistencies: the abstract reports an odds ratio (OR) of 0.08 with 95% confidence interval (CI) 0.02–0.94 ($p$=0.001), a combination that is internally inconsistent because a CI extending close to 1.0 would correspond to a borderline $p$ value near 0.05, not 0.001. Table 4 of the original article instead reported OR 0.08 with 95% CI 0.02–0.29 ($p$<0.001). These discrepancies raise further doubts about the reliability of the reported association.

Third, extubation time further illustrates internal inconsistency. Although the Methods section states extubation was performed only after train-of-four ratio >0.9, Table 2 shows identical times of 5.0 (5.0–10.0) minutes in both groups. Given sugammadex's well-established pharmacologic advantage, such equivalence is implausible. Meta-analyses consistently demonstrate that sugammadex accelerates extubation by several minutes compared with neostigmine.[3] The absence of difference here implies that extubation was driven largely by workflow factors or inconsistently applied criteria, undermining the validity of this endpoint.

Additional concerns include a likely mis-specified sevoflurane row in Table 4, lack of fresh gas flow reporting despite its central role in volatile consumption,[4] absence of data on preoperative rate-limiting medications or anesthetist/surgeon clustering, and unaddressed collinearity between bispectral index use and bundle exposures. A structured summary of these issues is provided in Supplementary Table 1.

We respectfully suggest redefining the exposure at the bundle level, re-justifying sample size under a binary outcome framework with fewer or penalized covariates, correcting reporting inconsistencies, and standardizing key variables such

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as fresh gas flow and extubation criteria. These clarifications would allow a more robust interpretation of whether bradycardia prevention relates to drug choice or broader anesthetic strategies.

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## Author Contributions

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