Etomidate and Treatment Propensity

To the Editor:

Wagner *et al.*[1] must be congratulated for their robust and interesting work into the effects of a single dose of etomidate on long-term outcomes. Nonetheless, we consider that several elements would benefit from greater information and discussion. First, the doses of etomidate administered were not reported and therefore any dose–response effect remains unclear; it may be that higher doses may induce decrements in long-term outcomes. Ideally, information on drug doses should be included. Perhaps the most important criticism relates to the case mix included in the analysis. When understanding whether etomidate is safe, it is necessary to compare the drug with other induction drugs. Inclusion of patients who did not receive an induction drug, such as those presenting in cardiogenic shock and already intubated, therefore appears inappropriate. The authors have recognized this to some degree: "We also performed a sensitivity analysis in which patients who did not receive any induction drugs were excluded from the analysis. The results from the sensitivity analysis were qualitatively similar to those reported in table 3." However, these are *the* critical data to report, as it excludes patients who did not receive the induction of anesthesia for surgery. Hence, these data should not be considered supplementary information rather we ask the authors to publish them in full. Other sensitivity analyses that are worth conducting include subgroup analyses for elective and emergency surgery as these factors may affect treatment propensity. Furthermore, although we consider that the authors' use of propensity scoring is appropriate,[2] we suggest that a propensity score-matching approach for "etomidate only" with other induction agents such as "propofol only" or "midazolam only" would also be of interest to provide a more direct comparison of the induction agents. This is also important, as midazolam appears to be associated with a shorter duration of mechanical ventilation and length of stay in hospital. Given the deleriogenic effects of midazolam,[3,4] this observation appears surprising, but may relate to superior cardiovascular stability with this approach. Nonetheless, this requires further discussion especially because patients with cardiogenic shock were more likely to receive "midazolam only." Of course the data are slightly more complex given the use of coinduction with midazolam and etomidate or propofol. Given that there is a clear clinical preference for coinduction, these two combinations should also be compared with each other by propensity score matching. Finally, the association of angiotensin-converting enzyme inhibitors with prolonged hospital length of stay, but not with mortality (although the point estimate is shifted toward increased mortality), is of interest given a recent meta-analysis suggesting increased mortality and acute kidney injury in cardiac surgical patients administered these drugs.[5] Here the authors may wish to consider adjusting for hypertension as a potential confounder by indication. In summary most of these criticisms could be approached by the publication of the sensitivity analysis removing patients with cardiogenic shock, as well as conducting some additional analyses. Despite our critique we applaud the authors for their hard work and robust statistical approach, they have identified an important topic for research and made substantial contributions to clarifying the role of etomidate for induction of anesthesia for cardiac surgery.

Competing Interests

The authors declare no competing interests.

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In Reply:

We thank Dr. Sanders *et al.* for their interest in our work.[1] We address their comments with additional summaries and responses to specific comments.

Sanders *et al.* requested that drug doses be used in our analyses. We recognize the lack of drug dose as a potential weakness to our analysis; however, all induction drugs, including etomidate (median dose of 0.15 mg/kg), were administered to achieve hypnosis. We did not model the induction dose of etomidate because etomidate suppresses