

Evidence for Better Results of Combined General and Epidural Anaesthesia in Esophagectomy

Sir,

We read with great interest the paper by Jiang *et al.* published in a recent issue of your esteemed journal.¹ The authors designed a clinical study comparing general and epidural anaesthesia (GAEA) with only general anaesthesia (GA) for esophagectomy. The authors concluded that GAEA might reduce the inflammatory response and cognitive dysfunction after esophagectomy.

Randomised controlled trials (RCTs) provide the highest level of evidence and, undeniably, are the design of choice to compare the effectiveness of GAEA vs. GA for esophagectomy. However, any study can have systematic errors, and readers should have a critical view and detect the main risk of bias.

Certain methodological aspects of Jiang *et al.*'s trial favoured bias. First of all, the study lacks a protocol. Protocols are pre-specified documents published in a database reporting the study's methodology and objectives, so that, the reader can check if the authors complied with the initially proposed plan. Besides, a protocol defines the outcomes to be evaluated. If a protocol is not well established, the reader cannot know if all the evaluated outcomes were reported, predisposing the study to report bias. The study protocol also should predefine if an intention-to-treat (ITT), per-protocol (PP), or as-treated (AS) analysis will be made.² Theoretically, if there is no pre-specified protocol, the authors could perform any of the three analyses and present only the one that fits better with the result they are looking for. Probably, that is not the case in Jiang *et al.*'s trial. However, a protocol would give transparency.

In Jiang *et al.*'s trial, there were eight exclusions related to surgery cancellation. Since there is no specification if the surgery suspension was related to any anaesthetic intercurrent, it is hard to know if this data loss could interfere with the final analysis. If an operation cancellation was related to the studied intervention, this exclusion would not be appropriate, and an ITT would be a better fit than a PP.

Another issue is that the authors did not clarify the randomisation process. Choosing an appropriate randomisation methodology (simple, block, stratified, or other) is essential to avoid selection bias and ensure the balance of groups' baseline characteristics.³ Despite the authors reporting that the groups' baseline characteristics were similar, no information was provided regarding the surgical techniques. McKeown, Ivor Lewis, and other esophagectomy techniques may differently impact patients' inflammatory responses.

Finally, there is no mention of how the authors estimated the sample size. An improper sample may induce type I and II errors. Readers should have a critical appraisal and know the limitations of any paper, even when the study design suggests the highest level of evidence.

COMPETING INTEREST:

The authors declared no competing interest.

AUTHORS' CONTRIBUTION:

FT: Conceptualisation and supervision.

MV: Writing and editing.

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AUTHOR'S REPLY:

Sir,

Thank you for your comments!

Since the journal requires that the manuscript should be less than 2500 words, some information was not shown in the paper. The procedures of this study were approved by the Affiliated Hospital of Traditional Chinese Medicine, Southwest

Medical University and were consistent with those described in this paper.

The eight patients did not undergo the surgery for patient's own or family factors, or economic reasons. All the operations were cancelled before anaesthesia, which was not related to anaesthesia.

The randomisation process was as follows: Each patient was assigned with an identifier, and each identifier was associated one-to-one with a random number generated using SPSS 24.0. Then, the random numbers were sorted to generate a random number table. The initial 71 patients in the random number table were allocated to the GA group and the final 71 to the GAEA group. In addition, all patients underwent the same esophagectomy technique (thoracoscopy combined with laparoscopy and esophagectomy).

The incidence of postoperative cognitive dysfunction (POCD) in the elderly is about 20%.^{1,2} Many clinical studies about the influence of anaesthetic techniques on postoperative cognitive function in elderly patients recruited 49, 50, 68 or 71 patients (each group).³⁻⁶ So, we recruited 142 patients.

Lastly, our research group once again thanks you for your meaningful suggestions. In the future, we will further optimise our design and scheme to show more meaningful clinical results.

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