

# Anesthesia and Surgery in Space: Reply

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## In Reply:

As pointed out by Drs. Covington and Moon,<sup>1</sup> in response to our recent article,<sup>2</sup> mitigating the risk of decompression sickness is of utmost importance for future missions to the Moon or Mars. This risk is proportional to the ratio  $R$  between the partial pressure of nitrogen in the tissues and the pressure of the spacesuit.<sup>3</sup> For future space exploration missions, an acceptable risk of decompression sickness is reached for an  $R$  less than 1.3 to 1.4.<sup>4</sup> Whereas the atmosphere inside the International Space Station is normoxic and normobaric (14.7 psi and 21% oxygen), the American spacesuit circulates pure oxygen pressurized at 4.3 psi (about 0.3 atm).<sup>3</sup> As a consequence, astronauts prebreathe oxygen for 4 h to wash out nitrogen from body tissues (to reduce the partial pressure in the tissues) before depressurization, with the option to enhance denitrogenation with physical exercise.<sup>3,4</sup> For a Mars mission that will potentially have almost daily extra-vehicular activities, 4 h of prebreathe time for each spacewalk will be operationally impractical.

Several solutions exist: lowering the ambient pressure of the habitat (at the cost of increasing the fraction of inspired oxygen and flammability) or raising the suit pressure (at the cost of increasing suit rigidity and the metabolic cost of movement).<sup>4</sup> Pretreatment with hyperbaric oxygen before decompression may also be effective in reducing the incidence of decompression sickness, although the evidence remains limited to animal models.<sup>5</sup> It is estimated that an atmosphere in the habitat of 8.0 psi and 32% oxygen would eliminate the need to prebreathe.<sup>4</sup> Another solution might come from innovative hybrid suit design, combining “mechanical counter-pressure” and gas pressure.<sup>4</sup> Finally, “smart suits” could progressively lower their internal pressure during the extra-vehicular activity to improve flexibility while keeping the  $R$  ratio within acceptable bounds.<sup>4</sup>

The challenge of spacesuit design, and more globally of manned spaceflight, elegantly illustrates the interactions between physiology and engineering in designing life support systems, very much like the applied physiology and physics that underpins submarine and diving activities, pressurized airplanes, high-altitude mountaineering, but also the delivery of anesthesiology and critical care on Earth.

## Competing Interests

The author has received speaker honoraria from GE Healthcare (Limonest, France) and consulting fees from Philips Healthcare (Eindhoven, The Netherlands).

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# Epidural Anesthesia and Postoperative Delirium: Comment

## To the Editor:

The recent article titled “Delirium in Older Patients after Combined Epidural–General Anesthesia or General Anesthesia for Major Surgery: A Randomized Trial”<sup>1</sup> explored whether combined epidural–general anesthesia reduces the incidence of postoperative delirium in elderly patients recovering from major noncardiac surgery. The authors suggested that delirium was significantly less common in the combined epidural–general anesthesia group than in the general anesthesia group. However, we have some commentary and questions for the authors on their conclusions.

Opioids are strongly associated with delirium<sup>2</sup>; the current study found that the combined epidural–general anesthesia reduced the incidence of delirium, supported by a decreased perioperative morphine equivalent consumption (mean difference, –32 mg; 95% CI, –41 to –23). But the occurrence of intraoperative hypotension events cannot be ignored. The authors reported that intraoperative hypotension (systolic blood pressure less than 80 mmHg) was more common in patients assigned to epidural anesthesia (421 [49%] vs. 288 [33%]), with more time with mean arterial pressure of less than 65 mmHg (17 min [interquartile range, 3 to 42] vs. 8 min [0 to 25]), and more epidural patients were given vasopressors (495 [58%] vs. 387 [45%]). The epidural anesthesia was associated with an increased risk of intraoperative hypotension, which is a well-known consequence of combining general and epidural anesthesia.<sup>2</sup> Previous studies have demonstrated that intraoperative hypotension is associated with an increased risk of delirium.<sup>3,4</sup> It is reasonable to take the intraoperative hypotension events into treatment-by-covariate interactions analysis. The benefit of combined epidural–general anesthesia thus needs to be balanced against potential risks of hypotension in individual patients (which strongly influences the number needed to treat). In the current study, the absolute risk reduction with combined epidural–general anesthesia was 3.2%, corresponding to the number-needed-to-treat to prevent a delirium event as close to 31.

In addition, we are wondering whether or not the patients had experienced multiple delirium and, if so, whether the subtype of delirium was evaluated each time and each event analyzed separately or as a composite. This point should be clarified for readers. Additionally, it would be useful if the authors could provide the durations of delirium.

### Competing Interests

The authors declare no competing interests.

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## Epidural Anesthesia and Postoperative Delirium: Reply

### In Reply:

We appreciate the comments from Zhang *et al.*<sup>1</sup> on our recent article “Delirium in Older Patients after Combined Epidural–General Anesthesia or General Anesthesia for Major Surgery: A Randomized Trial.”<sup>2</sup>

Consistent with many others,<sup>3</sup> our study also found that intraoperative hypotension occurred more frequently in patients given combined epidural–general anesthesia. Increasing evidence suggests that intraoperative hypotension is associated with an increased risk of postoperative delirium.<sup>4,5</sup> According to the suggestion of Zhang *et al.*,<sup>1</sup> we included intraoperative hypotension in a *post hoc* treatment-by-covariate interaction analysis for the primary outcome. Our results did not find significant interaction between treatment intervention and intraoperative hypotension. The effect of combined epidural–general anesthesia on delirium was similar in the subgroups with or without intraoperative hypotension (with intraoperative hypotension [systolic blood pressure < 80 mmHg]: relative risk 0.68; 95% CI,

0.20 to 2.37; without intraoperative hypotension: 0.33, 0.16 to 0.67; interaction  $P = 0.243$ ).

In our study, delirium was assessed twice daily with the Confusion Assessment Method for the Intensive Care Unit during the first 7 postoperative days. Immediately before assessing delirium, sedation or agitation was assessed with the Richmond Agitation-Sedation Scale. Patients who developed delirium were classified into three subtypes according to the Richmond Agitation-Sedation Scale assessment results. Hyperactive delirium was defined when the Richmond Agitation-Sedation Scale score was consistently positive (from +1 to +4). Hypoactive delirium was defined when the Richmond Agitation-Sedation Scale score was consistently negative or neutral (from -3 to 0). Mixed-type delirium was defined when both hyperactive and hypoactive episodes existed.<sup>6</sup> In accord with the results of others, hypoactive delirium was the most common subtype in our patients of the two groups.<sup>2</sup>

Among our patients, 58 (3.4%) developed delirium within the first 7 postoperative days; of those who developed delirium, 21 (36%) had two episodes or more. The duration of delirium (number of days with at least one episode of delirium) was shorter in patients given combined epidural-general anesthesia (median 0 days [interquartile range, 0 to 0] with combined epidural-general anesthesia *vs.* 0 days [0 to 0] with general anesthesia alone; mean difference -0.04, 95% CI, -0.08 to -0.01;  $P < 0.001$ ). Among 58 patients who developed delirium, the duration of delirium did not differ between the two groups (median 1 day [interquartile range, 1 to 2] *vs.* 1 day [1 to 2]; mean difference 0.42, 95% CI, -0.26 to 1.10;  $P = 0.546$ ).

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### Competing Interests

The authors declare no competing interests.

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