intensive care unit patients in previous studies.[3–6] However, our protocol is still based on the protocols that are widely used.[6,7] Anesthesia-induced atelectasis did not show definite B lines, which were used in the previous scoring system (B lines: hyperechoic vertical lines starting from the pleural line with the length of 8 cm or longer). Rather, anesthesia-induced atelectasis showed subpleural consolidations with short vertical lines starting from the margin of consolidation (pseudo B lines).[7] Accordingly, loss of A line with multiple subpleural consolidations has been reported as a more common and helpful finding to diagnose anesthesia-induced atelectasis.[7] In consideration of the development process of anesthesia-induced atelectasis, the grade 3 atelectasis, which is "loss of lung sliding and appearance of lung pulse," was added to our grading system. We found that the collapse of small bronchioles and alveoli leads to "loss of lung sliding and appearance of lung pulse" as subpleural consolidation progresses to a larger parenchymal consolidation.[8] This was also reported in previous studies.[8] Although we modified the scoring system for a more accurate diagnosis of anesthesia-induced atelectasis, it was not validated. We described this in the limitations to our study.

For the third question (sample size), we found that the power of our study did not meet the expectations and needed a larger number of patients. However, we understand that the probability of type II error (false negative) would have decreased as the sample size (power) increased, but the type I error (false positive) usually remains the same.[9] Therefore, we think our positive results would have been confirmed with more power if the sample size had increased.

We agree with Zaouter *et al.* that oxygen-free days or cumulative postoperative oxygen administration may be more important than the incidence of hypoxia as a secondary outcome. However, most patients received oxygen administration only on the night of surgery, and there was no difference in postoperative complications such as pneumonia and hospital stay between the two groups. So, we cautiously speculate that the time-weighted need for oxygen support would not have been different between the two groups.

Competing Interests

The authors declare no competing interests.

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Targeting Depth of Anesthesia to Prevent Delirium: Comment

To the Editor:

Brown *et al.*[1] nicely described their work comparing spinal anesthesia with targeted sedation based on Bispectral Index values compared with general anesthesia

(masked Bispectral Index) and the outcome of delirium. Intraoperative hypotension has been associated with delirium.[2,3] The adjusted hazard ratio associated with a 1-mmHg increase in time-weighted average of mean arterial pressure less than 65 mmHg was 1.11 (95% CI, 1.03 to 1.20).[2] The study by Brown *et al.*[1] found that the lowest mean arterial pressure was similar in both groups (general anesthesia, 59 [51 to 64] *vs.* spinal anesthesia, 60 [52 to 64]); however, the relationship between intraoperative hypotension and the subsequent development of delirium might be more of a cumulative exposure response than a single threshold. It would be of interest to know the hypotension exposure by time under the 65- or 60-mmHg threshold and to consider that in a treatment-by-covariate interactions analysis. In short, we appreciate Brown *et al.* for their great contributions to this important topic.

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Competing Interests

The authors declare no competing interests.

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Targeting Depth of Anesthesia to Prevent Delirium: Comment

To the Editor:

We read with great interest the recent article by Brown *et al.*[1] regarding the impact of Bispectral Index (BIS)–guided sedation on the incidence of postoperative delirium during spinal anesthesia for spine surgery compared with BIS-masked general anesthesia. We appreciated the originality and efforts of the authors to clarify a still controversial topic such as the connection between depth of the hypnotic component of anesthesia and postoperative delirium. Nevertheless, after careful reading of the trial and its conclusions, we would like to address some critical input to the authors.

First, in the "Materials and Methods" section, the authors report that they achieved spinal anesthesia using intrathecal bupivacaine or lidocaine. Spinal anesthesia with lidocaine carries the risk of transient neurologic symptoms.[2] Transient neurologic symptoms constitute an acute pain syndrome that could exacerbate postoperative pain and thus increase the incidence of postoperative delirium. In addition, acute postoperative urinary retention after spinal anesthesia could increase pain and discomfort and contribute to postoperative delirium.[3] Both complications could have influenced the reported results on postoperative delirium, but their incidence is not reported by the authors.

Second, we would have been happy to see more information on intraoperative hemodynamic stability, all the more since moderately high doses of intrathecal local anesthetic agents and prone position for surgery may have an impact on it. Despite the fact that the relationship between intraoperative hypotension and the incidence of postoperative delirium is still not clearly established, it would have been informative to report not only on the lower intraoperative mean arterial pressure but also, and more importantly, on the decrease from initial mean arterial pressure and time spent below a patient-adapted threshold value, *i.e.*, the time of relative cerebral hypoperfusion.[4,5] Indeed, cerebral perfusion

pressure beyond the autoregulatory limit is an independent risk factor for the development of neurologic complications, including postoperative delirium. Rightly, the authors report the incidence of postoperative stroke in their trial, but several publications have emphasized the importance of subclinical cerebral vascular events and their potential role in generating postoperative delirium.[6]

Third, and in accordance with the results of this study, the BIS is probably not the right tool to guide anesthesia depth with the aim of avoiding postoperative delirium. Drug-induced alterations of brain function are complex, and BIS catches only a very small part of them.[7] However, this does not mean that we should not seek a better understanding of the changes that are really relevant with regard to postoperative delirium and that should be prevented. The electroencephalogram is certainly the most accessible and noninvasive tool to be used in this respect, and several teams are currently performing an in-depth analysis of intraoperative electroencephalogram data to find out the most relevant markers. This must occur in a more general framework that takes account of the multifactorial nature of postoperative delirium, in which factors such as neuroinflammation, quality of organ perfusion, drug interactions, adequacy of antinociception, and patient comfort intervene.

Therefore, we should consider BIS as reflecting the tip of the iceberg only, while the immense mountain of ice remains hidden. Using BIS as the sole tool to prevent postoperative delirium is piloting a boat like the *Titanic*'s captain: the most important part of the problem could still be under the surface of the water.

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Competing Interests

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Targeting Depth of Anesthesia to Prevent Delirium: Reply

In Reply:

We thank Drs. Xiong *et al.*[1] and Carella and Bonhomme[2] for their comments regarding the shaping anesthetic techniques to reduce post-operative delirium (SHARP) study.[3] We agree that evaluating intraoperative hypotension as a potentially moderating factor in the SHARP trial would be interesting. We found no difference in the number of minutes at a mean arterial pressure less than 55 mmHg between the spinal anesthesia with targeted sedation group (median, 0 min; interquartile range, 0 to 5) and the general anesthesia group

(median, 0 min; interquartile range, 0 to 5; $P = 0.51$). Further, when the number of minutes at a mean arterial pressure less than 55 mmHg (considered as a categorical variable) was added to the main regression model as an interaction term, the interaction term was not significant, indicating that mean arterial pressure less than 55 mmHg did not modify the effect of anesthetic choice on postoperative delirium. Finally, the number of minutes at a mean arterial pressure less than 55 mmHg was not associated with delirium when added to the adjusted model described in the article.[3] We did not prospectively record hypotension exposure below a 60- or 65-mmHg threshold but will consider this for potential future studies.

A further question was whether transient neurologic symptoms or urinary retention after spinal anesthesia could have caused increased pain or discomfort and thus influenced the development of postoperative delirium. Since the pain scores were similar on postoperative day 1 between groups, we do not think these complications were strong factors that could have biased the study results. Finally, we agree that Bispectral Index may not be the optimal tool to guide anesthesia depth, and further work using the electroencephalogram is needed. However, we designed this study based on previous studies that suggested a beneficial role for Bispectral Index in guiding anesthetic depth, and we utilized an anesthetic regimen that allowed for sedation to a level lighter than general anesthesia, irrespective of BIS levels.

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Competing Interests

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