

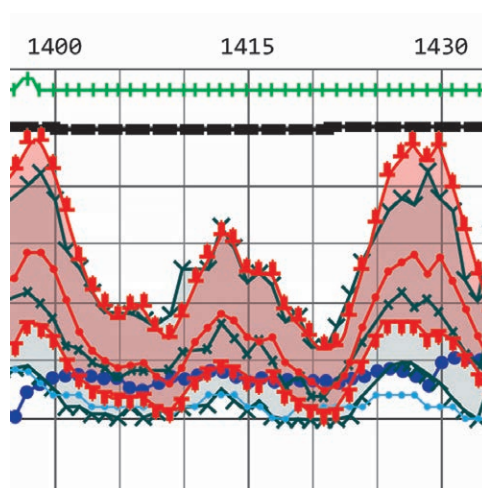
Wanted: Modifiable Risk Factors for Postoperative Delirium!

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Postoperative delirium is one of the most common complications in older patients recovering from surgery. Depending on the specific patient population, surgery type, and screening methods, research demonstrates that it affects between 10 and 50% of surgical patients older than 65 yr, which translates into millions of cases annually.¹ It is associated with prolonged hospital stay, increased healthcare costs, psychological distress for patients and families, and increased morbidity and mortality. Investigating predisposing and precipitating factors, particularly modifiable ones, is crucial for the development of preventive and therapeutic strategies.

In this issue of *ANESTHESIOLOGY*, Rössler *et al.* report on their investigation of the possible relationship between intraoperative hypotension and postoperative delirium.² In their retrospective analysis of nearly 40,000 non-cardiac surgeries, they found no causal association between the area under an intraoperative mean arterial pressure (MAP) threshold of 65 mmHg and postoperative delirium. Further analyses evaluating other methods to quantify intraoperative hypotension, postoperative hypotension, and blood pressure variability during and after surgery either found no associations or found statistically significant relationships with no clinically meaningful difference.

The lack of relationship between hypotension and postoperative delirium observed in this study may be partly



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explained by the relatively low incidence of delirium (6.5%). Postoperative delirium is a complex multifactorial phenomenon, and its diagnosis is often challenging due to its hallmark fluctuating nature. Any single questionnaire or test only captures a snapshot of the patient’s cognitive state, often resulting in underdiagnosis. Retrospective review of physician and nursing charts can uncover missed cases, and validated tools such as the Chart-based Delirium Identification Instrument (CHART-DEL) are valuable for identification of delirious behaviors documented throughout the hospitalization.³ Hopefully, artificial intelligence using large language models will assist us in efficiently reviewing patients’ electronic medical records and in detecting previously undiagnosed cases of postoperative delirium.

Another ongoing debate concerns the optimal timing of screening; disoriented behavior in the postanesthesia care unit was traditionally considered as emergence delirium rather than postoperative delirium. However, growing evidence suggests that delirium that continues into the inpatient stay may begin as early as in the postanesthesia care unit, and that early recognition, even amid logistical challenges, may be critical.⁴

Undoubtedly, age is an independent risk factor for delirium. The preoperative cognitive state of patients is also strongly associated with postoperative delirium, as patients with lower cognitive reserve are at risk.⁵ Similarly,

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frailty plays an important role in identifying patients at risk, but it is unclear whether the preoperative cognitive state or the cognitive reserve are modifiable.⁶ Several studies have explored prehabilitation strategies, such as physical conditioning, nutritional support, cognitive training, and psychosocial interventions, with mixed results due to heterogeneous study designs and patient populations.⁷ Since delirium also occurs in nonsurgical patients as well as before surgery, it is reasonable to assume that hospitalization, pain, and the unfamiliar environment are also contributing factors. However, by definition, postoperative delirium must occur after a surgical procedure, and surgery nearly always involves anesthesia. This raises important questions about the role of anesthesia in triggering or unmasking cognitive disturbances in at-risk individuals. It is therefore not surprising that intraoperative and anesthesia-related factors have been intensely investigated, although results remain inconclusive. Among these factors, intraoperative hypotension has received considerable attention.

Intraoperative hypotension has long been considered a plausible causal contributor to postoperative delirium, purportedly through mechanisms of cerebral hypoperfusion and reduced cerebral oxygen delivery.⁸ Given that intraoperative hypotension is potentially modifiable, much research has previously evaluated its role in the development of postoperative delirium but has largely failed to identify a reliable causal relationship.^{2,9}

It is surprising that while intraoperative hypotension is strongly associated with myocardial and kidney injury, this is not the case when the brain is the organ of interest. The answer to this discrepancy may lie within the unique cerebral hemodynamic profile of anesthesia-induced hypotension. Anesthesia-induced systemic hypotension is attributable to myocardial depression, systemic vasodilation, and decreased sympathetic activity. However, emerging evidence suggests that arterial dilatation with reduced systemic vascular resistance is the most significant factor.¹⁰ Interestingly, systemic arterial dilatation is accompanied by cerebral arterial dilatation, increased cerebral blood flow, and improved cerebral oxygenation. These effects occur with both propofol and inhaled anesthetics.¹¹ Paradoxically, the primary mechanisms by which general anesthetics induce hypotension may actually enhance cerebral blood flow and oxygen delivery, thereby mitigating potential effects of cerebral hypoperfusion and hypoxia. Moreover, the decreased cerebral metabolic rate and oxygen demand attributed to general anesthesia further contribute to a favorable cerebral oxygen supply and demand balance.

This cerebral vascular response is different than the expected effects of hypotension in critically ill patients admitted to the intensive care unit, in patients having cardiac surgery, and in patients experiencing postoperative hypotension. In these clinical conditions, systemic hypotension is likely associated with impaired cerebral perfusion

and oxygenation, and a causal relationship with postoperative delirium is therefore still plausible.

The complexity of postoperative delirium diagnosis and the unique cerebral vascular physiology warrant a comprehensive and nuanced approach to the study of hypotension and delirium. Future research should continue to advance postoperative delirium screening methods, focus on high-risk populations, and explore whether targeted intraoperative management can alter the postoperative cognitive trajectory.

Competing Interests

The authors are not supported by, nor maintain any financial interest in, any commercial activity that may be associated with the topic of this article.

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