

Is “Triple Low” of Low Blood Pressure, Low Bispectral Index, and Low Minimum Alveolar Concentration of Volatile Anesthesia an Independent Predictor for Postoperative Mortality?

To the Editor:

We read with great interest the recent article by Sessler *et al.*,¹ which suggested that a “triple low” of mean arterial pressure, bispectral index, and minimum alveolar concentration strongly predict postoperative mortality. We would like to congratulate them on their excellent and impressive study on this important subject. However, there are a few important points we wish to comment on.

The authors reported that triple low had four times the hazard of death within 30 days compared with patients who did not have a triple low after adjusting for patient age, sex, comorbidities, and surgical complexity. The following question arises: is intraoperative triple low an independent risk predictor or just a marker of hazard level of postoperative mortality? In fact, the results properly account for inherent variability in risk associated with differences in baseline characteristics (or severity of preexisting diseases) as well as differences in procedural complexity between patients with triple low and those without. From our perspective, it may be extrapolated that patients with triple low have more preoperative risk factors in comparison with those without. However, the authors did not analyze these differences between patients with triple low and those without. In addition, the inclusion of other perioperative risk factors in the multivariate analyses may increase the likelihood of identifying the independent association of intraoperative triple low and postoperative outcomes. Although the authors attempted to control for patient comorbidities and procedural risk using their recently published Risk Stratification Index,^{2,3} some important intra- and postoperative risk factors (*e.g.*, intraoperative blood transfusion and postoperative troponin T level) were not included in the multivariate analyses. Intraoperative blood transfusion was associated with an increased risk of 30-day mortality in patients undergoing noncardiac surgery.⁴ The postoperative troponin T level after surgery was significantly associated with mortality among patients undergoing noncardiac surgery.^{5,6} Moreover, triple low may offer an accurate characterization of patient risk contributing to mortality in the postoperative period when combined with other perioperative risk factors. Meanwhile, it would also be of essence to know the relationship between preoperative risk factors and the occurrence of intraoperative triple low. In this way, we might be able to identify patients with high-risk levels

preoperatively, who could receive intensive perioperative management to limit postoperative mortality.

However, adverse effects of intraoperative hypotension perhaps are related more to the cause of the hypotension (*e.g.*, hypovolemia, myocardial dysfunction, sepsis, or anesthetic overdose) than to the arterial blood pressure *per se*.⁷ Similarly, intraoperative cerebral state (*e.g.*, cerebral hypoxia or increased cerebral susceptibility to the effects of anesthetics), not low bispectral index and minimum alveolar concentration *per se*, is associated with adverse outcomes after surgery.⁷ Thus, it is unclear whether triple low results in the increased risk of postoperative mortality or simply detects patients with potential high risk of death. In our opinion, triple low may simply reflect severity of the patient’s underlying disease and serve as a marker of high risk of postoperative mortality, and indeed is attributable to the multiple preoperative risk factors the patient suffers from simultaneously. It is rational to consider that specific groups of patients may be more likely to exhibit or be affected by triple low, and this would warrant further subgroup analyses. However, the authors did not stratify patients into high-risk and low-risk groups based on the number of preexisting risk factors.

As mentioned by Drs. Kheterpal and Avidan in their accompanying Editorial, short-term 30-day mortality was the primary outcome, which increases the possibility of a causal contribution of intraoperative events.⁸ The authors also did not identify the causes of death, but based on a recent study, a substantial proportion of deaths are likely to be related to cardiovascular causes.⁵ It is essential that the sensitivity analysis of triple low, associated with different causes of death, should be performed.

The association of a triple low of mean arterial pressure, bispectral index, and minimum alveolar concentration with postoperative mortality in noncardiac surgical patients is a fascinating topic, and this impressive study is highly important for our understanding of this interesting phenomenon. Therefore, additional clinical trials are needed to confirm the prognostic value of triple low and establish whether interventions can alter patients’ risk of death based on triple low events during surgery.

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Concentration of Precious Sleep: Piloting Survival or Attending Death?

To the Editor:

Tailoring depth of anesthesia to the needs of each individual patient, while mastering the inevitable cardiovascular side effects represents a core anesthesiologist's skill. Novel inspiration to this daily challenge has recently been brought by Sessler *et al.*,¹ identifying the combination of low blood pressure, low bispectral index (BIS), and low minimum alveolar concentration of volatile anesthesia as a troika of death. Looking at the cutoff parameters of this “triple low” may cause a wave of reflection, if not immediate malaise in each anesthesiologist, as values below the mortality threshold are routinely tolerated. The question arises: Are we harming all these patients, if not worse?

All three phenomena are inextricably entwined and intraoperative management is largely dictated by patient characteristics and intraoperative course. Low blood pressure was shown to determine adverse outcome in relation to age and duration of surgery,² and the establishment of a causal relationship between low BIS values and intermediate-term outcome previously failed when malignancy and physical status were considered.³ Moreover, left ventricular dysfunction, systemic illness, or a complicated intraoperative course

was shown to account for accumulated low BIS values, with no relation to end-tidal anesthetic gas concentrations.⁴ The abovementioned results emphasize that anesthetic management is influenced not only by anesthesia-related, but also a plethora of surgery-related, and patient-specific factors. It seems difficult to control all these interfering factors to achieve clear-cut scientific conclusions; however, discrimination of at least American Society of Anesthesiologists physical status and cause of death seems mandatory. It is hard to believe that a triple low in a 20-yr-old American Society of Anesthesiologists class I patient has the same prognostic value, if any at all, as that of a 70-yr-old American Society of Anesthesiologists class III patient. Although Sessler *et al.* certainly would agree with these considerations, their current study misses the opportunity to provide conclusive new insights in conjunction with clinically applicable concepts as the predictive role of important variables such as comorbidities, American Society of Anesthesiologists physical status, duration and difficulty of surgery (*e.g.*, transfusion requirements), and cause of death were neglected. Moreover, no single low was associated with increased mortality, further impeding the identification of distinct manipulations of either mean arterial pressure, BIS, or minimum alveolar concentration as causal or pure epiphenomena. Hence, observation of a “double low,” and triple low should not be misinterpreted as differences in anesthetic sensitivity or outcome determinants *per se*. As before, attention is required not to injudiciously confound low BIS values as a pure reflection of anesthetic depth in the critically ill, just as the sufficient supply of minimum alveolar concentration values and provision of adequate perfusion pressures should be self-evident hallmarks of anesthesia.

However, despite its limitations, the study shines with its conceptual approach of desperately needed outcome research in anesthesiology. Many aspects of narcosis remain unexplored and things working as a matter of course on a daily basis are likely to impact patient morbidity and mortality. Prospective studies regarding the prognostic value of anesthetic characteristics are desirable, in particular, those targeting outcome improvement. Data supporting clinical decision making will help to manage the core anesthesiologist's task of tailoring anesthetic depth to each individual needs and answer the question: How can we make a difference for the better?

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