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Hypotension and Stroke in Cardiac Surgery: Comment

To the Editor:

I have long been concerned that anesthesiologists, at least occasionally, are unwittingly accepting intraoperative mean arterial pressures (MAPs) that may bring the central nervous system very close to the thresholds for ischemic injury.[1] The recent report by Sun *et al.* offered a caution about intraoperative hypotension and was therefore a result that I was inclined to welcome.[2] They reported, on the basis of a retrospective examination of a large electronic database, an association between MAPs less than 65 mmHg before, during, or after cardiopulmonary bypass (CPB) and the occurrence of postoperative stroke. However, in spite of my biases, I found myself with some uncertainties about the strength of their observations. I am concerned about unmeasured (or merely unreported) covariates. In part, the prompt for that concern was the nearly simultaneous publication of an investigation by Vedel *et al.* (about which Sun *et al.* inevitably had no opportunity to comment).[3] Vedel *et al.* assigned cardiac surgery patients to MAPs of either 40 to 50 or 70 to 80 mmHg on CPB. The investigation was randomized and prospective. The CPB parameters, which were reported in detail, were common to the two groups, with the exception of pressors and inotropes in the latter group. The primary endpoint was the volume of new diffusion weighted imaging lesions in the postoperative period. There were no differences between the groups in that endpoint or in several secondary endpoints. While relatively small numbers (98 and 99 patients per group) might be suspected of having resulted in type II statistical errors, every trend (diffusion weighted imaging lesion volume, stroke, cognitive dysfunction at the time of discharge, mortality) was in favor of the low pressure group.

I write to seek the opinions of Sun *et al.* as to possible explanations for the apparently contradictory results of the two studies. Their retrospective trial reports a stroke association with MAP less than 65 mmHg while the prospective, randomized trial reports no disadvantage to a MAP of 40 to 50 mmHg. That prompted my concern about covariates. I have several questions. First, why was there so much MAP variation, especially during CPB, within one cardiac surgery group? Were the lower MAPs in some patients a function of the perceived fragility of the aorta? The references cited by Sun *et al.* confirm the importance of aortic atherosclerosis as a conspicuous stroke risk factor.[4,5] Was an assessment of the severity of atherosclerotic disease of the aortic arch performed and recorded in their patients? Sun *et al.* provide little information about CPB technique and/or its variation among practitioners and over time. Were differences in the practices of individual surgeons, anesthesiologists, and perfusionists contributors to outcome differences among patients? More specifically, were the CPB techniques the same for all patients? As a reflection of the possible influence of variations in CPB technique, was the stroke rate constant over the 6-yr study period? I hope that this letter will present Sun *et al.* an opportunity to strengthen their work by providing information about potential covariates.

As a minor additional concern, to which I seek no response, I think that there are some references to the literature that are misrepresentations of the cited papers, or at a minimum will be misunderstood. An assertion offered in the Introduction is one such: "Optimal blood pressure thresholds for stroke

prevention have been described as MAP within 30% of baseline in a noncardiac, nonneurologic surgery cohort,[6] and… MAP of greater than 66 mmHg…during CPB.[7]" Neither of the cited papers makes recommendations about target MAPs for the prevention of stroke. Bijker *et al.* reported an association between stroke and intraoperative MAP greater than 30% below baseline.[6] However, they opined that "these associations should be interpreted cautiously and do not automatically imply causality." Joshi *et al.* identified the average lower limit of autoregulation on CPB to be 66 mmHg (notably, with a very wide CI and a poor correlation between baseline MAP and lower limit of autoregulation).[7] Their conclusion was that MAP targets based on clinical guestimates of a probable lower limit of autoregulation are likely to be frequently very wide of the mark. However, they did not make MAP recommendations. While my comments may appear to some to be mere caviling over semantics, my experience has been that too many third party reviewers take hold of misstatements of this nature in the published literature and, in the face of adverse outcomes, make them the basis of standard of care criticisms of clinicians. The semantics matter.

Competing Interests

The author declares no competing interests.

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Hypotension and Stroke in Cardiac Surgery: Reply

In Reply:

We appreciate the opportunity to respond to the questions raised by Ravn *et al.* and Dr. Drummond, as well as to clarify aspects of our clinical practice and methodology in response to these questions. We are grateful to Ravn *et al.* and Dr. Drummond for their interest in our paper.[1]

In response to the first comment by Ravn *et al.*, although we lack information on mean cardiopulmonary bypass (CPB) flow, the routine practice at our institution is to maintain flow at a minimum of 2.4 $l \cdot min^{-1} \cdot m^{-2}$ during CPB. This generally uses the estimated "lean body surface area" of the patient and, as such, warrants adjustment in the presence of obesity. To the second point by Ravn *et al.*, we are unable to comment on the impact of prolonged "low" CPB flow, since the relationship between pressure and flow is complex, and a "low" flow threshold number has yet to be clearly determined in cardiac surgery patients. Ravn *et al.* pointed out that in a recent randomized control trial, where the CPB flow rate was fixed and vasopressor infusions were used to manipulate mean arterial pressure (MAP) during CPB, patients in the high MAP group (70 to 80 mmHg) had lower cerebral saturation levels compared to those in the low MAP group (40 to 50 mmHg).[2] These findings likely result from the inverse relationship between flow and vascular resistance, as well as emphasize the merits of near infrared spectroscopy in the management of high-risk patients during CPB. Overall, the points by Ravn *et al.* provide support to the need for further studies examining CPB pressure–flow relationships in greater detail.

In response to Dr. Drummond, we hereby confirm that lower MAPs during CPB were not a function of the fragility of the aorta, since controlled hypotension, in the