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LETTER TO THE EDITOR

Is increased perfusion pressure really necessary during cardiopulmonary bypass?

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We read with great interest the work by Siepe *et al.* [1] investigating the effect of increased systemic perfusion pressure during cardiopulmonary bypass on cognitive dysfunction and delirium. In this revolutionary study questioning cerebral autoregulation, they found that maintaining mean perfusion pressure during normothermic cardiopulmonary bypass (CPB) at 80–90 mmHg is associated with less early cognitive dysfunction and delirium after coronary artery bypass grafting (CABG), and elevated perfusion pressure is not associated with increased morbidity and mortality. This finding may lead to severe changes in the routine practice of cardiac surgeons and anaesthesiologists including us. However, we believe that there are some issues that need to be addressed.

This study lacks a power and sample analysis and seems to have been conducted in a very small group of patients. For this reason, postoperative complications such as atrial fibrillation (19 vs 36%), bleeding requiring reoperation (2 vs 7%), use of blood products (50 vs 70), cessation of catecholamine support (26 vs 14 h), superficial wound infection (4 vs 7%) and pleural effusion (33 vs 48%) which may be statistically significant in a larger group of patients appears to be insignificant.

As the low perfusion group needed longer catecholamine support, it is easy to assume that they were in either low cardiac output (LCO) or vasoplegic state. The incidence of preoperative left ventricular dysfunction, which is a predictor of LCO, is not reported and should be included in the statistical analysis. Furthermore, it is well known that preoperative medication by inhibitors of angiotensin-converting enzyme in coronary artery patients is associated with vasoplegic shock early after CABG. This issue also needs to be addressed.

If low perfusion pressure during CPB is to be blamed, then the postoperative period should be comparable in both groups. However, as the LP group suffered from LCO postoperatively, measurement of neurochemical markers (S-100 beta and neuron-specific enolase) immediately after CPB might be appropriate.

It is clear that patients with delirium had longer CPB, ventilation and intensive care unit (ICU) stay times, and were still in LCO (probably still in ICU and under major depression) at the

time of Mini-Mental-State examination. All of these factors have been shown to be associated with postoperative delirium [2, 3].

Cerebral circulation during CPB may be affected by partial arterial oxygen (hyperoxaemia by impairing red cell rheology and microcirculation) and carbon dioxide pressure (by changing cerebral arteriolar reactivity) [4]. Thus, they should be monitored closely (more frequently than every 20 min) and kept similar in both groups.

Spot measurements of transcutaneous cerebral oxygen saturation as measured by near-infrared spectroscopy seem to be similar in both groups. However, it is reported that rSO₂ desaturation score, which is calculated by multiplying rSO₂ below 50% by time (s), is a more sensitive method of predicting early postoperative cognitive decline than spot measurements [5].

Nitric oxide (NO) formed via endothelial NO synthase and neuronal NO synthase plays crucial roles in the regulation of blood flow through vasodilatation and decreased vascular resistance. Endothelial and autonomic nitrergic nerve functions are impaired in patients with diabetes mellitus, resulting in regional blood flow decrease [6]. As the duration of the diabetes mellitus and insulin dependence may change from patient to patient, it seems necessary to exclude these patients or at least compensate for the severity of their disease.

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LETTER TO THE EDITOR RESPONSE

Reply to Alhan *et al.*

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We thank Dr. Alhan *et al.* for their constructive and important comment on our study [1]. They highlighted some relevant limitations [2] of this small randomized trial which we aim to address in our response in part. Alhan *et al.* have correctly asked for some unreported preoperative factors such as the ejection fraction, the pre-OP medication, including angiotensin-converting enzyme inhibitors, and the longevity of diabetes which are reported factors associated with postoperative cognitive dysfunction. We intended to exclude the possible bias by means of the study's randomized fashion and analysed these factors. The medication, the preoperative ventricular function and EuroSCORE were identical in the two groups. The most important limitation of this trial (as correctly stated by Alhan *et al.*) is the small size of the cohorts. More important questions with better defined secondary endpoints can only be answered in a bigger randomized multicentre trial. Factors such as the mentioned neurochemical markers, more meaningful values derived from transcutaneous oxygen saturation

must be included in a future trial as well as the intermediate and possibly late cognitive outcome measures. We hope that Alhan *et al.* and other readers will like to participate in the planning and conduction of such a trial. This type of input is crucial to derive more valid knowledge about the association between pressure, microperfusion and postoperative cognitive dysfunction in surgery with the use of cardiopulmonary bypass.

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LETTER TO THE EDITOR

Reviewing α -Gal in valve immunology

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