Ketamine for induction and maintenance during elective on-pump coronary artery bypass grafts

Editor—We read with interest the article on the alterations to the inflammatory response during cardiopulmonary bypass, after induction and maintenance with ketamine. However, we have a couple of questions for the authors.

Anaesthetic depth was monitored using the bispectral index. This is known to be an unreliable marker of anaesthetic depth in the presence of ketamine. This could therefore have resulted in more anaesthetic drugs being administered in the ketamine-treated group. Indeed, both midazolam and propofol doses were higher in this group. Since the definitive changes in ‘immune function’ caused by propofol and midazolam are still unclear, might not the altered cytokine response result solely from the extra use of these drugs? We also notice that attempts were made to blunt the sympathomimetic response to ketamine. The authors state that both β-blockers and antihypertensives were used as necessary. We would be interested to have more information, as some of these drugs are now being recognized to have additional properties, including alterations in the inflammatory cytokine response.

While the study demonstrates significantly different levels of interleukin 6, 8, and 10 in the early hours after cardiopulmonary bypass in the ketamine-treated group, the troponin and creatine kinase-MB levels were similar. There are few incidences where it is thought that manipulating the cytokine response to a major insult may be beneficial. However, there are also many incidences where no benefit or harm has been demonstrated. The overall clinical implications from the observed cytokine responses might be difficult to predict. We therefore believe that using ketamine as induction and maintenance on the basis of this study may be difficult to justify.

Conflict of interest
None declared.

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Reply from the authors
Editor—We would like to thank Drs Bigham and Jaggar for their comments on our study. They raise the question whether the use of higher doses of propofol and midazolam in the ketamine group, even though statistically not significant, could be responsible for the observed differences in cytokine responses. The fundamental difference between our study groups was the presence or absence of S-(+)-ketamine. Our results clearly show that the propofol and midazolam doses did not differ significantly between the groups. It is hence unlikely that differences in sedative drugs can explain the inhibition of proinflammatory cytokine release in the ketamine group. It is worth noting that the described differences in cytokine response were detectable despite high standard variation and non-normal distribution of data, while the data on propofol doses showed more homogeneity. Therefore, significant differences in propofol and midazolam dosing would have been detected with acceptable reliability. Furthermore, from the clinical and immunological perspective, it also appears questionable that 220 mg of propofol (i.e. approximately 0.5 mg kg⁻¹ h⁻¹) or 1.2 mg of midazolam applied during a 6 h anaesthetic can be made responsible for differences in the immune response. The study cited by Bigham and Jaggar was performed in rats and used a bolus injection of 10 mg kg⁻¹ propofol followed by an infusion of 10 mg kg⁻¹ h⁻¹. This suggests that at least 10-fold higher additional doses of sedatives are required to elicit a measurable effect on cytokine response. Monitoring of anaesthetic depth using bispectral index during ketamine administration is not an established procedure. However, recent experience suggests that ketamine may neither influence BIS values nor increase the incidence of postoperative delirium, if given in combination with other anaesthetics. β-Blockers have been thoroughly investigated for immune effects. However, we would like to emphasize that ~80% of the patients in both study groups were on β-blockers as their usual treatment. β-Blockade was continued on the day of surgery. Hence,