References

1. Deng C, Bellomo R, Myles P. Systematic review and meta-analysis of the perioperative use of vasoactive drugs on postoperative outcomes after major abdominal surgery. *Br J Anaesth* 2020; **124**: 513–24
2. Sandham JD, Hull RD, Brant RF, et al. A randomized, controlled trial of the use of pulmonary-artery catheters in high-risk surgical patients. *N Engl J Med* 2003; **348**: 5–14
3. Sterne JAC, Savović J, Page MJ, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. *BMJ* 2019; **366**: l4898
4. Stens J, Hering J-P, van der Hoeven CWP, et al. The added value of cardiac index and pulse pressure variation monitoring to mean arterial pressure-guided volume therapy in moderate-risk abdominal surgery (COGUIDE): a pragmatic multicentre randomised controlled trial. *Anaesthesia* 2017; **72**: 1078–87
5. Deng C, Myles P. *Effect of intraoperative administration of inotropic or vasoactive agents on postoperative outcomes following major abdominal surgery in adults: a systematic review and meta-analysis* 2018. PROSPERO 2018 CRD42018116213. Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42018116213. [Accessed 19 May 2020]
6. Guyatt GH, Oxman AD, Kunz R, et al. What is 'quality of evidence' and why is it important to clinicians? *BMJ* 2008; **336**: 995–8

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Perioperative use of vasoactive drugs on postoperative outcomes after major abdominal surgery. Response to *Br J Anaesth* 2020; 125: e353–4

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Keywords: cardiovascular; goal-directed therapy; haemodynamics; major abdominal surgery; perioperative care; postoperative outcome; vasoconstrictor agents

Editor—We thank Yonekura[1] for his interest in our systematic review,[2] and would like to address his comments.

Firstly, we accept that the denominator in our meta-analysis was inconsistent with the intention to treat principle. We have repeated the analysis with updated denominators reflecting intention to treat or modified intention to treat principles. This did not change the results of the meta-analysis (risk ratio of mortality at longest follow-up in intervention compared with control group of 0.83, 95% confidence interval 0.63–1.10, P=0.20). For missing data, 1851 of 1994 randomised participants in the study by Sandham and colleagues[3] had completed 1 yr of follow-up. Of those with missing long-term outcome data, 88 participants were excluded after randomisation as they did not meet the *a priori* inclusion criteria, and 55 were lost to follow-up (only 2.9% of the modified intention to treat population). We made a considered judgement that this does not represent significant loss to follow-up as the overall mortality rate was in the range of 16–18%. There is no evidence to suggest that the missingness is systematic (non-random). Furthermore, it is the original authors' responsibility to report the reason(s) for missing data and any assumptions or imputation methods used to handle missing data.

Secondly, we agree with Yonekura's[1] concern that heterogeneity posed a major limitation in our systematic review, as we had highlighted in our discussion. The aim of our systematic review was to assess whether the protocolised administration of vasoactive agents had an effect on postoperative outcome, which included studies comparing vasoactive medications as part of haemodynamic targeting with routine care. It would be considered unethical not to treat severe hypotension in the controlled arm of a trial, and as such the use of vasoactive agents in both arms of an intervention such as this is not surprising. This is not an equipoise problem, rather, methodological limitations of individual studies which we had addressed in our discussion.

Thirdly, we disagree that the Grading of Recommendations Assessments, Development and Evaluation (GRADE) framework is useful in this context. We did not publish clinical guidelines, but rather a synthesis of previously published research.

Declarations of interest

PM is an Australian National Health and Medical Research Council practitioner fellow and an editor of the *British Journal of Anaesthesia*. CD declares no conflict of interest.

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References

1. Yonekura H. Perioperative vasoactive drugs in patients undergoing major abdominal surgery. Comment on *Br J Anaesth* 2020;**125**: e353–4
2. Deng C, Bellomo R, Myles P. Systematic review and meta-analysis of the perioperative use of vasoactive drugs on postoperative outcomes after major abdominal surgery. *Br J Anaesth* 2020; **124**: 513–24
3. Sandham JD, Hull RD, Brant RF, et al. A randomized, controlled trial of the use of pulmonary-artery catheters in high-risk surgical patients. *N Engl J Med* 2003; **348**: 5–14

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Impact of neuraxial anaesthesia on short-term outcomes after elective open abdominal aortic aneurysm repair. Comment on *Br J Anaesth* 2020; 124: 544–52

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Keywords: abdominal aortic aneurysm; anaesthesia; mortality; neuraxial anaesthesia; outcome

Editor—We appreciate the insights offered by Salata and colleagues[1] in their retrospective study evaluating the impact of two anaesthetic approaches on outcomes for patients undergoing elective open abdominal aortic aneurysm (AAA) repair. By applying propensity score weighting for confounding adjustment, they found that patients who received combined general and regional anaesthesia experienced a higher 90-day survival rate and lower incidence of complications compared with those who received general anaesthesia. They also showed that, compared with general anaesthesia, combined anaesthesia was associated with a shorter mechanical ventilation period and hospital length of stay. Although the authors openly discussed the limitations of their findings, these results may have been influenced by biases. Accordingly, we would like to call attention to several confounding biases and statistical issues that we believe warrant further discussion.

First, the initial selection of anaesthetic approach may have been influenced by the confounding effects of severity and indication.[2] Regional anaesthesia is typically avoided for patients who have a severe burden of co-morbid illness (confounding by severity) or contraindications for neuraxial anaesthesia (confounding by indication). This trend was consistent with the study results: compared with those who received combined anaesthesia, patients in the general anaesthesia group were more likely to have a clinical history of congestive heart failure or peripheral arterial disease, a higher Charlson co-morbidity score, and a higher incidence of anticoagulant use (see Table 1 in Salata and colleagues[1] for a detailed summary of patient characteristics). These confounding biases for neuraxial anaesthesia suggest that the results of this study may have been fundamentally biased against the general anaesthesia group. It would be ideal to conduct an RCT to address confounding biases, but the limited external generalisability and need for large sample sizes make conducting an RCT difficult.

Second, although the authors used the Charlson Comorbidity Index and clearly acknowledged the limitations of not having assessments of physiological reserve, they did not take into account the direct effects of patients' ability to perform activities of daily living (ADL) or frailty in the preoperative period. Dependence in ADL is significantly associated with higher 1 yr mortality rates after major surgery, including AAA repair.[3] Frail patients are also significantly more likely to have higher mortality and morbidity after elective open AAA repair surgery.[4] Frailty is a multidimensional syndrome defined as a decline in physical performance, cognitive function, nutrition status, and mental health, which makes it difficult to be evaluated by a single measurement.[5,6] The aforementioned unmeasured preoperative factors may have introduced residual confounding effects.

Third, the authors used an inverse probability of treatment weighting (IPTW) approach using the propensity score for balancing background characteristics and controlling for confounding bias. Although the baseline characteristics between the two groups were well balanced after IPTW was applied, there were no details provided regarding the propensity score distribution. We are interested in examining whether or not there was sufficient overlap in propensity score distributions between the two groups, both before and after propensity score weighting, which is an essential step in statistical analyses that use propensity score weighting. Sufficient overlap in the propensity score distribution could support a reasonable clinical equipoise between the two groups.[7]

Fourth, considering the within-hospital clustering effects of clinical practice, we speculate that inter-institutional

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