3 days of storage, indicating increased haemolysis, and infusion of 40-day packed erythrocytes was recently suggested to lead to increased NO production from endothelial NOS, as a compensatory mechanism for reduced NO bioavailability caused by plasma oxyhaemoglobin scavenging of NO. However, although leucoreduced units of packed red blood cells contain fewer than $5 \times 10^{-6}$ white blood cells, it should be noted that neutrophils, which undergo spontaneous cell death, constitutively express large amounts of arginase and even small contamination of packed red cell bags by neutrophils might, therefore, produce significant levels of arginase activity, apart from that derived from the red cells themselves. Recently, we found raised levels of free arginase in blood stored for long periods, which could corroborate these arguments and have implications for patients in whom immunosuppression is a major challenge.

Thus, we suggest that increased haemolysis might be an important aspect in blood transfusion, leading to elevated levels of arginase and NOS, and, thereby, to l-arginine depletion that could eventually affect immune function and cancer progression.

**Declaration of interest**

None declared.

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**Reply from the author**

Editor—I have to thank Palomero-Rodrı´guez and colleagues for their important contribution to this topic as raised in our review. Certainly, l-arginine and arginase I and II are important modulators of the immune response after blood transfusion. No less important is the evidence provided by several investigators suggesting that a deficiency of l-arginine also occurs as part of the stress response to surgery and this deficiency has been implicated as one of the mechanisms behind the known shift from a Th1 to a Th2 response after surgery. This phenomenon may even have been worsened by the transfusion of mainly ‘old’ blood which would further deplete levels of l-arginine. Perhaps, a more relevant question to answer in the clinical setting is whether the administration of l-arginine in the context of perioperative immune-nutrition could ameliorate immunosuppression and perhaps improve long-term oncological outcomes in patients in whom blood transfusion cannot be avoided and undergo major surgery.

**Declaration of interest**

None declared.

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**Factors for perioperative delirium**

Editor—I read with interest the paper by Radtke and colleagues addressing the important issue of anaesthetic depth and its relationship with postoperative delirium. Any measure which may ameliorate delirium warrants attention, given the personal cost to the patient and patient’s family along with the financial strain that postoperative delirium carries with it for the healthcare system.

I do, however, kindly request clarification regarding two methodological issues with the paper that may affect interpretation of the results presented: (i) benzodiazepine administration and (ii) intraoperative hypotension.

First, perioperative benzodiazepine use is associated with emergence delirium based on earlier work by Radtke and colleagues; in a prospective observational study examining over 1800 patients, those receiving a benzodiazepine as premedication were 2.39 times (95% confidence interval 1.01–5.62) more likely to experience emergence delirium than patients who were not administered a benzodiazepine. According to the methods used in the current study, ‘in case a sedative premedication is needed midazolam is prescribed in a dosage of 0.1 mg per kg’. Given their conclusion that ‘intraoperative neuromonitoring is associated with a lower incidence of delirium’, and in an effort to contextualize their findings with the