Letter to the editor re : Association of preoperative anemia with postoperative mortality in neonates

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Dear Sir

I read with interest the recent article by Goobie and colleagues1 and the accompanying editorial by Higgins et al 2. Whilst I support the concept of preoperative optimisation (including haematocrit where appropriate) I could not agree more with the significant limitations of the study as highlighted in the editorial. Whilst I acknowledge that the independent association between low haematocrit and mortality cannot be refuted on statistical grounds, not to have included underlying surgical diagnosis as a confounding variable appears to represent a significant methodological flaw. I note that the majority of infants underwent a ‘general surgical’ procedure which from experience may have ranged in severity from elective inguinal hernia repair to emergent laparotomy for fulminant NEC. On closer inspection of the cohort of 93 infants who died in hospital, we find that 63% weighed <2kg, 69% were preterm, 82% of procedures were emergent and 51% underwent an intra-operative transfusion. These figures suggest a much greater severity of illness due to underlying diagnosis in the group that died than survivors, which may be (a) cause for low haematocrit and (b) also an independent risk factor for mortality. High mortality 3 is a feature of necrotising enterocolitis a diagnosis that is likely to have been present in a good number of non-survivors given the population demographics and clinical features. As emphasised in the editorial, ASA classification of 3-5, preoperative mechanical ventilation and preoperative inotrope support all had odds ratios for mortality higher than the odds ratios for low haematocrit and all were statistically significant on multivariate analysis. To ignore surgical pathology and select out anaemia alone as a focus for increased mortality risk would seem inappropriate and a significant over-simplication.

I also draw attention to the supplementary table. This compares infants included in this study on the basis that they had a pre-operative haematocrit measured with those who were not included since no haemotocrit was drawn. Almost all clinical features were significantly different between included and excluded groups suggesting important differences and raising the possibility of selection bias. By selecting out only the more unwell infants (who were noted to be unwell enough to warrant a preoperative haematocrit), the results may be significantly skewed. I am struck in particular by the bottom line of the supplementary table; just by having a haematocrit drawn infants had a 10 times higher mortality risk.

1. Goobie SM, Faraoni D, Zurakowski D, DiNardo JA. ASsociation of preoperative anemia with postoperative mortality in neonates. *JAMA Pediatrics.* 2016.

2. Higgins RD, Patel R, Josephson CD. PReoperative anemia and neonates. *JAMA Pediatrics.* 2016.

3. Thyoka M, De CP, Eaton S, et al. Advanced necrotizing enterocolitis part 1: mortality. *Eur J Pediatr Surg.* 2012;22(1):8-12.