

**Response to: Early laparoscopic-assisted surgery is associated with decreased post-operative inflammation and intestinal strictures in infants with necrotizing enterocolitis**

**George S Bethell<sup>1</sup> and Nigel J Hall<sup>1\*</sup>**

1. University Surgery Unit, Faculty of Medicine, University of Southampton, Southampton, United Kingdom.

\* Corresponding author - [n.j.hall@soton.ac.uk](mailto:n.j.hall@soton.ac.uk)

We read with interest your recent article by Montalva et al. and the invited commentary reporting and discussing the use of laparoscopy in necrotizing enterocolitis (NEC).(1, 2) We would like to draw readers' attention to an additional, and we believe important, difference between groups in this study which is only briefly mentioned in either the authors' original discussion or the invited commentary. The authors propose that with a new treatment pathway comprising initial diagnostic laparoscopy there is less inflammation and reduced stricture rate in infants with NEC. They contribute this benefit to the use of initial laparoscopy (citing CO2 pneumoperitoneum as being anti-inflammatory) despite the fact that 90% of cases subsequently went on to have laparotomy.

We would like to draw readers' attention to the difference in time between onset of NEC and surgery in the 2 groups: 3 days in the group having initial laparoscopy and 6 days in the historical control group. This was a statistically significant difference. We propose that it is more likely that the difference in outcomes seen was a consequence of these babies being operated on far earlier in their disease course than the historical control group and that as a consequence the pro-inflammatory drive arising from diseased intestine was interrupted sooner. This hypothesis of earlier surgery being associated with improved outcomes is supported by our recent work published in this journal in 2021.(3) In a large multicentre cohort we identified that infants whose indication for surgery was failed medical management, waited 30 hours longer for surgery than those who underwent surgery on the basis of pneumoperitoneum and were more likely to have a poor outcome (death or PN requirement at 28 days post-surgery).

In addition to the reduced inflammation and reduced stricture rate with earlier surgery reported by Montalva and colleagues, we note a lower need for diverting stoma. We also note some hints towards improvements in other outcomes. Although not statistically significant the early (laparoscopy first) approach was associated with higher use of primary anastomosis, lower mortality, and reduced need for reintervention. Further exploration of this early surgery approach in a larger sample size is certainly warranted to investigate these important outcomes further.

Finally, we wish to suggest that the difference in CRP levels between the groups may not be as inconsequential as the authors suggest. An important long-term outcome in NEC is neurodevelopment and it is highly likely that neurodevelopmental outcome is associated with the severity of inflammation and perhaps duration of exposure to severe inflammation.(4, 5, 6) Thus an early reduction in CRP associated with early surgery (whether laparoscopic or not) may not be of such uncertain significance as the authors suggest. Reduction in the severity and/or duration of the systemic inflammatory response may well be extremely important when considering the full range of outcomes for these babies.

We are pleased to see these data supporting earlier surgery in NEC and suggest this approach may have a role in improving outcomes. Finally we agree with Montalva and colleagues that an objective means to determine better early predictive factors of necrosis would be helpful.

## References

1. Montalva L, Incerti F, Qoshe L, Haffreingue A, Marsac L, Frérot A, et al. Early laparoscopic-assisted surgery is associated with decreased post-operative inflammation and intestinal strictures in infants with necrotizing enterocolitis. *J Pediatr Surg.* 2022.
2. Zani A. Invited commentary on Montalva L, et al.: Early laparoscopic-assisted surgery is associated with decreased post-operative inflammation and intestinal strictures in infants with necrotizing enterocolitis. *J Pediatr Surg.* 2022.
3. Bethell GS, Knight M, Hall NJ, BAPS-CASS B-CNIGobo. Surgical necrotizing enterocolitis: Association between surgical indication, timing, and outcomes. *J Pediatr Surg.* 2021;56(10):1785-90.
4. Jones IH, Hall NJ. Contemporary Outcomes for Infants with Necrotizing Enterocolitis-A Systematic Review. *J Pediatr.* 2020.
5. Lodha A, Asztalos E, Moore AM. Cytokine levels in neonatal necrotizing enterocolitis and long-term growth and neurodevelopment. *Acta Paediatr.* 2010;99(3):338-43.
6. Rose J, Vassar R, Cahill-Rowley K, Hintz SR, Stevenson DK. Neonatal Biomarkers of Inflammation: Correlates of Early Neurodevelopment and Gait in Very-Low-Birth-Weight Preterm Children. *Am J Perinatol.* 2016;33(1):71-8.