

Letter to the Editor

Anti-TNF Therapy Before Intestinal Surgery for Crohn's Disease and the Risks of Postoperative Complications

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We read with interest the 2020 ECCO guidelines on surgical treatment of Crohn's disease,¹ and noted that ECCO have reversed their 2018 guidelines in regards to the safety of preoperative anti-tumour necrosis factor [TNF] therapy. In 2018, ECCO concluded that administration of anti-TNF agents shortly before abdominal surgery is associated with an increased risk of postoperative septic complications [Statement 1B]. In 2020, ECCO stated that the current evidence does not support such an association, and that cessation of therapy is not mandatory [Statement 4.3].¹

We propose that this statement may be premature. At the time of publication of the 2020 guidelines, no less than three meta-analyses on this topic had recently been published. Two of those concluded that preoperative anti-TNF therapy was associated with an increased risk for infectious complications,^{2,3} and one found no increase in risks.⁴ Notably, all three found significant heterogeneity, with an I^2 in the 23–64% range.^{2–4}

There are several reasons for such heterogeneity. These drugs have a half-life of 1–2 weeks, but individual studies have used definitions of 'preoperative' administration that vary from 4 to 12 weeks preceding surgery. Any effects on postoperative outcomes are likely diluted in those studies that used the longer time periods. Another important issue is adjustment for disease severity, an obvious potential confounder in this literature. Insufficient adjustment may explain positive findings in some studies.

Despite these shortcomings in the literature, there are high-grade data that signal a real risk. Perhaps the most important is a French prospective multi-centre study in 592 patients undergoing ileocaecal resection, where adjustments for a range of disease severity markers were made both by multivariable regression and by propensity scoring.⁵ This study demonstrated an increase of overall morbidity (adjusted odds ratio [OR] 2.89) and intraabdominal septic complications [adjusted OR 2.22] in patients treated by preoperative anti-TNF therapy.

How did the authors of the 2020 ECCO guidelines support their updated recommendations? They cited only two references: the recent meta-analysis that did not demonstrate increased risks,⁴ and an as yet unpublished study of ulcerative colitis and Crohn's disease presented in abstract form in 2019.

In conclusion, a mixed picture emerges when the literature on the safety of preoperative anti-TNF therapy is examined, with some

high-grade evidence that raises concerns. The stakes are high in bowel resection for Crohn's disease: postoperative abdominal sepsis is common and intestinal failure is a real risk in this population. In light of these challenges, and clear signals of risk in the literature, we propose to err on the side of caution until more conclusive data emerge. We therefore propose that the recommendation to continue anti-TNF administration in the weeks preceding intestinal surgery for Crohn's disease is not supported by the available data on this issue.

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Conflict of Interest

MS has received consulting fees from 11 Health and Technologies Inc., Irvine, CA, USA. LH and JD declare that they have no competing interests.

Author Contributions

MS drafted the response in coordination with JD. LH revised and edited the letter. All the authors approved the final version of the letter.

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