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To cite this article: Marco Ettore Allaix, Andrea Resegotti & Mario Morino (2022): Effects of Preoperative Anti-TNF Therapy on Specimen Length in Crohn's Disease and Beyond, Journal of Investigative Surgery, DOI: [10.1080/08941939.2022.2048143](https://doi.org/10.1080/08941939.2022.2048143)

To link to this article: <https://doi.org/10.1080/08941939.2022.2048143>



Published online: 06 Mar 2022.



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COMMENTARY



Effects of Preoperative Anti-TNF Therapy on Specimen Length in Crohn's Disease and Beyond

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We have read with great interest the paper by Huang et al. [1], that aimed at evaluating the impact of preoperative treatment with anti-TNF agents (infliximab and adalimumab) on the length of resected bowel and at identifying risk factors for postoperative morbidity in patients undergoing ileocolic resection for Crohn's disease (CD). A total of 184 patients were included in this observational study of a prospective cohort: 66 (35.9%) patients received anti-TNF agents within 8 weeks before surgery. The mean length of the resected bowel was 10 cm shorter in those patients who had received preoperative anti-TNF therapy than those who had undergone ileocolic resection without preoperative treatment with anti-TNF ($P < 0.001$). The multivariate analysis showed that preoperative anti-TNF therapy was associated with a shorter length of the resected bowel. Systemic steroids, but not anti-TNF agents, were independent risk factors for overall complications and intra-abdominal sepsis, thus confirming the current evidence available in the literature.

This study brings some new interesting insights to the scientific community that handles with CD in the biologics era. During the last few decades, more and more patients with CD are receiving more intensive treatments, including anti-TNF drugs. However, the postoperative outcomes in terms of morbidity in patients preoperatively receiving anti-TNF and non-anti-TNF biologics are controversial [2], with some studies reporting increased complications [3, 4], and others similar morbidity rates [5]. The outcomes reported by Huang et al. support the evidence recently published by the Mayo Clinic group, showing 5.3% of intrabdominal septic complications in the anti-TNF group versus 4.4% in the non-biologic group in a retrospective analysis of 274 patients undergoing minimally invasive ileocolic resection for CD [6].

More importantly, the study by Huang et al. [1], fuels the debate if more intensive medical treatment might reduce the length of the resected bowel specimen. The potential clinical implications of this study are related to the fact that the preoperative administration of anti-TNF drugs might lead to shorter bowel resections, that in turns reflect into lower risk of short bowel syndrome in case of multiple bowel resections for CD recurrence, with no significantly increased perioperative morbidity and mortality. To date, there are only a few retrospective studies focused on this topic, reporting conflicting results. De Groof et al. [7]

retrospectively reviewed 195 patients undergoing ileocolic resection for CD between 1999 and 2014, aiming at evaluating if anti-TNF medical treatment might result in more limited ileocolic resection. Similar to Huang et al., 33% of patients ($N = 65$) were on anti-TNF before surgery. The comparison between patients exposed and non-exposed to anti-TNF showed a significantly longer time between diagnosis and surgical resection in the latter group, while no significant differences were observed in indications for surgery, age at surgery, operative time, conversion from laparoscopic to open surgery, stoma rate, postoperative morbidity. The length of the resected ileum was similar: 21 vs. 20 cm ($P = 0.87$). This result is consistent with that reported by Fu et al. in 2014 [8].

According to the existing controversy, further large prospective comparative (and possibly randomized) studies are needed to better define the role of these biologics in reducing the length of the resected specimens. Based on the study by Huang et al. [1], the use of anti-TNF biologics seems to achieve shorter specimens. However, we do not know if the length of the diseased bowel tract was already different before the medical treatment and before surgery in the two groups of patients. To date, there are no studies reporting robust evidence of a correlation between measurements done by radiologists and pathologists before and after medical therapy. Most importantly, the question that further studies will be asked to answer is: "Does the reduced resection reflect into higher rates of recurrence or not?" Indeed, if a diseased segment of bowel is not resected because it is in remission as a consequence of anti-TNF therapy, there is the theoretical risk of early recurrence in the same bowel segment after surgery when anti-TNF drugs are withdrawn.

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