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Letter to the Editor

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Comment on "The Severity of Rectal Inflammation and Pouch Surgery Outcome in Patients with Ulcerative Colitis: A Retrospective Cohort Study"

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Dear Editor,

We read with great interest the retrospective cohort study by Bækgaard et al., which investigates the association between preoperative rectal inflammation and ileo-pouch anal anastomosis (IPAA) outcomes in 434 patients with ulcerative colitis (UC).[1] This work addresses a critical clinical uncertainty—whether preoperative rectal inflammation should delay IPAA in refractory UC—and its use of standardized tools (eg, Nancy Index, Clavien-Dindo Classification) strengthens the reliability of findings. The long median follow-up (3133 days) further adds value, as it captures late-onset pouch failure, a key concern in UC surgical management. We commend the authors for advancing evidence to guide surgical timing decisions.

Critical Considerations and Constructive Reflections

While the study concludes that rectal inflammation does not increase the risk of pouch failure, three specific limitations warrant discussion to enhance its clinical applicability.

Initially, unaddressed data gaps can obscure potential correlations. The authors indicate that key variables have missing data: 12.7% (55/434) for preoperative BMI, 35.7% (155/434) for Mayo scores, and 10.8% (47/434) for pre-IPAA endoscopy status. The absence of Mayo scores, an endoscopic measure frequently used to direct UC management, is particularly troublesome. This is because macroscopic inflammation could be associated with outcomes in specific patient groups (for instance, those with severe mucosal friability). In comparable cohort studies on IPAA outcomes, multiple imputation has been demonstrated to mitigate bias from missing data by maintaining sample size and accounting for uncertainty.[2] The exclusion of this method here diminishes the confidence that the "no association" conclusion is not influenced by uneven missingness (eg, more missing data in patients with severe inflammation).

Secondly, the absence of centralized pathological review raises concerns regarding the consistency of the Nancy Index. The Nancy Index is validated for scoring UC histology, but its application relies on detailed documentation of crypt destruction and inflammatory infiltration.[3] The authors point out that pathology reports lacking Nancy grading were assessed by a single reviewer, without any inter-observer reliability assessment being conducted. In gastrointestinal pathology, inter-rater agreement for intermediate inflammation grades (eg, Nancy Grade 1-2) can be particularly variable—especially when original reports use ambiguous terms such as "mild inflammation" without providing crypt-level details.[3,4] A secondary review by an independent gastrointestinal pathologist could have reduced misclassification bias and enhanced the validity of inflammation-outcome analyses.

Third, subgroup analyses are necessary to clarify heterogeneous effects across surgical approaches. The cohort included patients with diverse surgical strategies: 62.7% underwent open surgery, 34.8% had laparoscopic IPAA, and 74.2% were performed with diverting ileostomies. Laparoscopic IPAA, which has been more widely adopted since 2000, is associated with lower perioperative morbidity, which could buffer any adverse effects of inflammation.[5] Similarly, diverting ileostomies reduce anastomotic pressure, potentially mitigating the risk of inflammation-related leakage. Stratifying outcomes by surgical approach or ileostomy use would clarify whether the "no association" finding holds uniformly—for example, in patients undergoing open IPAA without diverting stomas, who may face a higher baseline risk of complications.

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Actionable Recommendations for Future Research

Building on the strengths of this study, we propose three specific directions to refine IPAA outcome research:

1. *Implement a multi-center IPAA registry with standardized data capture*: A prospective registry that spans tertiary IBD centers should include mandatory variables (eg, complete preoperative inflammation assessments via Nancy Index/Mayo score, pouch failure etiologies) and patient-reported outcomes (eg, Pouchitis Disease Activity Index).[6] This would enable validation of the current findings in diverse populations and provide detailed data on why pouches fail (eg, refractory pouchitis vs. technical complications).
2. *Integrate biomarker profiling with clinical inflammation assessments*: Future studies should explore serum (eg, C-reactive protein) or fecal (eg, calprotectin) biomarkers alongside histologic/endoscopic measures.[7] Even if gross inflammation does not predict outcomes, a high fecal calprotectin level at surgery might identify patients at risk of late-onset pouchitis—enabling targeted post-operative monitoring.
3. *Develop a surgical timing algorithm for individualized care*: The current findings support moving beyond "wait for inflammation to resolve" protocols. A practical algorithm could weigh inflammation status against patient-specific factors (eg, symptom severity, quality of life, surgical approach) to guide decisions. For example, patients with severe UC symptoms but persistent inflammation could proceed with IPAA, while those with mild symptoms might delay surgery to optimize nutrition.

Conclusion

The study by Bækgaard et al. fills a critical gap in the surgical literature on ulcerative colitis (UC) by providing high-quality evidence that preoperative rectal inflammation does not increase the risks associated with ileal pouch-anal anastomosis (IPAA). This work has the potential to reduce unnecessary surgical delays for patients with refractory UC. The considerations and recommendations outlined above are intended to build on this foundation, ensuring that future research translates more directly to personalized clinical practice. We once again commend the authors for their rigorous approach and valuable contribution to inflammatory bowel disease (IBD) care.

Author Contributions

Xingmei Yang: Conceptualization, Writing—original draft, Writing—review & editing; Songqian Yang: Supervision, Writing—review & editing.

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Conflicts of Interest

The authors declare no conflicts of interest. X.Y. and S.Y. declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this comment.

Generative AI Use Statement

No generative AI tools were used in the preparation of this manuscript.

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