Are We Able to Accurately Assess Post IPAA Pathology?

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Post ileal pouch anal anastomosis (IPAA) pathology remains difficult to investigate, and thus truly difficult to understand. As a first step, we do not know how many patients are currently living in the United States with a pouch. Without a centralized database, we do not have an accurate denominator to define the real incidence and prevalence of acute pouchitis, chronic pouchitis, and Crohn disease of the pouch. In addition, even single center series are limited by lack of longitudinal follow-up, clinical follow-up only at times when patients are having trouble with their pouch rather than times of quiescent disease, and obtaining new pouch patients as pouch referrals without all the pre-IPAA data to understand the longitudinal disease course. While we do our best to extrapolate and compile data from various single center series, it is difficult to understand the reproducibility of the findings and application to multiple centers treating pouch patients. In attempt to overcome some of the limitations when studying pouch pathology, Barnes et al[1] in this issue of Crohn's and Colitis 360, utilized data from Sinai-Helmsley Alliance for Research Excellence, a multicenter prospective cohort database prospectively followed recruited pouch patients from 7 academic inflammatory bowel disease referral centers with follow-up questionnaires completed every 12 months.

Barnes et al set out to define resource utilization including medical therapy and surgical intervention post IPAA, and identify risk factors for acute pouchitis, chronic pouchitis, and Crohn disease of the pouch. The authors consented and enrolled at total of 468 pouch patients across the 7 centers and followed them for a median of 796 days. There were 3 things that were particularly striking about the findings in this cohort: (1) the use of biologics was quite high for both chronic pouchitis and Crohn disease of the pouch given the limited supporting data, (2) the rate of Crohn disease of the pouch, 41%, is much higher than that previously reported in single center series, and (3) the overall rate of pouch pathology seems remarkably high for an operation that we support so highly due to its good reported quality of life and functional outcomes.

At the start of the study, 11% of patients with chronic pouchitis and 50% of patients with Crohn disease of the pouch were taking biologics. Over the course of the study, at some point in their disease course, 25% of patients with chronic pouchitis and 70% of patients with Crohn disease of the pouch were taking biologic therapy. This rate of biologic use is quite high especially given the lack of supporting data. For chronic pouchitis, the rate of remission is approximately 10% with anti-tumor necrosis factor therapy, much lower than reported 64% reported with Crohn like complications of the pouch.[2] Similarly, vedolizumab is less effective in chronic pouchitis as compared to Crohn disease of the pouch,[3,4] and at the end of 14 weeks remission was variable between 14% and 64%. Even an investigation of ustekinumab found the same trend; 16% of those with chronic pouchitis had improved as compared to 84% with Crohn disease of the pouch.[5] Thus, while biologics may be useful, especially for Crohn disease of the pouch, they do not appear nearly as helpful for chronic pouchitis, underscoring the need for an accurate distinction between the 2 diagnoses.

However, this remains a challenge. Crohn disease of the pouch following a pre-IPAA diagnosis of ulcerative colitis is largely a clinical diagnosis given the limitations of finding pathognomonic transmural lymphoid aggregates and granulomas on pouchoscopy biopsy.[6] The challenge is that the inflammatory, fibrostenosing, and fistulizing phenotypes of Crohn disease can mimic alternative pathology. Chronic pouchitis can be difficult to distinguish from Crohn disease of the pouch, a chronic sinus or anastomotic leak may be mislabeled as a Crohn related fistula, and anastomotic stenosis may be thought to be related to Crohn disease. Thus, to make a diagnosis of Crohn disease of the pouch, one must consider the timing in relation to pouch construction and if there is additional supporting evidence (eg, proximal small bowel stricturing or skip lesions, upper gastrointestinal findings, or

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extraintestinal manifestations) that suggests Crohn disease vs complications from the pouch. The most commonly used definition is therefore a clinical diagnosis based on the development of proximal small bowel disease, stricture, or complex fistulas outside the ileoanal anastomosis and not on the findings of the pouch itself.[7] Without a consistent definition of Crohn disease of the pouch, it is difficult to determine the true incidence, but most single center series have reported rates ranging up to 10%—much lower than the 41% reported here.[7,8]

The largest series looking at longitudinal follow-up following IPAA report favorable outcomes.[9–12] A series from Cleveland Clinic by Fazio et al reported outcomes of 3707 IPAA patients and found that over a mean follow-up of 84 months, 33.9% reported pouchitis, 15.9% reported chronic pouchitis (defined as more than 3 attacks in a 12-month period), and only 5.3% reported pouch failure.[9] Other series have also reported chronic pouchitis at rates less than 20%.[8,13] And these rates are with duration of follow-up over 10 years. The study herein by Barnes et al in this issue of Crohn's and Colitis 360, reported that 80% had a pouch pathology of acute pouchitis, chronic pouchitis, or Crohn disease of the pouch. It is hard to understand whether this is a referral center bias given that all centers included are inflammatory bowel disease referral centers, or whether this is a bias of those patients interested and consenting for study inclusion had more problems with their pouch.

Regardless of potential center or patient bias, this study importantly highlights that pouch pathology is common. Thus, all patients should be appropriate counseled before IPAA as to what to expect in the early and late postoperative periods. While an IPAA offers a good quality of life and overall good durable pouch function, patients will have to develop a new normal way of experiencing bowel function and seek early attention when needed. As care providers, our job is to discover ways to better study the true incidence of pouch pathology, understand how these morbidities affect patients' quality of life, and determine patient preferences for restoration of intestinal continuity when fully educated about anticipated pouch function.

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