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EDITORIAL – GASTROINTESTINAL ONCOLOGY

Positive Margin for Low-Grade Appendiceal Mucinous Neoplasms (LAMN): To Observe or to Reoperate?

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Low-grade, appendiceal mucinous neoplasms (LAMNs) are rare and unique tumors of the appendix. Management options can be very broad, ranging from a simple appendectomy to cytoreductive surgery (CRS) with hyperthermic intraperitoneal chemotherapy (HIPEC) when there is peritoneal spread. Histologically, they are characterized by mucinous epithelium with low-grade cytologic atypia and absence of infiltrative growth, destructive invasion, or associated desmoplastic response.[1,2] These lesions are usually incidentally diagnosed after resection for suspected appendicitis and carry very low recurrence rates when completely resected, having disease confined to the appendix, and in the absence of rupture.[3] In these patients, appendectomy is almost invariably curative and further surgery, such as a right colectomy or ileocecectomy, is not needed.[4] However, some debate surrounds further management of resected LAMNs when there is a "microscopically positive margin" on final pathology.

In the study by Ibrahim et al., the authors try to answer this question of whether a positive resection margin for LAMN is associated with local recurrence.[5] They performed a retrospective analysis of their institution's pathology database from 2000 to 2020 to identify appendectomy specimens diagnosed as LAMN. Of the 98 patients identified, only eight had a positive margin. Of those, five underwent additional surgery; the remaining three had observation. In the five patients who had surgery (right colectomy or ileocecectomy), none had residual tumor on re-resection. Furthermore, none of the eight patients developed local recurrence or peritoneal disease over an average follow-up period of approximately 4 years. The authors also performed a literature review and found that none of the "uncomplicated" LAMN cases managed conservatively had disease recurrence. They concluded that in patients with uncomplicated LAMN and a positive margin, conservative management is a reasonable treatment choice.

One of the biggest issues with this study is the small sample size. Less than 100 patients were found over 20 years and ultimately only eight for further analysis. Performing a subset analysis on such a small group of patients makes obtaining meaningful results challenging. The authors attempted to correct this by pooling data from their cohort with those in the literature, thereby increasing the number of cases that meet inclusion criteria. Even then, some key granular data were missing. Nine of those 60 patients had no reported data on the type of treatment that they received following LAMN identification, making their inclusion in the "conservative management" arm questionable. Additionally, the surveillance strategy and frequency of follow-up for patients was not uniform. In their cohort, while five of eight patients underwent imaging, the remaining three only had physical examinations (without imaging) on follow-up making ascertainment of their true disease-free status possibly inaccurate. As with any retrospective analysis, additional confounding factors associated with why patients underwent additional surgery or why surgeons offered it versus observation are not known and could impact the results.

Despite the small sample size, the study population the authors used to answer this question was very appropriate. The patients were followed for a reasonable time period. With an average follow up of just less than 4 years, if patients were going to develop recurrence, it should have been detected. It is notable that the authors reevaluated all the pathology specimens to confirm the diagnoses of LAMN

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and the status of the resection margins according to the definitions they provided. This extra step is not often performed in retrospective studies, particularly ones that span a long time period, and warrants acclaim as it removes confusion regarding accurate assessment of a condition that still has much debate about terminology, despite PSOGI guidelines.[1]

The literature review presented in the manuscript is extensive, spanning more than three decades. The authors were diligent to select patients who satisfied the definitions that were presented in their manuscript in an effort to exclude any potential confounding factors that could have interfered with the findings. This also allowed for a uniform patient population where they could combine their institutional data with that from the literature to better answer this study question.

The results presented in this manuscript show that in patients with "uncomplicated LAMNs" with positive margins, conservative management without surgery is a reasonable approach. However, it needs to be emphasized that this is a very select group of patients. The authors are very clear that LAMN specimens cannot have evidence of perforation or scarring of the appendiceal wall and no cellular or acellular mucin on the serosal surface and mesoappendix. Furthermore, the appendix specimen requires detailed histologic examination and review by pathologists accustomed to this disease process and management by surgeons who are familiar with appendiceal neoplasms. Furthermore, all patients underwent surveillance, so when peritoneal recurrence does occur, these patients can be salvaged with surgery without impacting overall survival.

We applaud Ibrahim and colleagues for conducting a thorough investigation into identifying patients with uncomplicated LAMNs and a positive margin that can potentially forgo additional surgical resection. With the challenges of dealing with such a rare patient population, findings from projects such as this are needed to better understand this disease. We hope that these data can help to refine further the treatment strategies for patients with uncomplicated LAMNs.

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