What is the Incidence of Malignancy in Resected IPMN? An Analysis of Over 100 U.S. Institutions in a Single Year

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In this issue of the *Annals of Surgical Oncology*, Dr. Rym El Khoury and colleagues describe the current incidence of high-risk intraductal papillary mucinous neoplasms (IPMN) among pancreatic resections performed in the United States. They use the American College of Surgeons National Surgical Quality Improvement Project (ACS-NSQIP) dataset to address this question from a population-based perspective. With data available from more than 100 hospitals, approximately 10% of all pancreas resections in 2014 were performed for IPMN. This is in stark contrast to much lower rates published in older series.¹ High-risk disease (high-grade dysplasia or invasive cancer) was found in 23% of IPMN specimens.

The authors conclude the 23% rate of high-risk pathology among resected IPMNs is too low and therefore innovative biomarkers are needed to improve patient selection. This may not be the conclusion drawn by all readers. As mentioned in the article, the true incidence may have been higher if some pathology reports of adenocarcinoma did not report the IPMN component from which it arose. Even if we assume 20% accurately reflects the true incidence of high-risk pathology among resected IPMNs in the United States, it does not necessarily follow that 80% of the operations were of no utility. Some IPMN with low or moderate dysplasia may progress over time, and the rate and timing of this are not well described. Branch-duct IPMNs transition to malignancy in nearly 10% of patients after more than 5 years of surveillance.² Earlier

intervention for these patients even at the time of low-grade dysplasia might in fact be preferred, *if we could accurately predict which 10% will progress*.

In addition to reporting on the incidence of malignancy among resected IPMNs, the authors attempt to identify preoperative risk factors for high-risk pathology. This is limited, because some important factors are unavailable in the ACS-NSQIP database (e.g., imaging characteristics of the lesion). They do demonstrate that jaundice and weight loss are significant predictors. Presumably these factors motivated resection for many patients since the presence of symptoms is known to be associated with cancer risk in IPMN.³ One finding in the paper deserving special attention is the association of serum alkaline phosphatase with high-risk IPMN. Others have similarly reported this finding in addition to an association with serum CA 19-9.⁴ Elevated alkaline phosphatase increases the concern of experienced hepatopancreatobiliary surgeons in situations, such as indeterminate liver mass or pancreatic cystic lesion. The confirmation of this concern by the authors reminds us to continue teaching this clinical pearl to students and residents. Nevertheless, as the authors state, more sophisticated biomarkers are needed to accurately identify patients at risk for invasive disease, especially among those who are asymptomatic, as well as those at risk of progressing to invasive disease.

In the meantime, the surgical community is left wondering: what should the appropriate incidence of invasive disease be among IPMN specimens? The question is pressing in light of recent evidence that current international guidelines may not be adequate in helping surgeons best select patients.⁵ Presumably, if the incidence is too high, we may have allowed some IPMNs to progress to invasive disease while under surveillance. If the rate is too low, then perhaps some patients underwent resection unnecessarily if their IPMN was unlikely to progress to invasive disease during their lifetime. In the ultimate

question of surveillance versus resection for IPMN, we must admit this question primarily arises because of the complications associated with the pancreas operations. Endoscopic resection of completely benign polyps is widely endorsed as a means of preventing colorectal cancer. Are complications in low-risk IPMN patients more regrettable, because the operation is prophylactic not therapeutic? Should pancreatic surgeons weigh estimated risk more heavily in the decision to recommend operation for IPMN compared with cancer?

Dr. El Khoury and colleagues should be congratulated on this important study. With 10% of pancreas resections now being done for IPMN, we must be knowledgeable of the incidence of high risk lesions. Whether the current 23% incidence of high-risk IPMN is too low, too high, or just right remains to be debated. As with any IPMN under surveillance, time will tell.

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