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ASO Author Reflections: Improving Identification of Intraductal Papillary Mucinous Neoplasm Patients at Risk – Current Status and the Role of Molecular Biomarkers

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PAST

Within our generation, we have witnessed an evolution of surgery for cystic lesions of the pancreas, particularly intraductal papillary mucinous neoplasms (IPMNs).

Recommendations for surgical resection have progressed from resection of all lesions to resection of only selected IPMNs based on an estimation of malignant risk. Since the characterization and terminology of what constitutes an IPMN has evolved over the last 22 years since the WHO definition, the reported incidence of malignancy in surgically treated patients has fluctuated based on the time period of reporting. The purpose of the current study was to create a snapshot of the rate of malignancy in resected IPMNs that is reflective of the current surgical era post-establishment of recent international consensus guidelines.

PRESENT

This issue regarding which patients should undergo resection is only becoming greater as the number of incidental pancreatic cysts being evaluated is increasing exponentially secondary to ubiquitous cross-sectional imaging and advancements in imaging quality. This situation is further complicated since we only correctly identify the type of pancreatic cyst preoperatively approximately 50% of the time.¹ It is clear that there is a need to improve the accuracy of diagnosis and quantification of preoperative malignant risk. The decision on whether to perform surveillance or resection is challenging and is the topic of ongoing refinements to consensus guidelines. Although the sensitivity of these guidelines is satisfactory, the specificity remains poor.² Many guideline-negative lesions are found to harbor high-grade dysplasia or invasive cancer, and vice versa. Thus, the management of IPMNs is still an art that takes into account multiple variables and biases. Using a large national database, it was determined that 10% of all pancreatic resections are for IPMNs, and 77% of these lesions showed no evidence of high-risk disease.³ Although some may feel that this is appropriate to prevent progression to invasive disease of a cancer for which

current treatments are limited, it can be argued that, based on our limited understanding of the natural history of IPMNs, many of these lesions may be suitable for a surveillance strategy.

FUTURE

This information has not been previously established, and was critical to determine in order to define current surgical practice and to highlight areas of research that may help in both fine-tuning patient selection and advancing our understanding of the disease. Therefore, can we better predict the biologic behavior of incidental IPMNs preoperatively? Multiple oncogenes, tumor suppressor genes, glycoproteins, immune modulators, proteins, and genetic markers from tissue and IPMN fluid have been identified that can accurately differentiate low-risk from high-risk lesions.^{4,5} The next step for the field is to work collaboratively to pool resources and samples so that an optimal biosignature can be created and validated for this disease. In its final form, it is likely that preoperative prediction of biologic behavior will be a combination of molecular markers and radiographic variables. Although rare, an IPMN has become the most common cystic precursor lesion of pancreatic adenocarcinoma, and steps to improve our preoperative diagnostic accuracy of high-risk disease may enable the percentage of future resections to include less low-risk lesions while improving patient quality of life without the cost of missed malignancy.

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