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Editorial

Optimal Follow-up of Incidental Pancreatic Cystic Lesions without Worrisome Features: The Follow-up Strategy Is Still Evolving

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See "Optimal Follow-up of Incidental Pancreatic Cystic Lesions without Worrisome Features: Clinical Outcome after Long-term Follow-up" by Dong-Won Ahn, et al. on page 328, Vol. 18, No. 2, 2024

Surveillance of incidental pancreatic cysts, particularly presumed branch duct intraductal papillary mucinous neoplasms (BD-IPMNs) remains a challenge. The likelihood of malignancy is generally low in pancreatic cysts, which are more commonly found in elderly patients who often die from nonpancreatic-related diseases. In clinical practice, there is currently no consensus on the optimal method to surveil pancreatic cystic lesions, including the duration, interval, and discontinuation of the follow-up. Excessive surveillance frequency may cause a considerable burden on healthcare resources due to imaging costs and the risks associated with unnecessary procedures such as endoscopic ultrasound.[1] However, inadequate lengthening of the surveillance interval poses a significant concern for the malignant risk of the cyst itself or concomitant pancreatic ductal adenocarcinoma elsewhere in the pancreas. It is also unclear whether surveillance can be discontinued in patients with prolonged, stable incidental pancreatic cysts.

Therefore, it is welcome to see in this issue of the Journal, a study by Ahn *et al.*[2] from Korea evaluating the long-term clinical outcomes of incidental pancreatic cystic lesions for more than 10 years. The study showed that there was still a chance for malignancy to progress after 5 years of follow-up, and the majority of pancreatic cystic lesions without the development of worrisome features (WF) or high-risk stigmata (HRS) within 10 years had a good clinical prognosis even after 10 years. Optimal surveillance duration is an area of significant controversy. The American Gastroenterological Association proposes stopping surveillance after 5 years, if there are no changes in the cysts for 5 years after diagnosis.[3] In contrast, the American College of Gastroenterology, European Study Group, and International Association of Pancreatology recommend ongoing surveillance even after 5 years.[4] Although current guidelines have no consistency regarding follow-up intervals and the duration of surveillance, there is growing evidence to suggest that pancreatic cystic lesions may have a considerable risk of developing cancer, even after 5 years.

In this study, only 0.4% of the patients (1/227) had a risk of malignancy within 5 years; however, after 5 years, 1.4% of patients (3/210) developed malignancy. The findings of this study support the need for ongoing surveillance beyond 5 years for patients with pancreatic cystic lesions. However, it is difficult to draw definite conclusions from this study because not only the total number of enrolled patients (n=227) but also the number of patients with pancreatic cancer (n=4) was small. From a biological perspective, the risk of pancreatic cancer is anticipated to increase over time, not decrease. Studies have demonstrated that it can take 20 years for pancreatic cancer to develop after an initial mutation, providing a rationale for prolonging surveillance beyond 5 years. A multicenter prospective study in Japan, which evaluated 1,404 patients with IPMNs, found a cumulative incidence of pancreatic cancer of 3.3% at 5 years, 6.6% at 10 years, and 15% at 15 years.[5] However, the argument for stopping surveillance is that most patients with incidental pancreatic cysts will not develop pancreatic cancer and it is not feasible to follow patients indefinitely given the large number of patients with pancreatic cystic lesions. The approach of stopping surveillance after 5 years is supported by a retrospective study of 7,211 patients with pancreatic cysts in which only 79 (1.1%) developed

pancreatic cancer.[6] Similarly, a recent meta-analysis of 41 cohort studies reported that the malignant conversion rate during extended surveillance after 5 years for patients with stable BD-IPMN without WF or HRS at the 5-year time point was only 0.2%.[7]

The key question is how to identify the subgroup of patients, who are less or more likely to undergo malignant conversion after 5 years when considering the economic burden. The identification of this subgroup must be based on strong evidence of the natural history of BD-IPMN. Recently, a large-scale international cohort study by Han *et al.*[8] reported that malignant conversion was not observed in stable cysts that did not develop WFs during the initial 5-year surveillance, whereas it was observed in 12 changing cysts (1.7%). This finding suggests that patients with cysts smaller than 20 mm and who do not experience morphologic changes during the first 5 years of surveillance may consider stopping surveillance if they are unable to undergo surgery or have a life expectancy of 10 years or less.

At this time, there is not enough evidence to justify continuing surveillance for all incidental pancreatic cysts after 5 years according to the findings of this study. Equally, there are not enough data to support stopping surveillance universally after 5 years of stability based on the American Gastroenterological Association guidelines. The era of precision medicine can give a possibility that a combination of patient factors (age and comorbidity), cyst factors (histology subtype, presence of WF/HRS, cyst size), and more precise pancreatic cyst fluid biomarkers, will result in a more detailed and well-informed approach for stopping or continuing incidental pancreatic cysts surveillance.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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