Editorial

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Imaging for Screening/Surveillance of Pancreatic Cancer: A Glimpse of Hope

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Take-home points

- There are emerging opportunities in the early detection of Pancreatic ductal adenocarcinoma (PDAC) with improved outcomes in certain high-risk individuals using imaging surveillance with MRI/endoscopic ultrasound. Still, there remains a challenge regarding the feasibility of PDAC screening in general population where most PDACs occur.
- Surveillance with MRI is widely performed for patients with branch-duct intraductal papillary mucinous neoplasms (BD-IPMNs) although present imaging strategies may not be cost-effective. Further studies are needed to define a group that would benefit from a more intensive surveillance and another group that would not need surveillance by combining imaging and clinical/genetic features.
- Early-stage PDAC can be subtle on imaging, obscured by coexistent entities such as chronic pancreatitis or IPMNs. Focal pancreatitis can be misdiagnosed as PDAC. Therefore, screening for PDACs should be ideally performed in centers with high-volume pancreatic MRI and imaging expertise.

Keywords: Pancreas; Malignancy; Screening; Surveillance; Imaging

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Pancreatic ductal adenocarcinoma (PDAC) is highly lethal, with a 5-year survival rate below 10%. Early detection of PDAC, which enables surgical resection, is presently the only hope for curative treatment, and there has been increasing interest in screening for PDAC. However, the incidence of PDAC in the general population (lifetime risk < 2%) is unacceptably low. Even with very high specificity, a screening test would generate many false positives, potentially causing medical, financial, and emotional harm [1]. Further, imaging techniques and biomarkers have a limited capability in detecting early-stage PDAC or precursor lesions such as pancreatic intraepithelial neoplasia. Therefore, current screening efforts focus on high-risk individuals (HRIs) with a combination of family history and germline mutations. The results of earlier studies were disappointing due to a low detection rate of PDAC/precursor lesions as well as detection of advanced PDACs despite imaging surveillance.

RECENT PROMISING STUDIES ON SCREENING/ SURVEILLANCE OF PANCREATIC CANCER

Two recent studies from over 20 years of prospective data collection, utilizing MRI with or without endoscopic ultrasound (EUS), reported encouraging results that the surveillance of certain groups of HRIs leads to a detection of early-stage PDAC with improved resectibility and survival. The study by Klatte et al. [2] detected 36 PDACs in 347 carriers of a germline CDKN2A mutation with a cumulative incidence of 20.7% by age 70 years, 83.3% of whom were resectable with a 32.4% 5-year survival. Dbouk et al. [3] analyzed data combining Cancer of the Pancreas Screening (CAPS)–5 with other prior CAPS cohorts dating back to 1998 in genetic/familial HRIs. In their cohort, 5.15 PDACs were diagnosed per 1000 person-years of surveillance, and those with screen-detected PDAC showed a median survival of 9.8 years and

5-year survival of 73.3%. While these studies are impressive and promising, these HRIs with an underlying familial or genetic predisposition comprise only a small proportion of patients with PDAC. Unlike hepatocellular carcinomas where most cases occur in HRIs, the majority of PDACs occur sporadically without known risk factors.

SURVEILLANCE FOR PATIENTS WITH INTRADUCTAL PAPILLARY MUCINOUS NEOPLASMS

Intraductal papillary mucinous neoplasms (IPMNs) are recognized as a precursor of PDAC, which can develop from the cystic lesions or at a location different from the site of the cystic lesions [4]. Presently, patients with small branch-duct (BD) IPMNs are the most widely accepted population for imaging surveillance. Improved MRI technologies have enabled the detection of tiny pancreatic cystic lesions of presumed BD-IPMNs. These comprise many abdominal MRI examinations in various radiology practices, imposing an economic burden on healthcare systems and MRI availability. However, the efficacy and cost-effectiveness of adopting this surveillance are debatable [5]. The malignancy rate in BD-IPMNs entering surveillance is considerably low [6]. Suboptimal specificity in detecting malignancy leads to a substantial number of unnecessary surgeries for lesions with low-grade dysplasia due to worrisome features detected on imaging surveillance [7]. Further, PDACs are often caught with a locally advanced or metastatic stage, even when annual MRI surveillance is applied. IPMNs are known to be more prevalent among patients with familial pancreatic cancer or hereditary cancer predisposition syndromes [8]. Other clinical risk factors include age, new-onset diabetes, and elevated serum carbohydrate antigen 19-9. Further studies focusing on a better risk stratification of developing malignancy in BD-IPMNs by combining imaging and clinical/genetic parameters are needed to define a group that would benefit from a more intensive surveillance and another group that would not need surveillance. The need for discontinuation of surveillance of stable BD IPMN for a certain period of time should be also defined with evidence.

IMAGING TECHNIQUES

Regarding the imaging modalities for PDAC screening, transabdominal ultrasonography is easily accessible but has a suboptimal diagnostic performance [9]. CT has more than 90% sensitivity for detecting solid pancreatic nodules, but the sensitivity declines to approximately 77% for small (< 2 cm) tumors that can be iso-attenuating to the pancreatic parenchyma. Moreover, CT has inferior diagnostic performance compared with MRI/EUS in characterizing small cystic lesions [10]. Besides, radiation exposure and the risk of contrast-induced nephropathy are limiting factors for using CT as a screening tool. CT is still an alternative to MRI in patients with claustrophobia or pacemakers [11].

Typically, surveillance for PDAC is performed annually using MRI and EUS alternatively [11]. Both have similar diagnostic performance in differentiating cystic from small solid lesions and evaluating features of the cystic lesions, including septa, mural nodules, communication with the main pancreatic duct (MPD), and MPD dilatation. MRI is non-invasive and more widely available than EUS; however, EUS has shown a superior sensitivity for detecting sub-centimetre lesions and has the advantage of tissue sampling if needed [9]. Interestingly in the study by Klatte et al. [2], most PDACs were detected on MRI, but the number of performed MRIs was at least ten times higher than EUS.

Standardized MRI, including MR cholangiopancreatography and dynamic contrast-enhanced images, is preferred over unenhanced MRI because solid tumours can be missed on unenhanced MRI sequences alone [11]. Some pitfalls of early PDAC detection on MRI include increased susceptibility to motion artifacts and underlying chronic pancreatitis that causes pancreatic heterogeneity, obscuring small tumors. Also, focal pancreatitis may be indistinguishable from PDAC on imaging, and EUS-guided biopsy may be necessary. Scrutinizing the MPD for any new stricture helps detecting a small PDAC, given its high specificity as a secondary sign of an underlying obstructive PDAC [12]. Given these diagnostic challenges, imaging surveillance requires an expertise in centers with high-volume MRI for pancreatic abnormalities, and multidisciplinary teams should discuss the management of the detected lesions. This certainly limits the widespread use of imaging surveillance in larger population.

CONCLUSION

In summary, recent studies of PDAC screening with MRI/EUS shed a hope for an opportunity to detect early PDACs and improve patients' outcomes in certain HRIs [2,3]. However, it should be noted that most PDACs occur sporadically in patients without known risk factors in whom present screening methods are not cost-effective.

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Further studies are needed to widen appropriate high-risk populations that would benefit from screening and to optimize imaging modalities and intervals of surveillance.

Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

Author Contributions

Conceptualization: all authors. Supervision: Tae Kyoung Kim. Validation: Tae Kyoung Kim. Writing—original draft: all authors. Writing—review & editing: all authors.

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