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Cystic pancreatic lesions: when to watch and when to act?

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Cystic pancreatic lesions (CPLs) have gained significant attention in recent years due to their increased detection based on the development of different imaging techniques especially with the widespread use of cross-sectional imaging. These lesions, which can range from benign pseudocysts to potentially malignant intraductal papillary mucinous neoplasms (IPMNs), present a complex clinical challenge, particularly regarding their management. The presence of these lesions has become a significant burden on healthcare systems, as clinicians struggle to differentiate between benign lesions and those with malignant potential.

As a result, surveillance, treatment strategies, and decisions related to the risk of malignancy remain central issues in the management of CPLs. This editorial integrates insights from recent literature and explores the evolving landscape of managing CPLs, with a particular focus on malignant risk, surveillance approaches, and treatment strategies.

The rise in the detection of CPLs is largely attributed to advances in imaging modalities such as magnetic resonance imaging (MRI) and magnetic resonance cholangiopancreatography (MRCP), which have revealed that these lesions are not as rare as once thought. It has been reported that as many as 36.7% of cases present incidentally IPMNs on MRCP, especially among older populations (1). These CPLs can be divided into two broad categories: benign lesions such as serous cystadenomas (SCNs) and pseudocysts, and potentially malignant lesions, including mucinous cystic neoplasms (MCNs) and IPMNs (2).

IPMNs, particularly branch-duct (BD) variants, are the most commonly detected CPLs and present a major clinical challenge in terms of management. Although many of these BD-IPMNs are small, stable, and establish a minimal risk of malignant transformation (3), it remains uncertainty about when to prevent, treat, or just simply observe. In the other hand ~~contrast~~, main duct (MD) IPMNs carry a much higher risk of malignancy, with studies showing that malignancy rates for MD-IPMNs can range from 36% to over 90%, depending on various factors, such as cyst size, presence of mural

nodules, or duct dilation (2). This variability necessitates a precise risk stratification to guide the appropriate management decisions.

Assessing the risk of malignancy in CPLs is a delicate task. Recent studies have provided useful insights into how to stratify the risk of malignant transformation; however consensus remains lacking. The risk of malignancy in CPLs is often linked to the size of the cystic lesion, presence of high-risk features, and the specific type of CPLs. For example, large cysts, greater than 3 cm, cysts with mural nodules, or those with an enlarged main pancreatic duct are considered high-risk stigmata and typically warrant surgical intervention (4). However, these criteria also present some limitations. Studies have shown that a large proportion of BD-IPMNs, particularly those under 15 mm without high-risk or worrisome features, are unlikely to transform into invasive cancer, even when followed for large periods.

The concept of "trivial cysts" (5) has also emerged in recent research, referring to BD-IPMNs without high-risk features and remain stable for at least five years. For patients aged 65 or older, the likelihood of malignancy in such cysts is minimal, and the risks associated with continuing surveillance or surgical intervention may outweigh the benefits. Furthermore, studies have suggested that surveillance may be safely discontinued in patients over 75 years old, particularly when a cyst has remained stable for five years (6).

Despite these advances, significant challenges remain to be solved in terms of standardizing risk assessments. Different guidelines, such as those from the American Gastroenterological Association (AGA) and the International Association of Pancreatology (IAP), recommend varying approaches for surveillance intervals, highlighting the need for individualized, patient-centered strategies that consider age, comorbidities, and the cyst's characteristics.

Surveillance for CPLs remains a cornerstone of management, particularly in asymptomatic, low-risk lesions. The goal of surveillance is to detect early signs of

malignant transformation ~~early~~, enabling timely intervention. However, as the number of patients diagnosed with CPLs increases, the burden of surveillance has become a concern. Surveillance involves a combination of imaging techniques, such as MRI, MRCP, and endoscopic ultrasound (EUS), which can be costly and consuming big resource. Furthermore, the psychological burden of living with the uncertainty of a potentially malignant lesion can be significant for patients.

A critical issue in CPLs surveillance is the lack of consensus on the optimal duration and frequency of follow-up. Current guidelines suggest follow-up intervals that vary from six months to several years, depending on the type and characteristics of the CPLs (7). However, studies have indicated that surveillance may not always be necessary for all patients, particularly those with benign, stable lesions or those in whom the risk of surgery outweighs the potential benefits. The notion of "de-escalating surveillance" for certain patient populations, especially elderly individuals with comorbidities or those with trivial cysts, is gaining traction in the literature. By discontinuing surveillance for these patients, healthcare systems could better allocate resources and reduce unnecessary interventions. Unlike other cancer screening programs and strategies (8), there is no established age limit for starting or stopping surveillance of CPLs. Only the ACG guidelines (9) dare to establish 75 years as a limit after which the need for follow-up should be reconsidered. However, it is not specified whether it is appropriate to start follow-up from this age.

For CPLs with high-risk features or those suspected of harboring malignancy, surgical intervention has traditionally been the mainstay of treatment. However, the decision to perform surgery is hampered with multiple challenges. Pancreatic surgery, including pancreaticoduodenectomy or distal pancreatectomy, carries significant morbidity and mortality, particularly in older patients with comorbidities. Therefore, the decision to proceed with surgery must carefully weigh the patient's overall health, the risk of malignancy, and the potential benefits of surgical intervention (10).

In response to these challenges, alternative treatment strategies have emerged. EUS-guided ablation techniques, such as ethanol lavage, radiofrequency ablation, or EUS-guided laser ablation, offer a less invasive option for patients who are not candidates for surgery and for treating high-risk CPLs while minimizing patient morbidity (11).

Additionally, the increasing role of molecular diagnostics in CPLs cannot be overlooked. Next-generation sequencing of cyst fluid could help to identify genetic mutations, such as those in the KRAS and GNAS genes, which are associated with a higher risk of malignant transformation. The integration of genomic data with traditional imaging and clinical information may lead to more personalized and precise treatment strategies, allowing for better prediction of malignancy risk and more targeted surveillance.

As the understanding of CPLs continues to evolve, there is a growing shift toward personalized, risk-adapted management strategies. Emerging technologies, including artificial intelligence (AI), could further refine risk prediction models by integrating clinical, radiological, and molecular data.

Incorporating patient-reported outcomes into decision-making processes will also become increasingly important. The psychological impact of living with a pancreatic cyst, coupled with the uncertainty of its potential for malignancy, cannot be ignored. Future studies should explore how surveillance and treatment strategies affect patients' quality of life, mental health, and overall well-being, and incorporate these factors into clinical guidelines.

CPLs represent a growing challenge in gastroenterology, as their detection becomes more prevalent, and their management is increasingly complex. While many CPLs are benign and require only observation, others carry a significant risk of malignant transformation. The key to effective management relies in an accurate risk stratification, which can guide decisions regarding surveillance and treatment. As we move towards more personalized, patient-centered approaches, it is crucial to balance

the benefits of early detection and intervention with the risks of overtreatment and the psychological burden on patients. Advances in molecular diagnostics and imaging, combined with improved patient education and shared decision-making, will be essential in shaping the future of CPLs management. The goal is not only to improve patient outcomes but also to ensure that care is compassionate, cost-effective, and aligned with individual patient needs.

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