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REVIEW ARTICLE

Tailored Surveillance Strategies for Pancreatic Cancer in Patients with Chronic Pancreatitis

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Chronic pancreatitis, a significant risk factor for pancreatic cancer, necessitates monitoring for pancreatic cancer development. Chronic pancreatitis can be broadly categorized into hereditary and sporadic. Given the variability in the risk for pancreatic cancer based on the presence and type of genetic mutations, it is crucial to establish and be aware of guidelines for screening and surveillance tailored to each risk level. In cases of hereditary chronic pancreatitis with *PRSS1* mutations, patients demonstrated a high incidence of pancreatic cancer, justifying the rationale for screening and surveillance. However, the incidence of pancreatic cancer is relatively low in hereditary chronic pancreatitis with other genetic mutations and sporadic chronic pancreatitis; thus, precise screening and periodic surveillance are not recommended. For individuals with *PRSS1* mutation-related hereditary chronic pancreatitis, surveillance may be considered from the age of 40 years. While computed tomography or magnetic resonance imaging is suitable for pancreatic cancer screening, endoscopic ultrasonography is not recommended because of parenchymal inflammation, fibrosis, and calcification. However, in cases of sporadic chronic pancreatitis where various risk factors for pancreatic cancer coexist, the incidence of pancreatic cancer significantly increases. Therefore, in 5 years after the diagnosis of chronic pancreatitis, the pancreatic cancer incidence has been observed to continuously increase. In such cases, individualized screening tests and surveillance based on the patient's symptoms and specific circumstances must be considered.

Key Words: Chronic pancreatitis; Pancreatic neoplasms; Hereditary pancreatitis; Population surveillance

INTRODUCTION

In general, determining whether to conduct screening for a specific disease depends on the prevalence of the disease, the accuracy of the screening test, and the cost-effectiveness ratio of the screening. For screening to be justified, the ratio of true positives to false positives must be at least 1. Pancreatic cancer occurs at a rate of about 10 per 100,000 people annually worldwide, and chronic pancreatitis affects about 5–12 per 100,000 people, making it relatively uncommon. Therefore, it is not recommended to perform screening tests for all patients with chronic pancreatitis from an opportunity cost perspective. It is necessary to selectively monitor patients with chronic pancreatitis who are at high risk for pancreatic cancer. Additionally, appropriate screening methods for high-risk chronic pancreatitis patients requiring periodic pancreatic cancer screening have not yet been established. This paper aims to examine the classification of patients with chronic pancreatitis who require pancreatic cancer surveillance and the methods of monitoring.

MAIN SUBJECTS

Screening for pancreatic cancer in patients with hereditary chronic pancreatitis

Numerous studies have been conducted on the incidence and relative risk of pancreatic cancer in patients with chronic pancreatitis. Reported pancreatic cancer incidence rates in patients with chronic pancreatitis range from 0.7% to 2.9%, with relative risks varying from 7.6 to 68.1 times compared to the general population [1,2]. While chronic pancreatitis is a major risk factor for pancreatic cancer, international guidelines established in 2020 do not recommend routine pancreatic cancer screening for all chronic pancreatitis patients, considering the cost-effectiveness ratio [2]. However, hereditary pancreatitis shows a standardized incidence ratio of 53–87 times higher, particularly with *PRSS1* gene mutations, justifying regular surveillance for pancreatic cancer in these patients. Unlike sporadic chronic pancreatitis, autosomal dominant hereditary chronic pancreatitis with *PRSS1* gain-of-function mutations poses an extremely high relative risk of pancreatic cancer, up to 87 times.

The largest cohort study on *PRSS1* hereditary pancreatitis, the EUROPAC study, found that 26 out of 418 patients (6.2%) were diagnosed with pancreatic cancer [3]. Similarly, other cohort studies by the American Pancreatic Association and International Association of Pancreatology reported that 8 out of 246 *PRSS1* hereditary pancreatitis patients developed pancreatic cancer, with the risk increasing after age 40 [4]. Although there is no independently studied clear recommendation for the screening interval, the 2020 clinical guidelines by the American Gastroenterological Association suggest an annual screening interval for high-risk patients, including those with *PRSS1* hereditary pancreatitis [5]. Abnormal findings such as main pancreatic duct strictures or solid lesions smaller than 1 cm, or new-onset diabetes, may necessitate shortening the observation interval to 3–6 months. In *PRSS1* hereditary pancreatitis patients, the incidence of pancreatic cancer before age 40 is almost negligible, so surveillance is recommended to start after 40 and be discontinued when surgical treatment is no longer appropriate, according to expert consensus.

Standard imaging modalities for diagnosing pancreatic cancer, including computed tomography (CT), magnetic resonance imaging (MRI), and magnetic resonance cholangiopancreatography, are useful in screening for pancreatic cancer in chronic pancreatitis. Although endoscopic ultrasound (EUS) is valuable for early tumor detection in normal pancreatic parenchyma, it is not recommended for use in chronic pancreatitis due to difficulties distinguishing early tumors amid parenchymal inflammation, fibrosis, and calcification. Intensive pancreatic cancer surveillance and precise examination for *PRSS1* hereditary pancreatitis patients are strongly recommended by the 2020 international consensus guidelines (International Association of Pancreatology, American Pancreatic Association, Japan Pancreas Society, and European Pancreatic Club). However, other genetic mutations such as *SPINK1*, *CFTR*, *CTRC*, *CPA1*, and *CEL* do not justify screening and follow-up tests due to lower pancreatic cancer risks.

Screening for pancreatic cancer in patients with sporadic chronic pancreatitis

In clinical practice, sporadic chronic pancreatitis is more commonly encountered than hereditary chronic pancreatitis. The incidence of pancreatic cancer in sporadic chronic pancreatitis is relatively low compared to *PRSS1* hereditary pancreatitis (0.6–2.9% vs. cumulative incidence rates at age 50: 10.0%, age 60: 19.0%, age 75: 53.5%), making routine surveillance for pancreatic cancer unjustifiable in all sporadic chronic pancreatitis patients. However, when high-risk factors for pancreatic cancer coexist in sporadic chronic pancreatitis patients, proactive surveillance may be necessary considering the increased risk. Previous studies have identified factors such as obesity, pancreatic duct dilation, bile duct stricture, old age, new-onset diabetes, smoking, and alcohol consumption as highly associated with pancreatic cancer development in chronic pancreatitis [6]. The relative risks for newly diagnosed diabetes, pancreatic duct dilation, and bile duct dilation were 10.7, 10.5, and 9.2 times, respectively.

According to a retrospective study in Korea, among 727

patients diagnosed with chronic pancreatitis, pancreatic cancer was diagnosed in 16 patients (2.2%, annual incidence rate of 0.5%) over a median follow-up period of 3.6 years (range: 1.0–12.9 years) [7]. The average interval between chronic pancreatitis diagnosis and pancreatic cancer diagnosis was 2.4 years (range: 1.4–6.6 years). Pancreatic cancer patients were older and had more frequent exacerbations of pancreatitis and higher CA 19-9 levels. Among the 16 patients who developed pancreatic cancer, the characteristics of chronic pancreatitis were classified as follows: 10 patients (62.5%) with chronic obstructive pancreatitis, 4 patients (25.0%) with chronic obstructive and calcifying pancreatitis, 1 patient (6.3%) with chronic calcifying pancreatitis, and 1 patient (6.3%) with autoimmune pancreatitis. Factors associated with pancreatic cancer development included older age (hazard ratio [HR]: 4.830, p = 0.006), pancreatic duct stricture (HR: 2.706, p = 0.048), and high CA 19-9 levels (HR: 3.567, p = 0.014). Especially, age over 60 years (HR: 4.540, p = 0.009) and serum CA 19-9 levels over 100 U/mL (HR: 3.528, p = 0.015) were independent risk factors for pancreatic cancer. The combined presence of these factors is believed to further increase the risk, although specific studies on the extent of their interaction and the optimal surveillance strategies for pancreatic cancer are still lacking.

According to a meta-analysis, the risk of pancreatic cancer after a diagnosis of chronic pancreatitis is 6.09 times higher after 1 year, 16.16 times higher after 2 years, 7.90 times higher after 5 years, and 3.53 times higher after 9 years. This indicates that the incidence of pancreatic cancer remains significantly elevated for about 5 years following the diagnosis of chronic pancreatitis, with the highest risk occurring within the first 2 years and then declining thereafter [1]. These results suggest that the risk of pancreatic cancer remains significantly high for a long duration after chronic pancreatitis diagnosis, highlighting the importance of long-term and consistent surveillance for early detection.

Currently, there are no clear guidelines for the most appropriate screening method for pancreatic cancer in sporadic chronic pancreatitis patients. While CT or MRI is recommended, there is insufficient consensus and expert agreement, and EUS is not recommended due to difficulty in distinguishing early tumors amid inflammation, fibrosis, and calcification.

CONCLUSION

The risk of pancreatic cancer varies significantly depending on the presence and type of genetic mutations in chronic pancreatitis, making it essential to establish guidelines for pancreatic cancer screening tailored to each risk level. While pancreatic cancer surveillance is justified for *PRSS1* hereditary chronic pancreatitis, screening and periodic follow-up are not yet recommended for hereditary chronic pancreatitis with other genetic mutations and sporadic chronic pancreatitis. Surveillance can be considered for *PRSS1* hereditary chronic pancreatitis patients starting at age 40, with CT or MRI as suitable screening methods, but not EUS. In sporadic chronic pancreatitis patients with various pancreatic cancer risk factors, the incidence of pancreatic cancer significantly increases. Therefore, pancreatic cancer screening and surveillance based on individual symptoms and circumstances can be considered during the first five years after chronic pancreatitis diagnosis, when the incidence of pancreatic cancer remains high.

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CONFLICTS OF INTEREST

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

AUTHOR'S CONTRIBUTIONS

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