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Risk of pancreatic cancer after acute pancreatitis: A population-based matched cohort study

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ABSTRACT

Background: We investigated the short- and long-term risks of pancreatic cancer after the diagnosis of acute pancreatitis.
Methods: This population-based matched-cohort study used data from the Korean National Health Insurance Service database. Patients with acute pancreatitis (n = 25,488) were matched with the control group (n = 127,440) based on age, sex, body mass index, smoking status, and diabetes. We estimated the hazard ratios for developing pancreatic cancer in both groups using Cox regression analysis.
Results: During a median follow-up of 5.4 years, pancreatic cancer developed in 479 patients (1.9%) in the acute pancreatitis group and 317 patients (0.2%) in the control group. Compared with the control group, the risk of pancreatic cancer in the acute pancreatitis group was very high within the first 2 years, which gradually decreased over time. The hazard ratio for the risk of developing pancreatitis was 8.46 (95% confidence interval, 5.57–12.84) at 1–2 years, and then decreased to 3.62 (95% confidence interval, 2.26–4.91) at 2–4 years. However, even after 8–10 years, the hazard ratio was still statistically significantly increased to 2.80 (95% confidence interval, 1.42–5.53). After 10 years, there was no significant difference in the risk of pancreatic cancer between the two groups.
Conclusions: The risk of pancreatic cancer increases rapidly after acute pancreatitis diagnosis, gradually declines after 2 years, and remains elevated for up to 10 years. Further studies are needed to determine the long-term effects of acute pancreatitis on the risk of pancreatic cancer.

1. Introduction

The etiology of pancreatic cancer remains unclear. Smoking, obesity, diabetes, chronic pancreatitis, and genetic factors are widely known as risk factors for pancreatic cancer, and dietary habits and alcohol abuse have been reported as possible risk factors [1–3]. Acute pancreatitis is one of the most common gastrointestinal diseases that cause hospitalization worldwide [4]. Although gallstones and alcohol use are the most common causes of acute pancreatitis, pancreatic cancer is also an important cause that accounts for approximately 1.7–3.6% of all acute pancreatitis cases [5]. Acute pancreatitis is also known to be one of the early clinical manifestations of pancreatic cancer.

The association between acute pancreatitis and pancreatic cancer has not been clearly established as there are differences between reports. Most studies involved a small number of patients, and only a few large-scale studies have been conducted [6–8]. Population-based cohort studies have suggested that acute pancreatitis may be a risk factor for pancreatic cancer [5–9]. This association is mainly observed in cases of recurrent acute pancreatitis or its progression to chronic pancreatitis [7,10]. A meta-analysis indicated that acute pancreatitis might not be a risk factor for pancreatic cancer over a long period [11]. A recent population-based study reported that the risk of pancreatic cancer increased in the long term after acute pancreatitis, regardless of its etiology, and increased in proportion to episodes of recurrences [8]. Most previous studies were limited in that confounding factors could not be adjusted for. Furthermore, most of these studies have been conducted in Western countries, and studies on Asian populations are scarce. In addition, no study has considered smoking,

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diabetes, and obesity, which are the main risk factors for pancreatic cancer, in the control group.

We recently reported the risk factors for pancreatic cancer in Koreans [12]; therefore, matching risk factors with the control group was possible. We conducted this risk factor-matched cohort study to investigate the incidence of pancreatic cancer in the short and long terms after acute pancreatitis. This study aims to contribute to the early diagnosis of pancreatic cancer following acute pancreatitis and the selection of patients at high risk for pancreatic cancer.

2. Methods

This study was approved by the Institutional Review Board of National Health Insurance Service Ilsan Hospital (NHIMC 2021-03-017). The Board waived the requirement for informed consent because anonymized raw data were obtained from the database of the National Health Insurance Service (NHIS) of Korea. This study was conducted in accordance with the principles of the Declaration of Helsinki.

2.1. Data source

This study was based on data obtained from the NHIS database between 2002 and 2017, and the National Health Screening (NHS) program database between 2005 and 2006. The NHIS database includes all information about the medical services provided to patients, accounting for >98% of the Korean population. Furthermore, we used the NHS program database to obtain information regarding health and behavior. The NHIS recommends that subscribers and dependents participate in a standardized medical examination at least biennially [13].

2.2. Study population

The subjects of this study were selected from the population included in our previous study on risk factors for pancreatic cancer in Koreans [12]. Herein, we describe the process of identifying these cases. In this study, a two-step process was used to select subjects. The first step was the identification of subjects without a history of pancreatic diseases or cancer at the time of the health examination, which was performed as follows. Among the NHS participants from 2005 to 2006, those younger than 40 years, those with a cancer diagnosis between 2002 and the year of the health examination, and those with missing variables were excluded. In addition, subjects with a diagnosis code of acute or chronic pancreatitis, pancreatic cystic diseases, or benign neoplasms before the health examination were excluded. In the second step, we identified all patients with a first diagnosis of acute pancreatitis after the health examination, with the date of the first diagnosis of acute pancreatitis considered the index date. We also identified a control group with no history of acute pancreatitis prior to the index date. Patients with pancreatic cancer, chronic pancreatitis, pancreatic cystic disease, or benign neoplasms between the health examination and index date were excluded. Patients diagnosed with acute pancreatitis and pancreatic cancer during the same index admission period were excluded. Patients diagnosed with pancreatic cancer who were hospitalized within 3 days post-discharge after treatment for acute pancreatitis were considered to have the same index admission and were excluded.

2.3. Propensity score matching

Propensity score matching was used to select the control group and eliminate possible confounding factors. Obesity, smoking, and diabetes have been identified as significant risk factors for pancreatic cancer in several studies [1,14,15], including in our recent study in Koreans [12]. Therefore, unlike previous studies, these variables were used as matching variables in the present study. Propensity scores were derived from the predicted probabilities of subjects with and without acute pancreatitis using a logistic regression model adjusted for age, sex, body mass index (BMI), smoking status, and diabetes. A “greedy nearest-neighbor” algorithm was used to match patients in the two groups in a 1:5 ratio [16].

2.4. Categorization of variables at the health examination

Age was classified in 10-year intervals, and the income level was stratified into quintiles. BMI was calculated as weight divided by height squared (kg/m^2) and categorized as underweight or normal-weight (<23.0 kg/m^2), overweight (23.0–24.9 kg/m^2), and obese (≥25.0 kg/m^2) by modifying the World Health Organization (WHO) criteria for Asian populations [17]. Smoking status was categorized into non-smokers, former smokers, and current smokers. Alcohol intake was categorized as non-drinking, drinking 2–3 times per month, and drinking 1–2 times, 3–4 times, and ≥5 times per week. Physical activity was categorized as no exercise, and exercising 1–2, 3–4, and ≥5 times per week. Diabetes was defined as the presence of at least two claims per year with an ICD-10 code for diabetes (E10–14) during the year preceding the health examination, the identification of diabetes in a previous medical history questionnaire, or a blood fasting glucose level ≥126 mg/dL at a health examination. We calculated the Charlson comorbidity index (CCI) for each subject using ICD-10 diagnostic codes reported in NHIS from 1 year before the health examination and classified the values as 0, 1 and ≥ 2 [18,19].

2.5. Definition of disease conditions

Acute pancreatitis was defined as hospital admission with a primary diagnosis of acute pancreatitis (ICD-10 code, K85). Patients with an acute pancreatitis diagnosis code only as an outpatient were not considered as having acute pancreatitis. Chronic pancreatitis was defined as a diagnosis of chronic pancreatitis (K86) based on inpatient or outpatient claims. Pancreatic cystic diseases or benign neoplasms were defined using the diagnosis codes D136 (benign neoplasm of the pancreas), D377 (neoplasm of uncertain or unknown behavior of the pancreas), and K862 (cyst of the pancreas).

2.6. Follow-up and outcomes

All subjects in the acute pancreatitis and control groups were followed up from the diagnosis of acute pancreatitis (or the index date for the matched control group) until December 31, 2017, the date of diagnosis of pancreatic cancer, or death, whichever occurred first. Subjects in the control group were followed up for the same period as the matched patients in the same manner (Fig. 1). Newly developed pancreatic cancer during follow-up was defined as ICD-10 code C25 (pancreatic cancer) combined with claims to the NHIS for a rare and intractable disease (RID) registrations. Since 2005, newly diagnosed cancer patients have been registered in the RID program and reimbursed for medical expenses by the NHIS. This registration process ensures the reliability of cancer diagnosis [20].

2.7. Statistical analysis

Statistical analyses were conducted using the $\chi 2$ test and independent *t*-test to investigate differences in variables. Continuous

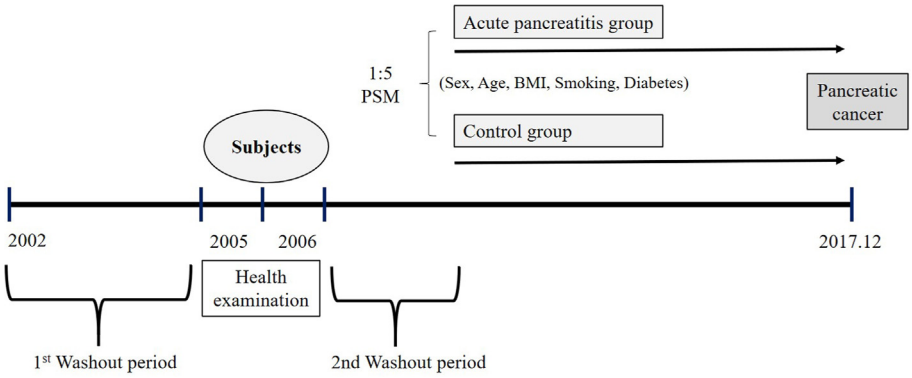

Fig. 1. The study design. PSM: propensity score matching, BMI: body mass index.

variables are presented as medians with interquartile ranges (IQRs). The cumulative incidence of pancreatic cancer was estimated using the Kaplan–Meier method, and the log-rank test was used to compare the differences between groups. Since there was a significant deviation in the hazard ratio (HR) according to the follow-up period, the follow-up period was divided into the following 10 groups: ≤2 months, 2–4 months, 4–6 months, 6–12 months, 1–2 years, 2–4 years, 4–6 years, 6–8 years, 8–10 years, and >10 years. Cox proportional hazard regression analysis with 95% confidence intervals (CIs) was used to determine the risk of pancreatic cancer in both groups after adjusting for sex, age, income level, BMI, smoking status, alcohol intake, physical activity, diabetes, and CCI. All statistical analyses were performed using SAS version 9.4 (SAS Institute, Inc., Cary, NC, USA) with a significance level of 5%.

3. Results

3.1. Study population

A total of 12,248,104 individuals who participated in an annual or biennial NHS program between 2005 and 2006 were identified from the NHIS data. After applying the eligibility criteria, 7,480,596 participants with no history of pancreatic diseases or cancer at the health examination were selected in the first step. Among these subjects, 28,946 had newly developed acute pancreatitis after the health examination. Finally, 25,488 patients with acute pancreatitis were included in acute pancreatitis group, excluding patients with pancreatic diseases between the health examination and diagnosis of acute pancreatitis (n = 2,706) and those diagnosed with acute pancreatitis and pancreatic cancer at the same index admission (n = 752). Among the subjects who did not develop acute pancreatitis after the health examination, 127,440 were selected as the control group using 1:5 propensity score matching (Fig. 2).

Table 1 shows the characteristics of the acute pancreatitis and matched control groups. After adjusting for sex, age, BMI, smoking status, and diabetes, no significant differences were found between the acute pancreatitis and control groups.

3.2. Pancreatic cancer incidence

In both groups, the median follow-up duration was the same at 5.4 (IQR 2.6–8.4) years. During the follow-up period, 479 patients (1.9%) in the acute pancreatitis group (n = 25,488) and 317 patients (0.2%) in the control group (n = 127,440) developed pancreatic cancer. The cumulative incidences of pancreatic cancer in both groups are shown in Fig. 3 (log-rank test, $p < 0.0001$).

The cumulative risks of pancreatic cancer in patients with acute pancreatitis versus controls were 1.1% versus 0.02% at 1 year, 1.4% versus 0.06% at 2 years, 2.0% versus 0.2% at 5 years, and 2.8% versus 0.5% at 10 years.

3.3. Pancreatic cancer risk based on the follow-up period

Compared with the control group, the risk of pancreatic cancer in the acute pancreatitis group was very high within the first 2 years which gradually declined over time (Fig. 4). The HR was the highest at 63.32 (95% CI, 25.73–155.85) within the first 2 months after the diagnosis of acute pancreatitis. After that, the HR decreased, but it was 8.46 (95% CI, 5.57–12.84) at 1–2 years. At 2–4 years after the diagnosis of acute pancreatitis, the HR for pancreatic cancer further decreased to 3.62 (95% CI, 2.26–4.91). However, even after 8–10 years, the HR was still statistically significantly elevated to 2.80 (95% CI, 1.42–5.53). There was no statistically significant difference in the risk of pancreatic cancer between the two groups after 10 years (Table 2).

4. Discussion

In this population-based matched cohort study, we found that patients with acute pancreatitis had an elevated risk of pancreatic cancer in the short and long terms after the diagnosis of acute pancreatitis. The most marked increase in risk was observed in the first 2 years after acute pancreatitis diagnosis. The risk was highest within 2 months after acute pancreatitis (HR, 63.32; 95% CI, 25.73–155.83) and gradually decreased thereafter. The HR was still high at 14.64 in 6–12 months and 8.46 in 1–2 years. Furthermore, even after the first 2 years, we found a substantially elevated risk of pancreatic cancer in the acute pancreatitis group. After 10 years, the difference in the risk was not statistically significant.

The association between acute pancreatitis and the risk of pancreatic cancer remains unclear. Pancreatic cancer can cause acute pancreatitis, and the diagnosis of pre-existing pancreatic cancer may be delayed in patients with acute pancreatitis. Therefore, the increased risk of pancreatic cancer in the short term after acute pancreatitis diagnosis is believed to be due to the late diagnosis of pancreatic cancer, which causes acute pancreatitis [5]. Whether acute pancreatitis increases the risk of pancreatic cancer in the long term is still debatable [5–7,11].

A Danish population-based cohort study including 41,669 patients with acute pancreatitis examined the risk of subsequent pancreatic cancer compared with matched comparison subjects [6]. The HR for the risk of pancreatic cancer was highest within the first 2 years (HR, 19.28; 95% CI, 14.62–25.41). After the first 2 years, the risk decreased over time but remained at a high level after more

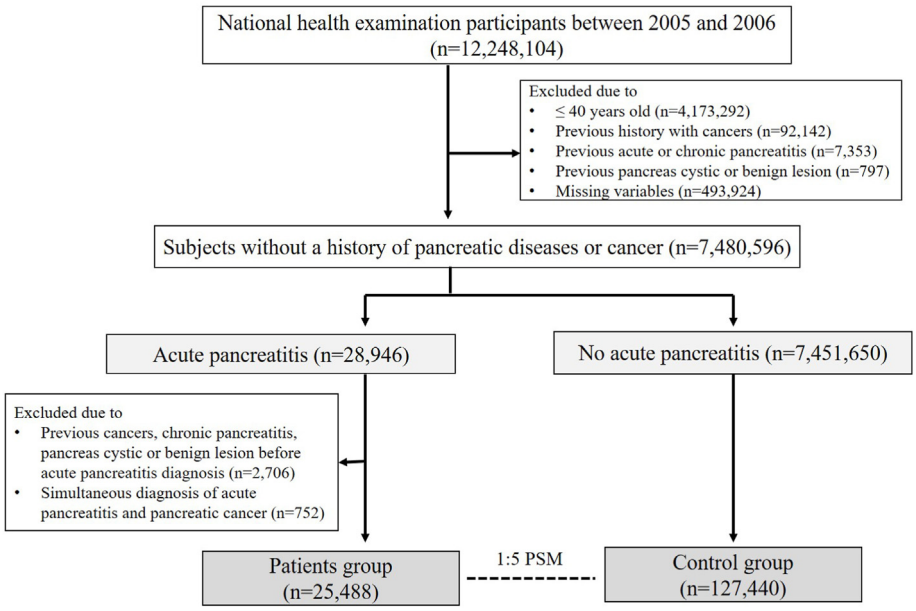

Fig. 2. The flow chart of the study population. PSM: propensity score matching.

Table 1
Baseline characteristics of the study population.

	Acute pancreatitis group	(n = 25,488)	Control group	(n = 127,440)	p value
	No,	%	No.	%	
Sex					
Male	15,996	62.8	79,979	62.8	0.9981
Female	9,492	37.2	47,461	37.2	
Ages (years)					
40–49	7,753	30.4	38,765	30.4	1.0000
50–59	7,027	27.6	35,135	27.6	
60–69	6,200	24.3	31,000	24.3	
70–79	3,923	15.4	19,615	15.4	
≥80	585	2.3	2,925	2.3	
Income level					
1 quintile	4,286	16.8	19,982	15.7	<0.0001
2 quintile	3,642	14.3	15,903	12.5	
3 quintile	4,866	19.1	22,107	17.3	
4 quintile	5,581	21.9	29,873	21.9	
5 quintile	7,113	27.9	41,575	32.6	
BMI (kg/m^2)					
<23	10,083	39.6	50,416	39.6	0.9999
23–24.9	6,408	25.1	32,045	25.1	
≥25	8,997	35.3	44,979	35.3	
Smoking					
Non-smokers	15,279	59.9	76,409	60.0	0.9986
Former smokers	2,347	9.2	11,722	9.2	
Current smokers	7,862	30.8	39,309	30.8	
Alcohol intake					
No	13,561	53.2	70,510	55.3	<0.0001
2–3 times/month	2,795	11.0	17,455	13.7	
1–2 times/week	4,036	15.8	22,392	17.6	
3–4 times/week	2,719	10.7	10,406	8.2	
≥5 times/week	2,377	9.3	6,677	5.2	
Physical activity					
No	14,819	58.1	68,121	53.5	<0.0001
1–2 times/week	5,696	22.3	31,499	24.7	
3–4 times/week	2,338	9.2	13,706	10.8	
≥5 times/week	2,635	10.3	14,114	11.1	
Diabetes					
No	20,856	81.8	104,280	81.8	1.0000
Yes	4,632	18.2	23,160	18.2	
CCI					
0	20,905	82.0	107,768	84.6	<0.0001
1	3,956	15.5	17,661	13.9	
≥2	627	2.5	2,011	1.6	

BMI: body mass index, CCI: Charlson comorbidity index.

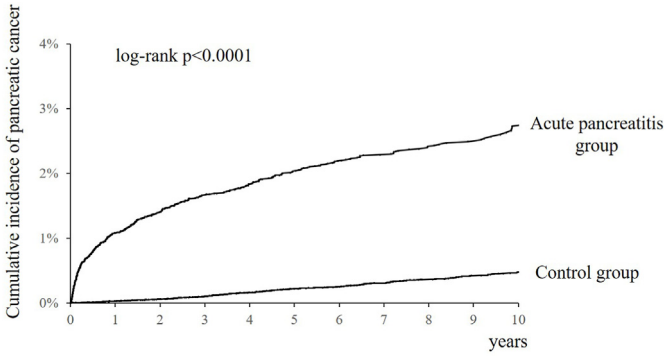

Fig. 3. The cumulative incidence of pancreatic cancer in the acute pancreatitis and control groups.

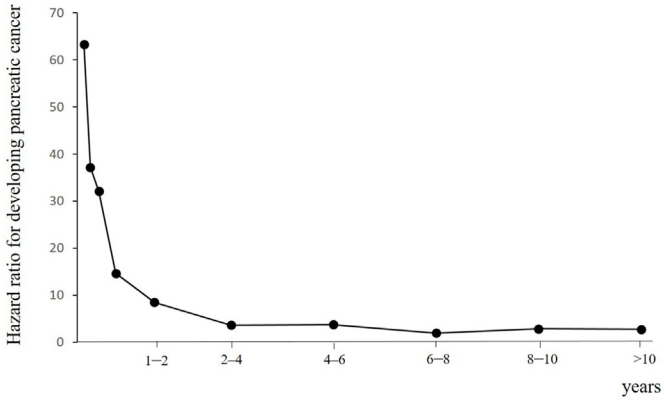

Fig. 4. Hazard ratios for developing pancreatic cancer in the acute pancreatitis group compared with the control group.

than 5 years (HR, 2.02; 95% CI, 1.57–2.61). These results suggest an association between acute pancreatitis and the long-term risk of pancreatic cancer. In addition, a Swedish population-based cohort study, including 49,749 patients with acute pancreatitis, reported that the risk of pancreatic cancer after acute pancreatitis diagnosis was very high within the first few years, then gradually decreased and became similar to that of the control group after 10 years [7]. In a recent study of 35,550 US military veterans with acute pancreatitis, there was an increased risk of pancreatic cancer in patients with acute pancreatitis compared with the control group at 3–10 years after acute pancreatitis diagnosis (HR, 1.7; 95% CI, 1.4–2.0) [8]. Other studies with smaller sample size have also reported a marked increase in the risk of pancreatic cancer after acute pancreatitis diagnosis [5,9,21]. According to a meta-analysis including 11 studies, the association between acute pancreatitis and the risk of pancreatic cancer was very high within 1 year (Effects Estimates (EEs), 23.47; 95% CI, 3.26–43.68) and declined over the long term [11]. In the subgroup analysis based on the follow-up period, there was no association between acute pancreatitis and the risk of pancreatic cancer after 10 years (EEs, 1.17; 95% CI, 0.78–1.57). This meta-analysis suggests that acute pancreatitis is not likely a causal factor of pancreatic cancer.

A rapid increase in the risk of pancreatic cancer within the first few years after acute pancreatitis diagnosis indicates a delayed diagnosis of pre-existing pancreatic cancer. The delayed diagnosis of pancreatic cancer in patients with acute pancreatitis can be explained as follows. Initial peri-pancreatic inflammation in acute pancreatitis may mask pancreatic cancer [22]. Moreover, pancreatic cancer can be mistaken for an inflammatory mass [7]. Most physicians preferentially investigate gallstones or alcohol as the cause of acute pancreatitis, and it is difficult to consider pancreatic cancer as the cause. Computed tomography (CT) which is appropriate for diagnosing pancreatic cancer, should be performed in the arterial and portal venous phases based on the pancreatic protocol [23]. Therefore, if CT is performed in a single phase rather than multiple phases when diagnosing acute pancreatitis, it may be challenging to diagnose pancreatic cancer. In addition, the diagnosis of pancreatic cancer may not be easy if CT shows an isoattenuating tumor, which occurs in 11–14% of all pancreatic cancers [24,25]. Therefore, it should always be noted that pre-existing pancreatic cancer may not be diagnosed in patients with acute pancreatitis. Cho et al. [22] recommended a follow-up CT scan within 3 months of discharge in selected patients, such as those with unknown causes of acute pancreatitis.

Pancreatic cancer that develops in the long term after acute pancreatitis diagnosis may be associated with chronic or recurrent acute pancreatitis. In a study by Sadr-Azodi et al. [7], the risk of pancreatic cancer did not increase 10 years after acute pancreatitis diagnosis when the follow-up for recurrent acute pancreatitis or chronic pancreatitis was censored. In a follow-up study of 731 patients with acute pancreatitis, pancreatic cancer developed in two of 51 patients who progressed to chronic pancreatitis. Compared with patients who did not progress to chronic pancreatitis, the risk of pancreatic cancer was nine times higher in patients who did [10]. Chronic pancreatitis is a well-known risk factor for pancreatic cancer. In a Danish population-based cohort study, the risk of pancreatic cancer was 6.9 times higher in patients with chronic pancreatitis than in the control group (HR, 6.9; 95% CI, 5.6–8.6) [26]. In a meta-analysis of 13 studies by Kirkegard et al., the risk of pancreatic cancer increased approximately 16-fold within 2 years

Table 2
Hazard ratio for developing pancreatic cancer based on follow-up period.

Follow-up period	Acute pancreatitis group			Control group			HR (95% CI)	p-value
	No. of events	No. at risk	person-years	No. of events	No. at risk	person-years		
≤2 months	119	25,488	21,095	5	127,440	21,095	63.32 (25.73–155.85)	<.0001
2–4 months	49	24,531	20,794	5	125,738	20,794	37.16 (14.71–93.86)	<.0001
4–6 months	26	23,918	20,447	3	123,714	20,447	32.05 (9.37–109.67)	<.0001
6–12 months	68	23,359	11,306	18	121,654	59,385	14.64 (8.67–24.72)	<.0001
1–2 years	66	21,884	20,496	34	115,832	109,912	8.46 (5.57–12.87)	<.0001
2–4 years	74	19,102	33,093	96	103,853	184,303	3.62 (2.26–4.91)	<.0001
4–6 years	44	14,109	23,843	62	80,668	139,001	3.72 (2.52–5.51)	<.0001
6–8 years	18	9,802	15,718	55	58,370	95,014	1.90 (1.11–3.26)	0.0186
8–10 years	12	5,930	8,566	30	36,654	53,927	2.80 (1.42–5.53)	0.0029
>10 years	3	2,687	2,772	9	17,262	18,090	2.70 (0.71–10.21)	0.1437

HR: hazard ratio, CI: confidence interval.
HRs were adjusted for sex, age, income level, body mass index, smoking status, alcohol intake, physical activity, diabetes, and Carlson comorbidity index.

of chronic pancreatitis diagnosis, and its association gradually decreased during long-term follow-up. The cumulative incidence of pancreatic cancer in patients with chronic pancreatitis increases with the follow-up duration [27]. The increased risk of pancreatic cancer within a short period after the diagnosis of chronic pancreatitis is believed to be due to the misclassification of pancreatic cancer as chronic pancreatitis [28,29]. In a recent study by Munigala et al., chronic pancreatitis had an additive effect; however, the increased risk of pancreatic cancer was not due to the progression to chronic pancreatitis [8]. Two previous studies on humans suggested that the long-term risk of pancreatic cancer increased proportionally with the number of episodes of recurrent acute pancreatitis and that repeated acute inflammation could promote pancreatic carcinogenesis [7,8]. Experimentally induced acute pancreatitis in a mouse model initiated and accelerated pancreatic carcinogenesis [30]. In an oncogenic K-ras mutant mouse model, acute pancreatitis induced acinar-to-ductal metaplasia and pancreatic cancer precursor lesion formations [31]. Oncogenic Kras-driven pancreatic intraepithelial neoplasia in a mouce model rapidly progressed to pancreatic cancer due to caerulein-induced acute pancreatitis [32]. Therefore, inflammation due to acute pancreatitis is likely associated with an increased risk of pancreatic cancer in the long term after acute pancreatitis diagnosis, and further studies are needed regarding this.

Smoking, obesity, and diabetes are the most well-known risk factors for pancreatic cancer [1–3]. Therefore, the consideration of these risk factors in the study on the risk of pancreatic cancer can diminish selection bias. Only two population-based matched cohort studies have been conducted on the association between acute pancreatitis and pancreatic cancer [6,7]. In these two studies, subjects with no history of acute pancreatitis were matched only by sex and age without including other important risk factors for pancreatic cancer such as smoking, obesity, and diabetes. Recently, our group conducted a population-based study and reported that smoking, high BMI, and diabetes were significant risk factors for pancreatic cancer in Koreans [12]. In this study, as a continuation of the previous study, BMI, smoking status, and diabetes were used as matching variables to adjust for confounding factors. This distinguishes this study from other population-based studies.

In this study, acute pancreatitis was strictly defined as patients hospitalized with a primary diagnosis (K85) to more accurately include patients with acute pancreatitis from NHIS data. For validation, we reviewed the medical records of 250 patients at our institution, and 236 patients met the definition of acute pancreatitis [33], with an accuracy of 94.4%.

This study has several limitations. First, because this study used the NHIS database, the diagnose of acute pancreatitis and pancreatic cancer depended on the diagnosis code. Pancreatic cancer can be suspected in some patients with acute pancreatitis; however, coding for the diagnosis of pancreatic cancer may be delayed. Therefore, the risk of pancreatic cancer within several months after acute pancreatitis diagnosis may have been overestimated. Second, because information regarding the etiology of acute pancreatitis was limited, an analysis of the risk of pancreatic cancer based on the cause of acute pancreatitis could not be performed. Third, as information regarding the diagnosis of chronic pancreatitis was not available, a subgroup analysis could not be performed for patients who progressed to chronic pancreatitis.

Nevertheless, this study has the following strengths: This was a large-scale population-based study that involved 25,488 patients with acute pancreatitis and used real-world data. In contrast to other studies, the influence of confounding factors was minimized by using BMI, smoking status, and diabetes as matching variables. Furthermore, acute and chronic pancreatitis, pancreatic cystic disease, and pancreatic benign neoplasms diagnosed before selection in this study were excluded, which contributed to reducing selection bias.

In conclusion, this population-based study, which matched the risk factors for pancreatic cancer, demonstrated that the risk of pancreatic cancer increased rapidly after acute pancreatitis diagnosis. The risk gradually declined after 2 years but remained elevated for up to 10 years. Since the increase in short-term risk of pancreatic cancer after acute pancreatitis diagnosis may be due to pancreatic cancer presenting as acute pancreatitis, careful attention should be paid to prevent delayed diagnosis of pancreatic cancer. Acute pancreatitis is associated with an increased long-term risk of pancreatic cancer. Further studies are needed to determine whether this increased risk is mediated by chronic pancreatitis or recurrent acute pancreatitis, and whether inflammation of acute pancreatitis is involved in pancreatic carcinogenesis.

Authors' contributions

Byung Kyu Park and Jeong Hun Seo designed the study and interpreted the data. Byung Kyu Park wrote the manuscript. Kang Ju Son and Jung Kyu Choi assisted with data interpretation and manuscript evaluation. Jeong Hun Seo supervised study development. All authors have read and approved the manuscript and agree to be accountable for all aspects of the research to ensure that the accuracy or integrity of any part of the work was appropriately investigated and resolved.

Declaration of competing interest

All authors have no conflicts of interest or financial ties to disclose.

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