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Incidence of and risk factors for pancreatic cancer in chronic pancreatitis: A cohort of 1656 patients

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ABSTRACT

Background: Risk of pancreatic cancer may increase in chronic pancreatitis patients.
Aims: This study aimed to identify the incidence of and risk factors for pancreatic cancer in chronic pancreatitis patients.
Methods: Chronic pancreatitis patients admitted to our center from January 2000 to December 2013 were enrolled. Cumulative rates of pancreatic cancer and survival rates were calculated. The standardized incidence ratio was calculated based on the pancreatic cancer incidence in general population of China. Risk factors for pancreatic cancer were identified.
Results: In a total of 1656 patients, the median follow-up duration was 8.0 years. Pancreatic cancer was detected in 21 patients (1.3%). The expected number of cases of pancreatic cancer was 1.039, yielding a standardized incidence ratio of 20.22. The standardized incidence ratios for patients with a >60 pack-year smoking history were much higher (145.82). Two risk factors for pancreatic cancer were identified: age at the onset of chronic pancreatitis (hazard ratio, 1.05) and a >60 pack-year smoking history (hazard ratio, 11.83).
Conclusion: The risk of pancreatic cancer is markedly increased in chronic pancreatitis patients compared with the general population, especially in patients with an older age at onset and a >60 pack-year smoking history. The high-risk populations were suggested to be followed up closely.

1. Introduction

The incidence of chronic pancreatitis (CP) in industrialized countries ranges from 3.5 to 10 people per 100,000 [1]. The damage to both the exocrine and endocrine compartments of the pancreas eventually results in severe maldigestion and diabetes. The histopathologic features of this disease include acinar atrophy, fibrosis, fatty replacement, chronic inflammation and abnormal ducts [1,2].

Chronic inflammatory conditions constitute predispositions to organ-specific cancers. CP patients reportedly represent a high-risk population for pancreatic cancer [3–10]. A recent meta-analysis that included 22 studies found an increased relative risk of developing pancreatic cancer of 13.3 in CP patients [11]. Pancreatic cancer is a severe clinical condition that is always diagnosed too late for surgical intervention. Moreover, the onset of pancreatic cancer is insidious in CP patients and the symptoms of pancreatic cancer may resemble the symptoms and clinical findings of CP [12]. Therefore, identifying risk factors for the development of pancreatic cancer in CP patients would be beneficial for early detection [13].

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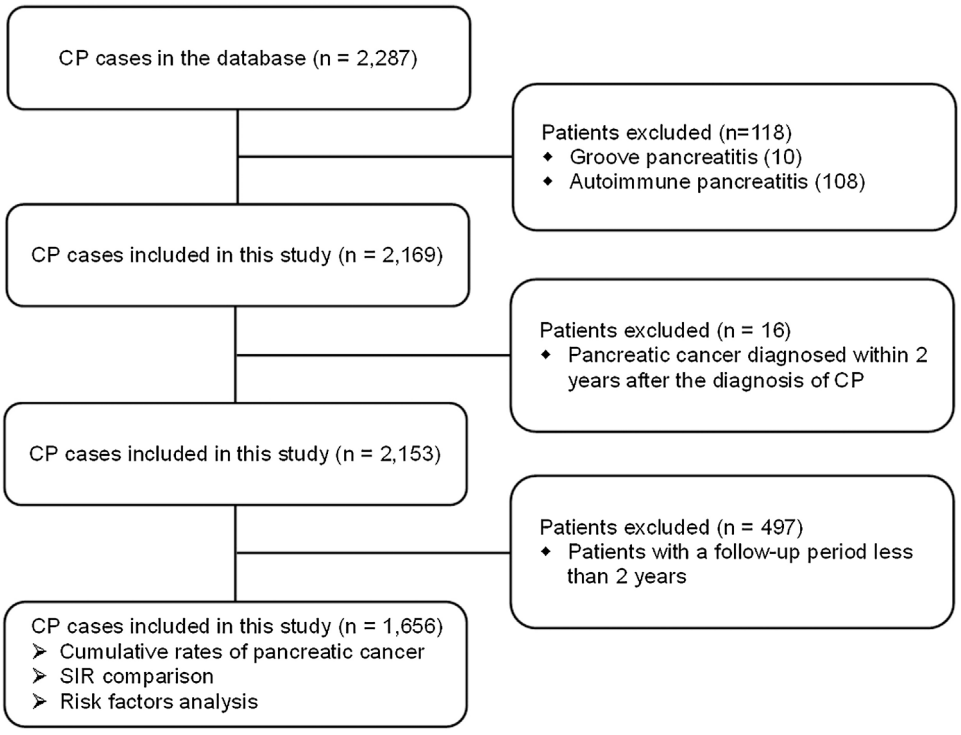

Fig. 1. Flow diagram of patient enrolment and the study design.

This study was based on a retrospective–prospective cohort of 1656 CP patients with a long follow-up history after the onset of CP. We aimed to determine the incidence of pancreatic cancer in CP patients and identify the risk factors for this disease.

2. Materials and methods

2.1. Patients and database

Since the 1990s, an electronic medical record system (GOODWILL Inc., Beijing, China) has been used in Changhai Hospital (Shanghai, China) and has facilitated several studies on CP [14–22]. To track changes consistently throughout the course of CP and facilitate the evaluation and the study of this disease, a dedicated database, the Changhai CP Database (version number 2.1, YINMA Information Technology Inc., Shanghai, China), was established in 2005 to collect the clinical data of CP patients who were admitted to Changhai Hospital. Data from January 2000 to December 2004 were retrospectively collected according to the electronic medical record system and were complemented through telephone, letter, and e-mail inquiries. Data were prospectively collected since January 2005. The following information was documented in detail: demographic data (age, sex, birthplace, etc.), the course of CP, medical history, history of other diseases, smoking and alcohol history, family history of pancreatic diseases and diabetes mellitus (DM), laboratory and imaging findings, and treatment strategy.

The database system was set to remind the investigators to call patients for clinical check-ups. In addition to clinic visits due to complaints of discomfort related to CP, all patients were periodically (at least annually) called for clinical check-ups and investigations. Transabdominal ultrasound, magnetic resonance imaging (MRI), or computed tomography (CT) was selected as the evaluation modality during each follow-up visit. Evaluations of each revisit or of telephone inquiries for patients who did not return to Changhai Hospital were added to the CP database. In December 2013, we contacted all the patients in our database for a final evaluation, except those who were lost to follow-up or had died. The duration of follow-up was defined as the duration from the onset of CP to the date of the last personal contact, death, or the end of follow-up (December 2013), whichever came first (Fig. 1).

The exclusion criteria were as follows: groove pancreatitis (GP) and autoimmune pancreatitis (AIP) [23]. In the present study, cases of pancreatic cancer diagnosed within 2 years after the diagnosis of CP [16,24] and patients with a follow-up period of less than 2 years (CP diagnosed after December 2011) were excluded.

The study was approved by the Ethics Committee of Changhai Hospital. Written informed consent was obtained from all participating patients. All of the diagnostic and therapeutic modalities were carried out in accordance with the approved guidelines.

2.2. Definitions

The diagnosis of CP was established according to the Asia-Pacific consensus [25]. Alcoholic chronic pancreatitis (ACP) was considered when alcohol intake exceeded 80 g/day for men or 60 g/day for women for at least 2 years in the absence of other causes [17,26]. Hereditary CP refers to two first-degree relatives or ≥3 second-degree relatives in ≥2 generations with recurrent acute pancreatitis and/or CP without any precipitating factors [27]. Although the abnormal anatomy of the pancreatic duct (including pancreas divisum and anomalous pancreaticobiliary junction) as a cause of CP remains controversial, we defined it as an etiology [28]. Patients were defined as having post-traumatic CP when there was a history of abdominal trauma with imaging evidence of pancreatic injury and subsequent ductal dilation. Hyperlipidemia is considered an etiology when blood triglycerides are >1000 mg/dL [29]. Patients with CP were considered idiopathic when none of the above causes were found.

The diagnosis of pancreatic cancer was established according to the National Comprehensive Cancer Network (NCCN) guideline [30,31]. Once the patient was diagnosed with pancreatic

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