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Original article

The seventh nationwide epidemiological survey for chronic pancreatitis in Japan: Clinical significance of smoking habit in Japanese patients

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ABSTRACT

Objectives: A nationwide survey was conducted to clarify the epidemiological features of patients with chronic pancreatitis (CP) in Japan.
Methods: In the first survey, both the prevalence and the incidence of CP in 2011 were estimated. In the second survey, the clinicoepidemiological features of the patients were clarified by mailed questionnaires. Patients were diagnosed by the Japanese diagnostic criteria for chronic pancreatitis 2009.
Results: The estimated annual prevalence and incidence of CP in 2011 were 52.4/100,000 and 14.0/100,000, respectively. The sex ratio (male/female) of patients was 4.6, with a mean age of 62.3 years. Alcoholic (67.5%) was the most common and idiopathic (20.0%) was the second most common cause of CP. Comorbidity with diabetes mellitus (DM) and pancreatic calcifications (PC) occurred more frequent in ever smokers independently of their drinking status. Among patients without drinking habit, the incidences of DM and PC were significantly higher in ever smokers than in never smokers. The multiple logistic regression analysis revealed smoking was an independent factor of DM and PC in CP patients: DM, Odds ratio (OR) 1.644, 95% confidence interval (CI) 1.202 to 2.247 ($P = 0.002$): PC, OR 2.010, 95% CI 1.458 to 2.773 ($P < 0.001$). On the other hand, smoking was not identified as an independent factor for the appearance of abdominal pain by this analysis.
Conclusion: The prevalence of Japanese patients with CP has been increasing. Smoking was identified as an independent factor related to DM and PC in Japanese CP patients.

Introduction

The epidemiology of chronic pancreatitis (CP) has not yet been fully investigated. In Japan, nationwide surveys of CP have been sequentially conducted six times by the Research Committee of Intractable Pancreatic Diseases (RCIPD) supported by the Ministry of Health, Labor and Welfare, Japan [1–3]. Since the first and second survey, which were conducted from 1970 to 1984, were not designed to investigate the prevalence of CP, the prevalence of CP in Japan was first clarified in the third nationwide survey conducted in 1994 [1]. After that, the fourth and the fifth surveys were conducted in 1999 and in 2002, respectively [2]. We previously reported the sixth nationwide survey, which was conducted targeting patients who were treated for CP in Japanese hospitals in 2007, and demonstrated that the prevalence of CP in Japan had been increasing [3].

After the sixth survey, Japanese diagnostic criteria for CP were revised in 2009 [4]. In the revised Japanese diagnostic criteria, the concept of early CP was newly defined in addition to definite and probable CP to aim at improving the long-term prognosis of CP

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patients, possibly by abstinence from both drinking and smoking in the early stage of CP. The diagnostic criteria of early CP is consisted of characteristic clinical features and imaging results. Two or more following clinical features are prerequisite before imaging examinations to diagnose early CP, 1) repeated upper abdominal pain, 2) abdominal pancreatic enzyme levels in the serum or urine, 3) abnormal pancreatic exocrine function, and 4) continuous heavy drinking of alcohol equivalent to or more than 80 g/day of pure ethanol. Besides the clinical features, it is necessary to satisfy the diagnostic criteria of early CP that the characteristic findings of pancreatic imaging be detected by endoscopic ultrasonography (EUS) or endoscopic retrograde cholangiopancreatography (ERCP) (Tables 1 and 2 [4].

This is the first report of a Japanese nationwide survey of CP after the revision of the Japanese diagnostic criteria in 2009. In this manuscript, we demonstrate the latest prevalence and incidence of CP in Japan and the clinical characteristics of Japanese CP patients. Moreover, we also demonstrate that cigarette smoking increased the risk of comorbidity with diabetes mellitus (DM) and pancreatic calcifications (PC) independently of alcohol drinking in Japanese CP patients.

Materials and methods

Diagnostic criteria and classification

CP was diagnosed and classified according to the diagnostic criteria for CP proposed by RCIPD, Japanese Pancreatic Society (JPS) and Japanese Society of Gastroenterology (JSGE) in 2009 [4]. Briefly, CP was classified as definite CP and probable CP by diagnostic reliability. In addition to definite and probable CP, early CP was newly defined in the criteria. Definite CP and probable CP were diagnosed according to typical findings of pancreatic imaging obtained from imaging tests such as ultrasonography (US), computed tomography (CT), magnetic resonance cholangiopancreatography (MRCP), EUS and ERCP, and pancreatic exocrine insufficiency measured by tubeless test and histology. Typical clinical features of CP were considered in the diagnosis for definite CP and were required for early CP (Table 1) [4]. Characteristic findings in pancreatic imaging obtained from EUS or ERCP are necessary for the diagnosis of early CP, as well (Table 2) [4].

Table 1
Japanese clinical diagnostic criteria for CP 2009 [4].

Diagnostic items for CP
1) Characteristic imaging findings
2) Characteristic histological findings
3) Repeated upper abdominal pain
4) Abnormal pancreatic enzyme levels in the serum or urine
5) Abnormal pancreatic exocrine function
6) Continuous heavy drinking of alcoholic equivalent to ≥80 g/day of pure ethanol
Definite CP: either a or b
a. Definite findings of 1) or 2)
b. Probable findings of 1) or 2), plus more than two items among 3), 4) and 5)
Probable CP
Probable findings of 1) or 2)
Early CP[a]
More than two items among 3)-6) plus imaging findings of early CP

Patients with more than two items among 3)-6) but without 1) and 2) are diagnosed as "possible CP" after ruling out other pancreatic diseases. Imaging examinations, such as endoscopic ultrasonography (EUS) are recommended for the patients with "possible CP" within 3 months after the diagnosis.
Patients with imaging findings of early CP plus rather 3) or 4) in whom other pancreatic disease are ruled out could have early CP; therefore, careful follow-up is required for the patients.
[a] The real nature of early CP will be clarified by a long-term prospective follow-up of the patients in this category.

Table 2
Imaging findings of early CP [4].

Either a or b:
a. More than two features among the following seven features of EUS findings including one of (1)–(4)
(1) Lobularity with honeycombing
(2) Lobularity without honeycombing
(3) Hyperechoic foci without shadowing
(4) Stranding
(5) Cysts
(6) Dilated side branches
(7) Hyperechoic MPD margin
b. Irregular dilation of more than three duct branches on ERCP findings

First survey

Our targeted subjects were patients with CP diagnosed by the Japanese diagnostic criteria for CP 2009 and treated in Japanese hospitals during the 1-year period from January 1st 2011 to December 31st 2011. The prepared list of hospitals for the survey was based on the "Listing of Hospitals" compiled by the Committee on Studies of Health Policies, Ministry of Health, Labour and Welfare, Japan, and was revised using newly received information. The departments of internal medicine, gastroenterology, digestive surgery, and surgery in each hospital were listed, and stratified, random sampling was used to select the departments to be surveyed. The sampling rates were approximately 5%, 10%, 20%, 40%, 80%, 100% and 100%, for the strata of general hospitals with less than 100 beds, 100 to 199 beds, 200 to 299 beds, 300 to 399 beds, 400 to 499 beds, 500 or more beds, and the affiliated university hospitals, respectively. Some relevant departments, where many patients with pancreatic diseases were expected to be treated, were classified as special strata and were all selected [3]. In the first survey, a simple questionnaire was used to inquire about the number of patients with CP who visited the hospitals and that of newly diagnosed patients in the year 2011. This questionnaire was directly mailed to the heads of 4175 departments randomly chosen as described above in June 12th 2012. The number of patients treated in 2011 was estimated, based on the assumption that the response from departments is independent of the frequency of patients. The number of patients in stratum k was estimated as.

$$\hat{a}_k = \frac{n_k}{N_k}\sum_i i \cdot N_{ki}$$

where n_k, N_k and N_{ki} denote the total number of departments, the number of responded departments, and the number of departments with i patients in stratum k, respectively. The 95% confidence interval of $\hat{a}_k$ was

$$(\hat{a}_k - 1.96\cdot s_k,\ \hat{a}_k + 1.96\cdot s_k)$$

$$s_k = \sqrt{\frac{\frac{1}{N_k}\sum_i i^2 \cdot N_{ki} - \left(\frac{1}{N_k}\sum_i i\cdot N_{ki}\right)^2}{n_k - 1}\cdot n_k^3\left(\frac{1}{N_k} - \frac{1}{n_k}\right)}$$

where s_k is the estimated standard error of $\hat{a}_k$. The total number of patients, $\hat{a}$ was computed as follows:

$$\hat{a}_k = \sum_k \hat{a}_k$$

the 95% confidence interval was.