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Original article

The sixth nationwide epidemiological survey of chronic pancreatitis in Japan

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A B S T R A C T

Objectives: A nationwide survey was conducted to clarify the epidemiological features of patients with chronic pancreatitis (CP) in Japan.
Methods: Two sequential surveys were conducted. In the first survey, both the prevalence and incidence of CP in Japan in 2007 were estimated by a questionnaire, which was mailed to 3027 randomly chosen Japanese facilities. In the second survey, the second questionnaire was then mailed to 1110 facilities selected by the first survey to clarify the clinicoepidemiological features of the patients.
Results: The estimated annual prevalence of CP was 36.9 per 100,000; 53.2 in males and 21.2 in females. The estimated annual incidence was 11.9 per 100,000. The prevalence and the incidence of CP gradually increased in Japan as compared to former surveys. The sex ratio (male/female) of definitive and probable CP patients was 4.5, with a mean age of 59.4 years; 59.2 years in males and 60.2 years in females. Alcoholic (69.7%) was most the common and idiopathic (21.0%) was the second most common cause of CP. The proportion of alcoholic CP increased as compared to the 55.5% found in 1994. The clinical features of overall Japanese patients with CP were: abdominal pain (60.6%), malabsorbtion (12.2%), diabetes mellitus (39.7%) and pancreatolithiasis (75.7%). Alcoholic patients were characterized by high morbidity as compared to nonalcoholic patients: abdominal pain (alcoholic 65.0% vs nonalcoholic 53.0%, $p < 0.0001$), diabetes mellitus (44.8% vs 31.4%, $p < 0.0001$) and pancreatolithiasis (84.0% vs 60.8%, $p < 0.0001$).
Conclusion: The prevalence and the incidence of CP, especially alcoholic CP, have been increasing in Japan.

1. Introduction

The epidemiology of chronic pancreatitis (CP) has not yet been fully investigated. Especially, only a few nationwide surveys have been available to estimate the prevalence and incidence of CP. [1,2]. Although it was mentioned that the prevalence of CP might have increased recently [3,4], the reported evidence is still insufficient to confirm recent changes of the estimated prevalence in the same population.

In Japan, nationwide surveys of CP have been conducted five times by the Research Committee of Intractable Pancreatic Diseases (RCIPD) supported by the Ministry of Health, Labor and Welfare, Japan. 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 [4,5]. We report here the sixth nationwide survey, which was conducted targeting patients who were treated for CP in Japanese hospitals in 2007. In this study, we demonstrated the latest prevalence and incidence of CP in Japan, discussed the clinicoepidemiological features of Japanese patients and compared the latest results to those of previous studies.

2. Materials and methods

2.1. Diagnostic criteria and classification

CP was diagnosed and classified according to the diagnostic criteria for CP proposed by Japanese Pancreatic Society (JPS) in 2001

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(JPS criteria 2001) [4,6]. Briefly, CP was classified as definite CP and probable CP by diagnostic reliability. Both were diagnosed according to typical findings of pancreatic imaging obtained from imaging tests such as ultrasonography (US), computed tomography (CT) and endoscopic retrograde cholangiopancreatography (ERCP), and pancreatic exocrine insufficiency measured by secretin and tubeless test and histology. The JPS criteria 2001 were based on the diagnostic criteria for CP proposed by JPS in 1995 (JPS criteria 1995) [7]. The JPS criteria 2001 were a version of the JPS criteria 1995 with minor revision including magnetic resonance cholangiopancreatography (MRCP) findings in the imaging criteria of probable CP [4,6].

2.2. First survey

Our targeted subjects were patients with CP diagnosed by the JPS criteria 2001 and treated in Japanese hospitals during the 1-year period from January 1st 2007 to December 31st 2007. The prepared list of hospitals for the survey was based on the "Listing of Hospitals 2003–2004" 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 stratum 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. Some relevant departments, where many patients with pancreatic diseases were expected to be treated, were classified as special strata and were all selected [8]. 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 2007. This questionnaire was directly mailed to the heads of 3027 departments randomly chosen as described above in November 2008. The number of patients treated in 2007 was estimated, based on the assumption that the response from departments is independent of frequency of patients. The number of patients in stratum k was estimated as:

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

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 $\hat{\alpha_k}$ was:

$$\left(\hat{\alpha_k} - 1.96 \cdot S_k,\ \hat{\alpha_k} + 1.96 \cdot S_k\right)$$

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

where s_k is the estimated standard error of $\hat{\alpha_k}$. The total number of patients $(\hat{\alpha})$ was computed as follows:

$$\hat{\alpha} = \sum_k \hat{\alpha_k}$$

and the 95% confidence interval was:

$$(\hat{\alpha} - 1.96 \cdot s, \hat{\alpha} + 1.96 \cdot s), s = \sqrt{\sum_k s_k^2}$$

where s is the estimated standard error of $\hat{\alpha}$. [1,9]

2.3. Second survey

After the first questionnaires were collected, the second questionnaires were forwarded to those departments from which patients with CP were reported on the first questionnaires. The second questionnaires were continued to be collected until December 2009 (until 9 months after the due date). This clinicoepidemiological information on individual patients including etiology/symptoms, diagnostic criteria, therapy and complications was collected from medical records of the patients. To obtain as many responses as possible, we mailed reminders before and after the due date for each survey. From the second survey, data on 1504 patients were collected. The response rate in the second survey was 23.7%. 1320 of them were classified into definite (1,182, 78.6%) and probable (138, 9.2%) cases. The other 184 patients were classified into possible cases [6] or inappropriate cases, and were excluded from this study. Eighty-four patients in the definite and possible cases were diagnosed as autoimmune pancreatitis (AIP). Because the morphology of AIP is reversibly improved by corticosteroid administration, the nature of AIP may be unsuitable for the concept of CP, which was defined as a disease with progressive and irreversible structural changes [10,11]. Therefore, the 84 patients with AIP were not included in this study. Finally, 1236 patients were enrolled in the study of the second survey. The study design was approved by the ethics committee of Tohoku University School of Medicine, article no. 2008-178.

3. Results

3.1. First survey

Table 1 shows a summary of the first survey. Of the 3027 departments where the first questionnaire was mailed, 1100 departments replied (response rate 36.7%) with descriptions of 6339 patients treated and 2217 patients newly diagnosed as having CP in 2007. We estimated the total number of patients treated for CP in 2007 as 47,100 (95% confidence interval (CI), 40,200–54,000) with a prevalence of 36.9 per 100,000, that of males as 33,100 (95% CI, 28,700–37,600) with a prevalence of 53.2 per 100,000, and that of females as 13,900 (95% CI, 11,300–16,400) with a prevalence of 21.2 per 100,000. We also estimated the number of newly diagnosed CP cases in 2007 as 15,200 (95% CI, 12,900–17,600), with an incidence of 11.9 per 100,000.

3.2. Second survey

3.2.1. Distribution of age and sex

From the second survey, the clinical data of 1236 patients were collected. The number of males and females with definite and possible CP was 1010 and 226, respectively, and the sex ratio (male-

Table 1
Summary of the first survey.

	Numbers	Sampling rate (%)	No. mailed questionnaires	No. of response	Response rate (%)
University hospital	316	100	316	183	57.9
Special strata	71	100	71	61	85.9
≥500 beds	681	100	681	235	34.5
400–499 beds	634	80	505	167	33.1
300–399 beds	1156	40	463	139	30.0
200–299 beds	1689	20	336	101	30.1
100–199 beds	3903	10	389	129	33.2
≤99 beds	5324	5	266	95	35.7
Total	13,774	–	3027	1110	36.7