Estimation of the prevalence and incidence of chronic pancreatitis and its complications

A prospective survey in adults attending gastroenterologists in France

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SUMMARY

Incidence and prevalence of chronic pancreatitis (CP) are poorly known and prospective nationwide epidemiologic estimation has never been performed.

Aims — To estimate prospectively national incidence and prevalence of patients attending gastroenterologists for CP in France.

Patients and methods — Study was proposed to all of the French gastroenterologists (N = 3215) of whom 753 accepted to participate (24% private, 40% hospital and 36% both). Were included all patients suffering from proved or suspected CP, from 04-2003 to 07-2003. Certain diagnostic criteria were pancreatic calcifications, ductal or histological abnormalities. For all of non-responder gastroenterologists, a tracking system was used (mail or by phone).

Results — A total of 456 gastroenterologists returned at least 1 case on 1748 patients. Median patient age was 51 years; sex-ratio was 5.07. Median duration between the first CP sign and the inclusion was 41 months. CP cause was alcoholism (84%), hereditary (1%), cystic fibrosis (1%), idiopathic (9%), other (6%). CP diagnosis was certain in 77%: calcifications (85%), ductal abnormalities (57%), cystic fibrosis (1%), idiopathic (9%), other (6%). CP diagnosis was certain in 77%; calcifications (85%), ductal abnormalities (57%), cystic fibrosis (1%), idiopathic (9%), other (6%). CP diagnosis was certain in 77%; calcifications (85%), ductal abnormalities (57%), cystic fibrosis (1%), idiopathic (9%), other (6%). CP diagnosis was certain in 77%; calcifications (85%), ductal abnormalities (57%), cystic fibrosis (1%), idiopathic (9%), other (6%).

Conclusion — New CP patients attending gastroenterologists are known in France, as well as in the rest of the world. The formal diagnosis of CP can be based only on the presence of one of the following three criteria: 1) duct anomalies, at least moderate, according to the Cambridge classification [1], 2) presence of pancreatic calcifications, or 3) fibrosis in histological specimen. The first two signs are late indicators, and generally appear several years after the onset of the symptoms [2]. Moreover, prior to the availability of pancreatic magnetic resonance imaging, duct imaging required an endoscopic retrograde pancreatography — an invasive procedure not devoid of risks and therefore not performed routinely. Lastly, an histological specimen obtained

rÉsUMÉ

Estimation de la prévalence et de l’incidence de la pancréatite chronique en France : une enquête prospective portant sur les adultes consultant en gastroentérologie en France

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L’incidence et la prévalence de la pancréatite chronique (PC) sont mal connues et aucune enquête épidémiologique prospective nationale n’a jamais été publiée.

Buts — Estimer prospectivement et au niveau national l’incidence et la prévalence des malades consultant en gastroentérologie pour PC.

Méthodes — L’enquête a été proposée à tous les gastroentérologues français (N = 3215) dont 753 ont accepté de participer (activité privée : 24 %, hospitalière : 40 %, mixte : 36 %). Les malades ayant soit une PC prouvée soit suspectée ont été inclus entre avril et juillet 2003. Les critères de diagnostic certain étaient la présence de calcifications pancréatiques, d’anomalies canalaires ou histologiques. Pour tous les gastroentérologues non répondants, un rappel a été fait par courrier ou téléphone.

Résultats — Au total, 456 gastroentérologues ont signalé au moins un cas pour un total de 1748 malades. L’âge médian des malades était 51 ans ; le sex ratio était 5.07. La durée médiane entre le premier signe de PC et l’inclusion était 41 mois. La cause de la PC était alcoolique (84 %), héritaire (1 %), la mucoviscidose (1 %), idiopathique (9 %), ou autre (6 %). Le diagnostic de PC était certain dans 77 % des cas : calcifications pancréatiques (85 %), anomalies canalaires (57 %), histologie (8 %). Les symptômes de la PC étaient : douleurs abdominales chroniques (53 %), pancréatite aiguë (67 %), pseudokyste (40 %), compression de la voie biliaire principale (21 %), diabète (32 %), insuffisance pancréatique exocrine (36 %). L’incidence maximale annuelle était de 4646 nouveau cas (incidence annuelle brute : 7,7 pour 10000 ; 12,9 pour les hommes ; 2,6 pour les femmes). La prévalence était de 13832 cas (prévalence brute : 26,4 pour 10000 ; 43,8 pour les hommes ; 9,0 pour les femmes).

Conclusion — Les nouveaux consultants en gastroentérologie pour PC représentent environ 5000 cas par an. La prévalence de la PC est d’environ 16000 malades. La fréquence des principales complications est proche des séries hospitalières, confirmant que les résultats issus de ces centres sont peu ou pas biaisés.

Introduction

The epidemiology of chronic pancreatitis (CP) is poorly known in France, as well as in the rest of the world. The formal
after surgical resection is rarely available, especially in the early stages of the disease. The formal diagnosis of CP is, therefore, often delayed and based essentially on a set of arguments [3]. Thus, the average length of time to diagnosis of CP when revealed as an acute alcohol-related pancreatitis is approximately 5 years [4].

A precise knowledge of the epidemiology of CP is important because it is suggested that CP is a widespread disease, for example, as chronic inflammatory intestinal disorders.

No exhaustive survey has been carried out involving all gastroenterologists in a country. The purpose of this study was to conduct a national survey in France, a country of 60,400,000 inhabitants, on the prevalence and incidence of patients attending gastroenterologists for CP and its complications.

Methods

This is an observational study having no impact on the nature or quality of patient management.

Recruitment of physicians

PRELIMINARY INVESTIGATION

Patients with CP may be treated by gastroenterologists, diabetologists or general practitioners. A preliminary telephone survey was carried out involving 195 general practitioners and 181 diabetologists randomly selected from the files of the Naxis Logistics Company (Lyon, France) in order to target the physicians who see these patients on a regular basis. The results of this survey showed that 41.4% of general practitioners and 63.9% of diabetologists saw in one year at least one patient with CP; averaging 2.7 ± 1.7 and 5.0 ± 4.8 patients, respectively. 70.8% of the patients managed by general practitioners and 73.5% of those managed by diabetologists were also treated by a gastroenterologist at the same time. Given these figures, we decided that only gastroenterologists would participate in the study.

RECRUITMENT AND RECALL

All gastroenterologists practising for adult patient in the private sector, general hospital or university hospitals (N = 3215) of Metropolitan France (Cédérom files, Boulogne-Billancourt) were contacted by mail in March 2003 to ask if they would accept to participate in this survey. Seven hundred and fifty-three (753) (23.4%) gastroenterologists agreed to take part in the study. Amongst these, 297 did not report any cases (so-called “inactive” physicians) and 456 reported at least one case (so-called “active” physicians). At the end of the survey, a letter was sent to the inactive physicians asking them to state their reasons for (1) including patients, giving them the choice between one of the two following answers: “(1) did not see any case of CP during the inclusion period”; “(2) saw cases but did not have time to report them”. The response rate to the mail was 63.3%. Amongst those who responded (N = 188), 51% (N = 96) declared that they had not seen any case and 49% (N = 92) said they had seen cases but did not have enough time to include them (so-called “potentially active” physicians). Extrapolating from these percentages, the overall number of “active” physicians would, therefore, have been 602 gastroenterologists.

Patient inclusion

All the patients (more than 14 year old) complying with the inclusion criteria and seen between 04/15/2003 and 07/15/2003, had to be included if they presented with sure signs of CP or if they had had recurrent attacks of acute pancreatitis without confirmed evidence of CP. Patients who experienced acute alcohol-related pancreatitis were included from the first attack since it is now clear that the vast majority of acute alcohol-related pancreatitis is the first manifestation of alcohol-related CP [4]. Diagnosis was considered as confirmed on the presence of one of the following criteria: a) duct anomalies that were, at least, moderate, according to the Cambridge classification [1]; b) pancreatic calcifications visible on ultrasound scanning, CT scan, echoendoscopy; c) histological examination. The decision to perform imaging procedures was left to the clinician in charge of the patient. Acute pancreatitis was defined by an association of typical acute pancreatitis pain associated with an elevation of amylase or lipase serum level above three times the upper limit of normal range. The patients were then classified as either with probable CP (alcohol-induced acute pancreatitis, or recurrent acute pancreatitis of other cause without formal criteria for CP diagnosis), or confirmed CP.

Data collected

Physician’s characteristics

The following data were collected: age, sex, type of activity (private or hospital practice, or both) and region of practice.

Patients’ characteristics

The following data were collected prospectively: identification of the physician; patient’s initials; date of inclusion; date of birth; gender; reported daily consumption of pure alcohol expressed in grams per day (< 40, between 40 to 120, > 120); duration of consumption expressed in years (< 10 years, between 10 to 20, > 20); existence of a period of alcohol abstinence and, if the case, its duration; date on which the first CP-related symptom was encountered; date of diagnosis; causes of CP (divided into alcohol-related cause in the event of daily alcohol consumption exceeding 60 g/day for more than 2 years, hereditary in the case of mutation of cationic trypsinogen, SPINK1 or CFTR genes, others and idiopathic causes); CP complications (chronic pain, attacks of acute pancreatitis, pseudocyst(s), compression of the bile duct with or without cholelithiasis, etc.); presence of exocrine pancreatic insufficiency (diagnosis based on clinical signs or functional examination of the stools) or endocrine (non-insulin-dependent or insulin-dependent diabetes mellitus); and number of consultations for CP within the last twelve months.

Patient duplicates were avoided by systematic comparison of patient’s initials and date of birth.

Statistical methods

Qualitative data are expressed as a percentage. Quantitative data are expressed in terms of median and extreme values or mean and standard error. The prevalence and national incidence were calculated in three different ways in order to obtain a range as closely as possible to reality: a) calculation No. 1 only taking into account confirmed cases of CP reported by active physicians; b) calculation No. 2 only taking into account confirmed or probable cases of CP reported by active physicians; c) calculation No. 3 only taking into account confirmed and probable cases of CP seen by “active” physicians and cases extrapolated from “potentially active” physicians. The calculation of national prevalence and incidence was extrapolated for one whole year and to all French gastroenterologists (multiplying factor: 3215/753). Incidence was calculated taking into account only those cases that were newly diagnosed during the period of reference. Regional and departmental prevalence and incidence rates could not be calculated because they could be modified by multiple inter-regional or inter-departmental factors that were also difficult to control (patients’ mobility, hospital cover of varying extent, existence of more or less important university hospitals, presence or absence of “reference centres” that can have an attraction effect, distribution of different types of practice (hospital/private/mixed), different population structures). National, regional and departmental demographic medical data were taken from data collected by the Research, Evaluation and Statistics Studies Directorate (Ministry for Social Affairs, Employment and Solidarity and Ministry of Health, Family and Handicapped Persons, Paris, September 2003) [5].

Results

Characteristics of gastroenterologists

Of the 456 gastroenterologists who included at least one patient, 424 gave their characteristics. The median age was 40 [range: 26-65] years and 86% were male. They practised in the private sector (N = 104), hospital sector (N = 167) and both private/hospital sector (152); missing data (N = 1).
General patient characteristics

During the three-month period, 1748 patients were included. The median age at the time of the survey was 51 (14-92) years. The distribution of the patients' age is shown in Figure 1. Gender distribution was male: 83.5%, female: 16.5%. CP was alcohol-related (83.6%), related to cationic trypsinogen or SPINK1 mutation (1.2%), mutation of the CFTR gene (0.8%), idiopathic (8.6%) or due to another cause (5.8%) (2 missing data). The distribution of the patients' age on entry into the study according to the cause of CP is shown in Figure 2. Amongst the patients with alcohol-induced CP, the declared daily intake of pure alcohol ranged from 40 to 120 g in 65.7% of patients and over 120 g in 32.2%. The duration of alcoholism was less than 10 years, between 10 and 20 years, and over 20 years in 9.3%, 52.6% and 38.1% of the patients, respectively. At the time of the survey, 60.1% of patients with alcohol-induced CP stated that they had not consumed alcohol for a median period of 13 (0-552) months. The distribution of the patients included in the study, according to the gastroenterologist's practice was as follows: private (12.8%), hospital (50.3%), both (36.9%).

Characteristics of chronic pancreatitis

The diagnosis of CP was probable in 399 patients (22.8%), 83.6% of whom with alcohol-induced CP, and certain in 1349 (77.1%) patients. Confirmed diagnosis was based on the presence of pancreatic calcifications (84.7%), duct anomalies (56.8%) or histological confirmation (7.6%). The median length of time elapsed between the first sign indicative of CP and diagnosis was 1 [0-384] month. The median length of time between the first CP-related sign and inclusion in the study was 41 [3-649] months.

The symptoms and signs of CP were as follows: 52.7% of patients had chronic pain, 66.7% had had at least one attack of acute pancreatitis, 39.5% a pseudocyst and 21.3% a compression of the common bile duct. Other varying complications (alteration of the general status, surgery and portal thrombosis) were reported in 18.8% of patients. Diabetes mellitus was present in 31.6% of patients; it was non-insulin dependent in 37.5% and insulin-dependent in 62.5%. Pancreatic exocrine insufficiency was observed in 35.8% of patients and absent in 64.2%. The diagnosis of exocrine pancreatic insufficiency was based on clinical signs in 76.7% of patients, on the measurement of faecal pancreatic enzymes (5.8%) or on the faecal fat rate (27.1%).

In the case of 206 patients, CP had just been diagnosed (incidental cases).

Incidence and prevalence of chronic pancreatitis

NATIONAL PREVALENCE

Calculation No. 1

Calculated with reference to all French gastroenterologists, the number of consultations by gastroenterologists for CP with a confirmed diagnosis can be estimated at 1349 X (3215/753), i.e. 5760 consultations within three months or 23,040 in one year. The annual number of consultations by patients to gastroenterologists was 2.49 +/- 2.45. The national prevalence of CP could be estimated at 9253 patients (23,040/2.49). The crude prevalence was 15.42 per 100,000 (men: 25.75; women: 5.09).

Calculation No. 2

Taking into account those patients with probable and confirmed CP diagnosis, the same calculation gives an overall national prevalence of 11,990 patients, i.e. a crude prevalence of 19.98 per 100,000 (men: 33.37, women: 6.59).

Calculation No. 3

Finally, by adding the cases not reported by “potentially active” physicians, the national prevalence can be estimated at 15,832 cases (crude prevalence: 26.38, 43.80 in men and 8.97 in women).

INCIDENCE

The number of new cases diagnosed during the 3-month period by 456 active physicians was 206. All of these incident cases were confirmed cases of CP; therefore, calculation No. 2 (taking probable diagnoses into account) was not carried out. By extrapolating this information to all French gastroenterologists over a period of 1 year, this gives a minimal incidence of 3518 new cases per year (crude incidence: 5.86 per 100,000, 9.79 in men and 1.93 in women). The number of cases seen by the 146 “potentially active” physicians could be estimated at 66, i.e. 272 incident cases in all over three months and in the sample. With the same calculation, the number of new cases seen by all the French gastroenterologists could be estimated at 1161 over a three-month period, i.e. a maximum estimation of the incidence of 4,646 cases in 1 year (crude incidence: 7.74 per 100,000, 12.85 in men and 2.63 in women).

Discussion

This study is the first nationwide epidemiological prospective survey devoted to the study of the prevalence and incidence of patients attending gastroenterologists for CP. We also estimated the frequency of the main complications of the disease occurring in the “real life” by contrast with reference centre series. The population of physicians who actively took part in this survey is consistent with the national French population of gastroenterologists [5] in terms of mean age (sample: 40.6 years vs. national population: 45.7 years), male predominance (86.0% vs. 80.9%) and the proportion of gastroenterologists working in the private sector (60.5% vs. 59.6%). The proportion of gastroenterologists (23.4%) who agreed to take part in the study is rather high for such a survey.

Most of the patients with CP are seen by gastroenterologists. This was confirmed by the preliminary survey conducted with general practitioners and endocrinologists — the only two specialist disciplines that may regularly treat patients with CP, apart from gastroenterologists. This survey showed that patients followed by general practitioners and endocrinologists were few in...
number and that almost three-quarters of them were also treated by a gastroenterologist at the same time. Thus, the “loss” of patients is probably minimal and, therefore, may be ignored. Some physicians who had agreed to report patients with CP failed to do so for various reasons. On the basis of a postal survey, we estimated the proportion of these “falsely inactive” physicians and extrapolated the results as if these physicians had ultimately recruited patients. Indeed, as every studies dealing with a disease which may be silent or uneventful, we did not detect patients with undetected or untreated CP.

The survey was carried out over a period of three months between 15 April and 15 July. There is no reference in the literature to any seasonal variation in terms of the manifestations of CP or to any wide variation from one year to another. In acute alcoholic-induced pancreatitis, it does not seem to exist any seasonal variation [6, 7] except, perhaps, during the summer months [8]. There is no reason to believe that our data have not correctly estimated the frequency of CP. It is legitimate to extrapolate our results for one quarter’s activity to the whole year.

The prevalence and incidence of CP were estimated in three ways. Calculation No. 1 has only taken into account confirmed cases of CP, with a diagnosis based on unquestionable criteria (duct anomalies, pancreatic calcifications or histological confirmation). Acute alcohol-induced pancreatitis has, in fact, proved to be the first manifestation of CP in over 90% of cases [4]. In this study, alcohol-related pancreatitis represented 83.6% of CPs with an only probable diagnosis. It was, thus, logical to include these cases when calculating the frequency of CP as we did in the second calculation.

We did not include paediatric centres and only focused on adults. This should lead to an under estimation of the prevalence. However, paediatric cases are much less frequent than adult ones.

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In this study, the investigators did not independently verify that the imaging criteria of CP were actually present or correctly interpreted. However, patient cases were included by experienced gastroenterologists and therefore, the risk of wrong diagnosis may be low. This risk is at least lower than in register studies (or based on diagnosis at discharge) in which the person who filled the record is not systematically a specialist or, even, a physician. To the best of our knowledge, this study is the first one assessing prospectively the epidemiology of CP.

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Thanks to the method employed, we can provide a range in which the true prevalence and incidence of patients with CP attending gastroenterologists in France may probably be. The national prevalence of CP is between 9253 and 15832 cases.
This study shows that CP is a relatively frequent disease. Therefore, the incidence and prevalence of CP were reported, shows that the sample is representative of the national forces the validity of the collection of data. From which to believe that recruitment was biased, and this reinforces the published data is also essential in order to validate the patient population included in this study. The median age was 51 years. The median duration of disease progression at baseline was 41 months. Therefore, it can be extrapolated that the average age at the onset of the disease was approximately 47 years. According to the literature, the age at which the first sign of CP appeared or when CP was diagnosed ranges from 36 to 54 years [14-22]. The percentage of men in this series is 83.5% compared with 72 to 96% in the literature [14-22]. The percentage of alcohol-induced CP is 83.6% in our study, and 68 to 96% in the literature [14-22]. The frequency of other clinical parameters or manifestations (age distribution, duration and quantity of alcohol consumption, pancreatic calcifications, frequency of pain, acute pancreatitis, pseudocysts, endocrine and exocrine pancreatic insufficiencies) are in the same range than that of the published data [14-17, 21, 23-38].

The global comparison of the cohort included in this study with the published series does not highlight any specific difference in the major symptoms of CP. Thus, there is no evidence from which to believe that recruitment was biased, and this reinforces the validity of the collection of data.

In conclusion, the prevalence and incidence of patients attending gastroenterologists for CP could be assessed by our survey for the first time at a national level and prospectively. A comparison of the major characteristics of the disease when they were reported, shows that the sample is representative of the natural history of CP. Therefore, the incidence and prevalence of this condition are probably within the estimate that we have given. This study shows that CP is a relatively frequent disease and underscores its burden in gastroenterologist practice.
REFERENCES


