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Pancreatic cancer in patients with chronic calcifying pancreatitis: Computed tomography findings – a retrospective analysis of 48 patients

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ABSTRACT

Objective: Chronic calcifying pancreatitis (CCP) is a risk factor for pancreatic cancer (PC). Symptoms of PC are non-specific in patients with CCP, and diagnostic imaging can be difficult. Some studies have shown that diagnosis may take several months, leading to delays in treatment (Lin et al., 2015; Lennon et al., 2014) [2,3]. The aim of this study was to describe the radiological signs of PC in patients with CCP.
Methods: This retrospective, single-center study was conducted between January 2004 and December 2014. Patients with CCP who were being monitored for PC were included. Each patient diagnosed with PC was matched with two CCP controls who did not develop PC.
Results: We studied 48 patients with CCP (30 men (62%) and 18 women (38%), mean age 69.4 years). Sixteen patients (with 18 tumor sites) who developed PC (1.52%) were compared with 32 controls who did not develop PC. A hypodense mass was observed in all of the patients with PC, predominantly in the pancreatic head (61.2%). No such masses were observed in the controls ($p < 0.001$). The average mass size was 36.3 mm, and the masses were observed to push aside the calcifications in all patients ($p < 0.001$). Calcifications were very abundant (>10) in 33.3% of the patients with PC and in 71.9% of the controls ($p = 0.0076$). The main pancreatic duct (MPD) was dilated in all of the patients with PC (average diameter 8.6 mm; homogeneous in 83.3%) and in only 46.9% of the controls (average 7.4 mm; homogeneous in 37.5%) ($p > 0.05$). Dilation of the intrahepatic bile ducts and common bile duct was observed in 15 (94.4%) of the patients with PC and in none of the controls ($p < 0.0001$). The average alcohol consumption was 1 g/day (0–5 g/day) in the PC group and 4.6 g/day (0–20 g/day) in the control group. In addition, the average smoking history was 14.25 pack-years (0–40 PY) in the PC group and 27.70 PY (0–60 PY) in the control group.
Conclusion: The presence of a pancreatic mass in a patient with CCP is suggestive of malignancy, especially when few pancreatic calcifications are observed (that are pushed aside by the tumor) and when the tumor causes dilation of the common bile duct and main pancreatic duct.

1. Introduction

Pancreatic cancer (PC) is rare, but its incidence has been increasing worldwide for approximately thirty years [1]. In France, PC is the 10th most common malignancy, with anestimated 9040 new cases diagnosed in 2011 [4]. The incidence peaks between the ages of 50 and 80 years. Some studies have shown that diagnosis may take several months, leading to delays in treatment [2,3]. Despite advances in the diagnosis and treatment of PC, the prognosis remains very

Abbreviations: CCP, chronic calcifying pancreatitis; PC, pancreatic cancer; CBD, common bile duct; SV, splenic vein; TSM, splenomesaraique trunk; SMA, superior mesenteric artery; SMV, superior mesenteric vein; DPC, pancreaticoduodenectomy; IPMT, intrapancreatic ductal papillary mucinous neoplasm.

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poor, with a 5-year survival rate of less than 5% (all stages) and a median survival time of less than 6 months [5–7]. Surgical resection is the only available curative treatment [8], but it is only feasible in the approximately 15% of patients without vascular involvement or distant extension.

Both endogenous and exogenous risk factors have been identified [9]. The two main exogenous risk factors are smoking [10,11] and chronic calcifying pancreatitis (CCP) [9]. PC is approximately 7.2 times more frequent in patients with CCP, with a risk of occurrence of approximately 1% to 2% per year [12–14]. Recent epidemiological studies have reported an increasing incidence of chronic pancreatitis [15]; in European countries, its incidence ranges from 4 cases per 100,000 in the UK to 13.4 cases per 100,000 in Finland [16,17].

Chronic pancreatitis has many possible causes, and the most frequent causes in Western countries are excessive alcohol consumption [12,18] and smoking [11,19,20]. Therefore, this disease is generally alcohol- and smoking-induced [19]. Pancreatic mesenchymal stellate cells are responsible for producing fibrotic tissue during chronic pancreatitis, and this fibrosis appears to be promoted by continuous alcohol consumption [22,23]. Chronic alcohol intoxication leads to abnormal secretion of pancreatic proteins and reduced lithostatin synthesis, thereby increasing the risk of intraparenchymal and intraductal calcification formation [17]. The fibrotic process can be stimulated by the combined effects of alcohol and smoking on pancreatic stellate cells. A recent study [20] has suggested that smoking, but not alcohol consumption, is a risk factor for exocrine pancreatic insufficiency and for the formation of pancreatic calcifications. When PC occurs in individuals with pancreatic insufficiency and abundant calcifications, it is often diagnosed late and is detected according to symptoms of parenchymal and ductal calcifications secondary to chronic pancreatitis. Diagnostic imaging of PC can be difficult in this context. Some studies have shown that diagnosis can take several months, thereby delaying treatment.

The aim of this study was to describe the radiological signs of PC in patients with CCP.

2. Patients and methods

2.1. Inclusion criteria

We conducted a retrospective, single-center study spanning a 10-year period between January 2004 and December 2014 and focusing solely on patients with CCP.

A search of digital radiological and pathological reports (DxCare software) resulted in the identification of 1050 patients with CCP who underwent CT at our center.

The inclusion criteria were as follows:

- Patients followed in the Hepatogastroenterology Department for CCP with the following CT features at diagnosis: calcifications, atrophy of the pancreatic parenchyma, and abnormalities of the main pancreatic duct (MPD).
- Patients managed between January 2004 and December 2014.
- Patients who had at least one available CT scan

The exclusion criteria were as follows:

- Patients who had not at least one available injected CT scan
- Patients who had not histologic confirmation of PC by examination of biopsy or surgical specimen

Among these 1050 patients, 16 CCP patients (10 men and 6 women, average age of 69.7 years) who were found to have PC, either at CCP diagnosis or during CPP monitoring, were included in the study. Histologic confirmation of PC was obtained by examination of biopsy or surgical specimen in all 16 patients (Fig. 1).

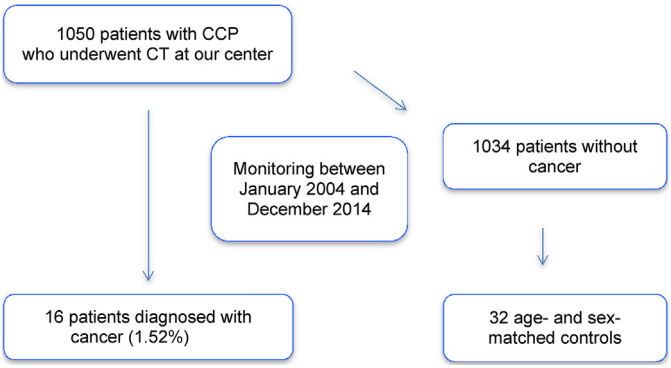

Fig. 1. Flow chart of the study population.

To search for discriminatory CT signs of PC in this setting, we compared the cancer group with a control group of CCP patients who did not develop PC. Each CCP patient diagnosed with PC was matched by age and sex with two CCP patients who remained cancer-free (32 controls).

The CT scans for each patient were reviewed, and the findings were recorded on a standard form (see Appendix A).

General data, such as age, sex, mode of PC discovery and prior cancer history, were recorded. Alcohol consumption (g/day) and smoking history (pack-years) were recorded when available.

2.2. Imaging data

All of the patients underwent at least one CT examination at our center, with and without injection of contrast material.

The following CT protocol was used: without injection phase (0 s), pancreatic phase (40–45 s), portal phase (80 s) and late phase (120 s).

Between 1.5 and 2 ml/kg of iodinated contrast agent (at least 300 g/l of iodine) was injected at a rate of 3 to 4 ml/s. The images were acquired in the cranio-caudal orientation.

2.3. Analysis of imaging data

The CT scans (General Electric Healthcare 16 or 64 slices) of the 48 patients were read by consensus by a senior radiologist (15 years' experience) and a junior radiologist (4 years' experience) who were blinded to the final diagnoses on a Windows Advantage ADW 4.5 post-processing console.

The following data were recorded on standardized forms (Appendix A):

- General and Radiological data, the most important being presence of a tissue mass; its location and size as well as number and location of calcifications

2.4. Statistical analysis

After anonymization, the data were recorded on an Excel spreadsheet (Microsoft Office). The Epidemiology Department of our institution provided assistance with statistical analysis. For the quantitative criteria (i.e., the sizes of the tumor and of the MPD), the mean values obtained by the two readers were analyzed.

These data were compared between the PC and control groups using the McNemar chi-square test for categorical variables and Student's paired *t* test for quantitative variables. Percentages were compared using the chi-square test or Fisher's exact test.