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Incidence and reasons of pancreatic resection in patients with asymptomatic serous cystadenoma

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ABSTRACT

Background/Objectives: Despite diagnostic refinements, pancreatic resection (PR) is eventually performed in some patients with asymptomatic serous cystadenoma (A-SCA). The aim of this study was to define incidence and reasons of PR in A-SCA.

Methods: A retrospective analysis of a prospectively maintained database was performed for all the patients referred for pancreatic cystic lesions (PCL) between January 2005 and March 2016.

Results: Overall, there were 1488 patients with PCL, including 1271 (85.4%) with incidental PCL (I-PCL). During the study period referral of I-PCL increased 8.5-fold. Surgery was immediately advised in 94 I-PCL (7.3%) and became necessary later on in 11 additional patients (0.9%), because of the development of symptoms. Overall, PR was performed in 105/1271 patients presenting with I-PCL (8.2%), including 27 with A-SCA (2.1%). All patients with A-SCA underwent ultrasonography and contrast-enhanced computed tomography. Magnetic resonance imaging was performed in 21 patients (77.8%), 18 F-FDG positron emission tomography in 8 (29.6%), endoscopic ultrasonography (EUS) in 2 (7.4%), and EUS-guided fine needle aspiration (EUS-FNA) in 1 (3.7%). These studies demonstrated a combination of atypical features such as solid tumor (3; 11.1%), oligo-/macrocystic tumor (24; 88.8%), mural nodules (14; 51.8%), enhancing cyst walls (17; 62.9%), dilation of the main pancreatic duct (3; 11.1%), and upstream pancreatic atrophy (1; 3.7%). Additionally, 14/27 patients (51.8%) were females with oligo-/macrocystic tumors located in the body-tail of the pancreas.

Conclusions: Management of patients with A-SCA entails a small risk of PR especially when these tumors demonstrate atypical radiologic features associated with confounding anatomic and demographic characteristics.

1. Introduction

Probably because of the more frequent use and better quality of cross-sectional imaging, incidental pancreatic cystic lesions (I-PCL) are identified in 2.5% of the patients [1,2]. Detection of I-PCL is higher using magnetic resonance imaging (MRI) (15%) versus computed tomography (CT) (3%) [3] and increases with ageing, being <0.5% until 40 years of age and exceeding 30% after 80 years of age [3,4]. To have a more immediate view of the proportions of this phenomenon, each year in the United States approximately 150,000 patients are diagnosed with I-PCL [5]. The risk of malignant degeneration of I-PCL is low, and is associated almost entirely to mucinous cysts. The prevalence of mucin-producing pancreatic carcinomas was calculated in a retrospective population-based cross-sectional study. Given a PCL prevalence rate of 2.5%, the

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total number of PCL in 137, 154, 960 adults was estimated to be 3,428,874. Mucin-producing pancreatic carcinomas were expected to be diagnosed in 1137 patients, with a prevalence of malignant degeneration of 33.2 per 100,000 population [6].

Despite the relatively benign course of nearly all I-PCL, their identification is associated to a cascade of imaging studies, including invasive testing, that requires high resource utilization [7] and generates anxiety in patients and in their families [8]. The recent publication of several guidelines by the Scientific Societies [9–15] has addressed many of the pending issues and has clarified the diagnostic-therapeutic algorithm for the majority of patients with PCLs. However, especially for patients with I-PCL, recommendations from guidelines are not always unambiguous, probably because of the availability of limited evidence and the incomplete definition of the biologic course of some of these lesions [16].

On practical grounds, the surgeon is sometimes confronted with the difficult decision of whether or not to resect an I-PCL. Resection of an I-PCL of undetermined nature provides a reliable diagnosis, and possibly prevents malignant degeneration of the tumor, but entails the surgical risks typically associated with these procedures [17]. On the other hand, a policy of surveillance spares the patient the risks of surgery, but is associated with the hazard of overlooking a cancer [18].

Although most of the controversy revolves around mucinous cysts, not all serous cystadenomas (SCA) are readily identified [19]. Indeed, all large series of resected PCLs include incidentally discovered SCA [17,20–24].

In this study we review our experience with resected SCA in asymptomatic patients (A-SCA), with the aim of define incidence and reasons of pancreatic resection in this patient population.

2. Materials and methods

A retrospective analysis of a prospectively maintained database was performed for all the patients referred with a diagnosis of PCL to the Division of General and Transplant Surgery of the University of Pisa, between January 2005 and March 2016.

The aim of this study was to identify patients who underwent pancreatic resection of an I-PCL of undetermined nature with a final diagnosis of SCA, and to define the reasons indicating surgery in this group of patients.

This study was approved by the Institutional Review Board of the University of Pisa.

Demographic data, patient history, information on serology, type of imaging studies performed, size of the cyst, characteristics of the cystic wall, associated findings (e.g. duct dilation), radiology reports, results from fine needle aspiration/citology, and pathology data were extracted from the database. Reports of pre-operative multidisciplinary tumor board were also reviewed.

Each patient was evaluated by ultrasonography (US), including contrast-enhanced ultrasound if required, multiphasic contrast-enhanced CT using either a 64-(Light Speed Plus VCT, GE Medical System, Milwaukee USA) or a 128-row scanner (Discovery HDx 750, GE Medical System, Milwaukee USA) according to a standardized protocol [25], and MRI/magnetic resonance cholangiopancreatography (MRCP) performed on a superconductive system operating at either 1.5 T (Signa HDx; GE Healthcare, Milwaukee, Wisconsin, USA) or 3 T (GE DISCOVERY MR750; GE Healthcare, Milwaukee, Wisconsin, USA) with an eight-channel phased-array body coil.

According to our multiphasic contrast-enhanced CT (MDCT) imaging protocol, following basal scanning, high-concentration iodinated contrast medium (370–400 mg iodine/ml) was injected intravenously at a flow rate of 3.5–4 mL/s, using a dual-head pump injector. Post-contrastographic study included 3 phases: pancreatic phase (at 35–40 s), venous phase (at 70 s) and late phase (at 180 s). The following scanning parameters were used: section reconstruction 2.5–1.25 mm; section interval 1.25–0.625 mm; pitch 6 (High Speed-HS modality) or beam pitch 0.984:1; anode voltage 100–120 kV; 300–350 mA or automatic tube current modulation (smart mA, noise index 21); 0.6/0.8-s rotation speed; 512 matrix size.

Our MRI protocol first included axial T1 and axial and coronal T2w images, MRCP and diffusion-weighted sequences. DW-MRI was performed using a spin-echo echo-planar sequence with multiple b-values (300, 500, 700 and 1000 s/mm^2 at 1.5 T; 150, 500, 1000, 1500 s/mm^2 at 3 T), obtaining an ADC map [26]. T1w sequences after contrast agent administration was obtained in half of our patients.

When requested after multidisciplinary discussion of each case at the tumor board, 18 F-FDG positron emission tomography/computed tomography (18 F-FDG PET/CT), and/or endoscopic ultrasonography (EUS) coupled with fine needle aspiration (FNA) of cystic fluid were also performed.

Data on post-operative morbidity and mortality were also analysed. In particular all events occurring within 90 days of surgery were recorded. Post-operative pancreatic fistula (POPF) [27], delayed gastric emptying (DGE) [28], and post-pancreatectomy hemorrhage [29] were identified and graded according to standard definitions. Grade B and grade C POPF were considered clinically relevant POPFs. Clavien–Dindo classification was used to define the severity of postoperative complications [30]. Complications graded $\geq$ IIIb were considered severe [31]. In patients with more than one complication, the highest grade was considered. The comprehensive complication index was also calculated [32].

When resection was indicated despite the lack of an established diagnosis and/or symptoms, patients were counselled not only about the short-term risks and the long-term consequences of surgery, but also about the possibility of a “negative” histology after resection. Patients had to sign an informed consent. Patients requiring a distal pancreatectomy, irrespective of anticipated possibility of sparing the spleen, received pre-operative vaccines against streptococcus pneumoniae, haemophilus influenzae type b, and neisseria meningitidis.

2.1. Statistics

Categorical variables are summarized as frequencies, percentages and rates. Continuous variables are expressed as mean $\pm$ SD if normally distributed or as median and interquartile range (IQR) if not. Student's t-test and chi–square test were used as appropriate for comparison of continuous and categorical variables, respectively. A p value < 0.05 were considered significant. Statistical analysis was performed using IBM SPSS Statistics 24.0 (SPSS Inc, Chicago, IL).

3. Results

A total of 1488 patients were referred to our Institution with diagnosis of a PCL, with an increase in the frequency of annual referral of 6-fold between the first and the last year of the study period. There was a 3-fold increase for symptomatic PCLs, and a 8.5-fold increase for I-PCLs (Fig. 1).

A total of 1271 patients were diagnosed with I-PCLs (85.4%). Pancreatic resection was immediately performed in 94 of such patients (7.3%). Eleven (0.9%) of the 1177 patients for whom follow-up was devised, developed symptoms and/or changes in imaging features after an initial period of watchful waiting, and were also eventually operated.

Overall, a pancreatic resection was performed in 105 (8.2%) out of 1271 patients with an initial diagnosis of I-PCL, including 27 patients with a final diagnosis of SCA. Three of these patients had

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