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Pancreatectomy for pancreatic incidentaloma: What are the risks?

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ABSTRACT

Background: Pancreatic incidentalomas (PI) are nowadays common but the benefit-risk balance of surgery remains difficult to determine.**Methods:** Monocentric retrospective study of 881 pancreatectomies comparing resected PI with symptomatic lesion. Univariate and multivariate (MV) analyses were done to identify risk factors of malignancy in PI undergoing surgery.**Results:** Overall, 32% of pancreatectomies were performed for PI. Median size of PI was 30 mm (vs 28 mm; $p = 0.15$) and 49% were cystic (vs 42%; $p = 0.197$). Resected PI were mostly located in distal pancreas (61% vs 34%; $p < 0.001$), less frequently malignant (49% vs 59%; $p = 0.004$). PNETs were more frequent in PI (50% vs 21%; $p < 0.001$). Distal pancreatectomy (36% vs 23%; $p < 0.001$) or parenchyma-sparing surgery (34% vs 13%; $p < 0.001$) were more frequently performed for PI. Overall mortality (1.1% vs 1.2%) and morbidity (70% vs 68%) were not significantly different between both groups. Severe morbidity was lower for PI (15% vs 22%; $p = 0.007$). In multivariate analysis, age > 55 years (HR 6.14; $p < 0.001$), size > 20 mm (HR: 26.7; $p < 0.001$) and biliary dilatation (HR 29.9; $p = 0.027$) were independent risk factors of malignancy and, when associated, the likelihood of malignancy was above 90%. **Conclusions:** PI represent about 30% of indications for pancreatectomy and when resected after careful selection are malignant in 50% of cases.

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Introduction

With the widespread use of high-quality cross-sectional imaging, an increased number of asymptomatic solid or more frequently cystic pancreatic lesions are being identified. The prevalence of these so called “incidentalomas”, *i.e.* asymptomatic mass fortuitously detected by imaging, is approximately 10% [1] in the population and may reach as high as 30% in patients over 70 years of age [2]. Pancreatic incidentaloma encompasses a wide spectrum of neoplasms, including serous cystadenomas (SCA), mucinous cystic neoplasms (MCN), mucinous cystadenocarcinomas, non-functional neuroendocrine tumors (PNET), solid and pseudopapillary neoplasm (SPPN) and intraductal papillary mucinous neoplasms (IPMN) [3]. The main issue in their management is that beyond

their comforting presentation, this heterogeneous group of lesions can be premalignant or even malignant.

This concern has led to an increasing number of resections for pancreatic incidentaloma in order to eradicate potentially threatening pancreatic lesions in their earliest stages. However, the mortality of pancreatic surgery ranges from 1% to 3% in high-volume centers [4,5], but increases up to 6–10% when nationwide data are considered [6–8]. Consequently, surgical indication must be carefully weighted in asymptomatic patients.

The aim of the present study is to describe patients with pancreatic incidentaloma selected for surgery from a large database of pancreatectomies performed at a single institution, to compare them with symptomatic patients, and to determine risk factors of malignancy.

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Abbreviations

PI	Pancreatic Incidentaloma
BMI	Body Mass Index
CT	Computed tomography
EUS	Endoscopic ultrasonography
FDG-PET	Fluorodeoxyglucose positron emission tomography
FNA	Fine needle examination
IPMN	Intraductal papillary mucinous neoplasms
ISGPS	International Study Group of Pancreatic Surgery
MCN	Mucinous cystadenoma
MRCP	Magnetic resonance cholangiopancreatography
MRI	Magnetic resonance imaging
PNET	Pancreatic neuroendocrine tumor
PDAC	Pancreatic ductal adenocarcinoma
SPPN	Solid pseudopapillary neoplasm

Material and methods

Inclusion criteria and data collection

After institutional review board approval (IRB 12-055), we reviewed the medical records of 881 consecutive patients who underwent a pancreatic resection between 2005 and 2013 for suspected pancreatic tumors in the Department of Hepatobiliary and Pancreatic Surgery - Beaujon Hospital, Clichy, France. Demographic variables, clinical presentation, intraoperative, postoperative course, and a definitive pathologic diagnosis were obtained from a prospective database with an additional retrospective medical record review. Care was taken to obtain the following information: date of diagnosis, presence of symptoms or not including jaundice, pain, abdominal mass, nausea, vomiting or new-onset diabetes. Patients were categorized into 2 groups: 1) patients with pancreatic incidentaloma (PI), *i.e.* patients with incidentally diagnosed pancreatic lesions defined as lesions with no clinical manifestations related to the pancreatic mass or hormonal secretion and 2) patients with symptomatic pancreatic lesions (NI). Surgery for supposed biliary, duodenal and ampullary lesions were excluded, due to the specific role of endoscopy in their diagnosis and management.

Preoperative workup and surgical indications

A minimal routine work-up required 3-phase contrast-enhanced multidetector computed tomography (CT). Magnetic resonance imaging (MRI) with magnetic resonance cholangiopancreatography (MRCP), nuclear imaging (somatostatin receptor scintigraphy and/or fluorodeoxyglucose positron emission tomography (FDG-PET) or endoscopic ultrasound (EUS) with or without fine needle aspiration (FNA) or cyst fluid aspiration, were left to surgical and medical team's discretion. Pancreatic lesions were measured at their largest diameter on cross-sectional imaging. Dilatation of common bile duct and main pancreatic duct were assessed mainly at EUS. All surgical indications were discussed in a multidisciplinary pancreatic tumor board that included surgeons, radiologists, gastroenterologists, and pathologists. Surgical indications were decided according to the guidelines of the International Association of Pancreatology (IAP) for IPMN [9,10], and the ENETS guidelines [11] for PNET. Procedures and postoperative management were performed as previously reported by our team [12–14]. A parenchyma-sparing pancreatectomy (enucleation,

central pancreatectomy) was considered in patients with a presumed benign tumor and favorable anatomical localization [12]. Conversely, any suspicion of malignancy was an indication for an oncologic pancreatectomy (pancreaticoduodenectomy or distal pancreatectomy) with appropriate lymphadenectomy.

Postoperative course and follow-up

Postoperative mortality included all deaths occurring during hospitalization or within 90-days. Morbidity included all complications following surgery until discharge and/or readmission and was graded according to the Dindo-Clavien classification of postoperative complications [15]. Postoperative pancreatic fistula, haemorrhage and delayed gastric emptying were defined according to the International Study Group of Pancreatic Surgery (ISGPS) [16–18].

Pathological analysis

Pancreatic lesions were classified according to the World Health Organization classification of exocrine and endocrine neoplasms of the pancreas [19]. In the following analysis, the “malignancy” group, refers to undebatable surgical indication and includes any lesions harboring either carcinoma *in situ*, invasive or metastatic features, *i.e.* pancreatic ductal adenocarcinoma [PDAC], malignant IPMN, including *in situ* carcinoma, mucinous cystadenocarcinoma, functioning PNET except insulinoma, non-functioning PNET ≥ 2 cm or with positive node or metastasis disease, pancreatic metastasis, sarcoma and cholangiocarcinoma. The “potentially malignant” group includes high-grade IPMN, MCN, and SPPN. The “benign lesions” group includes insulinoma, non-functioning PNET < 2 cm without positive node or metastatic disease, simple cyst and SCA. Patients who underwent surgery due to suspicion of pancreatic neoplasms, but eventually had an inflammatory disease (chronic pancreatitis, pseudocysts, autoimmune pancreatitis) on pathological examination were also included in the “non-malignant lesions”.

Statistical analysis

Values were expressed as median (interquartile range), or percentage, as appropriate. According to the distribution of variables, the Chi-square or Fisher's exact tests were used to compare the differences in discrete or categorical variables, and the *t*-test or Wilcoxon rank-sum test was used for continuous variables between the PI and NI groups.

A multivariate logistic regression analysis was performed to determine the independent preoperative risk factors of malignancy in incidentalomas. All preoperative clinical, biological and radiological variables achieving statistical significance at a 0.1 level in the univariate analysis were considered for multivariate analysis. A backward variable selection procedure was used to identify the independent predictive factors. The sensitivity (Se), specificity (Sp), positive predictive value (PPV) and negative predictive value (NPV) for malignancy of one, two or three of these factors was then assessed. The malignancy rate of a risk factor was also calculated using the following formula: malignancy rate of one risk factor = number of patients presenting with the only considered factor and having a malignant tumor/number of patients presenting with the only considered factor. Odds ratios (OR) with 95% confidence intervals (CI) are reported. All statistical tests were two-sided, and the statistical significance was set at $p < 0.05$. Data were analysed with STATA 11 statistical software (StataCorp. 2009. Stata Statistical Software: Release 11. College Station, TX: StataCorp LP).

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