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Incidental lesions of the pancreas. A clinicopathological study of 100 cases surgically treated

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ABSTRACT

Objective: the objective of the present study was to analyze the characteristics of resected incidental lesions of the pancreas.

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Material and methods: a retrospective study was performed of pancreatectomies due to incidentalomas between 1995 and 2018.

Results: one hundred pancreatectomies were performed due to incidental lesions; 64 (64%) were solid and 36 (36%) were cystic lesions. The cytological analysis agreed with the diagnosis in 67/71 (88.7%) cases. Thirty-six tumors were cystic, 48 were neuroendocrine and 16 were adenocarcinomas. Disease-free survival for patients with cystic, neuroendocrine tumors and adenocarcinomas was 100%, 79% and 57.7% ($p < 0.04$).

Conclusion: pancreatic incidentalomas have a heterogeneous phenotype and should be treated in experienced centers

Keywords: Incidental. Pancreatectomy. Cystic tumor. Neuroendocrine. Adenocarcinoma. Outcomes.

INTRODUCTION

Given the greater use and sensitivity of imaging techniques such as multidetector computed tomography (MDCT), ultrasonography (EUS) and magnetic resonance imaging, the incidental diagnosis of pancreatic lesions is increasing (1). The differential diagnosis and choice of therapeutic options are challenging, for both gastroenterologists and surgeons. This is due to the associated morbidity and mortality associated with pancreatic resections and the fact that they are usually diagnosed in patients > 70 years. In this study we analyze our experience of pancreatic resections of 100 incidentally diagnosed lesions.

MATERIAL AND METHODS

Patients and pre-operative data

This was an observational, retrospective and descriptive study based on a prospective database of pancreatic resections performed due to incidental lesions from 1995 to 2018. The study was approved by the local Ethics Committee and was performed following the Declaration of Helsinki and STROBE recommendations. Demographic data such as age, sex, body mass index and ASA status were collected.

Incidental lesions were identified by chance during imaging studies or as a consequence of elevated tumor markers and/or transaminases, with the absence of symptoms. Two authors (JAC and LHP) independently confirmed the diagnosis of lesions as incidental. Cytological analysis was performed in most patients using EUS- or CT-guided fine needle aspiration (FNA) (2). A positive correlation was retained when the pre-operative and definitive histopathological diagnosis were consistent.

Surgical management

Surgical management was decided during an interdisciplinary meeting. The surgical approach, surgery time and hospital stay were noted. From 2002, enucleation, central and distal pancreatectomies were performed laparoscopically with sparing of the spleen and splenic vessels (3). No pancreatic drains were left in place. Complications were defined according to the International Study Group of Pancreatic Surgery and those > IIIb Clavien-Dindo were considered as severe (4).

Histopathological analysis

Surgical specimens were analyzed following the guidelines of the American College of Pathologists. Neuroendocrine tumors (NETs) were also assessed (5). Pancreatic ductal adenocarcinomas (PDCAs) were staged using the TNM system (6). PDCA, *in-situ* carcinoma, high-grade dysplasia in intraductal papillary mucinous tumors, solid pseudopapillary tumors, cystic mucinous neoplasia and stage IIa-IIIb (T2N0-1) NETs were considered as invasive phenotypes (7).

Outcomes

All patients were monitored every three months during three years and then every six months for up to five years via laboratory and imaging examinations. Disease-free and overall survival were calculated from the date of surgery to the date of radiology or histology confirmed recurrence and to the date of death from any cause, respectively (or censored until the date of last follow-up).

Statistical analysis

All analyses were performed using Stata v.12 (StataCorp, Texas, USA). Categorical and continuous variables are expressed as percentages and means (SD). The Chi-squared or Fisher's tests were used for categorical variables and the Student's t-test for continuous variables. A $p < 0.05$ was considered as statistically significant. Disease-free-survival was calculated according to the Kaplan-Meier and log-rank tests; median and interquartile ranges were computed for patient follow-up.

RESULTS

Of 387 pancreatic resections, 100 (25.8%) were performed due to incidental lesions (mean age: 58.9 ± 13.2, 49% female). Tables 1 and 2 summarize the symptoms at diagnosis and patient characteristics. The most commonly used diagnostic technique was MDCT (79%) and FNA was performed in 71 patients, either guided by EUS (n = 67) or by MDCT (n = 4). Diagnostic agreement was retained in 63 cases (88.7%). The sensitivity and positive predictive value were 87.9-84.2% and 100-100% for neuroendocrine tumors and PDCAs, respectively. Invasive lesions were larger ($p < 0.001$) and were mostly located in the head of the pancreas ($p = 0.013$).

The mean hospital stay was 9.8 days (SD: 9.8), with a mortality of 1% and no early readmissions. Thirteen patients (13%) experienced severe complications and fluid collections were observed in 24 cases (24%), two of which (8.3%) required drainage. Pancreatic ductal adenocarcinoma staging was as follows: IA (n = 2), IB (n = 7), IIA (n = 2) and III (n = 5). Fourteen cases were treated with neoadjuvant therapy. The median follow-up was 47 months (IQR 14-93). Survival at five and ten years is shown in figure 1. Five-year overall for cystic tumors, neuroendocrine and PDCA was 100%, 83.9% and 60%%, respectively, and disease-free-survival was 97%, 79.6% and 57%, respectively.

DISCUSSION

In our study, 25.8% of all pancreatic resections were incidental, rising to 31.4% in the last ten years. This is similar to previous reports (1,8). As previously described, the most frequent locations were the body and tail (70%) (1,9). This may have an impact on the mean hospital stay (9.8 days), which is similar to the North-America series, but lower than those reported from European studies (1).

The most frequently used diagnostic techniques were MDCT and EUS. Most lesions were solid and the most frequent diagnosis was a non-functional NET. These results are similar to series in which all the phenotypes of incidental tumors were considered, but in contrast to those studies that analyzed specific tumor subtypes (1,10). In our series, the incidence of pancreatic fistulas was lower. This was probably due to the systematic use of intraoperative ultrasound of the Wirsung, sparing of the spleen and splenic vessels in distal pancreatectomies and the lack of drainage in the pancreatic cell (1,11). However, we observed peripancreatic fluid collections in 24% of cases, which spontaneously reabsorbed in most cases. Central and distal pancreatectomies were more frequent in our series and they have a lower morbidity and mortality than cephalic duodenopancreatectomies, leading to a potential bias in some outcomes (1,12).

According to other authors, 47% of the tumors had an invasive phenotype, principally due to neuroendocrine tumors (55.3%) and adenocarcinomas (34%). The incidental NETs resected in our center represent 53% of all resected NETs, which is a lower percentage compared to Birnbaum (61%) (13) and higher than that reported by Crippa (35%) (14). They also had a greater diameter compared to non-invasive type, justifying the resection of incidental neuroendocrine and cystic tumors > 2 cm in size (13). In our series, 16% of lesions were PDCAs, which is slightly higher compared to other series (10-12%) and lower than that reported by Takeda (12). Resected incidental PDCAs represented 8.5% of all resected PDCAs and the majority were initial clinical stages (I-II). In addition, the good oncologic outcomes in these resected tumors must be interpreted with caution. Firstly, they were diagnosed at earlier stages of their natural development, thus resulting in a longer follow-up and an artificially increased survival. Secondly, incidental tumors grow more slowly and have a longer latent or pre-symptomatic phase, which may lead to increased survival. Lastly, other authors described a less aggressive behavior than symptomatic tumors (15).

We are aware of the limitations of our study due to the retrospective design of a heterogeneous cohort. However, data were collected prospectively. In addition, a longer follow-up is lacking, especially in cystic lesions. The introduction of minimally invasive techniques and the fact that a higher proportion of distal/central

pancreatectomy were performed could also have influenced the results.

In conclusion, incidental pancreatic tumors are becoming increasingly common and their diagnosis and treatment remain a challenge. Phenotypical and cytological characteristics and a multi-disciplinary approach are key points to ensure that the treatment is tailored to the needs of the patient.

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Table 1. Comparison of clinical, surgical details and tumor characteristics between non-invasive and invasive phenotypes of incidental lesions

No. (%) of patients

Clinical variable	Overall (n = 100)	Non-invasive (n = 53)	Invasive (n = 47)	*p* value
Sex				
Male	51 (51)	24 (45.3)	27 (57.4)	0.31
Age, mean (SD) *y.*	58.9 (13.2)	60.2 (11.8)	57.5 (14.7)	0.32
BMI, mean (SD)	25.6 (4.8)	26.4 (4.8)	25.5 (4.9)	0.35
ASA class on admission				
1 (no disturbance)	4 (4)	1 (1.8)	3 (5.6)	
2 (mild disturbance)	46 (46)	27 (51)	19 (40.4)	
3 (severe disturbance)	45 (45)	23 (43.3)	22 (46.8)	
Missing data	5 (5)			
Tumor location				
Head or uncinated process	29 (29)	10 (18.9)	19 (40.4)	
Body	23 (23)	18 (34)	5 (10.6)	0.01
Tail	47 (47)	24 (45.3)	23 (48.9)	
Diffuse	1 (1)	1 (1.9)		
Tumor size (mm) mean (SD)	26.9 (23.2)	19.5 (16.7)	35.6 (26.9)	< 0.01
Type of surgery				
Enucleation	4 (4)	4 (7.5)	0	0.01
Whipple procedure	25 (25)	8 (15.1)	17 (36.2)	
Central pancreatectomy	13 (13)	11 (20.8)	2 (4.3)	
Lap/open	10/3	9/2	1/1	
Corporeo-caudal pancreatectomy	6 (6)	-	6 (12.8)	
Distal pancreatectomy	51 (51)	29 (54.7)	22 (46.8)	
Lap/open	41/10	25/4	16/6	
Total pancreatectomy	1 (1)	1 (1.9)		
Histopathology diagnosis				

Mucinous cystic neoplasm	8 (8)	7 (13.2)	1 (2.1)	< 0.01
Serous cystadenoma	15 (15)	15 (28.3)	-	
Solid pseudopapillary tumor	3 (3)	-	3 (6.4)	
IPMN	9 (9)	8 (15.1)	1 (2.1)	
Neuroendocrine neoplasm	48 (48)	22 (41.5)	26 (55.3)	
Ductal adenocarcinoma	16 (16)	-	16 (34)	
Chorystoma	1 (1)	1 (1.9)	-	
Operative time (min), mean (SD)	296 (149)	298.4 (184)	294.4 (100)	0.797
Postoperative course				
Pancreatic fistula (grades B/C)	7 (7)	3 (5.7)	4 (8.5)	0.47
Delayed gastric emptying	3 (3)	3 (5.7)	-	0.09
Intra-abdominal collection	24 (24)	17 (32.1)	7 (14.9)	0.07
Hospital stay (days) mean (SD)	9.8 (9.8)	8.1 (7)	11.7 (12.1)	0.09
Grade ≥ IIIb morbidity	13 (13)	6 (11.4)	7 (14.9)	
Oncologic outcomes				
Loco-regional recurrence	5 (5)	1 (1.9)	4 (8.5)	< 0.01
Distant recurrence	15 (15)	-	15 (31.9)	< 0.01
Mortality				
30 days	1	-	1	
90 days	1	-	1	

ASA: American Society of Anesthesiologists; BMI: body mass index (calculated as weight in kilograms divided by height in meters squared); IPMN: intraductal papillary mucinous neoplasm: SD: standard deviation

Table 2. Clinical characteristics regarding the final pathologic diagnosis

	No. (%) of patients					
	Mucinous cystic neoplasm (n = 8)	Intraductal papillary mucinous neoplasm (n = 9)	Serous cystadenoma (n = 15)	Solid pseudopapillary tumor (n = 3)	Neuroendocrine tumor (n = 48)	Ductal adenocarcinoma (n = 16)
Sex						
Male, n (%)	2 (25)	4 (44.4)	3 (20)	0	31 (64.6)	10 (66.7)
Age, mean (SD) *y.*	65.5 (14.7)	64.2 (7.8)	57.3 (14)	29.3 (4.9)	57.6 (11.9)	64.9 (7.8)
Diabetes, n (%)	1 (12.5)	2 (22.2)	1 (6.7)	0	7 (14.6)	4 (25)
Invasive, n (%)	1 (12.5)	0	0	3 (100)	26 (54.2)	16 (100)
Location						
Head	1 (12.5)	4 (44.4)	2 (13.3)	1 (33.3)	9 (18.8)	12 (75)
Body	3 (37.5)	3 (33.3)	5 (33.3)	1 (33.3)	11 (22.9)	0
Tail	4 (50)	1 (11.1)	8 (53.3)	1 (33.3)	28 (58.3)	4 (25)
Diffuse	0	1 (11.1)	0	0	0	0
Diameter, mean (SD) *mm*.	38.1 (33.3)	16.6 (5.7)	23.6 (13.9)	46.7 (14.3)	25.6 (24)	26.6 (18.6)
Type of surgery						

Enucleation	0	0	1 (6.7)	0	3 (6.3)	0
Whipple procedure	1 (12.5)	4 (44.4)	1 (6.7)	1 (33.3)	6 (12.5)	12 (75)
Corporeo-distal	0	0	0	0	5 (10.4)	1 (6.3)
pancreatectomy	2 (25)	2 (22.2)	2 (13.3)	1 (33.3)	6 (12.5)	0
Central pancreatectomy	2/0	2/0	1/1	0/1	5/1	0
Lap/open	5 (62.5)	2 (22.2)	11 (73.3)	1 (33.3)	28 (58.3)	3 (18.8)
Distal pancreatectomy	4/1	2/0	10/1	1/0	22/6	2/1
Lap/open	0	1 (11.1)	0	0	0	0
Total pancreatectomy						
Loco-regional recurrence, n (%)	0	1 (11.1)	0	0	5 (10.4)	0
Distant recurrence, n (%)	0	1 (11.1)	0	0	9 (18.8)	5 (31.3)
Free of disease, n (%)	8 (100)	8 (88.8)	15 (100)	3 (100)	36 (75)	11 (68.8)
Deceased, n (%)						
Tumor related	0	0	0	0	7 (14.6)	4 (25)
Non-tumor related	1 (12.5)	0	0	0	1 (2.1)	3 (18.8)

Fig. 1. Kaplan-Meier overall survival (A) and disease-free survival curves (B) for patients with incidental lesions who underwent pancreatectomy according to the type of lesion