Sporadic nonfunctioning pancreatic neuroendocrine tumors: Prognostic significance of incidental diagnosis

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Background. *Sporadic nonfunctioning pancreatic neuroendocrine tumors (NF-PNETs) are increasingly diagnosed as incidentalomas, and their resection is usually recommended. The prognostic significance of this diagnosis feature is poorly studied, and management of these tumors remains controversial. Clinical, pathologic characteristics and outcome of resected incidentally diagnosed NF-PNET (Inc) were compared with resected symptomatic NF-PNET (Symp) to better assess their biologic behavior and tailor their management.*

Methods. *From 1994 to 2010, 108 patients underwent resection for sporadic nonmetastatic NF-PNET. Diagnosis was considered as incidental in patients with no abdominal symptoms or symptoms unlikely to be related to tumor mass. Patients with Inc were compared with patients with Symp, regarding demographics, postoperative course, pathology, and disease-free survival (DFS).*

Results. *Of the 108 patients, 65 (61%) had incidentally diagnosed tumors. Pancreas-sparing pancreatectomies (enucleation/central pancreatectomy) were performed more frequently in Inc (62% vs 30%, P = .001). Inc tumors were more frequently <20 mm (65% vs 42%, P = .019), staged T1 (62% vs 33%, P = .0001), node negative (85% vs 60%; P = .005), and grade 1 (66% vs 33%, P = .0001). One postoperative death occurred in the Inc group, and postoperative morbidity was similar between the two groups (60% vs 65%, P = .59). DFS was substantially better in the Inc group (5-year DFS = 92% vs 82%, P = .0016).*

Conclusion. *Incidentally diagnosed NF-PNETs are associated with less aggressive features compared with symptomatic lesions but cannot always be considered to be benign. Operative resection remains recommended for most. Incidentally diagnosed NF-PNET may be good candidates for pancreas-sparing pancreatectomies. (Surgery 2014;155:13-21.)*

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Pancreatic neuroendocrine tumors (PNET) are rare, representing 1% to 2% of all pancreatic neoplasms.[1] They represent a heterogeneous group of tumors with an extremely variable clinical behavior mainly depending on histologic features and disease staging.[2] When possible, operation provides the best chance for a cure and provides 5-year overall survival exceeding 60%.[3-5]

In recent years, PNET, particularly sporadic nonfunctioning (NF) cases, have been increasingly diagnosed,[6] often as incidentalomas, because of the widespread use of cross-sectional imaging.[7,8] Our understanding of the natural history of incidentally discovered NF-PNET is limited, but despite the lack of high-level evidence, operative resection is usually recommended. This aggressive management recently has been challenged because of the substantial morbidity of pancreatic surgery[5,9-11] contrasting with the favorable long-term outcome of these lesions[12]—even if this remains controversial.[13]

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To expand our knowledge regarding this increasingly frequent situation, we retrospectively analyzed our experience of pancreatectomy for sporadic nonmetastatic NF-PNET by comparing patients with tumors incidentally discovered with the remaining population.

PATIENTS AND METHODS

Data collection. From 1994 to 2010, 108 patients underwent complete resection for sporadic, nonmetastatic, NF-PNET in the Department of Hepatobiliary and Pancreatic Surgery - Beaujon Hospital, Clichy, France. Demographic variables, clinical presentation, preoperative workup, and intraoperative data including type of resection, postoperative course, and pathology were obtained from a prospective database with additional retrospective medical record review. NF tumors were defined as lesions without symptoms related to hormonal excess. Patients with incidentally diagnosed lesions were defined as patients without any symptoms or abnormal liver tests, ie, cholestasis, and/or patients with clinical manifestations unlikely to be related to the mass.

Preoperative work-up, operative procedures, and pathologic analysis. Preoperative tumor staging was done by computed tomography and/or magnetic resonance, endoscopic ultrasound, or somatostatin receptor scintigraphy at the surgeon's discretion, as previously reported.[5] All operative indications were discussed in a multidisciplinary pancreatic tumor board, including surgeons, radiologists, pathologists, oncologists, and gastroenterologists. Diagnosis of PNET was based on conventional histology and immunohistochemistry (chromogranin A, synaptophysin, and Ki67). All cases were reviewed and classified according to the 2010 World Health Organization (WHO) classification and assigned an ENETS (European Neuroendocrine Tumor Society)/TNM-based stage and grading score.[14,15]

Operative procedures were preoperatively planed based on tumor localization and intraoperatively confirmed after operative exploration assisted by routine intraoperative ultrasonography for evaluation of the proximity of the tumor from the vascular structure and the main pancreatic duct. Enucleation was performed when the tumor was near to or at the surface of the head or body of the pancreas, far enough (at least 1 to 2 mm) from the main pancreatic duct. Regarding tumors of the neck and body of the pancreas, if enucleation was not possible, central pancreatectomy was performed if the remnant pancreas was at least 5–7 cm long. In this setting, the proximal remnant was overseen after elective ligation of the main pancreatic duct. Reconstruction of the distal pancreas was done by end-to-side pancreaticogastrostomy. Pancreaticoduodenectomy and distal pancreatectomy were performed as previously reported by our group.[5]

Intraoperatively, all standard resections included regional lymph node dissection. During central pancreatectomy and enucleation, all visible lymph nodes located up to 5 cm around the tumor were resected but frozen section analysis was not routinely done. At the end of the procedure, drainage was placed close to the enucleation cavity or the pancreatic anastomosis or section and removed progressively from postoperative day 5.

Postoperative course and follow-up. Postoperative mortality included all deaths occurring before hospital discharge or within 90 days. Morbidity included all complications after operation until discharge and/or readmission and was graded according to the Clavien-Dindo classification.[16] Postoperative pancreatic fistula, hemorrhage, and delayed gastric emptying were defined according to the International Study Group of Pancreatic Surgery.[17,18]

Follow-up was based on clinical, radiologic, and laboratory assessments and updated upon outpatient evaluation, routine postoperative visits, and correspondence. Visits were scheduled every 6 months for the first 5 years and annually thereafter. Detection of recurrence was based on thoracoabdominal computed tomography scan and chromogranin A serum level. In case of suspected recurrence, magnetic resonance imaging or octreoscan scintigraphy were performed according to the clinical situation.

Statistical analysis. Values are expressed as median (range), or percentage, as appropriate. The Fisher exact test was used to compare differences in discrete or categorical variables, and the Wilcoxon rank-sum test was used for continuous variables. Overall survival (OS) was calculated from the date of surgery to the date of death or last follow-up if no event had occurred. Disease-free survival (DFS) was calculated from the date of surgery to the date of the first evidence of recurrence or last follow-up if no event had occurred. Patients who died during the postoperative course were excluded from the survival analysis to assess tumor behavior only. OS and DFS were estimated by the method of Kaplan-Meier, and the log-rank test was used to compare survival curves.

All tests were two-sided. Data were analyzed with the STATA 12 statistical software (StataCorp. 2011.

Stata Statistical Software: Release 12. College Station, TX: StataCorp LP).

RESULTS

Clinical characteristics. Among the 108 patients who underwent complete resection for sporadic, nonmetastatic, NF-PNET, 61% (n = 65) had an incidentally diagnosed tumor. These 65 pancreatic incidentalomas (Inc group) were compared with the remaining 43 patients (39%) with symptomatic (Symp group) lesions either because of abdominal pain (86%; n = 37) or jaundice (14%; n = 6). The percentage of incidentally diagnosed NF-PNET increased from 40% in the period from 1995 to 1998 to 69% in the period from 2007 to 2010.

Patient and tumor characteristics are summarized in Table I. Briefly, patients had a median age of 58 years (range, 36–75) and most of them were women (n = 69; 64%). Tumors were mostly located in the head (n = 43; 40%) of the pancreas, with a median radiologic diameter of 20 mm (range, 9–130). When compared according to age, sex, body mass index, comorbidity, tumor size, and tumor location, no significant differences were observed between the two groups.

Operation and postoperative course. Operative procedures and postoperative course are summarized in Table II. Briefly, 27 patients (25%) underwent pancreaticoduodenectomy, 28 (26%) distal pancreatectomy with splenectomy in 23 (21%), 53 (49%) pancreatic sparing resection including enucleation in 34 (31%), and central pancreatectomy in 19 (18%). In eight patients (7%) vein resection was required. Overall, pancreatic sparing resections were more frequently performed for incidentally diagnosed lesions (62% vs 30%; P = .001).

Overall mortality was 1% (n = 1) because of pulmonary embolism on postoperative day nine in a 68-year-old woman with an incidentally diagnosed lesion operated by central pancreatectomy. Overall morbidity was 62% (n = 67), including severe complications (Clavien-Dindo grade 3–4) in 13% of patients (n = 14). Pancreatic fistula occurred in 50% of patients (n = 54), 29% (n = 31) having a clinically significant one (ie, grade B or C). Hemorrhage occurred in 5% (n = 5), leading to the only four reoperations. Five patients (5%) required radiologic percutaneous drainage. Operative time, intraoperative blood loss, and perioperative transfusions were less important in Inc patients, and in patients who underwent parenchyma-sparing surgery. In contrast, no substantial differences were observed regarding mortality, overall morbidity, severe morbidity, reoperation rate, and length of stay between both groups.

Table I. Patient and tumor characteristics according to circumstances of diagnosis

	Overall	*Incidentaloma,* n = *65 (%)*	*Symptomatic lesions,* n = *43 (%)*	P *value*
Age, y	58 (36–75)	57 (36–71)	58 (43–75)	.81
Male sex	39 (36)	21 (32)	18 (42)	.31
BMI, kg/m^2	23 (16–42)	24 (16–35)	23 (17–42)	.58
ASA (III/IV)	4 (4)	2 (3)	2 (5)	.89
Comorbidity				
Overall	67 (62)	39 (60)	28 (65)	.59
Diabetes mellitus	7 (6)	4 (6)	3 (7)	.86
Tumor location				
Head	43 (40)	24 (40)	19 (44)	.51
Body	30 (28)	19 (29)	11 (26)	
Tail	35 (32)	22 (34)	13 (30)	

ASA, American Society of Anaesthesiology; *BMI*, body mass index.

When we compared standard resection and pancreas-sparing pancreatectomies (PSPs), clinically significant (grade B/C) pancreatic fistula were more frequent in PSP (38%, n = 20 vs 20%, n = 11; P = .048); overall morbidity was not significantly more frequent in PSP (70% (n = 37) vs 55% (n = 30); P = .102); whereas major morbidity was not significantly different (13%, n = 7 vs 13%, n = 7; P = .941).

Pathologic findings. Results of pathologic analysis are summarized in Table III. In brief, median tumor size was 20 mm (range, 9–140 mm) and tumor-free margins (R0) were obtained for all but six patients (5.5%). Overall, most tumors were classified as T1 (n = 54; 50%) or T2 (n = 34; 31%) according to ENETS TNM classification. According to ENETS/TNM classification, 51 (47%) tumors were classified as stage I, 29 (27%) as stage II, and 28 (26%) as stage III.

Overall, symptomatic tumors were diagnosed at a more advanced stage and showed more aggressive features than incidentally diagnosed lesions. Stage I tumors were more frequent in the Inc group (P = .0001). In 23 patients (21%), no nodes were present in the pathologic specimen (Nx), 83% (n = 19) of them after PSPs, ie, 19 of the 53 patients having their lesion resected by PSP (36%). When present, an average of three (two to six) nodes and up to 16 were harvested after PSP versus 12 (7–20) and up to 39 after standard resection (P < .001). Metastatic regional lymph nodes were found in 27 patients (25%) and

Table II. Operative procedure and postoperative complications in the two groups

	Overall	*Incidentaloma,* n = *65*	*Symptomatic lesion,* n = *43*	P *value*
Operative resection				
Standard pancreatectomies	55 (51)	25 (38)	30 (60)	.001*
Pancreatic sparing resection	53 (49)	40 (62)	13 (30)	
With vein resection	8 (7)	2 (3)	6 (14)	.006*
Postoperative mortality	1 (1)	1 (2)	0 (0)	.41
Morbidity (Dindo)				
Overall	67 (62)	39 (60)	28 (65)	.59
1–2	53 (49)	33 (51)	20 (47)	.34
3–4	14 (13)	6 (9)	8 (19)	
Pancreatic fistula	54 (50)	34 (52)	20 (47)	.55
Hemorrhage	5 (5)	3 (5)	2 (5)	.99
Delayed gastric emptying	9 (8)	3 (5)	6 (14)	.08
Operative time, minutes	240 (40–720)	195 (40–560)	240 (120–720)	<.001*
Blood loss, mL	200 (30–3,000)	200 (30–1,000)	300 (50–3,000)	.001*
Red blood cells transfusions	14 (13)	5 (8)	9 (21)	.04*
Hospital stay, days	18 (6–70)	19 (6–70)	17 (7–66)	.65
De novo diabetes	13 (12)	5 (8)	8 (19)	.09
De novo exocrine insufficiency	14 (13)	8 (13)	6 (14)	.80

*Statistically significant.

Table III. Pathologic characteristics

	Overall	*Incidentaloma* (n = *65*) (%)	*Symptomatic lesion* (n = *43*) (%)	P *value*
Tumor size, mm	20 (9–140)	18 (9–100)	25 (9–140)	.02*
<20	60 (55)	42 (65)	18 (42)	.02*
TNM classification				
T1 (<2 cm)	54 (50)	40 (62)	14 (33)	<.001*
T2 (2–4 cm)	34 (31)	18 (28)	16 (37)	
T3 (>4 cm)	18 (17)	7 (11)	11 (26)	
T4 (invading adjacent organs)	2 (2)	0 (0)	2 (5)	
Nodal status				
N0/Nx	81 (75)	55 (85)	26 (60)	.005*
N1	27 (25)	10 (15)	17 (40)	
ENETS stage				
Stage I (T1N0M0)	51 (47)	38 (59)	13 (30)	<.001*
Stage II (T2 or T3, N0M0)	29 (27)	17 (26)	12 (28)	
Stage III (T4N0M0 or any T, N1M0)	28 (26)	10 (15)	18 (42)	
Stage IV (any T, any N, M1)	0	0	0	
Resection margin				
R0	102 (94)	63 (97)	39 (9)	.17
R1	6 (6)	2 (3)	4 (9)	
Tumor grade				
G1	57 (53)	43 (66)	14 (33)	<.001*
G2	51 (47)	22 (34)	29 (67)	
Microangio invasion	33 (31)	15 (23)	18 (42)	.04*
Perineural invasion	23 (21)	8 (12)	15 (35)	.005*
Mitotic count (/10 HPF)	1 (0–12)	1 (0–5)	2 (0–12)	<.001*
>2 mitosis/10 HPF	24 (22)	7 (11)	17 (40)	<.001*
Ki67	1 (1–25)	1 (1–12)	4 (1–25)	<.001*
>2%	40 (37)	15 (23)	25 (58)	<.001*

*Statistically significant.
HPF, High-power field.

were found more frequently in the Symp group ($n = 17$, 40% vs $n = 10$, 15%; $P = .005$). If we considered N0, N1, and Nx separately, the difference between Inc and Symp group remained significant ($P = .018$). During the 10 patients with incidentally diagnosed lesions and positive lymph nodes, only

three were less than 2 cm in size. When comparing incidentally diagnosed lesions according to their lymph nodes status, lymph node positive tumors had a significantly greater tumor size than lymph node negative tumors (27 mm [22–40] vs 17 [12–25]; $P = .005$). Of the 13 NF-PNETs less than 10 mm in size, 11 had lymph node sampling, and none were metastatic.

Regarding WHO grading classification, 57 tumors (53%) were classified as grade 1 and 51 (47%) as grade 2. Inc patients had more frequent tumors ≤20 mm (65%, $n = 42$, vs 42%, $n = 18$, $P = .019$), staged as T1 ($n = 40$, 62% vs $n = 14$, 33%; $P = .0001$), and N0 (N0/Nx = 55, 85% vs $n = 26$, 60%; $P = .005$) than Symp patients. Additionally, microangioinvasion (23% vs 42%; $P = .038$), perineural invasion (12% vs 35%; $P = .005$), mitotic count (1 vs 2; $P = .0002$), and Ki67 index (1 vs 4; $P = .0004$) were lower in incidentally diagnosed cases than in Symp tumors.

Survival. Excluding the only postoperative death, after a median follow-up of 42 months (range 5–187 months), the 1-, 3-, 5-, and 10-year OS rates were 100%, 96% (90–99), 96% (90–99), and 91% (70–97), respectively, with a difference between the two groups ($P = .029$) in favor of incidentally diagnosed tumors. Median survival time was not reached. Four patients died during follow-up, and only one death was related to tumor or treatment. Specific survival was not different between the two groups ($P = .345$).

The 1-, 3-, 5-, and 10-year DFS rates were 95% (89–98), 89% (81–94), 87% (78–93), and 62% (42–78), respectively. Five patients (5%) experienced local nodal recurrence and 14 patients (13%) a distant recurrence, mainly located in the liver (86%, $n = 12$); none were classified pNx. Median DFS was 130 months. DFS was better in patients with incidentally diagnosed tumors ($P = .003$), with a 1-, 3-, 5-, and 10-year DFS of 98% (89–99), 95 (85–98), 92 (79–97), and 92 (79–97), vs 90% (76–96), 82% (66–91), 82% (66–91), and 31% (9–57) for symptomatic diagnosed lesions (Fig).

At multivariate analyses, including usually reported PNET prognostic factors such as tumor size, presence of positive lymph nodes, and tumor grade, in addition to circumstance of diagnosis (incidentaloma yes/no), tumor size and tumor grade were found to be the only independent prognostic factors of DFS. In the multivariate model, there was a trend ($P = .055$) toward a better DFS in patients with incidentally diagnosed PNET.

Analysis of the subgroup of patients with a lesion size less than 2 cm. When comparing incidentally diagnosed ($n = 34$) and symptomatic NF-PNET ($n = 16$) less than 2 cm in size, demographic characteristics were not different between the two groups. Nevertheless, symptomatic tumors harbored more aggressive features, including more frequent grade 2 tumors ($P = .012$), more frequent perineural invasion ($P = .044$), and a greater Ki67 ($P = .020$). In addition, the presence of metastatic local nodes was more frequent in symptomatic lesions (25% vs 9%; $P = .19$) despite an equivalent tumor size, even if the difference did not reach significance. Overall, 91% of incidentally diagnosed NF-PNET less than 2 cm in size were N0/Nx. DFS was not different between the two groups ($P = .09$).

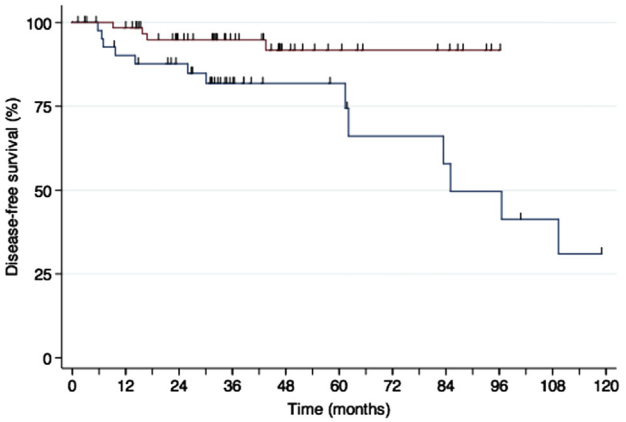

Fig. DFS of nonmetastatic sporadic NF-PNETs according to circumstance of diagnosis (incidentaloma, red line; symptomatic, blue line).

DISCUSSION

NF-PNET are more and more frequently diagnosed as *incidentaloma* because of the widespread use of cross-sectional imaging,[19-22] as confirmed in the present study, where more than half of patients were incidentally diagnosed. In recent series, this diagnostic feature accounts for more than one-third of all tumors and about one-half of NF-PNET,[14] most of these lesions being smaller than 2 cm in size.[19,23-25] The management of small sporadic NF-PNET is controversial, and the benefit of resection regarding OS and DFS has not been clearly established for lesions below 2 cm.[26,27]

We have shown here that sporadic incidentally diagnosed NF-PNET are associated with less aggressive features than symptomatic lesions but cannot be considered to be benign tumors. If operative resection should remain recommended for most of them, incidentally diagnosed NF-PNET frequently are amenable to pancreas-sparing pancreatectomies with an excellent long-term DFS.[5] Identification of a subgroup of patients

with indolent lesion amenable to a "wait-and-see" policy will be the next challenge for the medical and surgical community.

Our understanding of the natural history of incidentally diagnosed PNET is limited, and because NF-PNET are traditionally associated with aggressive behavior, most institutions have recommended their systematic operative resection.[21,28-30] Recently, few series have focused on the management of incidentally diagnosed PNET with conflicting results.[12,13] Some suggested that compared with symptomatic NF-PNET, incidentally diagnosed lesions had a better DFS after resection, this diagnostic feature being an independent prognostic factor. Although operative resection is curative in most cases, they suggested that clinical and radiographic surveillance might be an appropriate alternative for highly selected patients with asymptomatic and small tumors.[2] In contrast, the Massachusetts General Hospital group reported that incidentally diagnosed PNET can sometimes display aggressive behavior, even when small, and should undergo resection and careful postoperative surveillance, even when operative and pathologic findings suggest benign disease.[13] These studies underline the difficulty in assessing the biological behavior of NF-PNET. Regarding small lesions, ie, those less than 2 cm in size, they usually carry excellent long-term OS and DFS, but up to 10% are node-positive.[5,13,26] Even if the prognosis significance of node positivity is debatable, this low probability of distant disease justifies operative resection for most of these lesions. Not surprisingly, the number of lymph nodes present in the specimen after standard resection was greater than the one after PSP. Nevertheless, the extent of lymph node sampling can be tailored to the primary tumor size. As an example, this concept of a limited resection of the primary tumor with wide lymph node dissection is the standard procedure for sporadic gastrinomas.[31] It remains theoretically possible that LN positivity in limited resections is underestimated, even if none of the 19 patients with Nx status after PSP recurred.

Prognostic factors for PNET have been widely studied based on institutional review of operative patients[3,19,32,33] and several have been proposed,[34-36] including clinical parameters (age, functional status, presence of distant metastases), classification (TNM staging, WHO classification), or pathologic characteristics (macroscopically radical resection, tumor size, lymph node metastases, or angiolymphatic invasion).[3,34,35,37-39] To the best of our knowledge, we studied one of the largest single institution series evaluating incidentally diagnosed sporadic NF-PNET with specific attention paid to overall and DFS. Our study confirmed that asymptomatic NF-PNET less than 2 cm are more likely to be benign, ie, without long-term recurrence than larger and symptomatic lesions. Patients with incidental tumors smaller than 2 cm were more often staged T1, node negative, and graded 1, with a low rate of vascular and perineural invasion, pain, low mitotic count, and Ki67 than tumors measuring 2 cm or more. Interestingly, vascular and perineural invasion could explain symptoms in patients with abdominal pain. In addition, tumor grade and tumor size were the only independent prognostic factors of DFS in multivariate analyses, as reported by others[40,41] but incidental diagnosis was a nearly substantial prognostic factor (P = .05). In our series, DFS was 95%, 89%, 87%, and 62% at 1-, 3-, 5-, and 10-year, respectively, and was better in patients with incidentally diagnosed PNET. It now seems likely that incidentally diagnosed NF-PNET, especially small ones, harbor a better prognosis and less aggressive features than their symptomatic counterparts. What remains controversial is the clinical implication of this finding because a fraction of these patients will present at diagnosis with positive lymph nodes anyway, and will consequently be exposed to recurrences or distant metastasis. As in our study, most reports agree that a lymph node-positive disease does not preclude resection and does not dramatically affect overall survival,[32,33,37-39] most of recurrences being local, late, and amendable to re-resection. Association between size and PNET biologic behavior also has been clearly reported,[14,36,41-43] and overall, knowing the substantial morbidity and mortality of standard pancreatectomies, this favors a less-aggressive management from pancreas-sparing resection to even observation for a subset of patients with small indolent tumors, even if up to now, no high level evidence could support a "wait-and-see" policy.

The type and extent of operative resection for PNET remain controversial because of our inability to accurately predict which tumors are benign and which are malignant. Enucleation is now a standard of care for insulinoma because their benignity can be assumed most of the time. [44,45] Conversely, it is unclear whether pancreas-sparing pancreatectomies can be applied to small, sporadic NF-PNET because they are not optimal oncologic resections – with limited margins and no formal lymphadenectomy. Standard pancreatic resections

ie, pancreaticoduodenectomy and distal pancreatectomy, are associated, even in experienced hands, with a significant postoperative morbidity and mortality and disappointing long-term functional results.[9] The up to 30% reported rates of de novo diabetes following standard pancreatic resection[9,46] are no longer acceptable in the setting of asymptomatic patients with long life expectancy. Consequently, in our opinion standard pancreatic resections should be limited to large (>2 cm in diameter) and aggressive tumors requiring extensive lymphadenectomy. Conversely, parenchyma-sparing procedures could be offered to less aggressive PNET,[4,47] this includes NF-PNET less than 2 cm, especially when incidentally-discovered.[48] In our experience, about two-thirds of patients with incidentally diagnosed lesion underwent PSP, ie, every time than their anatomical location allowed it. With adequate patient selection, DFS is excellent, up to 90% at 5 years,[49-51] and in a recent study, when incidental small tumors were considered, only 6% were malignant and no patients died of disease.[26] Interestingly, as previously reported,[5] PSP carry a greater overall morbidity, especially regarding pancreatic fistula, but without significantly different severe morbidity or mortality.

The benefit of watchful surveillance can be discussed in the subgroup of patients with the smallest lesions, or in patients whose general condition precludes a safe operative resection. Extending this logic further, some authors suggested that for PNET less than 2 cm, a nonoperative management could be considered.[52] Our results could support this strategy. Indeed, most of the small incidentally diagnosed lesions were N0 and about 80% were grade 1, ie, nonaggressive neoplasms. A more accurate preoperative patient selection, using, for example, fine-needle aspiration to assess tumor grade, might be needed before extending a "wait-and-see" policy for small PNET. Until then, parenchyma-sparing surgery could represent an alternative for small incidentally diagnosed sporadic NF-PNET.

In conclusion, incidentally diagnosed NF-PNET is an increasing clinical situation now accounting for the majority of newly diagnosed patients. These tumors have more favorable histopathological characteristics than their symptomatic counterparts. Our results favor a less aggressive management of small incidentally diagnosed NF-PNET. In this setting, the value of PSP should be considered in these asymptomatic patients, who, ideally should remain asymptomatic, ie, as they were before operation.

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