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ORIGINAL ARTICLE

'Peripheric' pancreatic cysts: performance of CT scan, MRI and endoscopy according to final pathological examination

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Abstract

Objective: To assess the accuracy of pre-operative staging in patients with peripheral pancreatic cystic neoplasms (pPCNs).

Methods: From 2005 to 2011, 148 patients underwent a pancreatectomy for pPCNs. The pre-operative examination methods of computed tomography (CT), magnetic resonance imaging (MRI), endoscopic ultrasonography (EUS) were compared for their ability to predict the suggested diagnosis accurately, and the definitive diagnosis was affirmed by pathological examination.

Results: A mural nodule was detected in 34 patients (23%): only 1 patient (3%) had an invasive pPCN at the final histological examination. A biopsy was performed in 79 patients (53%) during EUS: in 55 patients (70%), the biopsy could not conclude a diagnosis; the biopsy provided the correct and wrong diagnosis in 19 patients (24%) and 5 patients (6%), respectively. A correct diagnosis was affirmed by CT, EUS and pancreatic MRI in 60 (41%), 103 (74%) and 80 (86%) patients (when comparing EUS and MRI; $P = 0.03$), respectively. The positive predictive values (PPVs) of CT, EUS and MRI were 70%, 75% and 87%, respectively.

Conclusions: Pancreatic MRI appears to be the most appropriate examination to diagnose pPCNs accurately. EUS alone had a poor PPV. Mural nodules in a PCN should not be considered an indisputable sign of pPCN invasiveness.

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Introduction

Pancreatic cysts are uncommon, representing approximately 5% of all pancreatic neoplasms.[1] The ability to differentiate cystic neoplasms from pancreatic carcinoma and pseudocysts is crucial to spare patients from high-morbidity surgery. In addition, there are histological subtypes of cystic neoplasms that should be differentiated owing to their variable natural history. On the one hand, a pancreatic cyst arising on the main pancreatic duct should be considered an intraductal papillary neoplasm (IPMN), and surgery is needed to spare the patient from possible transformation of the cyst into invasive carcinoma. On the other hand, the precise aetiology of 'peripheral' pancreatic cystic neoplasms (pPCNs; i.e. not arising on the main pancreatic duct) is difficult to ascertain. Indeed, all other subtypes except serous cystadenoma (SCA), which does not have a malignant potential except rare reported cases, share mucin-producing epithelia, and resection is recommended because of the malignant potential. The mucinous subtypes include mucinous cystadenoma (MCA), mucinous cystadenocarcinoma (MCADK), papillary cystic neoplasms and IPMNs.[1,2] Finally, some pPCNs might be resected, and the final histology might affirm rare pancreatic cystic tumours (e.g. neuroendocrine cystic tumours and pseudo papillary tumours). In the late 1990s, subtypes of pPCNs have been deemed indistinguishable without resection[3] and have led to the recommendation that all suspected pPCNs must be resected.[4] Improvement in imaging techniques [e.g. magnetic resonance imaging (MRI)] and endoscopic ultrasonography (EUS) associated with biopsies and/or fine needle aspiration (FNA) for cyst fluid carcinoembryonic antigen (CEA) level measurement led to an increase in the rate of appropriate pre-operative diagnoses. However, the accuracy of such examinations did not permit 100% reliable diagnoses. A pancreatic surgeon facing a

patient with a pPCN had to decide to resect it or not according to pre-operative imaging. The present study was designed so a pancreatic surgeon could be precise in which pre-operative imaging he could trust.

Patients and methods

From January 2005 to December 2011, 177 pancreatectomies for pPCNs were performed at the Institut Paoli-Calmettes (Marseille, France) and Hôpital Nord (Marseille, France). All of the patient data were entered prospectively into a clinical database, which was approved by the institutional review board of both institutions. A pPCN was defined by a unique or multiple cystic dilatation arising on pancreatic parenchyma with a normal main pancreatic duct identified at pre-operative imaging. Thus, all patients founded with the main pancreatic duct over 3 mm were excluded from the study (i.e. main pancreatic duct IPMNs or mixed IPMNs). Patients with a solid tumour (adenocarcinoma of the pancreas, neuroendocrine tumour, carcinoma of the duodenum, distal common bile duct tumour or ampulla of Vater tumour), IPMNs or invasive IPMNs arising on the main pancreatic duct (including mixed IPMNs) were excluded.

Pre-operative imaging

Pre-operative imaging included thin-section, contrast-enhanced, helical dual-phase scanning (CT), and/or EUS with or without pPCN biopsies, with or without FNA for CEA level measurement according to the endoscopist's preference/practice and/or pancreatic MRI. To reflect 'real' life, it was not required that pre-operative imaging was performed obligatorily at the institution that managed the patient. Indeed, some examinations were performed closer to the patient's home and were not performed again to eliminate any bias owing to the inexperience of the performing physician. For the present study, patients were selected patients who underwent at least a CT and EUS and/or pancreatic MRI. Thus, 148 patients comprised the present population study. After pre-operative imaging, the aetiology of the pPCN suggested by each examination was noted and compared with a final pathological examination.

Surgery

Surgery was performed using a laparotomy or a laparoscopic approach according to the tumour site and surgeon/centre preferences. Routine intra-operative section examination of the pancreatic remnant was performed to ensure complete resection of supposed IPMNs; in case of enucleation, the communicating duct was isolated and intra-operatively examined. A total pancreatectomy was achieved in the case of pPCN spread; enucleation was achieved if the pPCN was not close to the main pancreatic duct (the complete procedure was already described[5]).

Study parameters

The variables evaluated included: age, gender, maximal pPCN size (mm), defined as the maximum diameter on pathological analysis of the greater cyst in the case of multifocal disease, uni- or multifocal repartition of the pPCN, the presence of a mural nodule, cyst fluid CEA level measurement if performed (UI/ml), pre-operative biopsy results if performed and a final pathological examination.

Statistical analysis

Data analyses were performed using the GraphPad Prism software, version 5.0d (GraphPad Software Inc., La Jolla, CA, USA) and Microsoft Excel 2008 (Microsoft, Seattle, WA, USA). Statistical associations among categorical factors were assessed using Fisher's exact test. Statistical significance was set at a *P*-value less than 0.05.

Results

In this study, 94 patients (63.5%) underwent the 3 pre-operative examinations (i.e. CT, EUS and MRI), 93 patients underwent pancreatic MRI (63%), 139 patients (94%) underwent EE and a biopsy was performed in 79 patients (53%). The pPCN was unifocal in 95 patients (64%); the median pPCN size was 28.4 mm (range, 7–230 mm). Information regarding patient characteristics, pre-operative imaging and surgery are summarized in Table 1.

Mural nodules

A mural nodule was detected in 34 patients (23%). All patients with mural nodules underwent EUS and MRI. A mural nodule was identified by both examinations in 12 patients (35%). Mural nodules were only identified by EUS and MRI in 19 patients (56%) and 3 patients (9%), respectively. Only one patient (3%) with a mural nodule identified at pre-operative imaging had invasive IPMNs at the final pathological examination, 18 mural nodules (53%) showed mucin aggregation, 12 mural nodules were not retrieved (35%) and 3 mural nodules (9%) were benign. No significant difference was noted between EUS and MRI to identify the mural nodules correctly and provide the appropriate disease diagnosis.

Biopsies

In 55 patients (70%), the biopsy ($n = 79$) could not reveal the diagnosis; according to final pathological examination, the biopsy gave the correct and wrong diagnosis in 19 (24%) and 5 patients (6%), respectively.

Final pathological examination and correlation with pre-operative examinations (Table 2)

The final pathological examination affirmed 77 non-invasive branch duct IPMNs (52%), 38 MCAs (26%), 13 SCAs (9%), 8 neuroendocrine cystic tumours (5%), 7 pseudocysts (5%),

Table 1 Characteristics and Preoperative Imaging of patients with peripheral pancreatic cyst neoplasm

	All patients (n = 148)
Gender ratio Male/Female	0.4
Mean age (range)	59.7 (32–78)
CT-scan (%)	148 (100)
No diagnosis suggested (%)	54 (36)
EUS (%)	139 (94)
With biopsy (%)	79 (53)
With FNA for CEA measurement (%)	57 (39)
No diagnosis suggested (%)	1 (0.7)
MRI (%)	93 (63)
No diagnosis suggested (%)	1 (1)
Unifocal Cyst (%)	95 (64)
Mean Cyst Size (mm) (±SD)	28.4 (±23.8)
Mural Nodule (%)	34 (23)
Mean cyst fluid CEA level (UI/Ml) (±SD)	1133 (±430.7)
Type of pancreatectomy	
DP (%)	64 (43)
PD (%)	56 (38)
Enucleation (%)	14 (9)
MP (%)	10 (7)
TP (%)	4 (3)

CEA, carcinoembryonic antigen; DP, distal pancreatectomy; EUS, endoscopic ultrasonography; FNA, fine needle aspiration; MP, median pancreatectomy; MRI, magnetic resonance imaging; PD, pancreaticod duodenectomy; TP, total pancreatectomy.

3 invasive branch-duct IPMNs (2%), one pseudo papillary tumour (0.5%) and one case of cystic dystrophy of the duodenal wall (0.5%). CT, EUS and MRI could not provide a diagnosis in 54 patients (36.5%), 1 patient (0.7%) and 1 patient (1%), respectively. A correct diagnosis was affirmed by CT, EUS and MRI in 60 patients (41%), 103 patients (74%) and 80 patients (86%) (when comparing EUS and MRI; $P = 0.03$), respectively. Biopsies and cyst fluid CEA level measurement did not increase the EUS efficiency and MRI remained the better technique to predict a pPCN diagnosis. Hypothesizing that CT should have a better efficiency in large pPCNs (arbitrarily set at 4 cm), the accuracy of CT increased (54%) but remained significantly inferior to both EUS and MRI. When considering patients with multifocal cysts (n = 53), a correct diagnosis was affirmed by CT, EUS and MRI in 35 patients (66%), 48 patients (91%) and 51 patients (96%) (when comparing EUS and MRI; P = NS), respectively. In 14 patients, EUS and MRI did not suggest the same diagnosis; in such a situation, the correct diagnosis was affirmed by EUS and MRI in 4 patients (29%) and 8 patients (57%) (P = NS), respectively. The positive predictive values (PPVs) of CT, EUS and MRI were 70%, 75% and 87%, respectively.

Discussion

Our study showed that (a) MRI seemed to be the best examination to predict the diagnosis of pPCNs, (b) mural nodules were rarely (3%) associated with invasive pPCNs and (c) biopsy and cyst fluid CEA level measurement showed a poor efficiency and did not improve EUS accuracy.

Importantly, our study possessed several limitations. Indeed, it was not explained why a pancreatectomy was performed (i.e. pancreatitis, pain, or suspicion of invasive pPCNs). Thus, it cannot be argued that patients who underwent a pancreatectomy for SCA or a pseudocyst could have been spared from surgery. Moreover, a proportion of the patients (14% in our study) underwent a pancreatectomy for benign, non-degenerative pPCNs owing to the imaging limitation to predict the appropriate diagnosis. A second bias was the inability to differentiate between patients who underwent pre-operative imaging by an experienced physician. It is now accepted that the efficiency of EUS and MRI is strongly related to the physician's experience, and it would be interesting to compare EUS and MRI when performed by an experienced physician. However, our purpose was to determine the best examination to predict pPCN aetiology without consideration of the optimal situation of all the examinations being performed by an experienced

Table 2 Correlation between final pathological examination and diagnosis suggested by a pre-operative CT scan, endoscopic ultrasonography (EUS), and pancreatic magnetic resonance imaging (MRI)

	CT-scan diagnosis/FD (% RD)	EUS diagnosis/FD (%RD)	MRI diagnosis/FD (% RD)/p when comparing with EUS
IPMNs	41/35 (85)	84/73 (87)	65/59 (91)/NS
MCA	36/21 (58)	36/21 (58)	17/13 (76)/NS
Invasive MCA	3/0 (0)	6/0 (0)	0/0 (0)/NS
SCA	7/3 (43)	6/4 (67)	6/5 (83)/NS
Other diagnosis	7/17 (41)	6/5 (83)	4/3 (75)/NS
Total	94/66 (45)	138/103 (74)	92/80 (86)/0.03

EUS, endoscopic ultrasonography; FD, final diagnosis; IPMNs, intra pancreatic mucinous neoplasms; MCA, mucinous cystic adenoma; MRI, magnetic resonance imaging; RD, right diagnosis; SCA, serous cystic adenoma.

physician. Indeed, a pancreatic surgeon who examines a patient in the clinic who had already undergone EUS and/or MRI would not repeat these examinations, particularly if the two procedures produce concordant results. Finally, our study was not a double-blind study: the physician, who performed EUS or MRI, could know the diagnosis suggested by the previous examination and was possibly influenced about his or her diagnosis.

All other subtypes, except serous SCA, that did not have a malignant potential, share mucin-producing epithelia, and their resection is recommended because of the malignant potential. The major difficulty is to know the precise aetiology of pPCNs to have an optimal therapeutic algorithm (i.e. which patient must undergo resection and which patient could be spared from surgery). CT is an efficient examination to detect pPCNs, but not to affirm their precise aetiology. In our study, the PPV of CT was low [70% and always inferior to EUS and MRI even under optimized situations (large cysts or multifocal cyst)]. Thus, CT alone is a poor examination option to predict pPCN aetiology and must be completed by EUS or MRI. However, it was supposed that the CT efficiency is under estimated: the physician who performs CT for pPCNs did not make a fastidious study because the patient is expected to undergo a supplementary, more efficient examination.

At the end of the 20th century, resection of pPCNs has been recommended because of the lack of efficiency of EUS and MRI.[4] However, both examinations improved owing to technology and physician improvement. Thus, recent guidelines[6] recommend exploring pPCNs by CT and MRI. Indeed, the complication rate with simultaneous FNA is low in highly experienced centres,[7] but EUS remains an invasive procedure. Moreover, EUS morphology alone shows poor sensitivity and specificity in accurately classifying pPCNs: cyst morphology on EUS has an overall accuracy of 50–73%, and the sensitivity and specificity for EUS amount to 56–71% and 45–97%, respectively.[8] When EUS is associated with cyst fluid CEA level measurement, the results of cystic fluid analysis should always be interpreted in conjunction with findings on CT/MRI and EUS: EUS plus cyst fluid CEA level measurement can provide diagnostic help in some uncertain cases.[9] However, there is currently no evidence to suggest EUS as a routine method for the differential diagnosis of pPCNs. In our study, EUS had a poor PPV (75%) and could not be associated with CT alone to identify pPCN etiology precisely. Moreover, biopsy and CEA level measurement did not sufficiently increase the EUS efficiency to reach that of MRI. We supported that biopsies during EUS are useless and did not have to be performed to characterize pPCNs.

Regarding each pPCN aetiology in our study, it was noted that MRI and EUS showed equal efficiency, but the overall efficiency was significantly higher for MRI. MRI is not an invasive procedure and is less dependent on physician experience. Thus, in our experience, pancreatic MRI is the preferred examination to characterize pPCNs, and it is supported that patients who have undergone an MRI did not need an EUS. By contrast, it is strongly recommended performing an MRI for a patient with pPCNs who has already undergone CT and EUS. A recent prospective study[10] did not find an efficiency difference between EUS and MRI, but the series comprised patients whose examinations were all performed by an experienced physician. We support that EUS and MRI may have the same efficiency when performed by an experienced physician. However, the purpose of the present study was to determine which examination a pancreatic surgeon might trust regardless of the physician experience, a strategy that is a more realistic situation in everyday clinical practice.

Finally, it was surprisingly noted that the presence of a mural nodule was not strongly associated with an invasive pPCN (3%). Recently, Hirono *et al.*[11] showed that a mural nodule greater than 5 mm was a good predictor of invasive IPMNs. The mural nodule size was not noted; thus, emphatic conclusions about our findings could not be made. However, we support that detection of a mural nodule is a frequent indication of a pancreatectomy but should not be considered an indisputable sign of pPCN invasiveness.

Conclusions

In routine clinical practice (i.e. regardless of physician experience), pancreatic MRI seemed to be the most appropriate examination and was performed in each patient with a pPCN even if EUS had already been performed. EUS alone had a poor PPV, and biopsy and/or cyst fluid CEA level measurement did not permit EUS to reach the efficiency of MRI. Mural nodules in a pPCN should not be considered an indisputable sign of pPCN invasiveness.

Conflicts of interest

None declared.

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