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Endoscopic ultrasound of pancreatic cystic lesions

Shyam Prasad, Jarrad Wilson, Andrius Kalade, Paul Desmond and Robert Chen
Department of Gastroenterology, St. Vincent's Hospital (Melbourne), Fitzroy, Victoria, Australia

Key words
biopsy, endosonography, fine needle, pancreatic cyst, pancreatic neoplasms.

Abbreviations
CEA, carcinoembryonic antigen; CT, computed tomography; EUS, endoscopic ultrasound; FNA, fine-needle aspiration; IPMN, intraductal papillary mucinous neoplasm; MCN, mucinous cystic neoplasm; SCN, serous cystic neoplasm; SVH, St. Vincent's Hospital, Melbourne.

Correspondence
Dr. Robert Chen, Department of Gastroenterology, St. Vincent's Hospital (Melbourne), 35 Victoria Parade, Fitzroy, Vic. 3065, Australia. Email: robert.chen@svhm.org.au

S. Prasad PhD, MRCP; **J. Wilson** MB BS, FRACP; **A. Kalade** MB BS, FRACP; **P. Desmond** MD, FRACP; **R. Chen** MD, FRACP.

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Abstract

Background: The impact of endoscopic ultrasonography (EUS) on the management of pancreatic cystic lesions remains unclear, and there are no published studies of the Australian experience in this area. The aim of this study was to review the experience of EUS for such lesions within our institution.
Methods: A retrospective review was undertaken of data collected prospectively over a two-year period within the EUS database of St. Vincent's Hospital. Patients who underwent EUS for suspected pancreatic cystic lesions were identified. Data were collected on demographic variables, EUS findings, the results of EUS-guided fine-needle aspiration (FNA) and the findings on clinical and radiological follow-up.
Results: Fifty-nine patients were identified. Two thirds were female. Most lesions were located at the pancreatic head. Median diameter was 25 mm. FNA was performed in 36 cases (61%). On cytology, six (17%) showed features of mucinous tumours and five (14%) showed adenocarcinoma. The remainder contained either non-specific benign cells or insufficient epithelial tissue. Follow-up data on 48 cases (83%), after a median duration of 15 months, revealed that 15 lesions (31%) had been resected, including six serous and six mucinous tumours. The level of carcinoembryonic antigen in FNA specimens appeared to be higher in mucinous than in serous neoplasms. Twenty-four lesions had undergone repeat radiological imaging: only three had grown in size.
Conclusions: EUS and FNA are useful procedures for assessing pancreatic cystic lesions. Malignant features are demonstrated in only a small minority. The majority of the remainder show no signs of progression during follow-up.

Introduction

The diagnosis and management of cystic lesions of the pancreas is an increasingly recognized problem in clinical practice. The widespread use of high-resolution imaging modalities has led to their detection in as many as 1% of hospital inpatients.[1] Many of them are neoplastic and the majority are asymptomatic.[1,2] Of the non-neoplastic cysts, pseudocysts are most likely to cause symptoms. The natural history of neoplastic cysts remains unclear, and partly as a result of this, the optimal management of such lesions is the subject of debate. The World Health Organization histological classification of neoplastic pancreatic cysts broadly divides them into serous cystic neoplasms (SCNs) and mucinous cystic tumours, and the latter is classified further into the mucinous cystic neoplasms (mucinous cystadenomas or MCNs) and the intraductal papillary mucinous neoplasms (IPMNs).[3] This classification is useful because SCNs are thought to be very rarely malignant, whereas mucinous lesions can be either benign or malignant. Benign mucinous lesions have the potential to become malignant, although the rate at which this occurs is unknown. Thus, guidelines issued recently by both the International Association of Pancreatology and the American College of Gastroenterology have suggested that surgery should be considered for mucinous lesions, whereas a conservative approach may be considered for SCNs.[4,5]

In reality, a significant obstacle to this approach is the difficulty of distinguishing accurately between SCNs and mucinous lesions

without resecting them. MCNs, IPMN and SCNs are said to display differences when examined by imaging modalities, endoscopic ultrasonography (EUS) and cytological and biochemical analyses of cyst fluid. The performance characteristics of high-resolution computed tomography (CT) scanning in making these distinctions are, however, disappointing,[6,7] and its main role is, therefore, to determine the extent of any malignant spread. Cyst characterization by EUS may have some value in distinguishing SCNs from mucinous lesions. For example, SCNs are more likely to have a honeycomb appearance or multiple small (<3 mm) cysts.[8] However, cyst morphology alone distinguishes poorly in many cases, and furthermore, EUS may be limited by significant inter-observer variability.[9] EUS may therefore be most useful in facilitating fine-needle aspiration (FNA) of the cyst wall and cyst fluid for cytological and biochemical analysis.

One retrospective and two prospective studies have suggested that FNA fluid cytology can diagnose mucinous neoplasms with high (80–100%) specificity but low sensitivity (30–50%).[10–12] Many biochemical assays and estimations of tumour markers can be performed on FNA aspirates, of which the level of carcinoembryonic antigen (CEA) has the most supportive data for its use in practice. A high level of CEA (above a threshold of 192–400 ng/mL, depending on the study) is said to predict a mucinous tumour, with a sensitivity of 57–73% and a specificity of 84–100% reported in published studies, whereas a low level (below 4–5 ng/mL) is reported to be both highly sensitive (100%) and highly specific (86–93%) for a SCN.[12–15] A recent meta-analysis has supported these assertions.[16] However, the threshold values reported in these studies may not be applicable to other patient populations, methods of sampling or laboratories and so cannot be utilised in clinical practice without local quality assurance.

As few specific studies of pancreatic cystic lesions have been published, and none from Australian centres, the aim of this study was to review and report the experience of EUS and EUS-guided FNA for pancreatic cystic lesions from our institution.

Methods

EUS centre and patients

St. Vincent's Hospital, Melbourne (SVH) performs approximately 300 EUS procedures per year from a state-wide referral base. A retrospective review was conducted of its EUS database for a two-year period (April 2005–April 2007). Patients who underwent EUS for pancreatico-biliary indications were identified, and among these, all those with a suspected pancreatic cystic lesion were selected for analysis. There were no exclusion criteria, and EUS was performed on all those referred. The study was approved as a Quality Assurance exercise by the Human Research and Ethics Committee of SVH.

Endosonography and FNA

All EUS were performed by a single gastroenterologist with experience of more than 500 procedures during training overseas and more than 1000 procedures subsequently. The patients were sedated using intravenous midazolam and fentanyl with or without propofol.

The echoendoscopes used were radial (Olympus fibre-optic GF-UM20 or video GF-UM160, Olympus Australia, Mt Waverley, Australia) and curved linear array (Olympus GF-UC140P) with an Aloka Prosound SSD-5000 processor (Aloka America, Wallingford, Connecticut, USA). EUS-guided FNA was performed using either Olympus single-use aspiration 19- or 22-gauge needles (NA-200H-8022) or Wilson-Cook Quick-Core biopsy needles (EUSN-19-QC, Cooke Endoscopy, Winston-Salem, North Carolina, USA).

Data recorded at EUS included the site of the lesion within the pancreas, its maximum diameter and endosonographic features, and the presence of any adjacent lymph nodes. A lesion underwent FNA except where there was an infection risk (i.e. the risk of introducing infection exceeded any likely diagnostic yield, usually in cases of presumed pseudocysts or simple cysts), or because of technical difficulty (i.e. the lesion was deemed poorly accessible because either a vascular structure was interposed between the endoscope tip and the lesion or the lesion was very small (<1 cm diameter) or both). FNA was performed from both the cyst wall and any solid component. All specimens underwent cytological examination. In many cases, cyst fluid was tested for lipase, amylase and CEA levels. The patients undergoing FNA received prophylactic antibiotics with a single dose of intravenous ticarcillin and clavulanic acid (Glaxo-SmithKline, Boronia, Australia), followed by three days of oral roxithromycin (Arrow Pharmaceuticals, South Croydon, Australia). All complications were recorded.

Follow-up

Questionnaires were sent to all referring doctors to obtain follow-up data, including whether surgery had been performed, or, alternatively, the findings of any subsequent radiological imaging and the most recent clinical assessment. The final pathological diagnosis of any resected lesion was recorded and compared with the previous FNA results.

Results

Patients

Of the 255 EUS procedures performed for a pancreatico-biliary indication, 60 were for a suspected pancreatic cystic lesion in a total of 59 patients (one patient having undergone two procedures). These patients had been referred by 30 different physicians and surgeons. Thirty-nine patients (66%) were female and the mean age was 64 years (standard deviation (SD) 12 years).

EUS findings

EUS detected a lesion in the pancreas in 58 patients. The locations of these lesions within the pancreas are illustrated by Figure 1. Most (55%) were in the pancreatic head, with the remainder distributed across various regions of the pancreas. The maximum diameter of the overall lesion ranged from 2–82 mm (median 25 mm). Six lesions had a diameter of less than 10 mm, 16 a diameter of 11–20 mm, 19 a diameter of 21–30 mm and 17 a diameter of greater than 30 mm. Adjacent lymph nodes were noted in only eight cases (14%).

No complications were recorded.

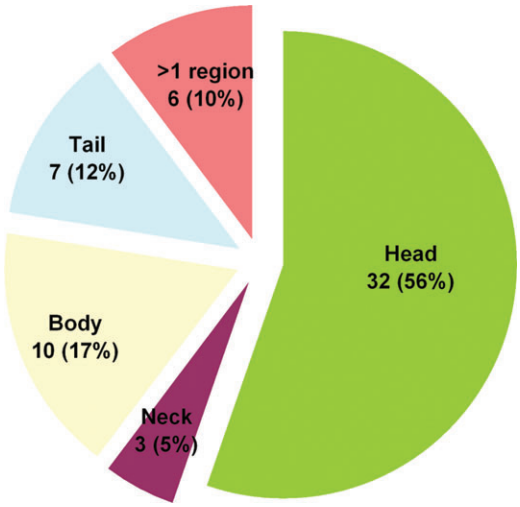

Fig. 1. Distribution of 58 pancreatic cystic lesions within the pancreas. The majority of lesions (55%) were found in the pancreatic head alone. The remainder were distributed throughout other regions or were found in more than one region.

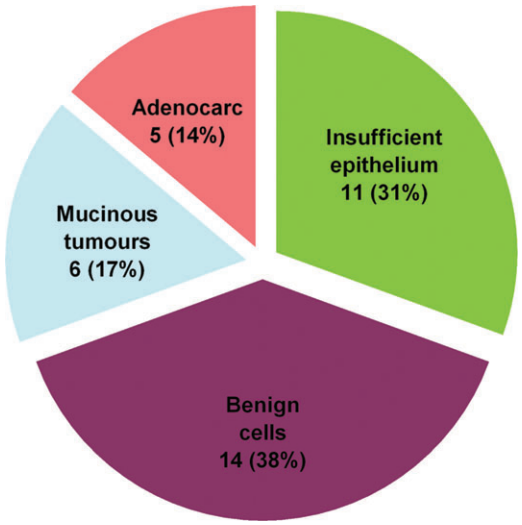

Fig. 2. Results of cytological analysis of specimens obtained from 32 cystic lesions of the pancreas by fine-needle aspiration. Adenocarcinoma was diagnosed in five cases (14%); mucinous tumours were suggested in a further six cases (17%). The remaining specimens either showed benign cells of no particular concern (39%) or contained insufficient cellular material for analysis (31%).

FNA

Thirty-six lesions (62%) underwent FNA, whereas 22 did not because of technical difficulty (15 cases), infection risk (six cases) and a decision to biopsy an adjacent structure (one case).

The results of FNA cytology are depicted in Figure 2. In 11 cases (31%), insufficient cellular material was obtained to make a valid assessment. In five cases (14%), the appearance strongly suggested the presence of adenocarcinoma. In six cases (17%), the appearance suggested the presence of a mucinous tumour. In the remaining 14 cases (39%), the specimen contained benign cells of no particular concern.

The levels of lipase, amylase and CEA were estimated in 20 cases. The results of each test varied widely between cases but showed no relationship to either EUS features or the results of FNA cytology.

Follow-up

Follow-up data were obtained in 48 of 58 cases (83%). The median duration of follow-up was 12 months (range 2–24 months).

Malignant cases

Of the five cases in which FNA cytology suggested adenocarcinoma, three underwent surgical resection and two received oncology-based care. The final pathological diagnoses in the three surgical cases were two mucinous adenocarcinomas and an undifferentiated carcinoma with osteoclastic giant cells and adjacent panin. All five patients were alive at the time of preparation of this paper.

Cases that underwent surgery

Thus far, 15 patients have undergone surgical resections. The final pathological diagnoses are listed in Table 1. Six lesions proved to be SCNs, whereas six other resections contained mucinous tumours. There was no difference between serous and mucinous tumours in the EUS-determined diameter of the largest cyst (medians of 25 mm and 23 mm for serous and mucinous tumours respectively). FNA cytology had suggested a mucinous aetiology in two of the five SCNs and four of the five mucinous lesions that had subsequently undergone surgery.

Table 1 Final pathological diagnosis after surgical resection of 15 pancreatic cystic lesions

Pathological diagnosis	Number of cases
Serous cystadenomas	6
Mucinous tumours	6
Mucinous cystadenoma	*1*
Mucinous adenocarcinomas	*3*
IPMN	*2*
Undifferentiated carcinoma	1
Neuroendocrine tumour	1
Lymphangioma	1
Total	15

Mucinous tumours have been subdivided into mucinous cystadenomas, mucinous adenocarcinomas and IPMN, and in total, make up 40% of resected lesions. Serous cystadenomas comprise a further 40% of resected lesions

Preoperative CEA levels had been measured in three of the resected SCNs (all <1 ng/mL) and three of the resected mucinous tumours (14, 167, 173 ng/mL), the difference in levels suggesting some value in distinguishing these groups.

Figure 3 shows EUS images from two subsequently resected lesions, a SCN (Fig. 3a) and a mucinous cystadenocarcinoma (Fig. 3b).

Cases that underwent radiological review

Twenty-four cases underwent radiological review without undergoing surgery after a median duration of six months (range 1–20 months). In 21 cases (88%) the lesions were unchanged, whereas in three, the lesions had increased in size: one was felt to be an enlarging pseudocyst in a patient with recurrent attacks of acute pancreatitis; a second was felt to be growing slowly and a conservative approach was adopted in this 82-year-old woman; the diagnosis of the third remains unclear and the patient is considering surgery.

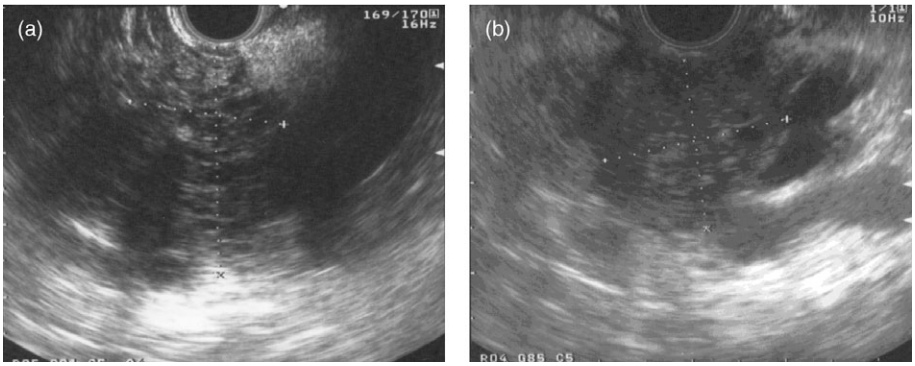

Fig. 3. Examples of images of pancreatic cystic lesions obtained by endoscopic ultrasonography. (a) Shows a multi-cystic lesion at the tail of the pancreas. The 'honeycomb' appearance of the lesion is suggestive of a serous cystadenoma. This diagnosis was confirmed after surgical resection of the lesion. (b) Shows a mixed solid and cystic lesion at the pancreatic body. This appearance suggests the possibility of a mucinous neoplasm undergoing malignant change. Cytology of a specimen obtained by fine-needle aspiration also suggested a mucinous adenocarcinoma, and the level of carcino-embryonic antigen in the sample (14 ng/mL) also suggested a mucinous tumour. Surgical resection confirmed a diagnosis of a mucinous adenocarcinoma.

Discussion

The principal clinical decision when managing a patient with a pancreatic cystic lesion is whether to offer a surgical resection or whether to observe. Where investigations suggest malignancy, surgery should, in general, be offered, unless the disease is deemed irresectable or the patient is unfit for the specific operation involved, in which case, there may be a role for chemotherapies in retarding disease progression.

In most cases, however, there is no evidence of malignancy. Recent evidence suggests that very small cysts (<1 cm) of whatever aetiology are unlikely to become malignant over a period of months.[17] For all but these lesions, EUS and especially, FNA should be considered, in order to help detect potentially malignant mucinous tumours, for which surgical resection is again the treatment of choice. However, the precise risks of occult malignancy and malignant transformation are poorly understood, although evidence suggests they are higher in IPMN than in MCNs and higher in main duct IPMN than in side branch IPMN.[18] These risks also probably increase with size; thus, a recent multi-centre study of smaller (<3 cm), asymptomatic, radiographically unconcerning cysts that had undergone resection suggests that the incidence of occult malignancy is modest (3.3%).[19] These risks must be weighed against the considerable risks of pancreatic surgery, particularly for lesions in the head. In addition, most patients are elderly and may carry significant co-morbidities. A decision to observe may therefore be acceptable to both surgeon and patient, particularly for small lesions in the pancreatic head in elderly or unfit individuals.[20]

Where imaging suggests a benign lesion, EUS reveals no features of a mucinous tumour and/or CEA level is low (below a threshold of perhaps 1 ng/mL), a strategy of observation also appears justifiable from our data, except in the small number that are large or symptomatic. Most lesions placed under radiological review were unchanged after a median of six months. Although we did not have data for longer durations of follow-up, it is reasonable to conclude that most lesions without malignant features at the outset grow slowly and can safely be observed for at least several months. Features that may suggest malignant transformation, such as an increase in size to greater than 2 cm, thickening, irregularity or calcification of the cyst wall, and solid regions within or adjacent to the cyst,[21,22] should provoke a reappraisal of the risk–benefit ratio of surgery. An absence of symptoms is not in itself evidence of a benign lesion because as many as one in six asymptomatic cysts may be malignant.[5]

In our series, cyst CEA was below 1 ng/mL in all three surgically proven SCNs, whereas it was much higher in the three resected mucinous tumours in which it had been measured. In view of the small number of cases, we cannot as yet report accurately the performance characteristics of this assay in our hands, but referring doctors could choose to incorporate the result into their decision-making. This would be supported by both a meta-analysis[16] and recently published practice guidelines.[4,5] As there is little evidence that CEA can distinguish benign from malignant mucinous neoplasms, there is no indication to perform repeated CEA measurements during follow-up EUS.

The use of CEA levels in decision-making is one subject of an ongoing prospective study in our unit. First, we are assessing the clinical impact of EUS and FNA on both diagnostic and management decisions made by the referring doctor. Second, we are prospectively examining the accuracy of diagnoses made by EUS and FNA by comparing them with the final pathological diagnosis of resected specimens.

Other assays are purported to distinguish between the causes of pancreatic cystic lesions. A CA 19-9 level above 50 000 U/mL is reported to confer a specificity of 81–90% for a mucinous tumour, but sensitivity varied widely (from 15–75%) in these studies.[13,23] The levels of CA 72-4 and CA 15-3 have shown some promise,[10–12,15] but these tests are less widely available than CEA and their evidence is less convincing. A low level of amylase is unlikely to occur in a pseudocyst,[16,23] whereas high levels have traditionally been stated to predict one. However, high levels are also reported in MCNs.[16,23] Furthermore, the use of FNA to diagnose pseudocysts is not recommended because of the risk of introducing infection, particularly into cysts that contain internal debris or necrotic tissue.[5] In most cases, the clinical history, coupled with the time frame over which the cyst appeared and the appearances on radiological imaging and EUS (pseudocysts are typically unilocular and communicate with the pancreatic duct) can be used to diagnose a pseudocyst. Highly viscous cyst fluid is also described as predictive of a mucinous

tumour. However, pseudocysts can also contain viscous fluid, and viscosity appears to perform less well than CEA[5]. Guidelines recommend its use only in support of other EUS and FNA findings.[5]

Molecular analysis of cyst aspirates is an area of growing interest. The detection of point mutations in the k-ras gene and analysis of a broad panel of tumour suppressor-linked microsatellite markers have been linked to the presence of malignancy in one prospective study.[24] A further multi-centre prospective study into these markers is currently in progress in the USA.

No complications occurred in our series, but caution needs to be retained in this regard as only 59 patients underwent EUS and 36 underwent FNA. The complication rate of EUS-guided FNA of pancreatic cysts is reported elsewhere to be approximately 2%, although most complications are mild.[25] Pancreatitis is the most common complication, whereas infection is rare. The benefit of prophylactic antibiotics is unknown. Transient abdominal pain following the procedure may be due to intracystic haemorrhage.[26] Overall, however, EUS-guided FNA appears to be safe.

In summary, this report confirms the usefulness and safety of EUS and EUS-guided FNA for pancreatic cystic lesions. In only a small minority (14%) does FNA show malignant cells. Of those lesions without malignant features at EUS, 28% had undergone surgical resection, whereas the vast majority of the remainder showed no signs of progression during clinical and radiological follow-up. Management of non-malignant pancreatic cystic lesions is a balance between the risks of malignant transformation and surgical resection. EUS and EUS-guided FNA can provide valuable information to help guide doctors and patients when making these decisions.

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References

1. Spinelli KS, Fromwiller TE, Daniel RA *et al*. Cystic pancreatic neoplasms: observe or operate. *Ann. Surg.* 2004; **239**: 651–7.
2. Walsh RM, Vogt DP, Henderson JM *et al*. Natural history of indeterminate pancreatic cysts. *Surgery* 2005; **138**: 665–70.
3. Kloppel G, Luttges J. WHO-classification 2000: exocrine pancreatic tumors. *Verh. Dtsch. Ges. Pathol.* 2001; **85**: 219–28.
4. Tanaka M, Chari S, Adsay V *et al*. International consensus guidelines for management of intraductal papillary mucinous neoplasms and mucinous cystic neoplasms of the pancreas. *Pancreatology* 2006; **6**: 17–32.
5. Khalid A, Brugge W. ACG practice guidelines for the diagnosis and management of neoplastic pancreatic cysts. *Am. J. Gastroenterol.* 2007; **102**: 2339–49.
6. Curry CA, Eng J, Horton KM *et al*. CT of primary cystic pancreatic neoplasms: can CT be used for patient triage and treatment? *AJR Am. J. Roentgenol.* 2000; **175**: 99–103.
7. Kawamoto S, Horton KM, Lawler LP. Intraductal papillary mucinous neoplasm of the pancreas: can benign lesions be differentiated from malignant lesions with multidetector CT? *Radiographics* 2005; **25**: 1451–68.
8. Song MH, Lee SK, Kim MH *et al*. EUS in the evaluation of pancreatic cystic lesions. *Gastrointest. Endosc.* 2003; **57**: 891–6.
9. Ahmad NA, Kochman ML, Brensinger C *et al*. Interobserver agreement among endosonographers for the diagnosis of neoplastic versus non-neoplastic pancreatic cystic lesions. *Gastrointest. Endosc.* 2003; **58**: 59–64.
10. Sperti C, Pasquali C, Guolo P, Polverosi R, Liessi G, Pedrazzoli S. Serum tumor markers and cyst fluid analysis are useful for the diagnosis of pancreatic cystic tumors. *Cancer* 1996; **78**: 237–43.
11. Sperti C, Pasquali C, Pedrazzoli S, Guolo P, Liessi G. Expression of mucin-like carcinoma-associated antigen in the cyst fluid differentiates mucinous from nonmucinous pancreatic cysts. *Am. J. Gastroenterol.* 1997; **92**: 672–5.
12. Brugge WR, Lewandrowski K, Lee-Lewandrowski E *et al*. Diagnosis of pancreatic cystic neoplasms: a report of the cooperative pancreatic cyst study. *Gastroenterology* 2004; **126**: 1330–6.
13. Hammel P, Levy P, Voitot H *et al*. Preoperative cyst fluid analysis is useful for the differential diagnosis of cystic lesions of the pancreas. *Gastroenterology* 1995; **108**: 1230–5.
14. Hammel PR, Forgue-Lafitte ME, Levy P *et al*. Detection of gastric mucins (M1 antigens) in cyst fluid for the diagnosis of cystic lesions of the pancreas. *Int. J. Cancer* 1997; **74**: 286–90.
15. Hammel P, Voitot H, Vilgrain V, Levy P, Ruszniewski P, Bernades P. Diagnostic value of CA 72-4 and carcinoembryonic antigen determination in the fluid of pancreatic cystic lesions. *Eur. J. Gastroenterol. Hepatol.* 1998; **10**: 345–8.
16. van der Waaij LA, van Dullemen HM, Porte RJ. Cyst fluid analysis in the differential diagnosis of pancreatic cystic lesions: a pooled analysis. *Gastrointest. Endosc.* 2005; **62**: 383–9.
17. Allen PJ, D'Angelica M, Gonen M *et al*. A selective approach to the resection of cystic lesions of the pancreas: results from 539 consecutive patients. *Ann. Surg.* 2006; **244**: 572–82.
18. Bassi C, Sarr MG, Lillemoe KD, Reber HA. Natural history of intraductal papillary mucinous neoplasms (IPMN): current evidence and implications for management. *J. Gastrointest. Surg.* 2008; **12**: 645–50.
19. Lee CJ, Scheiman J, Anderson MA *et al*. Risk of malignancy in resected cystic tumors of the pancreas < or =3 cm in size: is it safe to observe asymptomatic patients? A multi-institutional report. *J. Gastrointest. Surg.* 2008; **12**: 234–42.
20. Sahani DV, Saokar A, Hahn PF, Brugge WR, Fernandez-Del Castillo C. Pancreatic cysts 3 cm or smaller: how aggressive should treatment be? *Radiology* 2006; **238**: 912–9.
21. Zamboni G, Scarpa A, Bogina G *et al*. Mucinous cystic tumors of the pancreas: clinicopathological features, prognosis, and relationship to other mucinous cystic tumors. *Am. J. Surg. Pathol.* 1999; **23**: 410–22.
22. Gress F, Gottlieb K, Cummings O, Sherman S, Lehman G. Endoscopic ultrasound characteristics of mucinous cystic neoplasms of the pancreas. *Am. J. Gastroenterol.* 2000; **95**: 961–5.
23. Frossard JL, Amouyal P, Amouyal G *et al*. Performance of endosonography-guided fine needle aspiration and biopsy in the diagnosis of pancreatic cystic lesions. *Am. J. Gastroenterol.* 2003; **98**: 1516–24.
24. Khalid A, McGrath KM, Zahid M *et al*. The role of pancreatic cyst fluid molecular analysis in predicting cyst pathology. *Clin. Gastroenterol. Hepatol.* 2005; **3**: 967–73.
25. Lee LS, Saltzman JR, Bounds BC, Poneros JM, Brugge WR, Thompson CC. EUS-guided fine needle aspiration of pancreatic cysts: a retrospective analysis of complications and their predictors. *Clin. Gastroenterol. Hepatol.* 2005; **3**: 231–6.
26. Varadarajulu S, Eloubeidi MA. Frequency and significance of acute intracystic hemorrhage during EUS-FNA of cystic lesions of the pancreas. *Gastrointest. Endosc.* 2004; **60**: 631–5.