

## Cystic Neoplasms of the Pancreas: Current Diagnostic Modalities and Management

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### Abstract

Cystic neoplasm of the pancreas is a relatively uncommon condition covering a wide spectrum of pathology. The increasing incidence as a result of routine imaging tests in asymptomatic patients presents a diagnostic and therapeutic problem to the clinician. This paper discusses the role of the various investigative modalities in the management of cystic neoplasia of the pancreas.

Ann Acad Med Singapore 2009;38:251-9

**Key words:** Frantz tumour, Intraductal papillary mucinous neoplasm, Mucinous cystadenoma, Mucinous cystadenocarcinoma, Mucinous neoplasm of the pancreas, Solid pseudopapillary neoplasm

### Introduction

Cystic neoplasms of the pancreas are relatively uncommon conditions of the pancreas covering a wide spectrum of different pathological entities.<sup>1</sup> This condition accounts for less than 1% of all primary pancreatic tumours,<sup>2</sup> but has become increasingly important in clinical practice because of the rising occurrence of its detection in asymptomatic patients as a result of various imaging tests done for other reasons.<sup>3</sup> These tests would commonly be an abdominal ultrasound (US) or computed tomography (CT)<sup>4,5</sup> for investigation of abdominal symptoms or for staging and follow-up of patients with an abdominal malignancy. As the spectrum of diseases classified as cystic neoplasms of the pancreas can range from benign to frank malignancy and most of these patients are detected asymptotically, the condition presents a particular dilemma for the managing clinician. This difficult situation is further compounded by the frequent inability in establishing a definitive diagnosis preoperatively.<sup>6</sup> The present review aims to put into perspective the current role and limitations of the various investigations (Table 1) for use in this condition.

### Pathology and Clinical Scenario

The World Health Organisation (WHO) classifies cystic neoplasms of the pancreas into 3 main categories—benign, borderline (potentially malignant) and malignant.<sup>7,8</sup> The major histologic subtypes include (a) serous cystic

neoplasms (SCN), (b) mucinous cystic neoplasms (MCN), (c) intraductal papillary mucinous neoplasms (IPMN) and (d) solid pseudopapillary neoplasms (SPPN).<sup>1</sup> Rarer types include cystic pancreatic endocrine neoplasms (PEN), cystic ductal adenocarcinomas and acinar cell cystadenomas.<sup>1</sup> Presently, all cystic neoplasms are considered at the very least borderline malignant or malignant with the exception of SCN which are almost always benign,<sup>1</sup> although isolated cases of malignant SCN termed serous cystadenocarcinoma have been reported.<sup>9</sup>

It is important for the managing clinician to remember that the diagnosis of a non-neoplastic cystic lesion of the pancreas should be considered in the differential diagnosis of a cystic lesion of the pancreas.<sup>10</sup> The pancreatic pseudocyst is the most important non-neoplastic cystic lesion to consider as it is fairly common and its definitive management (which is beyond the scope of this review) is entirely different from cystic neoplasms of the pancreas.<sup>1,10</sup>

#### *Serous Cystic Neoplasm (SCN)*

Previously termed serous cystadenomas, SCN are lined by simple, glycogen-rich cuboidal epithelium.<sup>11,12</sup> Malignant change, although reported, is extremely rare, and the condition is considered benign.<sup>13</sup> There is a female predilection, and occurrence is mostly in the seventh decade of life. SCN can exhibit macroscopic variations in locule size and are now subdivided into (a) serous microcystic and

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Table 1. Typical Features of Various Pancreatic Cystic Lesions on Preoperative Investigations

	SCN	MCN	IPMN	SPPN	Cystic PEN	Pseudocyst
<b>Cross-sectional imaging features</b>	Microcystic or honey-combed cyst with central scar and calcifications	Macrocytic with thick wall septations and peripheral calcifications	Diffuse or segmental markedly dilated duct, ductal communication	Large mixed solid-cystic lesion	No specific features	Unilocular with evidence of pancreatitis
<b>Cyst fluid</b>						
<b>CEA</b>	Low	High	High	Low	-	Low
<b>CA 19-9</b>	Variable	Variable	Variable	-	-	High
<b>CA 72-4</b>	Low	High	High	-	-	Low
<b>CA 15-3</b>	Low	High	Low	-	-	Low
<b>CA 125</b>	Low	Variable	Low	-	-	Low
<b>Amylase</b>	Low	Low	High	-	-	High
<b>Cytology</b>	Monomorphic cuboidal cells glycogen-rich clear cytoplasm	Columnar mucinous cells with variable atypiaPresent	Columnar mucinous cells with variable atypiaPresent	Bland cells with round nuclei with papillary structures	Small cells with scant cytoplasm, monomorphic nuclei and positive staining for chromogranin and synaptophysin	Inflammatory cells without epithelial cells
<b>Mucin</b>	Absent	Absent	Absent	Absent	Absent	Absent

The data on cyst fluid analyses were obtained from Reference 13. Brugge WR, Lauwers GY, Sahani D, Fernandez-del Castillo C, Warshaw AL. Cystic neoplasms of the pancreas. *N Engl J Med* 2004;351:1218-26

(b) serous oligocystic adenomas,<sup>11</sup> the distinction being important in preoperative diagnosis and will be discussed later.<sup>14,15</sup>

The definitive management of symptomatic SCN is surgery. However, with asymptomatic tumours, management remains controversial; although most would observe,<sup>12</sup> a recent study suggests that large (>4 cm) SCN have a tendency to increase in size and cause symptoms at a later date<sup>16</sup> which may support the role of 'prophylactic resection' in this sub-group of patients.

#### *Mucinous Cystic Neoplasm (MCN)*

MCN are formed by mucus-producing cells and the presence of ovarian-like stroma is now considered a prerequisite for diagnosis.<sup>17,18</sup> These almost always occur in females, predominantly in the middle-aged and often in the body/tail of the pancreas. At present, all MCN are considered at least potentially malignant and all surgically-fit patients should undergo surgical resection.<sup>1,17,19</sup> The prognosis of patients after resection is significantly better when compared with patients with primary ductal adenocarcinoma of the pancreas.<sup>20,21</sup>

#### *Intraductal Papillary Mucinous Neoplasm (IPMN)*

First reported in 1982,<sup>22</sup> IPMN is now considered a distinct entity from MCN<sup>23</sup> and like MCN, produce mucin. A communication with the pancreatic duct is invariable,<sup>24</sup>

and patients may present with pancreatitis from ductal obstruction. The lesions are non-specific in location and can be multi-focal. IPMN are divided into (a) main-duct and (b) branch-duct type according to the involvement of the pancreatic ducts.<sup>19</sup> This distinction is of utmost importance as main-duct type IPMN have a reported prevalence of malignancy ranging from 57% to 92% compared to branch-duct type IPMN with a reported range from 6% to 46%.<sup>19</sup>

According to a recent consensus statement, all main-duct type IPMN should be resected because of the high malignancy rate whereas branch-duct type IPMN demonstrating favourable features (<3 cm size and absence of mural nodules) may be managed conservatively.<sup>19</sup>

#### *Solid Pseudopapillary Neoplasm (SPPN)*

First described by Frantz in 1959,<sup>25</sup> these occur almost exclusively in young women<sup>26</sup> although male cases have been reported.<sup>27</sup> The lesion is largely benign with low malignant potential and long-term survival is excellent after resection.<sup>28,29</sup> Surgery is advocated in all cases, as these lesions have the potential to grow to extremely large sizes and to metastasise.<sup>29</sup>

#### *Cystic Pancreatic Endocrine Neoplasm (PEN)*

PEN usually present as solid hypervascular lesions in the pancreas but may undergo cystic change, mimicking cystic

neoplasms of the pancreas.<sup>30</sup> The clinical behaviour of cystic PEN is similar to the solid counterparts and hence are considered morphological variants of the same pathological entity. There is a variable malignant potential determined by tumour size and mitotic activity. Presently, most cystic PEN are resected due to the difficulty in obtaining an accurate preoperative diagnosis and the belief that most PEN have malignant potential.<sup>30-32</sup>

### Imaging Modalities

Imaging modalities are the mainstay in the detection and diagnosis of cystic neoplasms. These range from the basic abdominal US for screening and detection, to higher definition cross-sectional imaging methods such as CT and magnetic resonance imaging (MRI), to invasive methods such as endoscopic ultrasound (EUS) and radionuclear imaging such as positron-emission tomography (PET) scanning.

#### CT

CT would be the main high definition imaging modality for the initial assessment of a cystic lesion of the pancreas. A key initial consideration would be the exclusion of a pancreatic pseudocyst,<sup>1</sup> and this is usually easily done based on a clinical history of pancreatitis, biochemical evidence of hyperamylasemia and radiologic evidence of pancreatitis such as gland atrophy, parenchymal calcification and swelling and ductal stones.<sup>1</sup> However, two potential pitfalls to remember is that IPMN may be complicated by pancreatitis and pancreatic pseudocyst may occasionally occur in asymptomatic patients.<sup>33</sup> Once a pancreatic pseudocyst has been excluded, the diagnosis of a pancreatic cystic neoplasm is considered.

Several important features on CT have been shown to be helpful in the diagnosis of pancreatic cystic neoplasms. These include (a) locularity (unilocular, oligolocular [ $< 6$  locules] or multi-locular [ $\geq 6$  locules]), (b) internal cysts (microcystic [ $< 2$  cm] or macrocystic [ $\geq 2$  cm]), (c) main pancreatic duct communication, (d) presence of mural nodules and (e) central or peripheral calcification.<sup>1,14,15,33</sup>

SCN tend to be well-demarcated, lobulated cystic lesions on CT with multiple thin or filmy septations that do not enhance and appear on CT as a conglomerate of multiple ( $> 6$ ) small cysts, each not more than 2 cm in size. This 'microcystic' appearance or 'honeycomb' appearance is presently considered pathognomonic of SCN (Fig. 1a).<sup>14,15</sup> In typical lesions, a central stellate scar with calcification confirms the diagnosis,<sup>34-36</sup> although this feature is only found in 1 of 5 patients.<sup>15</sup> Potential pitfalls of CT in the diagnosis of SCN are the inability to discern the fine septa and hence microcystic appearance and the existence of the morphological variant of SCN termed serous oligocystic

adenoma which appears as a macrocystic instead of microcystic lesion (Fig. 1b).<sup>11,15</sup>

MCN are more frequently seen in the body/tail of the pancreas, and appear unilocular commonly or occasionally multi-locular with septations that vary in thickness. Features on CT that suggest malignancy or a malignant potential include: (a) large size (usually  $> 2$  to 3 cm), (b) wall or septal enhancement, (c) nodularity of the wall or septae, (d) calcifications of the wall typically described as egg-shell calcification,<sup>4,37</sup> (e) solid components within the cyst<sup>38</sup> and (f) evidence of local invasion or (g) distant metastases.<sup>39-41</sup> A typical clinical scenario when the diagnosis of a MCN should be strongly considered is the detection of a large ( $> 4$  cm) macrocystic lesion with mural nodules and peripheral wall calcifications occurring in the body or tail of the pancreas of a middle-aged female (Fig. 2).

Main-duct IPMN has a typical appearance on CT which usually enables it to be distinguished from other cystic neoplasms of the pancreas.<sup>1</sup> The presence of a diffusely or segmentally dilated tortuous pancreatic duct with filling defects is highly suggestive of a main-duct IPMN (Fig. 3).<sup>1</sup>

Branch-duct IPMN frequently appears as a unilocular cyst and is difficult to distinguish from other cystic neoplasms, although diagnosis is clinched by the demonstration of communication with the pancreatic duct. The presence of multiple cysts is also suggestive of IPMN as multi-focality is a unique feature of IPMN not shared by the other cystic neoplasms. Alternatively, ductal dilatation distal to the cystic lesion provides supportive evidence for IPMN.<sup>42,43</sup>

SPPN typically present in young females (20s to 30s in age) as a large well-encapsulated lesion with mixed solid and cystic components giving rise to a heterogeneous appearance (Fig. 4). There may be peripheral wall calcification and contrast enhancement.<sup>29</sup>

Despite the typical features described, CT diagnosis of the specific type of lesion and the determination of benign versus malignant disease is often difficult if not impossible. While CT is good for defining location and adjacent structures, it is usually not specific enough to confirm a diagnosis preoperatively. Various studies have determined the diagnostic accuracy of CT in the differential diagnosis of cystic neoplasms of the pancreas to be between 20% and 90%. The wide difference in results may be attributed to the different diagnostic criteria and study designs adopted.<sup>15</sup> In essence, it is currently impossible to determine the true accuracy of CT in the diagnosis of cystic neoplasms of the pancreas although there is presently near-uniform agreement that cross-sectional imaging alone is not sufficiently accurate to provide a clinically useful diagnosis because of the great degree of overlap in the morphologic features of the various cystic neoplasms of the pancreas.<sup>33,44</sup>

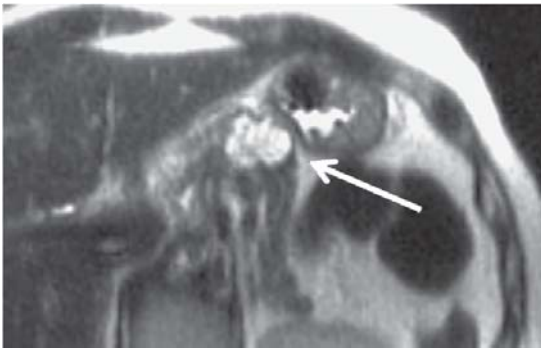


Figure 1. Features of SCN on imaging. (a) MRI showing typical microcystic appearance of an SCN (arrow); (b) MRI showing a large oligocystic SCN displacing the common bile duct but not causing obstructive dilatation.

Figure 1. (b).



Fig. 2.



Fig. 3.

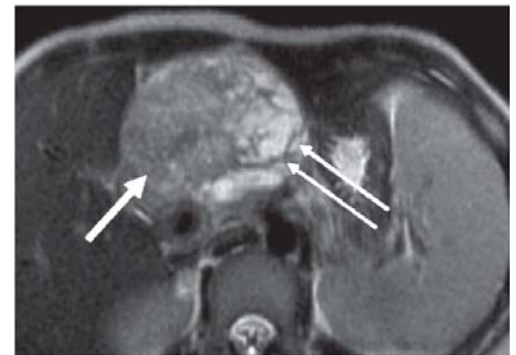


Fig. 4.

Figure 2. CT scan demonstrating features of a typical MCN with mixed solid and cystic areas as well as “egg-shell” calcification (arrows).

Figure 3. A main-duct IPMN demonstrating pancreatic ductal dilatation and filling defect (arrow) on an MRCP.

Figure 4. MRI demonstrating features of a typical SPPN in the head/neck of pancreas with mixed solid (single arrow) and cystic (double arrows) areas.

*Magnetic Resonance Imaging (MRI), MR Cholangio-pancreatography (MRCP)*

MRI has been described as being better at the characterisation of cystic pancreatic lesions than CT and may allow better delineation of a communication with the pancreatic duct.<sup>45</sup> In general, MRI features will closely mimic those described for CT.

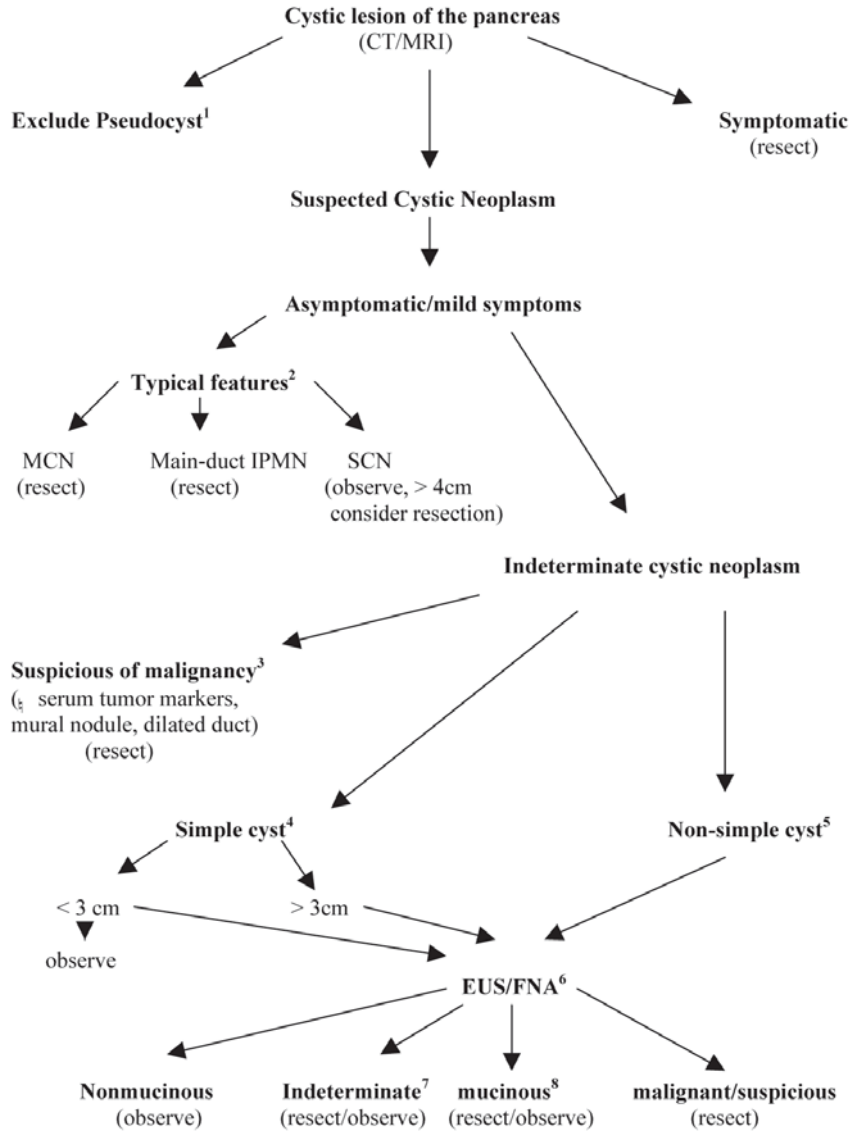
In SCN, the features of multi-locular small cysts less than 2 cm with a central scar are typical. In addition, low signal intensity in the lesion on T1 weighted images and high signal intensity on T2-weighted images support the diagnosis.<sup>46</sup> With MCN and IPMN, the features are again similar. MRI is especially useful for defining the extent of ductal dilatation and the size of intramural nodules within these mucin-secreting tumours.<sup>45,47,48</sup> The features of SPPN on MRI are not well described. The features of mixed solid and cystic areas seen on CT are expected. In addition, the papillary structures within the centre of the cyst have been

reported as better defined on MRI although these do not enhance with gadolinium contrast.<sup>27</sup>

*Endoscopic Ultrasound (EUS)*

Transcutaneous abdominal US for imaging the pancreas is often difficult because of overlying bowel and gas shadows and the need for the US waves to traverse a long distance. These problems have been addressed by EUS where the transducer is placed close to the target intra-abdominal organ via an endoscopic device. For pancreatic cystic lesions, EUS has been reported to increase the resolution for better definition of features which may help in diagnosis.

SCN will show the typical honeycomb appearance described earlier for CT and MRI. The finding of smaller than 3 mm, multiple cystic spaces within a cystic lesion is highly suggestive of serous cystadenoma with a diagnostic accuracy of up to 96%.<sup>49</sup> MCN are typically unilocular and occur in the body and tail of the pancreas. EUS findings of irregular and calcified septa,<sup>50,51</sup> mural nodules and papillary protuberances suggest malignancy. These features are also seen with IPMN, but with the additional supportive findings of distended pancreatic ducts. Although not part of EUS, a side viewing endoscope to visualise the ampulla of Vater may classically demonstrate mucin extruding from the



1. Pseudocysts may be diagnosed from a typical history and biochemical evidence of pancreatitis and cross-sectional imaging features.
2. Main-duct IPMN, SCN and MCN may demonstrate typical cross-sectional features which are almost pathognomonic.
3. Elevated serum tumor markers and the presence of suspicious cross-sectional imaging features such as the presence of solid component or mural nodules and dilated pancreatic duct have been shown to have a strong predictive value of a malignant or potentially malignant lesion.
4. Small incidental simple cysts are almost never frankly malignant and can be safely observed without the need for further investigations. Nonetheless, it is important to note that many of these are potentially malignant such as benign MCN and branch-duct IPMN.
5. Non-simple cysts are indeterminate cysts without suspicious features which commonly appear as macrocystic lesions.
6. The results of cyst fluid analysis via EUS/FNA may be malignant/suspicious if malignant cells, atypical cells or neuroendocrine cells are demonstrated.
7. An indeterminate result is obtained when the sample is insufficient or the cyst fluid CEA level is borderline i.e. neither high nor low enough to suggest or exclude a mucinous lesion. In this case, the cyst may be resected or observed depending on the particular risk-benefit ratio of surgery.
8. An elevated cyst fluid CEA or the presence of mucin staining strongly suggests a mucinous lesion. These in general should be resected as mucinous lesions are considered potentially malignant. However, recent evidence suggests that some of these may be observed i.e. small branch-duct IPMN without mural nodules.

Figure 5. Proposed management algorithm of a cystic lesion of the pancreas

pancreatic duct.<sup>52,53</sup> An endoscopic retrograde cholangiopancreatography (ERCP) is a possible adjunct investigation<sup>54,55</sup> but will probably only demonstrate duct obstruction, mural nodules or communication without defining the lesion.<sup>43,56</sup> As with CT and MRI, EUS

demonstrates a mixed solid and cystic appearance in SPPN. Although EUS can occasionally better define the features compared to CT and MRI, it is subject to inter-observer variability<sup>57</sup> and is unreliable in distinguishing benign from malignant lesions.<sup>58</sup> The current recommendation from the

guidelines of the American Society of Gastrointestinal Endoscopy (ASGE) suggests that cystic lesions of the pancreas are potentially malignant and that EUS by itself is not accurate enough to define the type of lesion and its malignant potential.<sup>59</sup>

#### *Positron Emission Tomography (PET)*

PET has been advocated as the imaging of choice for the detection of cancer and its staging. In combination with CT imaging as PET-CT, it allows for localisation of a functionally active lesion. The sensitivity and specificity for PET in pancreatic disease has been reported to be 94% and 97%, respectively.<sup>60</sup>

Unfortunately, despite its usefulness for pancreatic ductal adenocarcinoma, PET is unable to distinguish cystic from solid tumours and currently cannot replace traditional cross-sectional imaging as the imaging of choice for pre-operative evaluation.<sup>60</sup> More recently, PET scan has been shown by an Italian group to be extremely accurate in detecting overtly malignant cystic neoplasms of the pancreas with sensitivities and positive predictive values of more than 90%.<sup>1,60,61</sup> However, PET is unable to distinguish potentially malignant or borderline cystic neoplasms from benign cystic neoplasms and its potential clinical utility remains limited.

#### **Serum Tumour Markers**

Although serum tumour markers such as carcino-embryonic antigen (CEA) and carbohydrate antigen (CA) 19-9 have been useful in the diagnosis and staging of pancreatic adenocarcinoma, these are less useful in cystic neoplasms of the pancreas. More recently however, several investigators have demonstrated that elevation of serum CEA or CA 19-9 were actually useful in the initial triage of cystic neoplasms of the pancreas as it has a high positive predictive value (>90%) and specificity (>90%) in the detection of malignancy.<sup>33</sup> Nonetheless, in most cases of cystic neoplasms of the pancreas, serum tumour markers are within normal range and the sensitivity of these tests are extremely low (<50%).

#### *Cyst Fluid Cytology and Biochemical Markers*

While imaging methods can define the location of the pancreatic cystic neoplasms, it is unable to fully determine the nature and type of lesion. Cells and fluid aspirated from cystic neoplasms have been used in an attempt to better define the diagnosis. The acquisition of cells and fluid can be via a percutaneous needle aspiration approach under imaging guidance or more recently using EUS as a guide.

#### *Cytology and Cyst Fluid Nature*

Clear cystic aspirate and the finding of glycogen-rich cells from a lesion are typical for SCN. When mucin is

aspirated, the diagnosis of MCN is made although there will be difficulty in deciding malignant potential based on cytology alone. Occasionally with SPPN, branching papillae and a myxoid stroma may be diagnostic.<sup>62,63</sup> The presence of malignant cells or neuroendocrine cells on cytology may also guide the clinician towards surgical resection. However, accuracies with cytology reported in the literature have been variable, ranging from 54% to 97%.<sup>64-68</sup> The main limitation of cytologic examination of cyst fluid has been the difficulty in obtaining sufficient cells.<sup>1</sup>

#### *Markers in Cyst Fluid*

The finding of raised amylase levels within the cyst fluid should raise the suspicion of a pseudocyst or of a cystic lesion with ductal communication such as IPMN. A cyst fluid amylase <250 U/L has been reported to be useful in excluding a pseudocyst.<sup>1</sup>

A variety of tumour markers have also been studied in the cyst fluid. These include the traditional pancreatic markers such as CEA and CA 19-9 as well as other markers such as CA 125 and CA 72-4. With cyst fluid CEA levels, a value of greater than 400 ng/mL is highly indicative of a mucinous cystadenocarcinoma or a mucinous cystadenoma with borderline malignant potential,<sup>69,70</sup> although differing results have been reported and hence no definitive cut-off value is currently acceptable for clinical use.<sup>59</sup> Presently, cyst fluid CEA is widely regarded as the single most useful cyst fluid marker for the diagnosis of a mucinous cystic lesion. Using a cyst fluid CEA cut-off of >192 ng/mL, the Cooperative Pancreatic Cyst (CPC) Study Group demonstrated that there was a diagnostic accuracy of 79% in distinguishing mucinous from non-mucinous cysts.<sup>71</sup> In another pooled analysis of 12 studies, a cyst fluid CEA <5 ng/mL predicted a benign cyst with a sensitivity of 54% and a positive predictive value of 94%.<sup>72</sup>

High levels of CA 125 and CA 72-4 are also suggestive of a malignant or pre-malignant state.<sup>70,73</sup> CA 125 was found to be elevated in up to 60% of malignant cysts, and CA 72-4 has been reported to be highly specific in diagnosing pre-malignant neoplasia.<sup>74</sup> These markers are currently considered not accurate or specific enough to be of significant clinical use.<sup>59</sup> Although CA 19-9 has been the traditional marker for pancreatic ductal adenocarcinoma, its role in cystic neoplasms of the pancreas is limited because of variable levels in both benign and malignant lesions including pseudocysts.<sup>13,70</sup>

#### *Genetic Markers*

Genetic alterations have been detected in a wide variety of cancers. With pancreatic adenocarcinoma, point mutations of the K-ras oncogene have been reported to be of a significantly high occurrence to be of clinical use.<sup>75-77</sup>

However, these mutations are also found in normal and inflammatory pancreatic ducts,<sup>78,79</sup> thus limiting the value of its use in distinguishing benign from malignant lesions. The use of these genetic markers has not been well-studied with cystic neoplasms although more recently, DNA quality and number and sequence of mutations have been proposed as markers for distinguishing malignant from potentially malignant cystic neoplasms.<sup>80</sup>

## Conclusion

Cystic lesions of the pancreas are increasingly detected especially in asymptomatic patients due to imaging studies performed for other indications. A wide spectrum of disease entities have been recognised which may present as a cystic lesion of the pancreas and can range from obviously benign to indeterminate or borderline malignant potential lesions to overt malignancy. The role of imaging in detecting the lesions and confirming its location and proximity to surrounding structures is well recognised and CT or MRI is probably best for this purpose. Although the different pathological types have distinct features on imaging, cytology and markers, these are probably not specific enough at present to be used to discriminate between lesions and to determine their appropriate management. EUS including EUS-guided FNA for cytology and fluid studies has proven to be a useful addition to the diagnostic armamentarium of clinicians managing cystic lesions of the pancreas.

In the past, many have advocated an aggressive resectional approach<sup>1-3,6</sup> for all cystic neoplasms of the pancreas on the basis that almost all lesions, except for SCN, have the potential to be malignant and there are currently no reliable preoperative tests to determine malignant potential. However at present, a more tempered approach is being used at many centres, including ours. The current management of a cystic lesion of the pancreas should be tailored according to the risk-benefit ratio of surgical resection which is primarily determined by the risk of a cyst being malignant or becoming malignant versus the operative risk of pancreatic surgery. The risk of a cystic neoplasm being malignant can be determined preoperatively by the various preoperative diagnostic tests discussed previously whereas the operative risk will be determined primarily by the age and co-morbidities of the patient, surgical volume of the centre and the type of resection (distal pancreatectomy or pancreaticoduodenectomy) which in turn is determined by the size and location of the cystic neoplasm.

Based on our review of the literature, we propose a simple and practical approach towards the management of a cystic lesion of the pancreas (Fig. 5).

The initial characterisation of a cystic lesion of the pancreas is by CT or MRI, in particular to exclude a

pancreatic pseudocyst based on history, biochemistry and cross-sectional imaging.<sup>1</sup> It is imperative to remember that occasionally pseudocysts may not have typical symptoms of preceding pancreatitis and that cystic neoplasms such as IPMN may also cause pancreatitis.<sup>33</sup>

On confirming a diagnosis of cystic neoplasm of the pancreas, treatment should be resection if the patient is symptomatic or has complications from the tumour.

In those with mild or no symptoms, further evaluation is necessary. Lesions with typical features of MCN, SCN or main-duct IPMN are managed accordingly. More commonly, the pathognomonic features of a particular histologic subtype are absent and the indeterminate cystic neoplasm can be classified into (a) cyst with features suspicious of malignancy, (b) simple cyst and (c) non-simple cyst.

Cysts in the ‘suspicious of malignancy’ category demonstrate features such as mural nodules, solid components, lymph node enlargement, dilated pancreatic duct and elevated serum tumor markers and should in most instances undergo resection.<sup>33</sup> The findings of a recent study support this recommendation as cysts with suspicious features of malignancy had a more than 80% chance of harbouring a malignant or potentially malignant lesion.<sup>33</sup>

Simple cysts are unilocular cystic lesions with no septae, calcifications, dilated ducts and solid components. Simple small (<3 cm) cysts are almost never frankly malignant<sup>14,33,81</sup> and can be observed without further diagnostic investigations for more than 5 years.<sup>81</sup> Nonetheless, one should note that premalignant lesions such as benign IPMN and MCN form a significant proportion of small simple cysts.<sup>33</sup>

In this study, we classified non-simple cysts as cysts without features suspicious of malignancy but could not be classified as ‘simple’ as these were multi-locular and had calcifications. Non-simple cysts and simple cysts >3 cm need an EUS-FNA to further characterise the cysts.

The results of EUS-FNA can be categorised as-(a) suspicious or malignant category with malignant, atypical or neuroendocrine cells, (b) mucinous category with a high fluid CEA and/or mucin, (c) non-mucinous category when fluid CEA is low without mucin and (d) indeterminate category when the sample is insufficient or fluid CEA level is borderline.

The management of the suspicious or malignant category should be resection. Non-mucinous category can be observed. However, the management of the mucinous and indeterminate category is debatable and depends on the risk-benefit ratio of surgery. While most would previously advocate resection of lesions in the mucinous category, recent evidence suggests that many of these are branch-

duct type IPMN and can be managed conservatively if smaller than 3 cm without mural nodules.<sup>19,82</sup>

In summary, there are no ideal tests or combination of tests that can determine the type of cystic neoplasm or its malignant potential. It would be sensible for the managing clinician to take the tests in the context of the clinical situation to customise management for each individual patient. Our proposed management algorithm will aid the clinician towards tailoring an appropriate management approach for the individual patient.

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