Comparative analysis and assessment of diagnostic accuracy of 256 slice CT and endoscopic ultrasound in evaluation of pancreatic masses

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Abstract

Context: Pancreatic masses are routinely encountered on imaging and often present as a diagnostic dilemma. These masses range from benign inflammatory masses, requiring no intervention to malignant masses, which carry grave prognosis and hence require aggressive management. Aims: Compare the diagnostic accuracy of 256 multislice CT and endoscopic ultrasound (EUS) in characterization and assessment of resectability of pancreatic masses and compare the multidetector computed tomography (MDCT) and EUS findings with histopathological findings. Settings and Design: Prospective study. Subjects and Methods: 36 patients with pancreatic masses were included who underwent dual phase CT using pancreatic protocol and EUS using 5–13 MHz transducer. Fine needle aspiration cytology (FNAC) was done wherever feasible. Parameters regarding tumor size, location, imaging morphology, and vessel involvement were recorded. Findings were compared with histopathological/operative diagnosis/clinical follow-up. Statistical Analysis Used: Descriptive statistics with percentages and proportions and Chi-square test. Results: Multidetector computed tomography (MDCT) and EUS established diagnosis consistent with tissue diagnosis in 30 (83%) and 22 (61%) patients, respectively. However, the best results were obtained with the combined use of MDCT and EUS. The number of patients categorized as inconclusive by MDCT were lower compared to EUS. Assessing resectability for pancreatic adenocarcinoma, MDCT showed specificity and positive predictive value (PPV) of 100% compared to EUS, which had specificity and PPV of 75% and 92.3%, respectively. MDCT is the first-line imaging modality in detection, characterization of pancreatic masses, and assessment of resectability in malignant neoplasms. EUS is beneficial in the detection of masses <2 cm in size causing pancreatic contour deformity on CT, for guiding FNAC. MDCT and EUS with EUS-guided FNA are complementary not competitive tools in preoperative imaging of pancreatic masses.

Key words: Endoscopic ultrasound; multidetector CT; pancreas

Introduction

Pancreatic masses are commonly seen and present with similar clinical presentation, hence their differentiation dictates their management.
Multidetector computed tomography (MDCT) provides 3-D multiplanar reconstruction with improved spatial and temporal resolution enabling accurate determination of tumor involvement of the common bile duct (CBD), pancreatic duct, and peripancreatic vasculature. It also enables the detection of metastasis and loco-regional spread in cases of pancreatic carcinoma.

Endoscopic ultrasound, overcomes the limitations of transabdominal USG and has shown to be more sensitive than MDCT for visualization of pancreatic tumors <3 cm in size and allows concurrent biopsy. However, it is highly operator dependent.]

Our aim was to compare the role of CT and EUS in the evaluation of pancreatic masses and define their complementary roles if any.

Subjects and Methods

A cross-sectional, prospective study to evaluate pancreatic lesions using MDCT and Endoscopic USG along with Endoscopic USG guided FNAC/cyst aspiration was undertaken at our institute. Patient recruitment was done prospectively from May 2015 to January 2017. The study was approved by the Institutional Ethics Committee, and informed consent was taken from all the patients. Patients (≥10 years) with clinical (history, examination, serum markers like CA 19-9 in cases of pancreatic adenocarcinoma, C-peptide and insulin levels for neuroendocrine tumors particularly insulinomas) suspicion of pancreatic mass and/ or incidentally discovered pancreatic mass on any imaging modalities, like transabdominal ultrasound, CT abdomen or MRI abdomen were included. Exclusion criteria were pregnant females, contraindications to contrast enhanced CT abdomen and patients unable to undergo endoscopic ultrasonography for any reason.

Thirty-six patients were included in the study, who underwent contrast enhanced MDCT and Endoscopic ultrasound for characterization of pancreatic lesions (14 men, 22 women; age range 10–70 years). The interval between MDCT and Endoscopic ultrasound examinations was less than 2 weeks. A detailed clinical history was taken. Clinical findings, General physical examination, abdominal examination, laboratory investigations of all the patients were recorded. Clinical diagnosis was recorded. Findings on other imaging modalities done prior to CT abdomen and Endoscopic ultrasound were also recorded. This was followed by CT examination on 256-slice dual source multidetector CT and endoscopic ultrasound (EUS) with formulation of a CT diagnosis and EUS diagnosis. FNAC/ cyst aspiration (in case of cystic lesions) wherever required and feasible was performed. These findings were compared with histopathological diagnosis/operative diagnosis/ clinical follow up to arrive at the final diagnosis

Procedure for MDCT

All patients undergoing abdominal CT were instructed for overnight fasting. NCCT and CECT were acquired using a set protocol on Dual source 256 slice MDCT (Somatom Definition FLASH). Each patient was scanned from diaphragm to the pubic symphysis. Scans were obtained with a slice thickness of 1.5mm, at 120 kV and 250 effective mAs. Contrast enhanced CT scans were obtained using dual phase pancreatic imaging protocol comprising pancreatic parenchymal (at 35-40 seconds from start of I/V contrast) and portal venous phase (at 65-70 seconds from start of I/V contrast). Ninety to one hundred twenty millilitre of non-ionic iodinated contrast media (iodine 320 mgI mg/mL) was injected through an intravenous cannula using a pressure injector (at rate of 4 mL/s). Post processing of the axial data set was done and images were preserved in axial, coronal, sagittal and relevant MPR format. MIP format and VRT images were generated wherever deemed appropriate. CT images were reviewed by two radiologists who recorded their findings arrived at by common consensus on a predefined proforma.

Procedure for EUS

After overnight fasting the patient was taken for EUS procedure. An IV line was secured, all procedures were done under mild sedation using midazolam, 1–2.5 mg slow IV, under the supervision of a doctor.

All procedures were done by linear Olympus CLV 180 series scope (Olympus Corporn., Japan) with high-frequency transducer (5–13 Mhz) using station approach in the left lateral position. A transgastric approach was used to depict the pancreatic neck, pancreatic body and tail, splenic vein, whereas a transduodenal approach was used to reveal the pancreatic head, common bile duct, and portal vein and its confluence. The uncinate process, superior mesenteric artery, and superior mesenteric vein were seen using the second and third portions of the duodenum as an ultrasound window. All parameters regarding tumor size, location, the involvement of vessels, were recorded in the prescribed format. The whole of pancreas was evaluated. FNAC (via transduodenal route for pancreatic head and body lesions and via transgastric route for pancreatic tail lesions) was done using Echotip ultra 22 G needle (Cook Corporn.) and was evaluated by on- site pathologist.

After the procedure, the patient was monitored in recovery room for 4–6 h.

Statistical test used

Excel software was used to analyze the statistical data. Descriptive statistics with percentages and proportions of the occurrence of pancreatic masses were generated for the study patients according to age and sex, location of lesions, morphology of lesions, characterization of lesions using
MDCT study and EUS study, comparison of MDCT and EUS in characterization of pancreatic lesions individually and with combined use of both modalities (MDCT and EUS). Comparison of MDCT and EUS in determining operability of pancreatic ductal carcinoma (based on MD Anderson’s resectability criteria for pancreatic malignancy[6]) was done using 2x2 contingency table with calculation of sensitivity, specificity, PPV, NPV and the $P$ value using Chi-square test.

**Results**

A total of 36 patients were included in the study. Each of the patients included were subjected to an abdominal MDCT scan on a 256-slice scanner followed by a EUS examination.

The occurrence of pancreatic lesion, solid/solid cystic/cystic was seen to be more common in the females compared to males with a male is to female ratio of almost 1:1.5 in our study.

The pancreatic lesions including both malignant and benign masses were seen to occur most commonly in the 4th to 6th decades of life.

The most common site of occurrence of pancreatic masses was the pancreatic head region, with few lesions showing multiple sites of occurrence.

The pancreatic lesions encountered could be broadly classified as solid masses ($n = 26$), cystic masses ($n = 8$), and mixed solid-cystic masses ($n = 2$).

Amongst all cases of pancreatic masses, pancreatic adenocarcinoma emerged as the single most common pancreatic lesion.

The cystic lesions of the pancreas were relatively less common in occurrence compared to solid lesions, with nearly equal proportions of serous cystadenoma, mucinous cystadenoma, and intraductal papillary mucinous neoplasm encountered in our study.

**Characterization of Pancreatic lesions on MDCT in comparison to final diagnosis:**

It was noted that in 88% of cases of solid lesions encountered, MDCT diagnosis was consistent with the final tissue diagnosis. This percentage was 62% for cystic lesions, with 100% solid-cystic lesions being correctly diagnosed on MDCT [Table 1].

CT findings were considered ‘inconclusive’ in the setting of findings such as focal enlargement and fullness of the pancreas and dilatation of the pancreatic duct without evidence of an underlying mass.

**Characterization of Pancreatic lesions on EUS in comparison with the final diagnosis**

When comparing the results of EUS with tissue diagnosis, it was found that the diagnosis of EUS was consistent with gold standard tissue diagnosis in 73% of solid lesions, 36% of cystic lesions with none of the solid-cystic lesions being consistent with tissue diagnosis [Table 2].

EUS findings were considered ‘inconclusive’ in the setting where the lesion was categorized based on imaging morphology as cystic/solid/solid cystic with no definitive diagnosis.

**Comparison of multidetector computed tomography and Endoscopic ultrasound imaging in assigning definitive diagnosis**

The number of cases correctly diagnosed with MDCT when compared against the gold standard histopathological diagnosis were 30, with percentage of 83%, and with EUS

<table>
<thead>
<tr>
<th>Pancreatic lesions</th>
<th>Consistent with final diagnosis</th>
<th>Inconsistent with final diagnosis</th>
<th>Inconclusive</th>
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<tbody>
<tr>
<td>Lesions</td>
<td>Number</td>
<td>Number</td>
<td>Percentage</td>
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<tr>
<td>Solid</td>
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<td>23</td>
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<tr>
<td>Cystic</td>
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<td>5</td>
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</tr>
<tr>
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<td>2</td>
<td>2/2 = 100</td>
</tr>
<tr>
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*2 cases were inconclusive on CT

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<tr>
<td>Lesions</td>
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<td>Percentage</td>
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<tr>
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<td>26</td>
<td>19</td>
<td>19/26 = 73</td>
</tr>
<tr>
<td>Cystic</td>
<td>8</td>
<td>3</td>
<td>3/8 = 38</td>
</tr>
<tr>
<td>Solid-cystic</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>36</td>
<td>22/36</td>
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*10 cases were inconclusive on EUS
Table 3: Characterization of pancreatic lesions on MDCT and EUS: Out of the total 36 cases

<table>
<thead>
<tr>
<th></th>
<th>MDCT</th>
<th>EUS</th>
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<tr>
<td></td>
<td>Number</td>
<td>Percentage</td>
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<td>11</td>
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<tr>
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<td>6</td>
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<tr>
<td>Total</td>
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<td>100</td>
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<tr>
<td>Consistent with final diagnosis</td>
<td>30</td>
<td>83</td>
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The number of lesions categorized as inconclusive were less for MDCT compared to EUS, 2 vs 10 in number [Table 3].

Comparison of characterization of masses by individual and combined use of modalities

The best results for characterizing the pancreatic lesions were obtained with combined use of all modalities, MDCT, Endoscopic ultrasound imaging along with Endoscopic ultrasound guided intervention, with a percentage correct diagnosis of nearly 95% (34/36 cases). The same percentage for MDCT imaging alone was 83%, EUS imaging alone was 61% and MDCT and EUS imaging was 86% [Table 4].

Assessment for operability of Pancreatic adenocarcinoma

The main thrust of our study was detection and characterization of pancreatic lesions, however, a small subset of cases of pancreatic adenocarcinoma was assessed for resectability on both MDCT and endoscopic ultrasound, as both these modalities contribute significantly in determining tumor operability. Cases of pancreatic adenocarcinoma in our study were assessed for their resectability status based on the MD Anderson’s resectability criteria for pancreatic malignancy, with vessel involvement being assessed on axial sections using grading system proposed by Raptopoulos et al. [7] Figure 1 and classified into resectable, borderline resectable, and unresectable according to it. Our study showed that out of the sixteen cases of pancreatic malignancy presenting to us only four cases were found to be resectable at the time of presentation and rest twelve were unresectable, with none in the borderline resectability category [Tables 5 and 6].

Table 5: Pancreatic adenocarcinoma

<table>
<thead>
<tr>
<th>Pancreatic adenocarcinoma</th>
<th>Number</th>
<th>Percentage</th>
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<tbody>
<tr>
<td>Resectable</td>
<td>4</td>
<td>25</td>
</tr>
<tr>
<td>Unresectable</td>
<td>12</td>
<td>75</td>
</tr>
<tr>
<td>Total</td>
<td>16</td>
<td>100</td>
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The above findings concluded for our study that MDCT has higher specificity and PPV in determining resectability of pancreatic adenocarcinomas as compared to EUS, with sensitivity and NPV being similar for both modalities.

The P-value equals 0.66 using Chi-square test, which is not statistically significant.

Discussion

Pancreatic masses represent a myriad of pathologies, ranging from benign to malignant.

Amongst the malignant masses, the early detection of pancreatic ductal adenocarcinoma is of prime importance as early detection and diagnosis can greatly influence its resectability status. The 5-year survival rate in resectable tumors have been found to be as high as 20%–25%, compared to unresectable tumors, very few of whom survive 5 years after diagnosis.[7]

Cystic pancreatic neoplasms are rare entities, however, advancement in cross-sectional imaging techniques like MDCT, have led to an increase in the detection of these lesions. It is important to characterize these lesions as their management guidelines vary greatly. Mucinous cystic lesions are considered premalignant. Hence, surgery is recommended for all mucinous neoplasms and symptomatic cystic lesions.
As the pancreatic masses have a significant overlap in their clinical presentation, the role of imaging assumes a pivotal position in the management of pancreatic masses. There is a need for a systematic approach towards cases suspected with any pancreatic pathology.

Whenever a pancreatic mass is suspected on Pre MDCT and Pre EUS work up of patient, the next steps are, detection of the lesion on MDCT/EUS, characterization of the lesion and lastly to determine the extent of the disease (locoregional and distant spread of disease).

In our study, we found that the detection of a mass lesion on MDCT greatly depended on the size of the lesion. The sensitivity of CT in the detection of pancreatic cancers lies between 75%-100%. For tumors >2 cm the sensitivity may be as high as 98%. EUS has emerged as a useful, albeit invasive, modality in the diagnosis of pancreatic tumors with sensitivities and accuracy approaching 100% and specificity >95% even for lesions <2 cm in size. In the current scenario, a CT scan is still recommended as the first-line imaging modality to detect pancreatic lesions but in event of negative results with CT scan, EUS (when available) is indicated to confirm the absence of small pancreatic lesions. The early detection of a lesion is critical in the cases of pancreatic adenocarcinomas as it has been found that the size of the pancreatic tumor is a major determinant of resectability with up to 83% of tumors ≥20 mm being resectable compared to only 7% of tumors >30 mm in size.

Diagnosis of pancreatic neoplasm is challenging in patients with inconclusive findings on pancreatic multidetector CT. In a recent article ‘Use of EUS-FNA in diagnosing pancreatic neoplasm without a definitive mass on CT’, Wei Wang et al mention that in setting of ‘negative findings’ or ‘non-specific’ CT findings such as solely focal enlargement, fullness of the pancreas and dilation of the pancreatic duct without evidence of an underlying mass, further diagnostic work up is required. The next important step in pre-operative work up is characterization of the mass lesion based on their imaging morphology. With new age multidetector CT scanners which provide very thin slice cuts, high image resolution and fast acquisition, majority of the pancreatic lesions can be accurately characterized on MDCT alone. In our study the diagnosis made on MDCT was consistent with the final pathological diagnosis in 83% of the cases. Opposed to this the EUS diagnosis was consistent with final tissue diagnosis in 61% of the cases. EUS alone (without FNA) was unable to characterize the lesions in a large number of cases of our study and these were categorized as inconclusive.

The necessity of tissue acquisition by FNA during the evaluation of pancreatic masses is dependent on the clinical scenario and institutional practices. The tissue sample can be obtained either via a percutaneous route under CT/USG-guidance or endoscopically via EUS. The percutaneous approach is often risky with chances of bowel and vessel injury.

Endoscopic ultrasound has been shown to be a valuable imaging tool for the detection of pancreatic lesions. Additionally, EUS has a capability to perform fine-needle aspiration and provide concurrent tissue diagnosis at the time of EUS that has made it an essential tool in the diagnostic algorithm of solid pancreatic lesions. In cases of unresectable lesions, tissue diagnosis by FNA before committing patients to chemotherapy and/or radiation therapy is essential. The advantage of EUS-guided FNA over percutaneous FNA lies in the trans-duodenal approach for FNA in endoscopic EUS. The needle tract is along the tissues that would subsequently be resected in pancreateicoduodenectomy, thereby significantly lowering the risk of tumor seeding along the needle tract. The endoscopic US is also an optimal method for lymph node staging.

Owing to the morbidity associated with a surgical exploration, the pre-operative work up in case of pancreatic adenocarcinoma includes classifying the tumor as resectable vs borderline resectable vs unresectable. According to Brennan et al only a small percentage of patients, about 5-30% with pancreatic tumors have resectable tumors at the time of presentation. Our study analyzed a total of 16 cases of pancreatic adenocarcinoma, out of which only a small percentage, 25% were resectable at time of presentation.

The CT report of cases with suspected pancreatic adenocarcinomas conveyed information regarding, presence or absence of a primary tumor in the pancreas; presence or absence of peritoneal and hepatic, nodal metastases; description of the patency of the superior mesenteric vein-portal vein confluence and the relationship of these veins to the tumor; description of the relationship of the tumor to the superior mesenteric artery (SMA), celiac axis, and hepatic artery and any vascular anatomic variants. The major advantage of CT in comparison with EUS is its ability to provide an assessment of the entire abdominal cavity thus providing more information than EUS for distant metastases. Another important dimension to preoperative imaging is assessment of major vascular structures, for both evaluation of resectability and also regarding aberrant anatomy. EUS has proven to be more accurate in detecting portal vein or splenic vein invasion, with accuracy of 78-98%, especially in the area of portal confluence. MDCT is superior in detecting arterial invasion over a broader area, particularly in the region of superior mesenteric artery with a sensitivity rate at 71% versus that of 57% by EUS. In our study the sensitivity, specificity, PPV and NPV of MDCT and EUS were compared with
each other keeping peroperative findings as gold standard in determining 16 cases of pancreatic adenocarcinomas as resectable or unresectable or borderline resectable. We found that MDCT is superior to EUS in assessing tumor resectability preoperatively. EUS being an invasive modality compared to the non-invasive MDCT has certain potential risk of complications associated with it along with few technical disadvantages. EUS carries a 0.1-1% risk of pancreatitis.[6] The most dreaded complication with EUS is perforation which is very rare. As EUS requires the probe to be positioned in the duodenum for optimal evaluation, there can be technical difficulties as well as patient non-compliance for the same.

**MDCT vs EUS**

**Case 1**
The MDCT of a 48-year female who presented with an initial complaint of abdominal pain showed a contour irregularity within the body of the pancreas with no definite mass. The “fullness” was also noted to be isodense with the pancreatic parenchyma on all phases. A subsequent EUS of the patient revealed a well-defined hypoechoic mass showing internal vascularity. The mass was confirmed to be a neuroendocrine tumor on the histopathological diagnosis. EUS has an invaluable role in cases where MDCT shows no definite mass [Figure 2].

**Case 2**
The importance of EUS also lies in its ability to detect small lesions, which could be missed on MDCT. A 40-year-old male presenting with abdominal pain showed an intensely enhancing solitary lesion in the pancreatic neck on the pancreatic parenchymal phase, a diagnosis of pancreatic neuroendocrine tumors (NET) was given. EUS was, however, able to discover few other hypoechoic lesions of size <1 cm in the pancreas. The patient was operated for pancreatic NETs [Figure 3].

**Case 3**
The MDCT of a 43-year-old female demonstrated a hypodense mass in the head of the pancreas, with the

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**Figure 1:** Raptopoulos et al. grading of vessel involvement

**Figure 2 (A-E):** Axial CT pancreatic parenchymal (A), venous phase (B) and thin MIP (C) images showing contour deformity/’fullness’ (arrow) in body of pancreas, isodense on all phases. CT findings were inconclusive. EUS (D) showed a well-defined hypoechoic mass (arrow) in body of pancreas with internal vascularity. EUS guided FNA (E) Photomicrograph (H&E 220X) showed cells with eosinophilic granular cytoplasm and central oval nuclei.
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Figure 3 (A-E): Pancreatic parenchymal phase axial (A) and coronal (B) CT images showing a solitary avidly enhancing lesion in pancreatic neck (arrow) with dilated MPD and atrophic parenchyma. Diagnosis of NET was made. Endoscopic US shows multiple hypoechogenic SOLs in pancreatic neck (C), body (D) and tail (E), few of them sub-centimetric in size. EUS guided FNA showed them to be multiple NETs, confirmed on histology after enucleation

Figure 4 (A-F): Axial CT pancreatic parenchymal (A), image show a hypodense mass lesion (star) in pancreatic head. Axial (B-D) and sagittal (E) arterial MIP images show the fat plane between mass (star) and SMA (arrow) is preserved, rendering the mass resectable. The EUS (F) showing the mass (star) involving the SMA (arrow), suggesting the mass to be unresectable. Histologically mass was proven to be pancreatic adenocarcinoma
involvement of superior mesenteric vein (SMV), the fat plane between the lesion and superior mesenteric artery (SMA) was preserved. The mass was found to be resectable pancreatic adenocarcinoma on MDCT. EUS, however, differed in regard to SMA involvement by the mass lesion. EUS reported the mass to be unresectable owing to the SMA involvement. Peroperative findings showed that the SMA was not involved by the mass and the tumor was resectable [Figure 4].

Case 4
A heterogeneously enhancing mass lesion was seen on MDCT of a 40-year female. The SMA appeared normal at its origin and in its proximal course but was encased and attenuated in its mid-course. On EUS it was difficult to demonstrate such involvement of SMA due to the inability to angulate the transducer along the entire course of SMA [Figure 5].

These cases emphasized the importance of MDCT the in assessment of vascular structures to determine the operability of the mass

Case 5
A well-defined lobulated cystic lesion was seen on MDCT abdomen of a 60-year-old female who presented with pain in abdomen since 1 year. No obvious internal septations/enhancing mural nodule was seen on CT images. Possibilities of oligocystic variant of serous cystadenoma and mucinous cystadenoma were considered on CT. Endoscopic ultrasound following CT showed a well-defined cystic lesion in the pancreatic head in relation to the main portal vein. EUS-guided needle aspiration of the cyst revealed multiple microcysts, characteristic of serous cystadenoma around the primary cystic lesion with the aspiration of serous fluid from the cyst. EUS and EUS-guide cyst aspiration can contribute significantly in determining the internal features of a cyst and allow for fluid analysis aspirated from a cyst to reach the final diagnosis [Figure 6].

The best outcomes were obtained with combined use of MDCT and EUS imaging with addition of EUS guided interventions (EUS-FNA or EUS guided cyst aspiration). Thus, we support the fact that the most optimal use of these
modalities is as complimentary rather than as competing tools in preoperative work up of pancreatic lesions.

We accept that there are several limitations to our study. It was a single center prospective study, endoscopic ultrasound being an invasive modality was done only for cases with significant/equivocal findings on MDCT after obtaining proper consent & pre-anesthesia clearance of participating subjects. All these factors resulted in a small sample with a heterogenous mixture of pathologies. Owing to the limited sample size, sensitivity, specificity, PPV and NPV of MDCT and EUS could not be compared and calculated for characterization of lesions. Also, endoscopic ultrasound as a preoperative imaging modality for pancreatic tumors has been recently established at our center, therefore the percentage correct diagnosis, sensitivity and specificity is lower compared to literature value.

Conclusion

MDCT and Endoscopic US are important pre-operative imaging tools for evaluation of any pancreatic mass. MDCT is superior to EUS for characterization of pancreatic masses, assessing local and distant spread of disease owing to its larger coverage area and to look for vessel involvement by a mass lesion as well as to define vascular anatomy. EUS is superior to CT in cases where CT findings were equivocal/indefinite, lesions were <1 cm in size as a result of better resolution due to close proximity of ultrasound transducer to the pancreas and for lesions requiring concurrent tissue sampling/ fluid aspiration. Combined use of MDCT, EUS imaging, EUS guided interventions provided best results in our study and therefore a combination of these modalities should be used to reach the final diagnosis.

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Conflicts of interest
There are no conflicts of interest.

References


