

Contrast Enhanced Computed Tomography study of Cystic lesions of Pancreas with histopathological correlation.

Dr. Padma Badhe¹, Dr. Prasad Udmale², Dr. Anuja Kapadnis³

¹(Associate professor, Department of radiology, Seth G.S. medical college and KEM hospital, Mumbai, India)

²(Senior resident, Department of radiology, Seth G.S. medical college and KEM hospital, Mumbai, India)

³(Resident, Department of radiology, Seth G.S. medical college and KEM hospital, Mumbai, India)

Corresponding Author: Dr. Padma Badhe

Abstract: Aims and objectives: To identify lesions with cystic appearance in pancreas, to differentiate between pancreatic cystic lesion of neoplastic etiology after exclusion of pseudocyst due to pancreatitis, to differentiate cystic lesion into benign and malignant nature based of CECT morphology, to correlate histopathological reports with CECT morphology.

Materials and methods: It was a non-interventional prospective observational study in the department of radiology of Seth G.S. medical college and KEM hospital Mumbai. Patients meeting the inclusion criteria were studied over a period of 12 months. All patients who underwent contrast enhanced CT scan abdomen as advised by the respective physician/surgeon for further evaluation of already diagnosed pancreatic lesion or suspected cystic pancreatic lesion were included in study.

Results: We included 46 patients after application of inclusion and exclusion criteria and who underwent histopathological diagnostic procedure during follow up. Out of which 26 lesions turned out to be benign, 20 lesions showed malignant histopathology. After obtaining histopathological diagnosis of the lesion we studied CECT morphological criteria such as wall thickness, solid component, number of locules, size of cyst, largest locule size in multilocular cyst, pancreatic duct diameter.

Out of 46 patients, there were 20 patients with unilocular cyst, 12 multilocular cysts, 6 cases of IPMN (intraductal papillary mucinous neoplasm) and 6 cases of solid-cystic pancreatic lesions out of which 4 were adenocarcinoma and 2 were solid pseudopapillary neoplasm (SPEN).

Out of 20 unilocular cysts, 12 were pseudocysts. Hence, 8 patients were considered as true unilocular cysts and were evaluated with CECT morphological criteria such as size of cyst, wall thickness of cyst and solid component within cyst. A size of <3cm showed benign nature and >3cm showed malignant potential of lesion. A wall thickness of <2mm or >2mm predicted benign and malignant nature of lesion respectively. A lesion with solid component <5mm or >5mm predicted benign and malignant nature of lesion respectively.

14 patients of multilocular cystic lesions of pancreas were evaluated with criteria such as number of locules and size of locule. More than 6 locules was suggestive of benign nature and less than 6 locules predicted malignant nature. 6 cases of IPMN were seen and all of them were malignant.

Conclusion: The increasing use of Multidetector Computed Tomography has resulted in a marked increase in the incidental detection of cystic pancreatic lesions with advantages of improved spatial and contrast resolution have resulted in the differentiation of benign from malignant lesions. The purpose of this study was to address the diagnostic guidelines for the patients with cystic pancreatic lesions based on multiple morphological parameters of the cystic masses instead of conclusively interpreting any single criterion.

The most important and significant result derived from the study rests in the use of wall thickness and absence of solid component criteria for the diagnosis of benign lesions. Conclusively stating, wall thickness less than 2mm and absence of solid component are diagnostic of benign cysts with a Positive predictive value of 100% and 95.8% respectively. The observation was made during the study that a unilocular cyst with wall thickness less than 2mm, size less than 3cm and absent solid component is almost always benign. For multilocular cysts which are usually mucinous, serous or IPMNs benign histopathology was predicted with 85.71% accuracy and by the presence of multiple locules (more than 6). The size of largest locules less than 2cm indicated benign nature with a similar accuracy.

Key words: Cystic pancreatic lesions, contrast enhanced CT scan (CECT), histopathological correlation.

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I. Introduction

Imaging is indispensable in the evaluation of patients with cystic pancreatic lesions. Cystic neoplasms of the pancreas once considered extremely rare are being diagnosed in increasing numbers.

Studies using computed tomography (CT) and magnetic resonance imaging (MRI) have shown that the prevalence of pancreatic cysts (in individuals without history of symptoms of pancreatic disease) is about 2.5%, and that this increases with age to the point that 10% of persons 70 years or older have a pancreatic cyst. (1)

This corresponds with a prior autopsy study which found pancreatic cysts in 19% of those between the age of 70 to 79 years and 30% in those 80 to 89 years of age. (2)

The increasing numbers of cases that are surfacing is in part related to increased awareness of their existence, but certainly and mostly due to increased use of cross-sectional imaging, which has led to incidental discovery of many pancreatic cysts. Although the overall risk of malignancy is very low, the presence of these pancreatic cysts is associated with a large degree of anxiety due to concerns about malignancy.

There are two major aspects to the effective diagnosis and management of pancreatic cystic neoplasms. The first is the differentiation between pancreatic cystic neoplasms and pancreatic pseudocysts. Pancreatic pseudocysts can be excluded based on history of pancreatitis, serum pancreatic enzyme levels, obvious acute fat stranding on Contrast Enhanced CT Abdomen, Endoscopic Ultrasound or Percutaneous Aspiration. The other major aspect to the effective diagnosis of pancreatic cystic neoplasms is the understanding of the underlying pathologies of pancreatic cystic neoplasms, their varying degrees of malignant risk, and the role of imaging in sorting these issues out. This will be the focus of this review. Serous cystadenomas are benign tumours and in asymptomatic patients do not require surgical excision, whereas most mucin-producing lesions (e.g. IPMNs, mucinous cystic neoplasms) have malignant potential that warrants surgery. Occasionally, solid tumours of the pancreas such as islet cell tumours and adenocarcinomas have an associated cystic component or may undergo degeneration and can mimic a cystic neoplasm at imaging. Differentiating cystic neoplasms from pancreatic adenocarcinomas is important, since the prognosis for malignant cystic neoplasms is better than that for ductal adenocarcinomas. Hence, accurate preoperative characterization of the lesions aids in prognostication and guides therapeutic decision making. (3)

Transabdominal Ultrasonography is not the best imaging since it is difficult to visualize the complete pancreas due to overlying bowel or fat, and it is rather operator dependent. CT is an immensely useful imaging technique to visualize and differentiate pancreatic cysts based on morphologic features as size, microcystic/macrocytic aspect, presence of septation, nodules, and calcifications.

Bosniak's classification scheme for renal cysts based on morphologic criteria is well established and has proved to be a reasonably accurate method for assessing the risk of malignancy in renal cysts. Using a similar approach, pancreatic cysts can be classified into four subtypes: (a) unilocular cysts, (b) microcystic lesions, (c) macrocystic lesions, and (d) cysts with a solid component.

MDCT has a reported accuracy of 56– 85% for characterization of cystic pancreatic lesions, which is comparable to that of MRI. Increasingly, the morphologic pattern depicted on MDCT images is being used to categorize cystic pancreatic lesions broadly into mucinous and non-mucinous types and then subdivide them on the basis of complex features into aggressive and nonaggressive lesions. The presence of solid nodules, thick septation, and cyst wall thickening on MDCT images favours the diagnosis of an aggressive cystic lesion.

Formation of imaging based criteria for the characterisation of the pancreatic lesions is the need of the hour which would determine nature of lesion nature of lesion and guide management, especially in terms of need for surgery. Early detection of malignant lesion will help to reduce morbidity and mortality.

II. Aims & objectives

To identify lesions with cystic appearance in pancreas, to differentiate between pancreatic cystic lesion of neoplastic etiology after exclusion of pseudocyst due to pancreatitis, to differentiate cystic lesion into benign and malignant nature based of CECT morphology, to obtain histopathological reports if advised by treating physician/surgeon and correlate them with CECT morphology.

III. Materials & methods

It was a non-interventional prospective observational study done in the department of radiology of Seth G.S. medical college and KEM hospital Mumbai. Patients meeting the inclusion criteria were studied over a period of 12 months.

Inclusion criteria:

All the patients who are underwent contrast enhanced CT scan as advised by the respective physician/surgeon for further evaluation of already diagnosed pancreatic lesion or suspected cystic pancreatic lesion and were willing to participate into the study fulfilling the below mentioned criteria-patient having age

more than 18years, either male or female, patients having normal serum creatinine value (0.3-1.4 mg/dl), patients non-allergic to contrast, no prior history of GI surgery.

Exclusion criteria:

Any patient not willing for the study, any patient having increased serum creatinine levels (>1.4 mg/dl), any pregnant female patient, any patient having history of contrast allergy reaction and patients having clinical history, biochemical evidence or documented imaging evidence of pancreatitis were excluded from the study.

Study procedure:

Patients having symptoms related to pancreatic lesion such as epigastric pain, epigastric lump, nausea, and vomiting or weight loss were referred by treating physicians and surgeons. Patients incidentally detected on ultrasonography to have cystic pancreatic lesions or those symptomatic and detected by ultrasonography, who were advised CECT for further evaluation of the pancreatic lesions. Contrast enhanced CT scan was obtained in above patients as per requisition of the physician/surgeon.

After explaining the risk and benefits of examination a proper informed consent was obtained from patient. Consent was also taken regarding inclusion of study images in the study. Essential clinical history was obtained mainly regarding previous episodes of pancreatitis, any documented biochemical or radiological evidence of pancreatitis. Any surgery or intervention related to pancreas or any other intra - abdominal pathology

All studies were performed on Philips 64 slice Brilliance Computed tomography Unit.

CT data was obtained with following parameters:Field of view: 350 mm; Thickness: 2 mm; Pitch: 1.5:1 mm; Filter standard: B: Window width 60; Window length: 360; Matrix: 512 x 512.Age based standard low dose [Kv-120Mas/slice-220] CT protocol was used.

Non-contrast scan was used in standard biphasic pancreatic protocol with parenchymal phase (PP) and portal venous phase (PVP) with scan delay of 40 seconds for first phase and 70 seconds for second phase.

Followed by 1.5 ml/kg non-ionic iodinated contrast material was injected at rate of 4ml/sec using pressure injector.

Parenchymal phase scanning included lower thoracic aorta to abdominal aortic bifurcation. Portal venous phase scan included lung bases to pelvis. All the image data was sent electronically to a workstation [Aquarius Tera recon] for analysis.

Statistical Analysis:

After obtaining histopathological diagnosis of the lesion we studied CECT morphological criteria's as follows which were previously established by various studies (as under **table 1**)

	Benign Morphology	Malignant Morphology
All cystic pancreatic lesions	Wall thickness less than 2mm	Wall thickness more than 2mm
All cystic pancreatic lesions	Absence of solid component	Presence of solid component
Multilocular cysts	More than 6 locules	Less than 6 locules
Unilocular cyst	Less than 30mm diameter	More than 30mm in diameter
Multilocular cyst	Single largest compartment size less than 20mm	Single largest compartment size more than 20mm
Intraductal pancreatic mucinous neoplasm	Pancreatic duct less than 10mm	Pancreatic duct more than 10mm

Statistical test of significance used for categorical data to test whether there is statistically significant correlation between previously established criteria and final histopathological diagnosis was

Chi square test for categorical data

After establishing statistical significance between CECT morphology and histopathological diagnosis we calculated sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy.

Measurements:

Wall thickness was measured from outer wall of cystic lesion wherever it was maximum. Maximum length and breadth of the solid component was measured. In case of unilocular cysts largest dimension of the cyst was used. In case of multilocular cysts number of locules were measured having separate walls and longest dimension of largest locule was measured. In case of intraductal papillary mucinous neoplasm maximum pancreatic duct diameter was measured at the point of maximum dilatation.

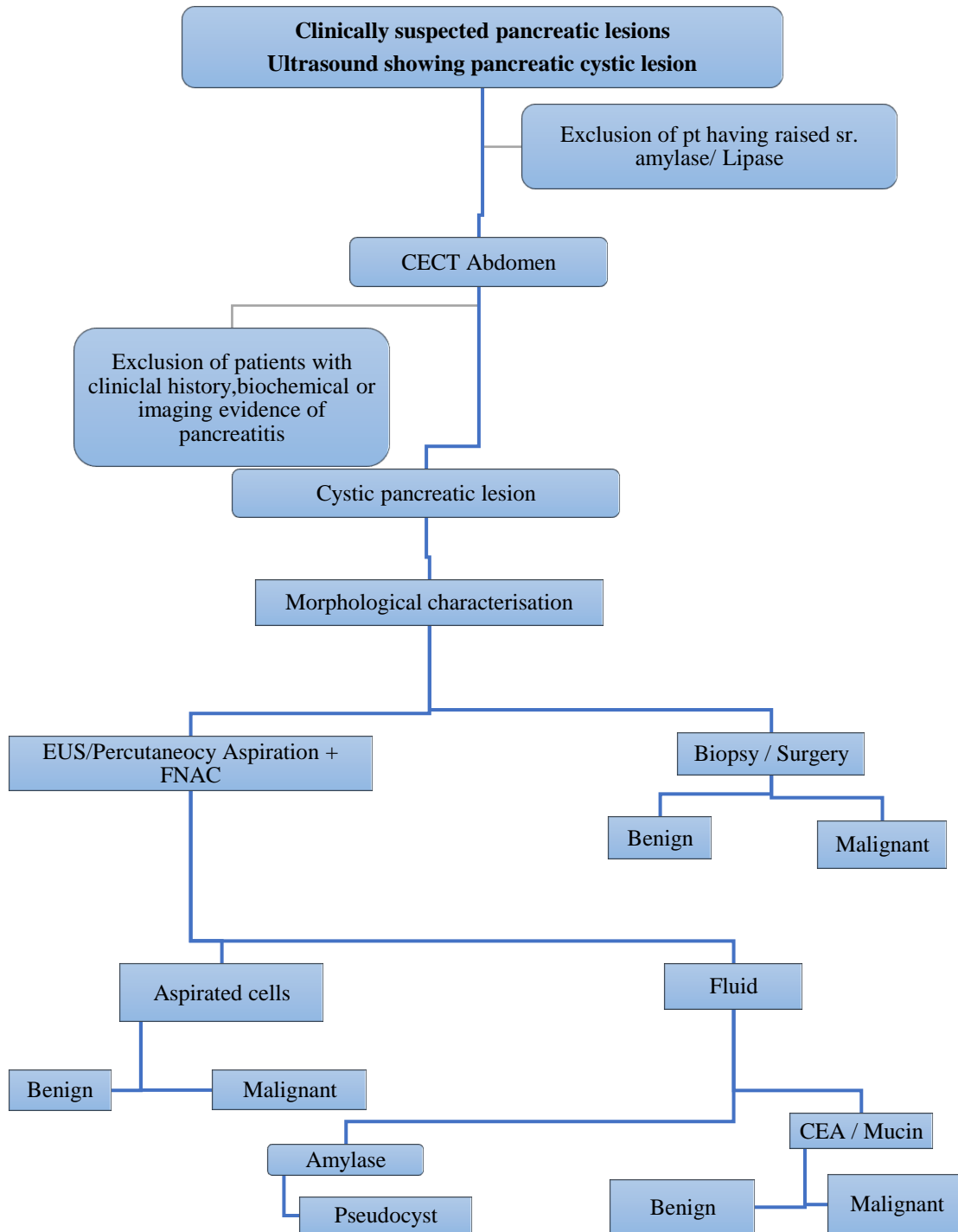


Fig.1: flowchart of clinically suspected case of cystic pancreatic lesion

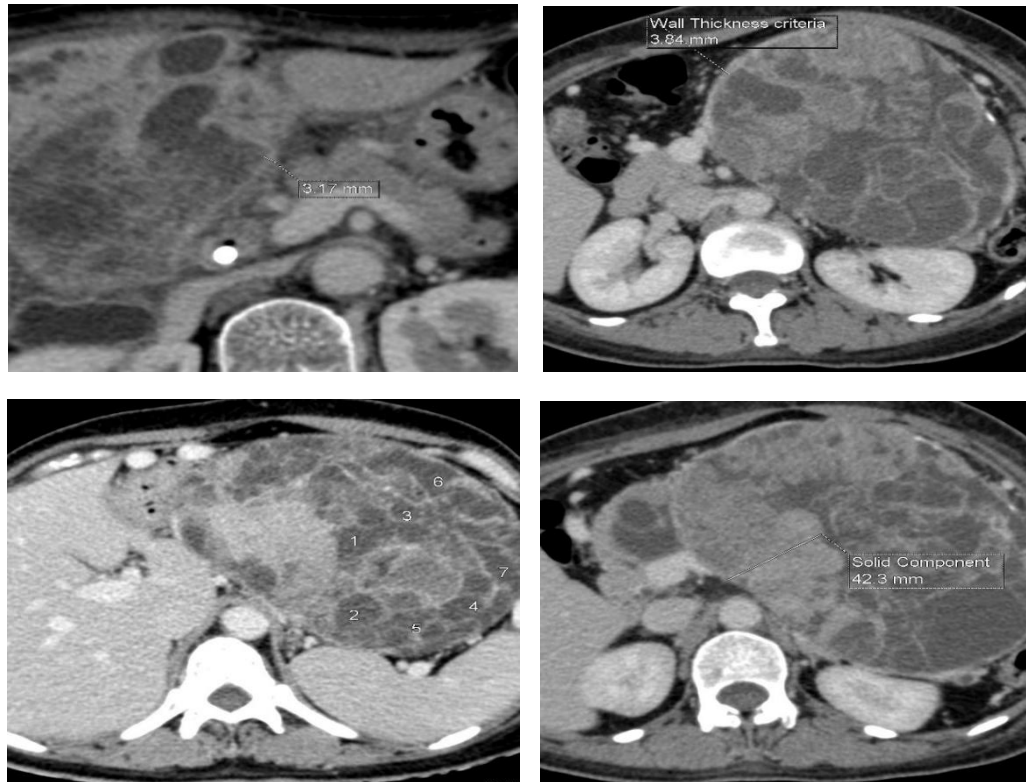


Fig 2: Representative images depicting different measurements for CECT morphological criteria

IV. Results

In tertiary care institute with dedicated super-speciality gastrointestinal surgery, endocrine and endocrine surgical department we encounter significant referral for pancreatic lesions with or with or without endocrine involvement. In our study of differentiating cystic pancreatic lesion based on contrast enhanced computed tomography we excluded patients with documented clinical history, biochemical or imaging evidence of pancreatitis.

After applying exclusion criteria 83 patients were included in the study having cystic pancreatic lesions, 15 patients were lost to follow up, and 22 patients did not undergo surgery, biopsy, aspiration cytology or FNAC and were excluded from study. 46 patients underwent histopathological diagnostic procedure during follow up ,26 lesions turned out to be benign ,12 lesions showed raised amylase levels with normal mucin levels in the aspirated fluid suggesting pseudocyst (attributed to subclinical or undocumented evidence of pancreatitis), 20 lesions showed malignant histopathology.

After comparing their CECT morphology and histopathological diagnosis, following results were obtained.

Lesions were classified in groups as follows

- Unilocular cyst
- Multilocular Cyst
- Solid cystic lesions
- Intraductal papillary mucinous neoplasm
- Microcystic lesions

On CECT, the morphological criteria were used to differentiate between benign and malignant lesions as per table 1. Following results were obtained after demographic analysis and statistical analysis

Demographic Analysis: The mean age of patients in our study was 54.4 years. Mean age of males in the study was 52.7 years and that for female patients was 54.14 years. Proportion of males was significantly higher in the age groups of less than 40 years and more than 70 years. In the age group of 31-70 years, the number of female patients was significantly higher. Young males showed preponderance of the benign lesions, while middle aged females showed preponderance of malignant lesions

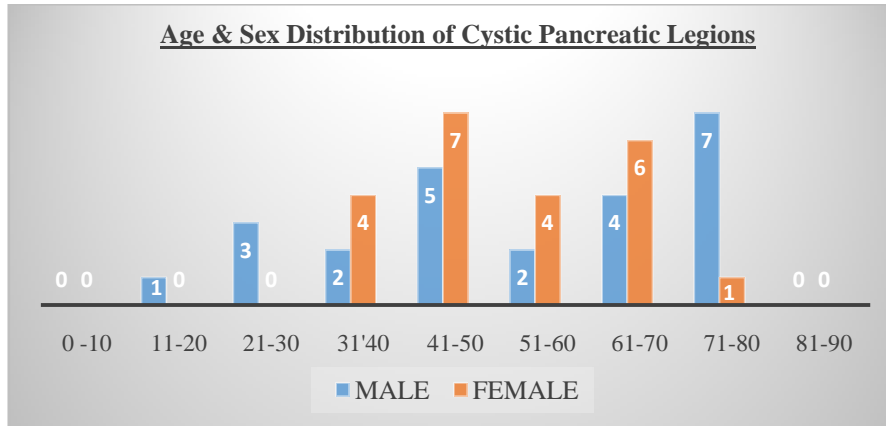


Fig.3: bar diagram showing age & sex distribution of cystic pancreatic legions

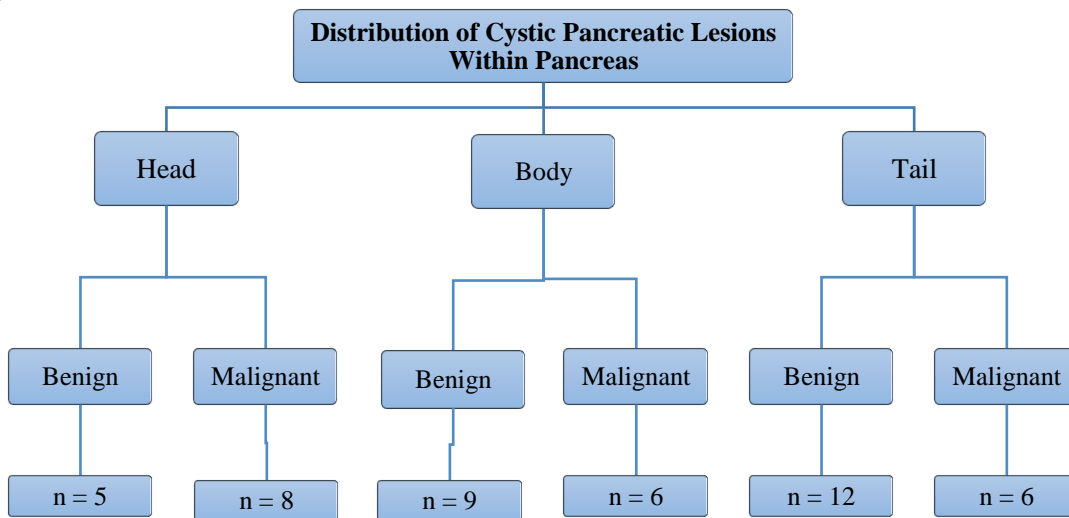


Fig.4: Distribution of cystic pancreatic lesions within pancreas

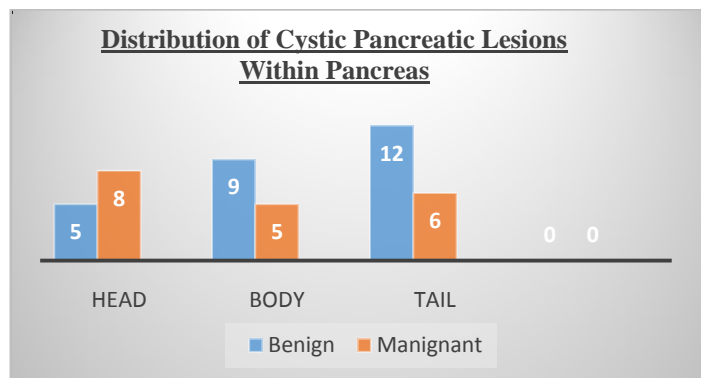


Fig.5: bar diagram showing distribution of cystic pancreatic lesions within pancreas

Histopathological distribution of cystic pancreatic lesions

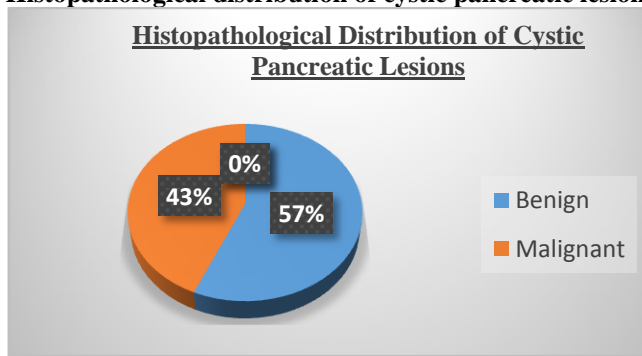


Fig 6: Pie chart showing histopathological distribution of cystic pancreatic lesions

Histopathological Distribution of Cystic Pancreatic Lesions	No. of Patients
Serous Cystadenoma	9
Mucinous Lesion	7
Intraductal papillary mucinous neoplasm (IPMN)	6
Cystic pancreatic neuroendocrine Lesion	1
Pseudocyst (After exclusion of documented pancreatitis due to subclinical / non-documented pancreatitis)	12
Adenocarcinoma with neurosis	4
Solid Pseudopapillary Neoplasm (SPEN)	2
Lymphoepithelial Cyst	1
Malignant Solid Cystic Lesion	4

Table 2: Histopathological Distribution of Cystic Pancreatic Lesions

For all cystic pancreatic lesions, CECT morphological criteria of Wall thickness and solid component were applied.

1) Pancreatic cystic lesions on wall thickness criteria to predict benign and malignant lesion:

(Based on contrast enhanced computed tomography morphology alone)

Out of 46 patients, 44 patients showed cystic morphology like unilocular cyst, multilocular cyst, microcystic lesion, IPMN and solid cystic lesions, excluding two intraductal type of IPMN which had predominantly solid morphology and intraductal nodule. We included remaining 44 patients in whom maximum outer wall thickness was measured, whether there was correlation between benign and malignant morphology with wall thickness less than 2mm predictive of benign nature and more than 2mm predictive of malignant nature was assessed by “Chi square test”. Following table of Observed frequency of the unilocular cystic lesion differentiation based on their maximum wall thickness on CT morphology alone

	Benign on Histopathology	Malignant on histopathology
Wall Thickness <2mm	22	0
Wall Thickness >2mm	4	18

On statistical evaluation with Chi square test to a $p < 0.001$ which was statistically significant.

Sensitivity and specificity, positive predictive value, negative predictive value and accuracy for above proposed criteria (i.e. based on wall thickness) were 84.6%, 100%, 100%, 81.81%, 90.9% respectively.

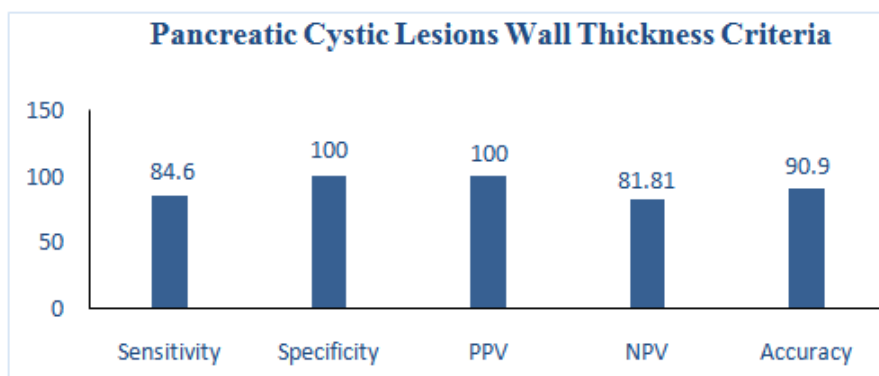


Fig 7: Bar diagram showing pancreatic cystic lesions wall thickness criteria

2) Pancreatic cystic lesions solid component criteria to predict benign and malignant lesion:

In our study, we compared whether presence of solid component i.e. solid enhancing component of at least 5mmX5mm size is associated with increased chances of the malignancy.

Out of 46 patients 26 patients showed benign histopathology, 2 lesions showed intermediate grade on histopathology (included as malignant for statistical evaluation) and 18 showed malignant histopathology. Solid component was present in 22 patients out of which 19 were malignant.

Observed frequency of the pancreatic cystic lesion differentiation based on presence or absence of solid component on CT morphology alone as follows

	Benign	Malignant
Solid component absent	23	1
Solid component present	3	19

On statistical evaluation with Chi square test to a $p < 0.001$ which was statistically significant.

So there exists statistically significant correlation between wall thickness and benign or malignant behaviour of cystic pancreatic lesions

Sensitivity and specificity, positive productive value, negative predictive value and accuracy for above proposed criteria (i.e. based on presence or absence of solid component on CT) were 88.4%,95%,95.83%,86.36%,91.30% respectively.

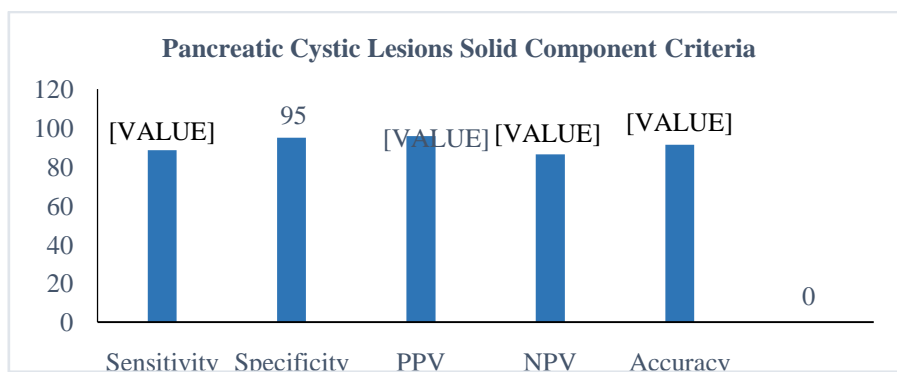


Fig. 8: Column chart showing pancreatic cystic lesions solid component criteria

Unilocular Cysts:

The CECT morphological criteria used were size criteria, wall thickness criteria, and solid component criteria.

1) **Size criteria** for unilocular cystic pancreatic lesions:

In this study, out of 46 patients, 20 patients were found to have unilocular cysts out of which 12 patients were to have pseudocysts on cytological and aspirational fluid analysis. 8 patients were evaluated for size criteria as follows:

	Benign on Histopathology	Malignant on Histopathology
<3cm	2	0
>3cm	1	5

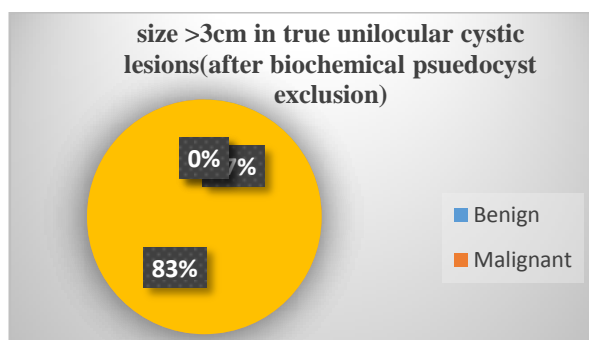


Fig.9: Pie chart showing >3cm in size unilocular cystic lesion distribution.

On statistical evaluation with Chi square test a P value=0.04 was obtained which is statistically significant. Hence in case of true pancreatic unilocular lesions there was significant correlation of size>3cm to predict malignant potential of lesion. Sensitivity and specificity, positive productive value, negative predictive

value and accuracy for above proposed criteria (i.e. based on size of unilocular cyst and histological findings) were 66.6%, 100%, 100%, 83.33%, 87.5% respectively.

There is statistically significant correlation between size < 3cm and benign morphology of the lesion:

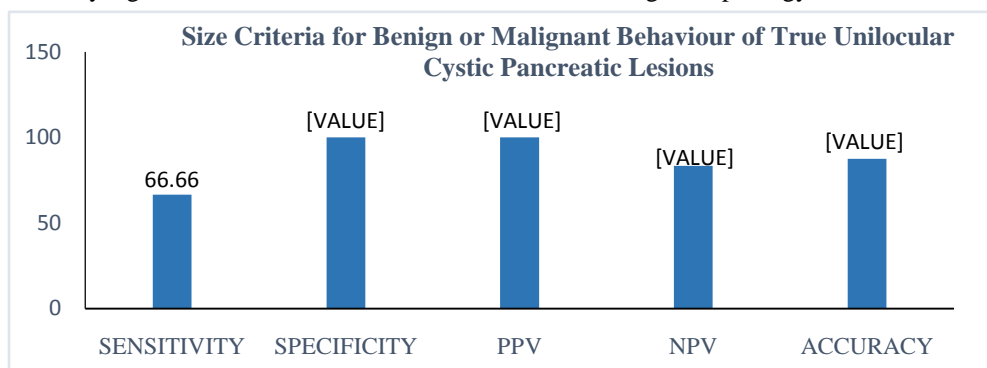


Fig 10: bar diagram showing size criteria for benign or malignant behaviour of true unilocular cystic pancreatic lesions

2) Wall thickness criteria for unilocular cystic lesion:

Observed frequency of the unilocular cystic lesion differentiated based on their maximum wall thickness on CT morphology alone

	Benign	Malignant
Wall Thickness < 2mm	14	0
Wall Thickness > 2mm	1	5

On statistical evaluation with Chi square test a p value of < 0.001 was obtained which is statistically significant.

So there exists statistically significant correlation between wall thickness less than 2mm and benign lesions.

Sensitivity and specificity, positive productive value, negative predictive value and accuracy for above proposed criteria (i.e. based on unilocular cystic lesion wall thickness criteria) were 93.3%, 100%, 100%, 83.33%, 95% respectively.

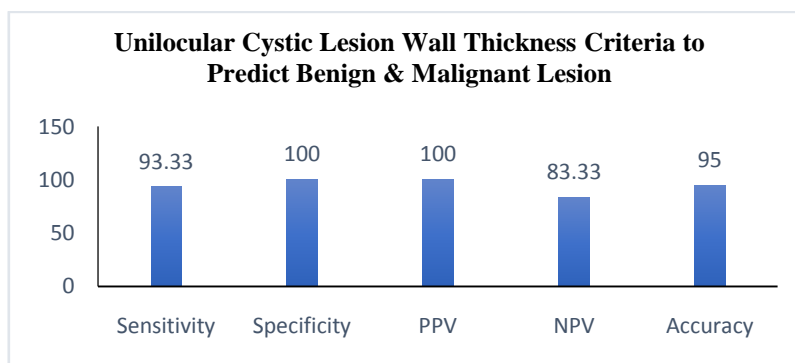


Fig.11: bar diagram showing unilocular cystic lesion wall thickness criteria to predict benign & malignant lesion

3) Solid Component Criteria in Unilocular Cystic Lesion:

Solid component is defined as more than 5x5mm sized component in both width & breadth.

Observed frequency of the unilocular cystic lesion based on CT morphology alone as follows

	Benign	Malignant
Solid Component Absent	14	1
Solid Component Present	1	4

On statistical evaluation with Chi square test a p value of < 0.001 was obtained which is statistically significant. Sensitivity and specificity, positive productive value, negative predictive value and accuracy for above proposed criteria (i.e. based on unilocular cystic lesion solid component criteria) were 93.3%, 80%, 93.33%, 80%, 90% respectively.

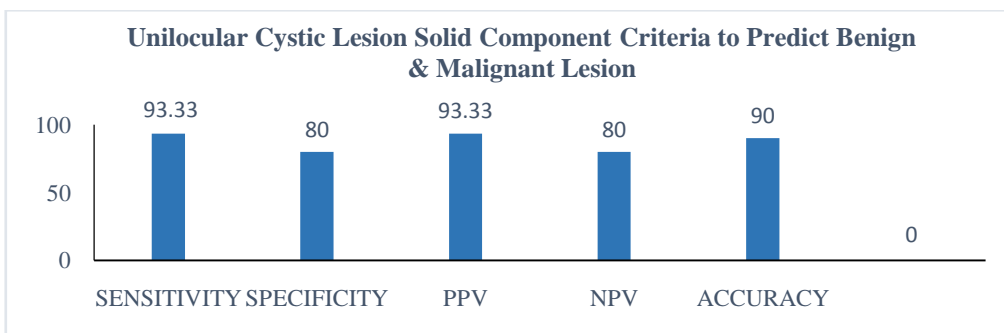


Fig.12: Column chart showing unilocular cystic lesion wall thickness criteria to predict benign & malignant lesion

Histopathological Distribution of Cystic Lesion in Unilocular Cyst:

Benign Mucinous Cystadenoma	2
Malignant Mucinous Cystadenocarcinoma	2
Intraductal Papillary Mucinous Neoplasm (Malignant)	2
Lymphoepithelial Cyst (Benign)	1
Cystic Pancreatic Neuroendocrine Neoplasm	1

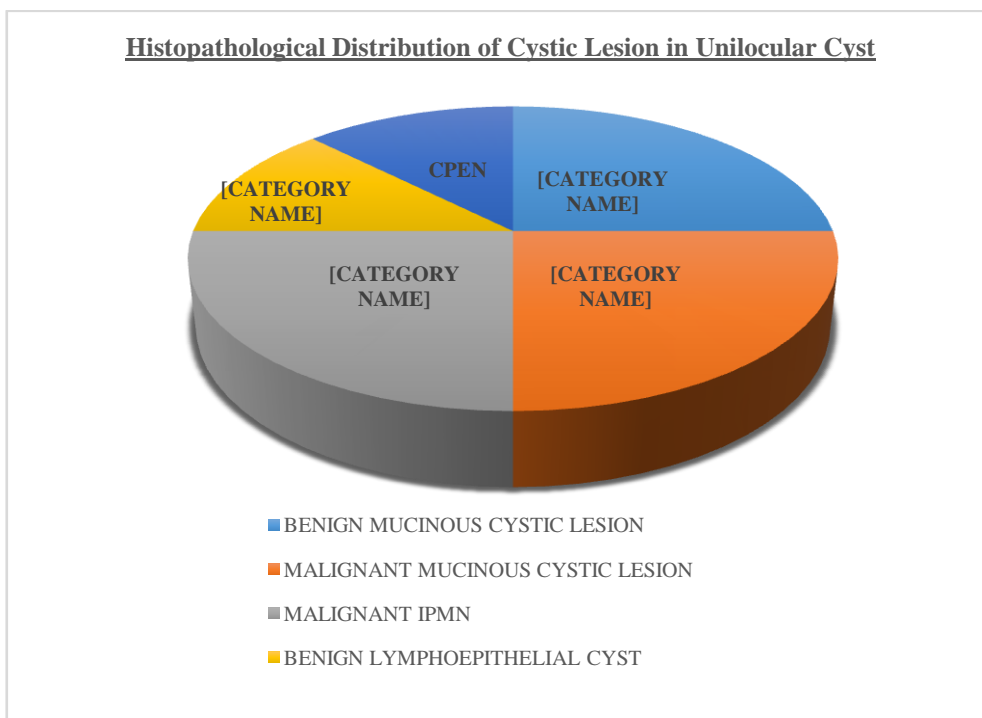


Fig.13: Pie chart showing histopathological distribution of cystic lesion in unilocular cyst

Unilocular pancreatic cystic lesions CECT morphology criteria to differentiate benign and malignant lesion on histopathological diagnosis:

	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Diagnostic accuracy
Size criteria for true cystic pancreatic lesion (after exclusion of pseudocyst by aspiration fluid analysis)	66.6	100	100	83.33	87.5
Wall thickness criteria based on CECT morphology alone	83.3	100	100	93.3	95
Solid component criteria based on CECT morphology alone	93.33	80	93.33	80	90

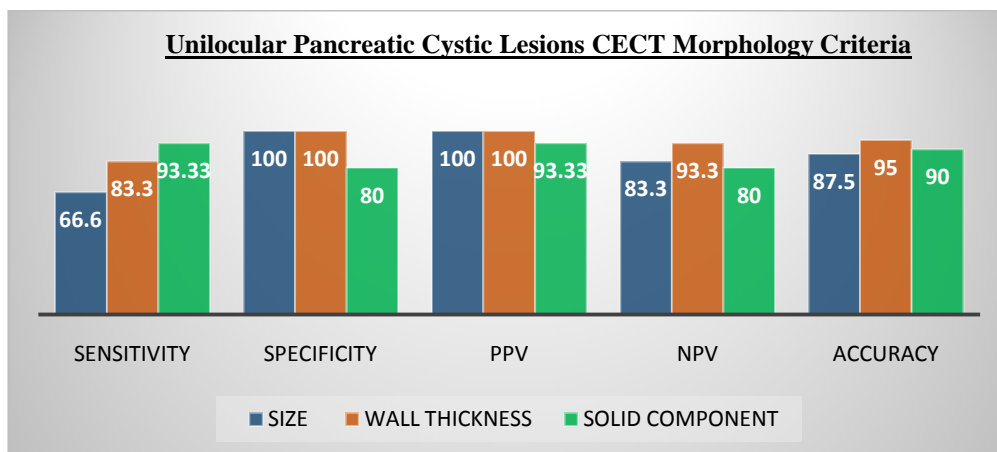


Fig. 14: Column chart showing unilocular pancreatic cystic lesions CECT morphology criteria

Multilocular cystic pancreatic lesions:

CECT morphology criteria used:

- Number of locules(Less than 6 locules and more than 6 locules)
- Size of largest locule(Size of largest locule <20mm or >20mm)

Cystic pancreatic lesions showing multilocular morphology on contrast enhanced computed tomography (14 patients showed more than one locule) which were:

- Serous cystadenoma
- Mucinous cystadenoma
- Mucinous cystadenocarcinoma
- IPMN side branch variant

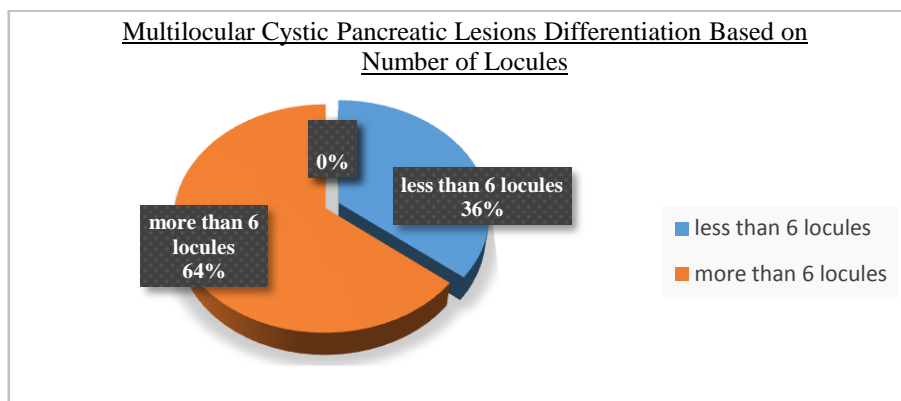


Fig.15: Column chart showing multilocular cystic pancreatic lesions differentiation based on number of locules

1) **Number of locules criteria** in multilocular cystic pancreatic lesions:

Observed frequency of the multilocular cystic lesion differentiated based on their number of locules on CECT morphology alone as follows

	Benign	Malignant
More than 6 locules	8	1
Less than 6 locules	1	4

On statistical evaluation with Chi square test a p value=0.009 was obtained which is statistically significant. So there exists statistically significant correlation between number of locules and benign and malignant behaviour in case of multilocular cystic pancreatic lesions. Sensitivity and specificity, positive productive value, negative predictive value and accuracy for above proposed criteria (i.e. based on number of locules observed on CECT in multilocular lesions) were 88.8%, 80%, 88.8%, 80% , 85.71% respectively.

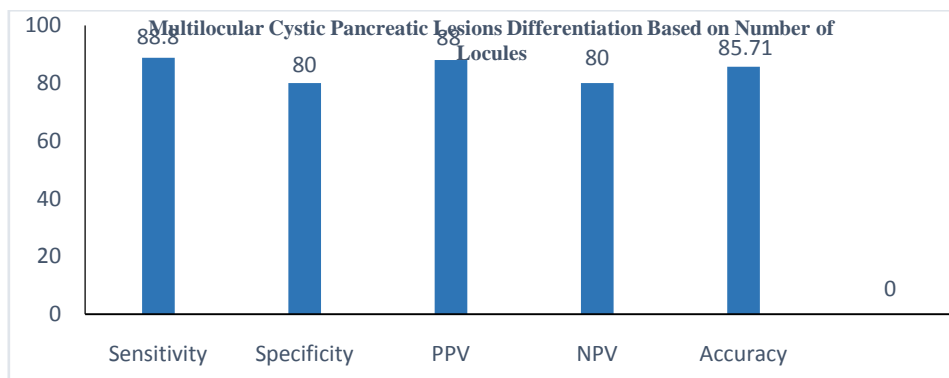


Fig.16: Column chart showing multilocular cystic pancreatic lesions differentiation based on number of locules.

2) **Size of locules criteria** in Multilocular cystic pancreatic lesions:

Observed frequency of the multilocular cystic lesion differentiated based on their number of locules on CECT morphology alone as follows

	Benign on histopathology	Malignant
Locule less than 20mm	7	0
Locule more than 20 mm	2	5

On statistical evaluation with Chi square test a p value=0.005 was obtained which is statistically significant. So there exists statistically significant correlation between size of locules and benign and malignant behaviour of the lesion in case of multilocular cystic pancreatic lesions. Sensitivity and specificity, positive productive value, negative predictive value and accuracy for above proposed criteria (i.e. based on size of locules observed on CECT in multilocular lesions) were 63%, 100%, 100%, 71.4%, 85.71% respectively.

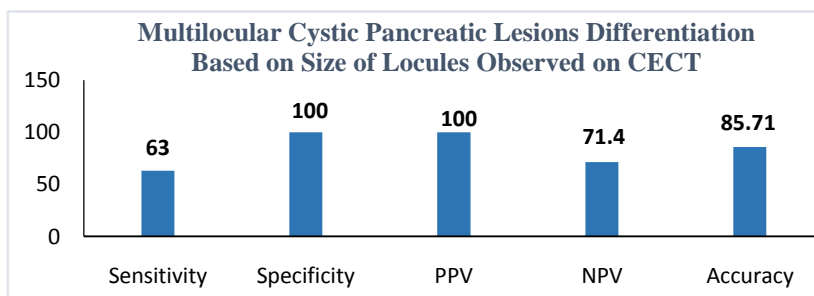


Fig 17:bar diagram showing multilocular cystic pancreatic lesions differentiation based on size

Specific criteria to predict malignant potential of IPMN

We have encountered 6 cases of Intraductal papillary mucinous neoplasm, all of them turned out to be malignant based on EUS biopsy or surgical histopathology. All 6 cases showed pancreatic duct dilated more than 10mm. Two of them showed solid nodule within pancreatic duct without any cystic component. 4 showed cystic morphology with 1 unilocular and 3 multilocular lesions. All 3 showed some solid component and communication with pancreatic duct was observed in 2 of them using CECT.

As we have not encountered any benign IPMN in our study duration, comparison between benign and malignant CECT morphological characteristics is not possible.

Of 6 patients, 5 were elderly males, 1 female and our study showed significant male predominance.

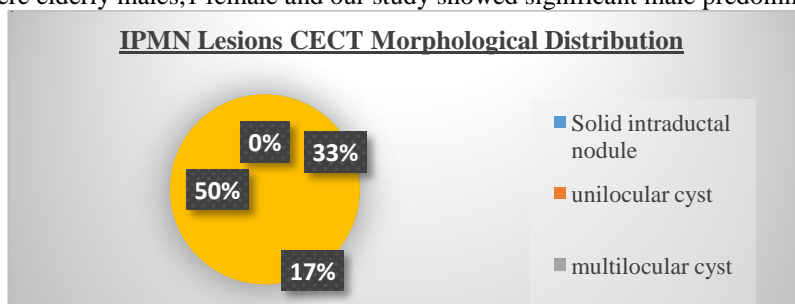


Fig.19: Pie chart showing IPMN lesions CECT morphological distribution

Sex distribution in IPMN encountered during our study

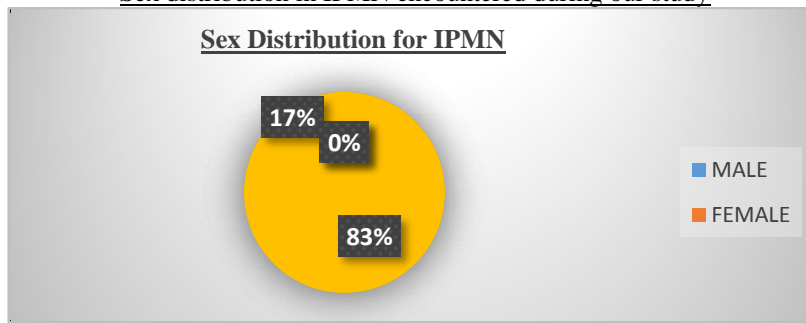


Fig.20: Pie chart showing sex distribution for IPMN

Pancreatic solid cystic pancreatic lesions:

In our study, 6 solid-cystic pancreatic lesions were seen, 4 of them showed adenocarcinoma with necrosis on histopathology, 2 of them were diagnosed as SPEN (Solid pseudopapillary neoplasm) showing large cystic components, diagnosis of SPEN (Solid pseudopapillary neoplasm) consistent with benign histopathology. 4 patients showed multilocular cysts, however due to significant solid component they are classified as solid cystic lesions. Two of them underwent percutaneous biopsy and showed high grade malignancy however definite diagnosis was not reached. Other two showed adjacent organ invasion, however histopathological diagnosis was not obtained.

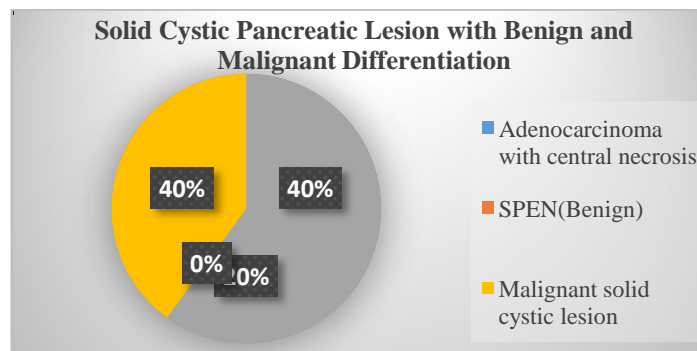


Fig.21: Pie chart showing solid cystic pancreatic lesion with benign and malignant Differentiation

Presence of solid component correlates with malignant nature of the lesion as shown above, 8 out of 10 lesions showing significant solid component turned out to be malignant. Two solid cystic lesions with histopathological diagnosis of solid pseudopapillary neoplasm of pancreas both of which were in tail of pancreas in young females.

V. Discussion

In this study in tertiary care hospital setting with dedicated gastrointestinal and endocrine and pancreatic super-speciality surgical units we experience significant patient load of the pancreatic lesions referred to us. Reasons for such high number of malignant lesions encountered in this study were likely to be due to patients referred requiring expert treatment to our tertiary care centre because of malignant nature of lesion and out of 85 lesions many patients who clearly showed benign morphology on CECT did not undergo any histopathological diagnostic procedure and we did not consider them for final evaluation

We have analysed our observation and tabulated the data in section observation and results under headings of

- Age and sex distribution
- Distribution of lesions within pancreas
- Histopathological diagnostic distribution of cystic pancreatic lesions
- CECT morphology wall thickness and solid component criteria
- For unilocular cysts size of lesion ,wall thickness and solid component criteria
- For multilocular cystic pancreatic lesions number of locules and size of largest locule criteria
- Pancreatic duct size criteria for intraductal papillary mucinous neoplasm
- Solid cystic pancreatic lesions

Age and sex distribution of the cystic pancreatic lesions. Out of 46 patients in our study 26 were male and 20 were female however this male preponderance could not be extrapolated as 10 male patients had pancreatic

pseudocyst (Secondary to subclinical or undocumented event of pancreatitis). If we exclude these 10 patients there is definite female preponderance in cystic pancreatic lesions with 56 % females. Compared to previous demographical data there is also female preponderance with 63% of the patients likely to be male in study by K. Spinelli and colleagues in study of 168 patients(5)

The mean age of patients with cystic pancreatic lesions in our study was 54.4years

Elderly female patients typically showed a benign serous cystadenoma on histopathology, middle aged females and elderly males showed significant number of malignant lesions. Middle aged female typically had mucinous pancreatic neoplasms (Cystadenoma or cystadenocarcinoma). Intra-ductal papillary mucinous neoplasms (IPMN) were typically seen in elderly males, 5 out of 6 patients.

Young males typically showed benign unilocular cysts, even after exclusion of known cases of pancreatitis on basis of history or biochemical and radiological evidence 12 unilocular cysts turned out to be pseudocysts (because of high amylase level of aspirated fluid on follow up) highlighting importance of considering pseudocyst as differential diagnosis in young males which could be attributed to mild, subclinical undocumented episode of pancreatitis. Our findings were consistent with demographic findings seen in study by Garg et al which showed elderly female predominance in serous cystadenoma and elderly male predominance in the IPMN(6)

Distribution of lesions within pancreas:

Maximum number of malignant cystic lesions were encountered in the head and uncinate region of pancreas 8 malignant lesions. Tail showed maximum number of benign lesions (n=12). Distribution within pancreas generally could not predict benign or malignant nature of lesions in our study with nearly equal distribution of both malignant and benign lesions in all regions of the pancreas.

CECT morphology distribution of cystic pancreatic lesions:

There were 20 unilocular lesions 15 out of 20 were benign lesions, out of 5 malignant lesions 4 were mucinous adenocarcinoma and 1 was side branch IPMN

Out of 14 multilocular lesions encountered in our study 9 showed benign histopathology all of them were serous cystadenoma, 3 lesion showed microcystic morphology of serous cystadenoma with central scarring and calcification. 10 lesions showed solid cystic lesions with predominant solid area and central necrosis mimicking cystic appearance. 8 out of 10 turned out malignant 4 showed definite histopathological diagnosis of adenocarcinoma with necrosis. 2 showed solid pseudopapillary neoplasm of pancreas both in the tail of pancreas of young women showing benign morphology. For remaining 4 lesions biopsy revealed highly aggressive undifferentiated neoplasm with probable consideration of adenocarcinoma or undifferentiated mucinous adenocarcinoma.

CECT morphology criteria to differentiate between benign and malignant nature of the lesion.:

MDCT has a reported accuracy of 56–85% for characterization of cystic pancreatic lesions, which is comparable to that of MRI(7). Visser et al found that Multi detector contrast enhanced CT had an accuracy of 76–82% in definitely establishing the diagnosis of malignancy in their study 58 histopathologically proven cystic pancreatic masses. Another study of 100 cystic pancreatic lesions, Chaudhari and colleagues (8) reported an accuracy of 71–79% for MDCT for discriminating premalignant or malignant lesions from benign lesions. Lee et al.(7) reported a comparable accuracy (63.9–73.5%) of MDCT for differentiating benign from malignant cystic pancreatic lesions.

However, most of the times sub classification of cystic lesions into histopathologic types is often difficult because of overlapping imaging features. Increasingly, the morphologic pattern depicted on MDCT images is being used to categorize cystic pancreatic lesions broadly into mucinous and non-mucinous types and then subdivide them on the basis of complex features into aggressive and nonaggressive lesions. In a study of 114 patients with 130 cystic pancreatic lesions, Sahani and colleagues (9) stratified the lesions into mucinous and non-mucinous subtypes with an accuracy of 82–85% and reported an accuracy of 85–86% for recognizing aggressive biologic features

Comparable diagnostic accuracy has been reported for small cystic pancreatic lesions less than 3 cm. Sainani et al.(10) found that MDCT had 71–84.2% accuracy for differentiating mucinous and non-mucinous subtypes of small cystic pancreatic lesions.

In the study we have tried to attempt benign and malignant nature prediction on CECT of pancreas alone, and tried to set definite criteria to differentiate between two as mentioned in table 1.

The presence of solid nodules, thick septation, and cyst wall thickening on MDCT images favour's the diagnosis of an aggressive cystic lesion (10)(4)

Sahani and colleagues (4) reported that pancreatic protocol MDCT had sensitivities of 93.6%, 71.4%, and 86.4% for detecting morphologic features such as septa, mural nodules, and main pancreatic duct communication.

Wall thickness criteria to differentiate benign and malignant lesions:

In previous studies Kim et al used >1mm as criteria to predict malignancy we however followed Morangoni A and colleagues and used thickness more than 2 mm as predictor of malignancy in all cystic pancreatic lesions.

After confirming statistical significance sensitivity specificity, PPV, NPV and accuracy obtained in the study and were 93.3%, 100%, 100%, 83.33%, 87.5% respectively.

Kim et al. (11) found that shape and wall thickness (> 1 mm) were two independent predictors of malignancy of a cystic pancreatic lesion. However, they do not give any specific values for characterisation except they mentioned that septa or wall thickness more than 1mm has specificity of 90% for predicting the diagnosis of malignant cystic lesion. Morgagni and et al encountered all Mucinous tumours and IPMN to have wall thickness of more than 2mm (100% of the lesions) (12)

Solid component criteria for all cystic pancreatic lesions to differentiate between benign and malignant nature

Tomimaru et al. (13) reported that the presence or absence of mural nodules on CT images had a sensitivity, specificity, and accuracy of 93%, 80%, and 86% in the diagnosis of malignant cystic pancreatic neoplasm.

The study showed sensitivity, PPV and accuracy for solid component criteria for all cystic pancreatic lesions as 93.33%, 93.33%, 90% respectively.

Unilocular cystic pancreatic lesions:

There were 20 unilocular lesions 15 out of 20 were benign lesions, out of 5 malignant lesions 4 were mucinous adenocarcinoma and 1 was side branch IPMN.

The study showed high PPV and specificity i.e. 100% for size criteria and wall thickness criteria to differentiate between benign and malignant nature. The study also showed high sensitivity and PPV (i.e. 93.33%) for solid component criteria.

Positive predictive value for benign unilocular cyst less than 3 cm in our study was 100% which was comparable with value of 97% found in study by Dushyant V Sahani and et al(14)

Hence, highlighting the fact that unilocular cysts less than 3 cm with a thin wall (less than 2mm) in the absence of any solid component are almost always benign in nature.

While evaluating unilocular cystic pancreatic lesions we have encountered 12 patients without documented clinical biochemical or imaging evidence of the acute or chronic pancreatitis and showed increased amylase and low mucin content of aspirated fluid highlighting two points

- Mild/subclinical pancreatitis can lead to pseudocyst formation and such episodes of pancreatitis may undergo unnoticed
- For unilocular cyst in pancreas aspiration of fluid and evaluation of amylase level and mucin remains only definitive method to exclude pseudocyst

Multilocular cystic lesions CECT morphological evaluation to differentiate benign and malignant nature:

Tanaka M and colleagues(15) has published guidelines for follow up multilocular cystic pancreatic lesions in which it has been recommended that multilocular lesions having >6 locules and <20mm sized largest locules are more likely to be benign and should be followed up on imaging.

Campbell F and colleagues in histopathological review of exocrine pancreatic lesions encountered more than 90% of MCNs have < 6 locules which are usually > 2 cm in size. The internal contents of the cyst may be hemorrhagic, necrotic or consist of mucinous material. MCNs typically have internal nodules, which histological may harbor high-grade dysplasia or invasive carcinoma

In these study, only one patient with mucinous cystic neoplasm had more than 6 locules and still had malignant histopathology.

In this study we found high sensitivity and PPV i.e. 88.8% for number of locules criteria to differentiate benign and malignant nature. Also, high specificity and PPV for largest size of locule criteria in the study.

All the malignant lesions in our study showed largest locule larger than 20mm, however sensitivity of this criteria was only 63% to predict benign nature of the lesion.

Hence, in the present study, it has been conclusively established that using the above parameters on Computed Tomography, pancreatic lesions can be classified as benign and malignant with considerable certainty. Especially important of these morphological criteria are wall thickness <2mm for benign lesions, which has a positive predictive value of 100% and >2mm is 100% specific for malignant lesions; and absence of solid component being positively predictive up to 95.8% for benign cystic masses and the presence being 95% specific for malignancy. For true unilocular cysts smaller than 3cm size, with wall thickness less than 2mm; and absence of solid masses the pancreatic cystic lesions are more likely to be benign and can be followed up on imaging (Positive predictive value 100%, 100% and 93% respectively). This study has been an attempt to formulate guidelines for treatment, particularly the decision of surgical management and to reduce unnecessary surgical morbidity associated with resection of benign masses and will help go a long way in determining patient diagnosis, management and prognosis.

Another important point highlighted in study that in case of unilocular cysts with thin wall, pseudocyst due to subclinical, undocumented episode of pancreatitis warrants consideration and cannot be excluded on basis of clinical history and imaging alone and needs to be excluded by amylase evaluation of aspirated fluid.

VI. Summary and Conclusion

The increasing use of Multidetector Computed Tomography has resulted in a marked increase in the incidental detection of cystic pancreatic lesions and the same advantages of improved spatial and contrast resolution have extrapolated the use of CT in the differentiation of benign from malignant lesions. The purpose of this study was to address the diagnostic guidelines for the patients with cystic pancreatic lesions based on multiple morphological parameters of the cystic masses instead of conclusively interpreting any single criterion.

The most important and significant result derived from the study rests in the use of wall thickness and absence of solid component criteria for the diagnosis of benign lesions. Conclusively stating, wall thickness less than 2mm and absence of solid component are diagnostic of benign cysts with a Positive predictive value of 100% and 95.8% respectively.

For unilocular cysts, size criterion, i.e. less than 3 cm in longest dimension, used additionally with the above two was found to be significantly associated with benign nature ($p=0.04$), however only after pancreatic pseudocysts had been ruled out on aspiration biochemistry.

Hence, the observation made during the study that a unilocular cyst with wall thickness less than 2mm, size less than 3cm and absent solid component is almost always benign. The accuracy of the above three for diagnosis of benign nature being 95%, 87.5%, 90% respectively can be cumulatively improved by using all the three tests simultaneously.

For multilocular cysts which are usually mucinous, serous or IPMNs; benign histopathology was predicted with 85.71% accuracy by the presence of multiple locules (more than 6). The size of largest locules less than 2cm indicated benign nature with a similar accuracy.

The most conspicuous confounding factor of pancreatic pseudocysts, which are common in young adults, of those that are subclinical were excluded by aspiration of the cyst and enzyme level estimation. Therefore, results derived after excluding these cases conformed to the size guidelines for predicting benign unilocular masses.

In cases studied of Intraductal Papillary mucinous neoplasm, measure of pancreatic duct dilatation, if more than 10mm, specifically associated with malignant IPMNs was confirmed as all the six cases studied showing duct dilatation were proven malignant on histopathology.

This study has been an attempt to study the association of pancreatic cystic morphology with the neoplastic pathology with the assistance of above cutoffs. However, more largescale studies would be necessary for review purpose and for formulation of guidelines and diagnostic scores or protocol on a universal level similar to the lines of IOTA guidelines for differentiating ovarian malignancy from benign or the Bosniak's classification of renal cysts.

Thus, the classification of cystic pancreatic lesions on the basis of their imaging morphologic features can simplify the differential diagnosis and be of value in management.



Fig.22: Multilocular cystic lesion pancreatic head

Axial CECT images showing multilocular cystic lesion with thick wall and solid component with few large locules suggestive malignant nature
Histopathological diagnosis: High grade mucinous neoplasm of pancreas

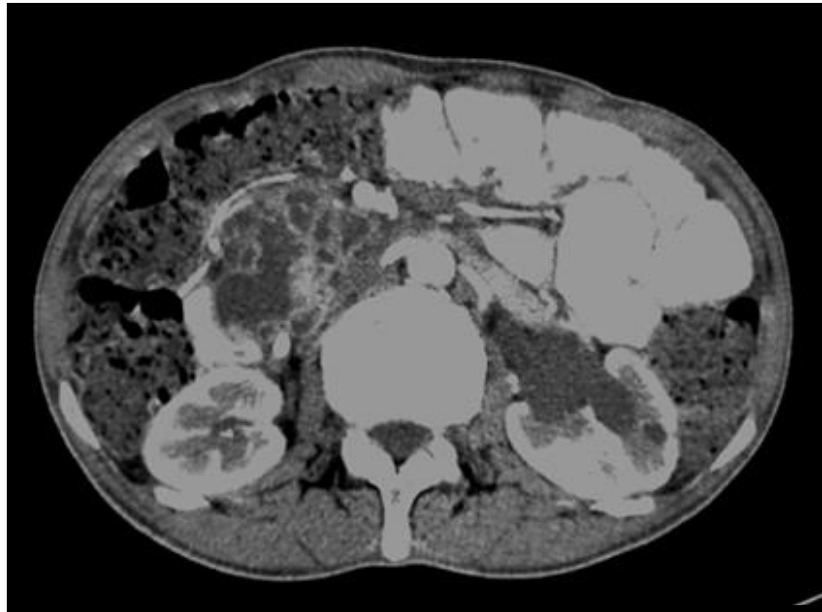


Fig.23: Multilocular cystic lesion pancreatic head: Axial CECT images showing multilocular cystic lesion with thick wall and solid component with few large locules suggestive malignant nature.
Histopathological diagnosis: High grade mucinous neoplasm of pancreas.

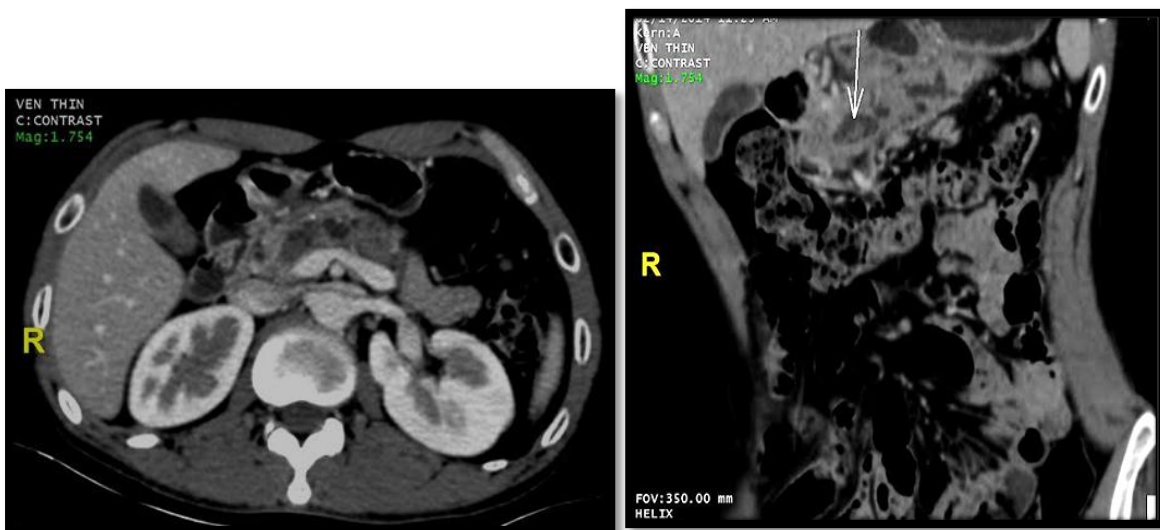


Fig.24: Intraductal Papillary Mucinous Neoplasm: Axial CECT images showing solid papillary enhancing mass within main pancreatic duct with both proximal and distal dilatation of the pancreatic duct.
Histopathological diagnosis: High grade intraductal papillary Mucinous Neoplasm.

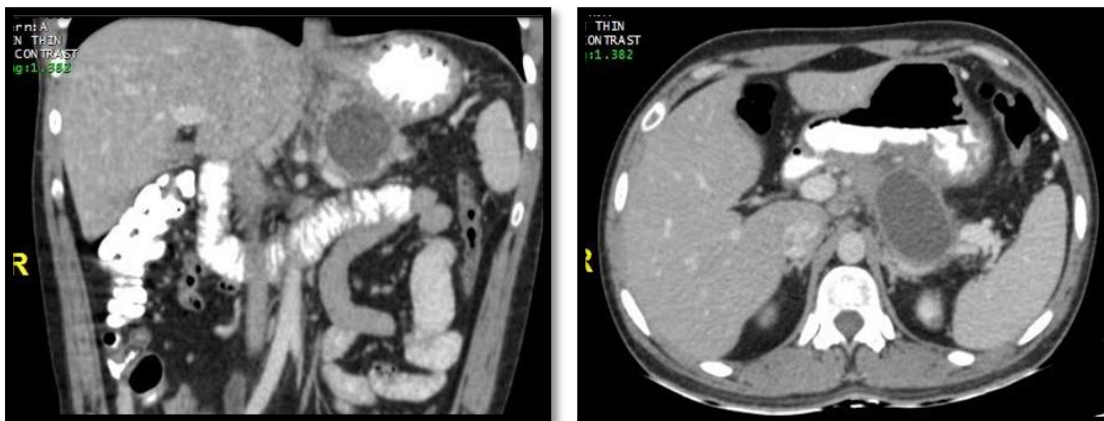


Fig.25: Pseudocyst of pancreas: Coronal Axial CECT images showing thin walled unilocular cyst without any solid component suggestive of benign etiology.

This lesion on aspiration of fluid showed raised fluid amylase, patient did not have documented pancreatitis. Also, not absence of peripancreatic fat.

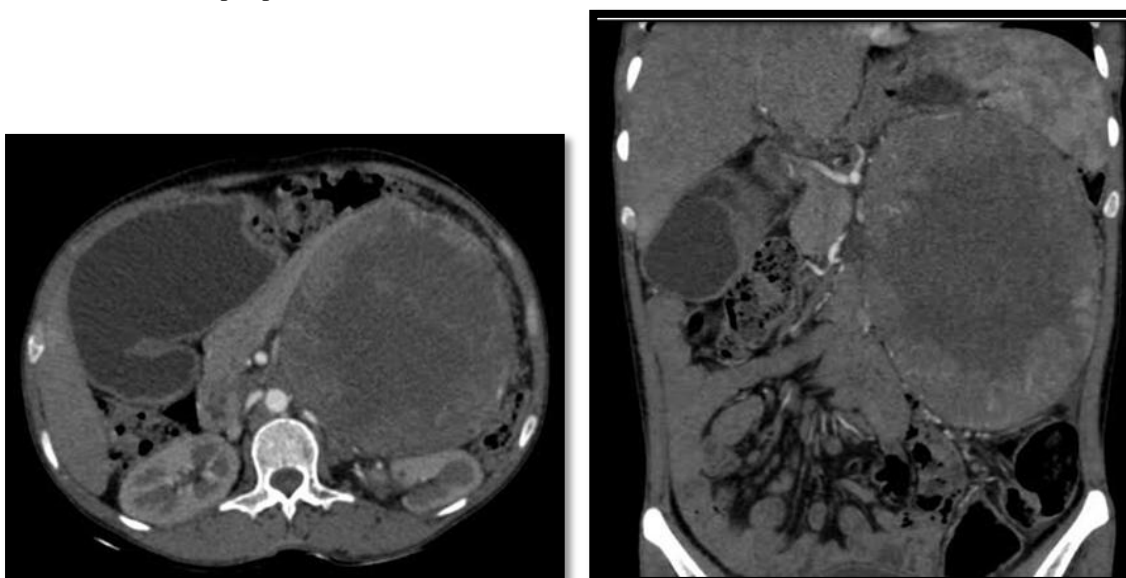


Fig.26: Solid cystic lesion: Axial and coronal CECT images showing large solid cystic lesion in the region of tail of pancreas, compressing left kidney pushing stomach and SMA and duodenojejunal junction anteriorly. Lesion shows large enhancing component and thick wall hence showing malignant criteria as per this study.

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