



Role of Endoscopic Ultrasound Guided Fine Needle Aspiration in the Diagnosis of Cystic Pancreatic Lesions

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Background: The diagnosis and management of cystic lesions of the pancreas is an increasingly recognized problem in clinical practice and many of the cystic pancreatic lesions are neoplastic and asymptomatic. Despite the significant advances occurred over the last decades, it remains difficulty to accurately distinguish between benign (serous cystic lesions) and malignant or potentially malignant (mucinous cystic lesions) pancreatic cysts before resecting them. Mucinous cystic neoplasms (MCNs), intrapapillary mucinous neoplasms (IPMN) and serous cystic neoplasms (SCNs) can display differences when examined by imaging modalities, endoscopic ultrasonography (EUS) and cytological and biochemical analyses of cyst fluid. The performance characteristics of high-resolution computed tomography (CT) scanning and magnetic resonance imaging (MRI) in making these distinctions are, however, disappointing. The aim of this study is to evaluate the role of endoscopic ultrasound guided fine needle aspiration (FNA) in diagnosis of cystic pancreatic lesions and its accuracy in discrimination between benign, malignant and potentially malignant cysts.

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Methods: The study was organized as a prospective study and conducted over 51 patients with identified cystic pancreatic lesions from prior radiological imaging (CT or MRI).

Results: EUS guided FNA has shown superior sensitivity, specificity, positive predictive value and negative predictive value in comparison to EUS alone in discriminating mucinous from non-mucinous cysts. This difference was remarkable specially for malignant cysts (mucinous cystadenocarcinoma, adenocarcinoma) and cystic lymphangioma. EUS-FNA associated with chemical and physical analysis of cyst fluid was 100% sensitive and specific. Cyst fluid CEA revealed significant importance in differentiating mucinous from non mucinous cysts. Cyst fluid amylase was significantly high in pseudocysts while mucin stain was important to discriminate mucinous from non-mucinous cystic lesions.

Conclusion: EUS-FNA has proven greater sensitivity and specificity, positive predictive, negative predictive value in differentiating mucinous and non-mucinous pancreatic cystic lesions as well as pathological categorization into subtypes.

Keywords: Endoscopic ultrasound; fine-needle aspiration; cystic pancreatic; malignant cysts.

1. INTRODUCTION

The diagnosis and management of cystic lesions of the pancreas is an increasingly recognized problem in clinical practice. The widespread use of high-resolution imaging modalities has led to their detection in as many as 1% of hospital inpatient admissions [1].

Many of the cystic pancreatic lesions are neoplastic with the majority being asymptomatic. The exact incidence of cystic pancreatic neoplasms is unknown, but it is frequently quoted that they constitute about 10% to 15% of all cystic lesions of the pancreas and less than 1% of all pancreatic neoplasms [2].

The WHO histological classification of neoplastic pancreatic cysts broadly divides them into serous cystic neoplasms (SCNs) and mucinous cystic neoplasms (MCNs), and the latter is classified further into mucinous cystadenomas or MCNs and intraductal papillary mucinous neoplasms (IPMNs). This classification is clinically useful because SCNs are rarely malignant, whereas mucinous lesions can be either benign or malignant. Benign mucinous lesions have the potential to become malignant, although the rate at which this occurs is unknown. Thus, guidelines issued recently by both the International Association of Pancreatology and the American College of Gastroenterology have suggested that surgery should be considered for mucinous lesions, whereas a conservative approach may be considered for SCNs [3,4].

In reality, a significant obstacle to this approach is the difficulty of distinguishing between SCNs and mucinous lesions without resecting them. MCNs, IPMN and SCNs are said to display

differences when examined by imaging modalities. However, the performance characteristics of high-resolution computed tomography (CT) scanning in making these distinctions are suboptimal, and its main role is, therefore, to determine the extent of any malignant spread [5,6].

The aim of this study was to evaluate the role of endoscopic ultrasound guided FNA (EUS-FNA) in diagnosis of cystic pancreatic lesions and its accuracy in discrimination between benign, malignant and potentially malignant cysts and in discriminating mucinous from serous cysts and detection of the histological subtype of the cyst .

2. PATIENTS AND METHODS

Our prospective study included 51 patients and was conducted between July 2017 and July 2019 at Tanta University Medical Center (Tanta, Egypt) after approval from Ethical Committee and after obtaining written informed consent from all participants.

The Inclusion criteria were adult age, and the presence of at least one cystic pancreatic lesions diagnoses by cross sectional radiological imaging tests (Trans-abdominal ultrasound, CT or MRI).

The exclusion criteria were the presence of solid pancreatic lesions identified by radiological imaging or EUS and patients with contraindication to EUS-FNA (e.g. coagulopathy) and patients who refused to participate in the study.

Before enrollment in this study, all participants were subjected to history taking, clinical

examination and laboratory investigations that included liver function tests, kidney function tests, serum levels of pancreatic enzymes (serum amylase) and serum levels of pancreatic tumor markers (CA 19.9, CEA).

Imaging modalities used for the diagnosis of pancreatic cystic lesions were transabdominal US, contrast enhanced CT scans of the abdomen and pelvis and contrast enhanced MRI of the abdomen and pelvis.

All EUS examinations were performed using a Pentax linear array EUS machine type EG-3870-UTK (HOYA Corporation, PENTAX Life care Division, Showanomori Technology Center, Tokyo, Japan) connected to a Hitachi EUB-7000 HV US unit (Hitachi Medical Systems, Tokyo, Japan). All tests were performed by one endosonographer and under sedation with IV propofol injection and with one dose of intravenous dose of prophylactic broad spectrum antibiotic 10 min before the endoscopy.

Fine needle aspiration: A Color Doppler image was used to exclude any vessel in the path of the needle. Needle punctures were made using a 22-gauge and 19 gauge needles (*Echotip®; Wilson-Cook, Winston Salem, NC, United States*) to obtain a representative sample of the cystic fluid.

Smaller (22) gauge needles were used for transduodenal FNA of the pancreatic head and uncinate process while a 19 G needles were used for cysts located in the body or in the tail of the pancreas. Cyst fluid underwent physical, and chemical analysis with assessment of cyst fluid Amylase and tumor markers such as carcinoembryonic antigen (CEA) using commercially available immunoassays (Roche Laboratories, Basel, Switzerland).

The diagnostic accuracy of EUS alone, EUS-FNA for the detection of malignant neoplastic pancreatic cysts was assessed by comparing the concordance between the pre- and post-operative diagnoses.

On the other hand, Patients whose provisional diagnosis was pseudocysts or serous cystadenomas with no symptoms or worrisome features were clinically observed and re-evaluated by EUS and FNAC after 6 months (it does not seem ethical to propose surgery for such benign conditions).

The diagnosis of reference was the post-operative histopathological report of all patients

who underwent surgical resection. The final diagnosis for patients who were not candidate or unfit for surgery was the matched and conclusive EUS guided fine needle aspiration cytology with good cellularity and physical, chemical criteria of the cyst fluid at time of diagnosis and follow up visit 6 months later.

Detection of the cystic lesion by EUS is shown in Fig. 1A. Color Doppler for the cystic lesion to assess the vascular structures at the needle pathway (Fig. 1B). Passage of the fine needle in the safest pathway into the center of the cyst in frequent times to obtain cyst fluid samples (Fig. 1C).

2.1 Statistical Analysis

Statistical presentation and analysis was conducted, using SPSS V.20.0. Categorical variables were expressed as frequency and percentage and were statistically analyzed by Chi-square test. The Kolmogorov-Smirnov test was used to verify the normality of distribution. Continuous variables were described using the range (minimum and maximum), the mean, and standard deviation if parametric, and median and IQR is non-parametric. The overall diagnostic performance was assessed by ROC curve analysis. All tests were two-tailed and P values less than 0.05 were considered statistical significant.

3. RESULTS

Most patients were females (58.8%) with mean age of 52.7 ± 10.65 years, 62.7% of them come from urban areas and only 25.5% were smokers. Asymptomatic patients represented 68.6% of the population. Among the symptomatic patients epigastric pain was the most common complaint (13.7%) followed by weight loss (9.8%), jaundice (7.8%) and the presence of an epigastric mass (5.9%). Tumor markers in serum (serum CEA, CA19-9) were normal in all the study group Table 1.

3.1 Cystic Lesion Characteristics

68.6% of the cysts were unilocular while 19.6% were multilocular and 11.8% were microcystic. Mural solid nodule existed in 29.4% of cysts while calcification of the cyst wall was noticed in only 17.6%. 47.1% of the pancreatic cystic lesions were communicating with the pancreatic duct, while 52.9% were non communicating. Moreover; pancreatic duct dilatation was noticed

in 19.6% of cases. 76.5% of the cases had a single pancreatic cyst while 23.5% of the cases had multiple cysts. Anatomically these cysts were distributed as follows: 52.5% at the pancreatic body, 25.5% at the head of pancreas, 7.8% at the pancreatic tail and 13.8% were diffusely distributed within the pancreas. The size of these cysts ranged from 2.3 cm to 15 cm with mean size 6.54 cm.

3.2 Biomarkers and Cytology Characteristics

Table 3 summarizes the mean level of cyst fluid amylase that was (951.29 I.U/ml \pm 2234.5) and the mean level of cyst fluid CEA was (1441.99 I.U/ml \pm 3586.60), This table also, shows that (33.3%) cases stained positive by mucin stain while (66.7%) were mucin stain negative Table 2.

3.3 Patient Outcomes

21 patients (41.2%) underwent surgical resection, while 2 patients (3.9%) were treated with percutaneous drainage, 2 patients (3.9%) have done endoscopic cystogastrostomy. the remaining 26 patients (51%) were managed conservatively and were followed in the outpatient settings after 6 months from the initial diagnosis.

At 6 months after the initial diagnosis, we found that 26 patients (42%) had a stable cystic lesion of the pancreas and 18 patients (35.3%) who underwent surgery had no recurrence of the cysts. On the other hand 2 patients died from postoperative complications and 5 patients had increasing size of their cystic lesions.

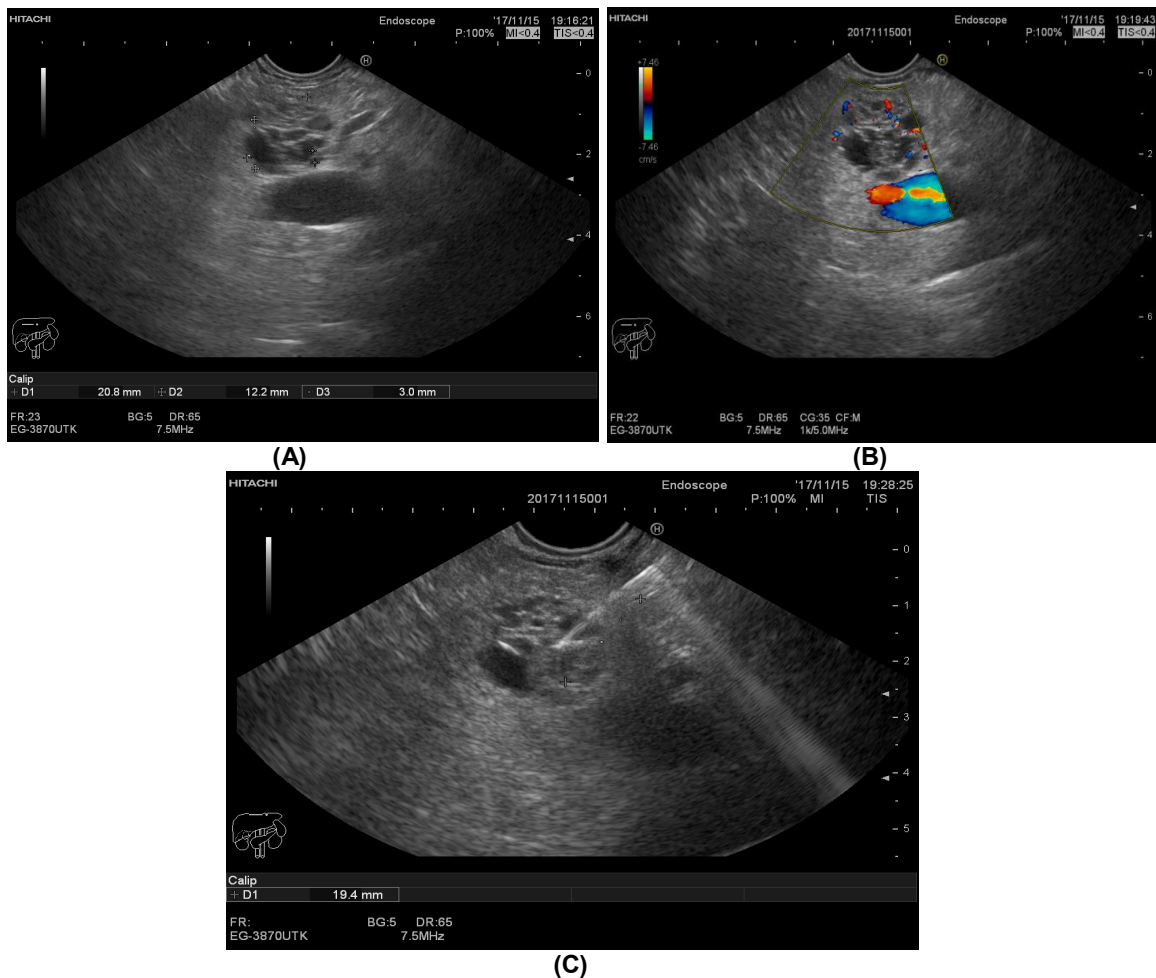


Fig. 1. Pseudopancreatic cyst within the pancreatic head (A) Color Doppler on the pancreatic pseudocyst (B) Introduction of the fine needle into the cyst (C)

Table 1. Demographic data, symptoms and laboratory parameter of the study group

Demographic data		N	%
Age	Range		35 – 75
	mean ± SD		52.75 ± 10.56
Sex	Male	21	41.2%
	Female	30	58.8%
Residence	Rural	19	37.3%
	Urban	32	62.7%
Smoking	Yes	13	25.5%
	No	38	74.5%
Abd. Pain		7	13.7%
Wt. loss		5	9.8%
Jaundice		4	7.8%
Mass		3	5.9%
Asymptomatic		35	68.6%
Serum Amylase	Range		10 – 1185
	Mean ± SD		174.14 ± 261.29
Serum Ca 19.9	Normal	51	100
	Abnormal	0	0
Serum CEA	Normal	51	100
	Abnormal	0	0

Table 2. Cyst morphological characteristics

Cyst characters by EUS		N	%
loculation	Unilocular	35	68.6%
	Multilocular	10	19.6%
	Microcystic	6	11.8%
Mural nodule	Yes	15	29.4%
	No	36	70.6%
Calcification	Yes	9	17.6%
	No	42	82.4%
Pancreatic duct communication	Yes	24	47.1%
	No	27	52.9%
Pancreatic duct dilatation	Yes	10	19.6%
	No	41	80.4%
Number	Single	39	76.5%
	Multiple	12	23.5%
Site	Head	13	25.5%
	Body	27	52.9%
	Tail	4	7.8%
	Diffuse	7	13.8%
Size (cm)	Range		2.3 – 15
	Mean ± SD		6.54 ± 2.85
Cyst Fluid Amylase	Range		2 – 10500
	Mean ± SD		951.29 ± 2234.5
Cyst fluid CEA	Range		0.2 – 16613
	Mean ± SD		1441.99 ± 3586.60
Mucin stain	+ve	17	33.3%
	-ve	34	66.7%

EUS has diagnosed IPMN, pancreatic lymphangioma at ratio of (21.6%, 35.3%, 17.6%, pseudocyst, serous cystadenoma, mucinous 25.5%, 0%, 0% and 0%) respectively. However cystadenoma, mucinous cystadenocarcinoma, EUS guided FNAC has diagnosed IPMN, pancreatic adenocarcinoma, cystic pancreatic pseudocyst, serous cystadenoma,

mucinous cystadenoma, mucinous cystadenocarcinoma, pancreatic adenocarcinoma, cystic lymphangioma at ratio of (21.6%, 33.3%. 15.7%, 17.6%, 2%, 5.9%, 3.9%) respectively. The final diagnosis was to some extent different ; the IPMN, pancreatic pseudocyst, serous cystadenoma, mucinous cystadenoma, mucinous cystadenocarcinoma, pancreatic adenocarcinoma, cystic lymphangioma were finally diagnosed at ratio of (19.6%, 33.3%. 17.6%, 13.7%, 5.9%, 5.9%, 3.9%) respectively Table 3.

EUS was 80% sensitive 93% specific with 73% PPV and 95% NPV in diagnosis of IPMN, while 94% sensitivity and 94% specificity with PPV 89% and NPV 97 % in case of pancreatic pseudocyst. On the other hand it had sensitivity 78% and specificity of 95% in diagnosis of serous cystadenoma and 71% sensitivity and

82% specificity in mucinous one. Eus could not diagnose cystic lymphangioma, mucinous cystadenocarcinoma and pancreatic adenocarcinoma at all Table 4.

EUS guided FNAC was 100% sensitive 98% specific with 91% PPV and 100% NPV in diagnosis of IPMN, while 100% sensitivity and 100% specificity with PPV 100% and NPV 100% in case of pancreatic pseudocyst. On the other hand it had sensitivity 89% and specificity of 100% in diagnosis of serous cystadenoma and 86% sensitivity and 93% specificity in mucinous cystadenoma. EUS with FNAC has diagnosed cystic lymphangioma and pancreatic adenocarcinoma with 100% sensitivity and specificity, while mucinous cystadenocarcinoma was diagnosed by 33% sensitivity and 85% specificity Table 5.

Table 3. Comparison between EUS alone, EUS guided FNAC and the final diagnosis as regard the pathological subtype

Diagnosis	EUS	FNAC	Final
IPMN	11 (21.6%)	11 (21.6%)	10 (19.6%)
Pancreatic pseudocyst	18 (35.3%)	17 (33.3%)	17 (33.3%)
Serous cystadenoma	9 (17.6%)	8 (15.7%)	9 (17.6%)
Mucinous cystadenoma	13 (25.5%)	9 (17.6%)	7 (13.7%)
Mucinous cystadenocarcinoma	0%	1 (2.0%)	3 (5.9%)
Pancreatic adenocarcinoma	0%	3 (5.9%)	3 (5.9%)
Cystic lymphangioma	0%	2 (3.9%)	2 (3.9%)

Table 4. EUS sensitivity and specificity in diagnosis of pathological subtype of the cyst

Diagnosis	EUS	Final (true)	Sensitivity	Specificity	PPV	NPV
IPMN	10	8	80	93	73	95
Pancreatic pseudocyst	17	16	94	94	89	97
Serous cystadenoma	9	7	78	95	95	78
Mucinous cystadenoma	7	5	71	82	38	95
Cystic lymphangioma	0	2	0	0	0	0
Mucinous cystadenocarcinoma	0	3	0	0	0	0
Pancreatic adenocarcinoma	0	3	0	0	0	0

Table 5. EUS guided FNAC sensitivity and specificity in diagnosing pathological subtype of the cyst

Diagnosis	FNAC (n)	Final (n)	Sensitivity	Specificity	PPV	NPV
IPMN	10	10	100	98	91	100
Pancreatic pseudocyst	17	17	100	100	100	100
Serous cystadenoma	9	8	89	100	100	98
Mucinous cystadenoma	6	1	86	93	67	97
Mucinous cystadenocarcinoma	1	3	33	85	13	95
Pancreatic adenocarcinoma	3	3	100	100	100	100
Cystic lymphangioma	2	2	100	100	100	100

EUS diagnosed 52.9% of the cysts as benign cysts and 47.1% of the cysts as pre malignant and detected no malignant cysts, while EUS guided FNAC has diagnosed 51% of the cysts as benign, 41.2% of cysts as premalignant and 7.8% as malignant. The final surgical diagnosis to some what was different; the benign cysts were 54.9% while the premalignant cysts constituted 33.3% of the cases and the malignant cysts constitute 11.8%.

EUS guided FNAC was 67% sensitive and 100% specific in detecting the malignant cystic lesion with 100% PPV and 95% NPV. EUS had diagnosed 47.1% of the cysts as mucinous and 52.9% as non mucinous, on the other hand EUS guided FNAC considered 43.1% as mucinous and 56.9% as non mucinous. The final diagnosis was different as it found 39.2% as mucinous and 60.8% as non mucinous.

EUS has diagnosed 24 cases as mucinous cysts when comparing them with final diagnosis we found 17 cases to be correct diagnosis and 7 cases to be incorrect diagnosis (non mucinous). EUS also has diagnosed 27 cysts to be non mucinous cysts when comparing them with the final diagnosis we found 24 cases of them to be correct diagnosis while 3 cases to be incorrect (non mucinous).

EUS has sensitivity of 85% and specificity of 77%, positive predictive value 71% negative predictive value 89% and 80% accuracy in

discriminating mucinous cysts from non mucinous cysts. Controversially; EUS associated with FNAC had sensitivity of 100% and specificity of 94%, positive predictive value 91% negative predictive value 100% and 96% accuracy in discriminating mucinous cysts from non mucinous cysts.

Cyst fluid CEA has 87% sensitivity, 80% specificity, 80% PPV and 87% NPV in differentiation of mucinous from non mucinous cysts at cut off level 250 ng/dl. AUC was 0.921 Fig. 2.

Cyst fluid CEA at cut off value 600 ng/dl has sensitivity of 83% and specificity of 80 % in predicting malignant cyst. AUC was 0.848 Fig. 3.

Cyst fluid amylase has 76% sensitivity, 71% specificity 56% PPV and 86% NPV in diagnosis of pancreatic pseudocyst at cut off value of 200 ng/dl. AUC was 0.859 Fig. 4.

4. DISCUSSION

EUS guided FNAC is a simple less complicated maneuver allowing sampling with subsequent physical, chemical and cytological assessment of the cyst fluid; 22 gauge and 19 gauge needles were used after pre- operative IV antibiotic dose and proper sedation. Cyst fluid biological markers like CEA and cyst fluid amylase were assessed as well.

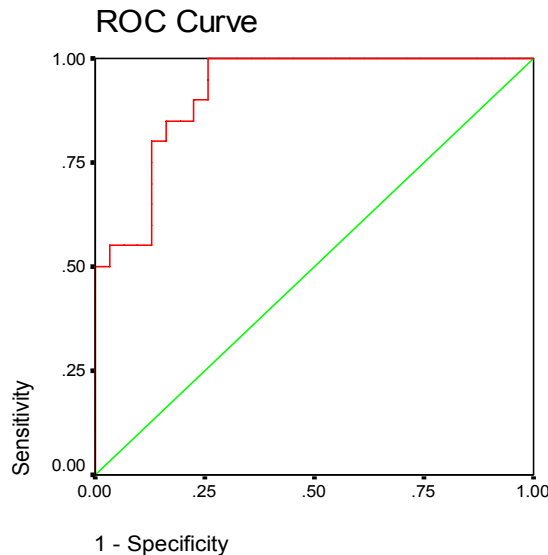


Fig. 2. ROC curve of CF CEA value in differentiating mucinous from non mucinous

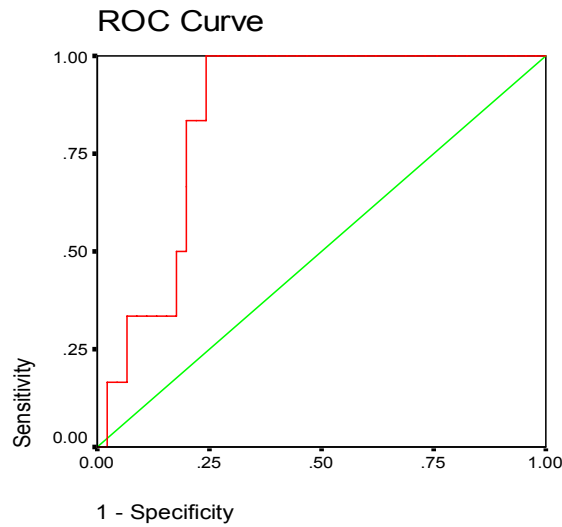


Fig. 3. ROC curve of cyst fluid CEA in malignancy prediction

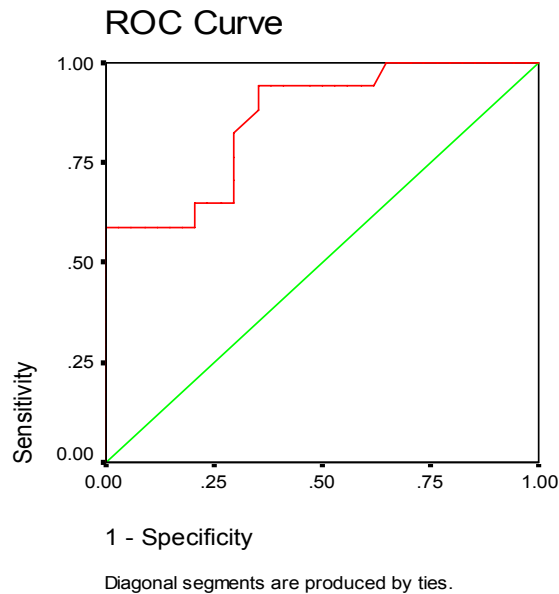


Fig. 4. ROC curve for cyst fluid amylase value in detection of pancreatic pseudocyst

The final results obtained by EUS morphologically, and that obtained by combined EUS and FNAC were compared with the final results obtained after surgical resections.

As regard cyst morphology by EUS, in agreement with us; Forssad et al. [7] who found most of the cystic lesions in his study to be located at the pancreatic body followed by head and tail.

In contrast to us; Lee et al. [8] found most of the cysts in his study to be at the pancreatic tail followed by the head and body.

On further sub analysis of the cyst site; we found 50% of *IPMNs* cysts to be; located at the pancreatic head, while 40% were diffuse and only 10% of cases were at the pancreatic body.

Eizaburo Ohno et al. [9] to some what agreed with us when they found 75% of the IPMN cases to be at the pancreatic head. This is also matching with established prevalence data in literatures.

Surprisingly; None of the cases of mucinous cystadenoma had occurred at the pancreatic head but 57% were at the pancreatic body and 28% were at the tail; even their malignant form (mucinous cystadenocarcinoma) was 100% at the pancreatic body.

Eizaburo Ohno et al. [9] also confirmed this results when they found 95% of the mucinous cysts to be located at the pancreatic body and tail.

The presence of a mural nodule within a cystic pancreatic lesion is a very important finding which can markedly help the diagnosis and judge the management.

In our study we surprisingly found mural nodules in 100% of malignant cysts, 41.1% of the premalignant cysts and 7.1% of the benign cysts with high statistical significance ($p < 0.001$). also; 50% of mucinous cysts contain mural nodules but only 16% of non mucinous cysts contain it.

In agreement with us; Kobayashi N, et al. and Ohno E, et al.; reported that. The presence and size of mural nodules are the most reliable findings in the differentiation of benign and malignant IPMNs. Koito et al. also reported the usefulness of mural solid nodules in benign - malignant differentiation [10,11].

Brugge et al.; also, reported that mural solid nodules has 51% accuracy in differentiating mucinous from non mucinous cysts.

In our opinion; despite the great importance of solid mural nodules in the pancreatic cyst classification , it remains a great challenge to differentiate them from mucus plugs within the cyst cavity making the use of a novel EUS techniques like contrast enhanced harmonic EUS to be of a great value in this aspect.

As regard cyst wall calcification; our study found that 66.7% of the malignant cysts show cyst calcification while only 14.3% of the benign cysts and 5.9% of the premalignant cysts show calcification this was statistically significant.

On further sub analysis; the 4 benign cases showing calcification; 3 of them were serous cystadenoma (about 33.3% of the serous cystadenoma cases in the study) and 1 of them was pancreatic pseudocyst (about 5.9% of the pancreatic pseudocysts in the study).

On the other hand; all the premalignant cysts showing calcifications were IPMNs. On analysis of the 4 malignant cases showing calcification; 3 of them were mucinous cystadenocarcinoma and 1 of them pancreatic adenocarcinoma.

Eizaburo Ohno et al. in 2019 and Curry CA, et al. [6] in 2001 agreed with us when they found pathognomonic central star shaped calcification in about 40% of the serous cystadenoma cases of their studies.

Taouli et al. in [12] had calculated 77% likelihood of malignancy when calcification present in mucin producing cystic neoplasms.

We explain the presence of calcification in pancreatic pseudocyst that it may be on background of chronic pancreatitis, while occurrence of calcification in cases of IPMNs due to the presence of mucin which has tendency to build up calcium salt deposits. However, pancreatic adenocarcinoma rarely to calcify, calcification can occur if carcinoma developed on background of chronic pancreatitis or if pancreatic duct obstruction by the tumour had occurred.

The role of cyst fluid CEA as a potential marker to differentiate between PCLs was first reported in the 1980s. Different cutoffs for CEA ranging from 5 ng/mL to 800 ng/mL have been utilized in multiple studies with varying ranges of sensitivity and specificity.

Our study revealed that the mean level of cyst fluid CEA was highest in mucinous cystadenocarcinoma, IPMNS , pancreatic adenocarcinoma and mucinous cystadenoma. On the other hand, the level was lowest in cystic lymphangioma, pancreatic pseudocysts and serous cystadenoma this was statistically significant.

In agreement with us Vander Waiji et al. [13] who found the lowest level of cyst fluid CEA in their study to be in serous cystadenoma and pancreatic pseudocyst, while mucinous cystadenoma and carcinoma show the highest

levels are strongly suspected when cyst fluid CEA exceeds 800 ng/ml.

Forssad et al., [7] also agreed that there was statistically significant difference among the different pathological subtypes in the cyst fluid CEA with the highest level was noticed in mucinous cyst adenocarcinoma and the lowest in serous cystadenoma.

On further sub analysis into mucin producing and non mucin producing cysts; we noticed that cyst fluid CEA was significantly elevated in the mucin producing group rather than the non mucin producing one. Cyst fluid CEA has 87% sensitivity, 80% specificity, 80% PPV and 87% NPV in differentiation of mucinous from non mucinous cysts at cut off level 250 ng/ml.

Forssad et al. [7] results in this aspect were different, they considered cyst fluid CEA more than 400 ng/ml to only have sensitivity of 13% and specificity of 75% in differentiating mucinous from non mucinous cysts.

Also, Snozek CL et al. in [14], considered cut off value of 30 ng/ml for differentiating mucinous from non mucinous cysts. This study however, suffered from less than ideal measures to define the diagnostic gold standard and we do not favor its use or suggested CEA threshold.

Rockacy M et al. in [15]; has considered cut off value 192 ng/ml for differentiating mucinous from non mucinous cysts.

Our study also, has found that cyst fluid CEA at cut off value more than 600 ng/ml has sensitivity of 83% and specificity of 80% in differentiating malignant cysts from other non malignant cysts.

Maire F et al. in [16] agreed with these results who assessed cyst fluid CEA value in benign malignant discrimination to have a sensitivity of 90%, specificity of 71%, PPV of 50% and NPV of 96% when CEA > 200 ng/mL.

The final results of our study revealed that; 17 (33.3%) patients were found to have pseudo pancreatic cyst, 10 patients with IPMN (19.6%), 9 patients with serous cystadenoma (17.6%), 7 patients with mucinous cystadenoma (13.7%), 3 patients with mucinous cystadenocarcinoma (5.9%), 3 patients with pancreatic adenocarcinoma (5.9%) and 2 cases of cystic lymphangioma (3.9 %).

On further analysis; 28 (54.9%) cysts were benign; most of them were pseudocysts while 17 (33.3%) cysts were pre malignant most of them were IPMNs. On the other hand, 6 (11.8%) cases had frankly malignant cysts.

These results were compatible with what is reported by [17], and [18] who found that pancreatic pseudocyst is the mostly prevalent cystic pancreatic lesions in their studies.

However, Forssad et al., 2005 had found most of the cases in his study as mucinous cystadenoma followed by IPMNs, but this can be easily explained that; the cohort of forssad study were those who were candidate for surgical resection and pseudo pancreatic cysts rarely need surgery so they were excluded from his study.

Also, the study performed by José Lario-Noia et al. in [19] revealed that; 47% of the cases to be IPMN while pseudo cysts constituted 17.46% only.

As regard EUS efficiency in diagnosis of the malignant potential of the cyst; EUS alone correctly identified 85.7% of the benign cyst and 82.4% of the pre malignant cysts and unfortunately; None of the malignant cysts were correctly diagnosed by EUS alone. so, our study revealed that EUS alone was insensitive tool in detecting malignant cysts in agreement with us; Ahmed and colleagues in 2003 [20,21,14,22,23] in their study which included 98 patients; who proven that EUS features alone could not be used reliably to differentiate benign from malignant pancreatic cysts.

4.1 However, when We Added FNAC to the EUS the Result Differs

EUS with FNAC correctly identified 92.9% of the benign cysts, 100% of the premalignant cysts and 66.7% of the malignant cysts. The sensitivity of EUS associated with FNAC in detection of malignant cyst become 67%, specificity about 100%, PPV 100% and NPV 95%.

Forssad et al. [7] agreed with us they showed that EUS-FNA improved the diagnostic ability compared with that of EUS morphological diagnosis alone. The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of EUS-FNA were 97%, 100%, 100%, and 95%, respectively.

Fernandez-del Castillo C et al., in [21,14,24] also agreed with us when he proved sensitivity of

EUS guided FNAC in malignancy detection to be 69% and specificity of 90%.

However, Gerke et al. [25] disagreed with us in their study on 66 patients who found EUS morphological characteristics to have 66% accuracy in benign – malignant differentiation. Ahmed et al.; also reported 40% accuracy of EUS morphological features in detecting malignant cysts.

When we studied the diagnostic efficiency of EUS and EUS FNAC in discriminating mucinous from non mucinous cysts: EUS had sensitivity of 85% and specificity of 77% with positive predictive value 71% and negative predictive value 89% in differentiating mucinous cysts from non mucinous cysts.

In agreement to these results, Zhang et al., [22,23,26-31] who reported 82% sensitivity and 80% specificity of EUS to discriminate mucinous from non mucinous cysts.

Brugge et al. [23,26-30], however, had reported lower accuracy of EUS morphological features (51%) in discriminating mucinous from non mucinous cysts in their study on 118 patients with pancreatic cysts.

On the other hand, Our study revealed that EUS associated with FNAC: had sensitivity of 100 % and specificity of 94%, positive predictive value of 91% and negative predictive value of 100% in differentiation between mucinous and non mucinous cysts.

Forssad et al., [7] revealed 100% sensitivity and 100% specificity for EUS guided FNAC in differentiating mucinous from non mucinous cysts on his study of 67 patients which met our inclusion criteria ,only one case in this study misdiagnosed as mucinous cystadenoma and proven latter to be IPMNs.

In contrast, Attasaranya et al. [28-32,8-13,15-19,24,25,33] who performed his study over 34 patients. He reported much lower sensitivity and specificity (63% and 73% respectively) of EUS guided FNAC in differentiating mucinous from non mucinous cysts.

This controversy is explained by that Attasaranya et al didn't use mucin stain in cytological assessment of their samples which is essential criteria of mucinous cysts, thus markedly reducing the diagnostic yield.

4.2 When We Comparing EUS and EUS Guided FNAC as Regard their Ability to Diagnose the Pathological Subtypes of Each Cyst Type We Found

In the aspect of IPMNS diagnosis: EUS had sensitivity of 80%, specificity of 93%. While EUS guided FNAC had sensitivity of 100%, specificity of 98%.

In disagreement with us, Forssad et al. [7]; he found EUS features alone to be 100% sensitive and specific in the diagnosis of IPMNs and the FNAC has no additional value in this pathological type.

In the aspect of pseudocyst diagnosis: EUS had proven sensitivity of 94%, specificity of 94%. While EUS guided FNAC had raised the sensitivity and the specificity up to 100%. Forssad and colleague [7] considered EUS features alone to be 100% sensitive and Specific in pseudocysts and FNAC had added nothing.

In my opinion EUS features alone in the absence of previous attack of pancreatitis may be confusing and can overlap with macrocystic serous cystadenoma or cystic lymphangioma. Even if the history of pancreatitis existed, pancreatitis can occur also in IPMNs or any cystic lesion which compresses or occludes the pancreatic duct not exclusive with pancreatic pseudocysts.

In the aspect of mucinous cystadenoma diagnosis: EUS had sensitivity of 71% and specificity of 82%. While EUS guided FNAC had sensitivity of 86% and specificity of 93%.

In the aspect of serous cystadenoma diagnosis: EUS had sensitivity of 78%, specificity of 95%. While EUS guided FNAC had sensitivity of 89%, specificity of 100%.

Forssad et al. [7] had found comparable results, they found EUS sensitivity and specificity in diagnosis of mucinous cystadenoma to be 65% and 84% which raised to 94% and 100% after addition of FNAC also when they studied serous cystadenoma EUS was 43% sensitive and 76% specific this was raised to 100% and 97% respectively after addition of FNAC.

So that we can conclude easily EUS has the highest sensitivity in pancreatic pseudocyst diagnosis and the least sensitivity in mucinous cystadenoma diagnosis and unfortunately,

insensitive to mucinous cystadenocarcinoma, cystic lymphangioma and pancreatic adenocarcinoma diagnosis.

As regard the complication of the maneuver of fine needle aspiration cytology ,our study results were surprising, we noticed that 82% of the cases passed without any complications, 9.8% of cases noticed post operative fever which passed within days of the maneuver with broad spectrum antibiotics. Only 3.9% of cases complained of self limited intra cystic bleeding and 3.9% of the cases complicated by post operative pancreatitis. No mortalities nor perforation or desaturation.

In agreement to us; Rodeguez-D'Jesus [30-32] et al. who reported pancreatitis in 1.92% of cases, hemorrhage in 1.5% of cases, fever in 4% of cases and unfortunately perforation in 0.21% of cases and desaturation in 0.23%.

Tumour seeding along needle tract or dissemination didn't occur in our study at all, Hirooka et al.and Yamabe [34,35] et al. reported tumour seeding and dissemination in their studies, however their studies were limited to IPMCs(intraductal papillary mucinous carcinoma cases).

5. CONCLUSION

Endoscopic ultrasound FNAC has proven greater sensitivity and specificity, positive predictive, negative predictive value in differentiating mucinous and non mucinous cyst as well as pathological categorization into subtypes.

CONSENT AND ETHICAL APPROVAL

Our prospective study included 51 patients and was conducted between July 2017 and July 2019 at Tanta University Medical Center (Tanta, Egypt) after approval from Ethical Committee and after obtaining written informed consent from all participants.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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