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Research Article

Endoscopic Ultrasound-Guided Fine Needle Aspiration Analysis of Pancreatic Cysts at Gastrointestinal and Liver Diseases Teaching Hospital in Sulaimani, Kurdistan Region, Iraq

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Abstract

Background: The extensive use of cross-sectional abdominal imaging (CT and MRI) has led to an increase in the occurrence of pancreatic cysts (PCs). ***Objectives***: Identifying different forms of PC lesions, discriminating between malignant and benign cysts, and determining the prevalence of neoplastic and non-neoplastic PC. ***Methods***: A retrospective cross-sectional analysis of 120 individuals with pancreatic cystic lesions was conducted between February 2023 and February 2024. There are 45 men and 75 women. The lesions were detected by EUS, MRI, CT, and TAUS. All patients underwent an EUS-guided FNA. Cytology and tumor markers (CA19-9 and CA-125) were used to evaluate the aspirated specimens. ***Results***: PCs were substantially more common in females (62.5%). Benign SCN was the most common kind (40%). Malignant cysts were detected in 35 patients (29.2%) (IPMN 62.9%), with men accounting for a statistically significant majority (71.4%). Malignant cysts significantly correlated with vomiting and weight loss (34.3% and 91.4%, respectively). CA-19-9 and CA-125 showed considerably larger elevations in malignant cysts than benign cysts (68.6% and 56.5%, respectively). EUS was the most effective imaging tool for cyst detection, with a sensitivity of 94.3% and a specificity of 91.8%, followed by MRI, CT scan, and TAUS. ***Conclusions***: Females were more likely to have PCs, whereas males had more malignant cysts. The most common and benign kind of PC was SCN. The most common form of malignant PC was IPMN, and EUS was the most effective way to diagnose PCs.

Keywords: Endoscopic ultrasound, CA19-9, CA–125, Pancreatic cysts.

تحليل الشفط بالإبرة الدقيقة الموجهة بالموجات فوق الصوتية بالمنظار لأكياس البنكرياس في المستشفى التعليمي لأمراض الجهاز الهضمي والكبد في السليمانية، إقليم كردستان، العراق

الخلاصة

الخلفية: أدى الاستخدام المكثف للتصوير البطني المقطعي (CT و MRI) إلى زيادة كشف تكيسات البنكرياس (PCs). **الأهداف**: تحديد الأشكال المختلفة لتكيسات البنكرياس، والتمييز بين الخراجات الخبيثة والحميدة، وتحديد مدى انتشار الأورام وغير الأورام. **الطريقة**: تم إجراء تحليل مقطعي بأثر رجعي لـ 120 فردا يعانون من آفات البنكرياس الكيسية بين فبراير 2023 وفبراير 2024. هناك 45 رجلا و 75 امرأة. تم الكشف عن الآفات بواسطة EUS و MRI و CT و TAUS. خضع جميع المرضى لـ FNA الموجه ب EUS. تم استخدام علم الخلايا وعلامات الورم (CA19-9 و CA-125) لتقييم العينات. **النتائج**: كانت تكيسات البنكرياس أكثر شيوعا لدى الإناث (62.5٪). كان SCN الحميد هو النوع الأكثر شيوعا (40٪). تم الكشف عن الخراجات الخبيثة في 35 مريضا (29.2٪) (IPMN 62.9٪) ، حيث يمثل الرجال أغلبية ذات دلالة إحصائية (71.4٪). ترتبط الخراجات الخبيثة بشكل كبير بالقيء وفقدان الوزن (34.3٪ و 91.4٪ على التوالي). أظهر CA-19-9 و CA-125 ارتفاعات أكبر بكثير في الخراجات الخبيثة من الخراجات الحميدة (68.6٪ و 56.5٪ على التوالي). كان EUS أداة التصوير الأكثر فعالية للكشف عن الكيس ، مع حساسية 94.3 ٪ وخصوصية 91.8 ٪ ، تليها التصوير بالرنين المغناطيسي ، والأشعة المقطعية ، و TAUS. **الاستنتاجات**: كانت الإناث أكثر عرضة لتكيسات البنكرياس، في حين أن الذكور لديهم أكياس خبيثة أكثر. كان النوع الأكثر شيوعا وحميدة من التكيسات هو SCN. كان الشكل الأكثر شيوعا لتكيس البنكرياس الخبيث هو IPMN ، وكان EUS هو الطريقة الأكثر فعالية لتشخيص تكيسات البنكرياس.

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INTRODUCTION

Pancreatic cystic lesions account for less than 1% of pancreatic neoplasms. However, high-resolution imaging has boosted incidental pancreatic cyst discovery [1]. In the United States, approximately 2.6% to 13.5% of persons have accidental pancreatic cysts [2,3]. Globally, pancreatic cancer causes significant morbidity and mortality [4]. Although it has one of the lowest 5-year survival rates of all cancers (3% in the UK) [5]. Poor survival is partly due to late

pancreatic cancer manifestation, as precursor lesions are challenging to identify, albeit diagnosis is improving. 3% of high-resolution abdomen CT scans reveal pancreatic cysts [6]. Pancreatic cysts constitute a diverse range of abnormal growths and encompass both benign and malignant cysts. Proper categorization and terminology of pancreatic cysts are crucial for accurate pathological and clinical diagnosis. Pseudocysts, retention cysts, lymphoepithelial cysts, benign epithelial cysts, and congenital cysts are examples of non-neoplastic cysts [1]. Non-neoplastic cysts are thought to indicate little or no risk of becoming cancerous. In general, neoplastic cysts are classified as mucinous or non-mucinous depending on the epithelial type they contain [7]. The mucinous cysts comprise two types of neoplasms: mucinous cystic neoplasms (MCN) and intraductal papillary mucinous cells (IPMN). Adenocarcinomas, solid pseudopapillary neoplasms (SPN), cystic pancreatic neuroendocrine tumors (PNET), cystic pancreatic ductal adenocarcinomas (PDA) and their variants, cholangiocarcinoma, acinar cell carcinoma, high-grade neuroendocrine carcinoma (small cell and large cell), pancreatoblastoma, lymphomas, sarcomas, and metastatic tumors are examples of non-mucinous cysts [1]. The neoplastic cysts are classified as either malignant (such as PDA and PNET) or having uncertain malignant potential (such as MCN, IPMN, and SPN). Within the category of mucinous cyst subtypes, it has been proposed that branch duct IPMN (BD-IPMN), although capable of becoming malignant, may display a more latent tendency in comparison to main duct IPMN [8,9]. A comprehensive analysis has been conducted on most pancreatic cysts to determine the need for surgery or further investigation [10]. During the diagnostic evaluation, specialized CT and MRI imaging tests are highly effective diagnostic methods for characterizing the morphological characteristics of pancreatic cysts [11,12]. Moreover, endoscopic ultrasonography has been highly useful in assessing pancreatic cystic lesions by offering precise information on the morphological features of the cyst [13]. In this study, we retrospectively studied 120 cases of pancreatic cysts through EUS-guided FNA to characterize their types and differentiate neoplastic from non-neoplastic types.

METHODS

Study design and settings

This is a retrospective, single-center, cross-sectional study designed to analyze data from 120 consecutive patients who underwent EUS-FNA performed by an expert endoscopist for pancreatic cysts between February 2023 and February 2024 at Gastrointestinal and Liver Diseases Teaching Hospital, Kurdistan Regional Government, Iraq.

Inclusion criteria

Patients 18 years or older with radiological evidence (CT, MRI, EUS, and TAUS) of pancreatic cysts.

Exclusion Criteria

Patients younger than 18 years, patients with pseudocysts, and patients with associated co-morbidities precluding general anesthesia.

Endoscopic ultrasound examination

An expert interventional gastroenterologist performed all EUS procedures. All patients were evaluated for fitness by an anesthetist. The procedure was carried out using a Pentax EG3830UT machine, manufactured by HOYA Corporation's PENTAX Lifecare Division at Shimamori Technology Center in Tokyo, Japan, connected to a Hitachi EUB-7000 machine. Fine needle aspiration (FNA) was performed with either a 22 or 19G Echo tip. (Cook, Endoscopy, Winston-Salem, NC). The aspirates were put into 2 tubes for cytopathology and tumor markers (CA19-9, CA-125) examination. The final diagnosis was based on cytopathological results.

Ethical considerations

The study is approved by the Research Protocol Ethics Committee of the Kurdistan Higher Commission of Medical Specialties. Written informed consent was obtained before the endoscopic procedure.

Statistical analysis

The Statistical Package for the Social Sciences (SPSS, IBM, Chicago, USA, version 27). The data were expressed as numbers and percentages for categorical data and mean (St. deviation) for numerical data. The chi-square test was used for categorical variables, and the Mann-Whitney U test was used to determine the association between numerical variables after performing the Shapiro–Wilk test. Sensitivity, specificity, PPV, NPV, and accuracy were estimated for the imaging modality of the pancreatic cyst. $p< 0.05$ was considered significant.

RESULTS

This study included a total of 120 patients (Figures 1 and 2); 75 (62.5%) patients were males, and 45 (37.5%) patients were females. Their ages ranged from 18 to 87 years, with a median age of 66 years, and 18 to 85 years, with a median age of 61 years, respectively. The commonest pancreatic cyst was SCN (40.0%, n=48), which were all benign. Thirty-five patients (29.2%) were found to have malignant cysts. Most of the malignant patients were males (71.4%, n=25), while most of the benign patients were females (76.5%, n=65). This outcome was statistically highly significant ($p< 0.001$). The residency of the enrolled

participants was not a substantial factor between both malignant and non-malignant groups (p= 0.128).

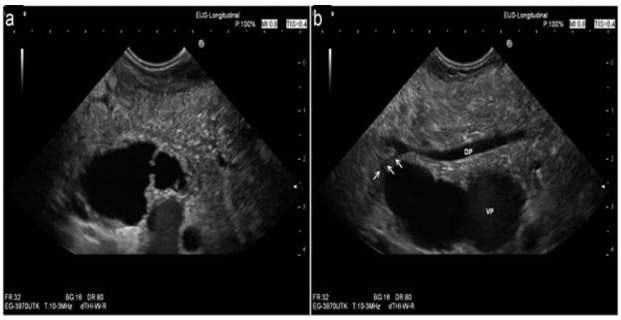

Figure 1: A 40-year-old male patient, EUS images of a typical BD-IPMN. grape-like agglomeration of cysts, communicating (a) with each other, and (b) with a side branch of the main pancreatic duct (arrows). Main pancreatic duct is slightly dilated. Pancreatic parenchyma is homogeneous.

While housewives were the predominant group (49.4%, 42 out of 85) possessing benign cysts, pancreatic cysts of retired participants were found to be mostly malignant (37.1%, 13 out of 35), and this was statistically significant (p= 0.001). The difference in ethnicity between patients with benign and malignant cysts was not statistically significant (p= 0.083). Of 35 patients with malignant cysts, 18 patients (51.4%) were smokers, and this was statistically highly significant (p< 0.001), indicating a strong association of smoking with malignant pancreatic cysts. None of the patients enrolled were consuming ethanol (Table 1).

Figure 2: A 28-Year-old pregnant female, Ultrasound of pancreatic mucinous cystic neoplasm (MCN) performed in the ninth week of gestation. (A) Abdominal ultrasound demonstrating a large cystic mass (14 cm Â 11 cm) with septations and mural nodules. (B) Blood flow was present around the mural nodule and a hypertrophic septum in the tumor.

Table 1: Sociodemographic distribution of patients.

Characteristics	Benign (n=85)	Malignant (n=35)	Total (n=120)	*p*-value
Age (year)				
Mean±SD	57.48±18.69	61.09±13.72	58.53±17.41	0.477
Gender n(%)				
Female	65(76.5)	10(28.6)	75(62.5)	<0.001
Male	20(23.5)	25(71.4)	45(37.5)	
Residency n(%)				
Inside city	47 (55.3)	14(40)	61(50.8)	0.128
Outside city	38 (44.7)	21(60)	59(49.2)	
Ethnicity n(%)				
Kurdish	67(78.8)	22(62.9)	89(74.2)	
Arabic	17(20)	13(37.1)	30 (25)	0.083
Christian	0(0.0)	1(2.9)	1(0.8)	
Smoking n(%)				
Smoker	14(16.5)	18(51.4)	32(26.7)	<0.001

n: number; SD: standard deviation. The data were analyzed using Man Whitney U test (age) and chi-square test (other variables).

Table 2 summarizes key clinical features of the patients with pancreatic cysts, divided into benign and malignant categories. There were no statistically significant differences regarding the presence of diarrhea (p=0.249), history of diabetes mellitus (0.065), drug history for chronic diseases (p= 0.143), history of previous surgery (p= 0.230), family history of hepato-pancreato-biliary diseases (p=*0.372)*, and lastly, history of pancreatitis (p= 0.775), between neoplastic and non-neoplastic patients. Vomiting and body weight loss (but not diarrhea) were statistically more apparent in the malignant pancreatic cyst group (p< 0.002 and <0.001, respectively) in comparison with the nonmalignant group. The mean weight loss was 9.45±2.94 kg in 4.66±2.2 months. Elevation of the cyst CA-19-9 and CA-125 was valuable in differentiating neoplastic from non-neoplastic lesions. In neoplastic lesions, the elevation of these tumor markers was 68.6% and 28.6%, respectively. On the contrary, in non-neoplastic lesions, these markers were elevated in only 12.9% (n=11) and 4.7% (n=4) patients, respectively. The difference in the elevation of the tumor markers in both groups was statistically significant (p < 0.001). Table 3 shows the different imaging procedures that have been performed on the patients studied for the detection of pancreatic cysts. EUS has the most effective ability in correctly identifying pancreatic cysts (sensitivity 94.3%) and correctly identifying patients without pancreatic cysts (specificity 91.8%). Except for EUS, MRI appeared to be more specific than other imaging modalities. TAUS was the least sensitive and was comparable in specificity when compared with CT examination. Table 4 presents the final diagnosis of pancreatic cysts categorized by the type of cystic lesion and their association with benign and malignant outcomes.

Table 2: Chief complaints of the patients studied

Chief complains	Benign (n=85)	Malignant (n=35)	Total (n=120)	*p*-value
Vomiting	9(10.6)	12(34.3)	21(17.5)	0.002
Weight loss	21(24.7)	32(91.4)	53(44.2)	<0.001
Diarrhea	3(3.5)	3(8.6)	6(5.0)	0.249
History of DM	24(28.2)	16(45.7)	40(33.3)	0.065
Drug history for chronic diseases	5(5.9)	0(0.0)	5(4.2)	0.143
History of surgery	8(9.4)	6(17.1)	14(11.7)	0.230
History of pancreatitis	6(7.1)	3(8.6)	9(7.5)	0.775
Family history of hepato-pancreato-biliary disease	6(7.1)	1(2.9)	7(5.8)	0.372
Elevation of CA 19-9	11(12.9)	24(68.6)	35(29.2)	<0.001
Elevation of CA 125	4(4.7)	10(28.6)	14(11.7)	<0.001

Data were expressed as number and percentage. CA: cancer antigen; DM: diabetes millets. The data were analyzed using chi-square test.

Table 3: Imaging modalities for diagnosis of pancreatic cysts

Imaging modality	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
EUS (n=120)	94.3	91.8	82.5	97.5	92.5
MRI (n=21)	75.0	88.2	60.0	93.8	85.7
CT (n=20)	83.3	78.6	71.4	91.7	80.0
TAUS (n=78)	62.5	81.5	60.0	81.5	75.6

n: number; EUS: Endoscopic ultrasound; TAUS: Transabdominal Ultrasound; MRI: Magnetic Resonance Imaging; CT: Computed tomography; PPV: positive predictive value; NPV: negative predictive value.

According to our study, the commonest pancreatic cyst was SCN (40.0%, n=48), followed by IPMN (31.7%, n=38), then MCN (15.0%, n=18), and lastly simple cysts (13.3%, n=16). IPMN has a significant portion of malignant cases (62.9%), with only 18.8% being benign.

Table 4: Final diagnosis of pancreatic cysts

Type of cystic lesion	Benign (n=85)	Malignant (n=35)	Total (n=120)	*p*-value
SCN	48(56.5)	0(0.0)	48(40.0)	<0.001
IPMN	16(18.8)	22(62.9)	38(31.7)	
MCN	5(5.9)	13(37.1)	18(15.0)	
Simple	16(18.8)	0(0.0)	16(13.3)	

Data were expressed as number and percentage. SCN: Serous Cystic Neoplasm; IPMN: Intraductal papillary mucinous neoplasm; MCN: Mucinous Cystic Neoplasm. The data were analyzed using chi-square test.

The *p*-value indicates a significant association, suggesting that IPMN is more likely to be malignant. Like IPMN, MCN shows a considerable proportion of malignancy (37.1%). The *p*-value is likely significant (though not explicitly stated), highlighting the potential for malignancy in MCN. Simple pancreatic cysts are entirely benign (16 patients), further supporting the notion that simple cysts do not typically harbor malignancy.

DISCUSSION

This study aimed to investigate the sociodemographic characteristics, clinical presentations, and final diagnoses of pancreatic cysts in patients assessed via EUS-guided FNA. The findings indicate significant differences between benign and malignant cystic lesions, with key variables impacting patient outcomes. The data reveal a notable gender disparity, with a higher proportion of females diagnosed with benign cysts, while males predominantly presented with malignant forms. This finding aligns with existing literature suggesting gender differences in pancreatic pathologies. Similarly, a study by Atef *et al*. reported that 66.0% of benign tumors occurred in females, compared to 57.1% of malignant tumors in males [14]. consistent with our results, as most patients were female. Additionally, de Jong *et al*. found that females constituted the dominant gender among pancreatic cyst patients [15]. Most of the patients were female rather than male; this aligns with the results of Le et al., who documented the same result [15]. Also, de Jon *et al*. noticed that the dominant gender of the pancreatic cyst patients was female [10]. The primary complaints varied significantly, with weight loss and vomiting being more prevalent in malignant cases. The high incidence of weight loss in malignant patients underscores the need for timely intervention and further investigation when such symptoms arise. Elevated tumor markers, particularly CA 19-9 and CA 125, were strongly associated with malignancy, reinforcing their value as diagnostic tools in clinical practice. Unintentional weight loss in patients with pancreatic cancer is highly prevalent and contributes to low therapeutic tolerance, reduced quality of life, and increased mortality [17]. Hendifar *et al*. hypothesized that unintentional weight loss is notably high among individuals diagnosed with pancreatic cancer, with potential causes including anorexia, malabsorption, and/or cachexia. Approximately 85% of pancreatic cancer patients meet the traditional criteria for cancer cachexia, yet there is currently no documented method for managing this condition [18]. EUS is the most effective modality for diagnosing pancreatic cysts, demonstrating high sensitivity, specificity, and accuracy. MRI and CT provide moderate results, with MRI outperforming CT in terms of sensitivity and accuracy. TAUS is the least effective option, particularly in sensitivity, which may lead to missed

diagnoses. Therefore, EUS is recommended as the first-line imaging modality for evaluating pancreatic cysts, while MRI can serve as a useful alternative. The roles of CT and TAUS may be limited due to their lower effectiveness. Wesali *et al*. found that EUS had a sensitivity of 93.7%, specifically of 87.5%, and overall accuracy of 91.2% in distinguishing pancreatic cancer from benign conditions [19]. Du *et al*. reported that the EUS model achieved a diagnostic sensitivity of 98.5% (67/68) and a classification ability of 92.6% (63/68) for pancreatic cystic neoplasms, surpassing CT (73.1%, $p< 0.001$) and MRI (81.3%, $p= 0.001$; 20.3%, $p< 0.001$) by 17.1% and 13.1%, respectively [20]. In terms of final diagnoses, serous cystic neoplasms (SCN) were exclusively benign, whereas intraductal papillary mucinous neoplasms (IPMN) and mucinous cystic neoplasms (MCN) were significantly present in malignant cases. The predominance of SCN among benign lesions and the association of IPMN and MCN with malignancy emphasize the importance of cyst type in management strategies. Non-mucinous pancreatic cystic neoplasms, such as SCN and simple cysts, are benign; however, mucinous cystic neoplasms like IPMN and MCN have potential pathogenic implications [21]. Scholten et al. also noted that the most observed pancreatic cystic neoplasms are IPMN, MCN, and SCN [21].

Conclusion

This study sheds light on the sociodemographic characteristics, clinical presentations, and final diagnoses of pancreatic cysts identified with EUS-guided FNA. The findings reveal major disparities between benign and malignant cystic lesions, specifically a gender imbalance in which females are more frequently diagnosed with benign cysts and males have a higher prevalence of malignant forms. The findings highlight the significance of certain clinical signs, such as weight loss and elevated tumor markers, in guiding prompt therapies and diagnostic procedures. EUS appears to be the most effective imaging technique for diagnosing pancreatic cysts, underscoring its importance in clinical practice. The identification of cyst types enables deciding therapeutic options, as benign diseases such as serous cystic neoplasms have different consequences than mucinous versions. Ultimately, this study enhances our comprehension of pancreatic cysts and establishes the groundwork for future investigations that aim to elucidate the underlying mechanisms and develop preventive treatments for individuals at risk.

Conflict of interests

No conflict of interest was declared by the authors.

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Data sharing statement

Supplementary data can be shared with the corresponding author upon reasonable request.

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