Management of Pancreatic Cystic Neoplasms: Single Institutional Study

Original Article

Ahmad N. Sallam[1], Kerollous M.F. Faltas[2], Sameh Abokoura[3], Mohammad T. Badawy[1], Khaled A. Abu-elela[1], Hesham Abdeldayem[1]

Departments of [1]HPB Surgery, [3]Diagnostic and Intervention Radiology, National Liver Institute, Menoufia University, Menoufia, [2]Department of HPB Surgery and Liver Transplantation, Egypt Air Hospital, Cairo, Egypt.

ABSTRACT

Background: The term "pancreatic cystic neoplasms" refers to a heterogeneous group of pancreatic cysts that have different clinical, radiological, and pathological characteristics. These include intraductal papillary mucinous neoplasms (IPMN), mucinous cystic neoplasms, serous cystic neoplasms, and solid pseudopapillary neoplasms.

Patients and Methods: This is a retrospective study from January 2006 to September 2022 that involved 50 patients who proved to have pancreatic cystic lesions. Patient preoperative laboratory results, computed tomography (CT), MRI with magnetic resonance cholangiopancreatography and endoscopic ultrasound (EUS) with cystic fluid analysis findings, postoperative pathological findings, types of resection and postoperative morbidity, such as pancreatic leak, were all gathered for study.

Results: Receiver operating characteristic curve is used to show the sensitivity of the investigation in relation to the pathological outcome. The sensitivity of MRI and EUS in the detection of premalignant pancreatic cystic lesions is more than CT, with more prognosis, less morbidity, and early detection of premalignant lesions before turning to malignancy. Also, the results show that the pancreatic leak is less clinically significant with IPMN but with no statistical significance in relation to other pancreatic cystic lesions.

Management: Pancreatic cystic lesions with malignant potential are treated by close surveillance or surgical excision. Different types of resection include pancreatico-dudenectomy, distal pancreatectomy, enucleation, and total pancreatectomy.

Conclusion: There is a diagnostic and therapeutic dilemma in the management of pancreatic cystic lesions. The results in MRI and EUS in relation to the pathological outcome postresection were highly specific and very sensitive in comparison to the results of dynamic CT. Also, the cytological biomarkers with EUS confirm the diagnosis and have a strong relation to the pathological diagnosis postresection. The early detection with resection of the premalignant cystic lesion has a good prognosis with less oncological morbidity. Complications postresection are mostly pancreatic leak, which is less clinically significant in IPMN than other cysts without obvious statistical significance.

Key Words: Intraductal papillary mucinous neoplasms, Mucinous cystic neoplasm, Pancreatic cystic lesions, Serous cystic lesion, Solid pseudopapillary neoplasm.

Received: 14 November 2024, **Accepted:** 8 November 2024, **Published:** 01 April 2025

Corresponding Author: Kerollous M.F. Faltas, MD, Department of HPB Surgery and Liver Transplantation, Egypt Air Hospital, Cairo, Egypt. **Tel.:** 01288212439 , **E-mail:** kerollousmedhat@gmail.com

ISSN: 1110-1121, April 2025, Vol. 44, No. 2: 799-806, © The Egyptian Journal of Surgery

INTRODUCTION

True pancreatic cystic neoplasms (PCN) are mostly accidentally discovered with a wide range of incidence (2–45% incidence) [1].

True pancreatic cystic lesions are a group of cysts with varying clinical, radiological, and pathological features that pose a medical challenge because of their biological activity, which can range from benign to malignant disease [2].

These cysts are solid pseudopapillary neoplasms (SPN), serous cystic neoplasms "microcysts and macrocysts," mucinous cystic neoplasms (MCN), and intraductal papillary mucinous neoplasms (IPMN) "main duct, side-branch and mixed type" [3].

MCN, SPN, and IPMN are classified as premalignant cystic lesions and require either surgical excision or closed follow-up, whereas serous cystic neoplasms are often

DOI: 10.21608/EJSUR.2024.336510.1279

benign and do not require observation or resection unless symptomatic macrocysts [3].

The majority of PCN cases accidentally appear on cross-sectional imaging since the majority of PCN patients do not show classic pancreatic symptoms, including pancreatitis, jaundice, or newly diagnosed diabetes mellitus.

Acute pancreatitis may develop in patients with IPMN who have main duct involvement due to their high mucus production with mucous plugs and obstruction of the main duct, with aggravation of pancreatitis [4].

Mucus plugs in the common bile duct or direct tumor invasion can also cause jaundice. Jaundice and pancreatitis are typically associated with advanced neoplasia, while they can occasionally occur in PCN patients without advanced neoplasia [5].

Imaging characteristics

IPMN may be categorized morphologically into main duct, side branch, and mixed type (Fig. 1), which are categories based on where they are located and how they extend throughout the ductal system.

The major pancreatic duct's sudden dilatation is a sign of main duct-IPMN. The dilatation of the major pancreatic duct's side branches or the presence of a cystic lesion that resembles a grape can be used to identify side branch IPMN.

Figure 1 MRI study: branch-duct IPMN with typical cystic hyperintense appearance on T2-weighted images [6]. IPMN, intraductal papillary mucinous neoplasms.

Clinical and imaging signs that have been linked to an elevated risk of cancer and are described as "high-risk" or "worrisome" characteristics [7].

High-risk clinical features include obstructive jaundice without other explanation, recurrent pancreatitis due to a pancreatic cystic lesion, a significantly elevated serum carbohydrate antigen 19-9 level, or, if cytology is obtained, the presence of cells demonstrating high-grade dysplasia or neoplasia, and new-onset or worsening diabetes.

Worrisome characteristics include main pancreatic duct dilation greater than or equal to 5mm, cyst size greater than or equal to 3cm, and the presence of a solid component or mural nodule in the pancreatic cystic lesion.

Cyst fluid analysis

Measuring the tumor marker carcinoembryonic antigen (CEA) for separating mucinous from nonmucinous. An increased amount of amylase in the cyst fluid indicates a link between the cyst and the pancreatic ductal system (IPMN) (Table 1).

PATIENTS AND METHODS:

The hepato-pancreato-biliary medical record database of roughly 50 patients from the inpatient wards of the National Liver Institute's hepatobiliary and pancreatic surgery department was used in this retrospective analysis, which ran from January 2006 to September 2022.

The investigation included patients of all ages who had been diagnosed with pathologically confirmed true pancreatic cysts.

Patients having pseudocysts in the pancreas were not included.

Data were gathered at Menoufia University's National Liver Institute following institutional review board approval of the study procedure.

Data collection

Data were collected through a well-designed questionnaire and included the following.

Demography

Standard demographic variables, including age and sex.

Clinical presentation

After reviewing medical records, information about symptoms and medical history was gathered.

Preoperative laboratories

Serum tumor marker levels, pancreatic enzymes, and biomarkers for cystic content were among the baseline laboratory data that were also collected.

Preoperative radiology

Diagnostic modalities

Pancreatic protocol computed tomography (CT).

Gadolinium-enhanced MRI with magnetic resonance cholangiopancreatography (MRCP).

Endoscopic ultrasound (EUS) with cyst fluid cytology and biomarkers.

Cyst fluid analysis

Measuring the tumor marker CEA for separating mucinous from nonmucinous. An increased amount of amylase in the cyst fluid indicates a link between the cyst and the pancreatic ductal system (IPMN).

Intraoperative resection modalities

Data on operative treatment were collected.

Resections were classified according to the following categories:

(1) Whipple procedure (pancreatico-duodenectomy).

(2) Distal pancreatectomy.

(3) Enucleation.

(4) Total pancreatectomy.

Postoperative follow-up

Morbidities that arise during the first day to 30 days after surgery are known as postoperative complications, and they are defined as issues that call for radiologic, endoscopic, or surgical intervention.

Pancreatic leak issues were among the 30-day postoperative complications considered in our study.

Management

Patients with high-risk pancreatic cystic lesions and those with known high-risk malignancy, such as solid pseudopapillary tumors, mucinous cystic lesions, and main-duct IPMN, were referred for surgical excision based on postoperative correlation with the pathological outcome. These patients were identified by MRI, MRCP, or EUS and cystic biomarkers.

Any detectable quantity of intraabdominal fluids with an increased amylase level greater than three times the normal serum level after day 3 postoperatively was indicative of a postoperative pancreatic leak.

RESULTS:

Our study included 50 patients which discovered accidentally by enhanced CT by cystic pancreatic lesions, two (4%) patients had multicenteric pancreatic cystic lesion, 23(46%) patients had microcystic pancreatic lesion, eight (16%) patients had pancreatic head/uncinate process pancreatic lesions with PD dilatation, eight (16%) patients had pancreatic body/tail pancreatic lesions with PD dilatation, seven (14%) patients had pancreatic head/uncinate process macrocystic pancreatic lesions without PD dilatation, two (4%) patients had pancreatic body/tail macrocystic pancreatic lesions without PD dilatation (Table 2).

Our study included 50 patients which discovered accidentally by dynamic MRI with MRCP by cystic pancreatic lesions, one (2%) patient had multicenteric pancreatic cystic lesions with dilatation of main duct (multiloculated IPMN), seven (14%) patients had multiple side-branches pancreatic cystic lesions (side-branches-IPMN), five (10%) patients had pancreatic head/uncinate process cystic lesion with dilated duct (main duct-IPMN), four (8%) patients had pancreatic body and tail cystic lesion with dilated duct (main duct-IPMN), seven (14%) patients had macrocystic head/uncinate process lesion without dilated duct (mucinous cyst), nine (18%) patients had macrocystic body and tail lesion without dilated duct (mucinous cyst), 10(20%) patients had microcytic simple lesion (serous cyst), two (4%) patients had macrocystic simple lesion (serous cyst), two (4%) patients had pancreatic head solid lesion (SPN), three (6%) patients had pancreatic body and tail solid lesion (SPN) (Table 3).

Figure 2 show cross-tabulation between CT findings in relation to the findings of the pathology postresection, showing that CT has 51.6% sensitivity and 57.9% specificity.

Our study included 50 patients, two (4%) patient had multicenteric pancreatic cystic lesion, 23 (46%) patients had microcystic pancreatic lesion, eight (16%) patients had pancreatic head/uncinate process pancreatic lesions with PD dilatation, eight (16%) patients had pancreatic body/tail pancreatic lesions with PD dilatation, seven (14%) patients had pancreatic head/uncinate process macrocystic pancreatic lesions without PD dilatation, two (4%) patients had pancreatic body/tail macrocystic pancreatic lesions without PD dilatation.

Figure 3 shows cross-tabulation between MRI and MRCP findings in relation to the findings of the pathology postresection, showing that MRI with MRCP has 77.4% sensitivity and 94.7% specificity.

Our study included 50 patients, one (2%) patient had multicentric pancreatic cystic lesions with dilatation of main duct (multiloculated IPMN), seven (14%) patients had multiple side-branches pancreatic cystic lesions (side-branches IPMN), five (10%) patients had pancreatic head and uncinate process cystic lesion with dilated duct (main duct-IPMN), four (8%) patients had pancreatic body and tail cystic lesion with dilated duct (main duct-IPMN), seven (14%) patients had macrocystic head and uncinate process lesion without dilated duct (mucinous cyst), nine (18%) patients had macrocystic body and tail lesion without dilated duct (mucinous cyst), 10(20%) patients had microcytic simple lesion (serous cyst), two (4%) patients

had macrocystic simple lesion (serous cyst), two (4%) patients had pancreatic head solid lesion (SPN), three (6%) patients had pancreatic body and tail solid lesion (SPN).

Figure 4 show cross-tabulation between EUS findings in relation to the findings of the pathology postresection, showing that EUS has 67.7% sensitivity and 94.7% specificity:

(1) Our study included 50 patients.

(2) One patient had multicentric pancreatic cystic lesions with dilatation of the main duct (multiloculated IPMN) (2%).

(3) Seven patients had multiple side-branch pancreatic cystic lesions (side-branch IPMN) (14%).

(4)Five patients had a pancreatic head and uncinate process cystic lesion with dilated duct (main duct-IPMN) (10%).

(5) Four patients had pancreatic body and tail cystic lesions with dilated duct (main duct-IPMN) (8%).

(6) Seven patients had macrocystic head and uncinate process lesion without dilated duct (mucinous cyst) (14%).

(7) Nine patients had macrocystic body and tail lesions without dilated duct (mucinous cyst) (18%).

(8) Ten patients had microcytic simple lesions (serous cysts) (20%).

(9) Two patients had macrocystic simple lesions (serous cysts) (4%).

(10) Two patients had a pancreatic head solid lesion (SPN) (4%).

(11) Three patients had a pancreatic body and tail solid lesion (SPN) (6%).

Receiver operating characteristic curve is used to show the sensitivity of the investigation, MRI and EUS near 1 in the area under the curve than CT. This indicates the sensitivity of MRI and EUS more than CT in detecting pancreatic cystic lesions (Table 4 and Fig. 5).

Figure 6 shows cross-tabulation between pancreatic leak in relation to the various types of pancreatic cystic lesions according to the findings of the pathology postresection, showing that there is no statistically significant.

Our study included 50 patients, 17 patients with IPMN, four patients had postoperative pancreatic leak, 34 patients had other types of PCNs, eight patients had postoperative pancreatic leak.

Table 1: Differences between pancreatic cysts in biochemical cystic fluid analysis.

	IPMN cyst	Mucinous cyst	Serous cyst	Pseudocyst
Amylase	+ve	−ve	−ve	+ve
CEA	+ve	+ve	−ve	−ve
Mucin	+ve	+ve	−ve	−ve

CEA: Carcinoembryonic Antigen; IPMN: Intraductal Papillary Mucinous Neoplasms.

Table 2: Statistics of suspicious cystic pancreatic lesions by computed tomography.

	Frequency	Percent
Valid		
Pancreatic head and tail cystic hypodense lesions with dilatation of the main duct	2	4.0
Microcystic pancreatic lesion	23	46.0
Pancreatic head/uncinate process cystic hypodense lesion with dilatation of the main duct	8	16.0
Pancreatic body/tail cystic hypodense lesion with dilatation of the main duct	8	16.0
Pancreatic head/uncinate process macrocystic hypodense lesion without dilatation of the main duct	7	14.0
Pancreatic body/tail macrocystic hypodense lesion without dilatation of the main duct	2	4.0
Total	50	100.0

Table 3: Statistics of suspicious cystic and solid lesions by MRI and magnetic resonance cholangiopancreatography.

	Frequency	Percent
Valid		
Multicentric pancreatic cystic lesions with dilatation of the main duct (multiloculated IPMN)	1	2.0
Multiple side-branch pancreatic cystic lesions (side-branch IPMN)	7	14.0
Pancreatic head and uncinate process cystic lesion with dilated duct (main duct-IPMN)	5	10.0
Pancreatic body and tail cystic lesion with dilated duct (main duct-IPMN)	4	8.0
Macrocystic head and uncinate process lesion without dilated duct (mucinous cyst)	7	14.0
Macrocystic body and tail lesion without dilated duct (mucinous cyst)	9	18.0
Microcytic simple lesion (serous cyst)	10	20.0
Macrocystic simple lesion (serous cyst)	2	4.0
Pancreatic head solid lesion (solid pseudopapillary neoplasm)	2	4.0
Pancreatic body and tail solid lesion (solid pseudopapillary neoplasm)	3	6.0
Total	50	100.0

IPMN: Intraductal Papillary Mucinous Neoplasms.

Table 4: Receiver operating characteristic curve table shows the test result variables between computed tomography findings and MRI findings in detecting pancreatic cystic lesions.

Area under the curve	
Test result variable(s)	**Area**
MRI and MRCP findings	0.861
EUS findings	0.812
CT findings	0.548

CT: Computed Tomography; EUS: Endoscopic Ultrasound; MRCP: Magnetic Resonance Cholangiopancreatography. The test result variable; (s): MRI and MRCP findings; EUS findings, and CT findings have at least one tie between the positive actual state group and the negative actual state group. Statistics may be biased.

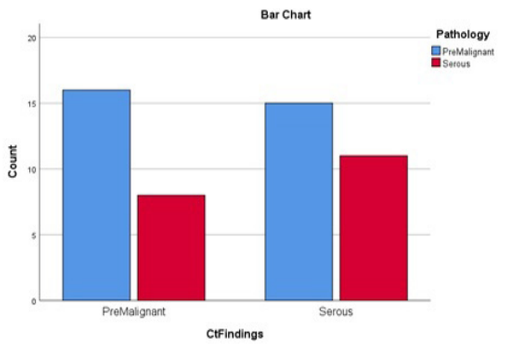

Fig. 2: CT findings; *: Pathology postresection cross-tabulation; CT: Computed Tomography.

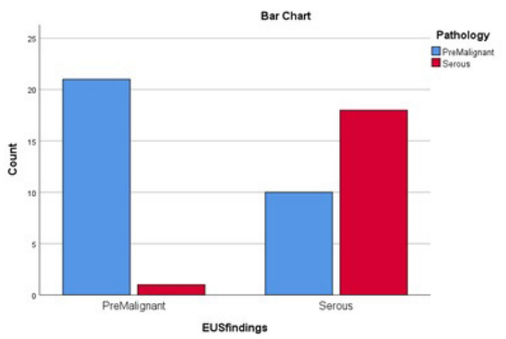

Fig. 4: EUS findings; *: Pathology Postresection Cross-tabulation; EUS: Endoscopic Ultrasound.

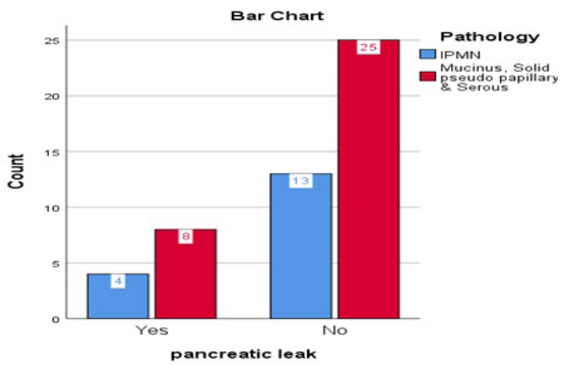

Fig. 6: Pancreatic leak; *: Pathology Cross-tabulation.

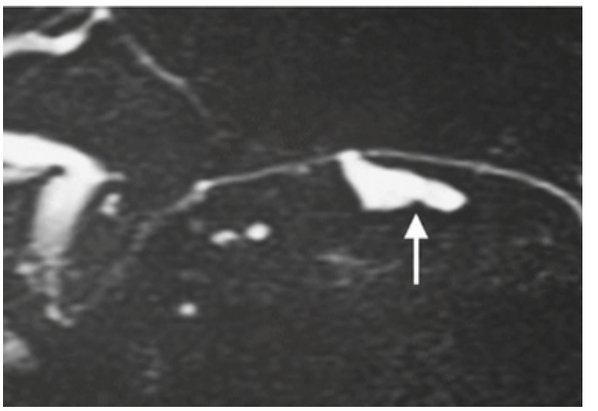

Fig. 1: MRI study: branch-duct IPMN with typical cystic hyperintense appearance on T2-weighted images [6]; IPMN: Intraductal Papillary Mucinous Neoplasms.

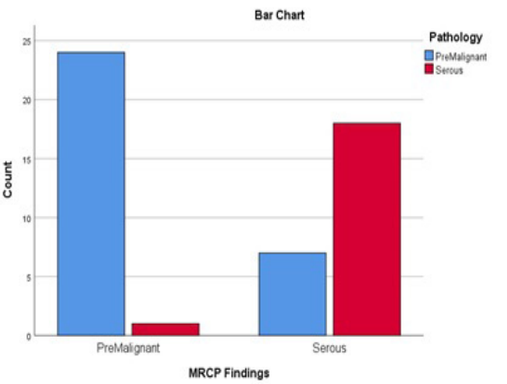

Fig. 3: MRI and MRCP findings; *: Pathology Postresection Cross-tabulation; MRCP: Magnetic Resonance Cholangiopancreatography.

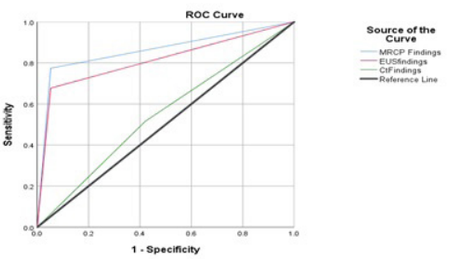

Fig. 5: ROC: Curve Shows Sensitivity and Specificity between CT findings and MRI findings in detecting pancreatic cystic lesions; CT: Computed Tomography; ROC: Receiver Operating Characteristic.

DISCUSSION

In our study, radiological assessment of pancreatic cystic lesions was variable from CT with contrast to MRI, MRCP, and even EUS.

There are obvious results in MRI and EUS accuracy compared to results from enhanced CT. As in enhanced CT, especially in microcysts and side-branch cysts, the accuracy was low (specificity 2% and sensitivity 58%). But the results in MRI and EUS in comparison with the pathological results postresection were highly specific and very sensitive (specificity 78% and sensitivity 95% for MRI and 68% sensitivity and 95% specificity for EUS).

According to a study by Taya *et al.,* [8], MRI, including MRCP sequences, is the most common method used for the diagnostic evaluation of pancreatic cystic lesions. This method is more accurate than multidetector CT.

These pancreatic cystic lesions were detected in 8% of imaging investigations as multidetector CT in a meta-analysis involving 48 860 asymptomatic patients [8].

In most cases, biochemical examination of pancreatic cyst fluids can distinguish mucinous from nonmucinous lesions that would appropriately prompt resection and distinguish IPMN from mucinous cystic lesions.

In a study by Thornton *et al*., [9], one meta-analysis of cytopathological cyst fluid analyses for differentiation between mucinous and nonmucinous, PCN reported a sensitivity of 54% and specificity of 93%.

Among biochemical analyses performed on pancreatic cystic fluid, the quantification of levels of the tumor marker CEA is the most useful for differentiation between mucinous and nonmucinous PCN [10].

A systematic review published as an Abstract in 2018 with individual patient data meta-analysis, however, showed an optimal cut-off value of 20ng/ml with sensitivity and specificity of 91 and 93%, respectively [11].

In our study, the cytological biomarkers with EUS confirm the diagnosis and have a strong relation to the pathological diagnosis postresection (68% sensitivity and 95% specificity). The cytological indicators of a mucinous neoplasm were the presence of background mucin and CEA cystic level. Cystic amylase level can distinguish between IPMN and mucinous cystic lesions.

In a study by Kang *et al.,* [12], the use of preoperative axial imaging studies to predict postoperative pancreatic fistula formation by characterizing its enhancement patterns. Preoperative imaging can provide some insight into important factors such as the consistency of the future remnant pancreas and also the presence of pancreatic ductal dilatation, as in IPMN. In a cohort of 29 patients undergoing pancreatic resection, MRI findings of a higher pancreas-to-muscle signal intensity ratio on T1 images were associated with a higher risk of postoperative pancreatic fistula.

In our study, we find that clinically the rate of postoperative pancreatic fistula is lower with IPMN due to the dilatation of the duct makes the anastomosis more efficient in Whipple operation and makes the closure easier in distal pancreatectomy in relation to other pancreatic cystic lesions. However, statistically, there is no specific significance between the two groups.

Our management of pancreatic fistula includes:

(1) Prevention of fistula:

By secured pancratico-jujonostomy anastomosis, external or internal pancreatic stenting, and pancreatic anastomotic glue.

(2) Management of fistula:

(a) Conservative management has the upper hand with good drainage of the leak and follow-up of the amount, amylase level, and culture from the drain.

(b) Follow up with complete blood count, C-reactive protein, and procalcitonin.

(c) Abdominal US or CT with percutaneous drainage if any collection.

(d) If there is blood vessels erosion from the leak, CT angiography with intervention, radiology embolism, or stenting for the erosive vessels.

CONCLUSION

True pancreatic cysts are unintentionally found during cross-sectional imaging, particularly in patients who have gastrointestinal symptoms, obstructive jaundice, or pancreatitis.

The probability of malignancy depends on the kind of pancreatic cystic lesion.

The best modalities for identifying high-risk and concerning characteristics, determining the type of cyst, and thus determining the management strategy

are dynamic MRI with MRCP and EUS with cyst biomarkers.

Surgery should be used to treat pancreatic cystic lesions with high-risk characteristics and those that have a known high risk of malignancy, such as solid pseudopapillary tumors, MCN, and main duct IPMNs.

Since advanced neoplasia is unlikely to arise in cysts that are asymptomatic and do not meet any high-risk criteria, such as serous cystic lesions and side-branch IPMN, active observation is advised.

Pancreatic leak, which is defined as any detectable volume of intraabdominal fluids with a high amylase level greater than three times the serum level, is the most common postoperative complication.

Pancreatic leaks are often treated conservatively.

Between the various kinds of pancreatic cystic lesions, there is still no statistically significant difference in postoperative pancreatic fistula. Clinically, however, IPMN has a lower rate of fistula because of the large duct and rather hard pancreas.

CONFLICT OF INTEREST

There are no conflicts of interest.

REFERENCES

1. Chang YR., Park JK., Jang JY., *et al.,* Incidental pancreatic cystic neoplasms in an asymptomatic healthy population of 21,745 individuals: large-scale, single-center cohort study. Medicine (Baltimore) 2016; 95:e5535.

2. Girometti R., Intini S., Brondani G., *et al*., Incidental pancreatic cysts on 3D turbo spin echo magnetic resonance cholangiopancreatography: prevalence and relation with clinical and imaging features. Abdom Imaging 2011; 36:196–205.

3. Tanaka M., Fernández-Del Castillo C., Kamisawa T., *et al.*, Revisions of international consensus Fukuoka guidelines for the management of IPMN of the pancreas. Pancreatology 2017; 17:738–753.

4. Tsutsumi K., *et al.*, A history of acute pancreatitis in intraductal papillary mucinous neoplasms of the pancreas is a potential predictive factor for malignant papillary subtype. Pancreatology 2010; 10:707–712.

5. Pelletier AL., *et al*., Acute pancreatitis in patients operated on for intraductal papillary mucinous neoplasms of the pancreas: frequency, severity, and clinicopathologic correlations. Pancreas 2010; 39:658–661.

6. Giovanni M., Mirko D., Paola C., *et al*., Imaging and Pathology of Pancreatic Neoplasms. Intraductal Papillary Mucinous Neoplasm (IPMN). Milano: Springer; 2015.

7. Ohtsuka T., Fernandez-Del Castillo C., Furukawa T., *et al*., International evidence-based Kyoto guidelines for the management of intraductal papillary mucinous neoplasm of the pancreas. Pancreatology 2023; 28.

8. Taya M., Hecht EM., Huang C., Lo GC., *et al*., Pancreatic cystic lesions: imaging techniques and diagnostic features. Gastrointest Endosc Clin N Am 2023; 33:497–518.

9. Thornton GD., *et al*., Endoscopic ultrasound guided fine needle aspiration for the diagnosis of pancreatic cystic neoplasms: a meta-analysis. Pancreatology 2013; 13:48–57.

10. Dumonceau JM., *et al*., Indications, results, and clinical impact of endoscopic ultrasound (EUS)-guided sampling in gastroenterology: European Society of Gastrointestinal Endoscopy (ESGE) clinical guideline — updated January 2017. Endoscopy 2017; 49:695–714.

11. van Huijgevoort NCM., *et al*., Su1347 — the diagnostic accuracy of carcinoembryonic antigen in differentiating mucinous and non-mucinous pancreatic cystic neoplasms — a systematic review and individual patient data meta-analysis. Gastroenterology 2018; 154 (Suppl. 1):S-528.

12. Kang JH., Park JS., Yu JS., *et al*., Prediction of pancreatic fistula after pancreatoduodenectomy by preoperative dynamic CT and fecal elastase-1 levels. PLoS ONE 2017; 12:e0177052.

13. Berland LL., *et al*., Managing incidental findings on abdominal CT: white paper of the ACR Incidental Findings Committee. J Am Coll Radiol 2010; 7:754–773.

14. Waters JA., *et al.*, CT vs MRCP: optimal classification of IPMN type and extent. J Gastrointest Surg 2008; 12:101–109.

15. Sugiyama M., Atomi Y. Intraductal papillary mucinous tumors of the pancreas: imaging studies and treatment strategies. Ann Surg 1998; 228:685–691.

16. Al- Rashdan A., et al., Fluid analysis prior to surgical resection of suspected mucinous pancreatic cysts. A single centre experience. J Gastrointest Oncol 2011; 2:208–214.

17. Wu J., *et al.,* Whole-exome sequencing of neoplastic cysts of the pancreas reveals recurrent mutations in components of ubiquitin-dependent pathways. Proc Natl Acad Sci USA 2011; 108:21188–21193.

18. Majumder S., Philip NA., Singh Nagpal SJ., *et al.*, High-grade dysplasia in resected main-duct intraductal papillary mucinous neoplasm (MD-IPMN) is associated with an increased risk of subsequent pancreatic cancer. Am J Gastroenterol 2019; 114:524–529.

19. Mirko D., Giorgia T., Nicolò C., *et al*., Magnetic resonance (MR) for mural nodule detection studying intraductal papillary mucinous neoplasms (IPMN) of pancreas: Imaging-pathologic correlation. Pancreatology. 2021; 21:180–187.