Mucinous Pancreatic Cysts: Comparison of Cyst Size and Location in Certain Mucinous Cyst Subgroups

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ABSTRACT

Background: *There are studies reporting that the location of intraductal papillary mucinous neoplasia (IPMN) predicts malignancy. Therefore, we evaluated the cyst location's relationship with malignancy, and the possibility of using cyst size and location to distinguish between non-main duct (non-MD)-IPMNs, mucinous cystic neoplasia (MCN), and cystic pancreatic ductal adenocarcinoma (PDAC).*

Methods: *We performed a retrospective analysis of data from 122 patients with a definite cyto-histological diagnosis of non-MD-IPMNs, LR-MCNs, and cystic PDACs via endoscopic ultrasound fine-needle aspiration between October 2011 and October 2020. We grouped the cyst locations as head, uncinate, neck (HUN), and corpus or tail (CT). On histology, low-grade dysplasia and intermediate-grade dysplasia were considered low risk (LR), whereas high-grade dysplasia and invasive carcinoma were considered high risk (HR).*

Results: *Of the 122 patients (61 (50%) women, median age 61.5 years (range 19-85), there were 34 (27.9%) LR-non-MD-IPMNs, 33 (27%) HR-non-MD-IPMNs, 19 (15.6%) LR-MCNs, and 36 (29.5%) cystic PDACs. We found no significant difference between LR- and HR-non-MD-IPMN locations (P = .803). Low-risk non-MD-IPMNs were significantly smaller than HR-non-MD-IPMNs (P < .001), LR-MCNs (P = .002), and cystic PDACs (P < .001). The area under the receiver operating characteristic curve (AUROC) was 0.819 (95% CI: 0.716-0.902; P < .0001), and demonstrated a cyst size cut-off <2.2 cm to differentiate LR cysts, while cysts <1.6 cm had a negative predictive value (NPV) of 100% in non-MD-IPMNs.*

Conclusion: *Cyst location is not predictive of malignancy in non-MD-IPMNs. Low-risk non-MD-IPMNs were smaller than HR-non-MD-IPMNs, LR-MCNs, and cystic PDACs. The cyst size cut-off was 2.2 cm; however, <1.6 cm had a 100% NPV differentiating LR- from HR-non-MD-IPMNs.*

Keywords: *Pancreatic mucinous cysts, cyst size, cyst location, intraductal papillary mucinous neoplasia, cystic pancreatic cancer*

INTRODUCTION

Pancreatic cystic lesions (PCLs) are divided into 2 groups according to mucin content, as mucinous and non-mucinous. Mucinous PCLs have a 15% risk of malignancy.[1] Intraductal papillary mucinous neoplasms (IPMNs), mucinous cystic neoplasms (MCNs), intraductal oncocytic papillary neoplasms, cystic changes in ordinary ductal adenocarcinomas, and other invasive carcinomas, such as cystic pancreatic ductal adenocarcinoma (PDAC), are included in the mucinous PCL group.[2]

For predicting whether neoplastic cysts need surgery or conservative management, the frequently used methods in diagnosis are cross-sectional imaging and endoscopic ultrasonography (EUS), with or without fine-needle aspiration (FNA). Also, in recent years, there are many emerging techniques such as needle-based confocal laser endomicroscopy, microforceps biopsy from the cyst wall, and DNA and molecular analysis of the cystic fluid for cyst evaluation.[3]

When pancreatic cysts are detected in cross-sectional or EUS imaging, compliance with the criteria described in guidelines such as Fukuoka 2012, AGA 2015, Revised Fukuoka 2017, and AGA 2018 is being investigated, since there is not a single gold standard test to make a definitive diagnosis. However, the determinants of these criteria are unfortunately limited to detect early malignancy in mucinous PCLs.[4-7]

Cyst sizes are essential in identifying malignant cysts, but size alone is insufficient to predict malignancy (8). Also, in many studies conducted on IPMNs earlier, it has been stated that the location of the cyst in the head or uncinate or neck (HUN) of the pancreas predicts malignancy.[9-14] Accordingly, we aimed to compare cyst location

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and size to evaluate the relationship between cyst location and malignancy and distinguish between non-main duct (non-MD)-IPMNs, MCNs, and cystic PDACs, which have been diagnosed cyto-histologically.

METHODS

Study Design and Participants

Demographic data, medical history, and cross-sectional imaging results were retrieved from the electronic medical records of 122 cyto-histologically diagnosed mucinous PCL patients evaluated with EUS-FNA at an academic tertiary medical center between October 2011 and October 2020. We included non-MD-IPMNs, benign MCNs, and cystic PDACs from the mucinous PCL group. We excluded all patients with main duct (MD)-IPMNs and pancreatic PDACs without cystic components. We removed MD-IPMNs because these lesions had high malignant potential and did not have apparent cystic formations. Where available, the results of patient demographic data, EUS findings, and cytological or histopathological diagnoses were recorded from the electronic database. All procedures were carried out according to the principles in the Declaration of Helsinki. The local ethics committee approved the study protocol for this retrospective study (03/68. February 16, 2021).

Endoscopic Ultrasound Technique

All patients underwent EUS examination (Pentax; A121091, H121645, H121435, H121637; Pentax Medical Co., Montvale, NJ, USA; Fujinon K1U047K062) after checking their coagulation status, international normalized ratio, and adequate platelet count. Any anticoagulant or antiplatelet drug was replaced with subcutaneous low-molecular-weight heparin before the procedure to obtain adequate coagulation. Endoscopic ultrasound-FNA was performed with either a 22- or 25-gauge FNA needle (Cook Medical, Bloomington, IN, USA, or Boston Scientific, Marlborough, MA, USA). All patients received prophylactic, single-dose, intravenous antibiotics before the procedure.

MAIN POINTS

- *We found that the location of benign and malignant cysts in non-main duct (non-MD)-intraductal papillary mucinous neoplasia (IPMN) did not differ significantly between pancreas head or uncinate or neck (HUN) and corpus or tail (CT).*
- *Low-risk (LR) non-MD IPMNs' sizes were significantly smaller than high risk (HR) non-MD-IPMNs, LR mucinous cystic neoplasia (MCN), and cystic pancreatic ductal adenocarcinoma (PDAC).*
- *Our single-center results determined the cyst size cut-off value of 2.2 cm among LR/HR non-MD-IPMNs by calculating the area under the receiver operating characteristic curve (AUROC), with 87.8% sensitivity, 67.6 % specificity, 72.5 % positive predictive value (PPV), and 85.2 % negative predictive value (NPV).*
- *We found the NPV of cysts below 1.6 cm as 100% to differentiate LR cysts in non-MD-IPMNs.*

Diagnostic Criteria for Pancreatic Cystic Lesions

Endoscopic Ultrasound Imaging

After the EUS evaluation of the cyst morphology and location and the demographic and clinical data, a preliminary diagnosis was made. Cyst locations were divided into 2 groups. Cysts in the HUN were included in group 1, and cysts in the corpus or tail (CT) were included in group 2.

Cytology

The cystic fluid aspirate was analyzed for cell morphology and mucin presence. All cytological analyses were carried out or reviewed by an expert cytopathologist. Sample reports were categorized as diagnostic (with mucinous epithelium) or non-diagnostic (samples that contained either a non-mucinous epithelium or no epithelial cells).

Histology

Histological interpretations of the surgical specimens were performed or reviewed by the study pathologist. For MCN diagnosis, an ovarian-type stroma was required. The World Health Organization classification system was used to categorize the resected cystic lesions.[15] Pathological diagnosis was established following the 2010 WHO classification and the Baltimore consensus meeting, according to which a mucinous epithelium was graded based on the degree of cytoarchitectural dysplasia as LR, low-grade dysplasia (LGD), or intermediate-grade dysplasia (IGD), or HR, high-grade dysplasia (HGD) or invasive carcinoma (16). Therefore, the resected MCNs and IPMNs were classified as LR (LGD or IGD) or HR (HGD or invasive carcinoma).

Final Diagnosis

According to the suggestions of valid guidelines such as Fukuoka 2012, AGA 2015, Revised Fukuoka 2017, or ACG 2018,[4-7] the approach to patients was based on multidisciplinary council decisions. The final diagnosis was based

on cytohistological examination of surgical resection specimens or EUS-FNA of a solid component or cyst wall.

Data Collection

All data were retrospectively collected from an electronic database. The study group consisted of patients with specific final diagnoses based on cytology or specimen histology. The receiver operating characteristic (ROC) curve was plotted for cyst sizes to differentiate LR-non-MD-IPMNs from HR-non-MD-IPMNs. The area under the ROC curve (AUROC) was calculated. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated for cyst size cut-off level to maximize the ratio of correct diagnoses of HR-non-MD-IPMNs.

Statistical Analysis

All statistical analyses were done with SPSS Statistics software version 25 (IBM Corp., Armonk, NY, USA) and MedCalc Statistical Software version 19.2.5 (MedCalc Software Ltd., Ostend, Belgium; https://www.medcalc.org; 2020). The Kolmogorov–Smirnov and Shapiro–Wilk tests indicated a non-parametric data distribution. Descriptive analyses have been presented using median (min-max) for non-parametric and ordinal variables. Categorical variable comparisons were made using the chi-square or Fisher's exact (for cases with frequencies lower than 5) tests, as appropriate. Cyst size was compared among the 4 cyst types: LR-MCNs, LR-non-MD-IPMNs, HR-non-MD-IPMNs, and cystic PDACs using the non-parametric Kruskal–Wallis test. When the Kruskal–Wallis test results were statistically significant, the 4 groups were compared in pairs in a total of 6 comparisons using the Mann–Whitney test. We used Bonferroni's adjustment. The group included 4 subgroups (LR-MCNs, LR-non-MD-IPMNs, HR-non-MD-IPMNs, and cystic PDACs). Due to multiple pairwise comparisons, a *P*-value of <.013 was required for significance. Cyst size data were used to plot a ROC curve to differentiate LR-non-MD-IPMNs from HR-non-MD-IPMNs, and the AUROC was calculated. The AUROC was defined as low (0.5 to <0.7), moderate (0.7 to <0.9), or high (≥0.9). MedCalc Statistical Software version 19.2.5 (MedCalc Software Ltd., Ostend, Belgium; https://www.medcalc.org; 2020) was used to accurately determine the cyst size cut-off level diagnostic differentiation of LR-non-MD-IPMNs from HR-non-MD-IPMNs. A *P*-value of <.05 was considered significant.

RESULTS

Patient Characteristics

Of the cyto-histologically diagnosed cases, 122 patients (median age 61.5 years, range, 19-85 years; 61 (50 %) women) were included. The demographic data, diagnostic methodology, and available cytological and histopathological results of patients are shown in Table 1.

Comparison of Locations Among Non-main duct-IPMNs, Low-risk-Mucinous Cystic Neoplasias, and Cystic Pancreatic Ductal Adenocarcinomas

LR-MCNs were significantly CT localized when compared to non-MD-IPMNs and cystic PDACs. While LR/HR non-MD-IPMNs were primarily located in the HUN of the pancreas, cystic PDACs were mainly located in the CT but were not significant (Table 2).

Table 1. Baseline Patient Characteristics and Cyst Types (n = 122)

Characteristic	Data
Age, y , median (min-max)	61.5 (19-85)
Female	59 (19-80)
Male	65 (36-85)
Gender*	122
Female	61 (50)
Male	61 (50)
Cyto-histology*	122 (100)
FNA cytology	106 (86.8)
Resection material	50 (40.9)
Cyst types with final diagnosis*	122 (100)
LR-non-MD-IPMNs	34 (27.9)
HR-non-MD-IPMNs	33 (27)
LR-MCNs	19 (15.6)
Cystic PDACs	36 (29.5)
Cyst diameter in subgroups (mm), median (min-max)	
LR-non-MD-IPMNs	20 (9-60)
HR-non-MD-IPMNs	35.0(17-90)
LR-MCNs	45.0 (10-130)
Cystic PDACs	37.5 (12-80)
Location (HUN/CT)	
LR-non-MD-IPMNs	20 (61.8)/13 (38.2)
HR-non-MD-IPMNs	18 (54.5)/14 (42.4)
LR-MCNs	1 (5.3)/18 (94.7)
Cystic PDACs	16 (44.4)/20 (55.6)

*Values are represented as n (%).
CT, corpus or tail; FNA, fine-needle aspiration; HR; high risk, HUN, head or uncinate or neck; IPMN, intraductal papillary mucinous neoplasia; LR; low risk; MCN, mucinous cystic neoplasia; MD, main duct; PDAC, pancreatic ductal adenocarcinoma; y, years.

Table 2. Comparison of Locations Among Non-MD-IPMNs, LR-MCNs, and cystic PDACs

Cyst Types		Location		*P*
		HUN	CT	
IPMN*	LR	21 (61.8)	13 (38.2)	.803
	HR	18 (56.3)	14 (43.8)	
IPMN* vs LR-MCN	All IPMNs*	39 (59.1)	27 (40.9)	<.001
	LR-MCNs	1 (5.3)	18 (94.7)	
LR-MCN vs Cystic PDAC	Cystic PDAC	16 (44.4)	20 (55.6)	.002
	LR-MCNs	1 (5.3)	18 (94.7)	
LR-IPMN* vs Cystic PDAC	LR-IPMN*	21 (56.8)	13 (39.4)	.161
	Cystic PDAC	16 (44.4)	20 (55.6)	
HR-IPMN* vs Cystic PDAC	HR-IPMN*	18 (56.3)	14 (43.8)	.466
	Cystic PDAC	16 (44.4)	20 (55.6)	

Values are represented as n (%).
*Non-main duct.
P shows the differences between the groups and significant <.05.
CT, corpus or tail; HR; high risk, HUN, head or uncinate or neck; IPMN, intraductal papillary mucinous neoplasia; LR; low risk; MCN, mucinous cystic neoplasia; PDAC, pancreatic ductal adenocarcinoma.

Distribution of Cysts by Gender in Non-main duct-IPMNs and Cystic Pancreatic Ductal Adenocarcinomas

When we evaluated cyst location according to gender, we found that cysts in women were significantly located on CT (*P* = .002). After MCNs were excluded, we compared the location of non-MD-IPMNs and cystic PDACs between females and males. CT placement was higher in females (56%), while HUN placement was higher in males (60.7%), but we found no significant difference (*P* = .109). Among HR-non-MD-IPMNs, cysts were present in both regions of the pancreas in a female patient.

Evaluation of Cyst Sizes Between Non-main duct-IPMNs, Low-risk Mucinous Cystic Neoplasias, and Cystic Pancreatic Ductal Adenocarcinomas

We found that cyst sizes in LR-non-MD-IPMNs were significantly smaller than LR-MCNs, HR-non-MD-IPMNs, and cystic PDACs. The significance persisted after Bonferroni correction (*P* < .013). Besides, we found no significant difference in cyst sizes between LR-MCNs, HR-non-MD-IPMNs, and cystic PDACs (Table 3).

The Results of Our Center in Determining Cyst Size Cut-Off Value Between LR and HR Cysts in Non-main Duct-IPMNs

We calculated the cyst size cut-off value to differentiate LR cysts from HR cysts using the ROC curve in non-MD-IPMNs (Figure 1).

Table 3. Comparison of Cyst Sizes Between Mucinous PCL Subgroups

Mucinous Cysts Types (n = 122)	Cyst Size, cm, Median (Min-Max)	*P*-value
LR-MCNs (n = 19)	4.5 (1-13)	<0.001¥, 0.002*, <0.001**, <0.001***, 0.487†, 0.634‡, 0.295
LR-non-MD IPMNs (n = 34)	2 (0.9-6)	
HR-non-MD IPMNs (n = 33)	3.5 (1.7-9)	
Cystic PDACs (n = 36)	3.75 (1.2-8)	

P shows the differences between all groups. ¥Kruskal–Wallis test: LR-nonMD IPMN versus LR-MCN versus HR-nonMD IPMN versus Cystic-PDAC.
P shows the differences among the two groups, significant <.05. Mann–Whitney U test: *LR-non-MD IPMN versus LR-MCN, **LR versus HR-non-MD IPMN, ***LR-non-MD IPMN versus cystic PDAC, †HR-nonMD IPMN versus LR-MCN, ‡HR-non-MD IPMN versus cystic PDAC, ¶Cystic PDAC versus LR-MCN.
LR; low risk, HR; high risk, MCN, mucinous cystic neoplasm; MD, main duct; IPMN, Intraductal papillary mucinous neoplasm; PDAC, pancreatic ductal adenocarcinoma.

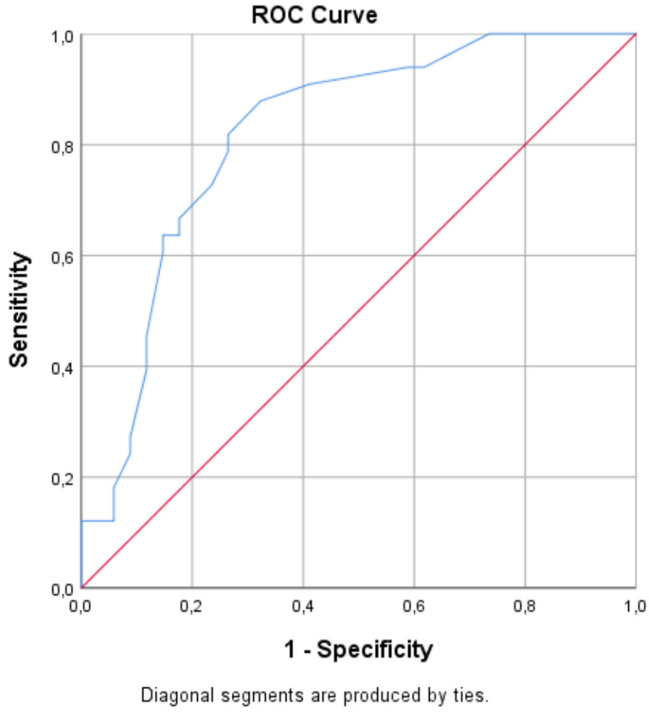

Figure 1. ROC analysis to differentiate LR/HR-non-MD-IPMNs. Cyst size cut-off value >2.2 cm resulted in an AUC of 0.819 (95% CI: 0.716 to 0.902) (*P* < .0001).

Using AUROC calculation, we detected a cut-off of 2.2 cm between LR cysts and HR cysts in the non-MD-IPMN group. We found the diagnostic validation of 2.2 cm cut-off value between LR cysts and HR cysts as: sensitivity, 87.8%; specificity, 67.6%; PPV, 72.5%; and NPV, 85.2%. Besides, according to ROC analysis results, the NPV of cysts below 1.6 cm was 100%.

When we evaluated the cysts below 2.2 cm in the non-MD-IPMN group, we found that the cyst size of 10 patients with LR was 2.2 cm and above. Seven of them were sent for resection according to the decision of the multidisciplinary council, and 3 of them had a conservative follow-up for 11, 60, and 60 months, respectively. On the other hand, we found that 3 patients (2 cytological, 1 resected) with a cyst size of 2.2 cm or less (1.7, 1.7, and 2.2 cm, respectively) were diagnosed with HR-non-MD-IPMN. However, we did not detect any signs of malignancy in cysts smaller than 1.6 cm in the non-MD-IPMN group.

DISCUSSION

In this study, we compared the localization areas and cyst sizes between LR- and HR-non-MD-IPMNs, LR-MCNs, and cystic PDACs. We included 122 (61 (50%) women), median age 61.5 years, (range 19-85)) patients with a definite cyto-histological diagnosis in this retrospective study. Of these patients, 34 (27.9%) were diagnosed with LR-non-MD-IPMNs, 33 (27%) with HR-non-MD-IPMNs, 19 (15.6%) with LR-MCNs, and 36 (29.5%) with cystic PDACs.

We compared the locations and sizes of the cysts between these specific mucinous PCL subgroups. Accordingly, we found that cysts were significantly localized in HUN in men and CT in women (P = .002). In this study, we detected all MCNs in women and they were located in the CT region. Therefore, we have determined that the location of cysts in LR-MCNs is significantly different from non-MD-IPMNs and cystic PDACs (P < .001 and P = .002, respectively).

Jun et al. concluded that cyst size and location were not significant in predicting invasive IPMNs.[17] However, most recently, Kerlakian et al. stated that among IPMNs, those located in the HUN region significantly predicted malignancy.[9] Also, older studies are supporting this conclusion of Kerlakian et al.[9-14] In this study, when we compared the LR and HR cyst locations in the non-MD-IPMN group, we found that LR (60%) and HR (56.3%) cysts were located more often in the HUN region, but this was not significant (P = .812). In addition, we did not find a significant localization difference between cystic PDACs and LR or HR-non-MD-IPMNs (P = .161 and .466, respectively). However, studies that find significant HUN localization in malignant IPMNs might have a selection bias, since they only cover patients with resection. Therefore, our study data includes not only those that suggested for resection but also the conservative oncologic management patients in whom we made a definitive diagnosis with adjunct cytological findings in addition to cross-sectional and EUS imaging diagnoses.

The current PCL surveillance guidelines define that the cyst size cut-off value is determined as 3 cm in the differentiation of benign and malignant IPMNs.[4-7] We found the optimal cyst size cut-off value to discriminate LR cysts to be 2.2 cm, with a significant AUROC 0.831 (95% CI: 0.716 to 0.914) in non-MD-IPMNs (P < .0001) (Figure 1). The diagnostic ability of this cut-off level to differentiate LR cysts in non-MD-IPMNs had a sensitivity of 87.8%, specificity of 67.6%, a PPV of 72.5%, and a NPV of 88.2%. Han et al.[18] followed-up 1369 BD-IPMN patients with a cyst size of less than 3 cm with cross-sectional imaging (CT) at regular intervals for a median of 62 months, and they were able to detect HR cysts in only 13 (0.9%) of 46 patients who were operated on with HR findings.

While evaluating non-MD-IPMN cyst sizes with the ROC curve, we found the NPV of cysts below 1.6 cm for malignancy as 100%. This cut-off value is consistent with the results of 2 sizeable 5-year follow-up studies conducted in BD-IPMNs in recent years.[19,20] Pergolini et al.'s 5-year BD-IPMN surveillance study found that cyst sizes were ≤1.5 cm in 108 (30%) patients out of 577 BD-IPMN patients. In addition, they observed that malignancy developed in only 1 patient (0.9%) in the follow-up of this 108-patient subgroup over 5 years.[21] Accordingly, they stated that the cut-off value of ≤1.5 cm showed an NPV for malignancy of 99%. Therefore, our cyst size cut-off with an NPV of 100% is the same as Pergolini et al. with a value of <1.6 cm. However, there are some differences between our cohort and the cohorts of the other 2 studies. The first difference is that most patients (459, 79.5%) in the 577-PCL group of Pergolini et al. were diagnosed only by MRI, CT, and EUS imaging. Similarly, Crippa followed 144 patients diagnosed with magnetic resonance imaging (MRI) for 5 years and reported the development of malignancy as an independent predictor in patients with cyst size >1.5 cm at the time of diagnosis.[19] However, our cohort consisted of 77 non-MD-IPMNs with gold standard cyto-histologic confirmation, in addition to cross-sectional and EUS imaging. The second difference is that while Crippa et al.'s and Pergolini et al.'s cohorts consisted of only BD-IPMNs, our cohort consisted of mixed-type IPMNs and BD-IPMNs.[19,21] Accordingly, we may exclude the possibility of malignancy in non-MD-IPMNs below 1.6 cm, at least at the time of diagnosis. Additionally, Crippa et al., Pergolini et al., and Lee et al. stated that cysts ≤1.5 cm

in BD-IPMNs have a much lower risk of malignant transformation than cysts >1.5 cm in the first 5 years of follow-up.[19-21]

In this study, we found that LR-non-MD-IPMNs were significantly smaller than HR-non-MD-IPMNs ($P < .001$), LR-MCNs ($P = .003$), and cystic PDACs ($P < .001$). Besides, we did not find a significant difference in cyst sizes between HR-non-MD-IPMNs, cystic PDACs, and LR-MCNs.

The strengths of our study include that in addition to the data of patients who underwent resection in our study, we think that the current study is more applicable to real-life data since it includes data from patients with cytological diagnosis. Therefore, we think that our study results reflect the relationship between cyst localization and malignancy prediction more accurately in terms of "real-life data" in non-MD-IPMNs.

The limitation of our study is that it is a retrospective single-center study utilizing a single-center cohort. This may or may not limit the generalizability of our results.

In conclusion, the location of the cyst is not predictive of malignancy in non-MD-IPMNs. LR-non-MD-IPMNs were the smallest among HR-non-MD-IPMNs, LR-MCNs, and cystic PDACs. According to our single-center data, the optimal cyst size cut-off value to discriminate LR cysts was 2.2 cm, and cysts below 1.6 cm had a 100% NPV in non-MD-IPMNs.

Ethics Committee Approval: Authors declared that the research was conducted according to the principles of Helsinki "Ethical Principles for Medical Research Involving Human Subjects".

Informed Consent: Since our study was designed as a retrospective study, we did not obtain informed consent from the patients.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – İ.H.K., H.Ş.; Design - İ.H.K., Ş.E., Z.G.; Supervision - H.Ş., Ş.E., F.U.M.; Resource - H.Ş., Ş.E., F.U.M.; Materials - H.Ş., Z.G., F.U.M.; Data Collection and/or Processing - İ.H.K.; Analysis and/or Interpretation - İ.H.K.; Literature Search - İ.H.K., H.Ş.; Writing - İ.H.K.; Critical Reviews - H.Ş., Ş.E., Z.G.

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REFERENCES

1. Al-Haddad M, El Hajj II, Eloubeidi MA. Endoscopic ultrasound for the evaluation of cystic lesions of the pancreas. JOP. 2010;11(4):299-309.
2. Basturk O, Coban I, Adsay NV. Pancreatic Cysts: Pathologic classification, differential diagnosis, and clinical implications. Arch Pathol Lab Med. 2009;133(3):423-438. [CrossRef]
3. ASGE Standards of Practice Committee, Muthusamy VR, Chandrasekhara V, et al. The role of endoscopy in the diagnosis and treatment of inflammatory pancreatic fluid collections. Gastrointest Endosc. 2016;83(3):481-488. [CrossRef]
4. Tanaka M, Fernández-del Castillo C, Adsay V, et al. International consensus guidelines 2012 for the management of IPMN and MCN of the pancreas. Pancreatology. 2012;12(3):183-197. [CrossRef]
5. Vege SS, Ziring B, Jain R, et al. American Gastroenterological Association institute guidelines on the diagnosis and management of asymptomatic neoplastic pancreatic cysts. Gastroenterology. 2015;148(4):819-22; quize12. [CrossRef]
6. 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(5):738-753. [CrossRef]
7. Elta GH, Enestvedt BK, Sauer BG, Lennon AM. ACG clinical guideline: Diagnosis and management of pancreatic cysts. Am J Gastroenterol. 2018;113(4):464-479. [CrossRef]
8. Kaplan JH, Gonda TA. The use of biomarkers in the risk stratification of cystic neoplasms. Gastrointest Endosc Clin N Am. 2018;28(4):549-568. [CrossRef]
9. Kerlakian S, Dhar VK, Abbott DE, et al. Cyst location and presence of high-grade dysplasia or invasive cancer in intraductal papillary mucinous neoplasms of the pancreas: A seven-institution study from the central pancreas consortium. HPB (Oxford). 2019;21(4):482-488. [CrossRef]
10. Park J, Lee KT, Jang TH, et al. Risk factors associated with the postoperative recurrence of intraductal papillary mucinous neoplasms of the pancreas. Pancreas. 2011;40(1):46-51. [CrossRef]
11. Yogi T, Hijioka S, Imaoka H, et al. Risk factors for postoperative recurrence of intraductal papillary mucinous neoplasms of the pancreas based on a long-term follow-up study: Proposals for follow-up strategies. J Hepatobil Pancreat Sci. 2015;22(10):757-765. [CrossRef]
12. Shin SH, Han DJ, Park KT, et al. Validating a simple scoring system to predict malignancy and invasiveness of intraductal papillary mucinous neoplasms of the pancreas. World J Surg. 2010;34(4):776-783. [CrossRef]
13. Suzuki Y, Nakazato T, Yokoyama M, et al. Development and potential utility of a new scoring formula for prediction of malignant intraductal papillary mucinous neoplasm of the pancreas. Pancreas. 2016;45(9):1227-1232. [CrossRef]
14. Li B, Shi X, Gao S, et al. Nomogram for the prediction of high-grade dysplasia and invasive carcinoma in patients with intraductal papillary mucinous neoplasms of the pancreas based on variables of noninvasive examination. Front Oncol. 2021;11:609187. [CrossRef]
15. Adsay NV, Fukushima N, Furukawa T, et al. Intraductal neoplasms of the pancreas. In: Bosman FT, Caneiro F, Hruban RH, Theise ND, eds. WHO Classification of Tumors of the Digestive System. Lyon; 2010:304-313.
16. Basturk O, Hong SM, Wood LD, et al. A revised classification system and recommendations from the Baltimore Consensus meeting for neoplastic precursor lesions in the pancreas. Am J Surg Pathol. 2015;39(12):1730-1741. [CrossRef]

17. Jun DY, Kwon HJ, Kim SG, et al. Predictive factors for invasive intraductal papillary mucinous neoplasm of the pancreas. Korean J Hepatobiliary Pancreat Surg. 2011;15(4):237-242. [CrossRef]
18. Han Y, Lee H, Kang JS, et al. Progression of pancreatic branch Duct Intraductal Papillary Mucinous Neoplasm Associates With Cyst Size. Gastroenterology. 2018;154(3):576-584. [CrossRef]
19. Crippa S, Pezzilli R, Bissolati M, et al. Active surveillance beyond 5 years is required for presumed branch-duct intraductal papillary mucinous neoplasms undergoing non-operative management. Am J Gastroenterol. 2017;112(7):1153-1161. [CrossRef]
20. Lee BS, Nguyen AK, Tekeste TF, et al. Long-term follow-up of branch-duct intraductal papillary mucinous neoplasms with no change in first 5 years of diagnosis. Pancreatology. 2021;21(1):144-154. [CrossRef]
21. Pergolini I, Sahora K, Ferrone CR, et al. Long-term risk of pancreatic malignancy in patients with BD-IPMN in a referral center. Gastroenterology. 2017;153(5):1284-1294.e1. [CrossRef]