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Surveillance of Small Side-Branch Intraductal Papillary Mucinous Neoplasms: Is Long-Term Follow-Up Necessary?

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Abstract

Purpose:

Side-branch intraductal papillary mucinous neoplasms (SB-IPMNs) are mucin-producing cystic lesions originating from the secondary branches of the main pancreatic duct and are characterized by low-grade dysplasia with malignant potential. Incidentally detected pancreatic cystic foci are followed for up to 10 years with MRI to monitor for the progression to invasive carcinoma (IC). The purpose of this study was to investigate the risk of malignant transformation in small SB-IPMNs, defined as measuring < 1 cm at baseline, with additional sub-analysis of lesions measuring ≤ 5 mm.

Methods:

A multicenter retrospective cohort study was performed using data collected from eight hospitals. MRI/MRCP reports referencing SB-IPMNs were extracted from the electronic health record. Patients with less than two years of follow-up were excluded. Multiple variables were then collected from the imaging reports, such as the size and characteristics of SB-IPMNs. Pathology reports were also extracted to determine SB-IPMNs that resulted in biopsy-proven carcinoma. After additional exclusions were applied from the collected variables, 800 patients remained. Statistical analysis was then performed.

Results:

Of the 800 patients, 354 had SB-IPMNs < 1 cm, and 446 had SB-IPMNs ≥ 1 cm. A total of 120 patients had SB-IPMNs ≤ 5 mm. Four patients in the < 1 cm group developed pancreatic carcinoma (1.1%), compared with five patients in the ≥ 1 cm group (1.1%), with no significant difference between groups ($p > .99$). One patient in the SB-IPMN ≤ 5 mm group developed carcinoma. No significant difference was observed when comparing carcinoma conversion rate amongst SB-IPMNs ≤ 5 mm with those > 5 mm, (0.8% vs 1.2%, $p > .99$). Although no statistically significant differences were identified, the overall carcinoma conversion rate in the ≤ 5 mm group was 0.8%, below the 1% threshold commonly used in pulmonary nodule surveillance.

Conclusion:

To our knowledge, this is the first study to specifically evaluate SB-IPMNs ≤ 5 mm. Additional studies are needed to further characterize these very small lesions and refine surveillance recommendations for incidentally detected pancreatic cystic foci, with the potential to reduce unnecessary follow-up imaging.

Introduction

With advances in MRI techniques and the increasing use of cross-sectional abdominal imaging, incidental detection of pancreatic cystic lesions has become more common. The most common of these is the intraductal papillary mucinous neoplasm (IPMN), with an estimated reported prevalence of 10.9% [1]. IMPNs are cystic lesions originating from the pancreatic duct or its branches, and are characterized by the production of mucin and varying degrees of dysplasia depending on the subtype [2, 3]. IPMNs are morphologically divided into three main subtypes: main duct, side branch duct, and mixed types (Fig. 1). Main duct IPMNs demonstrate focal or diffuse dilation of the main pancreatic duct, whereas side branch IPMNs (SB-IPMNs) involve dilation of side-branch ducts that communicate with the main duct. Mixed-type IPMNs exhibit features of both [2]. Although all IPMNs contain dysplastic epithelium, main duct and mixed-types have a significantly higher rate of malignancy, reported as high at 60%, and are therefore closely followed and often resected [4]. In contrast, SB-IPMNs have a lower reported rate of conversion to invasive carcinoma (IC), but are typically followed with MRI/MRCP for 5–10 years. Current guidelines, based on the revised Fukuoka criteria, recommend surveillance of SB-IPMNs measuring < 1.5 cm for up to 10 years with the interval dependent on the patient's age [5]. More recently, Wehrle et al. reported a 1.4% rate of conversion to invasive carcinoma in SB-IPMNs measuring < 1 cm at baseline and a 1.8% rate in those ≥ 1 cm [6].

Incidentally found subcentimeter pancreatic cystic foci are typically presumed to represent SB-IPMNs and are followed with imaging surveillance, given that communication with the main pancreatic duct is often not visualized. Similar to Wehlre et al., this study sought to determine the rate of conversion to invasive carcinoma, particularly among subcentimeter cystic foci. However, whereas Wehlre et al. required a minimum imaging follow-up interval of 6 months, this study established a minimum follow-up of 2 years in order to specifically evaluate long-term outcomes of presumed SB-IPMNs [6]. A subanalysis of SB-IPMNs measuring 5 mm or less was also performed, given the increasing incidental detection of very small cystic foci in current practice. These findings present a management challenge for radiologists, particularly in older patients, in whom the benefit of imaging surveillance relative to life expectancy is often uncertain.

Existing guideline recommendations are supported by the findings of Wehlre et al., who reported conversion rates to invasive carcinoma greater than 1% in both subcentimeter and ≥ 1 cm cyst groups. Additionally, they reported that up to 25% of subcentimeter cysts progressed to invasive carcinoma or high-grade dysplasia within 8 years of diagnosis, including lesions that had remained stable for the first 5 years. Based on these findings, they recommended surveillance for at least 10 years, if not longer [6]. This study aims to assess the malignant potential of subcentimeter pancreatic cystic foci, particularly the smallest SB-IPMNs (≤ 5 mm), in order to better inform risk stratification and guide evidence-based surveillance strategies.

Methods

A multicenter retrospective cohort study was conducted across eight hospitals and their associated imaging centers from July 1, 2006 to July 20, 2024. Using 18 keywords, MRI/MRCP abdomen imaging

reports were extracted from the EHR that mentioned SB-IPMNs in some capacity. Because SB-IPMNs are not always described in a standardized way, keywords such as “cystic foci” were utilized to maximize report capture. The initial query resulted in 9,821 patients aged 18–89 years old. Patients with < 2 years of follow-up were then excluded. Pathology reports were extracted from the EHR, which included fine needle aspiration and surgical pathology.

To determine the variables to extract for analysis, the revised Fukuoka guidelines were referred to for guidance in defining clinically relevant progression.

Suspicious features were defined as including any of the following:

1. Worrisome features: enhancing mural nodule of < 5 mm, thick and/or enhancing cyst wall, main pancreatic duct (MPD) dilation (5–9 mm), abrupt change in MPD caliber, or rapid rate of cyst growth of > 5 mm.
2. High-risk stigmata: symptoms (pancreatitis), enhancing nodule of ≥ 5 mm, or main duct dilation of ≥ 1 cm [5].

Similar to Wehlre et al., size > 3 cm was not considered a suspicious feature as it has not shown to correlate with dysplastic potential [6, 7]. Multiple data points were then extracted from the imaging reports, including:

- size of the cystic lesions
- characteristics of the cysts (such as mural nodularity, wall thickening)
- findings of pancreatitis
- size of the MPD, if dilated (> 4 mm)
- abdominal lymphadenopathy (> 1 cm)
- change in caliber of the MPD with distal atrophy
- any other pancreatic malignancy/lesions
- if any follow-up with endoscopic ultrasound or surgical/GI consultation was recommended

Based on baseline cyst size, patients were divided into two categories: SB-IPMNs < 1 cm and SB-IPMNs ≥ 1 cm. After the initial data was collected, additional exclusions were applied based on the following criteria:

1. Patients with any prior pancreatic surgery on initial imaging.
2. Patients with cystic foci that were followed but were determined to be pseudocysts, main duct IPMN, or mixed IPMNs.
3. Patients with pancreatic adenocarcinoma/pancreatic mass on initial imaging.
4. Pancreatic cysts that were resected after the first imaging and were thus not followed by imaging.

After the final exclusions were applied, 800 patients remained. Statistical analysis was performed between the two size groups of SB-IPMNs (< 1 cm and ≥ 1 cm), comparing cyst size, growth rate, rate of conversion to invasive carcinoma, and other variables initially collected. An additional subanalysis was performed for SB-IPMNs measuring ≤ 5 mm, compared with those measuring > 5 mm within the dataset. Fisher's exact tests and Kruskal–Wallis rank-sum tests were used for group comparisons, depending on the variable analyzed.

Results

Patients Demographics and Groups

Of 9821 patients identified by the initial query, 800 patients were included in the final study cohort after application of exclusion criteria. Of these patients, 354 were classified as group A (< 1 cm IPMNs at first imaging) and 446 as group B (≥ 1 cm IPMNs at first imaging). Patient demographic characteristics are summarized in Table 1. Patients with IPMNs ≥ 1 cm were slightly older at initial and final imaging compared with those < 1 cm ($p < .001$). There was a female predominance overall (63.5%) ($p = .01$). By race, 705 of 800 patients (88.0%) were White or Caucasian, 47 (5.9%) Black or African American, 22 (2.7%) Asian, 24 (3.0%) Other, and 3 (0.4%) American Indian or Alaska Native.

Table 1

Baseline demographic characteristics of the study cohort stratified by intraductal papillary mucinous neoplasm (IPMN) size. Group A included patients with IPMN < 1 cm, and Group B included patients with IPMN ≥ 1 cm. Continuous variables are presented as mean (standard deviation) and median (interquartile range); categorical variables are presented as a percentage. P-values reflect between-group comparisons.

Patient Demographics Stratified by IPMN Size (< 1 cm vs ≥ 1 cm)					
Group		Group A (IPMN < 1 cm)	Group B (IPMN ≥ 1 cm)	Overall	p-value
Number of patients		N = 354	N = 446	N = 800	
Age at Initial Study (years)	Mean (SD)	64.8 (± 10.1)	67.2 (± 10.2)	66.1 (± 10.2)	*< .001*[1]
	Median (IQR)	65.7 (57.4–71.6)	69.0 (61.9–74.3)	67.8 (59.8–73.4)	
	Range	24.2–86.1	32.2–84.8	24.2–86.1	
Age at Last Study (years)	Mean (SD)	69.9 (± 9.9)	72.4 (± 10.1)	71.3 (± 10.1)	*< .001*[1]
	Median (IQR)	70.9 (62.9–76.5)	74.5 (67.1–79.3)	72.8 (65.3–78.2)	
	Range	29.4–89.8	36.6–89.9	29.4–89.9	
Sex	Male	112 (31.6%)	180 (40.4%)	292 (36.5%)	*= .01*[2]
	Female	242 (68.4%)	266 (59.6%)	508 (63.5%)	
Race	White or Caucasian	316 (89.3%)	388 (87.0%)	704 (88.0%)	
	Black or African American	0 (0.0%)	3 (0.7%)	3 (0.4%)	
	Asian	10 (2.8%)	12 (2.7%)	22 (2.8%)	
	American Indian or Alaska Native	19 (5.4%)	28 (6.3%)	47 (5.9%)	
	Other	9 (2.5%)	15 (3.4%)	24 (3.0%)	

1 = Kruskal-Wallis rank sum test

2 = Fisher's Exact Test for Count Data

Cyst Characteristics and Growth

Cyst characteristics and growth patterns are summarized in Table 2. Initial cyst size differed significantly between groups (p< .001), reflecting the predefined size categories. This difference remained significant at final follow-up (p< .001). A size increase of ≥ 5 mm occurred in 104 of 446 patients (23.3%) in the ≥ 1

cm group and 53 of 354 patients (15.0%) in the < 1 cm group (p= .003). Mean growth rate was significantly higher in the < 1 cm group (32.7% vs 9.4%, p< .001). Suspicious features were identified in 146 of 446 patients (32.7%) in the ≥ 1 cm group and 91 of 354 patients (25.7%) in the < 1 cm group (p= .04). Carcinoma was identified with biopsy in 9 of 800 patients (1.1%), including 4 of 354 (1.1%) in Group A and 5 of 446 (1.1%) in Group B (p > 0.99).

Follow-up recommendation for EUS or gastrointestinal/surgical consultation occurred in 18 of 354 patients (5.1%) in Group A and 108 of 446 patients (24.2%) in Group B (p< .001).

Table 2

Cyst characteristics and longitudinal growth patterns stratified by intraductal papillary mucinous neoplasm (IPMN) size (< 1 cm vs ≥ 1 cm). Continuous variables are presented as mean (standard deviation), median (interquartile range), and range, and categorical variables as a percentage. P-values reflect between-group comparisons.

Cyst Characteristics and Growth by IPMN Size (< 1 cm vs ≥ 1 cm)					
Group		Group A (IPMN < 1 cm)	Group B (IPMN ≥ 1 cm)	Overall	p-value
Number of patients		N = 354	N = 446	N = 800	
Follow-up length (years)	Mean (SD)	5.1 (± 1.8)	5.2 (± 1.7)	5.1 (± 1.8)	*= .09*[2]
	Median (IQR)	4.6 (3.6–6.1)	4.8 (3.8–6.3)	4.7 (3.7–6.3)	
	Range	3.0–11.6	3.0–13.0	3.0–13.0	
Initial IPMN size (mm)	Mean (SD)	6.4 (± 1.9)	17.2 (± 7.1)	12.4 (± 7.7)	*< .001*[2]
	Median (IQR)	6.0 (5.0–8.0)	15.0 (12.0–20.0)	11.0 (7.0–16.0)	
	Range	2.0–9.0	10.0–66.0	2.0–66.0	
Final IPMN size (mm)	Mean (SD)	8.3 (± 4.3)	18.7 (± 9.3)	14.1 (± 9.1)	*< .001*[2]
	Median (IQR)	7.0 (5.2–9.0)	17.0 (12.0–23.0)	12.0 (7.0–18.0)	
	Range	1.0–30.0	5.0–75.0	1.0–75.0	
Size increase by ≥ 5 mm?	Yes	53 (15.0%)	104 (23.3%)	157 (19.6%)	*= .003*[1]
	No	301 (85.0%)	342 (76.7%)	643 (80.4%)	
Growth Rate (%)	Mean (SD)	32.7 (± 62.8)	9.4 (± 32.1)	19.7 (± 49.5)	*< .001*[2]
	Median (IQR)	12.5 (0.0–50.0)	5.9 (-7.7–23.1)	6.6 (0.0–33.3)	
	Range	-66.7–350.0	-68.4–150.0	-68.4–350.0	
Suspicious features of IPMN	Yes	91 (25.7%)	146 (32.7%)	237 (29.6%)	*=.04*[1]

Cyst Characteristics and Growth by IPMN Size (< 1 cm vs ≥ 1 cm)					
	No	263 (74.3%)	300 (67.3%)	563 (70.4%)	
Positive biopsy	Yes	4 (1.1%)	5 (1.1%)	9 (1.1%)	*>.99*[1]
	No	350 (98.9%)	441 (98.9%)	791 (98.9%)	
Follow-up EUS or gastrointestinal/ surgical consultation	Yes	18 (5.1%)	108 (24.2%)	126 (15.8%)	*<.001*[1]
	No	336 (94.9%)	338 (75.8%)	674 (84.2%)	
1 = Kruskal-Wallis rank sum test 2 = Fisher's Exact Test for Count Data					

Main Duct and Pancreatic Findings

Main duct dilation was present in 76 of all 800 (9.5%) patients overall, including 31 of 354 patients (8.8%) in Group A and 45 of 446 patients (10.1%) in Group B (p = .55; Table 3). Among the 107 patients with MPD measurements available, the mean MPD size was 6.5 ± 2.4 mm in Group A and 8.0 ± 3.5 mm in Group B (p= .02). Additional pancreatic findings are shown in Table 3. Notably, pancreatitis occurred in 31 of 800 patients (3.9%). Between groups A and B, pancreatitis (p= .71), other pancreatic lesions (p= .23), and lymphadenopathy greater than 1 cm (p= .34) did not differ significantly.

Table 3
Main pancreatic duct and pancreatic findings stratified by intraductal papillary mucinous neoplasm (IPMN) size (< 1 cm vs ≥ 1 cm). Categorical variables are presented as a percentage. P-values reflect between-group comparisons.

Main Duct and Pancreatic Findings by IPMN Size (< 1 cm vs ≥ 1 cm)					
Group		Group A (IPMN < 1 cm)	Group B (IPMN ≥ 1 cm)	Overall	p-value
Number of patients		N = 354	N = 446	N = 800	
Main Pancreatic Duct Dilation Present	Yes	31 (8.8%)	45 (10.1%)	76 (9.5%)	*= .55*[1]
	No	323 (91.2%)	401 (89.9%)	724 (90.5%)	
Pancreatitis?	Yes	15 (4.2%)	16 (3.6%)	31 (3.9%)	*=.71*[1]
	No	339 (95.8%)	430 (96.4%)	769 (96.1%)	
Additional pancreatic lesions?	Yes	7 (2.0%)	4 (0.9%)	11 (1.4%)	*=.23*[1]
	No	347 (98.0%)	442 (99.1%)	789 (98.6%)	
Lymphadenopathy of > 1 cm?	Yes	15 (4.2%)	13 (2.9%)	28 (3.5%)	*=.34*[1]
	No	339 (95.8%)	433 (97.1%)	772 (96.5%)	
1 = Kruskal-Wallis rank sum test					

Subgroup Analysis: Small IPMNs (≤ 5 mm)

Patients were further stratified into Group C (≤ 5 mm, n = 120) and Group D (> 5 mm, n = 680), with demographics presented in Table 4 and analysis presented in Table 5. The mean growth rate was 44.4% in group C and 15.3% in group D (p< .001), with corresponding median growth rates of 25.0% and 5.3%, respectively. Cyst size increase ≥ 5 mm occurred in 10.8% of Group C and 20.9% of Group D (p = 0.008). Suspicious features were identified in 213 of 680 patients (31.3%) in Group D compared to only 24 of 120 (20%) in Group C (p< .012). Positive biopsy results occurred in 1 of 120 patients (0.8%) in Group C and 8 of 680 patients (1.2%) in Group D, with no significant difference between groups (p> .99).

Table 4

Subgroup analysis of baseline demographic characteristics stratified by intraductal papillary mucinous neoplasm (IPMN) size. Group C included patients with IPMN ≤ 5 mm, and Group D included patients with IPMN > 5 mm. Continuous variables are presented as mean (standard deviation) and median (interquartile range); categorical variables are presented as a percentage. P-values reflect between-group comparisons.

Patient Demographics in a Subgroup Stratified by IPMN Size (≤ 5 mm vs > 5 mm)					
Group		Group C (IPMN ≤ 5 mm)	Group D (IPMN > 5 mm)	Overall	p-value
Number of patients		N = 120	N = 680	N = 800	
Age at Initial Study (years)	Mean (SD)	64.0 (± 9.7)	66.5 (± 10.3)	66.1 (± 10.2)	*= .003*[1]
	Median (IQR)	64.3 (57.1–70.5)	68.2 (60.2–73.8)	67.8 (59.8–73.4)	
	Range	32.5–83.6	24.2–86.1	24.2–86.1	
Age at Last Study (years)	Mean (SD)	69.0 (± 9.6)	71.7 (± 10.1)	71.3 (± 10.1)	*< .001*[1]
	Median (IQR)	69.7 (62.6–75.0)	73.2 (65.7–78.5)	72.8 (65.3–78.2)	
	Range	37.3–89.8	29.4–89.9	29.4–89.9	
Sex	Female	80 (66.7%)	428 (62.9%)	508 (63.5%)	*= .47*[2]
	Male	40 (33.3%)	252 (37.1%)	292 (36.5%)	
Race	White or Caucasian	110 (91.7%)	594 (87.4%)	704 (88.0%)	
	Black or African American	0 (0.0%)	3 (0.4%)	3 (0.4%)	
	Asian	4 (3.3%)	18 (2.6%)	22 (2.8%)	
	American Indian or Alaska Native	4 (3.3%)	43 (6.3%)	47 (5.9%)	
	Other	2 (1.7%)	22 (3.2%)	24 (3.0%)	

1 = Kruskal-Wallis rank sum test

2 = Fisher's Exact Test for Count Data

Table 5

Cyst characteristics and longitudinal growth patterns stratified by intraductal papillary mucinous neoplasm (IPMN) size (≤ 5 mm vs > 5 mm). Continuous variables are presented as mean (standard deviation), median (interquartile range), and range, and categorical variables as a percentage. P-values reflect between-group comparisons.

Subgroup IPMN Characteristics and Analysis (≤ 5 mm vs > 5 mm)					
Group		Group C (IPMN ≤ 5 mm)	Group D (IPMN > 5 mm)	Overall	p-value
Number of patients		N = 120	N = 680	N = 800	
Follow-up length (years)	Mean (SD)	5.0 (± 1.7)	5.2 (± 1.8)	5.1 (± 1.8)	*= .38*[1]
	Median (IQR)	4.6 (3.6–5.9)	4.8 (3.7–6.3)	4.7 (3.7–6.3)	
	Range	3.0–9.9	3.0–13.0	3.0–13.0	
Initial IPMN size (mm)	Mean (SD)	4.2 (± 0.8)	13.8 (± 7.4)	12.4 (± 7.7)	*< .001*[2]
	Median (IQR)	4.0 (4.0–5.0)	12.0 (8.0–18.0)	11.0 (7.0–16.0)	
	Range	2.0–5.0	6.0–66.0	2.0–66.0	
Final IPMN size (mm)	Mean (SD)	6.0 (± 3.0)	15.5 (± 9.1)	14.1 (± 9.1)	*< .001*[2]
	Median (IQR)	5.0 (4.0–7.0)	13.0 (9.0–20.0)	12.0 (7.0–18.0)	
	Range	1.0–18.0	3.0–75.0	1.0–75.0	
Size increase by ≥ 5 mm?	Yes	13 (10.8%)	142 (20.9%)	155 (19.4%)	*=.008*[1]
	No	107 (89.2%)	538 (79.1%)	645 (80.6%)	
Growth Rate (%)	Mean (SD)	44.4 (± 68.0)	15.3 (± 44.1)	19.7 (± 49.5)	*< .001*[2]
	Median (IQR)	25.0 (0.0–60.0)	5.3 (-5.9–28.8)	6.6 (0.0–33.3)	
	Range	-50.0–350.0	-68.4–300.0	-68.4–350.0	
Suspicious features of IPMN	Yes	24 (20.0%)	213 (31.3%)	237 (29.6%)	*= .012*[1]
	No	96 (80.0%)	467 (68.7%)	563 (70.4%)	
Positive biopsy	Yes	1 (0.8%)	8 (1.2%)	9 (1.1%)	*>.99*[1]
	No	119 (99.2%)	672 (98.8%)	791 (98.9%)	

1 = Kruskal-Wallis rank sum test

2 = Fisher's Exact Test for Count Data

Discussion

To our knowledge, this is the first study to specifically analyze the smallest SB-IPMNs, measuring ≤ 5 mm, in the context of malignant transformation risk. Our results demonstrate an overall low rate of invasive carcinoma (IC) across all size groups, with no significant difference between cysts < 1 cm and ≥ 1 cm (1.1% vs 1.1%). These rates are lower than those reported by Wehrle et al., who observed IC conversion rates of 1.4% in cysts < 1 cm and 1.8% in those ≥ 1 cm [6]. Similarly, Han et al. reported a malignant conversion rate of 1.3% for cysts < 1 cm, which progressively increased with larger cysts, reaching 28.5% in cysts > 3 cm [8]. While their findings of low risk among subcentimeter cysts align with ours, the absence of a significant difference between size groups in our cohort suggests that size alone may be a less meaningful discriminator of malignant potential among SB-IPMNs.

An additional significant finding in our study is the discordance between cyst growth and malignant transformation. Although cysts with an initial size < 1 cm demonstrated significantly higher relative growth rates compared with those that were ≥ 1 cm (32.7% vs 9.2%), this was not associated with an increased risk of IC. This trend suggests that interval growth, particularly in small cysts, may reflect earlier detection rather than aggressiveness. This interpretation is supported by the younger mean age of the subcentimeter cohort compared with the ≥ 1 cm cohort (64.8 vs 67.2 years). A similar trend was seen when comparing the mean age between the ≤ 5 mm and > 5 mm (64.0 vs 66.5 years). Mean follow-up in years amongst the groups was similar in the main analysis and the subgroup analysis.

These findings are consistent with prior studies. El Chafic et al. demonstrated that cyst growth is not reliably associated with high-risk pathology, and Wehrle et al. similarly reported no correlation between growth rate and high-risk disease [6, 9]. Although some studies have identified cyst growth as a potential risk factor for malignant progression, our findings, suggest that growth alone may be an unreliable predictor of malignancy, particularly in smaller SB-IPMNs.

In our subgroup analysis, SB-IPMNs measuring ≤ 5 mm demonstrated an IC conversion rate of 0.8%, compared to 1.2% in cysts > 5 mm, however, without statistical significance. Notably, this rate falls below the 1% malignancy threshold utilized in pulmonary nodule screening guidelines. These findings are consistent with prior literature demonstrating that stable small pancreatic cysts carry a very low risk of malignancy, particularly in the absence of high-risk features [10, 11]. Meziani et al., in a recent systematic review and meta-analysis, demonstrated that small cyst size (≤ 1.5 cm) is strongly associated with a markedly reduced risk of malignant transformation [10]. Similarly, Ciprani et al. found that cysts < 1.5 cm have a low baseline risk of malignancy (1.7%) that decreases over time, falling below 0.2% after five years of surveillance [11].

Imaging features traditionally considered worrisome demonstrated limited predictive value for the development of IC in our cohort. Although some patients who developed IC demonstrated suspicious features such as ductal dilation or pancreatitis, these findings were inconsistent and not uniformly present. Out of the 9 patients who developed IC, 2 had ductal dilation, one of whom also had ductal caliber change with distal atrophy. The other patient also had chronic pancreatitis. One additional patient

had imaging findings of chronic pancreatitis (overall 2/9). Notably, none of the SB-IPMNs that developed carcinoma exhibited mural nodularity, enhancing wall thickening, or septations. 2 of the 9 patients had an interval suspicious growth of 5 mm or more. Follow-up suggestions with either GI or surgical consultation or EUS were also inconsistent. 5 of the 9 patients had suspicious features, but only 2 of these had follow-up recommendations. 1 patient did not demonstrate suspicious features but had a follow-up recommended due to a size greater than 3 cm. 2 of the 9 had upper abdominal lymphadenopathy. None had any additional pancreatic lesions.

Although the revised Fukuoka guidelines remain a backbone in the management of pancreatic cysts, our findings suggest that their applicability to the smallest SB-IPMNs may be limited. This is consistent with evolving recommendations, including the Kyoto consensus, which acknowledges that surveillance strategies may be individualized or potentially discontinued in select low-risk patients after a period of stability. Importantly, continued surveillance in current guidelines is driven not only by the risk of IPMN-related malignant transformation, but also by concern for the development of concomitant pancreatic ductal adenocarcinoma, which remains a key rationale for continued follow-up even in low-risk lesions [12].

The findings presented above have important clinical implications. The increasing use of cross-sectional imaging has led to more frequent detection of incidental pancreatic cysts, particularly those measuring only a few millimeters. This has contributed to a substantial rise in surveillance imaging, increasing health care utilization, and associated costs. It has also likely contributed to patient anxiety, despite a low conversion rate to IC. This is supported by multiple aforementioned cohort studies and meta-analyses demonstrating low rates of malignant transformation in small, stable cysts [11, 12, 13, 14]. Together, this data suggests that surveillance strategies may be safely de-escalated or discontinued in low-risk patients, such as those with SB-IPMNs measuring 5 mm or less.

This study has several limitations. As a retrospective analysis, it is subject to potential selection bias related to the inclusion of patients who underwent imaging and had sufficient follow-up. For example, the patient population had a higher proportion of females (63.5% female vs 36.5% male). Additionally, biopsy results were available in only a subset of patients, which may underestimate the true rates of malignant pathology. The low number of developed ICs limits the statistical power to detect differences between the groups based on cyst size. Furthermore, although patients had at least 2 years of follow-up, some remained under active surveillance at the time of analysis, therefore, future malignant transformation events may not have been fully captured. Lastly, 88.0% of our study population were White Americans, limiting generalizability to other races and ethnicities.

Conclusion

Although pancreatic cancer is a highly morbid condition associated with substantial and rising healthcare costs, imaging surveillance should be tailored with careful consideration of overall patient risk. While SB-IPMNs measuring > 5 mm should undergo continued surveillance according to current

guidelines, our findings suggest there may be an opportunity to reduce imaging follow-up for the smallest SB-IPMNs.

Declarations

Ethics approval and consent to participate:

*This study was approved by the **Corewell Health Institutional Review Board.**

*Need for consent to participate was waived by **Corewell Health Institutional Review Board.**

*Human Ethics and Consent to Participate declarations: not applicable

*Consent to Participate: not applicable

*Consent for publication: not applicable.

*All experiments were performed in accordance with relevant guidelines and regulations

*The datasets generated and/or analysed during the current study are not publicly available due to patient privacy but are available from the corresponding author on reasonable request.

Author Contribution

Aaiz Hussain - Wrote the main manuscript, data collection and analysisAlexander Pietroski - Wrote the main manuscript, data collection and analysisAhmed Ahmed - Wrote the main manuscript, data collection and analysisAazif Hussain - Wrote the main manuscriptEmily Jagenburg - Data collectionMyra Esmail - Data collectionMichael Nazmifar - Data collectionJonathan Chapman - Principle Investigator

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Chen Shen - Assisted with data analysis.Lihua Qiu - Assisted with extracting patient data from EHR.

Data Availability

The datasets generated and/or analysed during the current study are not publicly available due to patient privacy but are available from the corresponding author on reasonable request.

References

1. de la Fuente J, Chatterjee A, Lui J, et al. Long-Term Outcomes and Risk of Pancreatic Cancer in Intraductal Papillary Mucinous Neoplasms. JAMA Netw Open. 2023;6(10):e2337799.

10.1001/jamanetworkopen.2023.37799. Published 2023 Oct 2.

2. Oo J, Brown L, Loveday BP. Intraductal papillary mucinous neoplasm: Overview of management. Aust J Gen Pract. 2024;53(11):835–9. 10.31128/AJGP-05-23-6822.
3. Boraschi P, Tarantini G, Donati F, Scalise P, Cervelli R, Caramella D. Side-branch intraductal papillary mucinous neoplasms of the pancreas: outcome of MR imaging surveillance over a 10 years follow-up. Eur J Radiol Open. 2020;7:100250. 10.1016/j.ejro.2020.100250. Published 2020 Aug 21.
4. Salvia R, Fernández-del Castillo C, Bassi C, et al. Main-duct intraductal papillary mucinous neoplasms of the pancreas: clinical predictors of malignancy and long-term survival following resection. Ann Surg. 2004;239(5):678–87. 10.1097/01.sla.0000124386.54496.15.
5. 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):738–53. 10.1016/j.pan.2017.07.007.
6. Wehrle CJ, Walsh RM, Kumar P, et al. Surveillance of subcentimeter side-branch intraductal papillary mucinous neoplasms: risk of invasive disease and follow-up recommendations. J Gastrointest Surg. 2025;29(4):101959. 10.1016/j.gassur.2025.101959.
7. Wehrle CJ, Hossain MS, Perlmutter B, et al. Consequences of a Surveillance Strategy for Side-branch Intraductal Pancreatic Mucinous Neoplasms: Long-term Follow-up of One Thousand Cysts. Ann Surg. 2024;280(4):683–92. 10.1097/SLA.0000000000006383.
8. Han Y, Kwon W, Lee M, et al. Optimal Surveillance Interval of Branch Duct Intraductal Papillary Mucinous Neoplasm of the Pancreas. JAMA Surg. 2024;159(4):389–96. 10.1001/jamasurg.2023.7010.
9. El Chafic A, El Hajj II, DeWitt J, et al. Does cyst growth predict malignancy in branch duct intraductal papillary mucinous neoplasms? Results of a large multicenter experience. Dig Liver Dis. 2018;50(9):961–8. 10.1016/j.dld.2018.04.022.
10. Meziani J, Sprij MLJA, Fuhler GM, Bruno MJ, Marchegiani G, Cahen DL. Small cyst size and lack of growth as negative predictors of malignant transformation in low-risk intraductal papillary mucinous neoplasms of the pancreas: A systematic review and meta-analysis. United Eur Gastroenterol J. 2025;13(1):7–20. 10.1002/ueg2.12666.
11. Ciprani D, Weniger M, Qadan M, et al. Risk of malignancy in small pancreatic cysts decreases over time. Pancreatology. 2020;20(6):1213–7. 10.1016/j.pan.2020.08.003.
12. 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. 2024;24(2):255–70. 10.1016/j.pan.2023.12.009.
13. Johansson K, Kaprio T, Nieminen H, et al. A retrospective study of intraductal papillary neoplasia of the pancreas (IPMN) under surveillance. Scand J Surg. 2022;111(1). 10.1177/14574969221076792.
14. Marchegiani G, Pollini T, Burelli A, et al. Surveillance for Presumed BD-IPMN of the Pancreas: Stability, Size, and Age Identify Targets for Discontinuation. Gastroenterology. 2023;165(4):1016–e10245. 10.1053/j.gastro.2023.06.022.

Figures

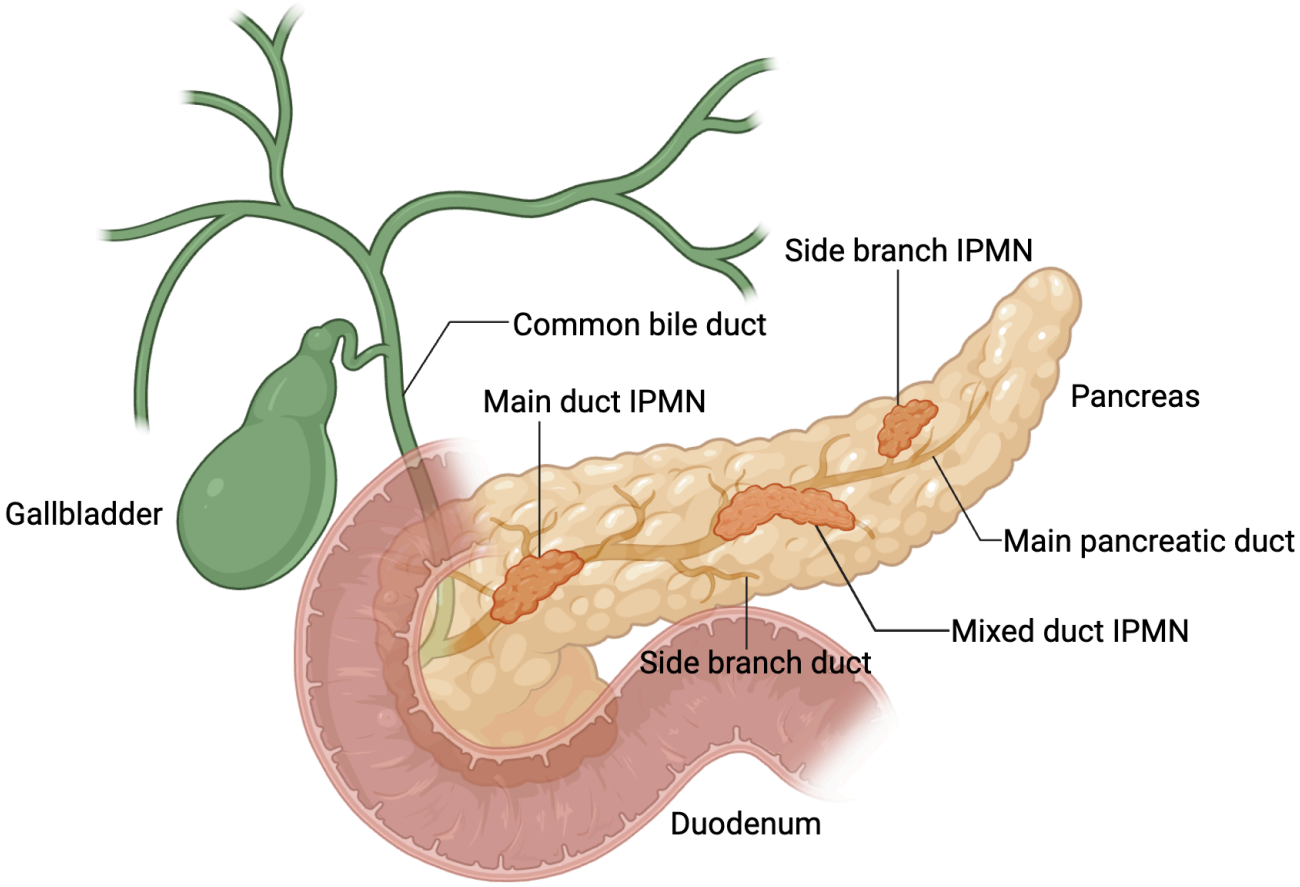


Figure 1

Schematic illustration of intraductal papillary mucinous neoplasms (IPMNs) arising from the main pancreatic duct, side branches, or both (mixed type). Created in https://BioRender.com.