



Retrospective Cohort Study

Optimizing branch-duct intraductal papillary mucinous neoplasms surveillance: Data-driven dimensional grouping for risk stratification and cost-effectiveness

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Abstract

BACKGROUND

The rising detection of branch-duct intraductal papillary mucinous neoplasms (BD-IPMN) has led to updated surveillance guidelines, yet the true malignant transformation rate and the cost-effectiveness of these strategies remain uncertain. Current protocols are based on expert opinion rather than validated data, leading

to conflicting recommendations and significant healthcare costs. This study addresses the need for an evidence-based approach to optimize surveillance by identifying robust risk factors and creating a more efficient protocol.

AIM

To determine the rate of BD-IPMN malignant progression, identify independent risk factors, and develop a surveillance protocol optimized for both diagnostic accuracy and cost-efficiency.

METHODS

This is a multicentric retrospective cohort study using prospectively collected data from four Italian tertiary care centers. A total of 333 patients undergoing surveillance for BD-IPMN between January 2017 and August 2023 were included. Multivariate Cox regression and segmentation analysis identified predictors and derived novel size thresholds for malignancy risk stratification. We then compared the diagnostic accuracy and 3-year surveillance costs of a proposed protocol against the Fukuoka 2017 and Kyoto 2024 guidelines.

RESULTS

Among 333 patients (median follow-up, 4 years), malignant transformation occurred in 11 (3.3%). Independent risk factors for malignancy included high risk stigmata (HRS) [hazard ratio (HR) = 4.4, 95% confidence interval (CI): 1.1-17.8, $P = 0.04$], the development of ≥ 2 worrisome features (WFs) (HR = 5.8, 95% CI: 1.5-22.4, $P = 0.01$), and cyst size (HR = 2.0, 95% CI: 1.3-3.0, $P < 0.001$). Two new cut-offs (1.5 cm and 3.0 cm) defined dimensional categories with distinct malignant potential (HR = 6.6, 95% CI: 1.7-25.4, $P = 0.007$, HR = 9.8, 95% CI: 1.1-89.7, $P = 0.04$). A proposed surveillance protocol preserved diagnostic accuracy while reducing 3-year costs by 11% *vs* Fukuoka and 21.4% *vs* Kyoto ($P < 0.001$). Scenario analysis confirmed cost-effectiveness.

CONCLUSION

IPMN degeneration is rare. HRS and at least two WF may independently predict malignancy. Our surveillance protocol based on data-driven size cut-offs (1.5 cm and 3 cm) may enhance cost-effectiveness over current guidelines while maintaining diagnostic precision.

Key Words: Pancreatic cyst neoplasms; Intraductal papillary mucinous neoplasm; Risk stratification; Surveillance strategy; Cost-effectiveness; Pancreatic cancer; Evidence-based medicine; Health care costs

Core Tip: Malignant degeneration of branch-duct intraductal papillary mucinous neoplasms is rare. Surveillance strategies can be optimized for both safety and cost-effectiveness. This study identifies data-driven cyst size thresholds of 1.5 cm and 3.0 cm and finds that the presence of at least two worrisome features, not just one, is an independent predictor of malignancy. A new surveillance protocol based on these findings maintains diagnostic accuracy while reducing 3-year costs by up to 21.4% compared to current international guidelines, particularly by safely extending follow-up intervals for the majority of patients with small cysts.

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INTRODUCTION

In recent decades, the diagnosis of pancreatic cystic neoplasms has increased significantly, with branch-duct intraductal papillary mucinous neoplasms (BD-IPMN) being the most common type[1,2], largely due to improved imaging and longevity[3]. While often asymptomatic, their malignant potential raises clinical concern[4]. Several guidelines recommend the surveillance of these lesions, including the recent Kyoto guidelines and the earlier Fukuoka guidelines from the International Association of Pancreatology (IAP), as well as those issued by the European Study Group on Cystic Tumours of the Pancreas and the American Gastroenterological Association (AGA)[5-8]. These guidelines rely on expert opinion and lack evidentiary support, particularly regarding follow-up protocols. This results in conflicting surveillance recommendations, both in terms of timing and identification of high-risk patients. Consequently, this has an inevitable impact on patients, who are recommended to undergo iterative third-level examinations, as well as healthcare systems that should support surveillance strategies already deemed not cost-effective by various authors[9,10]. It is, therefore, crucial to provide clinicians with data-driven evidence on how to optimize the surveillance management strategy of patients with BD-IPMN. This study aimed to evaluate the natural history of BD-IPMN under primary surveillance to identify specific risk categories, which could serve as the basis for proposing a new, more cost-effective follow-up strategy.

MATERIALS AND METHODS

Study design

This multicentric retrospective cohort study used prospectively collected data from the PACMANS database (Pancreatic Cysts Management and Surveillance), a consortium involving four Italian tertiary care centers.

The STROBE guideline was followed[11]. All data were retrospectively evaluated, preserving patients' anonymity. According to the Italian Medicines Agency det. March 20, 2008 on retrospective observational studies using anonymous data, approval by an ethics committee was not mandatory, and informed consent was waived. The study complied with the Declaration of Helsinki (2024 revision).

Patient selection and data collection

We included patients under surveillance for BD-IPMN from January 2017 to August 2023. To ensure the inclusion of patients with a clear indication for clinical surveillance, we excluded those with follow-up < 6 months, baseline high risk stigmata (HRS), previous pancreatic ductal adenocarcinoma or previous pancreatic surgery.

We collected demographic, clinical [including age-adjusted Charlson comorbidity index (ACCI)], imaging, endoscopic, surgical and surveillance cost data, along with IPMN features [worrisome features (WF) and HRS] as defined by IAP guidelines[12].

Definition of clinicopathological and follow-up criteria

Follow-up intervals and indications, while variable depending on physician/patient preferences, were based on the 2017 Fukuoka guidelines.

Standard imaging included computed tomography (CT), magnetic resonance imaging (MRI), and endoscopic ultrasound (EUS). All examinations were performed across four Italian tertiary referral centres with established multidisciplinary teams for pancreatic cysts. MRI followed pancreatic-dedicated protocols (T2-weighted sequences, magnetic resonance cholangiopancreatography, and contrast-enhanced phases), with only minor institutional variations. EUS was conducted by experienced endosonographers routinely involved in pancreatic cyst evaluation. Despite slight differences in equipment, all centres adhered to standard diagnostic criteria and surveillance pathways for BD-IPMN.

A pancreatic cystic lesion was classified as BD-IPMN if typical morphology was present with clear communication with main pancreatic duct (MPD) branches. According to Fukuoka guidelines, MRI and CT were first-line, EUS was indicated after WFs detection to evaluate mural nodules or cyst wall thickening. Cyst size was the longest diameter. For multiple lesions, the largest was the index cyst. Mural nodules were hyperdense nodules on CT/MRI with contrast or vascular protrusions on EUS. The MPD was considered dilated when ≥ 5 mm; cyst wall thickening when ≥ 2 mm.

Surveillance time was calculated from baseline to last follow-up, surgery, or death. Malignancy was predefined as high-grade dysplasia (HGD) or invasive carcinoma (IC), confirmed histologically [surgery or EUS-fine-needle aspiration/biopsy (FNA/FNB)], or by metastasis without another primary tumor. Malignancy-free survival was time from baseline to HGD/IC/censoring. IPMN size-increase was defined as ≥ 3 mm growth. Surgical indications followed IAP guidelines, tailored by institutional experience and patient preference.

Study endpoints

The primary endpoint was the pancreatic malignancy rate and associated risk factors, particularly WF and HRS.

Secondary endpoints included operatively identifying IPMN size thresholds to better stratify surveillance strategies. Based on these findings, we aimed to develop an optimized surveillance strategy and perform a simulation of per-patient surveillance costs. Cost-effectiveness of the proposed strategy (based on regional fee schedules for healthcare services) was compared with Fukuoka 2017 and Kyoto 2024 guidelines.

Statistical analysis

Analyses were performed using R (v4.3.2). Normality was assessed using the Kolmogorov-Smirnov test. Continuous variables are presented as mean $\pm$ SD or median (interquartile range). Univariate and multivariate Cox regression identified predictors of HGD/IC, using Wald-test for non-binary categorical variables. Segmentation analysis derived new dimensional thresholds for risk stratification. It was conducted using segmented logistic regression to identify potential breakpoints in the association between cyst size and malignant transformation. The breakpoint was selected based on model-fit criteria, and subsequently corroborated through Kaplan-Meier analysis. Kaplan-Meier curves estimated malignancy-free survival; group differences used the log-rank test. A *P* value < 0.05 was significant. A *post-hoc* power analysis (Schoenfeld's approximation) estimated the minimum detectable hazard ratio (HR) at 80% power ($\alpha = 0.05$) for predictors with varying prevalence. *Post-hoc* power analysis (Schoenfeld's approximation) estimated the minimum detectable HR at 80% power ($\alpha = 0.05$) for predictors by prevalence. Threshold accuracy for malignancy risk was evaluated with receiver operating characteristic (ROC) analysis. Threshold stability was assessed *via* 70/30 split validation and bootstrap resampling to derive sensitivity/specificity confidence intervals (CIs).

Economic analysis

Based on the size thresholds identified in our cohort, we defined a proposed surveillance protocol specifying follow-up intervals by cyst size and risk features. We then calculated and compared the per-patient 3-year follow-up costs of our proposed strategy against the Fukuoka 2017 and Kyoto 2024 guidelines, using regional tariffs for imaging modalities. Cost differences between the three strategies were assessed using the Kruskal-Wallis test with *post-hoc* Bonferroni correction. A scenario analysis estimated the incremental cost-effectiveness ratio, expressed as the additional cost per

extra malignant case detected, under varying willingness-to-pay (WTP) thresholds. Sensitivity analyses identified break-even points for cost-equivalence between the strategies.

RESULTS

Study population

Of 367 patients screened, 34 were excluded (< 6 months follow-up, HRS/unfit for surgery, or main duct/mixed type-IPMN). The final population included was 333 patients ([Supplementary Figure 1](#)).

Median age was 67 (58-75) years, 57.1% were female, and median follow-up period was 4 (2-6) years. Median lesion diameter at enrollment was 1.2 cm (0.8-1.9), increasing to 1.4 cm (0.9-2.2) at the end of follow-up. Most IPMNs were ≤ 1.5 cm (216, 64.8%), located in the pancreatic head (52%) or body (35.7%). Baseline characteristics are in [Table 1](#). Patients underwent a median of 4 (3-6) imaging assessments, primarily MRI (mean 3.2/patient), then EUS (1.0) and CT (0.65). EUS was performed after WFs appeared.

BD-IPMN evolution and malignant degeneration

Malignant degeneration occurred in 11 patients (3.3%). Ten patients (3%) underwent surgery. Seven (70%) had HGD-IPMN ($n = 4$, 40%) or IC ($n = 3$, 30%), while 3 presented low grade dysplasia-IPMN (30%). EUS FNA/FNB detected malignancy in 4/7 cases. In 3 patients it failed to detect malignant evolution (57% diagnostic yield). The remaining malignant cases were diagnosed clinically from metastases without another identifiable primary tumor, in accordance with our predefined definition of malignancy.

At enrollment, 64 patients (19.2%) had ≥ 1 WF, and 15 had two (4.5%). During follow-up, eight (2.4%) developed ≥ 1 HRS, 139 (41.7%) ≥ 1 WF, and 53 (15.9%) ≥ 2 WFs. All 11 malignant cases had ≥ 1 WF, 8/11 (72.7%) had ≥ 2 WFs, and 4/11 (36.4%) had HRS.

Malignancy rates were higher in patients with HRS (4/8, 50%) or ≥ 2 WFs (8/53, 15.1%) compared to those with a single WF (3/86, 2.4%) ($P < 0.001$). Among 8 patients with HRS, 6 had ≥ 2 WFs (3/6 malignant) and 2 had 1 WF (1/2 malignant). Details in [Table 2](#).

Predictors of malignancy, HRS and WFs

HRS, development of ≥ 1 WF, and ≥ 2 WFs demonstrated varying predictive abilities for BD-IPMN malignant progression. Their specificity, sensitivity, positive (+LR) and negative likelihood ratio (-LR), positive predictive value and negative predictive value in predicting malignancy are in [Supplementary Table 1](#).

Multivariate Cox regression identified three independent predictors of BD-IPMN malignant degeneration: HRS, with a 4.4-fold increased risk (HR = 4.4, 95%CI: 1.1-17.8, $P = 0.04$). At least two WFs, with a 5.8-fold increased risk (HR = 5.8, 95%CI: 1.5-22.4, $P = 0.01$). Cyst diameter, with a doubling of risk per cm increase (HR = 2.0, 95%CI: 1.3-3.0, $P < 0.001$).

Forest plots are shown in [Figure 1](#), results of Cox regression and malignancy-free survival curves for HRS and two WFs BD-IPMN are in [Supplementary Table 2](#) and [Supplementary Figure 2](#), respectively.

IPMN size and risk of neoplastic progression

The independent predictive role of IPMN size was confirmed by ROC analysis [area under the curve (AUC) = 0.91, 95%CI: 0.84-0.97]. This curve is presented in [Figure 2](#), reporting sensitivity and specificity for different cyst diameters.

The optimal cutoff for ROC analysis was 3.3 cm (94.6% specificity, 54.5% sensitivity) for predicting degeneration.

In the segmentation analysis, a segmented logistic regression model identified the IPMN size at which the most significant change in risk for malignant progression occurs. The analysis identified an estimated breakpoint at 1.5 cm ($P = 0.19$), with 100% sensitivity and 53% specificity in predicting degeneration.

The 1.5 cm and 3 cm thresholds (approximated from 3.3 cm) proved complementary. Lesions < 1.5 cm rarely progressed (100%, 53% specificity), while those > 3 cm carried a sharply increased risk (73% sensitivity, 88% specificity). A 70/30 split validation yielded an AUC of 0.885. Details in [Supplementary Table 3](#).

These thresholds identified two critical inflection points for changes in neoplastic risk, defining three size categories (< 1.5 cm, 1.5-3 cm, and > 3 cm). Malignancy-free survival analysis confirmed these cutoffs, showing a stepwise increase in risk across categories (log-rank trend test, $P < 0.001$). IPMNs > 3 cm had a 6.6-fold higher risk than those 1.5-3 cm (HR = 6.6, 95%CI: 1.7-25.4, $P = 0.007$), which had a 9.8-fold higher risk than lesions < 1.5 cm (HR = 9.8, 95%CI: 1.1-89.7, $P = 0.04$) ([Figure 3](#)).

Surveillance simulation based on proposed new cutoffs

We conducted a simulation implementing the following recommendations: For IPMNs ≤ 1.5 cm, those provided by IAP Fukuoka guidelines for lesions < 1 cm: Initial check at 6 months, then biennial[5]. For IPMNs 1.5-3 cm, those provided by IAP Fukuoka guidelines for lesions 1-2 cm: Annual for 2 years, then lengthening intervals[5]. For IPMNs with WF/HRS or > 3 cm, those provided by Kyoto IAP guidelines, largely overlapping with the Fukuoka[6]. [Figure 4](#) illustrates the recommendations of our proposal for IPMNs without WFs or HRS.

In the simulation, our strategy's costs were compared to those obtained if patients were managed according to the Fukuoka and Kyoto guidelines. Median time to malignant diagnosis was comparable across strategies: Fukuoka 14 (10.5-38.5) months, our proposal 13 (11-38), Kyoto 13 (11-37) ($P = 0.97$).

Table 1 General characteristics of the study population, *n* (%)

Clinical value	<i>n</i> = 333
Sex (female)	190 (57.1)
Age at diagnosis, median (IQR)	67 (58-75)
Total follow-up time, median (IQR)	4 (2-6)
Initial diameter, cm, median (IQR)	1.2 (0.8-1.9)
Final diameter, cm, median (IQR)	1.4 (0.9-2.2)
IPMN size	
≤ 1 cm	146 (43.8)
> 1 cm, ≤ 2 cm	121 (36.3)
> 2 cm, ≤ 3 cm	40 (12.0)
> 3 cm	26 (7.9)
IPMN location	
Body	119 (35.7)
Head	173 (52.0)
Tail	41 (12.3)
ACCI	
0-3, mild	160 (48.0)
4-10, moderate-severe	173 (52.0)
Congestive heart failure	19 (5.7)
Connective tissue disease	2 (0.6)
COPD	21 (6.3)
Dementia	2 (0.6)
Diabetes	56 (16.8)
Leukemia	2 (0.6)
Liver disease	84 (25.2)
Lymphoma	7 (2.1)
Myocardial infarction history	13 (3.9)
Severe chronic kidney disease	12 (3.6)
Solid tumor history	64 (19.2)
Stroke history	9 (2.7)

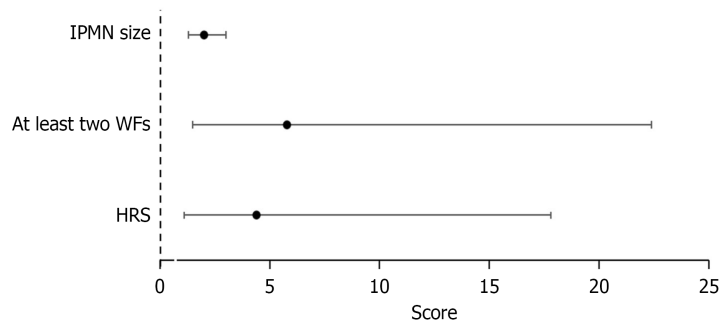
IQR: Interquartile range; IPMN: Intraductal papillary mucinous neoplasms; ACCI: Age-adjusted Charlson comorbidity index; COPD: Chronic obstructive pulmonary disease.

Follow-up costs over 3 years per patient were lower with our proposal [Euro 587.0 (347.1-930.3)] compared to Fukuoka [Euro 670.0 (407.3-1130.3)] and Kyoto [Euro 747.3 (547.2-1026.9)] ($P < 0.001$). Savings reached 11% *vs* Fukuoka and 21.4% *vs* Kyoto ($P < 0.001$), with the largest reductions in ≤ 1.5 cm cysts (24.6% and 40.8%, respectively). For 1.5-3 cm lesions savings were 19.4% *vs* Fukuoka and 9% *vs* Kyoto ($P = 0.16$), while for > 3 cm, costs were comparable ($P = 0.9$). Overall cost results in [Figure 5](#), per-patient costs in [Supplementary Figure 3](#). In the scenario analysis, the incremental cost-effectiveness ratio of each guideline compared with the proposed strategy was calculated as the difference in cost divided by the difference in malignant cases detected. With a WTP of Euro 20000 per additional malignancy detected, the break-even point corresponded to a missed detection rate exceeding 0.415% for Fukuoka and 0.802% for Kyoto per patient over 3 years. Scenario analyses' results are detailed in [Supplementary Table 4](#).

Table 2 Intraductal papillary mucinous neoplasms characteristics during surveillance, *n* (%)

IPMN characteristics during FU	<i>n</i> = 333
Malignant degeneration	11 (3.3)
At least one WF at enrollment	64 (19.2)
At least two WFs at enrollment	15 (4.5)
At least one WF at the end of FU	139 (41.7)
At least two WFs at the end of FU	53 (15.9)
HRS during FU	8 (2.4)
Surgery histology	
Adenocarcinoma	3 (30)
IPMN HGD	4 (40)
IPMN LGD	3 (30)
EUS histology	
Adenocarcinoma	4 (16.0)
IPMN HGD	1 (4.0)
IPMN LGD	14 (56.0)
Not diagnostic	6 (24.0)
Death for other reason during FU	10 (3.0)

IPMN: Intraductal papillary mucinous neoplasms; FU: Follow up; WFs: Worrisome features; HRS: High risk stigmata; EUS: Endoscopic ultrasound; HGD: High-grade dysplasia; LGD: Low-grade dysplasia.



Variable	Hazard ratio	<i>P</i> value
High risk stigmata	4.4 (1.1-17.8)	0.04
At least two WFs	5.8 (1.5-22.4)	0.01
IPMN size	2.0 (1.3-3.0)	< 0.001

IPMN, intra ductal papillary mucinous neoplasm; WF, worrisome feature; HRS, high-risk stigmata

Figure 1 Statistically significant predictors of malignant degeneration. IPMN: Intraductal papillary mucinous neoplasms; WFs: Worrisome features; HRS: High risk stigmata.

DISCUSSION

Our findings underscore that WFs, HRS, and specific dimensional criteria (1.5 cm and 3 cm), derived from operational mathematical analyses are crucial for optimizing BD-IPMN surveillance, ensuring diagnostic accuracy while improving cost-effectiveness. While malignant transformation remains rare, its poor prognosis and rising BD-IPMN prevalence underscore the need for a unified, data-driven management protocol to address discrepancies across international guidelines.

Recent studies report malignant transformation rates of 0.94%-3.3% at 5 years, 2.3%-6.6% at 10 years, and 7.6%-15% at 15 years[6], correcting earlier overestimates from surgical series[12-14]. Our 3.3% rate at 4 years aligns with the upper

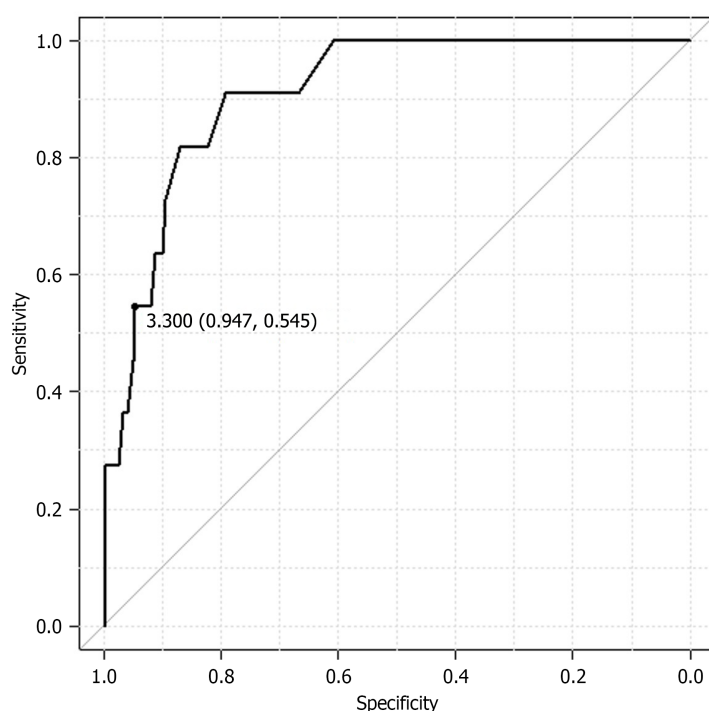


Figure 2 Receiver operating characteristic curve, intraductal papillary mucinous neoplasms size accuracy in predicting malignancy.

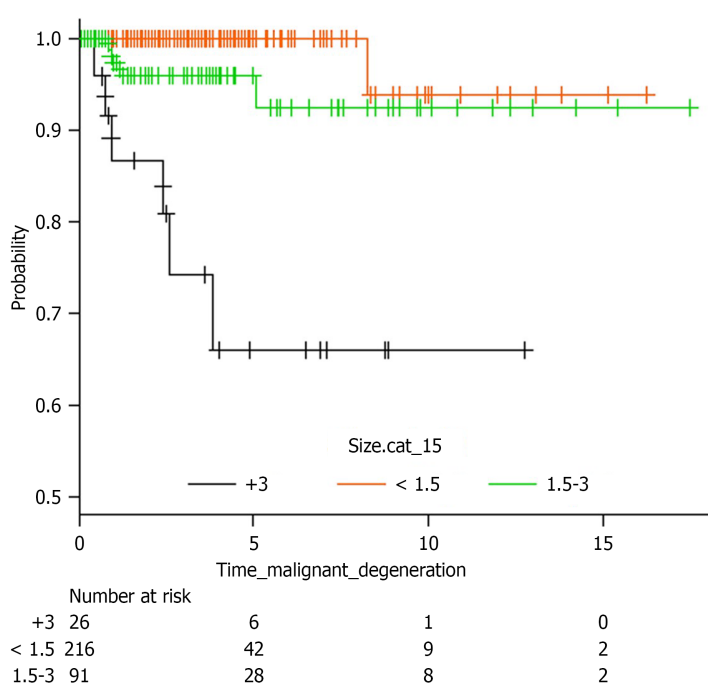


Figure 3 Kaplan-Meier malignancy-free survival curves stratified by intraductal papillary mucinous neoplasms size.

limits, likely reflecting a higher baseline prevalence of WFs (19%) compared to other studies (12% in a study by Han *et al* [15] (5.1% at 6.9 years), 0 WFs in the work by Marchegiani *et al* [16] (1.7% at 4 years).

The presence of WFs/HRS has been central in guidelines since 2012, when their malignant predictive value was first acknowledged [13]. However, the relative risk of each WF and HRS in comparison to others has not been exhaustively investigated yet [17]. In our cohort a single WF was not predictive of degeneration, while ≥ 2 WFs or any HRS markedly increased risk, a result confirmed by multivariate analysis. Similar evidence comes from Zelga *et al* [18], showing diagnostic accuracy rising with WF number. Remarkably, none of the individual WFs alone had significant predictive value for HGD/IC, as confirmed by another recent multicenter study [16]. Likewise, Sharib *et al* [19] reported 90% specificity with three WFs, while two were sufficient to predict HGD/IC, with risk increasing for each additional WF.

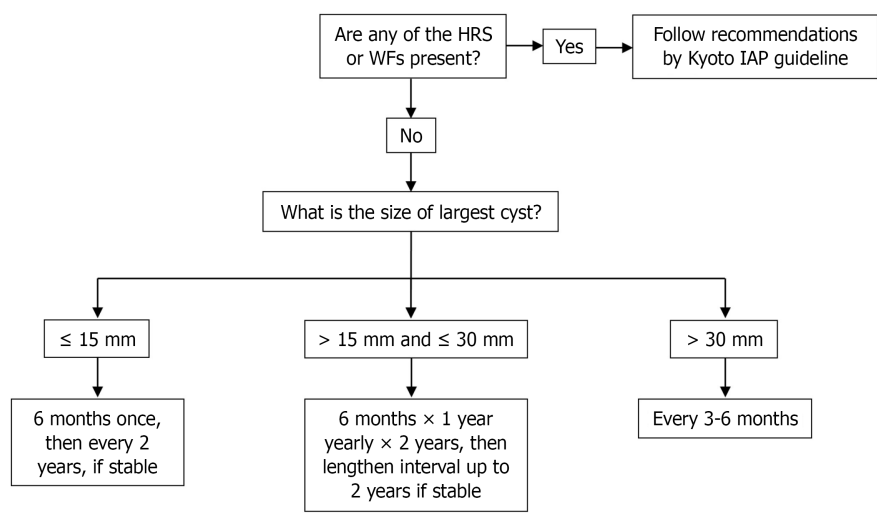


Figure 4 Proposed algorithm for the management of suspected branch-duct intraductal papillary mucinous neoplasms without high risk stigmata or worrisome features. IAP: International Association of Pancreatology; WFs: Worrisome features; HRS: High risk stigmata.

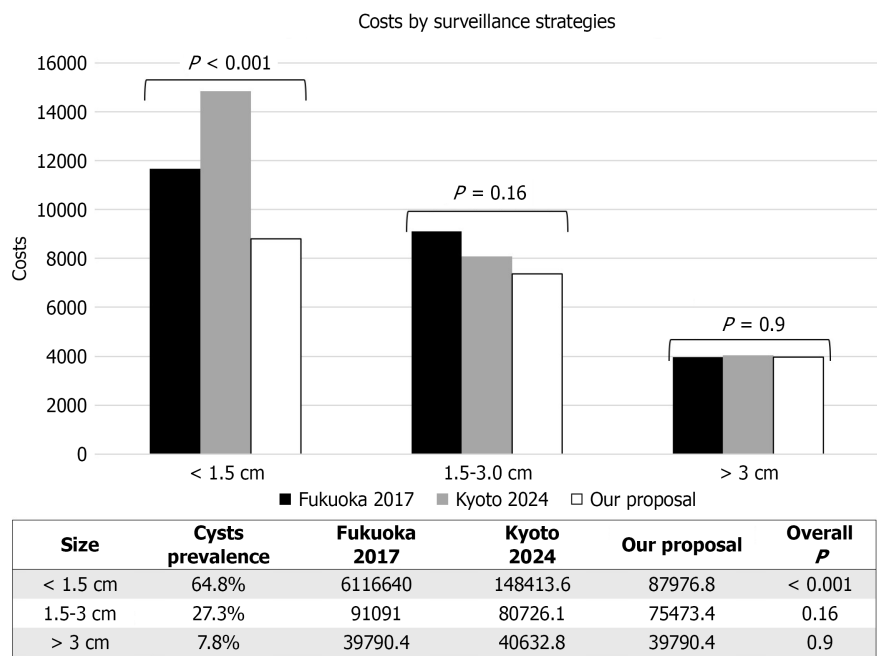


Figure 5 Total costs per-3 years of follow up by surveillance strategies.

The dimensional criterion is a critical factor in BD-IPMN surveillance, but current guideline cutoffs are empirical rather than analytically derived. These thresholds come from single studies that predefined cut-offs without testing alternatives.

For example, most studies set the lower cut-off at 1 cm, 1.5 cm, or 2 cm, without justification, showing that smaller cysts degenerate less often than larger ones. Our study documents that this risk doubles with every additional centimeter in cyst diameter (HR = 2.0, 95%CI: 1.3-3.0, $P < 0.001$).

Segmentation and ROC curve analysis (Figure 2) identified 1.5 cm and 3 cm as key thresholds, defining three risk categories with corresponding surveillance recommendations (Figure 4). This strategy matched Fukuoka/Kyoto guidelines accuracy but significantly reduced costs (Figure 5), mainly by improving small-cyst monitoring. Importantly, the upper 3 cm breakpoint is broadly consistent with the Kyoto and European frameworks, which consider cysts ≥ 30 -40 mm as having increased malignant potential and therefore warranting intensified surveillance and, in selected cases, surgical consideration. In contrast, our < 1.5 cm category lies entirely within the Kyoto “low-risk” class (< 2 cm) and refines this assumption by identifying a very-low-risk subgroup in whom extending surveillance intervals appears safe. Optimizing surveillance for small cysts, which form the majority of cases (64.8% were ≤ 1.5 cm and 80.4% ≤ 2 cm in our cohort), is crucial for sustainability. Our 1.5 cm and 3 cm thresholds align with prior evidence. For cysts > 3 cm, the odds ratio for degeneration in two retrospective studies was 3.9 (95%CI: 0.42-88.45)[19] and 2.35 (95%CI: 0.96-5.76), respectively [20,21]. A prospective study reported a 16.4 HR (95%CI: 3-304)[22]. Several studies showed, conversely, that cysts $<$

1.5 cm are the lowest-risk category[23–27]. Notably, our 1.5 cm threshold is strongly supported by a recent meta-analysis showing very low progression for cysts < 1.5 cm (relative risk = 0.37)[28]. However, Oyama *et al*[29] showed that cysts < 1.5 cm confer a higher risk than the general population over short- and long-term follow-up.

Optimizing surveillance also involves refining follow-up timing for lesions without WF/HRS, where guidelines diverge. The Fukuoka guidelines recommend intervals based on size, 6-months initially, then biennial for cysts < 1 cm, and progressively shorter intervals for larger cysts[5]. The 2018 European guidelines recommend MRI/EUS every 6 months in year 1, then annually[7]. The AGA guidelines suggest MRI at 1 then biennially for 5 years if < 3 cm[8]. The Kyoto guidelines redefined low-risk (< 2 cm), recommending follow-up at 6 then every 18 months[6]. This was based primarily on Han *et al*[15], who reported cyst doubling times of 1.1–2.2 years for cysts < 2 cm, though this cutoff was arbitrary and data for < 1.5 cm were lacking. Johansson *et al*[30] suggested biennial follow-up for < 1.5 cm. Additionally, in a cohort of 1369 patients an average doubling time of 2.5 years for cysts < 1 cm was observed, also supporting biennial follow-up[31]. Our study supports initial 6-month follow-up, then biennial, not only for its clinical accuracy comparable to previous guidelines, but also for its cost-effectiveness, reducing imaging and clinical visits (3 *vs* 4 in 5 years) and cutting costs by 25% for the majority of patients. We maintained the initial 6-month follow-up, consistent with guidelines, as an early checkpoint to detect rapidly progressing lesions, thereby prioritizing patient safety.

Our strategy demonstrated consistent cost savings over 3 years *vs* Fukuoka (-11%) and Kyoto (-21.4%), especially for cysts ≤ 1.5 cm (-25% *vs* Fukuoka, -40% *vs* Kyoto). Our economic evaluation expressed value as the cost per additional malignant case detected rather than quality-adjusted-life-years (QALYs), as no standardized WTP threshold exists for BD-IPMN, and because formal QALY-based modeling was beyond the scope of this study. Assuming a WTP Euro 20000 per extra malignant case detected, break-even analysis indicated that the proposed strategy would become less economically favorable only if it missed > 0.415% of cases compared with Fukuoka or > 0.802% compared with Kyoto over 3 years. These margins are substantially greater than the differences observed in our cohort, supporting both the robustness and economic resilience of our approach under conservative assumptions. To avoid overinterpretation, we note that these results represent a cost-minimization comparison under the assumption of comparable short-term diagnostic performance, rather than a full cost-effectiveness analysis.

A critical unresolved issue is when to stop surveillance. AGA advises stopping if cysts remain stable for 5 years. Recent proposals combine stability, size, and age, suggesting discontinuation in > 75 years with < 3 cm stable for ≥ 5 years, or > 65 years with ≤ 1.5 cm stable within the first 5 years[16]. Others argue that risk persists and suggest testing shorter surveillance[32], while several studies support lifelong monitoring due to ongoing malignant risk[24,29,33].

The Kyoto guidelines propose discontinuing follow-up for cysts < 2 cm stable for 5 years and/or life expectancy < 10 years, but consider both “stop” and “continue” approaches acceptable[6,16,34]. This reflects current practice: Only 18% of physicians would stop surveillance after 5 years, while most cite insufficient evidence that lifetime follow-up reduces mortality[35]. In our study, we did not address this issue due to a median follow-up duration of < 5 years. Nonetheless, in our cohort, only 6/333 patients had stable cysts < 2 cm and life expectancy < 10 years (per ACCI) and only 6/80 cases with follow-up > 5 years (7.5%). It is therefore plausible that few patients qualify for discontinuation, limiting cost-reduction effects of this strategy. A recent prospective study, however, proposes a third approach, using MPD size to guide extension or cessation of surveillance[36].

Strengths and limitations

Limitations include retrospective design, an uncontrolled surveillance protocol and surgical indications, though generally IAP-based. However, prospective standardized long-term studies are hardly feasible given IPMN’s indolent course, healthcare variability and sociomedical differences. Our cohort was smaller than some studies but excluded tertiary centers prone to selection bias, improving generalizability compared with single-center or referral-based cohorts. Given few malignant events, effect estimates require caution, as precision in time-to-event analyses depends mainly on event count; a *post-hoc* power assessment confirmed that only relatively large effect sizes could be detected with adequate power. This also explains the wide CIs of some HRs. Nevertheless, our findings were consistently supported by ROC analysis, segmentation modelling, and Kaplan-Meier stratification. This limitation affects most BD-IPMN studies; however, our event numbers matched prior multicenter series, and key associations aligned with sensitivity analyses and existing evidence. For this reason, the multivariable Cox model estimates were used only to support the direction of associations already observed in univariable analyses, ROC thresholds, segmentation output and Kaplan-Meier curves. Another limitation relates to the cost analysis, which was based on tariffs from the Italian National Health Service. As a publicly funded system, Italy has lower imaging costs compared with private or insurance-based healthcare models. Therefore, while our absolute cost values may not directly apply to all international settings, the proportional cost reductions observed (11% compared with Fukuoka and 21.4% compared with Kyoto over 3 years) are likely generalizable, as they result mainly from differences in resource utilization rather than local pricing structures. Indeed, in higher-cost systems, these proportional savings may translate into even greater absolute economic benefit.

Notably, this is the first study proposing a surveillance strategy grounded in clinical data while evaluating its economic impact. Further validation is needed, but our data offer insights into BD-IPMN history and support the development of evidence-based follow-up strategies.

CONCLUSION

Most BD-IPMNs remain benign, but some progress to malignancy with poor outcomes. Our data support personalized, size-based surveillance: After an initial 6-month follow-up, biennial surveillance for cysts ≤ 1.5 cm, annual for 2 years

then extended for cysts 1.5-3 cm, and IAP-based protocols for cysts with WFs, HRS, or > 3 cm. This approach appears more cost-effective than current guidelines but requires validation in larger, longer-term cohorts.

REFERENCES

- 1 **Ferrone CR**, Correa-Gallego C, Warshaw AL, Brugge WR, Forcione DG, Thayer SP, Fernández-del Castillo C. Current trends in pancreatic cystic neoplasms. *Arch Surg* 2009; **144**: 448-454 [RCA] [PMID: 19451487 DOI: 10.1001/archsurg.2009.36] [FullText]
- 2 **Pezzilli R**, Buscarini E, Pollini T, Bonamini D, Marchegiani G, Crippa S, Belfiori G, Sperti C, Moletta L, Pozza G, De Nucci G, Manes G, Mandelli ED, Casadei R, Ricci C, Alicante S, Vattiato C, Carrara S, Di Leo M, Fabbri C, Giovanelli S, Barresi L, Tacelli M, Mirante VG, Conigliaro R, Antonini F, Macarri G, Frulloni L, De Marchi G, Sassatelli R, Cecinato P, Del Vecchio Blanco G, Galli A, Pezzullo A, Fantin A, Graffeo M, Frego M, Stillitano D, Monica F, Germanà B, Capurso G, Quartini M, Veneroni L, Cannizzaro R, Falconi M. Epidemiology, clinical features and diagnostic work-up of cystic neoplasms of the pancreas: Interim analysis of the prospective PANCY survey. *Dig Liver Dis* 2020; **52**: 547-554 [RCA] [PMID: 32122771 DOI: 10.1016/j.dld.2020.02.003] [FullText]
- 3 **Gardner TB**, Park WG, Allen PJ. Diagnosis and Management of Pancreatic Cysts. *Gastroenterology* 2024; **167**: 454-468 [RCA] [PMID: 38442782 DOI: 10.1053/j.gastro.2024.02.041] [FullText]
- 4 **Matsubara S**, Tada M, Akahane M, Yagioka H, Kogure H, Sasaki T, Arizumi T, Togawa O, Nakai Y, Sasahira N, Hirano K, Tsujino T, Isayama H, Toda N, Kawabe T, Ohtomo K, Omata M. Incidental pancreatic cysts found by magnetic resonance imaging and their relationship with pancreatic cancer. *Pancreas* 2012; **41**: 1241-1246 [RCA] [PMID: 22699201 DOI: 10.1097/MPA.0b013e31824f5970] [FullText]
- 5 **Tanaka M**, Fernández-Del Castillo C, Kamisawa T, Jang JY, Levy P, Ohtsuka T, Salvia R, Shimizu Y, Tada M, Wolfgang CL. Revisions of international consensus Fukuoka guidelines for the management of IPMN of the pancreas. *Pancreatology* 2017; **17**: 738-753 [RCA] [PMID: 28735806 DOI: 10.1016/j.pan.2017.07.007] [FullText]
- 6 **Ohtsuka T**, Fernandez-Del Castillo C, Furukawa T, Hijioka S, Jang JY, Lennon AM, Miyasaka Y, Ohno E, Salvia R, Wolfgang CL, Wood LD. International evidence-based Kyoto guidelines for the management of intraductal papillary mucinous neoplasm of the pancreas. *Pancreatology* 2024; **24**: 255-270 [RCA] [PMID: 38182527 DOI: 10.1016/j.pan.2023.12.009] [FullText]
- 7 **European Study Group on Cystic Tumours of the Pancreas**. European evidence-based guidelines on pancreatic cystic neoplasms. *Gut* 2018; **67**: 789-804 [RCA] [PMID: 29574408 DOI: 10.1136/gutjnl-2018-316027] [FullText] [Full Text(PDF)]
- 8 **Vege SS**, Ziring B, Jain R, Moayyedi P; Clinical Guidelines Committee; American Gastroenterology Association. American gastroenterological association institute guideline on the diagnosis and management of asymptomatic neoplastic pancreatic cysts. *Gastroenterology* 2015; **148**: 819-22; quiz12 [RCA] [PMID: 25805375 DOI: 10.1053/j.gastro.2015.01.015] [FullText]
- 9 **Sharib J**, Esserman L, Koay EJ, Maitra A, Shen Y, Kirkwood KS, Ozanne EM. Cost-effectiveness of consensus guideline based management of pancreatic cysts: The sensitivity and specificity required for guidelines to be cost-effective. *Surgery* 2020; **168**: 601-609 [RCA] [PMID: 32739138 DOI: 10.1016/j.surg.2020.04.052] [FullText] [Full Text(PDF)]
- 10 **Lobo JM**, Scheiman JM, Zaydfudim VM, Shami VM, Sauer BG. Clinical and Economic Outcomes of Patients Undergoing Guideline-Directed Management of Pancreatic Cysts. *Am J Gastroenterol* 2020; **115**: 1689-1697 [RCA] [PMID: 32558682 DOI: 10.14309/ajg.0000000000000730] [FullText]
- 11 **Vandenbroucke JP**, von Elm E, Altman DG, Gøtzsche PC, Mulrow CD, Pocock SJ, Poole C, Schlesselman JJ, Egger M; STROBE Initiative. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE): explanation and elaboration. *Int J Surg* 2014; **12**: 1500-1524 [RCA] [PMID: 25046751 DOI: 10.1016/j.ijsu.2014.07.014] [FullText]
- 12 **Bannay A**, Chaignot C, Blotière PO, Basson M, Weill A, Ricordeau P, Alla F. The Best Use of the Charlson Comorbidity Index With Electronic Health Care Database to Predict Mortality. *Med Care* 2016; **54**: 188-194 [RCA] [PMID: 26683778 DOI: 10.1097/MLR.0000000000000471] [FullText]
- 13 **Tanaka M**, Fernández-del Castillo C, Adsay V, Chari S, Falconi M, Jang JY, Kimura W, Levy P, Pitman MB, Schmidt CM, Shimizu M, Wolfgang CL, Yamaguchi K, Yamao K; International Association of Pancreatology. International consensus guidelines 2012 for the management of IPMN and MCN of the pancreas. *Pancreatology* 2012; **12**: 183-197 [RCA] [PMID: 22687371 DOI: 10.1016/j.pan.2012.04.004] [FullText]
- 14 **Goh BK**, Thng CH, Tan DM, Low AS, Wong JS, Cheow PC, Chow PK, Chung AY, Wong WK, Ooi LL. Evaluation of the Sendai and 2012 International Consensus Guidelines based on cross-sectional imaging findings performed for the initial triage of mucinous cystic lesions of the pancreas: a single institution experience with 114 surgically treated patients. *Am J Surg* 2014; **208**: 202-209 [RCA] [PMID: 24530043 DOI: 10.1016/j.amjsurg.2013.09.031] [FullText]
- 15 **Han Y**, Kwon W, Lee M, Jung HS, Yun WG, Cho YJ, Chae YS, Fernández-Del Castillo C, Marchegiani G, Salvia R, Goh BKP, Lee WJ, Jang JY. Optimal Surveillance Interval of Branch Duct Intraductal Papillary Mucinous Neoplasm of the Pancreas. *JAMA Surg* 2024; **159**: 389-396 [RCA] [PMID: 38231494 DOI: 10.1001/jamasurg.2023.7010] [FullText]
- 16 **Marchegiani G**, Pollini T, Burelli A, Han Y, Jung HS, Kwon W, Rocha Castellanos DM, Crippa S, Belfiori G, Arcidiacono PG, Capurso G, Apadula L, Zaccari P, Noia JL, Gorris M, Busch O, Ponweera A, Mann K, Demir IE, Phillip V, Ahmad N, Hackert T, Heckler M, Lennon AM, Afghani E, Vallicella D, Dall'Olio T, Nepi A, Vollmer CM, Friess H, Ghaneh P, Besselink M, Falconi M, Bassi C, Goh BK, Jang JY, Fernández-Del Castillo C, Salvia R. Surveillance for Presumed BD-IPMN of the Pancreas: Stability, Size, and Age Identify Targets for Discontinuation. *Gastroenterology* 2023; **165**: 1016-1024.e5 [RCA] [PMID: 37406887 DOI: 10.1053/j.gastro.2023.06.022] [FullText]
- 17 **Ohno E**, Balduzzi A, Hijioka S, De Pastena M, Marchegiani G, Kato H, Takenaka M, Haba S, Salvia R. Association of high-risk stigmata and worrisome features with advanced neoplasia in intraductal papillary mucinous neoplasms (IPMN): A systematic review. *Pancreatology* 2024; **24**: 48-61 [RCA] [PMID: 38161091 DOI: 10.1016/j.pan.2023.12.002] [FullText]
- 18 **Zelga P**, Hernandez-Barco YG, Qadan M, Ferrone CR, Kambadakone A, Horick N, Jah A, Warshaw AL, Lillemoe KD, Balakrishnan A, Fernández-Del Castillo C. Number of Worrisome Features and Risk of Malignancy in Intraductal Papillary Mucinous Neoplasm. *J Am Coll Surg* 2022; **234**: 1021-1030 [RCA] [PMID: 35703792 DOI: 10.1097/XCS.000000000000176] [FullText]
- 19 **Sharib JM**, Fonseca AL, Swords DS, Jaradeh K, Bracci PM, Firpo MA, Hatcher S, Scaife CL, Wang H, Kim GE, Mulvihill SJ, Maitra A, Koay EJ, Kirkwood KS. Surgical overtreatment of pancreatic intraductal papillary mucinous neoplasms: Do the 2017 International Consensus Guidelines improve clinical decision making? *Surgery* 2018; **164**: 1178-1184 [RCA] [PMID: 30170819 DOI: 10.1016/j.surg.2018.07.014] [FullText]

- 20 **Kanno A**, Satoh K, Hirota M, Hamada S, Umino J, Itoh H, Masamune A, Asakura T, Shimosegawa T. Prediction of invasive carcinoma in branch type intraductal papillary mucinous neoplasms of the pancreas. *J Gastroenterol* 2010; **45**: 952-959 [RCA] [PMID: 20383536 DOI: 10.1007/s00535-010-0238-0] [FullText]
- 21 **Lee JH**, Lee KT, Park J, Bae SY, Lee KH, Lee JK, Jang KT, Heo JS, Choi SH, Choi DW, Rhee JC. Predictive factors associated with malignancy of intraductal papillary mucinous pancreatic neoplasms. *World J Gastroenterol* 2010; **16**: 5353-5358 [RCA] [PMID: 21072900 DOI: 10.3748/wjg.v16.i42.5353] [FullText] [Full Text(PDF)]
- 22 **Ohno E**, Itoh A, Kawashima H, Ishikawa T, Matsubara H, Itoh Y, Nakamura Y, Hiramatsu T, Nakamura M, Miyahara R, Ohmiya N, Ishigami M, Katano Y, Goto H, Hirooka Y. Malignant transformation of branch duct-type intraductal papillary mucinous neoplasms of the pancreas based on contrast-enhanced endoscopic ultrasonography morphological changes: focus on malignant transformation of intraductal papillary mucinous neoplasm itself. *Pancreas* 2012; **41**: 855-862 [RCA] [PMID: 22481289 DOI: 10.1097/MPA.0b013e3182480c44] [FullText]
- 23 **Crippa S**, Pezzilli R, Bissolati M, Capurso G, Romano L, Brunori MP, Calculli L, Tamburrino D, Piccioli A, Ruffo G, Fave GD, Falconi M. Active Surveillance Beyond 5 Years Is Required for Presumed Branch-Duct Intraductal Papillary Mucinous Neoplasms Undergoing Non-Operative Management. *Am J Gastroenterol* 2017; **112**: 1153-1161 [RCA] [PMID: 28244498 DOI: 10.1038/ajg.2017.43] [FullText]
- 24 **Pergolini I**, Sahara K, Ferrone CR, Morales-Oyarvide V, Wolpin BM, Mucci LA, Brugge WR, Mino-Kenudson M, Patino M, Sahani DV, Warshaw AL, Lillemoe KD, Fernández-Del Castillo C. Long-term Risk of Pancreatic Malignancy in Patients With Branch Duct Intraductal Papillary Mucinous Neoplasm in a Referral Center. *Gastroenterology* 2017; **153**: 1284-1294.e1 [RCA] [PMID: 28739282 DOI: 10.1053/j.gastro.2017.07.019] [FullText]
- 25 **Capurso G**, Crippa S, Vanella G, Traini M, Zerboni G, Zaccari P, Belfiori G, Gentiluomo M, Pessarelli T, Petrone MC, Campa D, Falconi M, Arcidiacono PG. Factors Associated With the Risk of Progression of Low-Risk Branch-Duct Intraductal Papillary Mucinous Neoplasms. *JAMA Netw Open* 2020; **3**: e2022933 [RCA] [PMID: 33252689 DOI: 10.1001/jamanetworkopen.2020.22933] [FullText] [Full Text(PDF)]
- 26 **Lee BS**, Nguyen AK, Tekeste TF, Chang K, Girgis A, Adeyemo M, Hanna MS, Yao JF, Kwok KK, Giap AQ, Hunt GC, Chaya CT, Kao KT, Attam R, Ko A, Pio JR, Tovar S, Lim BS. Long-term follow-up of branch-duct intraductal papillary mucinous neoplasms with No change in first 5 Years of diagnosis. *Pancreatol* 2021; **21**: 144-154 [RCA] [PMID: 33309223 DOI: 10.1016/j.pan.2020.10.040] [FullText]
- 27 **Ciprari D**, Weniger M, Qadan M, Hank T, Horick NK, Harrison JM, Marchegiani G, Andrianello S, Pandharipande PV, Ferrone CR, Lillemoe KD, Warshaw AL, Bassi C, Salvia R, Fernández-Del Castillo C. Risk of malignancy in small pancreatic cysts decreases over time. *Pancreatol* 2020; **20**: 1213-1217 [RCA] [PMID: 32819844 DOI: 10.1016/j.pan.2020.08.003] [FullText]
- 28 **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 European Gastroenterol J* 2025; **13**: 7-20 [RCA] [PMID: 39370669 DOI: 10.1002/ueg2.12666] [FullText]
- 29 **Oyama H**, Tada M, Takagi K, Tateishi K, Hamada T, Nakai Y, Hakuta R, Ijichi H, Ishigaki K, Kanai S, Kogure H, Mizuno S, Saito K, Saito T, Sato T, Suzuki T, Takahara N, Morishita Y, Arita J, Hasegawa K, Tanaka M, Fukayama M, Koike K. Long-term Risk of Malignancy in Branch-Duct Intraductal Papillary Mucinous Neoplasms. *Gastroenterology* 2020; **158**: 226-237.e5 [RCA] [PMID: 31473224 DOI: 10.1053/j.gastro.2019.08.032] [FullText]
- 30 **Johansson K**, Kaprio T, Nieminen H, Lehtimäki TE, Lantto E, Haglund C, Seppänen H. A retrospective study of intraductal papillary neoplasia of the pancreas (IPMN) under surveillance. *Scand J Surg* 2022; **111**: 14574969221076792 [RCA] [PMID: 35333109 DOI: 10.1177/14574969221076792] [FullText]
- 31 **Han Y**, Lee H, Kang JS, Kim JR, Kim HS, Lee JM, Lee KB, Kwon W, Kim SW, Jang JY. Progression of Pancreatic Branch Duct Intraductal Papillary Mucinous Neoplasm Associates With Cyst Size. *Gastroenterology* 2018; **154**: 576-584 [RCA] [PMID: 29074452 DOI: 10.1053/j.gastro.2017.10.013] [FullText]
- 32 **Deng H**, Dou W, Pan Y. The Surveillance for Presumed BD-IPMN of the Pancreas. *Gastroenterology* 2024; **166**: 939-940 [RCA] [PMID: 37549750 DOI: 10.1053/j.gastro.2023.07.023] [FullText]
- 33 **Khannoussi W**, Vullierme MP, Rebours V, Maire F, Hentic O, Aubert A, Sauvanet A, Dokmak S, Couvelard A, Hammel P, Ruszniewski P, Lévy P. The long term risk of malignancy in patients with branch duct intraductal papillary mucinous neoplasms of the pancreas. *Pancreatol* 2012; **12**: 198-202 [RCA] [PMID: 22687372 DOI: 10.1016/j.pan.2012.03.056] [FullText]
- 34 **Crippa S**, Marchegiani G, Belfiori G, Rancoita PVM, Pollini T, Burelli A, Apadula L, Scarale MG, Socci D, Biancotto M, Vanella G, Arcidiacono PG, Capurso G, Salvia R, Falconi M. Impact of age, comorbidities and relevant changes on surveillance strategy of intraductal papillary mucinous neoplasms: a competing risk analysis. *Gut* 2024; **73**: 1336-1342 [RCA] [PMID: 38653539 DOI: 10.1136/gutjnl-2023-329961] [FullText]
- 35 **Marchegiani G**, Salvia R; Verona EBM 2020 on IPMN. Guidelines on Pancreatic Cystic Neoplasms: Major Inconsistencies With Available Evidence and Clinical Practice- Results From an International Survey. *Gastroenterology* 2021; **160**: 2234-2238 [RCA] [PMID: 33609506 DOI: 10.1053/j.gastro.2021.02.026] [FullText]
- 36 **Hamada T**, Oyama H, Nevo D, Tange S, Takaoka S, Kawaguchi Y, Ishigaki K, Noguchi K, Saito T, Sato T, Suzuki T, Takahara N, Tanaka M, Hasegawa K, Ushiku T, Nakai Y, Petrov MS, Fujishiro M; TOP-CREATE Study Group. Risk factors for pancreatic cancer in individuals with intraductal papillary mucinous neoplasms and no high-risk stigmata during up to 5 years of surveillance: a prospective longitudinal cohort study. *Gut* 2025; **74**: 971-982 [RCA] [PMID: 39870394 DOI: 10.1136/gutjnl-2024-333259] [FullText]

FOOTNOTES

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