European Journal of Radiology Open 11 (2023) 100531

Contents lists available at ScienceDirect

European Journal of Radiology Open

journal homepage: www.elsevier.com/locate/ejro

Intraductal papillary mucinous neoplasms of the pancreas: Uncommon imaging presentation, evolution and comparison of guidelines

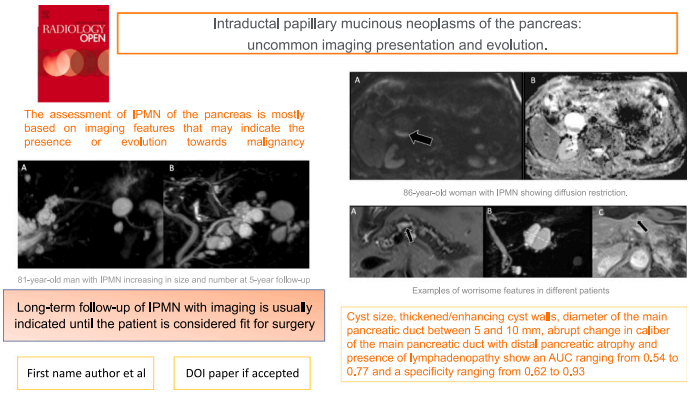
Chiara Minelli [a], Federico Balducci [a], Cristina Cavalleri [a], Anna Caterina Milanetto [b], Francesco Ferrara [c], Filippo Crimì [a], Emilio Quaia [a], Federica Vernuccio [d,*]

[a] Institute of Radiology, Department of Medicine-DIMED, University of Padova, 35128 Padova, Italy
[b] Chirurgia Generale 3, Department of Surgery, Oncology and Gastroenterology - University of Padova, 35128, Padova, Italy
[c] Gastroenterology Unit - University Hospital of Padova, 35128 Padova, Italy
[d] Department of Radiology, University Hospital of Padova, 35128 Padova, Italy

HIGHLIGHTS

- Most frequently IPMN are less than 10 mm in size at the time of detection, and in the majority of cases they have an indolent course.
- The assessment of IPMN of the pancreas is mostly based on imaging features that may indicate the presence or evolution towards malignancy.
- Long-term follow-up of IPMN with imaging is usually indicated until the patient is considered fit for surgery.

GRAPHICAL ABSTRACT



ARTICLE INFO

Keywords:
Pancreatic Intraductal Neoplasms
Pancreatic Neoplasms
Magnetic Resonance Imaging
Follow-Up Studies

ABSTRACT

Pancreatic cystic lesions are often asymptomatic, incidentally detected and include a range of entities with varying degrees of concern for malignancy. Among these, intraductal papillary mucinous neoplasms (IPMN) are considered premalignant pancreatic lesions, with a broad pathological spectrum ranging from lesions without dysplasia, which can be managed conservatively, to malignant lesions that require surgical resection. The increasing use of CT and MRI has led to increased recognition of this entity incidentally, with branch-duct IPMN representing the most common subtype and the most challenging lesions in terms of patient management. The main imaging modality involved in diagnosis and surveillance of IPMN is MRI. Radiologists play an important role in the management of patients with IPMN, including lesion detection, characterization, follow-up and

Abbreviations: IPMN, intraductal papillary mucinous neoplasms; CT, Computed Tomography; MRI, Magnetic Resonance Imaging; BD-IPMN, branch-duct IPMN; MD-IPMN, main-duct IPMN; MRCP, Magnetic Resonance Cholangiopancreatography; EUS, Endoscopic ultrasound; AUC, area under the curve; HRS, high-risk stigmata; WF, worrisome feature; HGD, High grade dysplasia; AGA, American Gastroenterological Association; IAP, International Association of Pancreatology; CA 19–9, Carbohydrate Antigen 19–9; CEA, Carcino-Embryonic Antigen; ROC, Receiver Operating Characteristics.

* Corresponding author at: Department of Radiology, University Hospital of Padova, Via Niccolò Giustiniani n.2, 35128, Padova, Italy.
E-mail address: federicavernuccio@gmail.com (F. Vernuccio).

https://doi.org/10.1016/j.ejro.2023.100531
Received 4 August 2023; Received in revised form 29 September 2023; Accepted 10 October 2023

prognostication, allowing early MRI identification of features that are concerning for malignancy. The main aim of this pictorial review is to illustrate MRI features of IPMN and to discuss risk stratification scores based on different guidelines, with a main focus on branch-duct IPMN. The secondary aims include the presentation of common and uncommon imaging evolution of BD-IPMN as well as the discussion on current controversies on the appropriate management of IPMN.

1. Introduction

Pancreatic cystic lesions are often asymptomatic, incidentally detected and are being increasingly recognized in up to 49 % of abdominal MRI studies [1,2]. Among pancreatic cystic lesions, intraductal papillary mucinous neoplasms (IPMN) are the most common and are considered premalignant pancreatic lesions, with a broad pathological spectrum ranging from low grade to high grade and eventually to invasive carcinoma [2–4]. IPMN are intraductal proliferation of mucinous epithelial cells. They are mainly distinguished into main-duct IPMNs (MD-IPMN), which originate from the main pancreatic duct, branch-duct IPMNs (BD-IPMN), which originate from the ductal branches of the main duct and are the most common, and mixed IPMNs which combine MD-IPMN and BD-IPMN characteristics with an average risk of dysplastic evolution.

Magnetic Resonance Cholangiopancreatography (MRCP) is the recommended imaging technique for assessment of IPMN at baseline and at follow-up, allowing recognition of septa, nodules and duct communication [5,6]. Most frequently IPMN are less than 10 mm in size at the time of detection [1,2], and in the majority of cases they have an indolent course [1,6,7]. Secretin-enhanced MRI may help accentuate BD-IPMN communication with the main pancreatic duct and differentiate chronic pancreatitis and MD-IPMN [8,9], although experts' recommendations indicate the little benefit of secretin-enhanced MRI beyond standard MRCP in patients with cystic pancreatic neoplasms overall [10]. Additional MR imaging features may help further delineate cystic pancreatic lesions; in this setting, diffusion-weighted imaging (DWI) and apparent diffusion coefficient (ADC) values could represent a useful tool in the differential diagnosis of pancreatic cystic lesions, with higher ADC values observed in the mucinous lesions compared with serous cystadenomas [11].

Endoscopic ultrasound should be considered if there are imaging features worrisome for malignancy on MRCP or if the patient is symptomatic [5]. MRI and EUS are comparable in terms of diagnostic accuracy in the differentiation between benign and malignant IPMN, with the former having the advantage of being non-invasive [12]. To another hand, EUS could be completed in unclear cases with the contrast-enhanced images evaluation (for instance distinguishing mural nodules vs. mucinous intra-cystic plugs) as well the intracystic fluid aspiration for biochemical or cytological analysis. In this setting, the combination of all the features, such as EUS morphology, cytology and cyst fluid CEA, provide greater accuracy in detecting mucinous PCN than either EUS morphology or cytology alone [13].

Surgery for MD-IPMN is universally accepted considering the high-rate of malignancy due to MD-IPMN. Conversely, malignancy development has been reported in about 1.9–7.8 % of BD-IPMN [14–18], with this malignancy rate being likely overestimated [19]; therefore, management of BD-IPMN is considered challenging and has been debated over the years. Therefore, radiologists – together with the clinicians, such as surgeons and gastroenterologists, involved in the patients' management – nowadays play a pivotal role in the evaluation of BD-IPMN both at baseline and at follow-up indicating the need for further diagnostic assessment and identifying suspicious features of malignancy.

The main aim of this pictorial review is to illustrate MRI features of IPMN and to discuss risk stratification scores based on different guidelines, with a main focus on branch-duct IPMN. The secondary aims include the presentation of common and uncommon imaging evolution of IPMN as well as the discussion on current controversies on the appropriate management of IPMN.

Table 1
Main epidemiology, clinical, imaging and outcomes of the most common pancreatic cystic lesions.

	IPMN	Serous Cystic Neoplasm	Mucinous Cystic Neoplasm
Sex	Both M and F	F > M	Almost exclusively F
Age (decade)	4th-5th	6th-7th	6th-7th
Asymptomatic	~ 50 %	Mostly when small	~ 50 %
Location	All tracts	Head > Body	Tail/Body
Cyst size	Variable	Microcystic > Macrocystic	Macrocystic
Number	Often multiple	Usually single	Usually single
Solid components	When malignant	Central scar	When malignant
Calcifications	- (occasionally within the duct)	Within central scar in 30 %	Peripheral/ septal
MR imaging signal intensity	T1: hypo/hyper T2: hyper	T1: hypo T2: hyper	T1: hypo/hyper T2: hyper
Enhancement	Walls, nodule if malignant	Central scar, septa	Variable
Main pancreatic duct communication	Side branch: present Main duct: dilatated	Absent	Absent

2. IPMN and differential diagnoses

The most common pancreatic cystic lesions are IPMN, followed by serous cystadenoma, and mucinous cystadenoma [2]. In the setting of pancreatitis, pseudocyst and walled-off necrosis may occur as cystic lesions occurring 4 weeks after interstitial edematous and necrotizing pancreatitis, respectively [20].

Most pancreatic cystic lesions are benign, although some of them hold malignant potential. Table 1 summarizes the main epidemiology, clinical, imaging and outcomes of the most common pancreatic cystic lesions [21–25]. Herein, the main imaging features of the most common pancreatic cystic lesions are presented:

-MD-IPMN: focal or diffuse dilatation of the main pancreatic duct with a cut-off of 5 mm or 7 mm, depending on Fukuoka guidelines or American College of Radiology white paper [5,25].

- BD-IPMN: unilocular cysts communicating with the main pancreatic duct or cluster of small cysts with lobulated margins and septa, also known as grapelike lobulated appearance, with communication with the main pancreatic duct.

- serous cystadenoma: multiple small cysts giving the appearance of a multilobulated multiloculated cystic lesion, also known as honeycomb pattern, with a central scar with stellate calcifications in up to 30 % of cases, and lack of communication with the main pancreatic duct (Fig. 1) or, more rarely, a rare macro/oligocystic variant;.

- mucinous cystic neoplasm: oligocystic lesion without any communication with the main pancreatic duct; septa, nodules or capsular calcifications may be present.

Other less common pancreatic cystic lesions include solid pseudopapillary neoplasm, pancreatic cystic neuroendocrine tumor (Fig. 2), retention cyst, lymphoepithelial cyst, cystic acinar cell carcinoma

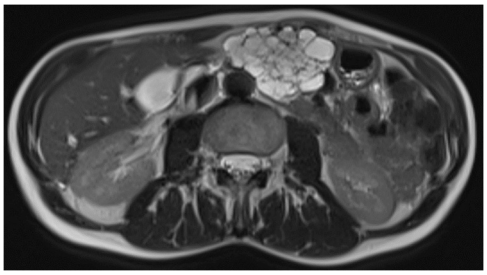


Fig. 1. 50-year-old woman with serous cystadenoma. T2-weighted non-fat sat sequence in the axial plane shows a multiloculated cystic lesion, with the honeycomb pattern, and lack of communication with the main pancreatic duct.

(Fig. 3), epidermoid cyst, intraductal oncocytic papillary neoplasms and intraductal tubulopapillary neoplasms, with these two latter entities, which cannot be distinguish by radiology, but only at final histology, having been indicated as distinct neoplasms from IPMN only in the most recent classification of the World Health Organization (WHO) published in 2019 [3,4].

3. Management of IPMN based on different guidelines and scoring systems

The assessment of IPMN of the pancreas is mostly based on imaging features that may indicate the presence or evolution towards malignancy [26]. Among these imaging features, a diameter of the main pancreatic duct 10 mm or greater, the presence of an enhanced solid component, and lymphadenopathy show a large AUC (0.95, 0.89, and 0.89, respectively) and a high specificity (0.98, 0.95, and 0.97, respectively), but a low sensitivity (0.14, 0.38, and 0.09, respectively) [26]. The remaining imaging features include cyst size, thickened/enhancing cyst walls, diameter of the main pancreatic duct between 5 and 10 mm, abrupt change in caliber of the main pancreatic duct with distal pancreatic atrophy and presence of lymphadenopathy show an AUC ranging from 0.54 to 0.77, a specificity ranging from 0.62 to 0.93, and a sensitivity ranging from 0.17 to 0.59 [26]. Compared with conventional MRI alone, the acquisition of diffusion weighted imaging improves diagnostic accuracy (Fig. 4) with increased specificity for differentiating malignant from benign IPMNs of the pancreas and provides a "biological" information to morphological data obtained by MRI [27]. Similarly, 18-FDG-PET proved to be sensitive, specific, and accurate in detecting malignant IPMNs (80 %, 95 %, and 87 %, respectively) [28,29].

Clinical and imaging evaluation based on the aforementioned imaging features in patients affected by BD-IPMN has been investigated in many studies and has been included in different clinical guidelines:

- The International Association of Pancreatology (IAP) published the first International Consensus Guidelines (Sendai guidelines) for the evaluation and management of IPMN in 2006 and recommended resection only for BD-IPMN with the following features: symptomatic cysts; asymptomatic cysts size of 3 cm or larger; main pancreatic duct dilation of 6 mm or more; presence of a mural nodule [30]. In 2012, the IAP updated these criteria, referred to as the Fukuoka guidelines and established the following new classification of features based on potential clinical and radiologic predictors of high-grade dysplasia (HGD)/malignancy: high-risk stigmata (HRS) and worrisome features (WFs). Factors associated with HRS due to the high risk of HGD/malignancy include obstructive jaundice, an enhancing solid component and a dilation of the main pancreatic duct of 10 mm or more and in these cases surgical resection is recommended by these guidelines. The WFs (Fig. 5) include a cyst size of 3 cm or larger, thickened/enhancing cyst walls, a diameter of the main pancreatic duct of 5–9 mm, abrupt changes in the caliber of the main pancreatic duct with distal pancreatic atrophy, non-enhancing mural nodule (Fig. 4) [23]. In the presence of WFs further assessment by

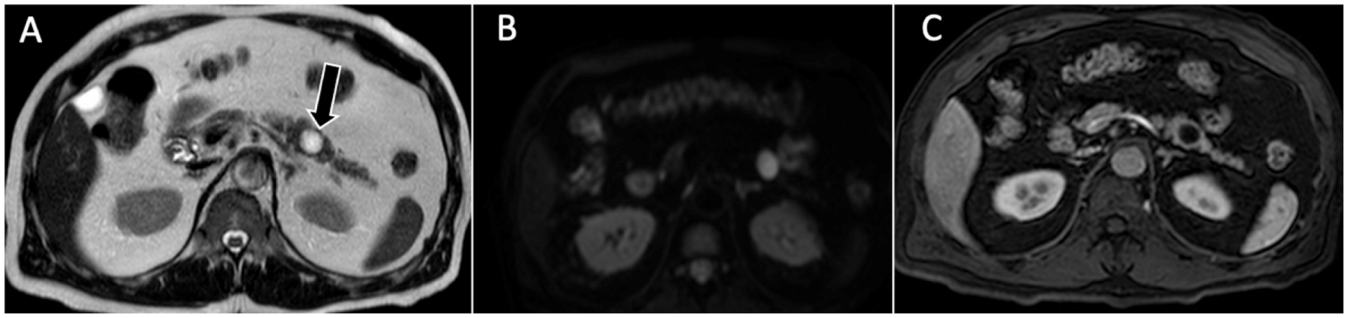


Fig. 2. 63-year-old man with cystic pancreatic neuroendocrine tumor. A. T2-weighted non-fat sat sequence in the axial plane shows a uniloculated cyst (arrow), with lack of septa. B. On diffusion-weighted-image the lesion shows diffusion restriction. C. On contrast-enhanced T1-weighted MR image a thin enhancing wall is evident.

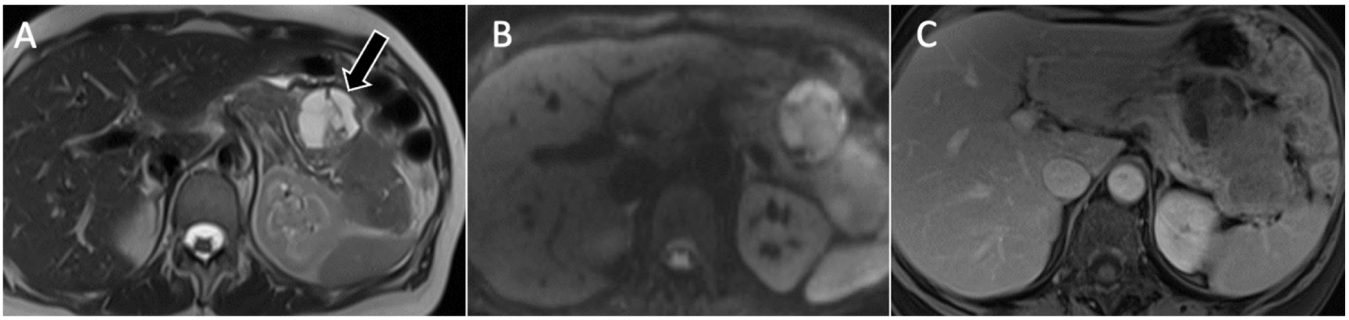


Fig. 3. 60-year-old woman with cystic acinar cell carcinoma. A. T2-weighted non-fat sat sequence in the axial plane shows a uniloculated cyst (arrow), with thick septa and a mural nodule. B. On diffusion-weighted-image the lesion shows diffusion restriction. C. On contrast-enhanced T1-weighted MR image a thin enhancing wall is evident and the mural nodule shows mild enhancement.

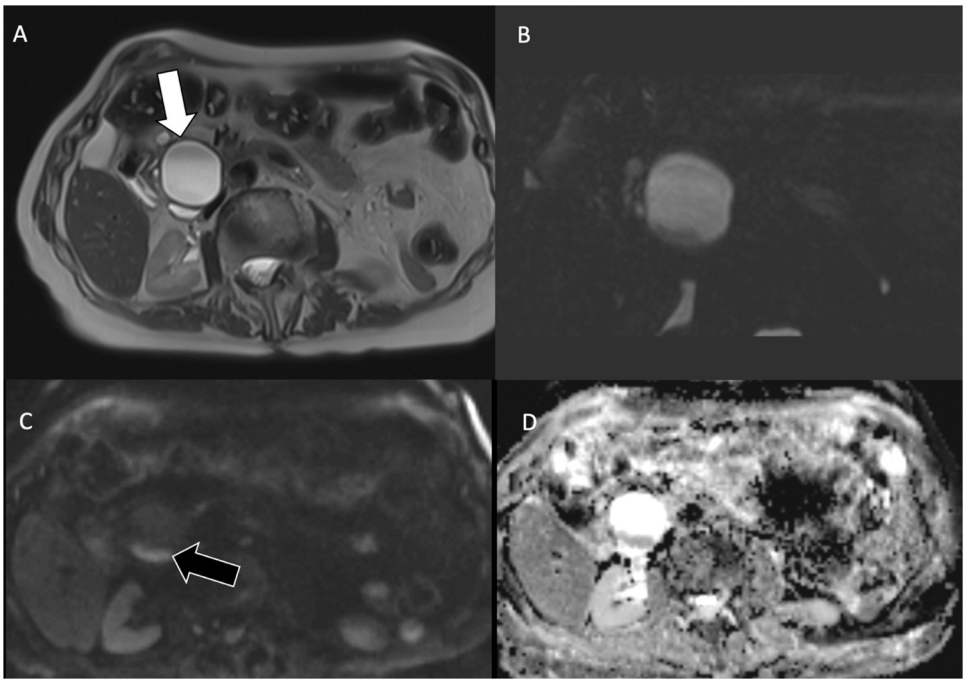


Fig. 4. 86-year-old woman with IPMN. A. T2 weighted image and B. MRCP image show a hyperintense lesion (white arrow) consistent with a cystic lesion, in communication with the main pancreatic duct, consistent with IPMN with. C. Diffusion weighted image shows a slight posterior hyperintensity (black arrow) on high b value. D. ADC map shows hypointensity corresponding to the hyperintense area on diffusion weighted image, consistent with true diffusion restriction.

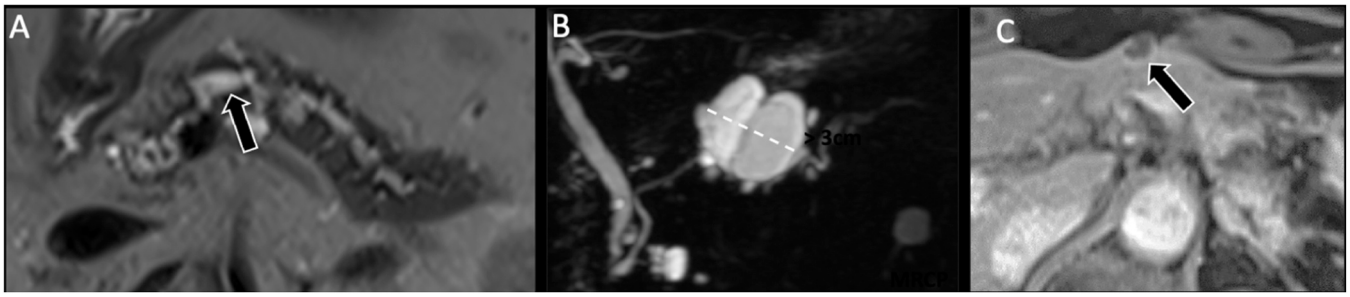


Fig. 5. Examples of worrisome features in different patients. A. T2-weighted non-fat sat sequence in the axial plane shows a dilated main pancreatic duct (arrow) of up to 7 mm. B. Coronal MRCP image shows a cyst that is larger than 3 cm. C. Contrast-enhanced T1-weighted MR image shows a thin enhancing wall.

endoscopic ultrasound is recommended. The latest update, published in 2017, made only minor revisions and put particular emphasis on the size of enhancing mural nodule for predicting HGD/malignancy, while adding lymphadenopathy and cyst growth rate as WFs [5]. Fig. 6 summarizes the Fukuoka guidelines based on the proposed management.

- In 2015, the guidelines of the American Gastroenterological Association (AGA) For asymptomatic pancreatic neoplastic cysts, suggested that patients with pancreatic cysts smaller than 3 cm without a solid component or a dilated pancreatic duct should undergo MRI for surveillance in 1 year and then every 2 years for a total of 5 years if there is no change in size or characteristics, while patients with pancreatic cysts with at least two high-risk features (i.e. size ≥3 cm, main pancreatic duct dilation and solid component) should be examined by endoscopic ultrasound with fine needle aspiration [31]. In addition, endoscopic ultrasound with fine needle aspiration is indicated in these guidelines in case of significant changes in the characteristics of the cyst, including the development of a solid component, increasing size of the pancreatic duct, and/or diameter ≥3 cm [31]. AGA guidelines recommend resection in patients with both a solid component and a dilated pancreatic duct and/or concerning features on endoscopic ultrasound with fine needle aspiration [31].
- In 2018, the European evidence-based guidelines were published as a joint initiative of the European Study Group on Cystic Tumors of the Pancreas, the United European Gastroenterology, the European Pancreatic Club, the European-African Hepato-Pancreato-Biliary Association, European Digestive Surgery and the European Society of Gastrointestinal Endoscopy and involved both European and non-European experts [13]. These guidelines established "relative and absolute indications'' for surgery similar to the concepts of HRS and WFs established by the IAP. Indeed, the European evidence-based guidelines consider jaundice (tumor related), the presence of an enhancing mural nodule of at least 5 mm or a solid component, positive cytology, or a main pancreatic duct measuring at least 10 mm highly predictive of malignancy and absolute indications for surgery in those patients that are fit for surgery [13]. In patients with IPMN and an absolute indication for resection, an oncologic resection including standard lymphadenectomy is the preferred choice by these guidelines. Main pancreatic duct dilatation between 5 and 9.9 mm, cystic growth-rate ≥5 mm/year, increased level of serum CA 19.9 (>37 U/mL), symptoms, enhancing mural nodules

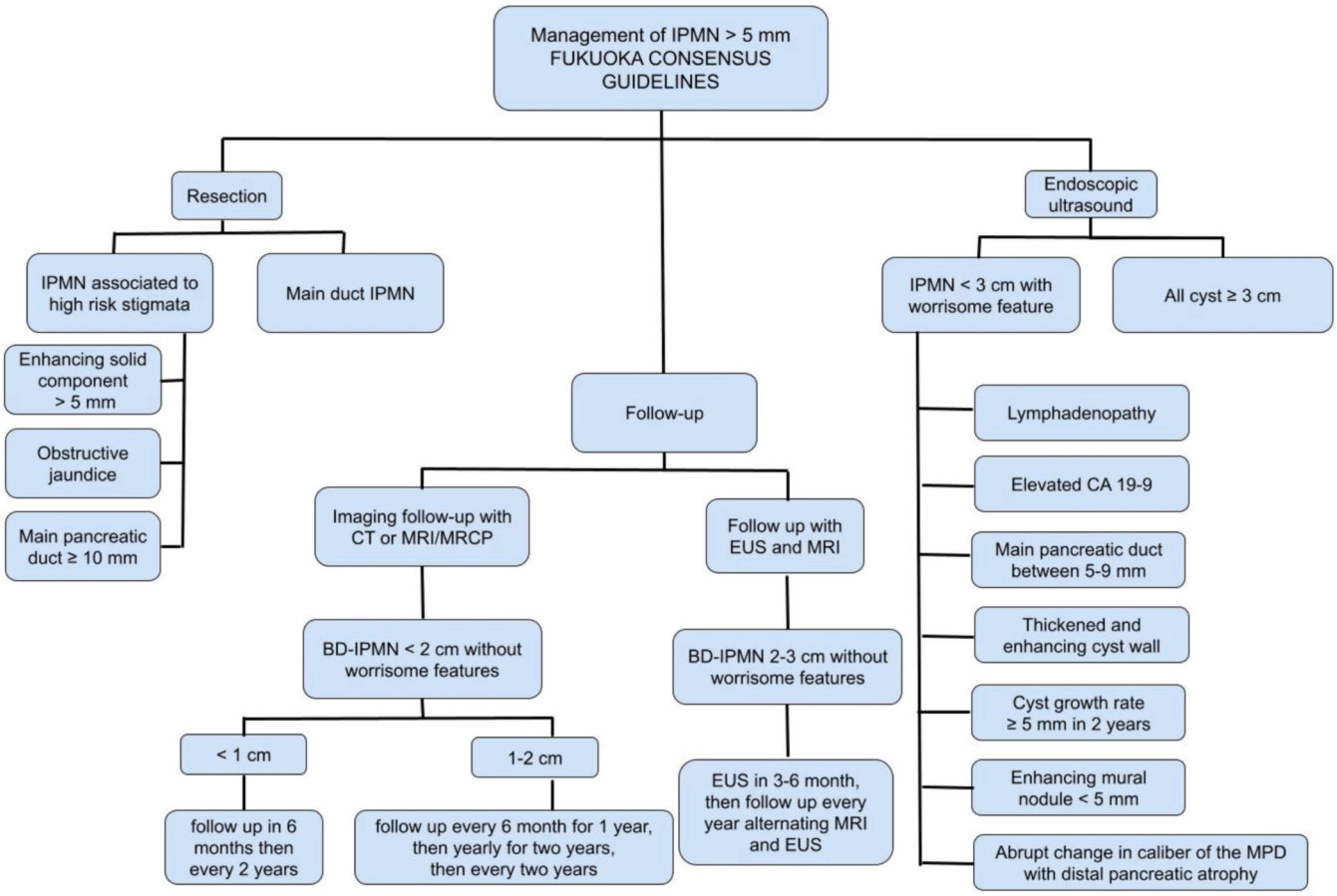


Fig. 6. Flowchart of the management of IPMN based on the Fukuoka consensus guideline.

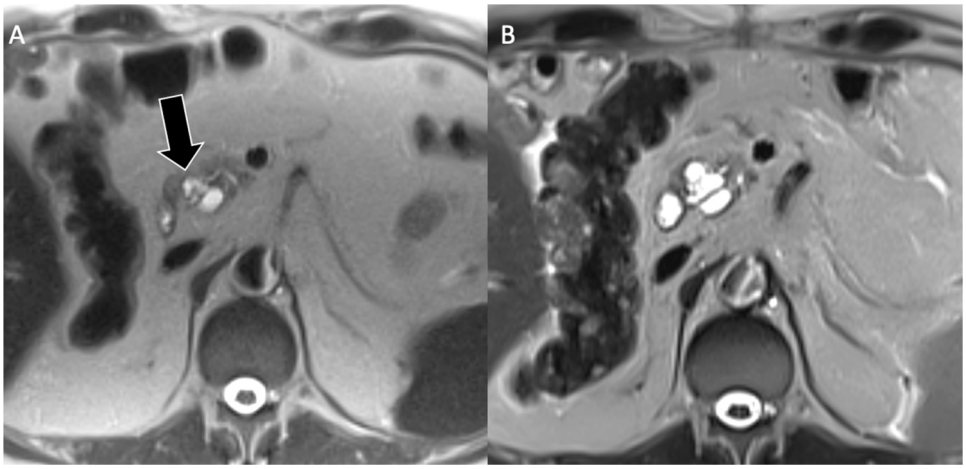


Fig. 7. Shin scoring system. A. T2-weighted non-fat sat sequence acquired in 2014 shows a BD-IPMN (arrow) in a 54-year-old man with CA19.9 of 23.9 IU/mL, with a Shin score of 0. B. T2-weighted non-fat sat sequence acquired in the same patients in 2022 when the patient was aged 67, showed a size increase of the BD-IPMN accompanied by an increase of the CA19.9 to 109.5 IU/mL with a final Shine score of 2.

(<5 mm), a cyst diameter ≥40 mm, new onset of diabetes mellitus, and acute pancreatitis caused by IPMN are considered as features indicating an increased risk for HGD and are indicated as relative indications for surgery [13].

- The Shin Score, published in 2010 in an Asian cohort, comprises five variables: age ≥ 60 years, history of pancreatitis, serum CA19.9 > 37 IU/mL, MPD diameter ≥ 6 mm and presence of mural nodules [32]. Shin et al. [32] indeed demonstrated that these five variables were independently predictive of malignant IPMN at multivariate analysis with odds ratios of 4.81 for presence of mural nodule(s), 4.55 for diameter of main pancreatic duct > 6 mm, 3.87 for history of pre-operative pancreatitis, 3.20 for age ≥ 60 years, 3.58 for and CA-19–9 > 37 U/mL. Since the difference in the odds ratios was small, authors assigned one point to each variable, with a final score from 0 to 5 (Fig. 7). Shin score of 0 or 1 had a specificity of 93.0 %, a sensitivity of 34.0 %, and a positive predictive value (PPV) of 90 %

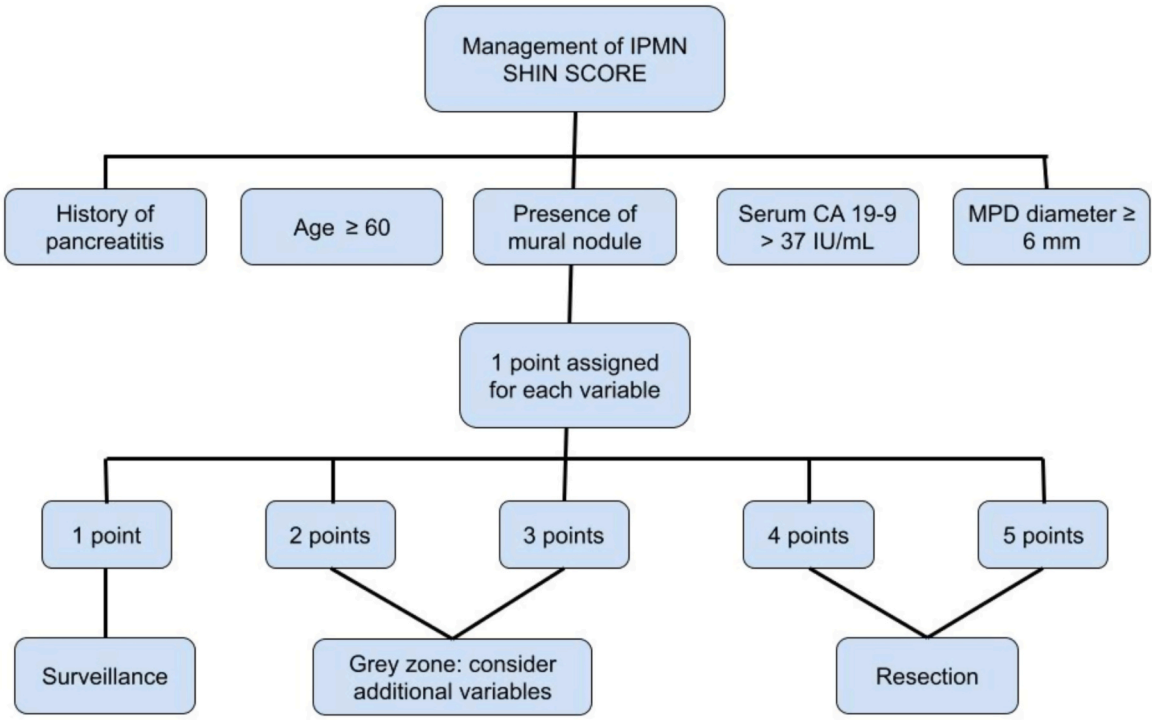


Fig. 8. Flowchart of the management of IPMN based on the Shin score.

for benignity in their cohort [32]. With a cut-off of 3, the Shin scoring system could predict malignancy with a sensitivity of 50.7 % and a specificity of 90.1 % in the authors' cohort [32]. The 5-year survival was also different based on the Shin scoring system ranging from 94.4 % in score 0–1 group, to 71.8 % in score 4–5 group. The Shin scoring system was later validated in a European cohort involving 11 countries and 567 patients overall: sensitivity and specificities for predicting malignancy were respectively 57.3 % and 64.4 % for a Shin score of 3, 21.7 % and 90.4 % for a Shin score of 4 %, and 4.2 % and 98.6 % for a Shin score of 5 [33]. Authors conclude that a Shin score of 1 or less should be monitored, while those with scores of 4 or more should undergo surgery [33]. Fig. 8 summarizes the application of the Shin score [33].

- In 2011, Hwang et al. [34] proposed two scoring systems for predicting malignancy and invasiveness as follows: malignancy-predicting score = 22.4 (presence of mural nodule [0 or 1]) + 0.5 (size of cyst [mm]) and invasiveness- predicting score = 36.6 (presence of mural nodule [0 or 1]) + 32.2 (elevated serum concentration of CEA [0 or 1]) + 0.6 (size of cyst [mm]), with the optimal cutoffs being respectively 14 and 21. Based on their results authors concluded that a BD-IPMN with mural nodule should be regarded as malignant IPMN itself [34].

Regarding the comparative performance of the above-mentioned guidelines and scores, in 2017 Xu et al. [35] published a retrospective study showing that overall diagnostic accuracy of the AGA guidelines was at 75.8 % versus 49.8 % for the 2012 Fukuoka guidelines, the miss-rate for HGD or cancer was 92.7 % if the AGA guidelines for resection were applied and 26.8 % with the 2012 Fukuoka guidelines, while the percentage of unnecessary surgery was 11.8 % with the AGA guidelines and 54 % with the 2012 Fukuoka guidelines. In 2021, Crippa et al. indicated that European and International guidelines have a relatively low diagnostic accuracy, being European guidelines more aggressive [36] and Vanden Bulcke et al. [37] reported a sensitivity of 96 % for the European guidelines, 80 % for the AGA guidelines and 67 % for the IAP guidelines, a specificity respectively of 11.3 %, 43.8 % and 26.8 %, a missed malignancy rate respectively of 1.5 %, 7.7 % and 11.3 % and a surgical overtreatment respectively of 59.1 %, 34.6 % and 48.4 %. More recently, in 2023 van Huijgevoort et al. [38] compared the diagnostic accuracy of the AGA, IAP, and European guidelines for detecting advanced neoplasia in intraductal papillary mucinous neoplasm/neoplasia demonstrating that the IAP and European guidelines were superior in detecting advanced neoplasia in IPMN as compared to the AGA (94 %−96 % versus 27 %, respectively) albeit at the cost of a higher rate of unnecessary surgery (76 %−83 % versus 8.6 %, respectively). In addition, the ROC curve comparison analyses showed that European (AUC 0.599) was superior to the IAP guideline (AUC 0.557) in identifying advanced neoplasia ($p = 0.009$) [38].

Table 2 summarizes the different recommendations, scores and algorithms illustrated above. Fig. 9 provides an overview of the clinical management [13].

4. Common and uncommon evolutions

Benign imaging evolution is quite common in low-risk BD-IPMN: most BD-IPMNs increase in size in the first 5 years (Fig. 10) and cysts with baseline size larger than 20 mm continued to grow beyond 5 years at a faster rate; however, growth rate usually does not exceed 1.7 mm/year, and less than 10 % of cysts develop worrisome features [39,40]. Unfortunately, delayed growth (Fig. 11), development of WF, HRS or invasive carcinoma even after 5 years has been also reported, thus supporting long-term follow-up with imaging until the patient is considered fit for surgery [41–43]. There is no clear marker that can predict with certainty how an IPMN is going to progress.

In a study including patients with a minimum follow-up of 10 years on MRI, Boraschi et al. [44] demonstrated that BD-IPMN remained dimensionally unchanged or slightly reduced in size in 26.2 % (Figs. 12) and 4.3 % of cases respectively and WF and HRS developed in 14.5 % and 4.3 % cases (Fig. 13), respectively, with an incidence of pancreatic cancer in patients with BD-IPMN of 2.9 %. In a recent systematic review and metanalysis published in 2023, the pooled incidence of WF/HRS among low-risk BD-IPMNs during initial and extended surveillance was

Table 2
Comparison the different recommendations and proposed scores and algorithms for the management of IPMN.

Guideline – Score - Algorithm	Year	Factors Taken Into Consideration And Consequent Clinical Decision
First International consensus guidelines from the International Association of Pancreatology (IAP) ("Sendai Guidelines")	2006	- "Sendai positive" if tumor size was ≥ 3 cm, symptomatic, mural nodules or thickened wall, or accompanied by a dilated MPD of ≥ 6 mm. Patients who did not meet these criteria were considered "Sendai negative."
The Shin Score	2010	• Age ≥60 years; • History of pancreatitis; • Serum CA19.9 > 37 IU/mL; • MPD diameter ≥ 6 mm and presence of mural nodules. Authors conclude that a Shin score of 1 or less should be monitored, while those with scores of 4 or more should undergo surgery.
Hwang et al.	2011	Proposed two scoring systems for predicting malignancy and invasiveness as follows: • Malignancy-predicting score = 22.4 (presence of mural nodule [0 or 1]) + 0.5 (size of cyst [mm]); • Invasiveness- predicting score = 36.6 (presence of mural nodule [0 or 1]) + 32.2 (elevated serum concentration of CEA [0 or 1]) + 0.6 (size of cyst [mm]). The optimal cutoffs being respectively 14 and 21. Based on their results authors concluded that a BD-IPMN with mural nodule should be regarded as malignant IPMN itself.
Update of the first international consensus guidelines of the International Association of Pancreatology (IAP), also called "Fukuoka guidelines"	2012	New classification of features based on potential clinical and radiologic predictors of high-grade dysplasia (HGD)/malignancy: high-risk stigmata (HRS) and worrisome features (WFs). • WFs: cyst size of 3 cm or larger, thickened/enhancing cyst walls, a diameter of the main pancreatic duct of 5–9 mm, abrupt changes in the caliber of the main pancreatic duct with distal pancreatic atrophy, non-enhancing mural nodule. • HRS: obstructive jaundice, an enhancing solid component and a dilation of the main pancreatic duct of 10 mm or more. In the presence of WFs further assessment by endoscopic ultrasound is recommended; in the presence of HRS, surgical resection is recommended. The latest update, published in 2017, made only minor revisions and emphasized the size of enhancing mural nodule for predicting HGD/malignancy, while adding lymphadenopathy and cyst growth rate as WFs.
American Gastroenterological Association (AGA) guidelines	2015	• Patients with pancreatic cysts smaller than 3 cm without a solid component or a dilated pancreatic duct should undergo MRI for surveillance in 1 year and then every 2 years for a total of 5 years if there is no change in size or characteristics. • Patients with pancreatic cysts with at least two high-risk features (i.e., size ≥3 cm, main pancreatic duct dilation and solid component) should be examined by endoscopic ultrasound with fine needle aspiration. Endoscopic ultrasound with fine needle aspiration is indicated in case of significant changes in the characteristics of the cyst, including the development of a solid component, increasing size of the pancreatic duct and/or diameter ≥ 3 cm. Resection is recommended in patients with both a solid component and a dilated pancreatic duct and/or concerning features on endoscopic ultrasound with fine needle aspiration.
European evidence-based guidelines as a joint initiative of the European Study Group on Cystic Tumors of the Pancreas, the United European Gastroenterology, the European Pancreatic Club, the European-African Hepato-Pancreato-Biliary Association, European Digestive Surgery and the European Society of Gastrointestinal Endoscopy	2018	Established "relative and absolute indications'' for surgery similar to the concepts of HRS and WFs established by the IAP. The European evidence-based guidelines consider jaundice (tumor related), the presence of an enhancing mural nodule of at least 5 mm or a solid component, positive cytology, or a main pancreatic duct measuring at least 10 mm highly predictive of malignancy and absolute indications for surgery in those patients that are fit for surgery. In patients with IPMN and an absolute indication for resection, an oncologic resection including standard lymphadenectomy is the preferred choice by these guidelines. Main pancreatic duct dilatation between 5 and 9.9 mm, cystic growth-rate ≥ 5 mm/year, increased level of serum CA 19.9 (>37 U/mL), symptoms, enhancing mural nodules (<5 mm), a cyst diameter ≥ 40 mm, new onset of diabetes mellitus, and acute pancreatitis caused by IPMN are considered as features indicating an increased risk for HGD and are indicated as relative indications for surgery.

2.2 % and 2.9 % patient-years, respectively, whereas the incidence of advanced neoplasia was 0.6 % and 1.0 % patient-years, respectively. Among BD-IPMNs with initial size stability, extended surveillance after 5 years had a WF/HRS and advanced neoplasia incidence of 1.9 % and 0.2 % patient-years, respectively [45].

Given the wide variability of long-term outcome and the low incidence of cancer among BD-IPMN, management of patients is still a matter of debate. Currently, most newly diagnosed BD-IPMNs do not require surgery. The indication to surgery is based considering above-mentioned guidelines, patient's life expectancy, comorbidities, location of the cyst and patient willingness. There is no good long-term data indicating whether surveillance can be safely spaced every 2 years or even more or when patient follow-up should be stopped. While the AGA suggests against continued surveillance of pancreatic cysts if there has been no significant change in the characteristics of the cyst after 5 years

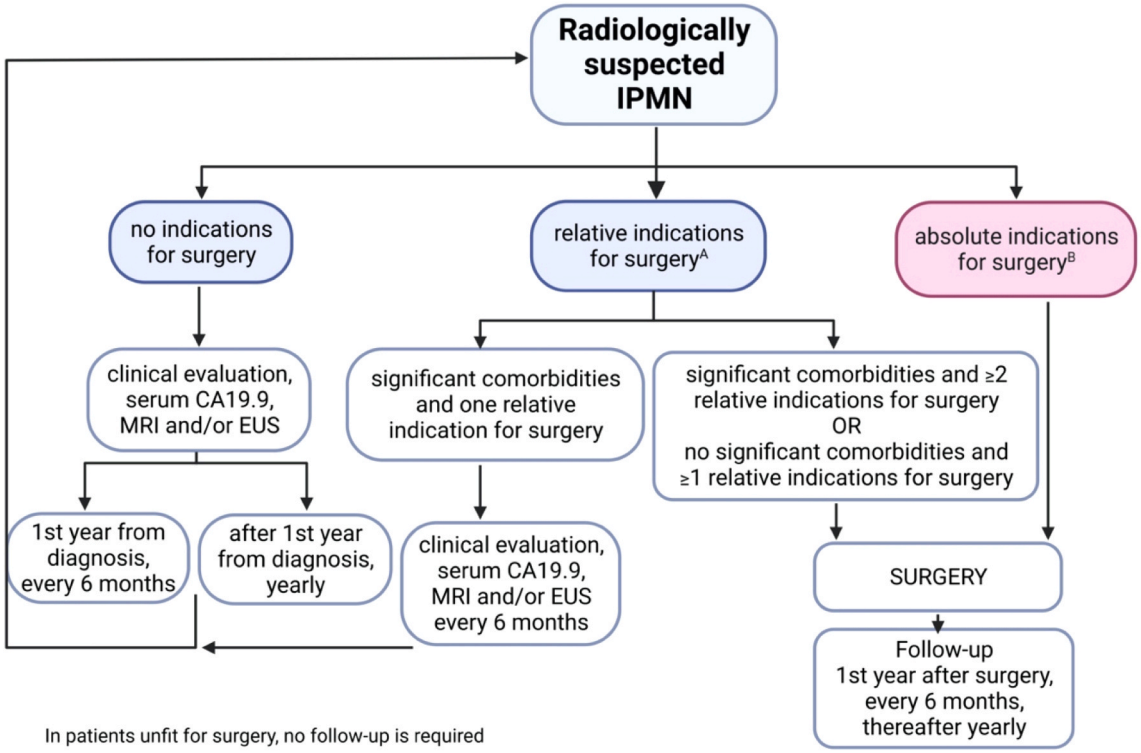


Fig. 9. Flowchart of the management of IPMN based on the European guidelines proposed by multiple societies, including European Study Group on Cystic Tumors of the Pancreas, the United European Gastroenterology, the European Pancreatic Club, the European-African Hepato-Pancreato-Biliary Association, European Digestive Surgery and the European Society of Gastrointestinal Endoscopy. Adapted from European Study Group on Cystic Tumours of the Pancreas. European evidence-based guidelines on pancreatic cystic neoplasms. Gut. 2018;67(5):789–804. doi: 10.1136/gutjnl-2018–316027 [13].

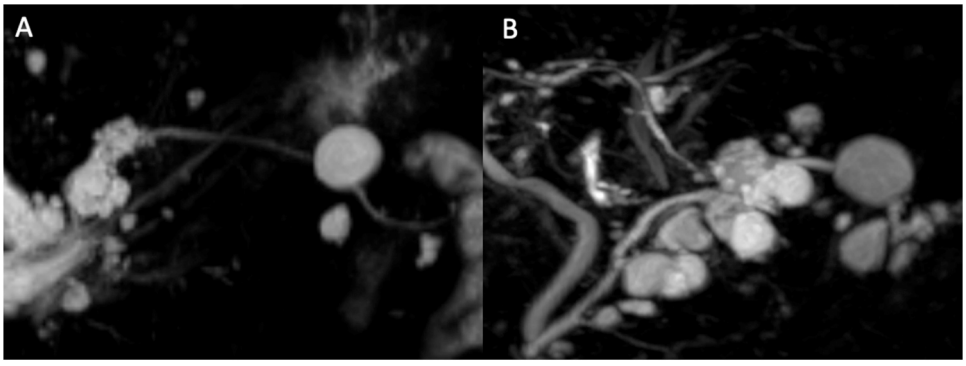


Fig. 10. 81-year-old man with IPMN increasing in size and number. A. MRCP image acquired in 2017 shows at least four BD-IPMN communicating with the main pancreatic duct. Ca19.9 in 2017 was 13,9 IU/mL. B. MRCP image in 2022 showed increase in number and size of the BD-IPMN. Ca19.9 in 2022 was also increased to 63,9 IU/mL.

of surveillance or if the patient is no longer a surgical candidate, the European-based guidelines suggest patient follow-up until the patient is fit for surgery, also in those patients that have already been resected for IPMN [13,31].

5. The role of Radiomics and other possible risk factors for malignancy

Radiomics and deep learning have emerged in the recent years for advanced imaging analysis for many diseases, including pancreatic cystic lesions [46]. In a recent study, Lee et al. [47] demonstrated that CT radiomics may have superior predictive ability for malignant IPMN compared to the 2017 international consensus Fukuoka guideline CT radiomics.

Recent reports suggest that pancreatic fatty infiltration may probably induces chronic inflammation caused by the release of various cytokines and chemokines by adipose tissue, leading to the development of cancer. Indeed, in the study proposed by Sotozono et al. [48], the pancreatic proton density fat fraction (PDFF) with multi-echo 3D DIXON, which is a quantitative index of pancreatic steatosis using MRI, was significantly higher in the patients with IPMN with a concomitant invasive carcinoma than in the patients with normal pancreas or with non-degenerated

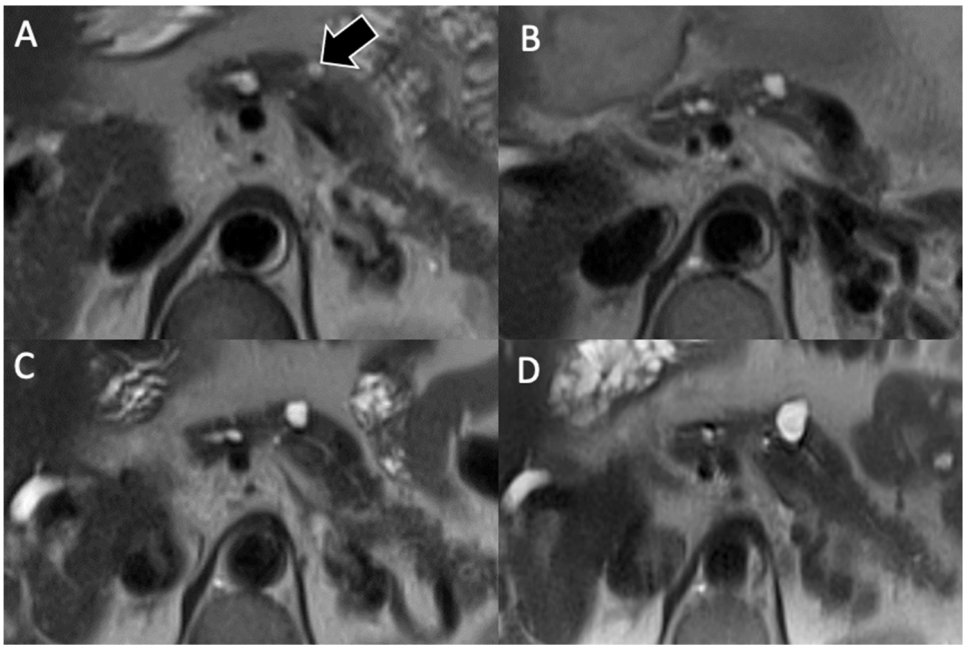


Fig. 11. 61-year-old man with IPMN increasing in size after 8 year stability. T2-weighted non-fat sat sequence acquired in 2010 (A), 2015 (B), 2018 (C) and 2020 (D), show a BD-IPMN (arrow) with a maximum diameter of 7 mm, 8 mm, 10 mm and 16 mm, respectively.

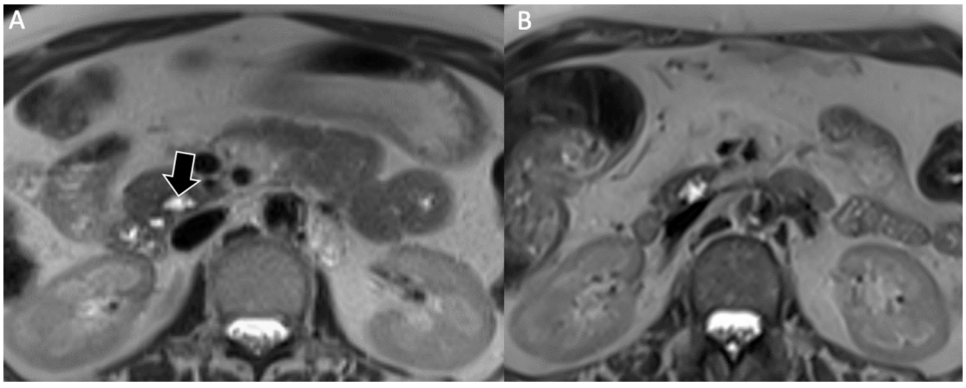


Fig. 12. 51-year-old woman with IPMN stable in size at 4-year-follow-up. T2-weighted non-fat sat images acquired in 2018 (A) and 2022 (B), show a BD-IPMN (arrow) that remains stable in size over time.

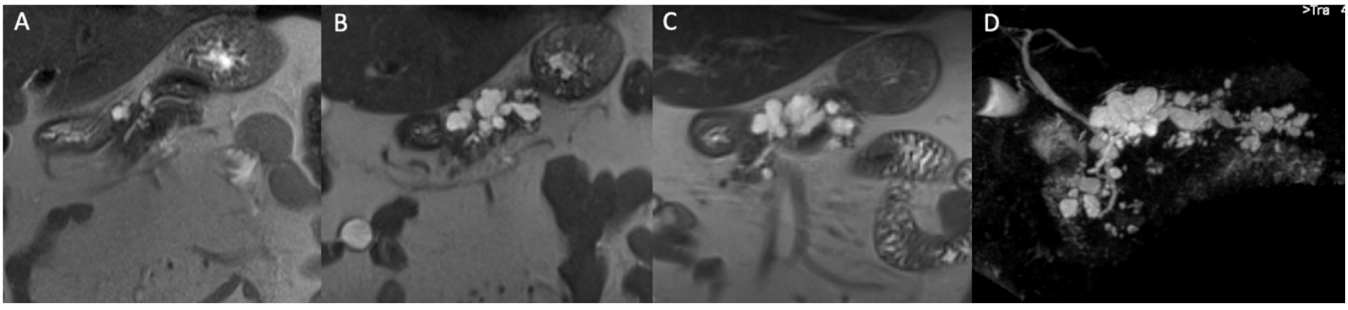


Fig. 13. 77-year-old man with IPMN and appearance of high-risk stigmata at follow-up. MR images in the coronal plane acquired in 2010 (A), 2021 (B) and 2022 (C and D), show multiple BD-IPMN that increase in number and size over time and appearance of dilatation of the main pancreatic duct over 10 mm in the last imaging follow-up.

IPMN. Evrimler et al. [49] investigated the association between MRI-derived pancreatic fat fraction and malignancy in patients with IPMN and concluded that the mean fat fraction was significantly higher in the high-risk IPMN group compared to the low-risk IPMN group. With regard to CT, Abe et al. [50] compared pancreatic density on CT between high-grade dysplasia/malignancy and low-grade dysplasia/no malignancy groups in patients undergoing surgical resection for IPMN and suggested that decreased CT density of the pancreas can be a reliable

biomarker for detecting patients with IPMN having malignancies.

6. Conclusion

Radiologists play an important role in the management of patients with IPMN. Radiologists need to be aware of common/uncommon evolutions of IPMNs, well-known and novel worrisome features to identify malignancy within IPMN, as well as common and uncommon differential diagnosis with other cystic pancreatic lesions.

CRediT authorship contribution statement

Minelli Chiara: Writing – original draft, Investigation, Conceptualization. **Milanetto Anna Caterina:** Writing – original draft, Visualization, Methodology, Conceptualization. **Ferrara Francesco:** Writing – review & editing, Conceptualization. **Balducci Federico:** Writing – review & editing, Data curation. **Cavalleri Cristina:** Writing – review & editing, Methodology, Data curation. **Vernuccio Federica:** Writing – review & editing, Visualization, Supervision, Project administration, Methodology, Conceptualization. **Crimì Filippo:** Writing – review & editing, Resources. **Quaia Emilio:** Writing – review & editing, Visualization, Validation, Supervision, Investigation, Data curation.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

[1] M.L. Kromrey, R. Bülow, J. Hübner, C. Paperlein, M.M. Lerch, T. Ittermann, H. Völzke, J. Mayerle, J.P. Kühn, Prospective study on the incidence, prevalence and 5-year pancreatic-related mortality of pancreatic cysts in a population-based study, Gut 67 (1) (2018) 138–145, https://doi.org/10.1136/gutjnl-2016-313127.

[2] R. Girometti, S. Intini, G. Brondani, G. Como, F. Londero, F. Bresadola, C. Zuiani, M. Bazzocchi, Incidental pancreatic cysts on 3D turbo spin echo magnetic resonance cholangiopancreatography: prevalence and relation with clinical and imaging features, Abdom. Imaging 36 (2) (2011) 196–205, https://doi.org/10.1007/s00261-010-9618-4.

[3] Assarzadegan N., Babaniamansour S., Shi J. Updates in the Diagnosis of Intraductal Neoplasms of the Pancreas. Front Physiol. 2022;13:856803. doi: 10.3389/fphys.2022.856803. Erratum in: Front Physiol. 2022;13:923917.

[4] WHO Classification of Tumours Editorial Board. Digestive System Tumours, 5th edn., International Agency for Research on Cancer, Lyon (France), 2019 https://doi.org/10.1111/his.13975.

[5] M. Tanaka, C. Fernández-del Castillo, T. Kamisawa, J.Y. Jang, P. Levy, T. Ohtsuka, et al., Revisions of international consensus Fukuoka guidelines for the management of IPMN of the pancreas, Pancreatology 17 (5) (2017) 738–753, https://doi.org/10.1111/his.13975.

[6] E.M. Hecht, G. Khatri, D. Morgan, S. Kang, P.R. Bhosale, I.R. Francis, et al., Intraductal papillary mucinous neoplasm (IPMN) of the pancreas: recommendations for Standardized Imaging and Reporting from the Society of Abdominal Radiology IPMN disease focused panel, Abdom. Radio. 46 (4) (2021) 1586–1606, https://doi.org/10.1007/s00261-020-02853-4.

[7] M. Kayal, L. Luk, E.M. Hecht, C. Do, B.A. Schrope, J.A. Chabot, T.A. Gonda, Long-term surveillance and timeline of progression of presumed low-risk intraductal papillary mucinous neoplasms, AJR Am. J. Roentgenol. 209 (2) (2017) 320–326, https://doi.org/10.2214/AJR.16.17249.

[8] Purysko A.S., Gandhi N.S., Walsh R.M., Obuchowski N.A., Veniero J.C. Does secretin stimulation add to magnetic resonance cholangiopancreatography in characterising pancreatic cystic lesions as side-branch intraductal papillary mucinous neoplasm? Eur Radiol;24(12):3134–41. doi: 10.1007/s00330–014-3355-y.

[9] P. Boraschi, F. Donati, R. Cervelli, F. Pacciardi, Secretin-stimulated MR cholangiopancreatography: spectrum of findings in pancreatic diseases, Insights Imaging 7 (6) (2016) 819–829, https://doi.org/10.1007/s13244-016-0517-2.

[10] J. Swensson, A. Zaheer, D. Conwell, K. Sandrasegaran, R. Manfredi, T. Tirkes, Secretin-enhanced MRCP: how and why— AJR expert panel narrative review, 1139–49, Am. J. Roentgenol. 216 (5) (2021), https://doi.org/10.2214/AJR.20.24857.

[11] P. Boraschi, P. Scalise, M.T. Casotti, E.F. Kauffmann, U. Boggi, F. Donati, Cystic lesions of the pancreas: is apparent diffusion coefficient value useful at 3 T magnetic resonance imaging? J. Comput. Assist Tomogr. 46 (3) (2022) 363–370, https://doi.org/10.1097/RCT.0000000000001302.

[12] H. Liu, Y. Cui, J. Shao, Z. Shao, F. Su, Y. Li, The diagnostic role of CT, MRI/MRCP, PET/CT, EUS and DWI in the differentiation of benign and malignant IPMN: a meta-analysis, Clin. Imaging 72 (2021) 183–193, https://doi.org/10.1016/j.clinimag.2020.11.018.

[13] uropean Study Group on Cystic Tumours of the Pancreas, European evidence-based guidelines on pancreatic cystic neoplasms, Gut 67 (5) (2018) 789–804, https://doi.org/10.1136/gutjnl-2018-316027.

[14] M. Moris, M. Raimondo, T.A. Woodward, et al., International intraductal papillary mucinous neoplasms registry: long-term results based on the new guidelines, Pancreas 46 (2017) 306–310, https://doi.org/10.1097/MPA.0000000000000750.

[15] H. Maguchi, S. Tanno, N. Mizuno, et al., Natural history of branch duct intraductal papillary mucinous neoplasms of the pancreas: a multicenter study in Japan, Pancreas 40 (2011) 364–370, https://doi.org/10.1097/MPA.0b013e31820a5975.

[16] G. Malleo, G. Marchegiani, A. Borin, et al., Observational study of the incidence of pancreatic and extrapancreatic malignancies during surveillance of patients with branch-duct intraductal papillary mucinous neoplasm, Ann. Surg. 261 (2015) 984–990, https://doi.org/10.1097/SLA.0000000000000884.

[17] I. Pergolini, K. Sahora, C.R. Ferrone, et al., Long-term risk of pancreatic malignancy in patients with branch duct intraductal papillary mucinous neoplasm in a referral center, e1, Gastroenterology 153 (2017) 1284–1294, https://doi.org/10.1053/j.gastro.2017.07.019.

[18] S.H. Choi, S.H. Park, K.W. Kim, J.Y. Lee, S.S. Lee, Progression of unresected intraductal papillary mucinous neoplasms of the pancreas to cancer: a systematic review and meta-analysis, e4, Clin. Gastroenterol. Hepatol. 15 (2017) 1509–1520, https://doi.org/10.1016/j.cgh.2017.03.020.

[19] D.T. Weaver, A.P. Lietz, S.F. Mercaldo, M.L.B. Peters, C. Hur, C.Y. Kong, B. M. Wolpin, A.J. Megibow, L.L. Berland, A.B. Knudsen, P.V. Pandharipande, Testing for verification bias in reported malignancy risks for side-branch intraductal papillary mucinous neoplasms: a simulation modeling approach, AJR Am. J. Roentgenol. 212 (3) (2019) 596–601, https://doi.org/10.2214/AJR.18.20180.

[20] K. Zhao, S.Z. Adam, R.N. Keswani, J.M. Horowitz, F.H. Miller, Acute pancreatitis: revised atlanta classification and the role of cross-sectional imaging, AJR Am. J. Roentgenol. 205 (1) (2015) W32–W41, https://doi.org/10.2214/AJR.14.14056.

[21] C. Delavaud, G. d'Assignies, J. Cros, P. Ruszniewski, P. Hammel, P. Levy, et al., CT and MR imaging of multilocular acinar cell cystadenoma: comparison with branch duct intraductal papillary mucinous neoplasia (IPMNs), Eur. Radio. 24 (9) (2014) 2128–2136, https://doi.org/10.1007/s00330-014-3248-0.

[22] H. Osman, D.R. Jeyarajah, Pancreas cystic lesions, Surg. Clin. North Am. 100 (3) (2020) 581–588, https://doi.org/10.1016/j.suc.2020.02.006.

[23] M. Tanaka, C. Fernández-del Castillo, V. Adsay, S. Chari, M. Falconi, J.Y. Jang, et al., International consensus guidelines 2012 for the management of IPMN and MCN of the pancreas, Pancreatology 12 (3) (2012) 183–197, https://doi.org/10.1016/j.pan.2012.04.004.

[24] K.S. Burk, D. Knipp, D.V. Sahani, Cystic pancreatic tumors, Magn. Reson. Imaging Clin. North Am. 26 (3) (2018) 405–420, https://doi.org/10.1016/j.mric.2018.03.006.

[25] A.J. Megibow, M.E. Baker, D.E. Morgan, et al., Management of incidental pancreatic cysts: a white paper of the ACR incidental findings committee, J. Am. Coll. Radio. 14 (7) (2017) 911.

[26] W. Zhao, S. Liu, L. Cong, Y. Zhao, Imaging features for predicting high-grade dysplasia or malignancy in branch duct type intraductal papillary mucinous neoplasm of the pancreas: a systematic review and meta-analysis, Ann. Surg. Oncol. 29 (2) (2022) 1297–1312.

[27] K.M. Jang, S.H. Kim, J.H. Min, S.J. Lee, T.W. Kang, S. Lim, D. Choi, Value of diffusion-weighted MRI for differentiating malignant from benign intraductal papillary mucinous neoplasms of the pancreas, AJR Am. J. Roentgenol. 203 (5) (2014) 992–1000, https://doi.org/10.2214/AJR.13.11980.

[28] S. Serafini, C. Sperti, A.R. Brazzale, D. Cecchin, P. Zucchetta, E.S. Pierobon, A. Ponzoni, M. Valmasoni, L. Moletta, The role of positron emission tomography in clinical management of intraductal papillary mucinous neoplasms of the pancreas, Cancers (Basel) 12 (4) (2020) 807, https://doi.org/10.3390/cancers12040807.

[29] Pasquali C., Milanetto, A.C. (2016). PET Scan in Cystic Tumors of the Pancreas. Cystic Tumors of the Pancreas: Diagnosis and Treatment, 97–106. 10.1007/978–3-319–31882-0_8 Marco Del Chiaro (Editor), Stephan L. Haas (Editor), Richard D. Schulick (Editor) Publisher: Springer 1st ed. 2016.

[30] M. Tanaka, S. Chari, V. Adsay, F.D. Carlos Castillo, M. Falconi, M. Shimizu, et al., International consensus guidelines for management of intraductal papillary mucinous neoplasms and mucinous cystic neoplasms of the pancreas, Pancreatology 6 (1–2) (2006) 17–32, https://doi.org/10.1159/000090023.

[31] S.S. Vege, B. Ziring, R. Jain, P. Moayyedi, M.A. Adams, S.D. Dorn, et al., American gastroenterological association institute guideline on the diagnosis and management of asymptomatic neoplastic pancreatic cysts, Gastroenterology 148 (4) (2015) 819–822, https://doi.org/10.1053/j.gastro.2015.01.015.

[32] S.H. Shin, D.J. Han, K.T. Park, Y.H. Kim, J.B. Park, S.C. Kim, Validating a simple scoring system to predict malignancy and invasiveness of intraductal papillary mucinous neoplasms of the pancreas, 776–83, World J. Surg. 34 (4) (2010), https://doi.org/10.1007/s00268-010-0416-5.

[33] A. Manuel-Vázquez, A. Balakrishnan, P. Agami, B. Andersson, F. Berrevoet, M. G. Besselink, et al., A scoring system for predicting malignancy in intraductal papillary mucinous neoplasms of the pancreas: a multicenter EUROPEAN validation, Lange Arch. Surg. 407 (8) (2022) 3447–3455, https://doi.org/10.1007/s00423-022-02687-2.

[34] D.W. Hwang, J.Y. Jang, C.S. Lim, S.E. Lee, Y.S. Yoon, Y.J. Ahn, et al., Determination of malignant and invasive predictors in branch duct type intraductal papillary mucinous neoplasms of the pancreas: a suggested scoring formula, J. Korean Med. Sci. 26 (6) (2011) 740, https://doi.org/10.3346/jkms.2011.26.6.740.

[35] M.M. Xu, S. Yin, A.A. Siddiqui, R.R. Salem, B. Schrope, A. Sethi, et al., Comparison of the diagnostic accuracy of three current guidelines for the evaluation of asymptomatic pancreatic cystic neoplasms, Medicine (Baltimore) 96 (35) (2017), e7900, https://doi.org/10.1097/MD.0000000000007900.

[36] S. Crippa, A. Fogliati, R. Valente, O. Sadr-Azodi, U. Arnelo, G. Capurso, A. Halimi, S. Partelli, Z. Ateeb, P.G. Arcidiacono, J.M. Lohr, M. Falconi, M. Del Chiaro, A tug-of-war in intraductal papillary mucinous neoplasms management: comparison between 2017 International and 2018 European guidelines, Dig. Liver Dis. 53 (8) (2021) 998–1003, https://doi.org/10.1016/j.dld.2021.03.009.

[37] A. Vanden Bulcke, J. Jaekers, H. Topal, D. Vanbeckevoort, V. Vandecaveye, T. Roskams, B.A. Weynand, J. Dekervel, E. Van Cutsem, H. van Malenstein, C. Verslype, W. Laleman, S. van der Merwe, Evaluating the accuracy of three international guidelines in identifying the risk of malignancy in pancreatic cysts: a retrospective analysis of a surgical treated population, Acta Gastroenterol. Belg. 84 (3) (2021) 443–450, https://doi.org/10.51821/84.3.006.

[38] N.C.M. van Huijgevoort, S.A.M. Hoogenboom, S.J. Lekkerkerker, O.R. Busch, M. Del Chiaro, P. Fockens, I. Somers, J. Verheij, R.P. Voermans, M.G. Besselink, J. E. van Hooft, Diagnostic accuracy of the AGA, IAP, and European guidelines for detecting advanced neoplasia in intraductal papillary mucinous neoplasm/neoplasia, Pancreatology 23 (3) (2023) 251–257, https://doi.org/10.1016/j.pan.2023.01.011.

[39] M. Kayal, L. Luk, E.M. Hecht, C. Do, B.A. Schrope, J.A. Chabot, T.A. Gonda, Long-term surveillance and timeline of progression of presumed low-risk intraductal papillary mucinous neoplasms, AJR Am. J. Roentgenol. 209 (2) (2017) 320–326, https://doi.org/10.2214/AJR.16.17249.

[40] A. Arlix, B. Bournet, P. Otal, et al., Long-term clinical and imaging follow-up of nonoperated branch duct form of intraductal papillary mucinous neoplasms of the pancreas, Pancreas 41 (2) (2012) 295–301, https://doi.org/10.1097/MPA.0b013e3182285cc8.

[41] N.C.M. van Huijgevoort, M. Del Chiaro, C.L. Wolfgang, J.E. van Hooft, M. G. Besselink, Diagnosis and management of pancreatic cystic neoplasms: current evidence and guidelines, Nat. Rev. Gastroenterol. Hepatol. 16 (11) (2019) 676–689, https://doi.org/10.1038/s41575-019-0195-x.

[42] S. Crippa, R. Pezzilli, M. Bissolati, et al., Active surveillance beyond 5 years is required for presumed branch-duct intraductal papillary mucinous neoplasms undergoing non-operative management, Am. J. Gastroenterol. 112 (7) (2017) 1153–1161, https://doi.org/10.1038/ajg.2017.43.

[43] W. Khannoussi, M.P. Vullierme, V. Rebours, F. Maire, O. Hentic, A. Aubert, A. Sauvanet, S. Dokmak, A. Couvelard, P. Hammel, P. Ruszniewski, P. Lévy, The long term risk of malignancy in patients with branch duct intraductal papillary mucinous neoplasms of the pancreas, Pancreatology 12 (3) (2012) 198–202, https://doi.org/10.1016/j.pan.2012.03.056.

[44] P. Boraschi, G. Tarantini, F. Donati, P. Scalise, R. Cervelli, D. Caramella, Side-branch intraductal papillary mucinous neoplasms of the pancreas: outcome of MR imaging surveillance over a 10 years follow-up, Eur. J. Radio. Open 7 (2020), 100250, https://doi.org/10.1016/j.ejro.2020.100250.

[45] A. Chhoda, S. Singh, A.H. Sheth, A.A. Grimshaw, C.G. Gunderson, P. Sharma, J. W. Kunstman, A. Sharma, N. Ahuja, T.A. Gonda, J.J. Farrell, Benefit of extended surveillance of low-risk pancreatic cysts after 5-year stability: a systematic review and meta-analysis, Clin. Gastroenterol. Hepatol. 21 (6) (2023) 1430–1446, https://doi.org/10.1016/j.cgh.2022.04.025.

[46] C. Huang, S. Chopra, C.W. Bolan, H. Chandarana, N. Harfouch, E.M. Hecht, G. C. Lo, A.J. Megibow, Pancreatic cystic lesions: next generation of radiologic assessment, Gastrointest. Endosc. Clin. N. Am. 33 (3) (2023) 533–546, https://doi.org/10.1016/j.giec.2023.03.004.

[47] D.Y. Lee, J. Shin, S. Kim, S.E. Baek, S. Lee, N.H. Son, M.S. Park, Radiomics model versus 2017 revised international consensus guidelines for predicting malignant intraductal papillary mucinous neoplasms, Eur. Radiol. (2023), https://doi.org/10.1007/s00330-023-10158-5.

[48] H. Sotozono, A. Kanki, K. Yasokawa, A. Yamamoto, H. Sanai, K. Moriya, T. Tamada, Value of 3-T MR imaging in intraductal papillary mucinous neoplasm with a concomitant invasive carcinoma, Eur. Radio. 32 (12) (2022) 8276–8284, https://doi.org/10.1007/s00330-022-08881-6.

[49] S. Evrimler, M.T. Yip-Schneider, J. Swensson, M. Soufi, R. Muraru, T. Tirkes, C. M. Schmidt, F. Akisik, Magnetic resonance imaging-derived fat fraction predicts risk of malignancy in intraductal papillary mucinous neoplasm, Abdom. Radio. (NY) 46 (10) (2021) 4779–4786, https://doi.org/10.1007/s00261-021-03146-0.

[50] T. Abe, D. Yamada, K. Asukai, S. Hasegawa, A. Tomokuni, H. Wada, W. Fujii, K. Ikezawa, N. Fukutake, K. Ohkawa, N. Shinno, H. Hara, Y. Yanagimoto, Y. Takahashi, K. Sugimura, K. Yamamoto, H. Ushigome, N. Haraguchi, J. Nishimura, M. Yasui, T. Omori, H. Miyata, M. Ohue, M. Yano, M. Sakon, H. Takahashi, Decreased CT-number in the pancreatic parenchyma is a reliable imaging biomarker of the presence of malignancies in patients with high-risk intraductal papillary mucinous neoplasm, Pancreatology 20 (3) (2020) 442–447, https://doi.org/10.1016/j.pan.2020.02.014.