Lesioni Cistiche del Pancreas

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Timeline of published guidelines spans more than a decade

- **2006** Consensus (Sendai)
- **2010** Radiology
- **2012** Consensus (Fukuoka)
- **2013** European
- **2014** Italian
- **2015** AGA Institute
- **2016** ASGE
- **2017** Revised Fukuoka
- **2018** ACG
- **2018** European

Diagnostics **2023**, *13*, 749

Pancreatic Cysts

An Overview

- ✓ Frequent
- ✓ Potentially malignant
- ✓ Need for surgery

The questions!

How many?

- ✓ Stressfull condition for patients *(and non-expert doctors)*

Pancreatic cyst: What clinician needs?

Stefano Francesco Crinò, Luca Frulloni
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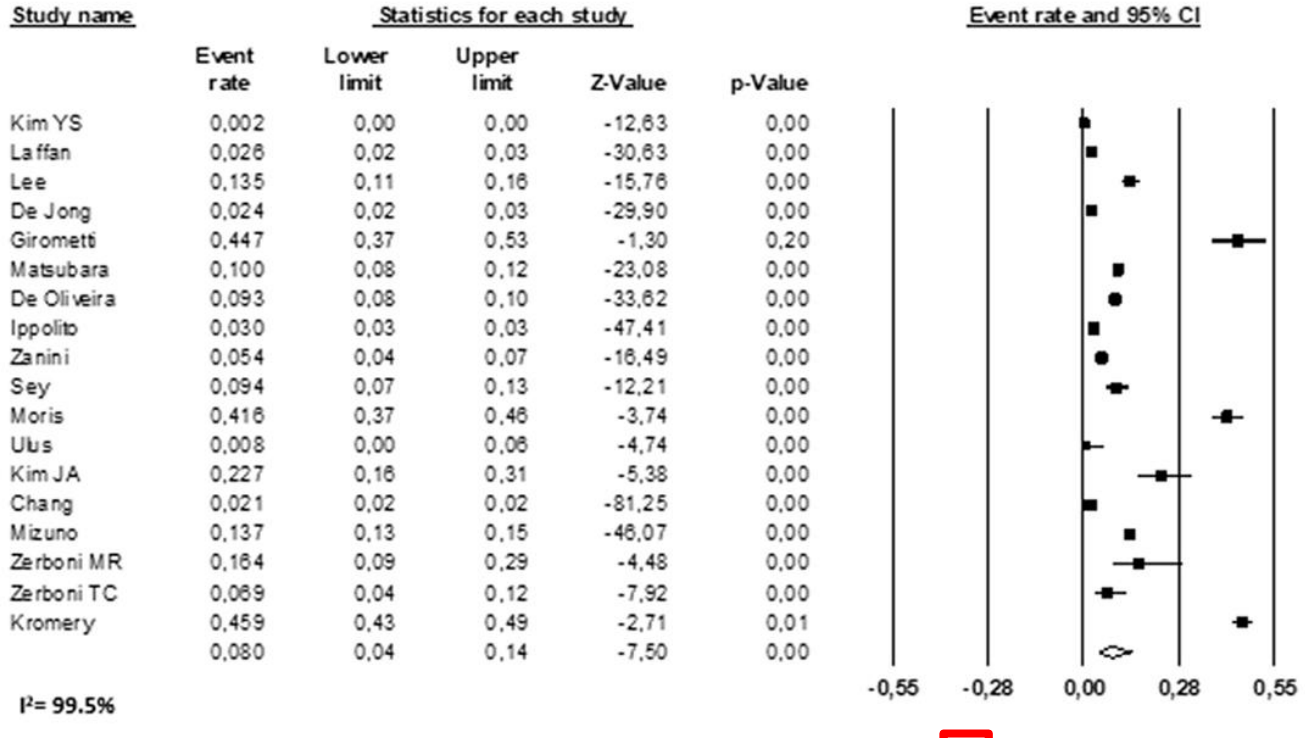
Table 1. Prevalence of pancreatic cyst in large series of cross-sectional studies on healthy patients

Author, year	Imaging	Area	Patients (*N*)	Patients with cyst(s) (*N*)	Prevalence (%)
Zhang *et al.*, 2002[5]	MR	USA	1444	283	19.6
Laffan *et al.*, 2008[6]	CT	USA	2832	73	2.6
de Jong *et al.*, 2010[7]	MR	Ned	2803	66	2.4
Lee *et al.*, 2010[8]	MR	USA	616	83	13.5
de Oliveira *et al.*, 2015[9]	MR	Brazil	2583	239	9.3
Zanini *et al.*, 2015[10]	CT	Italy	650	35	5.4
Sey *et al.*, 2015[11]	EUS	USA	341	32	9.4
Moris *et al.*, 2016[12]	MR	USA	500	208	41.6
Soroida *et al.*, 2016[13]	US	Japan	5198	182	3.5
Kromrey *et al.*, 2018[14]	MR	Germany	1077	494	49.1
Martínez *et al.*, 2018[15]	EUS	Spain	298	64	21.5
Total	-	-	15,822	1941	12.3

MR: Magnetic resonance, CT: Computed tomography, US: Ultrasound

Systematic review and meta-analysis: Prevalence of incidentally detected pancreatic cystic lesions in asymptomatic individuals

Giulia Zerboni [a], Marianna Signoretti [a], Stefano Crippa [b, d], Massimo Falconi [b, d], Paolo Giorgio Arcidiacono [c], Gabriele Capurso [c, *]



Study name	Event rate	Lower limit	Upper limit	Z-Value	p-Value
Kim YS	0,002	0,00	0,00	-12,63	0,00
Laffan	0,026	0,02	0,03	-30,63	0,00
Lee	0,135	0,11	0,16	-15,76	0,00
De Jong	0,024	0,02	0,03	-29,90	0,00
Girometti	0,447	0,37	0,53	-1,30	0,20
Matsubara	0,100	0,08	0,12	-23,08	0,00
De Oliveira	0,093	0,08	0,10	-33,62	0,00
Ippolito	0,030	0,03	0,03	-47,41	0,00
Zanini	0,054	0,04	0,07	-16,49	0,00
Sey	0,094	0,07	0,13	-12,21	0,00
Moris	0,416	0,37	0,46	-3,74	0,00
Ulus	0,008	0,00	0,06	-4,74	0,00
Kim JA	0,227	0,16	0,31	-5,38	0,00
Chang	0,021	0,02	0,02	-81,25	0,00
Mizuno	0,137	0,13	0,15	-46,07	0,00
Zerboni MR	0,164	0,09	0,29	-4,48	0,00
Zerboni TC	0,069	0,04	0,12	-7,92	0,00
Kromery	0,459	0,43	0,49	-2,71	0,01
	0,080	0,04	0,14	-7,50	0,00

Fig. 2. Pooled prevalence of all pancreatic cystic lesions (PCLs) in the 17 examined studies. The pooled prevalence resulted of 8% (95% CI 4%–14%), with considerable heterogeneity ($I^2 = 99.5\%$).

Systematic review and meta-analysis: Prevalence of incidentally detected pancreatic cystic lesions in asymptomatic individuals

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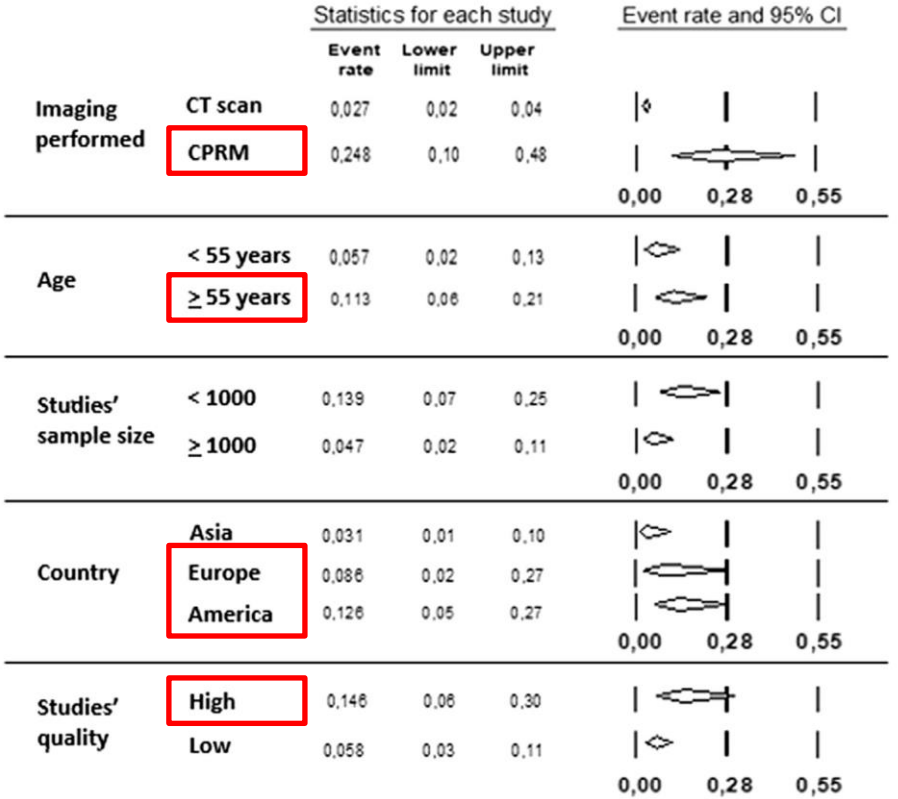


Pancreatic Cyst Prevalence and the Risk of Mucin-Producing Adenocarcinoma in US Adults

Timothy B. Gardner, MD[1], Lisa M. Glass, MD[1], Kerrington D. Smith, MD[2], Gregory H. Ripple, MD[3], Richard J. Barth, MD[2], David A. Klibansky, MD[1], Thomas A. Colacchio, MD[3], Michael J. Tsapakos, MD[4], Arief A. Suriawinata, MD[5], Gregory J Tsongalis, PhD[5], J. Marc Pipas, MD[3] and Stuart R. Gordon, MD[1]

Table 1. Calculation of pancreatic cyst prevalence in the US population in patients between 40 and 84 years old

	US population[a]	Cyst prevalence rate[b](%)	Total number of cysts
Total population	137,154,960	2.5	3,428,874
40–49-year-olds	43,599,555	1.35	588,594
50–59-year-olds	41,962,930	2.05	860,240
60–69-year-olds	29,253,187	3.25	950,729
70–79-year-olds	16,595,961	7.3	1,211,505
80–84-year-olds	5,743,327	8.7	499,669

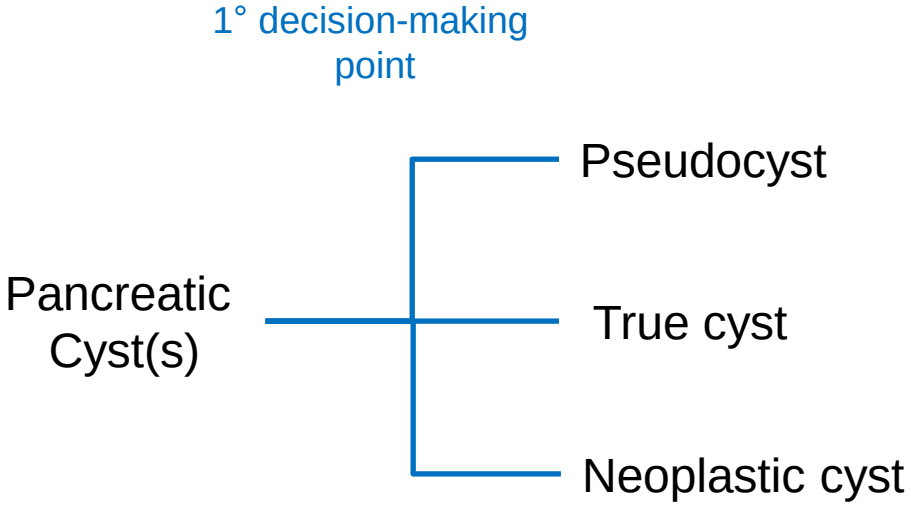
[a]US population determined from 2010 United States census information (17).

[b]The cyst prevalence rate was determined by combining the mean cyst rate of the two most scientifically rigorous cross-sectional imaging studies on cyst prevalence (1,2).

Am J Gastroenterol 2013; 108:1546–1550

Pancreatic Cysts

A Clinical Approach



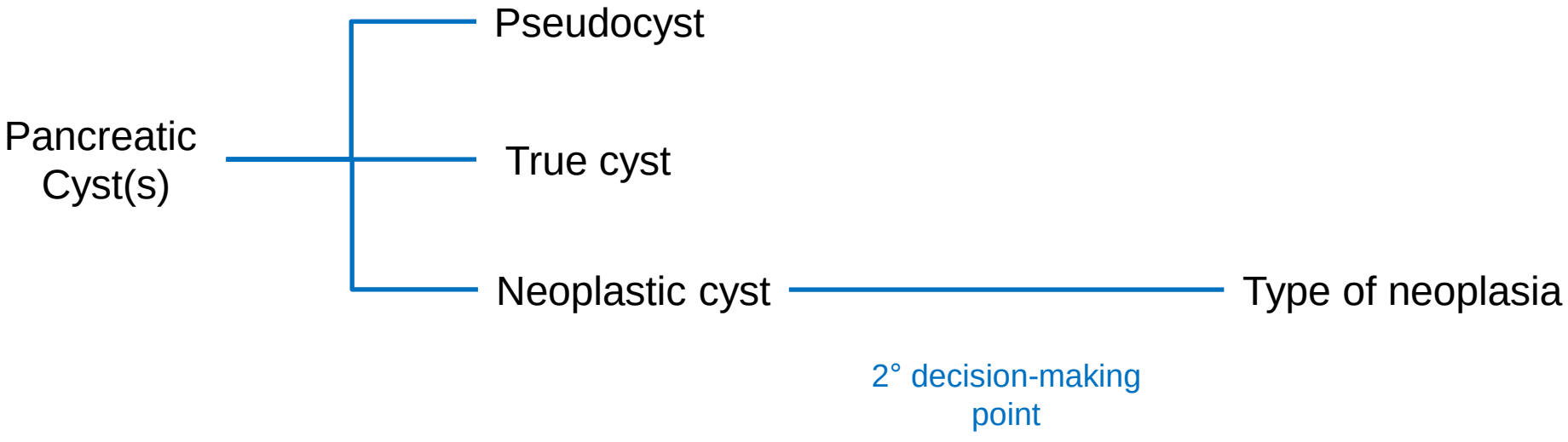
Pancreatic Cysts

Classification

	Pseudocyst	True cyst(s)	Neoplastic cyst(s)
Prevalence	Quite rare	?	Frequent
Clinical Scenario	Previous AP	Asymptomatic	Asymptomatic
Behaviour	Benign	Benign	Benign/Malignant
Diagnosis	Easy	Not possible	Depending on ∅

Pancreatic Cysts

A Clinical Approach



European evidence-based guidelines on pancreatic cystic neoplasms

The European Study Group on Cystic Tumours of the Pancreas

90%

Epithelial neoplastic	Epithelial non-neoplastic
Intraductal papillary mucinous neoplasm all types Mucinous cystic neoplasm Serous cystic neoplasm	Lymphoepithelial cyst Mucinous non-neoplastic cyst Enterogeneous cyst Retention cyst/dysontogenetic cyst Peri-ampullary duodenal wall cyst
Serous cystadenocarcinoma Cystic neuroendocrine tumour G1–2 Acinar cell cystadenoma Cystic acinar cell carcinoma Solid pseudopapillary neoplasm Accessory-splenic epidermoid cyst Cystic hamartoma Cystic teratoma (dermoid cyst)	Endometrial cyst Congenital cyst (in malformation syndromes)
Cystic ductal adenocarcinoma Cystic pancreatoblastoma Cystic metastatic epithelial neoplasm	
Others	

Non-epithelial neoplastic	Non-epithelial non-neoplastic
Benign non-epithelial neoplasm (eg, lymphangioma) Malignant non-epithelial neoplasms (eg, sarcomas)	Pancreatitis-associated pseudocyst Parasitic cyst

Gut 2018;**67**:789–804

Pancreatic Cysts

Type of Neoplasia

Serous Cystoadenoma	Mucinous Cystoadenoma	Intraductal Mucinous Papillary Neoplasm *(IPMN)*	Others *(acinar, endocrine, papillary-cystic, …)*

Pancreatic Cysts

Type of Neoplasia

Serous Cystoadenoma

Mucinous Cystoadenoma

Mucinous Cysto-adenocarcinoma

Intraductal Mucinous Papillary Neoplasm *(IPMN)*

IPMN adenocarcinoma

Others

(acinar, endocrine, papillary-cystic, …)

Malignancy

Incidental pancreatic cystic neoplasms in an asymptomatic healthy population of 21,745 individuals

Large-scale, single-center cohort study

Ye Rim Chang, MD, MS[a,b], Joo Kyung Park, MD, PhD[c,d], Jin-Young Jang, MD, PhD[a,*], Wooil Kwon, MD, MS[a], Jeong Hee Yoon, MD, PhD[e], Sun-Whe Kim, MD, PhD, FACS[a]

Characteristics of incidental pancreatic cystic neoplasms.

Parameter	N=457 (2.1%)
Age (median±SD, y)	58.0±10.0 (43.0, 75.0)*
Sex (male)	236 (51.6%)
Radiologic diagnosis	
IPMN	376 (82.3%)
Indeterminate	55 (12.0%)
SCN	19 (4.2%)
MCN	7 (1.5%)
Tumor size (median±SD, mm)	8.0±7.2 (3.0, 23.0)*
Tumor location (head/body/tail/diffuse)	166/167/120/4
Multiplicity	48 (10.5%)
Operated cysts†	8 (1.8%)
Tumor size of operated cysts (median±SD, mm)	32.5±14.9 (19.0, 57.0)‡
Pathologic diagnosis	
IPMN§	7 (1.5%)
SCN	1 (0.3%)

IPMN=intraductal papillary mucinous neoplasm, MCN=mucinous cystic neoplasm, SCN=serous cystic neoplasm, SD=standard deviation.

pre-test probability

Mucinous > 80%
Serous < 5%

Medicine (2016) 95:51(e5535)

Pancreatic Mucinous Neoplasia/Others

The critical question!

How frequent is malignant progression?

Pancreatic Cysts

Surgeons Got Us in a Big Trouble!

IPMN

25%
of branch ducts

75%
of main duct

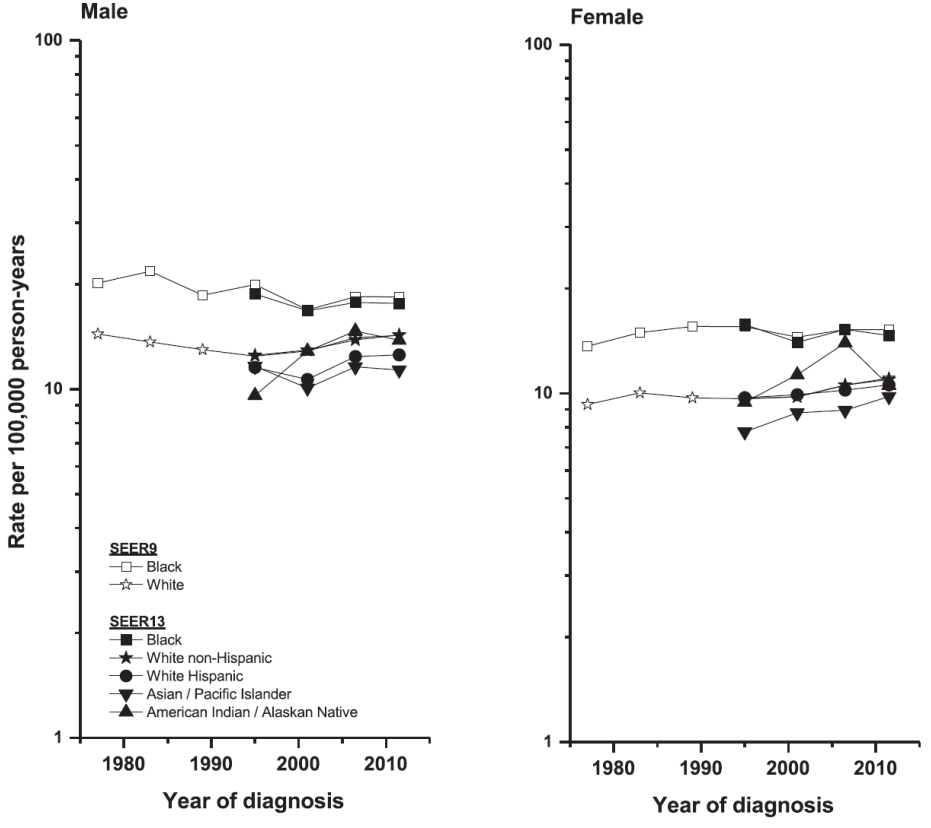
malignancy

Conclusions made on surgical series

Original article

Pancreatic cancer incidence trends: evidence from the Surveillance, Epidemiology and End Results (SEER) population-based data

Vanessa L. Gordon-Dseagu,[1]* Susan S. Devesa,[1] Michael Goggins[2] and Rachael Stolzenberg-Solomon[1]



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International Journal of Epidemiology, 2017, 1–13

Original article

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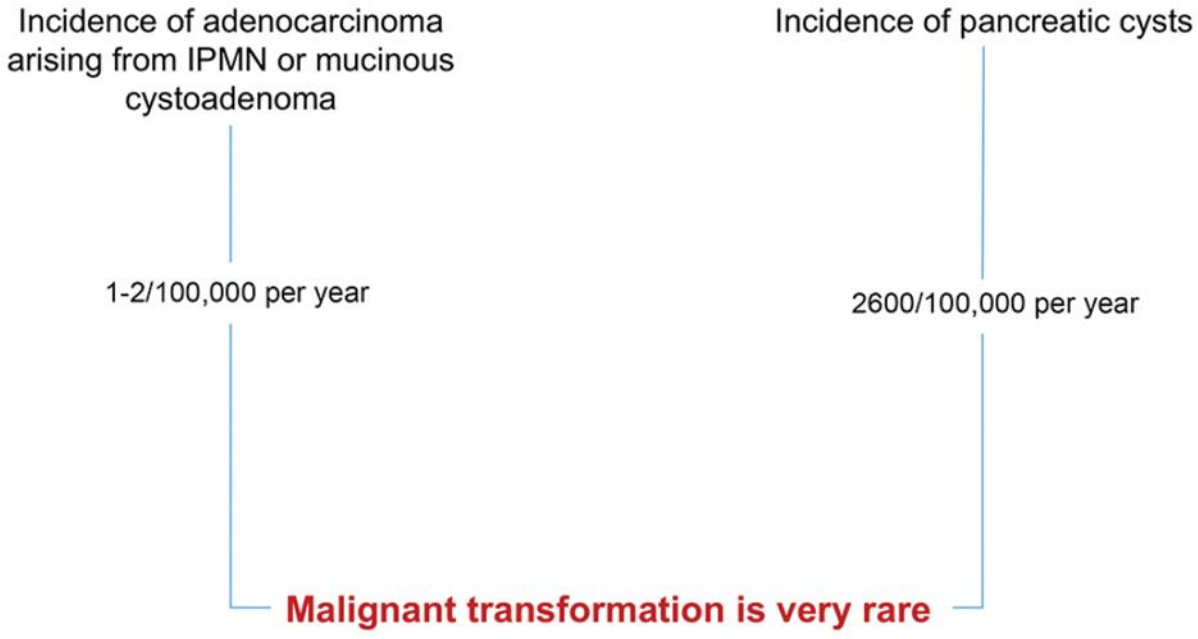
Histologic type*															
Male															
Adenocarcinoma, NOS	18 538	1.33	1.09	1.56	2 233	2.02	1.19	2.85	2 899	0.10	−0.60	0.81	2 218	0.28	−0.53	1.10
Ductal Adenocarcinoma	2 706	5.41	4.62	6.20	296	5.22	2.51	8.00	384	3.01	1.27	4.78	381	3.55	1.05	6.10
Ductal specified as Mucinous	1 254	−3.47	−4.94	−1.99	143	−4.89	−7.75	−1.95	170	−3.80	−6.08	−1.46	140	−2.09	−4.85	0.76
Endocrine: Non-Secretory	1 270	6.02	4.96	7.10	141	~	~	~	163	~	~	~	147	6.83	3.32	10.46
Poorly Specified	2 601	−1.92	−2.64	−1.20	369	−1.90	−3.96	0.21	481	−1.92	−4.43	0.64	356	0.17	−1.87	2.24
Female															
Adenocarcinoma, NOS	17 088	1.45	1.11	1.79	2 236	0.83	−0.02	1.68	3 183	0.89	0.26	1.52	2 231	1.79	1.04	2.54
Ductal Adenocarcinoma	2 546	4.94	3.91	5.99	318	7.10	4.51	9.75	418	3.31	1.75	4.89	437	5.47	3.58	7.40
Ductal specified as Mucinous	1 236	−2.28	−3.63	−0.90	189	−3.14	−5.54	−0.68	198	−2.99	−5.31	−0.61	156	−2.39	−4.87	0.17
Endocrine: Non-Secretory	870	6.18	4.85	7.53	124	~	~	~	160	~	~	~	131	7.34	3.60	11.22
Poorly Specified	2 360	−1.21	−2.18	−0.22	370	−0.88	−2.51	0.78	472	−3.54	−5.02	−2.05	322	−1.42	−3.11	0.31

mucinous
< 10%
of all pancreatic carcinomas

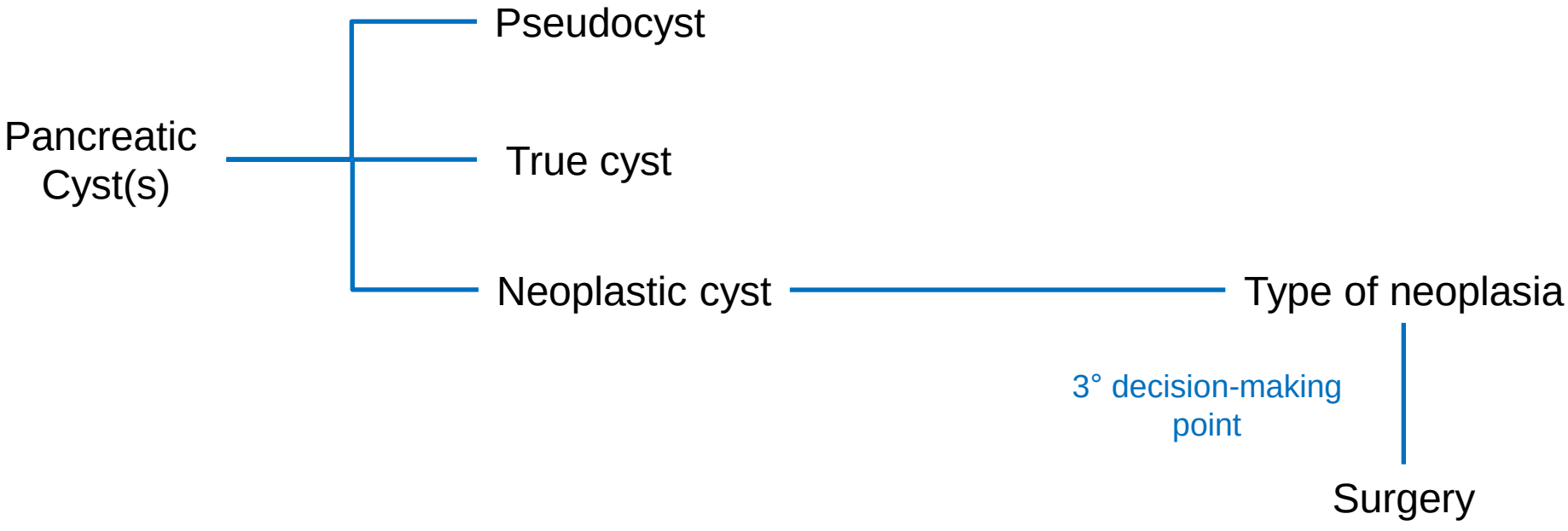
Pancreatic cyst: What clinician needs?

Stefano Francesco Crinò, Luca Frulloni
Department of Medicine, Pancreas Institute, University of Verona, Verona, Italy



Pancreatic Cysts

A Clinical Approach



Diagnosis of Pancreatic Cysts Operated in Verona

Preoperative Vs. Histological Diagnosis – January 2016-June 2017

	Histology					
Preoperative Diagnosis	IPMN	CAM	CAS	Other	PDAC	**Total**
IPMN	35	-	2	5	10	52
CAM	-	16	-	4	2	22
CAS	-	1	6	-	-	7
Other	-	-	-	7	-	7
Total	35	17	8	16	12	88

Correct diagnosis 64 out of 88=73%

Diagnosis of Pancreatic Cysts Operated in Verona

Preoperative Vs. Histological Diagnosis – January 2016-June 2017

	Histology					
Preoperative Diagnosis	IPMN	CAM	CAS	Other	PDAC	**Total**
IPMN	35	-	2	5	10	52
CAM	-	16	-	4	2	22
CAS	-	1	6	-	-	7
Other	-	-	-	7	-	7
Total	35	17	8	16	12	88

Preoperative diagnosis confirmed

35 out of 52=65%

16 out of 22=73%

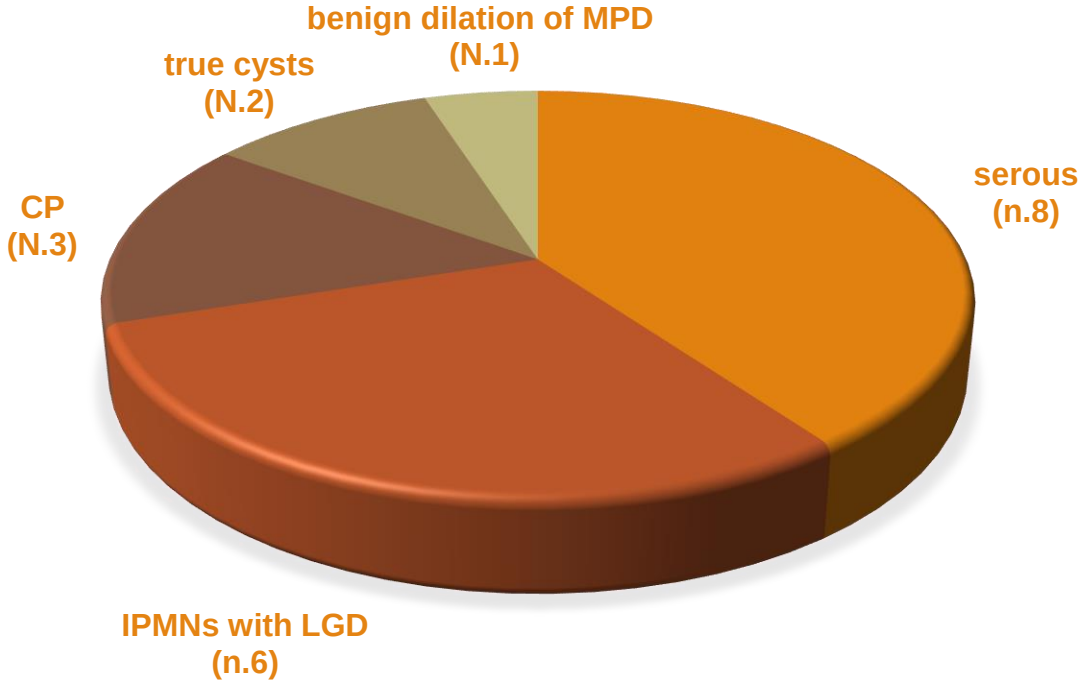
6 out of 7=86%

7 out of 7=100%

Pancreatic Cysts Operated in Verona

Benign findings at histology – January 2016-June 2017

20 out of 88 patients (23%)



9 out of 20 with clinical indication for surgery
(recurrent pancreatitis or ∅)

11 out of 88 with unnecessary surgery = 12%

MPD= main pancreatic duct
CP=chronic pancreatitis
LGD=low grad dysplasia

Table 3 Absolute and relative indications for surgery in IPMN

Absolute indications	Relative indications
Positive cytology for malignancy/HGD	Grow-rate ≥5 mm/year
Solid mass	Increased levels of serum CA 19.9 (>37 U/mL)*
Jaundice (tumour related)	MPD dilatation between 5 and 9.9 mm
Enhancing mural nodule (≥5 mm)	Cyst diameter ≥40 mm
MPD dilatation ≥10 mm	New onset of diabetes mellitus
	Acute pancreatitis (caused by IPMN)
	Enhancing mural nodule (<5 mm)

*In the absence of jaundice.
HGD, high-grade dysplasia; IPMN, intraductal papillary mucinous neoplasm; MPD, main pancreatic duct.

BILIARY AND PANCREATIC

Validation of European evidence-based guidelines and American College of Gastroenterology guidelines as predictors of advanced neoplasia in patients with suspected mucinous pancreatic cystic neoplasms

Liqi Sun,*,[1] Wei Wang,*,[1] Yang Wang,[†,1] Fei Jiang,* Lisi Peng,* Gang Jin[‡] and Zhendong Jin*

Departments of *Gastroenterology, [†]Radiology, and [‡]Hepatobiliary Pancreatic Surgery, Changhai Hospital, Navy Military Medical University, Shanghai, China

Table 2 Clinical features and pathological outcomes for the overall study cohort

Clinical features	
Median age, y (IQR)	60.5 (51–68)
Sex, n (%)	
Female	81 (40.9)
Male	117 (59.1)
Median cyst size, mm (IQR)	27 (16–39)
Cyst location (Head/body/tail/diffuse)	112/27/44/15
Cyst size ≥ 3 cm, *n* (%)	88 (44.4)
Cyst size ≥ 4 cm, *n* (%)	48 (24.2)
Pathology, *n* (Benign/HGD/IC)	
IPMN	82/11/33
MCN	10/0/3
SCN	28/0/0
SPT	0/0/4
Ductal adenocarcinoma	0/0/10
NET	3/0/0
Chronic pancreatitis	4/1/0
Pseudocyst	7/0/0
Retention cyst	1/0/0
Schwannoma	1/0/0

HGD, high-grade dysplasia; IC, invasive carcinomas; IPMN, intraductal papillary mucinous neoplasm; IQR, interquartile range; MCN, mucinous cystic neoplasm; NET, neuroendocrine tumor; SCN, serous cystic neoplasm; SPT, solid pseudopapillary tumor.

Retrospective analysis in a prospective cohort
Period 2013-2018

61 out of 198 (31%)
operated with HGD/IC

The European evidence-based guidelines on pancreatic cystic neoplasms (PCN) in clinical practice: The development of relative and absolute indications for surgery during prospective IPMN surveillance

Yrjö Vaalavuo [a, b], Antti Siiki [a, b], Anne Antila [a, b], Irina Rinta-Kiikka [b, c], Juhani Sand [a, b], Johanna Laukkarinen [a, b, *]

[a] Department of Gastroenterology and Alimentary Tract Surgery, Tampere, Finland
[b] Faculty of Medicine and Health Technology, Tampere University, Tampere, Finland
[c] Dept. of Radiology, Tampere University Hospital, Tampere, Finland

6 out of 23 (26%) operated upfront

Table 2a
Indication for surgery, upfront operated patients.

Indication for surgery	n
Absolute indication	
Malignant histology	2
MPD diameter ≥10 mm	2
Jaundice	1
Two relative indications	
Cyst diameter ≥40 mm and MPD diameter 5–9.9 mm	4
cyst diameter ≥40 mm and elevated levels of CA 19.9 (>37U/mL)	1
MPD diameter 5–9.9 mm and elevated levels of CA 19.9 (>37U/mL)	1
cyst diameter ≥40 mm and cyst growth rate ≥5 mm/year	1
One relative indication	
cyst diameter ≥40 mm	6
MPD diameter 5–9.9 mm	5

MPD, Main pancreatic duct.
HGD, High grade dysplasia.
LGD, Low grade dysplasia.
SCN, Serous cystic neoplasy

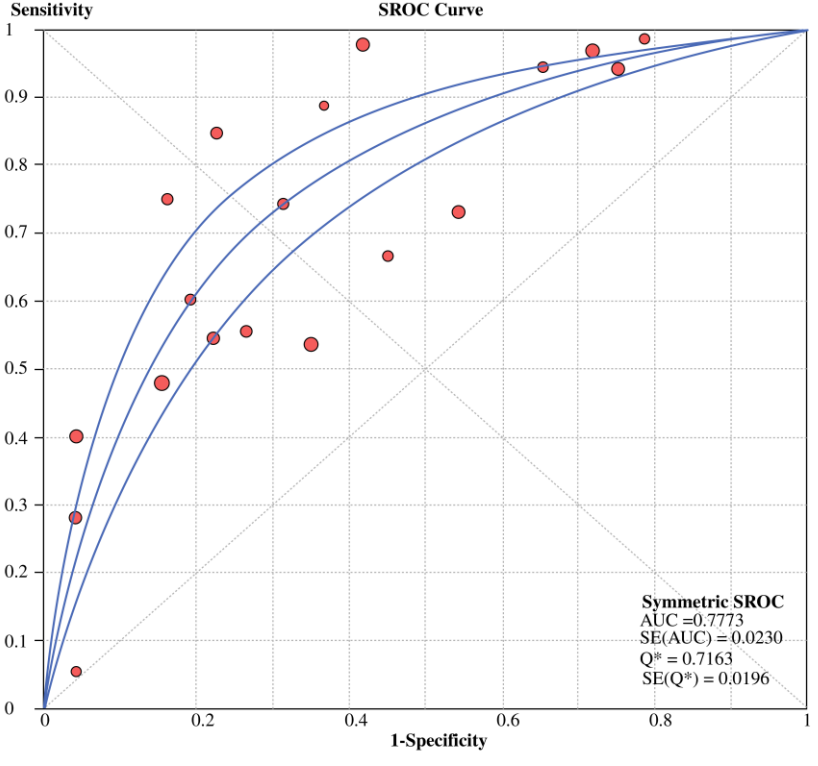
Table 2b
Histology and type of surgery, upfront operated patients.

Histology	N
Adenocarcinoma	2
IPMN-carcinoma	2
MD-IMPN HGD	1
BD-IMPN HGD	1
MX-IPMN LGD	7
MD-IPMN LGD	3
BD-IPMN LGD	3
SCN	3
Chronic pancreatitis	1
Type of surgery	
Pancreaticoduodenectomy	9
Distal pancreatic resection	7
Total pancreatectomy	6
Surgical exploration	1

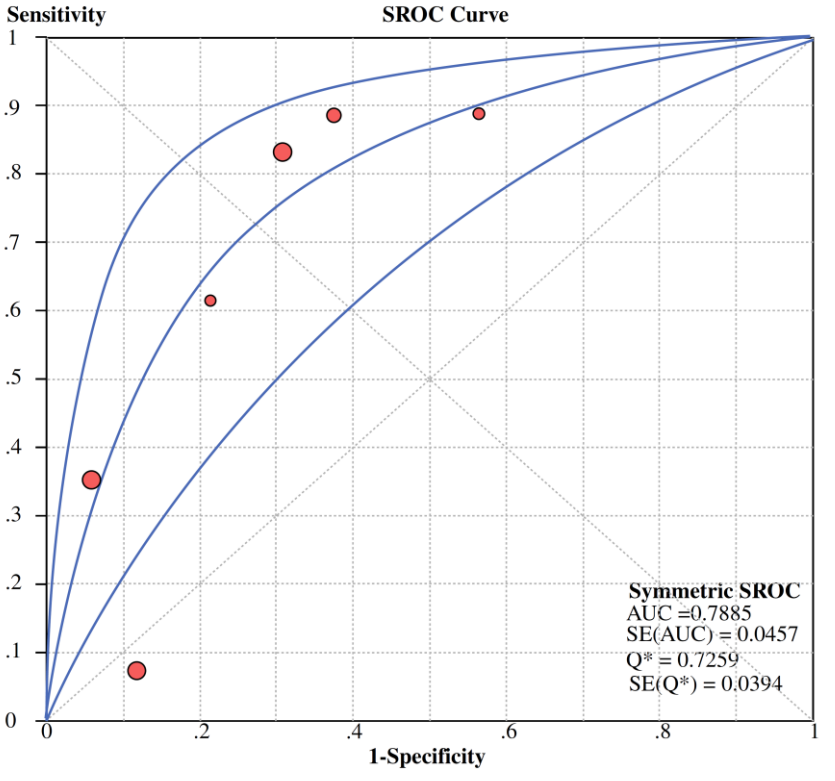
Retrospective analysis in a prospective cohort
Period 2013-2018

Pancreatology 20 (2020) 1393–1398

Accuracy of Fukuoka and American Gastroenterological Association Guidelines for Predicting Advanced Neoplasia in Pancreatic Cyst Neoplasm: A Meta-Analysis



Fukuoka



American Gastroenterological Association

Ann Surg Oncol (2019) 26:4522–4536

Validation of European evidence-based guidelines and American College of Gastroenterology guidelines as predictors of advanced neoplasia in patients with suspected mucinous pancreatic cystic neoplasms

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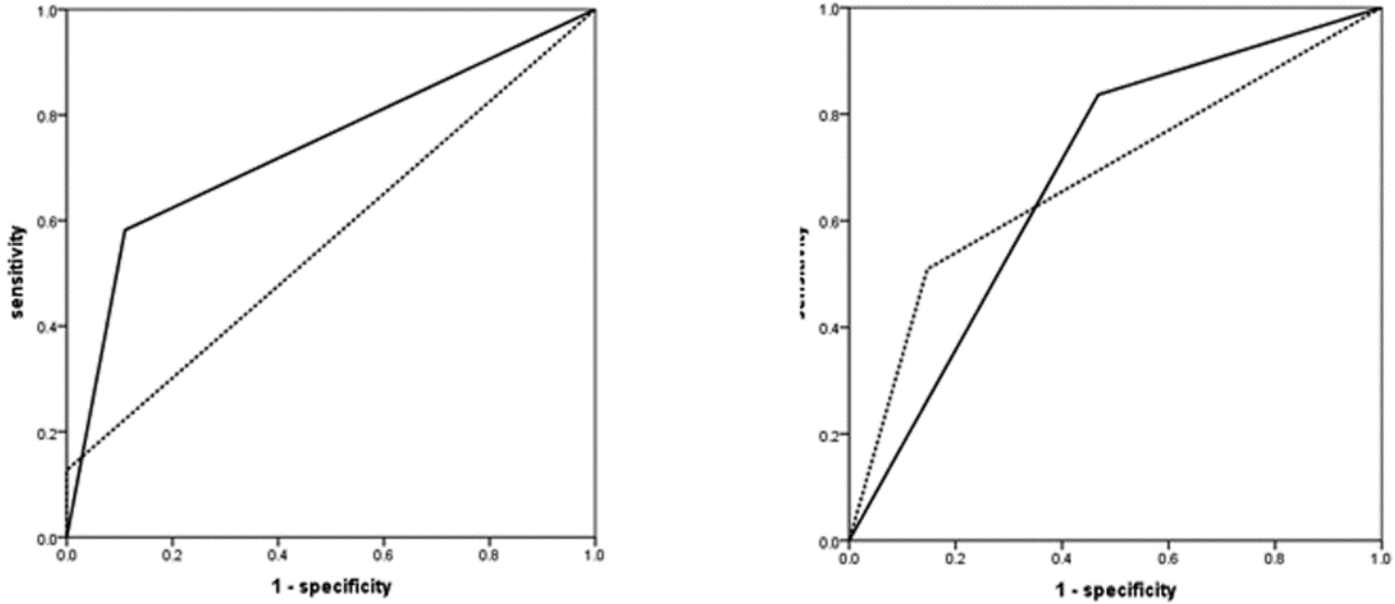

Figure 1 Performance of European evidence-based guidelines indication for IPMN or MCN. (a) EEG absolute indications for IPMN. (b) EEG relative indications for IPMN. (c) EEG indication for MCN. EEG, European evidence-based guidelines; IPMN, intraductal papillary mucinous neoplasm; MCN, mucinous cystic neoplasm. —, ≥ 1 criteria; ····, ≥ 2 criteria.

TABLE 1 Characteristics of the included studies

References	Region	Study design	Recruitment time	*N*	Age, years	Male [*n* (%)]	Cyst size, mm (range)	Guidelines
Zhou et al.[23]	China	Retrospective	2008–2015	197	Median 57	78 (29.9)	Median 30 (22–48)	Fukuoka
Lekkerkerker et al.[24]	Netherlands	Retrospective	2006–2015	75	Mean 60	32 (42.6)	Median 40 (30–61)	Fukuoka, AGA
Ge et al.[25]	USA	Retrospective	2004–2014	300	Mean 62.6	113 (37.7)	NR	AGA
Sighinolfi et al.[26]	USA	Retrospective	2007–2016	209	Mean 62.18	93 (44.5)	Mean 39.16 ± 31.17	Fukuoka, AGA
Xu et al.[27]	USA	Retrospective	2008–2013	269	Mean 67.0	78 (23.9)	Mean 28.5 ± 17.0	Fukuoka, AGA
Kimura et al.[28]	Japan	Retrospective	1994–2015	98	Mean 68.3	54 (55.1)	Mean 29.4 ± 17.5	Fukuoka
Singhi et al.[29]	USA	Retrospective	2014–2015	41	Median 62	20 (48.8)	Median 35 (23–49)	AGA
Ma et al.[30]	USA	Retrospective	2000–2014	239	Median 65	78 (36.8)	Median 27 (17–39)	Fukuoka, AGA
Ridtitid et al.[31]	USA	Retrospective	2001–2013	135	Mean 65.2	71 (52.6)	Mean 26 ± 16	Fukuoka
Robles et al.[32]	France	Retrospective	2006–2014	120	Mean 57.9	65 (54.2)	Mean 22 ± 11	Fukuoka
Hsiao et al.[33]	Taiwan	Retrospective	2000–2015	138	Median 64	67 (48.6)	NR	Fukuoka
Han et al.[34]	Korea	Retrospective	1996–2011	230	Median 63	153 (66.5)	Mean 36	Fukuoka
Watanabe et al.[35]	Japan	Retrospective	2006–2014	49	Median 73	29 (59.2)	NR	Fukuoka
Kaimakliotis et al.[36]	USA	Retrospective	2000–2008	194	Median 58	74 (38.1)	Median 33 (2–204)	Fukuoka
Jang et al.[37]	Korea	Retrospective	1995–2012	350	Mean 63.4	216 (61.7)	Mean 32.1 ± 15.0	Fukuoka
Fritz et al.[38]	Germany	Retrospective	2004–2012	233	Median 65	93 (39.9)	NR	Fukuoka
Roch et al.[39]	USA	Retrospective	1992–2012	340	Mean 68.2	165 (48.5)	NR	Fukuoka
Aso et al.[40]	Japan	Retrospective	2006–2013	100	Median 67	70 (70.0)	NR	Fukuoka
Goh et al.[41]	Singapore	Retrospective	1991–2012	114	Median 59	40 (35.1)	NR	Fukuoka
Nguyen et al.[42]	USA	Retrospective	1996–2012	66	Median 69	24 (36.4)	Median 24 (13–30)	Fukuoka
Sahora et al.[43]	USA	Retrospective	1995–2012	226	Median 65	94 (39.2)	Mean 24 ± 12	Fukuoka

NR none reported, *AGA* American Gastroenterological Association

Pancreatic Cysts

Clinical Aspects

1. Frequent and increase with age
2. Fit for surgery decreases with age
3. Very low rate of malignant transformation
4. Behavior of mucinous carcinomas is similar to ductal adenocarcinoma
5. Malignant signs evaluable by different imaging modalities
6. Symptoms associated with pancreatic cysts not necessarily related to malignancy

Pancreatic Cysts

What a Clinician Ask to Imaging Modalities

1. To differentiate serous with mucinous
2. To diagnose malignancy or alterations highly suggestive for malignancy
3. To use the cheaper and less invasive imaging modality
4. To limit invasive tests (biopsies)
   - *to very selected patients*
   - *only if they change the clinical decision (i.e. surgery)*