Pancreatic Cystic neoplasms

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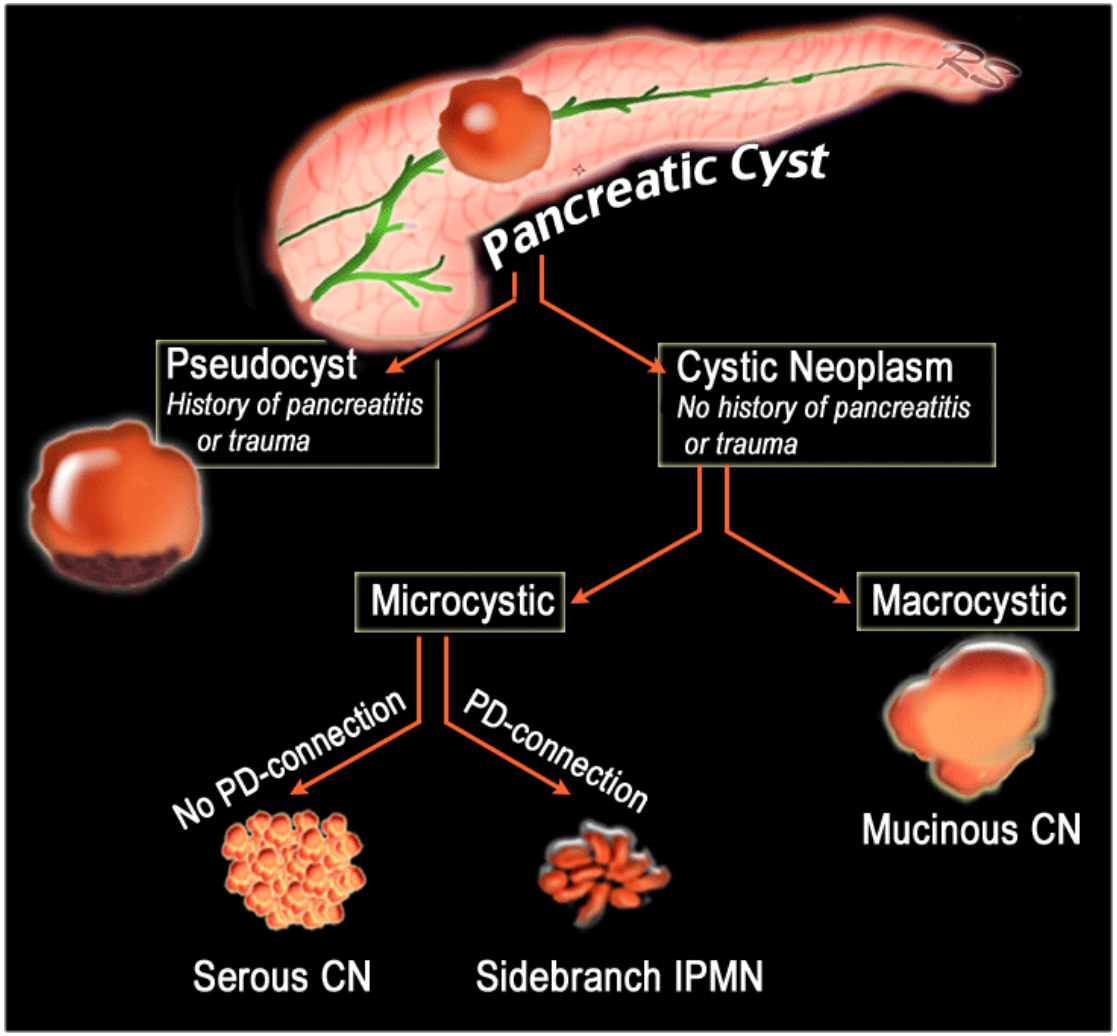
BC Pancreatic Cystic neoplasms



How frequent are neoplastic pancreatic cystic lesions ?

Average: 2.5%

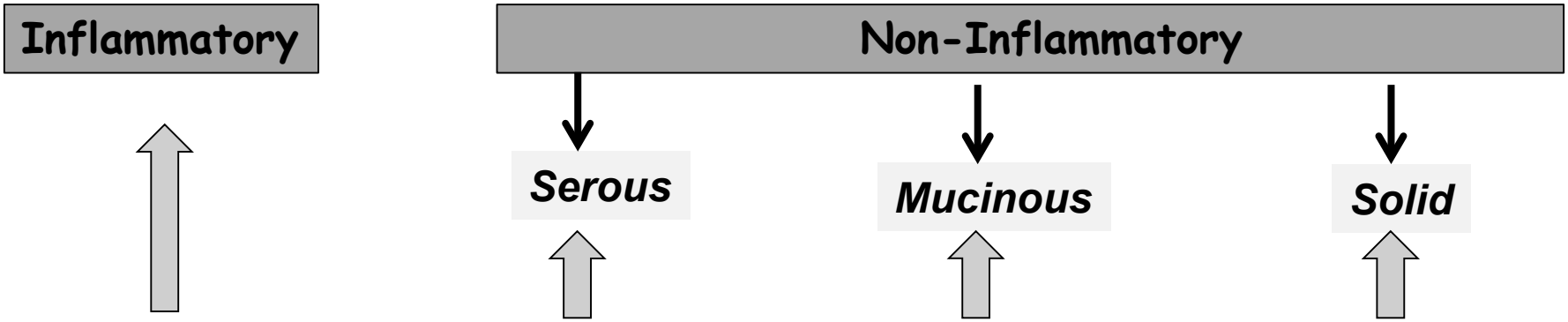
Age > 70 years: up to -**20%***

Age > 80: up to 37%

*: MRI in non-pancreatic disease: 20% of 1444 patients; Zhang XM et al. Radiology 2002
up to 44.7% Lee et al. AJG 2010

higher prevalence in MRI compared to CT (2.6%vs1.2%) Laffan TA Am J Roentgenol 2008

What categories and what type of pancreatic cysts exist?



Pseudocyst (PC)

Acute fluid collection
Walled-off-pancreatic necrosis (WOPN)
Abscess

Serous Cystadenoma **(SCA)**

Intraductal papillary mucinous neoplasm **(IPMN)**

Mucinous cystic neoplasm **(MCN)**

Solid Pseudo-papillary Neopl. **(SPN)**

Kongenital, Rentention/Lymphoepithel-Cyst, enterogen, Carvenous hemangioma
Parasitic Cyst

Cystic Endocrine **(CPEN)**
Metastatic cyst
Cystic degeneration of solid tumors
Acinar cell carcinoma
Pancreatoblastom
Sarkom, Lymphagniom

How to describe a cystic pancreatic lesion?

Typical morphological aspects

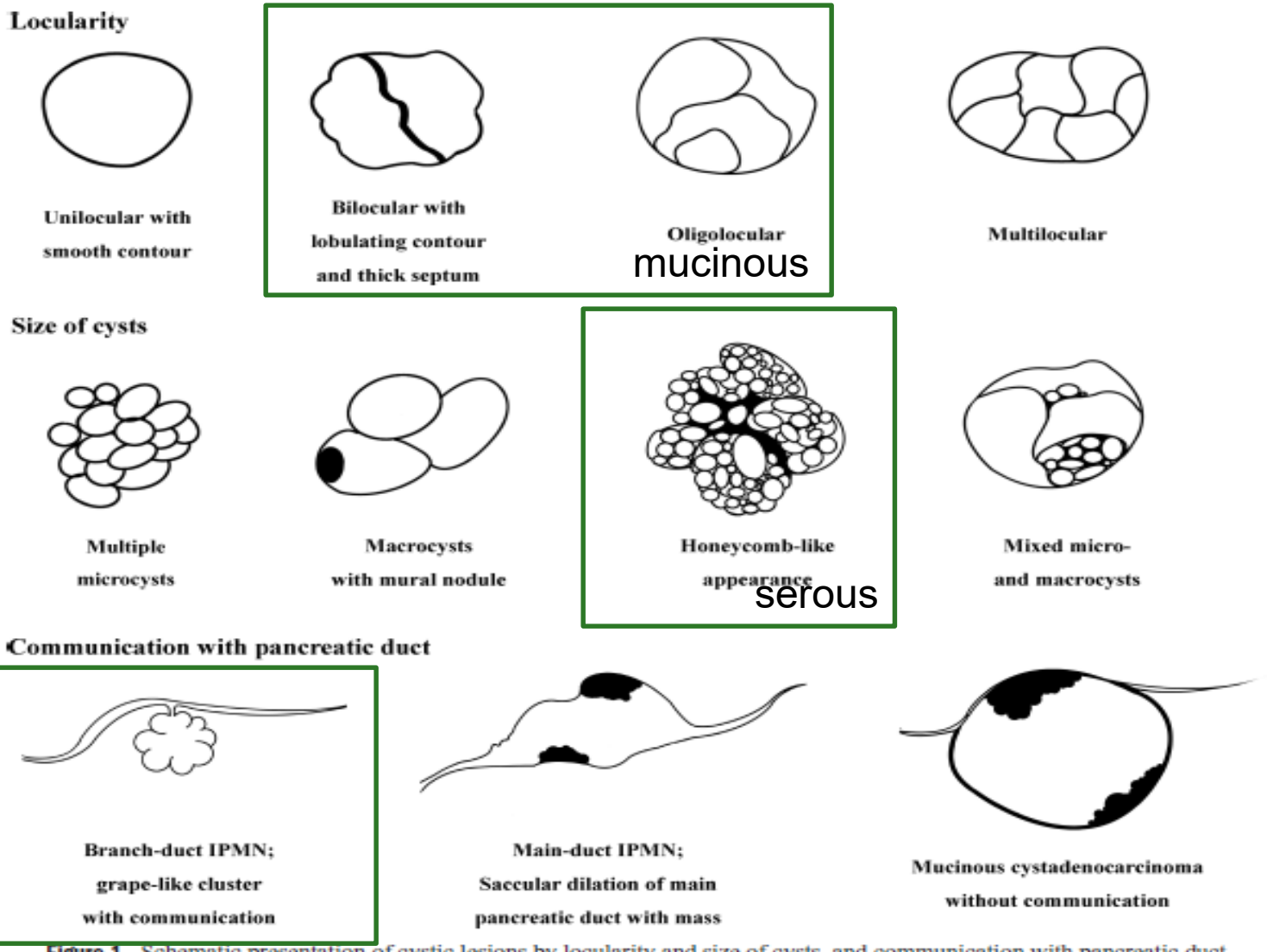
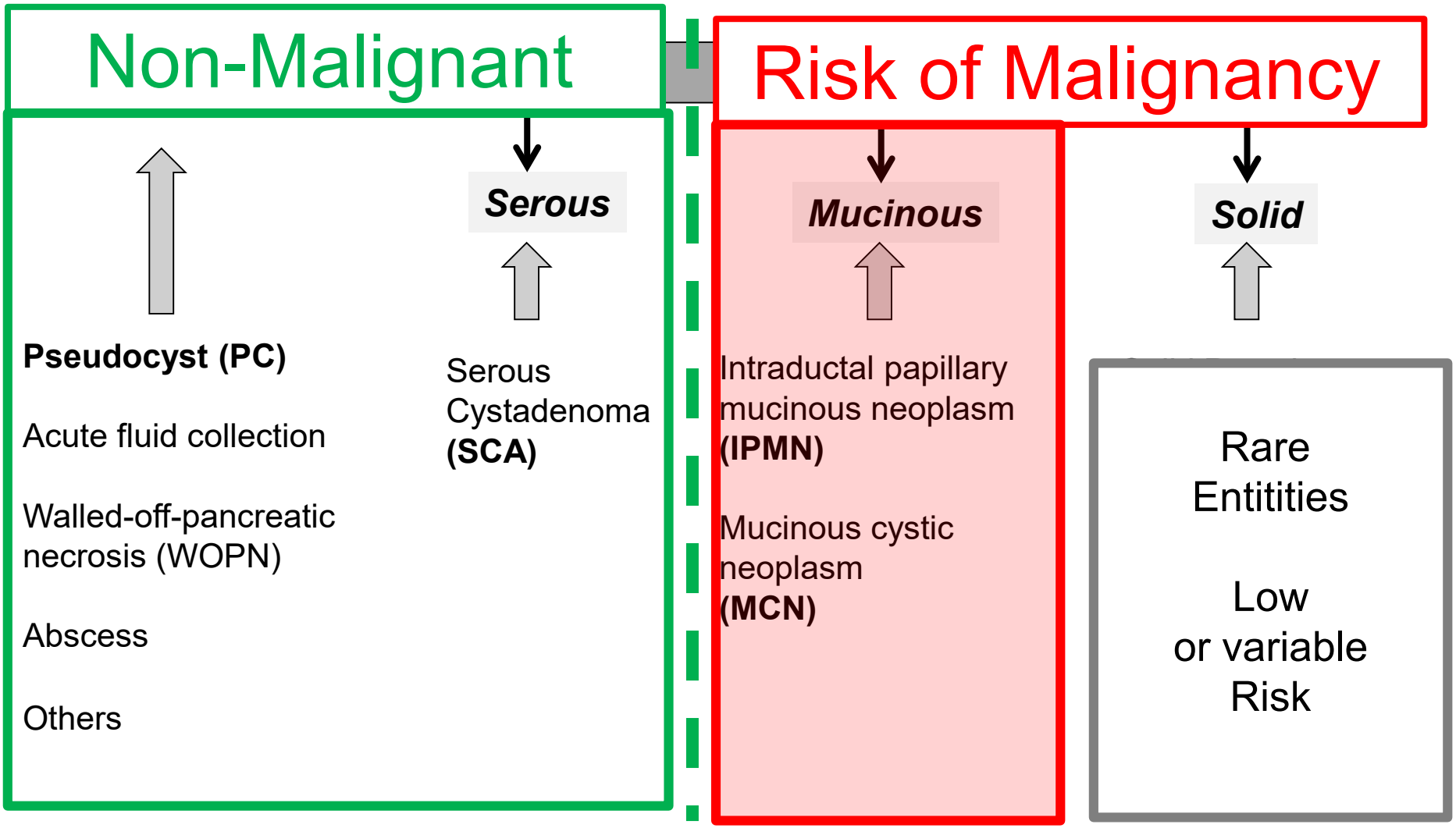


Figure 1. Schematic presentation of cystic lesions by locularity and size of cysts, and communication with pancreatic duct.

Oh et al Am J Gastro 2008

What entity of pancreatic cyst can become – or may be already malignant ?


Non-Malignant
Risk of Malignancy
Serous
Mucinous
Solid
Pseudocyst (PC)
Acute fluid collection
Walled-off-pancreatic necrosis (WOPN)
Abscess
Others
Serous Cystadenoma (SCA)
Intraductal papillary mucinous neoplasm (IPMN)
Mucinous cystic neoplasm (MCN)
Rare Entitities
Low or variable Risk

Accidental finding of pancreatic cyst 15 mm in abdominal ultrasound – no history of pancreatitis what next ?

CT or MRI with MRCP
is recommended for a cyst of >l cm

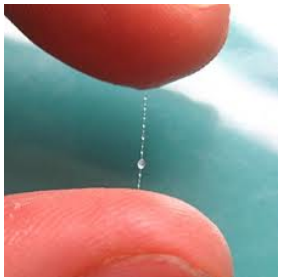
MDCT and MRCP
are most useful for distinguishing BD-IPMN from other cysts by showing multiplicity and a connection to the main pancreatic duct

ERCP is not recommended

History of pancreatitis ?

Family history of pancreatic cancer ?

How to separate serous from mucinous pancreatic cysts ?



Fluid: «String-Sign», definiert: > 1cm (> 1 sec.)

	CEA (> 200ng/ml)	String	CEA+String
PPV	**96%**	**94%**	**96%**
NPV	**73%**	**60%**	**81%**
Accuracy	**83%**	**72%**	**89%**

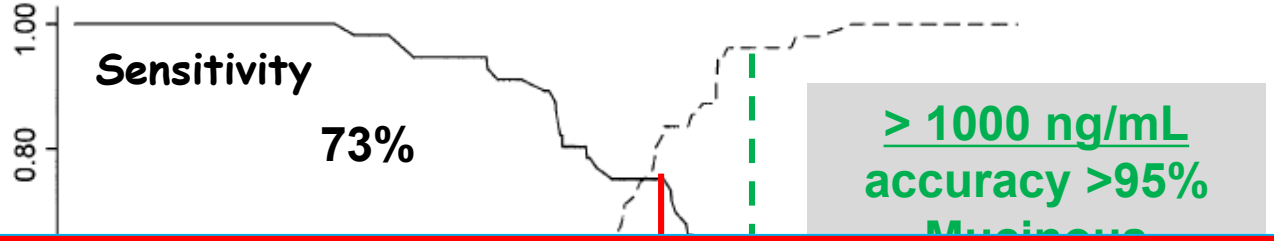
String vs. CEA (with > 800 ng/ml) equal sens./specificity

Bick BL et al. Endoscopy 2015

How to seperate mucinous cysts from others ?

Endoscopic Ultrasound (EUS) with Fine-Needle-Aspiration (FNA)

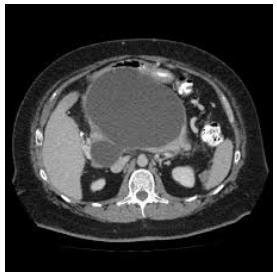
Fluid: CEA



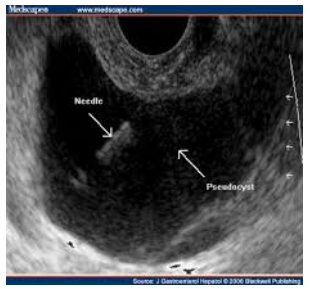
CEA most sensitive marker for mucinous lesion:
Better diagnostic accuracy than EUS morphology and/or cytology
No correlation with malignancy
CAVE: and a low CEA level does not exclude a mucinous cyst.

Brugge W et al. Gastroenterol 2004; Cizginer et al. Pankreas 2011

Serous pancreatic Cyst/s: Pseudocyst vs. SCA Specific features ?



Differentiation
pancreatic pseudocyst - cystic tumor ?

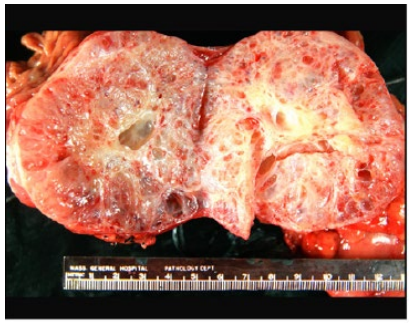


Feature	Pseudocyst	Cystic Tumor
Anamnese	Pancreatitis or Trauma	No history *
Septae	None (unilocule)	Evtl. Multi-loculized
Wall	Thin (< 4 mm)	Evtl. thick
Communication Pancreatic Duct	> 65%	No *
Fluid: Encymes Amylase/Lipase	High (> 2000/ > 5000 IU/ml)	Low *
Zytology	Inflammatory, degenerative	Pre-/malignant cells Tumor-markers

*** Exception: for IPMN/MCN**

Adapted from Garcia GIE 2008

Key features: Serous Cystic Neoplasm



- **Malignant potential:** **NO (only case reports)**
- **Location:** **throughout the pancreas (50% body/tail)**
- **Demographics, rate:** **(older) women (70%), 15-20% of PCNs**
- **Morphology:** **micro-, oligo-, macrocystic**

typically: multicystic cluster (each < 2 cm) = honeycumbed

No communication with pancreatic duct

Pathognomonic: central calcified stellate scar: 30% cases

Which syndrome associates with multiple/ oligocystic SCN ?

Hippel-Lindau-Syndrome

When if at all could/should be a SCN be resected ?

If symptomatic/ aggressive behavour/pa-head

EUS with FNA
What to measure in cyst fluid ?

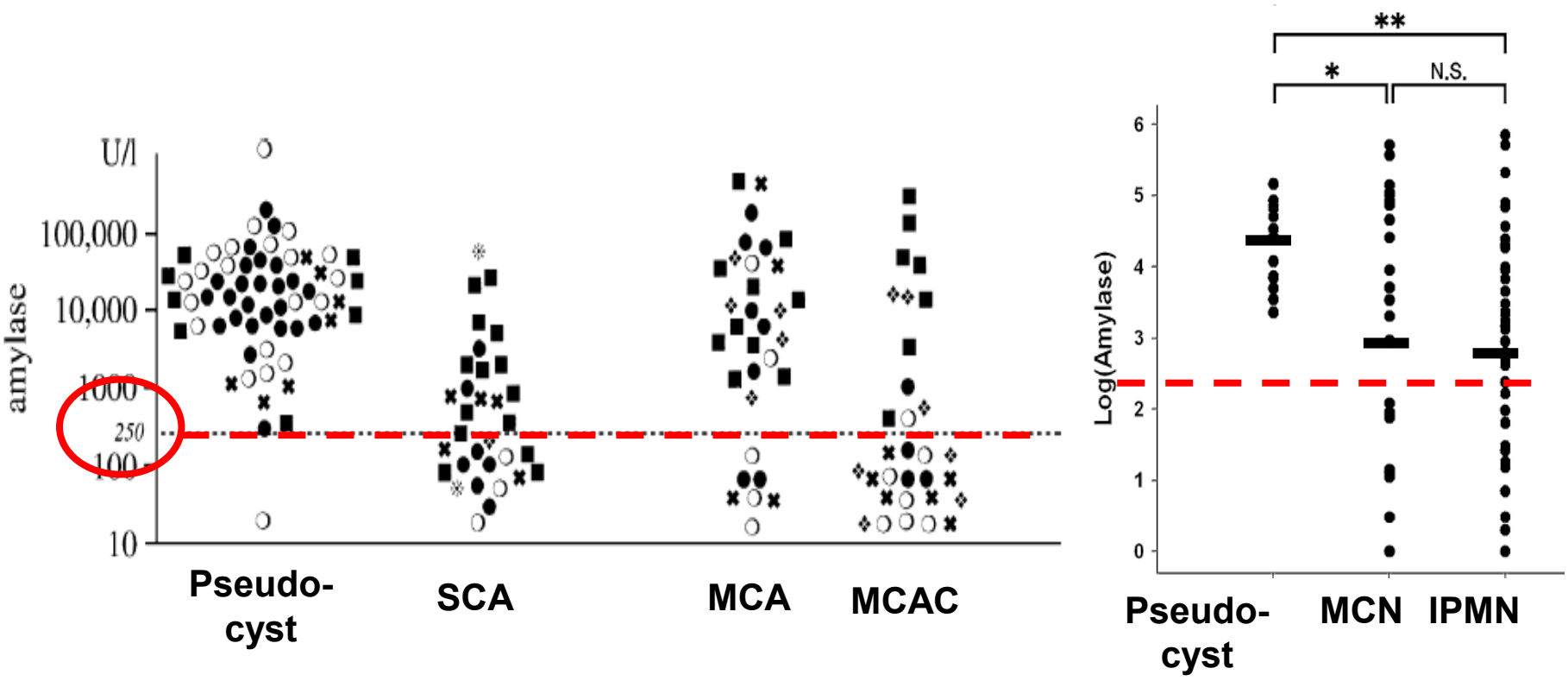
What conclusion can be derived from Cyst Amylase-/Lipase-levels ?

Fluid Analysis and Type of Cysts

Typ	Pseudocyst	MCN	IPMN	SPN	SCA
Viscosity /Mucin	**Low**	**High**	**High**	**NA**	**Low**
Amylase =duct-communication	**High**	**Low**	**Variable**	**Low**	**-**
CEA	**-**	**High**	**High**	**-**	**-**
Cytology	**«dirty material»** Macrophages, Inflammatory cell	**mucin-** containing column cells	papillary clusters of **mucin-** column cells, **atypia**	Branching papillae cuboid or cylindric cells, high cellularity, myxoid stroma	**negative** or Glyogen-con-taining cuboid cells

*: Low Amylase < 250 U/ml: basically excludes Pseudocyst
Ident. Lipase

Is Fluid Analysis for Amylase helpful ?



Cysts with an amylase concentration > 250 U/L were SCA, MCA, or MCAC

< 250 U/L virtually excluded Pseudocyst

Van der Waaii et al. GIE 2005; Brugge W et al. Gastroenterol 2004

Glucose-level and diagnostic yield in mucinous cysts

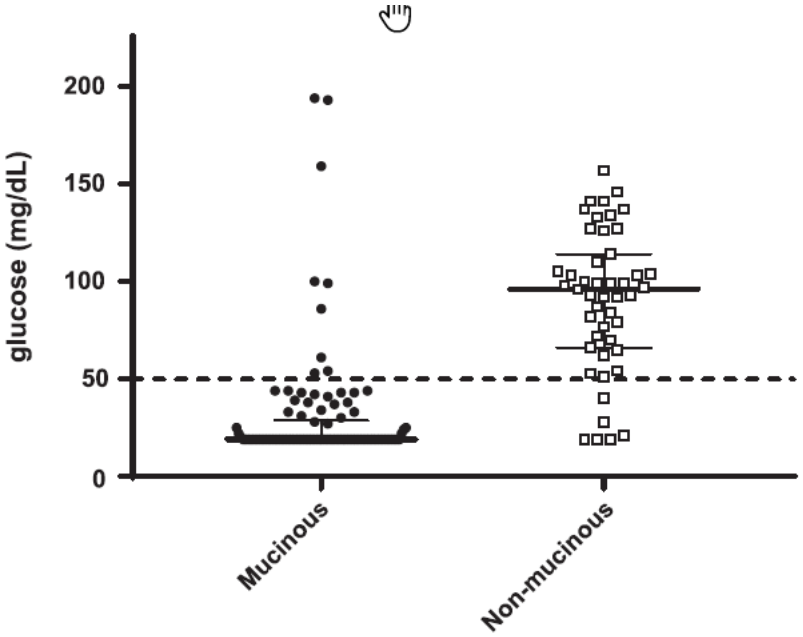


Fig. 1. Pancreatic cyst fluid glucose in mucinous versus nonmucinous pancreatic cysts. Cyst fluid glucose (y-axis) is compared between mucinous and nonmucinous cysts on the x-axis. The thick horizontal bars represent median values. Bordering median bars are thin, IQR bars. The horizontal dashed line identifies the cutoff value of 50 mg/dL for detecting mucinous pancreatic cysts.

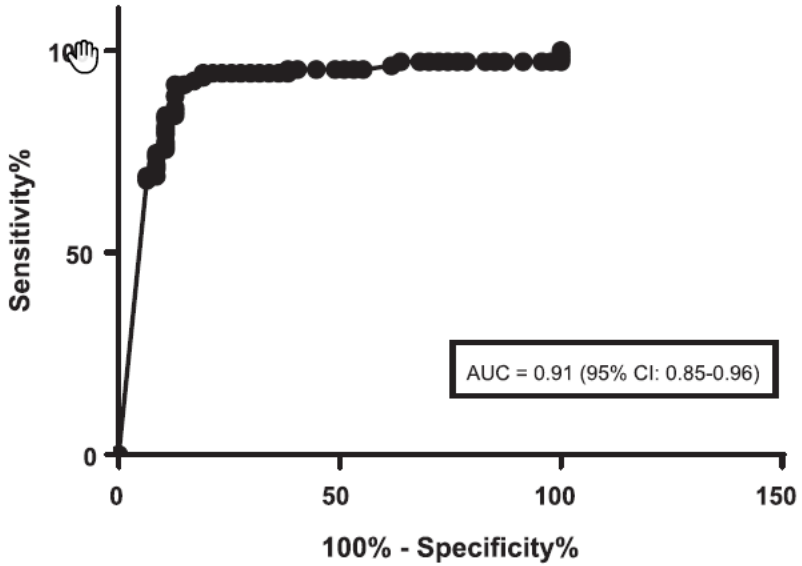


Fig. 3. Pancreatic cyst fluid glucose ROC curve analysis. The AUC for cyst fluid glucose is 0.91.

Carr et al. Surgery 2018

Combining Glucose and CEA criteria
Sensitivity 95%, Specificity 85%
Accuracy 93%
AUC 0.95
For mucinous etiology

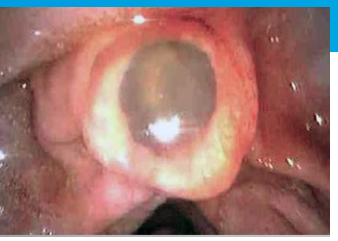
NGS of pancreatic cyst fluid

- highly accurate in cyst classification and detection of advanced neoplasia
- mutations in *KRAS* and/or *GNAS* → 89% sensitive and 100% specific for mucinous PC.
- the presence of *KRAS* and/or *GNAS* mutations 100% sensitivity for IPMNs, and the presence of *GNAS* mutations was 100% specific for an IPMN.
- *KRAS* mutations are detected in only 30% of MCNs.
- While mutations in KRAS are common in MCNs, the prevalence of these activating mutations is reported to increase with the severity of dysplasia.

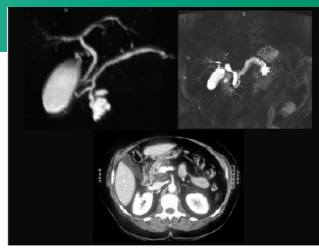
Hr B.H. 70 yo

Mucinous Cysts (IPMN/MCN)
Risk of malignancy:

Rank MD-, BD-IPMN, MCN and give 5year risk for HGD/Carcinoma



What factors determine malignant risk in IPMN/MCN?



Differentiation between types of mucinous cysts ?

Type – entity - Cyst

IPMN:

Main-Duct- :

Branch-Duct-:

MCN:

Surgical series:

> 30%

missclassified pre-operatively

Can fluid analysis differentiate

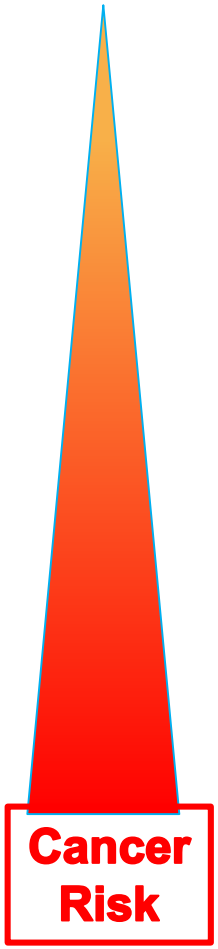
BD-IPMN from MCN ?

No

1: Sakorafas GH et al. Surg Oncol. 2011; 2 Sakorafas GH et al. Surg Oncol 2012; Tanaka et al. Pancratology 2012

IPMN
What histological types exist
And what differences in terms of malignant risk?

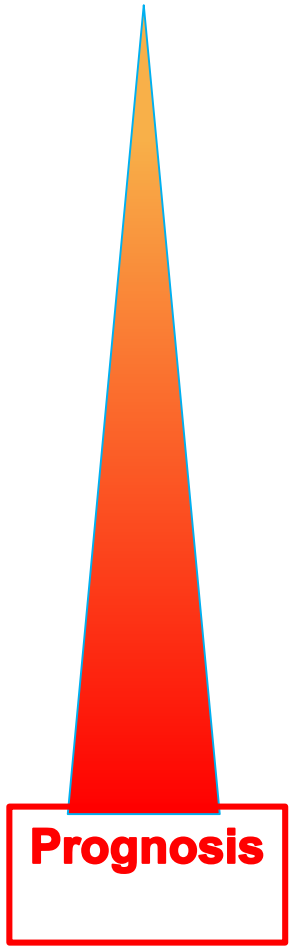
The histologic subtypes of IPMN have clinicopathologic signiflcance



Oncocytic type/
gastric type
typically low grade,
only small percentage of carcinoma

intestinal-type
can have invasive carcinoma, colloid type

pancreatobilary type
more frequently develops cancer,
usually aggressive



Mucinous Cysts (IPMN/MCN)
Revised Fukuoka-Criteria:

What are high-risk-stigmata and Worrisome features ?

Revised Fukuoka criteria for IPMN

Obstructive jaundice (cystic lesion in pa-head), enhanced mural nodule >5 mm, MPD size of >10 mm)

No

Cyst size > 3 cm, enhancing mural nodule <5 mm, main duct 5-9 mm, thickened enhanced cyst walls, abrupt change in the MPD caliber with distal pancreatic atrophy, lymphadenopathy, elevated (CA)19-9, rapid rate of cyst growth > 5 mm/2 years

EUS +/- FNA suspicious

Tanaka et al. Pancreatology 2017

If no High-Risk-Stigmata:
What are «worrisome features» in IPMN ?

Prediction of malignancy in pathological confirmed IPMNs (41 studies, 5788 patients)

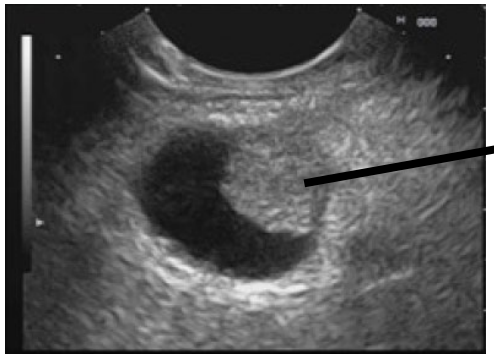
	OR
Size > 3 cm	**62/ 3**
Intramural nodule	**7.3/ 7.7**
Dilation main duct > 6 mm	**9.3/2.3**
Main-vs. BD-duct IPMN	**4.7/-**
Symptoms	1.6/-

Anand ClinGastroHep. 2013/ AGA technical Review Gastro 2015

Increased serum CA19-9; diagnostic accuracy 82%

Fritz et al. BJSurg 2014

EUS-feature: Role of intramural nodule in IPMN ?



Intramural Nodule

Main duct involvement

Cyst Size

	> 3 cm	< 3 cm
Intramural Nodules	54/165 (32.7%)	40/367 **(10.9%)**

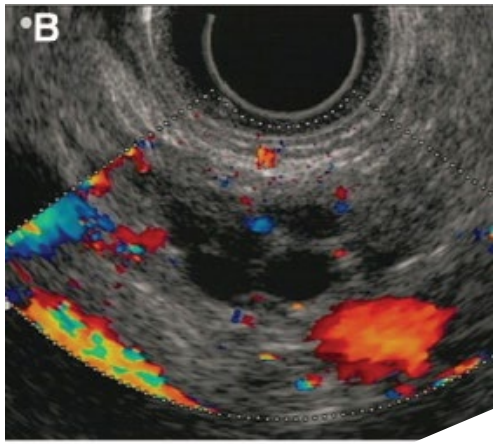
Wall

NO intramural nodules:

rate of malignancy extremely low (0-11%)

Meierle et al. Der Chirurg 2012

Contrast-EUS and IPMN: Sub-types + risk malignancy



Typ I:

low papillary Nodule

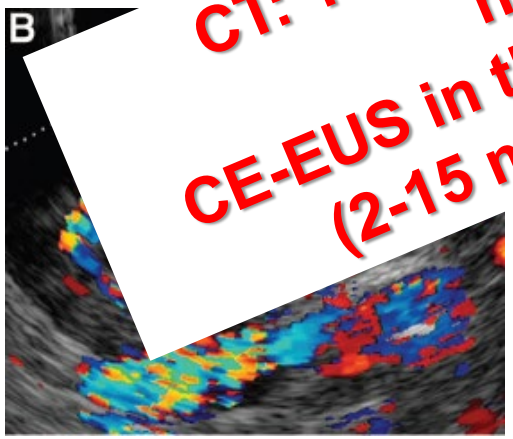
Fine pro

Typ II:

polypoid Nodule

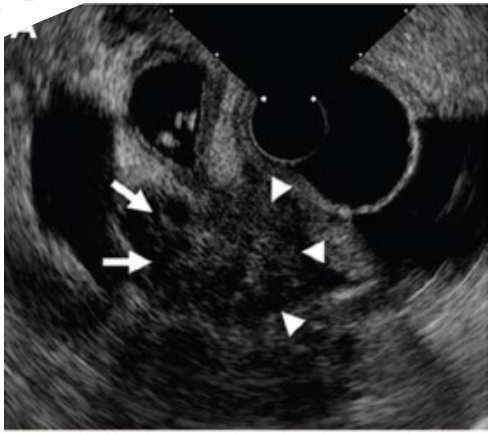
ooth surfaced
Component protr.

CT: 15 no malignant featurs (nodules):
histology: malignant
CE-EUS in these cases: nodules detectable
(2-15 mm, im schnitt 6 mm gross)!!



papillary Nodule

Protruding+
Thickend wall



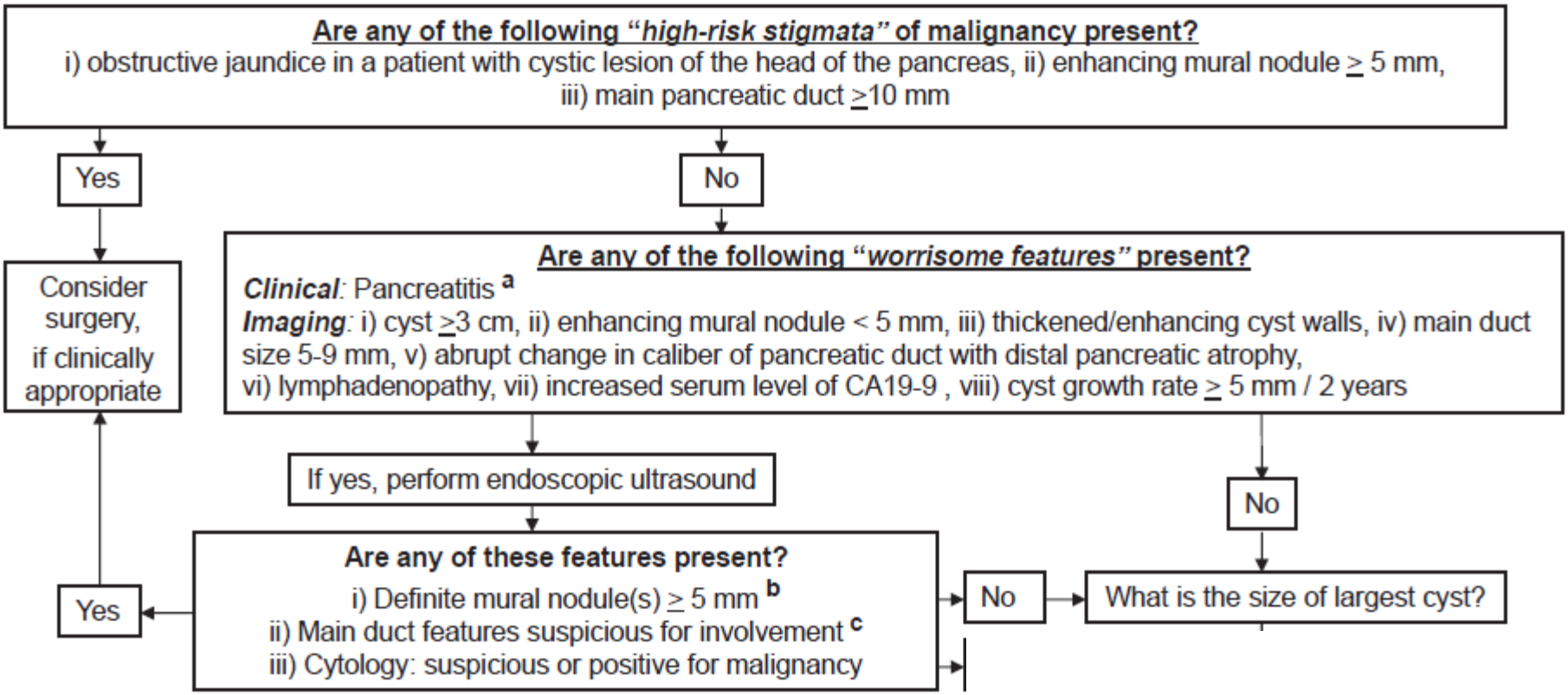
Typ IV:

invasive Nodule

Ill-defined
Hypoechoic area

Ohno et al. Ann Surgery 2009

IPMN:
When surgical resection ?


Are any of the following "high-risk stigmata" of malignancy present?
i) obstructive jaundice in a patient with cystic lesion of the head of the pancreas, ii) enhancing mural nodule ≥ 5 mm,
iii) main pancreatic duct ≥10 mm
Yes
No
Consider surgery, if clinically appropriate
Are any of the following "worrisome features" present?
Clinical: Pancreatitis a
Imaging: i) cyst ≥3 cm, ii) enhancing mural nodule < 5 mm, iii) thickened/enhancing cyst walls, iv) main duct size 5-9 mm, v) abrupt change in caliber of pancreatic duct with distal pancreatic atrophy,
vi) lymphadenopathy, vii) increased serum level of CA19-9 , viii) cyst growth rate ≥ 5 mm / 2 years
If yes, perform endoscopic ultrasound
No
Are any of these features present?
i) Definite mural nodule(s) ≥ 5 mm b
ii) Main duct features suspicious for involvement c
iii) Cytology: suspicious or positive for malignancy
Yes
No
What is the size of largest cyst?

Mucinous Cysts (IPMN/MCN) Follow-up:

In fukuoka-negative cysts in dependency on cyst size when/how to control?

How to perform surveillance for BD-IPMN and MCN?

< 1 cm:

1-2 cm:

540 BD-pts.

No HGD

No Cancer

Do NOT

request EUS + FNA

for cysts < 1-(2) cm

*:initial control 6 months

2-3 cm:

EUS in 3-6 months

Lengthen interval, alternating EUS and MRI

Consider surgery in young, fit patients (long surveillance)

> 3 cm:

EUS with close surveillance

alternating with MRI every 3 months

Strongly consider surgery (in young, fit patients)

Additiv: Serum CA19-9; diagnostic accuracy 82%

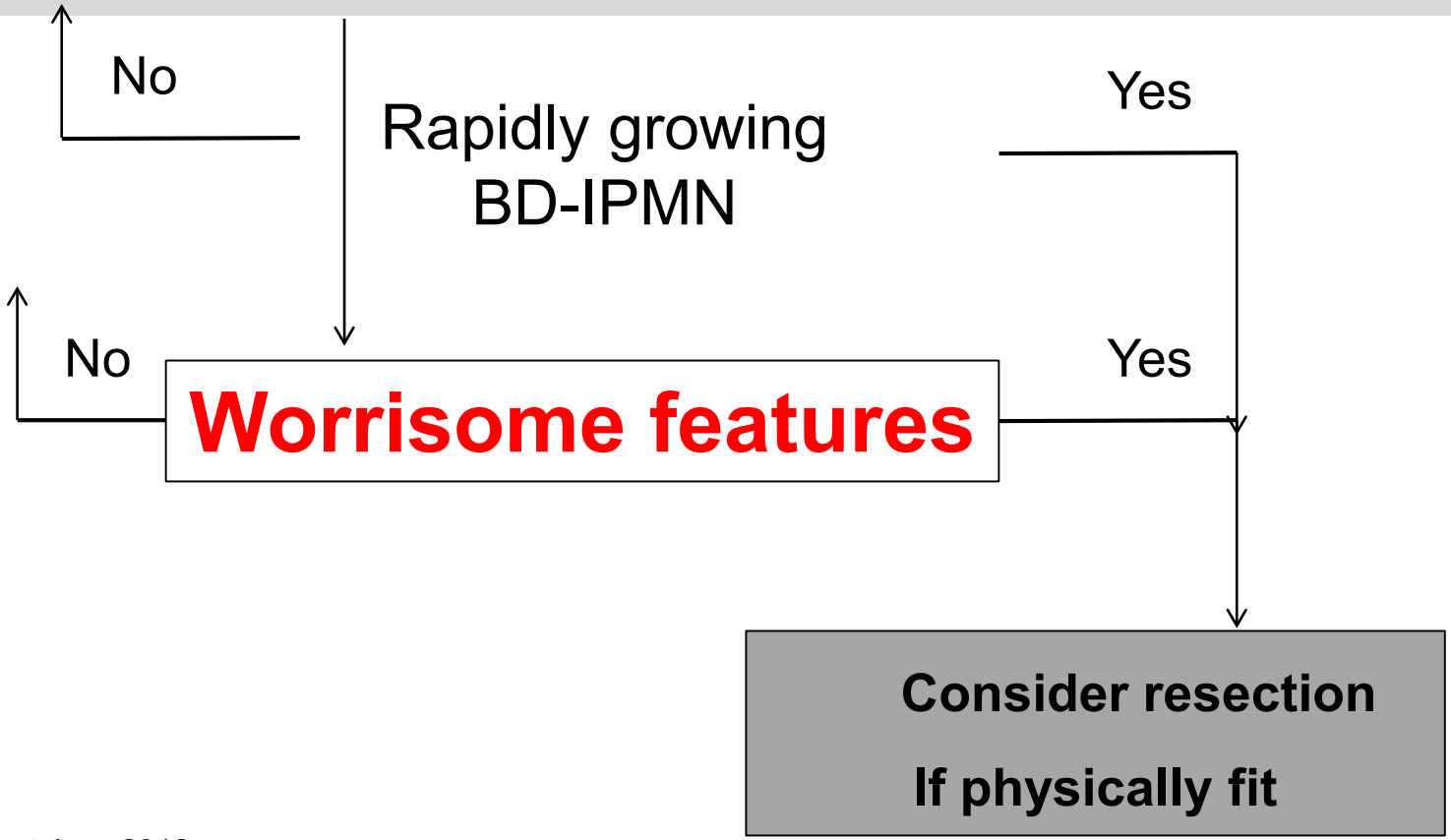
Tanaka et al. Pancreatology 2012

Fritz et al. BJSurg 2014

Mucinous Cysts - Follow-up:

In patients with two or more first degree relatives with pancreatic cancer ?

aggressive surveillance
by MRI/MRCP (or CT) every 3 (-6) months
and EUS annually



Tanaka et al. Pancreatology 2012

Mucinous Cysts - Follow-up:

What is the risk of concomitant Adeno-carcinoma in BD-IPMN?

Concomitant Pancreatic-Cancer in BD-IPMN

102 pts. with BD-IPMN: 6-monthly surveillance with EUS (CT,MRI)

NO progression of BD-IPMN: but pancreatic cancer otherwise

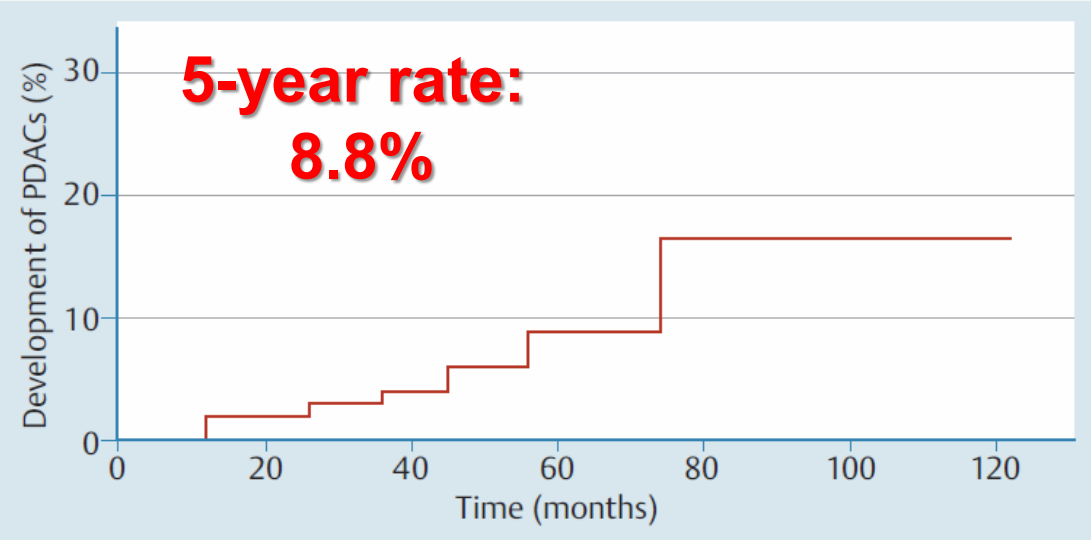


Fig. 3 Rate of intraductal papillary mucinous neoplasm (IPMN)-concomitant pancreatic ductal adenocarcinomas (PDAC) development during the follow-up of branch duct IPMNs, as analyzed by the Kaplan–Meier method.

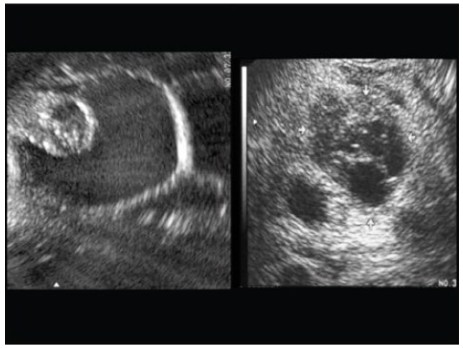
CT after EUS-Diagnosis:

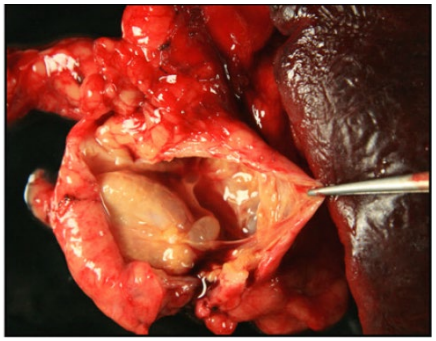
only 43%!!!! detectable with CT

Kamata et al. Endoscopy 2014

What characterizes MCN and when to resect?

Key features: MCN





- **Malignant potential:** **Yes (but lower than IPMN)**
- **Location:** **Body/tail (95%), always single lesion!**
- **Demographics, rate:** **Middle-aged women (95%), 25% of PCNs**
- **Morphology:** **thick-walled single cyst, capsule = „Orange“-like, often septations, epithelial layer with mucin-producing cells, ovarian-like stroma;**

No communication with pancreatic duct

Surgicâl resection is recommended for MCN

- ✓ all surgically fit patiens

- ✓ for MCNs of < 4 cm without murål nodules, laparoscopic resection or parenchyma-sparing resections or distal pancreatectomy should be considered

Tanaka et al. Pancreatology 2012

After surgical resection:

How to perform surveillance in IPMN/MCN?

Non-invasive MCNs:

no surveillance necessary after resection

IPMNs need surveillance:

based on the resection margin status:

High-gade dysplasia-> fruther resection
no residual lesions-> repeat examinations at 2 and 5 years*+
moderate-grade dysplasia-> unknown
low-grade or moderate-grade dysplasia -> MRCP twice a year

*: remnant BD-IPMN (multilocal cases); surveillance as in normal algorithm
+: others: **CT/MR initally every 6 months due to PDAC-risk (up to 2%/year) and then yearly (European Consensus)**

Tanaka et al. Pancreatology 2017

Vielen Dank