

Gastrohighlights 2018

Pankreas

Rainer Schöfl

# Interessenskonflikte

- Vortragshonorare: Gebro, Takeda, Janssen
- Advisory Boards: Sandoz, Norgine, Olympus
- Unterstützung abteilungseigener Veranstaltungen
- Unterstützung der wissenschaftlichen Gesellschaft

- akute Pankreatitis
- chronische Pankreatitis
- Pankreastumore
- Pankreaszysten

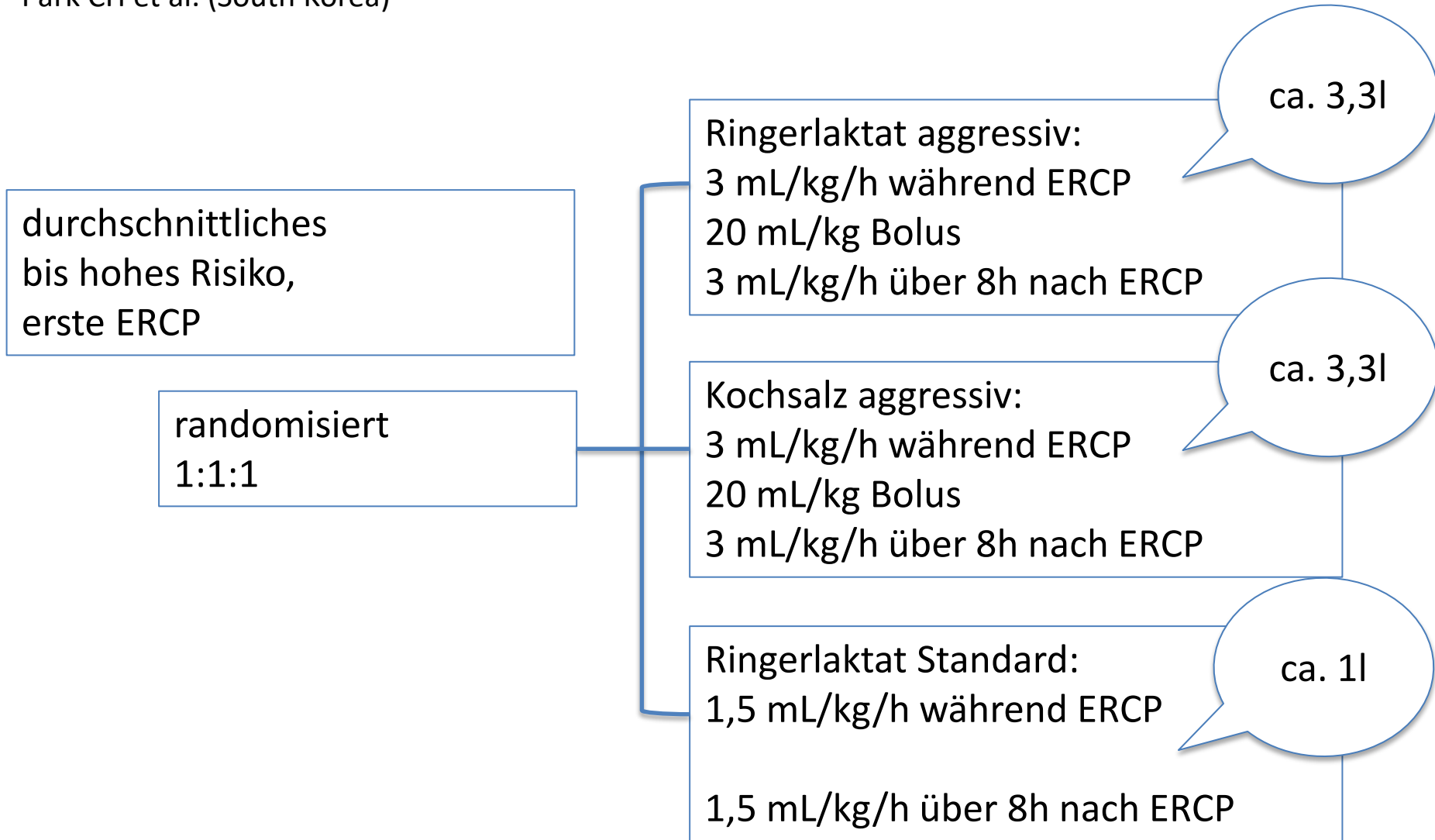
**Risk of Pancreatitis following Treatment of Irritable Bowel Syndrome with Eluxadoline.**

Gawron AJ, Bielefeldt K (USA)

- **Eluxadolin** (Truberzi<sup>®</sup>) ist ein Opioidrezeptormodulator ( $\delta$ -antagonist,  $\mu$ -Agonist), in der CH seit 2018 für diarrhoe-dominantes Reizdarmsyndrom zugelassen
- **“Pancreatitis-risk: 53 cases required hospitalization, 2 fatalities”**
- **“Conclusion: ... should prompt reassessment of the risk-benefit ratio.”**

**Aggressive intravenous hydration with lactated Ringer's solution for prevention of post-ERCP pancreatitis: a prospective randomized multicenter clinical trial.**

Park CH et al. (South Korea)



**Aggressive intravenous hydration with lactated Ringer's solution for prevention of post-ERCP pancreatitis: a prospective randomized multicenter clinical trial.**

Park CH et al. (South Korea)

395 Patienten rekrutiert, 385 wurden protokollgemäß behandelt

	PEP %	PEP n
aggressives Ringerlaktat	<b>3%</b>	4/132
aggressives Kochsalz	<b>6,7%</b>	9/134
Standard Ringerlaktat	<b>11,6%</b>	15/129

} p = 0.008  
} p = 0.17  
} p = 0.03

20% prophylaktische Pankreasstents, 0 NSAR zusätzlich

**Lactated Ringer's solution in combination with rectal indomethacin for prevention of post-ERCP pancreatitis and readmission: a prospective randomized, double-blinded, placebo-controlled trial.**

Mok SRS et al.

- aim was to evaluate the efficacy of IND with or without bolus LR in patients at high-risk for PEP
- 192 patients (48 per group) who completed follow-up at 24 hours and at 30 days post-ERCP
- all had at least 1 high-risk criterion for PEP, and 56% had >1

	Ringerlaktat + Indomethacin	Ringerlaktat + Plazebo	Kochsalz + Plazebo	Kochsalz + Indomethacin
PEP	3 (6%) *	9 (19%)	10 (21%)	6 (13%)
Readmission	1 (2%) *	2 (4%)	6 (13%)	2 (4%)

\* p < 0.03 bzw. 0.04

Endoscopy 2018; 50(1): 33-39

**Transpancreatic precut papillotomy versus double-guidewire technique in difficult biliary cannulation: prospective randomized study.**

Sugiyama H et al. (J)

- difficult (>15' or >3x pancreatography) biliary cannulation: 68 pts. randomly allocated: TPPP 34, DGT 34
- TPPP significantly **higher success rate (94.1 %)** than DGT (**58.8 %**)
- post-ERCP pancreatitis: **2.9 % in both groups**
- **no significant difference** in the overall rate of **complications**
- Conclusion: if biliary cannulation cannot be achieved, **TPPP should be selected first** after unintentional pancreatic duct cannulation



Pancreas 2018; 47(4): 444-453

## **Early Endoscopic Retrograde Cholangiopancreatography Versus Conservative Treatment in Patients With Acute Biliary Pancreatitis: Systematic Review and Metaanalysis of Randomized Controlled Trials**

Coutinho LMA et al.

- 10 RCTs, 1091 Patienten
- „early ERCP“:
  - **signifikant weniger**: lokale Komplikationen, Zeit bis schmerzfrei, Zeit bis fieberfrei, KH-Aufenthaltsdauer, Kosten
  - **nicht signifikant**: systemische Komplikationen, akute Cholangitis, Mortalität

Gut 2018; 67(4): 697-706

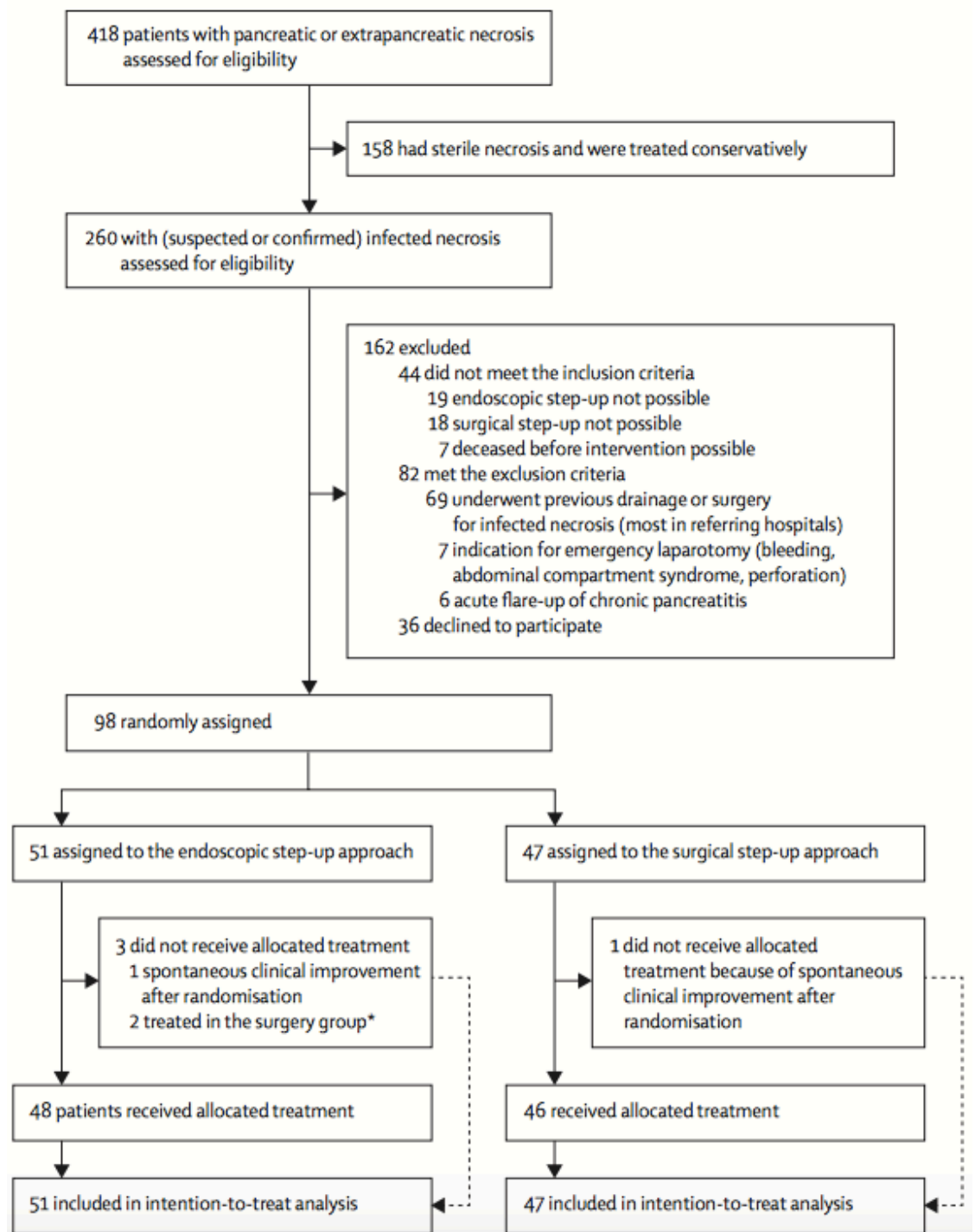
## Minimally invasive and endoscopic versus open necrosectomy for necrotising pancreatitis: a pooled analysis of individual data for 1980 patients.

van Brunschot S et al. (NL)

- 15 published and unpublished patient cohorts, retro- and prospective
- logistic multivariable regression and propensity score matching
- 1167 open necrosectomy, 467 minimally invasive surgical, 346 endoscopic
- **lower risk of death for minimally invasive surgical necrosectomy (OR 0.53; p=0.006) and endoscopic necrosectomy (OR, 0.20; p=0.006)**

Propensity Score Matching	low risk <5% Mortalität	intermediate risk 5-15% Mortalität	high risk 15-35% Mortalität	very high risk >35% Mortalität
MIC vs. offen				42 vs. 59/111 <b>RR 0,7</b> (0,52-0,95) p=0.02
endoskopisch vs. offen			3 vs. 12/40 <b>RR 0,27</b> (0,08-0,88) p=0.03	12 vs. 28/57 <b>RR 0,43</b> (0,24-0,77) p=0.005

Lancet 2018; 391(10115): 51-58  
**Endoscopic or surgical step-up approach for infected necrotising pancreatitis: a multicentre randomised trial**  
 van Brunschot S et al.



Lancet 2018; 391(10115): 51-58

**Endoscopic or surgical step-up approach for infected necrotising pancreatitis: a multicentre randomised trial**

van Brunschot S et al. (NL)

- multicentre, randomised superiority trial from 19 hospitals in the Netherlands, 2011-2015, ITT-analysis
- adult patients with infected necrotising pancreatitis and an indication for invasive intervention
- 418 patients screened, 98 patients enrolled
- either endoscopic or surgical step-up approach
  - endoscopic approach: EUS-guided transluminal drainage followed, if necessary, by endoscopic necrosectomy (n=51)
  - surgical approach: percutaneous catheter drainage followed, if necessary, by video-assisted retroperitoneal debridement (n=47)
- primary endpoint: composite of major complications or death during 6mo follow-up

Lancet 2018; 391(10115): 51-58

**Endoscopic or surgical step-up approach for infected necrotising pancreatitis: a multicentre randomised trial**

van Brunschot S et al. (NL)

	<b>endoscopic step-up</b>	<b>surgical step-up</b>	<b>p</b>
Primärer Endpunkt: Majorkomplik. o. Tod	43%	45%	0.88
Mortalität	18%	13%	0.5
Fisteln	5%	32%	0.001
Aufenthaltsdauer	53d	69d	0.014

Medicine (Baltimore) 2018; 97(1): e9417

**Evaluation of HVHF for the treatment of severe acute pancreatitis accompanying MODS.**

Abulimiti A et al. (China)

prospektiv, nicht randomisiert

<b>n = 40 (18/22)</b>	<b>Hämofiltration</b>	<b>Kontrollen</b>
APACHE II 3 d	6,3 +/- 1,7	9,2 +/- 2,1
APACHE II 7d	3,3 +/- 0,8	6,2 +/- 1,7
Mortalität	16,7%	31,8%
Komplikationsrate	11,1%	40,9%

J Laparoendosc Adv Surg Tech A 2017; 27(11): 1145-1150

## Effect of Laparoscopic Peritoneal Lavage and Drainage and Continuous Venovenous Diahemofiltration on Severe Acute Pancreatitis

Wang G et al. (China)

RCT, n = 245	Standard	Peritoneale Lavage	Hämofiltration	Peritoneale Lavage + Hämofiltration
Mortalität	20%	11,3%	12,3%	6,9%
Komplikationen	30%	5,8%	9,2%	10,3%
KH-Dauer	61,4d	31,3d	35d	25,6d
KH-Kosten	8.300\$	5.800\$	5.500\$	6.600\$

# Fazit Akute Pankreatitis

- auf Opiatrezeptormodulatoren wegen Pankreatitis-Risiko aufpassen
- an der Hydratation zur Prophylaxe der post-ERCP-Pankreatitis scheint was dran zu sein
- Dauerbrenner Precut-Technik bei schwieriger Papille und ERCP-Zeitpunkt/-Indikation bei biliärer Pankreatitis
- Nekrosektomie: Endoskopie ex aequo Minimal Invasive Chirurgie vor offener Chirurgie
- Hämofiltration und Peritoneal-Lavage bei nekrotisierender Pankreatitis ?



Gastroenterology 2017 Dec; 153(6): 1544-1554

**Development and Validation of a Chronic Pancreatitis Prognosis Score in 2 Independent Cohorts.**

Beyer G et al. (Germany)

- prospective study of 91 patients with chronic pancreatitis at academic centers in Europe from January 2011 through April 2014
- correlations between clinical, laboratory, and imaging data with number of hospital readmissions and in-hospital days over the next 12 months
- the parameters with the highest degree of correlation were used to develop a 3-stage chronic pancreatitis prognosis score (COPPS)
- predictive strength was validated in 129 independent subjects.

**Development and Validation of a Chronic Pancreatitis Prognosis Score in 2 Independent Cohorts.**

Beyer G et al. (Germany)

- **pain, HbA1c, CRP, BMI and platelet count** were used to develop the COPPS system
- patients' median COPPS was 8.9 points (5-14)
- accurately discriminated stages of disease severity: A (5-6 points), B (7-9), and C (10-15)

**Table 2.** Chronic Pancreatitis Prognosis Score (COPPS)

	1 point	2 points	3 points
NRS (1–10), most intense day within the past 7 d	0–2	3–6	7–10
HbA1c, %	>6.0	5.5–6.0	<5.5
CRP, mg/L	<3.1	3.1–20	>20
BMI, kg/m <sup>2</sup>	>25	18–25	<18
Thrombocytes, Gpt/L	150–400	100–150	<100, >400

**COPPS A = 5–6 points    COPPS B = 7–9 points    COPPS C = 10–15 points**

CRP, C-reactive protein; NRS, numeric rating scale for pain: 0 = no pain, 10 = worst imaginable pain.

# Fazit Chronische Pankreatitis

- neues klinisches Klassifikationssystem für cP mit prognostischem Wert
- Charakterisierung der Typ 2 Autoimmunpankreatitis mit CED
- Tetrahydrocannabinol hilft nicht bei Schmerzen der chronischen Pankreatitis

Scand J Gastroenterol. 2017 Dec; 52(12): 1435-1441

**22G versus 25G biopsy needles for EUS-guided tissue sampling of solid pancreatic masses: a randomized controlled study.**

Woo YS et. al.

- Diagnostic accuracy in 3 passes was 97.1% for the PC22 and 91.3% for the PC25. Noninferiority of PC25 to PC22 was not shown
- 2 passes was non-inferior to 3 passes in the PC22 (96.1% vs. 97.1%) but not in the PC25 group (87.4% vs. 91.3%)

Clin Gastroenterol Hepatol 2017; 15(7): 1071-1078

**Increasing Number of Passes beyond 4 does not increase Sensitivity of Detection of Pancreatic Malignancy by Endoscopic Ultrasound-Guided Fine-Needle Aspiration.**

Mohamadnejad M et al..

- 4 passes of EUS-FNA (22G, continuous suction, on-site-pathologist) were sufficient to detect malignant pancreatic masses; increasing number of passes did not increase sensitivity
- greater number of passes required to evaluate masses < 2 cm

Pancreas 2018; 47(3): 296-301

**Per-Pass Performance Characteristics of Endoscopic Ultrasound-Guided Fine-Needle Aspiration of Malignant Solid Pancreatic Masses in a Large Multicenter Cohort.**

Ge PS et al.

- Using a 25G needle, the maximal diagnostic yield of EUS-FNA for a solid pancreatic mass (91%-96%) is reached after 4 needle passes.

Br J Surg 2017 Oct; 104(11): 1443-1450

**Randomized clinical trial of laparoscopic versus open pancreatoduodenectomy for periampullary tumours.**

Palanivelu C et al. (India)

- 268 patients screened, 64 were randomized, 32 to each group
- postoperative hospital stay longer for open surgery (13 vs. 7d ; p = 0.001)
- duration of operation longer in the laparoscopy group
- blood loss greater in the open group (401 vs. 250 ml; p < 0.001)
- number of nodes retrieved and R0 rate similar
- no difference in delayed gastric emptying, pancreatic fistula or haemorrhage
- overall complications similar
- one death in each group

Gut Liver 2017; 11(4): 567-573

**Efficacy of a Multiplex Paclitaxel Emission Stent Using a Pluronic® Mixture Membrane versus a Covered Metal Stent in Malignant Biliary Obstruction: A Prospective Randomized Comparative Study.**

Jang SI et al. (South Korea)

- no significant differences in stent patency or patient survival

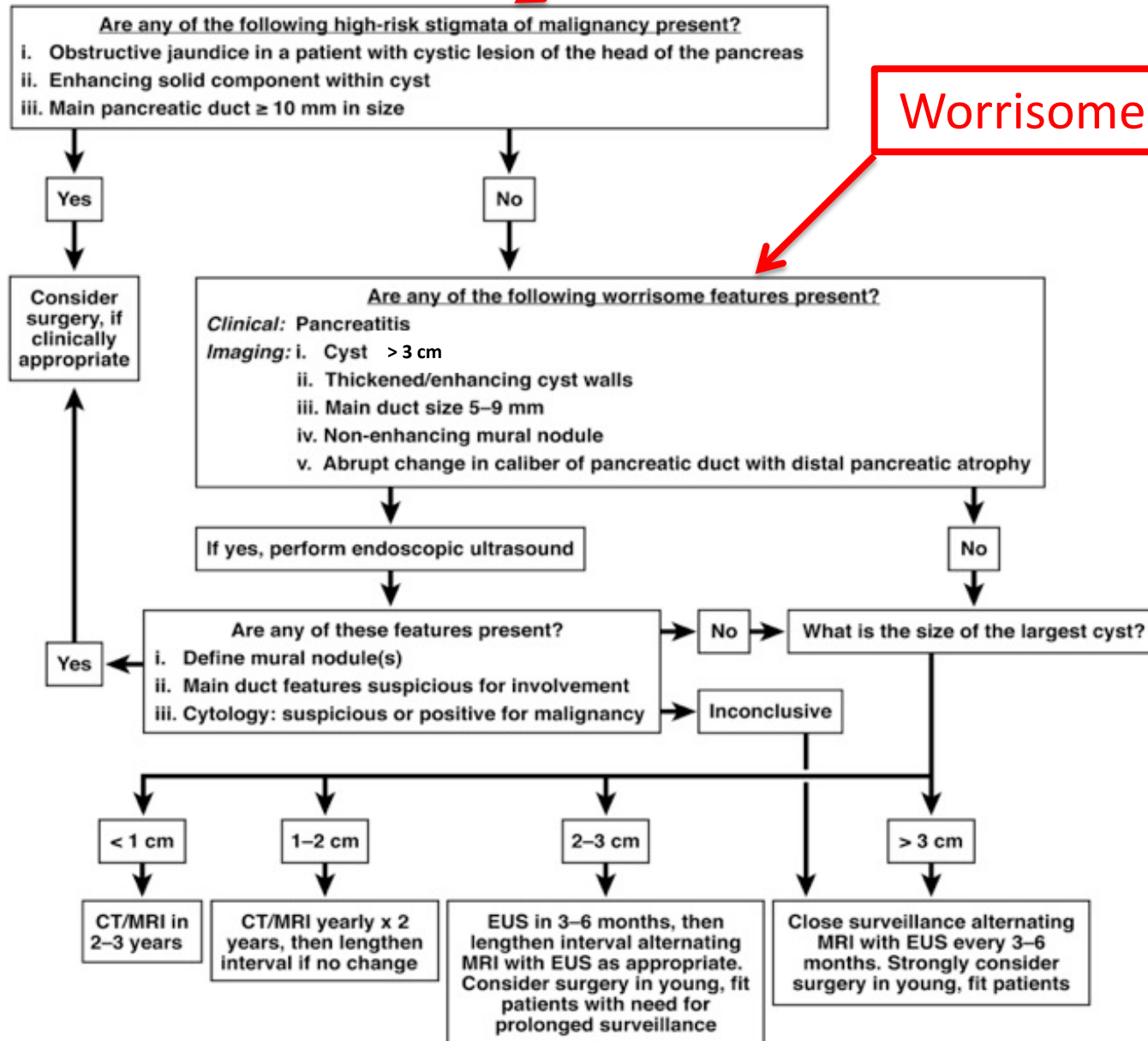
# Fazit Pankreastumore

- EUS-FNA Pankreastumor:
  - 22G und 25G sind ok
  - Sog und Pull-Technik sind ok
  - 25G braucht bis zu 4 Stiche, 22G möglicherweise nur 2
- laparoskopische Pankreatoduodenektomie scheint der offenen Operation gleichwertig
- drug eluting biliäre Stents bringen wahrscheinlich nichts

# Fukuoka Guidelines

High Risk Stigmata

Worrisome Features





Gut 2018; 67(1): 138-145

**Prospective study on the incidence, prevalence and 5-year pancreatic-related mortality of pancreatic cysts in a population-based study.**

Kromrey ML et al. (Germany)

- baseline prevalence: 49.1%
- 5-year follow-up: 12.9% new pancreatic cysts

Gastroenterology 2017 Nov; 153(5): 1284-1294

**Long-term Risk of Pancreatic Malignancy in Patients With Branch Duct Intraductal Papillary Mucinous Neoplasm in a Referral Center.**

Pergolini I et al. (Italy, USA)

- cancer developed in 10 years in 4.4%, worrisome features at 5 years 18,8%
- cysts  $\leq 1.5$  cm for more than 5 years might be considered low-risk for progression

Gastroenterology 2018; 154(3): 576-584

**Progression of Pancreatic Branch Duct Intraductal Papillary Mucinous Neoplasm Associates With Cyst Size.**

Han Y et al. (South Korea)

- retrospective; 1369 patients
- annual growth rate 0.8 mm over 61 months
- 3.4% underwent surgery because of disease progression
- worrisome features in 15.3% during surveillance

**Progression of Unresected Intraductal Papillary Mucinous Neoplasms of the Pancreas to Cancer: A Systematic Review and Meta-analysis.**

Choi SH et al. (South Korea)

- 10 studies of low-risk IPMNs (n = 2411) and 9 studies of non-low-risk IPMNs (n = 825)

Krebsinzidenz	1 Jahr	3 Jahre	5 Jahre	10 Jahre
low risk IPMN	0,02%	1,4%	3,12%	7,77%
non low risk IPMN	1,95%	5,69%	9,77%	24,68%

Am J Gastroenterol 2017; 112(8): 1330-1336

**Competing Risks for Mortality in Patients With Asymptomatic Pancreatic Cystic Neoplasms: Implications for Clinical Management.**

Kwok K et al. (USA)

- 402/1.800 Todesfälle (22.3%) während 5.7 Jahren:
  - 43 Pankreaskarzinome und 359 andere Todesursachen

Clin Transl Gastroenterol 2018; 9(6): 158

**Long-term follow-up of low-risk branch-duct IPMNs of the pancreas: is main pancreatic duct dilatation the most worrisome feature?**

Petrone MC et al. (Italy)

- Hauptgangdilatation ist das stärkste “worrisome feature”

# Fazit Pankreaszysten

- Pankreaszysten sind häufig (ca. 50% bei mittlerem Alter von 56 Jahren), in 5 Jahren entstehen bei ca. 13% neue Zysten
- ca. 15-20% entwickeln in 5 Jahren Überwachung Warnzeichen („worrisome features“) mit einem Karzinomrisiko von ca. 25% in 10 Jahren
- ca. 4-8% der primär harmlos aussehenden Seitenast-IPMNs werden in 10 Jahren zu Karzinomen
- die Kriterien „worrisome features“ und „high risk stigmata“ für die Überwachung der Zysten scheinen zu funktionieren