Pankreas

Gastrohighlights 2022

Rainer Schöfl

Linz

Interessenskonflikte

- Vortragshonorare (Novartis, Grünenthal, Medtronic, Boston Scientific)
- Reisestipendien diverser Firmen für die MA der Abteilung
- Unterstützungen der Abteilung für Veranstaltungen, ANPs, App-Entwicklung

Gliederung

- akute Pankreatitis
- chronische Pankreatitis
- Pankreaszysten
- Pankreastumore

akute Pankreatitis

Clin Gastroenterol Hepatol 2021; 19(8): 1652-60

Genetic Variants Associated With Increased Plasma Levels of Triglycerides, via Effects on the Lipoprotein Lipase Pathway, Increase Risk of Acute Pancreatitis

Signe E J Hansen, Christian M Madsen, Anette Varbo et al. (Dänemark)

- **even mild to moderate HTGL (177-886 mg/dL) associated with increased risk of AP?**

- **variants in Lipoproteinlipase** (APOA5, APOC3, ANGPTL3, ANGPTL4) result in increased or reduced TGL levels - **associations between these variants and AP in a general population?**

- **prospective cohort study,** men and women randomly selected from Copenhagen invited to complete a questionnaire and provide blood samples for biochemical and genetic analyses from 2003 through 2015
- TGL measurements from 117,427 participants, examined for 15 genetic variants, that are associated with lipoprotein lipase function

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- 970 diagnoses among participants in the genetic analysis and 527 among participants in the observational study were obtained from Danish registries
- pts. with the highest vs. the lowest genetic allele score **OR for AP 1.55** (1.08-2.23)
- **every 1 mmol/L** (89 mg/dL) increase in TGL associated with an **increase in OR of 1.09** (95% CI, 1.05-1.14)
- strategies to reduce plasma levels of triglycerides by **increasing lipoprotein lipase function might be developed for prevention** of acute pancreatitis

Lipoprotein-Lipase-Mangel

Lipoprotein-Lipase-Mangel (LPLD) ist eine seltene, autosomal-rezessiv vererbte Stoffwechselkrankheit. Aufgrund einer Mutation im Gen der Lipoproteinlipase (LPL) sind die produzierten LPL-Enzyme defekt oder funktionell eingeschränkt.
LPL Enzyme werden für den Abbau und die Verarbeitung von Chylomikronen benötigt, welche Triglyceride im Körper transportieren. Wenn diese Verarbeitung gestört ist, steigt die Konzentration von Triglyceridfetten im Blut um ein Vielfaches (10-100x) an.
Die meist noch jungen Patienten berichten von diffusen Abdominalschmerzen, sowie Unverträglichkeiten gegenüber Milch und fetthaltigen Speisen. Die erhöhten Blutfettwerte können Auslöser für rezidivierende Pankreatitiden mit Folgenekrosen und erhöhten Pankreaskrebsrisiko sein. Häufigkeit 1 / 1 000 000.

Diagnose

Eine Stammbaumanalyse kann hinweisführend sein.
Die Diagnose basiert auf dem klinisches Erscheinungsbild mit Bauchschmerzen, Xanthomen und rezidivierenden Pankreatitiden und einer Unverträglichkeit gegenüber Milchprodukten.
Die Labordiagnostik zeigt milchig verfärbtes Blut. Eine genetische Analyse des LPL-Gens im Blut sichert die Diagnose.

Therapie

Es sollte eine strenge fettarme Diät eingehalten werden (unter 20% der Gesamktkalorienmenge sollte durch Fett zugeführt werden) sowie eine strikte Alkoholkarenz.
Eine neue Form der Therapie ist die Gentherapie:Patienten erhalten einmalig mehrere intramuskuläre Injektionen Adeno-assoziierten Viren **Glybera®** mit einem intakten Gen der LPL. Infolgedessen kann der Körper LPL erneut produziert werden und die Pankreatitiden können verhindert werden.

Clin Transl Gastroenterol 2021 Oct; 12(11): e00415

Rectal Indomethacin does not mitigate the Systemic Inflammatory Response Syndrome in Acute Pancreatitis: a Randomized Trial

Jorge D Machicado, Rawad Mounzer, Pedram Paragomi et al. (USA)

- rectal indomethacin vs. placebo in reducing SIRS in high-risk AP

- single-center, blinded, 1:1 placebo-controlled RCT
- subjects with AP and SIRS within 72 hours of presentation without organ failure
- indomethacin rectally every 8 hours for 6 doses

- 42 subjects (mean age 52 years, 55% men), indomethacin (n=18) or placebo (n=24)

- **no differences** in SIRS scores after 24h, 48h, 72h or in CRP after 48h

- 2 adverse events occurring in the placebo and none in the indomethacin arm

PEP = Post-ERCP-Pankreatitis

Lancet Gastroenterol Hepatol. 2021 Sep; 6(9): 733-42

Non-steroidal anti-inflammatory drugs, intravenous fluids, pancreatic stents or their combinations for the prevention of post-endoscopic retrograde cholangiopancreatography pancreatitis: a systematic review and network meta-analysis

Venkata S Akshintala, Christina J Sperna Weiland, Furqan A Bhullar et al. (USA, NL, Indien)

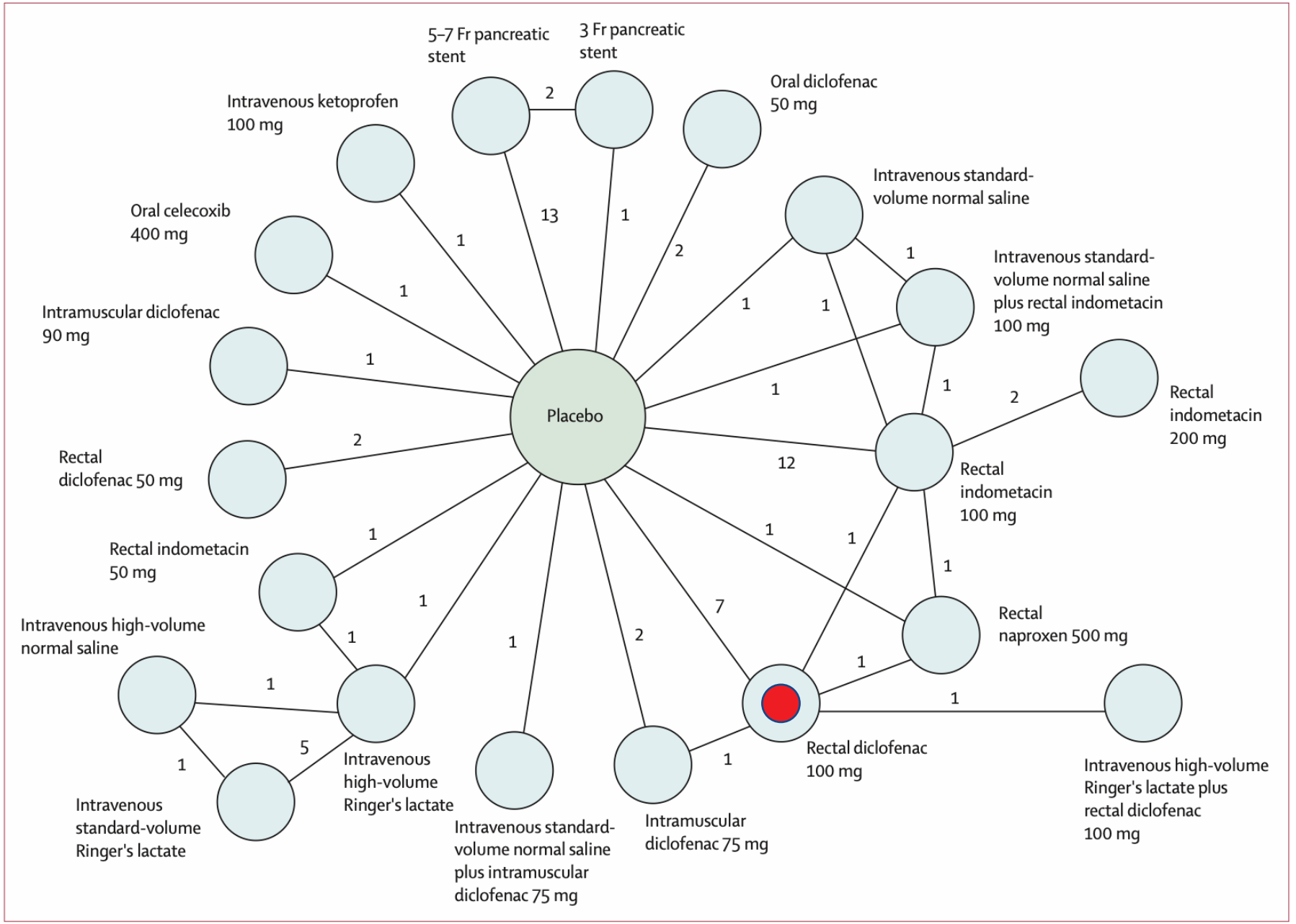
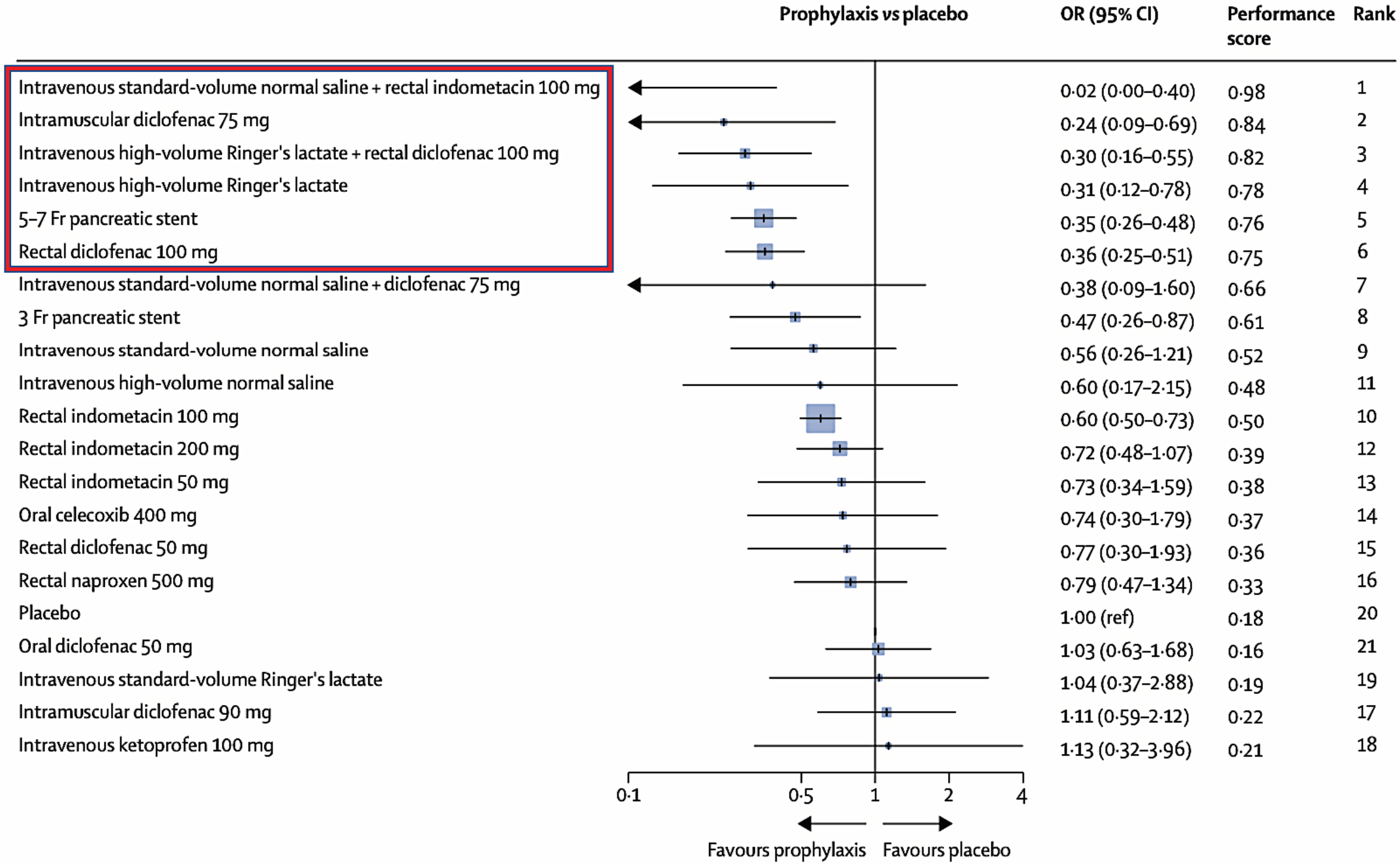


***Figure 2*: Network of randomised controlled trials comparing NSAIDs, pancreatic stents, and intravenous fluids, or combinations of these**

The number adjacent to the lines connecting agents indicate the number of RCTs. Some of the included RCTs have multiple comparative arms; therefore, the total number of RCTs in the figure is greater than 55. Fr=French. RCT=randomised controlled trials. NSAID=non-steroidal anti-inflammatory drug.


Prophylaxis vs placebo
OR (95% CI)
Performance score
Rank
Intravenous standard-volume normal saline + rectal indometacin 100 mg
0·02 (0·00–0·40)
0·98
1
Intramuscular diclofenac 75 mg
0·24 (0·09–0·69)
0·84
2
Intravenous high-volume Ringer's lactate + rectal diclofenac 100 mg
0·30 (0·16–0·55)
0·82
3
Intravenous high-volume Ringer's lactate
0·31 (0·12–0·78)
0·78
4
5–7 Fr pancreatic stent
0·35 (0·26–0·48)
0·76
5
Rectal diclofenac 100 mg
0·36 (0·25–0·51)
0·75
6
Intravenous standard-volume normal saline + diclofenac 75 mg
0·38 (0·09–1·60)
0·66
7
3 Fr pancreatic stent
0·47 (0·26–0·87)
0·61
8
Intravenous standard-volume normal saline
0·56 (0·26–1·21)
0·52
9
Intravenous high-volume normal saline
0·60 (0·17–2·15)
0·48
11
Rectal indometacin 100 mg
0·60 (0·50–0·73)
0·50
10
Rectal indometacin 200 mg
0·72 (0·48–1·07)
0·39
12
Rectal indometacin 50 mg
0·73 (0·34–1·59)
0·38
13
Oral celecoxib 400 mg
0·74 (0·30–1·79)
0·37
14
Rectal diclofenac 50 mg
0·77 (0·30–1·93)
0·36
15
Rectal naproxen 500 mg
0·79 (0·47–1·34)
0·33
16
Placebo
1·00 (ref)
0·18
20
Oral diclofenac 50 mg
1·03 (0·63–1·68)
0·16
21
Intravenous standard-volume Ringer's lactate
1·04 (0·37–2·88)
0·19
19
Intramuscular diclofenac 90 mg
1·11 (0·59–2·12)
0·22
17
Intravenous ketoprofen 100 mg
1·13 (0·32–3·96)
0·21
18
0·1
0·5
1
2
4
Favours prophylaxis
Favours placebo

Pancreas 2021; 50(8): 1236-42

Is the Combination of Rectal Diclofenac and Intravenous Ringer Lactate Superior to Individual Therapy for Prophylaxis of Post-Endoscopic Retrograde Cholangiopancreatography Pancreatitis: A Prospective, Open-Label, Single-Center Randomized Trial

Ravi Thanage, Shubham Jain, Sanjay Chandnani et al. (Indien)

- open-label randomized trial
- 57 patients at high risk for PEP, randomized into 3 treatment groups: Diclofenac suppository group, Ringerlactate group and a Combination group

- 14% in the diclofenac group, 16% in the RL group and 10.5% in the combination group developed **PEP**, **not statistically significant** (p=0.70)

- post-ERCP pancreatitis is usually mild to moderate (95%); female sex, age < 50 years, a benign indication of ERCP and low bilirubin levels have higher chances of PEP

- **combination** of rectal diclofenac and hydration with RL **does not offer better protection**

N Engl J Med 2021; 385(15): 1372-81

Immediate versus Postponed Intervention for Infected Necrotizing Pancreatitis

Lotte Boxhoorn, Sven M van Dijk, Janneke van Grinsven et al. (NL)

- infected necrotizing pancreatitis is treated with a step-up approach with catheter drainage often delayed until encapsulated. **Outcomes improved by earlier catheter drainage?**
- multicenter, randomized superiority trial
- primary end point: Comprehensive Complication Index (all complications over 6 mo)

	immediate	postponed
n	55	49
CCI (complication index)	57	58
mortality	13%	10%
interventions	4,4	2,6

- incidence of adverse events was similar in the two groups
- in the postponed-drainage group 19 patients **(39%) were treated conservatively with antibiotics and did not require drainage**; 17 of these patients survived

Cureus 2022; 14(7): e26485

Immediate Catheter Drainage Versus Delayed Drainage in the Management of Infected Necrotizing Pancreatitis

Wahidullah Dost, Farzad Qasemi, Wahida Ali et al. (Indien)

- prospective, controlled, not randomised trial, n=130
- Group A: immediate percutaneous catheter drainage (within 24h of admission, n=65)
- Group B: delayed drainage (after 24h)
- outcome: complication rate, mortality, length of hospital and ICU stay

- **no significant differences**
- mortality rate was 15.4% in Group A and 10.8% in Group B (p=0.44)
- multiple organ failure and wound infections statistically insignificant (p=0.08, p=0.61)

- Conclusion: the **timing of drainage did not impact the prognosis** of patients with necrotizing pancreatitis

Expert Rev Gastroenterol Hepatol 2022 Mar; 16(3): 297-305

Endoscopic versus percutaneous drainage for the management of infected walled-off necrosis: a comparative analysis

Jayanta Samanta, Jahnvi Dhar, Gaurav Muktesh et al. (Indien)

- 218 patients (175 males; 80.3%), 102 percutaneous (PCD), 116 EUS-guided (EUS-D)

- **clinical success** significantly higher with EUS-D (**92.1%** vs. **64.6%;** p<0.0001)
- also for infected WON (n=128) with higher and faster organ failure resolution (p<0.0001)
- **mortality significantly higher in the PCD-Group**
- PCD with >40% solid component had the worst clinical success rates, while EUS-D with <40% solid component had the best outcomes

- Conclusion: **EUS-D should be preferred** over PCD in the management of WON, infected or not (higher clinical success and faster resolution of organ failure). **PCD should be avoided in WON with >40% solid component**.

Endoscopy 2021; 53(6): 603-10

Impact of disconnected pancreatic duct syndrome on endoscopic ultrasound-guided drainage of pancreatic fluid collections

Lillian Wang, Sherif Elhanafi, Andrew C Storm et al. (USA)

- aim of study was outcomes of EUS-guided transmural drainage of pancreatic fluid collections (PFCs) in patients with disconnected pancreatic duct syndrome (DPDS)

- overall treatment success was determined by PFC resolution on follow-up imaging or stent removal without recurrence

- 141 pts, DPDS in 57 (40 %), walled-off necrosis most frequent type of PFC (55 %)

- DPDS was **not associated** with lower **immediate** clinical success, increased number of repeat interventions, or increased time to PFC resolution
- DPDS more often treated with **permanent plastic** double-pigtail stents (OR 6.4; $p<0.001$)
- when stents were removed, DPDS was associated with **increased PFC recurrence** after stent removal (OR 8.0; $p=0.04$)

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- when stents were removed, DPDS was associated with **increased PFC recurrence** after stent removal (OR 8.0; p=0.04)

wait, drain and see?
transpapillary stent?
somatostatine-analogues?
surgery?

Fazit Akute Pankreatitis

- je 90mg% TGL mehr erhöhen das Pankreatitisrisiko um je 10%
- rektales Indomethacin nutzt bei schwerer akuter Pankreatitis nichts
- als PEP-Prophylaxe sind rektales Diclofenac oder Indomethacin 100mg, aggressive Hydrierung (3l+) oder 5-7F Pankreasstents alle etwa gleich wirksam, die Kombination bietet keine zusätzliche Vorteile
- Walled Off Nekrosen (WONs) sollen, wenn klinisch möglich, spät drainiert werden
- Walled Off Nekrosen (WONs) sollen besser endosonographisch drainiert werden
- der abgehängte Pankreasgang bleibt trotz EUS-Drainage mit LAMS und/oder Plastik eine Langzeit-Herausforderung

chronische Pankreatitis

J Inflamm Res 2022 Aug; 15: 4737-49

Aspirin Ameliorates Pancreatic Inflammation and Fibrosis by Inhibiting COX-2 Expression in Experimental Chronic Pancreatitis

Xiao-Fan Xu, Jian-Wei Fan, Jia-Qi Xin et al. (China, BRD)

- Conclusion: ASA has an ameliorating effect in murine models of CP through inhibition of pancreatic inflammation and fibrosis, which may be a promising option for treatment

Am J Gastroenterol 2020 Mar; 115(3): 473-80

Prevention of Severe Acute Pancreatitis With Cyclooxygenase-2 Inhibitors: A Randomized Controlled Clinical Trial

Zhiyin Huang, Xiao Ma, Xintong Jia et al. (China)

- 190 Patienten mit vorhergesagter SAP, Parecoxib 40 mg/d iv für 3 Tage und Celecoxib 200 mg po zweimal täglich für 7 Tage
- zu einer **SAP** kam es in **21%** vs. **40%,** p= 0.005
- Reduktion **später lokaler Komplikationen 19%** vs. **34%,** p= 0.016

Cystic Fibrosis Transmembrane Conductance Regulator Modulator

medikamentöse Behandlung der Krankheitsursache orientiert sich an den sechs Mutationsklassen:

- für Klasse-I und -II Mutationen sind sogenannte *Korrektoren* (Ersatz) in Entwicklung
- für Klasse-III-Mutationen *Potentiatoren* (sollen die Funktionalität oder die Anzahl der Chloridkanäle erhöhen)

Ziel ist, die CFTR-Funktion auf mindestens 5% des Normalwertes anzuheben (Annahme, dass ab diesem Wert die Symptome erheblich reduziert oder die wichtigsten Manifestationen der Krankheit eliminiert werden können)

Kalydeco® (ivacaftor), **Orkambi**® (lumacaftor/ivacaftor), **Symdeko**® (tezacaftor/ivacaftor), **Trikafta**® (elexacaftor/tezacaftor/ivacaftor)

Am J Gastroenterol. 2021; 116(12): 2446-54

Cystic Fibrosis Transmembrane Conductance Regulator Modulator Use Is Associated With Reduced Pancreatitis Hospitalizations in Patients With Cystic Fibrosis

Mitchell L Ramsey, Yevgeniya Gokun, Lindsay A Sobotka et al. (Ohio, USA)

- **acute pancreatitis occurs among patients with pancreas-sufficient cystic fibrosis** (PS-CF) but is **less common among patients with pancreas-insufficient cystic fibrosis**
- incidence of AP may be influenced by cystic fibrosis transmembrane conductance regulator (CFTR) modulator use
- **can CFTR modulators reduce AP hospitalizations**, with the greatest benefit in PS-CF?

- 10.417 patients with CF identified, 1.795 received a CFTR modulator

- **AP relative reduction during CFTR modulator use was 67% and 62%**

- **AP was more common in PS-CF than PI-CF** (2.9% vs. 0.9%, p = 0.007)

Pregabalin (z.B. Lyrica® 75mg)

- ein Gabapentinoid
- Antikonvulsivum, Antipsychotikum. Analgetikum gegen neuropathische Schmerzen
- Dosierung 2-3 x 1, bis zu 8/d
- NW: Kopfschmerzen, Benommenheit, Gewichtszunahme, GI

Antioxidantien

- Vitamine A, C, E, organisches Selen und Methionin

unklare Datenlage bei chronischer Pankreatitis

Dig Dis Sci 2021; 66(11): 4017-25

Efficacy of Pregabalin and Antioxidants Combination in Reducing Pain in Chronic Pancreatitis: A Double Blind Randomized Trial

Sathasivam Sureshkumar, Agrawal Omang, Amaranathan Anandhi et al. (Indien)

- prospective, double blind, superiority RCT in patients with CP for 8 weeks
- primary outcome: change in **maximum pain intensity** assessed by VAS and Izbicki pain score
- secondary outcomes: painful days, opioid and non-opioid requirements, quality of life, hospital admissions and patient satisfaction

n = 90	PREGA + AntiOx	placebo	p
pain (VAS) reduction	2 +/- 0,8	1,3 +/- 0,9	0.007
analgetics-days	54,4 +/- 2,9	55,7 +/- 1,5	0.014
hospital admission	0,2 +/- 0,5	0,6 +/- 0,7	0.002
satisfaction	18%	11%	0.03

Pankreasgangsteine

- nicht Ursache, sondern Folge
- assoziiert mit Ätiologie?
- Kalziumkarbonat
- Therapie:
  - Extraktion nach EPT_{Pa}, primär kaum erfolgreich
  - dzt. ESWL, z.B. 3x; ohne vorherige EPT? Extraktion der Fragmente?
  - Pankreatikoskopie mit EHL dzt. Zweitlinie, Zugang limitiert, aufwändig und teuer

J Dig Dis 2021 Oct; 22(10): 572-81

Peroral pancreatoscopy-guided lithotripsy for the endoscopic management of pancreatolithiasis: A systematic review and meta-analysis

Edson Guzmán-Calderón, Belen Martinez-Moreno, Juan A Casellas, José Ramón Aparicio (Peru, Spanien)

Although ESWL is considered the first-line treatment, per-oral pancreatoscopy (POP) has emerged as a useful method for treating pancreatic stones.

- 15 studies, 11 retrospective and 4 prospective; 370 pts., 66.4% male; 218 EHL and 155 LL
- **technical and clinical success rate 88.1% and 87.1%**
- for EHL-POP technical success rate was 90.9% and clinical success rate was 89.8%
- for LL-POP technical and clinical success rate was 88.4% and 85.8%
- 43 adverse events occurred **(12.1%)**

„Further large randomized controlled trials are needed to compare EHL-POP and LL-POP with ESWL and evaluate whether POP may replace ESWL as the first-line management of pancreatolithiasis“

Gastrointest Endosc 2022 May; 95(5): 905-14

Pancreatoscopy-guided electrohydraulic lithotripsy for the treatment of obstructive pancreatic duct stones: a prospective consecutive case series

Sophia E van der Wiel, Pauline M C Stassen et al. (NL)

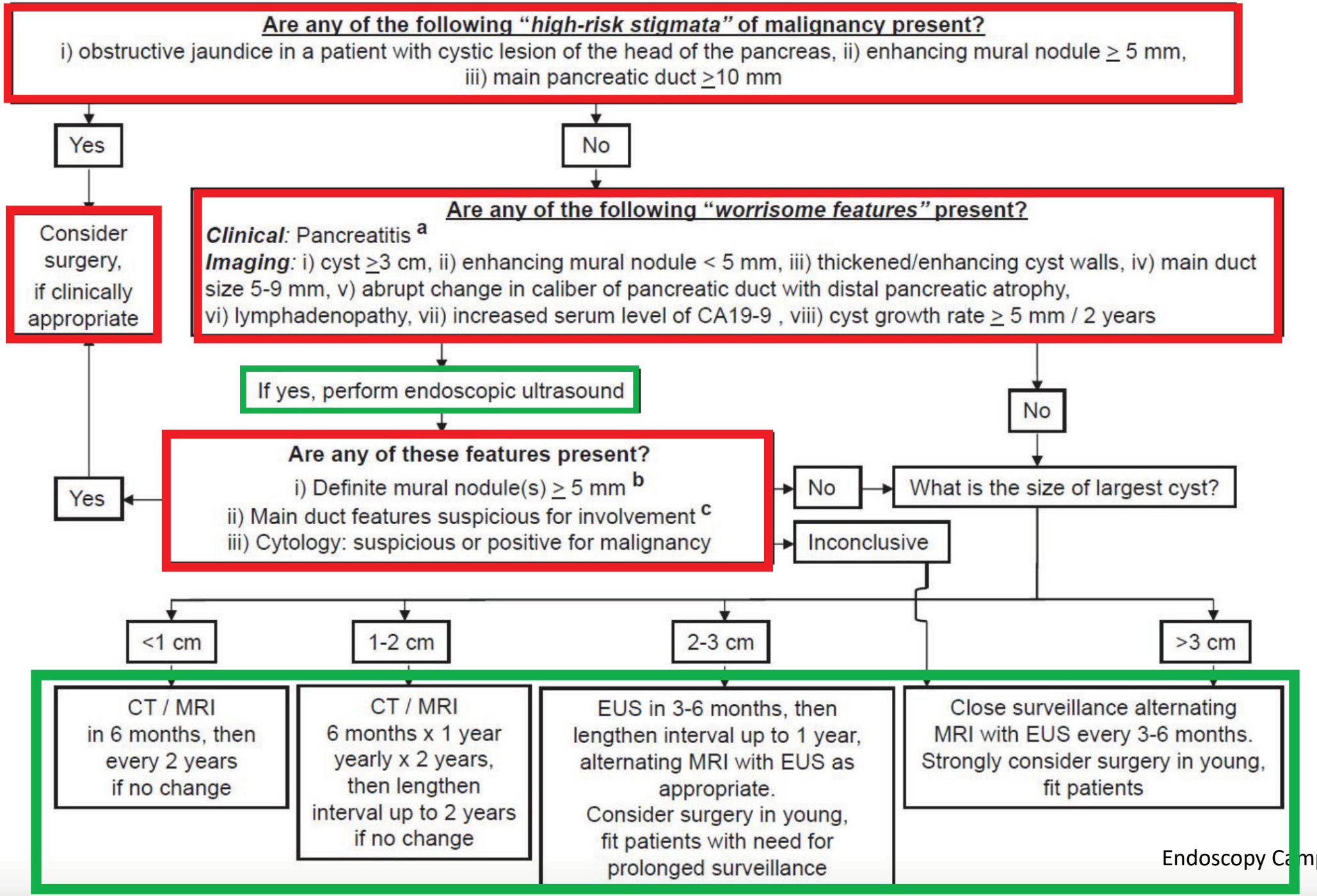
- EHL as first-line therapy of pancreatic stones?
- prospective, single-center, consecutive case series
- symptomatic patients with obstructing stones >5 mm in the head or neck of the pancreas
- primary outcome: technical success
- secondary outcomes: clinical success, adverse events and number of interventions

- 34 consecutive patients
- **failure to cannulate (n = 5) or resolution of stones after stent placement (n = 3)**
- **technically successful in 24 of 26 patients (92.3%)**
- **complete stone clearance 80%, partial clearance 20% after a median of 2 procedures**
- mean Izbicki score dropped from **62.3 ± 23.1 to 27.5 ± 35.0** at 6-mo ($p < 0.001$)
- adverse events: **acute pancreatitis (n=7)**, all mild and treated conservatively

Fazit Chronische Pankreatitis

- Aspirin hemmt Entzündung und Fibrose bei CP im Tiermodell
- CFTR-Korrektoren und Potentiatoren reduzieren auch das Pankreatitisrisiko bei Mukoviszidose (Jahrestherapiekosten ca. € 275.000)
- sind Pregabalin und Antioxidantien zur Schmerzbehandlung den Aufwand wert?
- primäre Pankreatikoskopie mit EHL wird wohl ESWL bei obstruierenden Pankreassteinen ablösen

Pankreaszysten



Ann Gastroenterol 2021; 34(5): 743-750

Comparing accuracy of high-risk features (HRF) for detecting advanced neoplasia in pancreatic cystic lesions: a systematic review and meta-analysis

Abhiram Duvvuri, Harikrishna Bandla, Vivek Chandrasekar Thoguluva et al.

- systematic review and meta-analysis comparing diagnostic accuracy of using ≥1 vs. ≥2 HRF for assessing the risk of advanced neoplasia (AN) when performing EUS in PCL
- AN was defined as adenocarcinoma, high-grade dysplasia in IPMN or MCA, pancreatic intraepithelial neoplasia and pancreatic neuroendocrine tumors
- HRF included cyst size ≥3 cm, solid component and dilated pancreatic duct ≥5 mm
- **primary outcome was the sensitivity and specificity of using ≥1 vs. ≥2 HRF as an indicator for EUS to detect AN**

Table 2 Performance characteristics of number of high-risk features in predicting advanced neoplasia in pancreatic cystic lesions

Measure	≥2 high-risk features (95%CI)	≥1 high-risk features (95%CI)
Sensitivity	41.7% (19.5-67.8%)	77.1% (66.1-85.3%)
Specificity	90.8% (81.9-95.5%)	72.7% (50.4-87.5%)
Positive predictive value	30.4% (19.4-44.2%)	17.9% (10.3-29.4%)
Negative predictive value	94.3% (89.6-97.0%)	98.1% (90.8-99.6%)

CI, confidence interval

Duvvuri et al. Ann Gastro 2021

Table 2 Performance characteristics of number of high-risk feat s in predicting advanced neoplasia in pancreatic cystic lesio

Measure	≥2 high-risk features (95%	(95%CI)
Sensitivity	41	77.1% (66.1-85.3%)
Specificity	.9-95.5%)	72.7% (50.4-87.5%)
Positive pr	0.4% (19.4-44.2%)	17.9% (10.3-29.4%)
N ve	94.3% (89.6-97.0%)	98.1% (90.8-99.6%)

CI, confidence interval

EUS with ≥1 HRF could offer greater sensitivity in detecting AN compared to ≥2 HRF, with a similar negative predictive value

Duvvuri et al. Ann Gastro 2021

Gastrointest Endosc 2021 Nov; 94(5): 881-9

Contrast-enhanced EUS for the characterization of mural nodules within pancreatic cystic neoplasms: systematic review and meta-analysis

Andrea Lisotti, Bertrand Napoleon, Antonio Facciorusso et al.

- presence of **enhanced** mural nodules represents a significant risk factor for malignancy
- primary outcome was pooled sensitivity for identification of HGD or invasive carcinoma

	CE-EUS	CH-EUS
n	532 (10)	320 (8)
sensitivity	88,2%	97%
specificity	79,1%	90,4%
accuracy	89,6%	95,6%
NN to diagnose	1,5	1,2

- at 42% disease prevalence a pos. vs neg. CH-EUS changed probability to 88% vs 2%

Endosc Ultrasound 2021; 10(4): 270-9

EUS-guided biopsy versus confocal laser endomicroscopy in patients with pancreatic cystic lesions: A systematic review and meta-analysis

Bojan Kovacevic, Giulio Antonelli, Pia Klausen et al. (Dänemark, Italien)

- two diagnostic tools have recently been introduced: through-the-needle biopsy (TTNB) and needle-based confocal laser endomicroscopy (nCLE)
- meta-analysis - diagnostic yield, performance, safety and technical success?

n = 1023 (20 studies)	EUS-TTNB	EUS-nCLE	p
diagnostic yield	74%	85%	<0.0001
sensitivity	80%	86%	>0.05
specificity	80%	83%	>0.05
adverse events	5%	3%	0.302
technical success	94%	99%	0.07

Gastroenterology 2017; 153(5): 1295-303

The Safety and Efficacy of an Alcohol-Free Pancreatic Cyst Ablation Protocol (CHARM trial)

Matthew T Moyer, Setareh Sharzehi, Abraham Mathew et al. (USA)

Background & aims: Endoscopic ultrasound (EUS)-guided **chemoablation with ethanol lavage followed by infusion of paclitaxel** is effective for the treatment of mucinous pancreatic cysts. However, complications arise in 3%-10% of patients ....

Conclusions: In this prospective, randomized, controlled trial, we found that **alcohol is not required** for effective EUS-guided pancreatic cyst ablation, and when alcohol is removed from the ablation process, there is a **significant reduction in associated adverse events**.

A multi-agent chemotherapeutic ablation mixture did not appear to significantly improve rates of complete ablation.

Clin Gastroenterol Hepatol 2022 Feb; 20(2): 326-29

The Durability of EUS-Guided Chemoablation of Mucinous Pancreatic Cysts: A Long-Term Follow-Up of the CHARM trial

Courtney Lester, Leonard Walsh, Kayla M Hartz et al. (USA)

- of 39 patients treated in the CHARM trial, 36 were included in the long-term analysis
- at baseline mean cyst diameter was 27.6 mm
- most cysts clinically diagnosed as IPMNs (69.4%) or mucinous cystic neoplasms (22.2%)
- **follow-up imaging performed at a mean of 36.5 months**

- of 23 patients who achieved complete resolution initially, 20 **(87.0%) sustained those results** at latest follow- up, other 3 patients maintained their response of 91%–93% reductions in cyst volume at follow-up.

- 4 cysts classified primarily as partial responders (n = 3) or non-responders (n = 1) have completely resolved at latest follow-up, 2 cysts initially classified as nonresponders achieved partial resolution.

treatment response	12mo	long term
complete	23 (64%)	24 (67%)
partial	7 (19%)	8 (22%)
nonresponse	6 (17%)	4 (11%)

Erfolg hält !

Fazit Pankreaszysten

- nicht auf 2 Highrisk-Zeichen beim IPMN warten, 1 genügt für OP-Indikation
- CE-EUS und noch besser CH-EUS zur Dysplasie-/Karzinomentdeckung in Pankreaszysten effektiv
- needle-based confocal laser endomicroscopy (nCLE) treffsicherer, aber aufwändiger wie through-the-needle biopsy (TTNB) zur Zysten-Charakterisierung
- Erfolge der EUS-Zystenablation mit Paclitaxel im CHARM-Trial halten über Jahre an

Pankreastumore

J Am Coll Surg 2021 Dec; 233(6): 730-9

Long-Term Quality of Life after Minimally Invasive vs Open Distal Pancreatectomy in the LEOPARD Randomized Trial

Maarten Korrel, Anne Roelofs, Jony van Hilst et al. (NL)

- more than 3 years after distal pancreatectomy **no improvement in QALYs and overall QoL was seen after Minimally Invasive Distal Pancreatectomy**, whereas cosmetic satisfaction was higher as compared with Open Distal Pancreatectomy.

Surgery 2022 Jun; 171(6): 1658-64

Incidence and impact of postoperative pancreatic fistula after minimally invasive and open distal pancreatectomy

Nicky van der Heijde, Sanne Lof, Olivier R Busch et al. (NL)

- postoperative pancreatic **fistula rate after minimally invasive distal pancreatectomy was significantly higher** than that after open distal pancreatectomy (28.7% vs 16.9%, p=.029)

Medicine (Baltimore) 2021; 100(35): e26918

Optimal extent of lymphadenectomy for radical surgery of pancreatic head adenocarcinoma: 2-year survival rate results of single-center, prospective, randomized controlled study

Ziyao Wang, Nengwen Ke 1 , Xin Wang et al. (China)

- in multimodality therapy systems the efficacy of chemotherapy should be based on the appropriate lymphadenectomy extent, and the standard extent of lymphadenectomy is optimal for resectable pancreatic head adenocarcinoma, **extended lymphadenectomy did not result in survival benefits**.

Ann Surg 2021 Dec; 274(6): 935-44

Influence of the Retrocolic versus Antecolic Route for Alimentary Tract Reconstruction on Delayed Gastric Emptying after Pancreatoduodenectomy: A Multicenter, Noninferiority Randomized Controlled Trial

Hirochika Toyama, Ippei Matsumoto, Takuya Mizumoto et al.

- The alimentary tract **should not be reconstructed via the retrocolic route** after pancreatoduodenectomy to prevent delayed gastric emptying.

Lancet 2022 May; 399(10338): 1867-75

Algorithm-based care versus usual care for the early recognition and management of complications after pancreatic resection in the Netherlands: an open- label, nationwide, stepped-wedge cluster- randomised trial

F Jasmijn Smits, Anne Claire Henry, Marc G Besselink et al. (NL)

- early recognition and management of postoperative complications, before they become clinically relevant, can improve postoperative outcomes of pancreatic resection

- **nationwide randomised trial of all patients having pancreatic resection during a 22mo period** in the Netherlands with all 17 centres that did pancreatic surgery

- a smartphone app was designed that incorporated the algorithm and included the daily evaluation of clinical and biochemical markers, when to do abdominal CT, radiological drainage, start antibiotic treatment, and remove abdominal drains

- primary outcome was a **composite of bleeding that required invasive intervention, organ failure and 90-day mortality**

Lancet 2022 May; 399(10338): 1867-75

Algorithm-based care versus usual care for the early recognition and management of complications after pancreatic resection in the Netherlands: an open- label, nationwide, stepped-wedge cluster- randomised trial

F Jasmijn Smits, Anne Claire Henry, Marc G Besselink et al. (NL)

- from Jan 2018 to Nov 2019 all 1805 patients who had pancreatic resection in the Netherlands were included, 57 patients who underwent resection during the wash-in phase were excluded from the primary analysis, **1748 patients (885 receiving usual care and 863 receiving algorithm-centred care)** remained

- primary outcome occurred in fewer patients in the algorithm-centred care group than in the usual care group **(8% vs 14%; RR 0·48; p<0·0001)**

- among patients treated according to the algorithm, compared with patients who received usual care there was a decrease in bleeding that required intervention (5% vs 6%; RR 0·65; p=0·046), organ failure (5% vs 10%; RR 0·35; p=0·0001), and 90-day mortality (3% vs 5%; RR 0·42; p=0·029)

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Algorithm-based care versus usual care for the early recognition and management of complications after pancreatic resection in the Netherlands: an open- label, nationwide, stepped-wedge cluster- randomised trial

F Jasmijn Smits, Anne Claire Henry, Marc G Besselink et al. (NL)

- **Interpretation:** The algorithm for the early recognition and minimally invasive management of complications after pancreatic resection considerably improved clinical outcomes compared with usual care. This difference included an **approximate 50% reduction in mortality at 90 days.**

Ann Surg 2022 Jun; 275(6): 1043-9

Results of a Phase II Study on the Use of Neoadjuvant Chemotherapy (FOLFIRINOX or GEM/nab-PTX) for Borderline-resectable Pancreatic Cancer (NUPAT-01)

Junpei Yamaguchi, Yukihiro Yokoyama, Tsutomu Fujii et al.

- These results indicate that **neoadjuvant chemotherapy with FOLFIRINOX or GEM/nab-PTX is feasible and well tolerated, achieving an R0 resection rate of 67.4%.** The survival of patients was even found to be favorable in the intention-to-treat analysis.

J Clin Oncol 2022 Apr; 40(11): 1220-30; vgl. auch: Ann Surg 2022 May; 275(5): 979-84

Neoadjuvant Chemoradiotherapy Versus Upfront Surgery for Resectable and Borderline Resectable Pancreatic Cancer: Long-Term Results of the Dutch Randomized PREOPANC Trial

Eva Versteijne, Jacob L van Dam, Mustafa Suker et al. (NL)

- **Neoadjuvant gemcitabine-based chemoradiotherapy followed by surgery and adjuvant gemcitabine improves OS compared with upfront surgery and adjuvant gemcitabine** in resectable and borderline resectable pancreatic cancer.
- it did not increase the incidence of surgical complications or mortality and reduced the rate of postoperative pancreatic fistula after resection in borderline-resectable pts.

Oncologist 2022 Feb; 27(1): 67-78

Effects of a 12-Week Multimodal Exercise Intervention Among Older Patients with Advanced Cancer: Results from a Randomized Controlled Trial

Marta K Mikkelsen, Cecilia M Lund, Anders Vinther et al.

- 84 adults ≥65 years with advanced pancreatic, biliary tract or non-small cell lung cancer receiving systemic treatment randomized 1:1 to intervention group or control group

- 12-week multimodal exercise-based program (supervised exercise twice weekly), protein supplement, home-based walking program and nurse-led support and counseling

- multimodal exercise intervention with targeted support proved effective in improving physical function in older patients, **significant beneficial effects were seen for physical endurance** (6-minute walk test), **hand grip strength, physical activity, symptom burden, symptoms of depression and anxiety, quality of life and lean body mass**

- **no effects were seen for dose intensity, hospitalizations or survival**

Ann Surg 2022 Sep; 276(3): 522-31

Long-term Outcomes of Parenchyma-sparing and Oncologic Resections in Patients With Nonfunctional Pancreatic Neuroendocrine Tumors <3 cm in a Large Multicenter Cohort

Louisa Bolm, Martina Nebbia, Alice C Wie et al. (USA)

- in small <3 cm nonfunctional pNETs **parenchyma sparing resections and lymph node-sparing resections are associated with lower complication rates**, lower blood loss and shorter operative times compared to oncologic resections and have similar long-term oncologic outcomes

Endosc Int Open 2021; 9(8): E1178-85

Long-term outcome after EUS-guided radiofrequency ablation: Prospective results in pancreatic neuroendocrine tumors and pancreatic cystic neoplasms

Marc Barthet, Marc Giovannini, Mohamed Gasmi et al.

- long-term efficacy of EUS-RFA in patients with NETs or pancreatic cystic neoplasms (PCNs) over at least 3 years?

- 12 patients had 14 NETs with a mean 13mm size (10-20) and 17 patients had cystic tumors (16 IPMN, 1 MCA) with a 29mm mean size (9-60)

- mean duration of follow-up was 42.9 months (36-53), 4 died from unrelated diseases
- **at 1-year follow-up in 85.7% complete disappearance was seen, after 45.6mo in 85.7%**
- a late liver metastasis occurred in a patient with initial failure of EUS-RFA

- at 1-year follow-up a significant response was seen in 70.5% of 15 patients with PCNs, at the end of the follow-up there was a significant response in 66.6%
- 2 cases of distant pancreatic adenocarcinoma unrelated to IPMN occurred

Fazit Pankreastumore

- laparoskopische Pankreaslinksresektion bzgl. Fistel nachteilig, bzgl. QOL nicht besser, ausgen. Kosmetik
- radikalere Duodenopankreatektomien bringen nichts
- neoadjuvante chemo(-radio)-therapeutische Konzepte scheinen primärer OP überlegen
- ein postoperativer Überwachungs-Algorithmus ist mortalitätswirksam
- Trainingsprogramm und EW-Supplemente fördern QOL, nicht aber das Überleben
- kleine nicht-funktionelle NETs des Pankreas - belassen? RFA? reduziert radikale OP?
- RFA von pNETs und IPMNs langfristig in 86% wirksam

World J Gastroenterol 2022 Apr; 28(14): 1455-78

Clinical classification of symptomatic heterotopic pancreas of the stomach and duodenum: A case series and systematic literature review

Michael T LeCompte, Brandon Mason, Keenan J Robbins et al. (USA)

- **at a single center** 29 patients were identified with HP with 6 having clinical symptoms, clinical manifestations included gastrointestinal bleeding, gastric ulceration with/without perforation, pancreatitis, and gastric outlet obstruction

- **Systematic Review** of the literature yielded 232 publications with only 20 studies describing ≥ 10 patients. Single and multi-patient studies were combined to form a cohort of **934 symptomatic patients**:

  abdominal pain (67%), dyspepsia (48%), pancreatitis (28%), gastrointestinal bleeding (9%), gastric outlet obstruction (9%)

  majority of cases (90%) underwent surgical or endoscopic resection with 85% reporting resolution or improvement in their symptoms