

Surgical Interventions for Chronic Pancreatitis in Children

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Disclosures

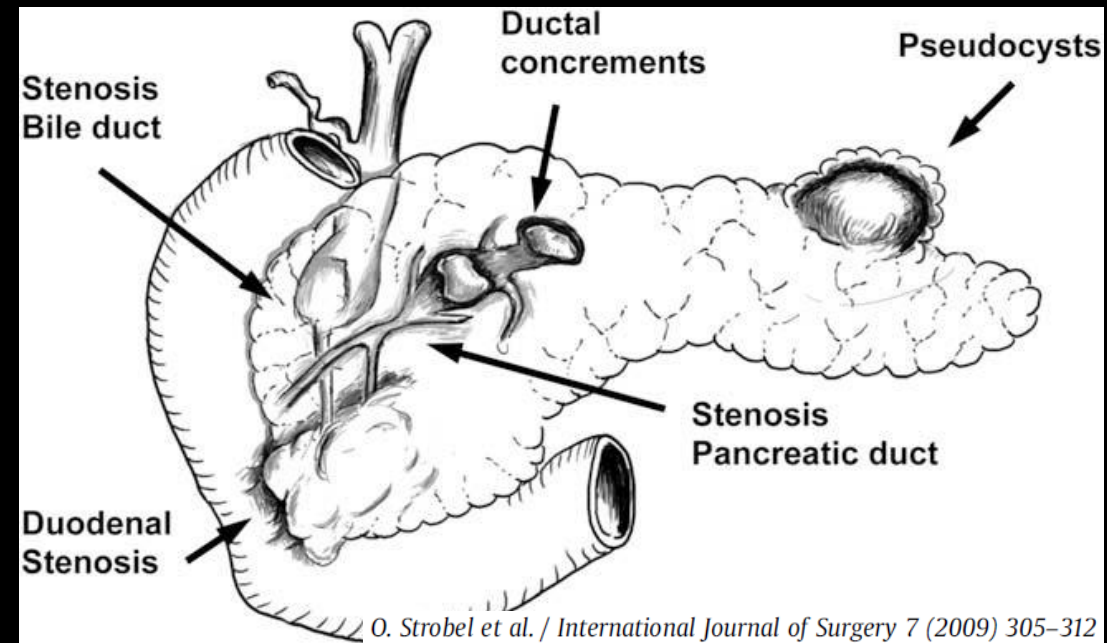
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Disclosure: Old General Surgery Adage



Indications for Surgery in CP

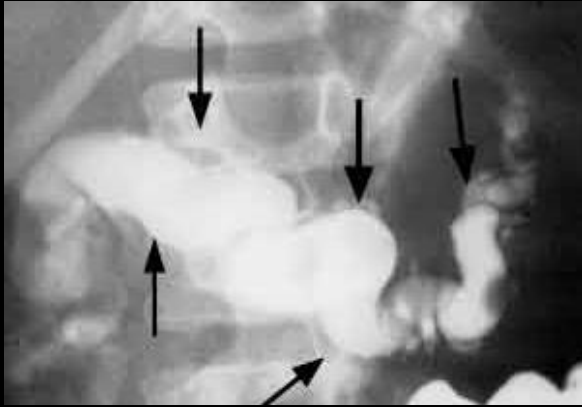
- 50 – 75% of CP patients eventually require surgery^{1,2}
- **Classic indications:**
 - Bile duct or duodenal obstruction
 - Pseudocysts
 - Suspicion of malignancy
 - Debilitating pain that fails to respond to medical and endoscopic treatment options – **most common**



¹Mitchell et al. Lancet 2003;361:1447-1455.

²Issa et al. Dig Surg 2013;30:35-50.

Approach to Surgery



Large duct disease



Inflammatory mass in head of pancreas



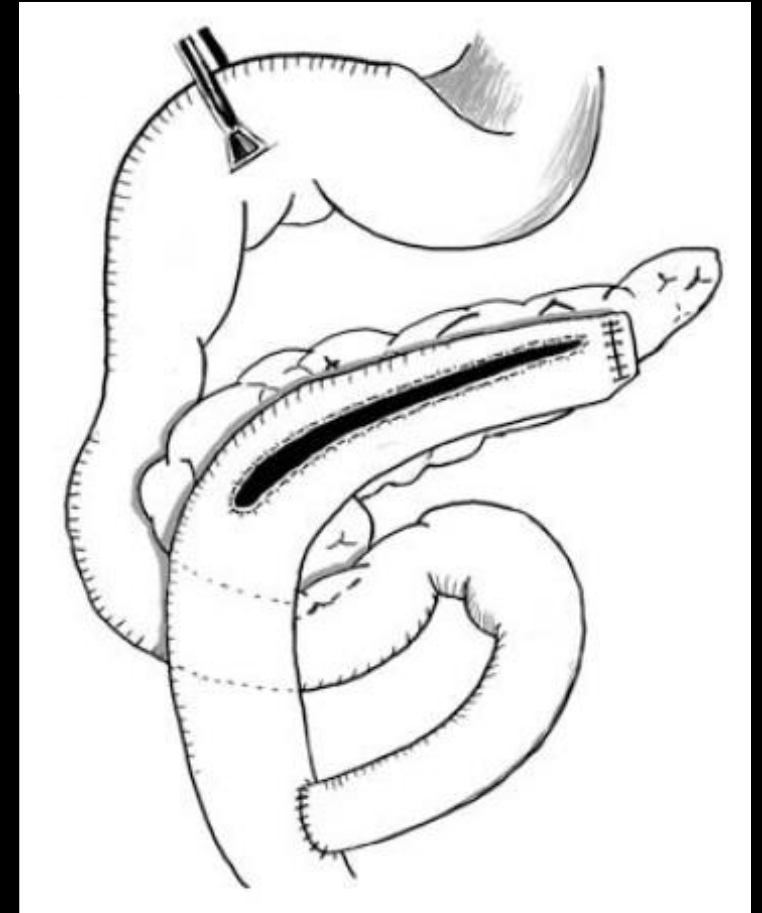
Distal stricture with focal disease

Preoperative assessment of morphology of disease determines the most appropriate surgical procedure

No single surgical procedure recommended for all patients with chronic pancreatitis

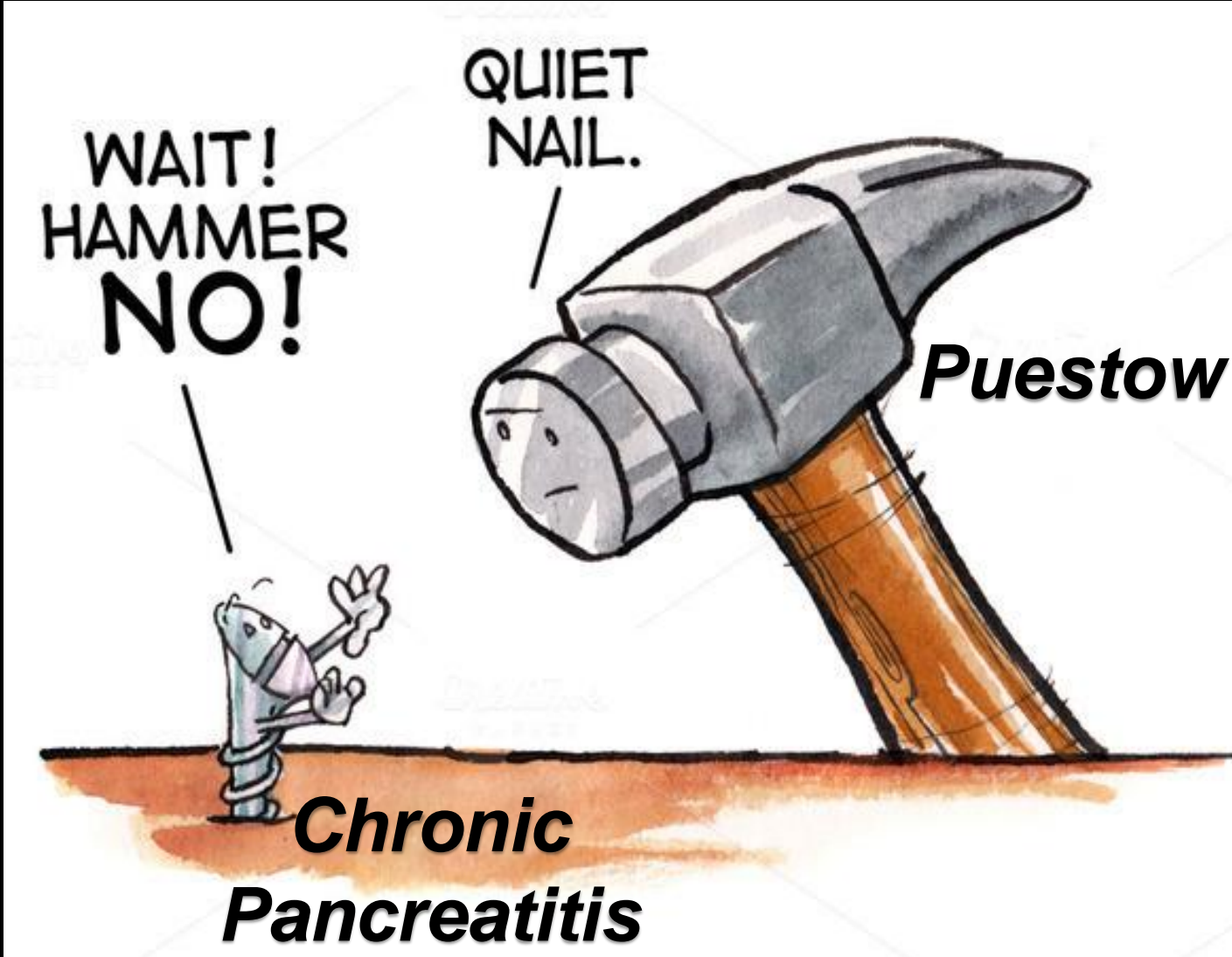
Drainage Procedures

- **Longitudinal pancreaticojejunostomy (Partington-Rochelle “modified Puestow”)**
 - Rationale: alleviate PD pressure in large duct disease
 - Short-term pain relief 75%
 - Recurrent pain in >50%
 - Indication: isolated PD dilation (>5 mm) or chain of lakes **without** inflammatory head mass and **without** genetic risk factor



Strobel et al. Int J Surg 2009;7:305-312.

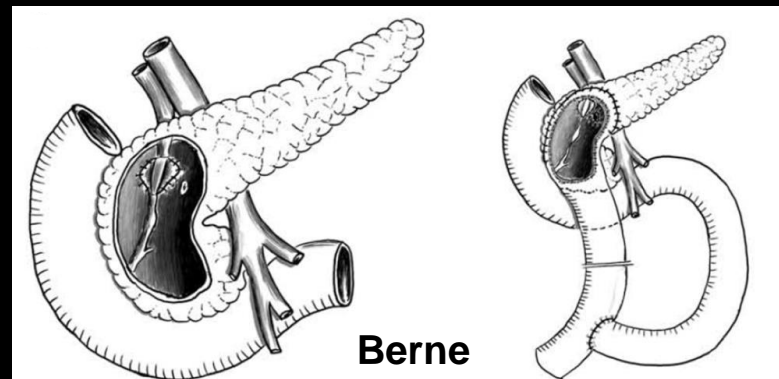
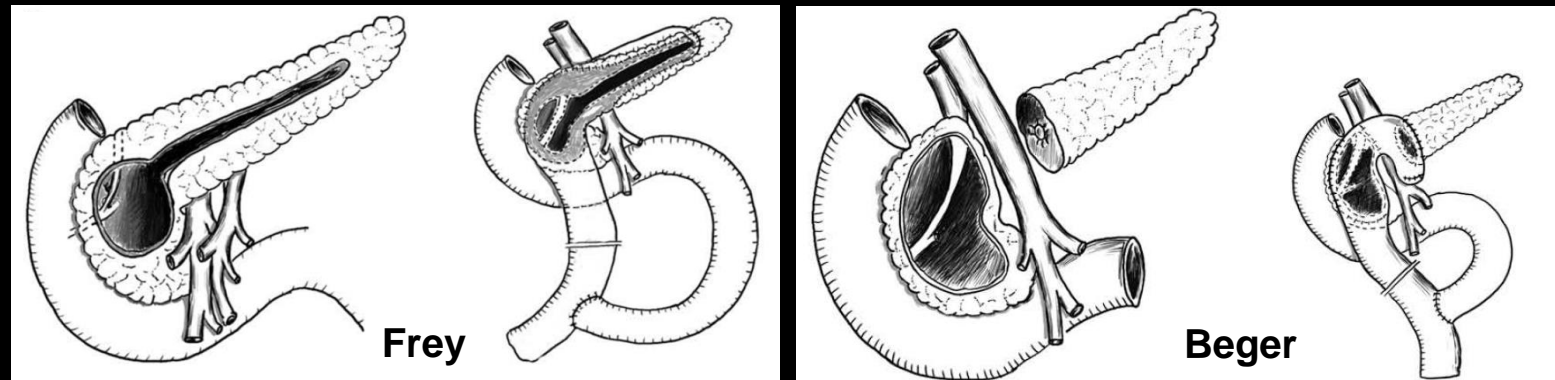
Markowitz et al. Arch Surg 1994;129:374-359.
Laje et al. J Ped Surg 2013;48:2271-2275.



Drainage + Partial Resection

- **Duodenum-preserving pancreatic head resection**

- Rationale: resect inflammatory head mass, decompress PD, preserve bile duct and GI continuity
- Pain relief 50 – 94%, EPI 10 – 34%, 10 – 26% endo insufficiency

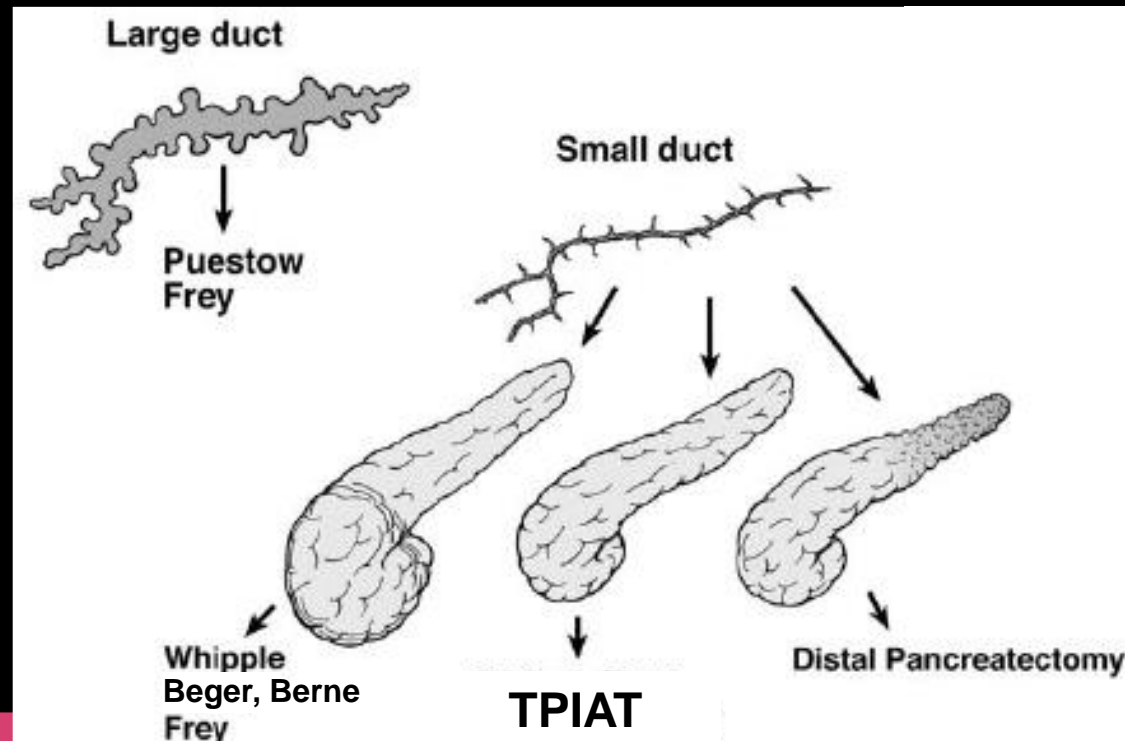


Strobel et al. Int J Surg 2009;7:305-312.

Although conventional surgeries for CP result in initial pain relief, pain recurs in more than 50% of patients over the long-term

Failure of conventional surgery is considered an indication for total pancreatectomy with islet autotransplantation (TPIAT)

Debilitating chronic pancreatitis without a conventional surgical option is an indication for TPIAT



Modified from
Howard et al. J
Gastrointest Surg
2008;12:2087-96.

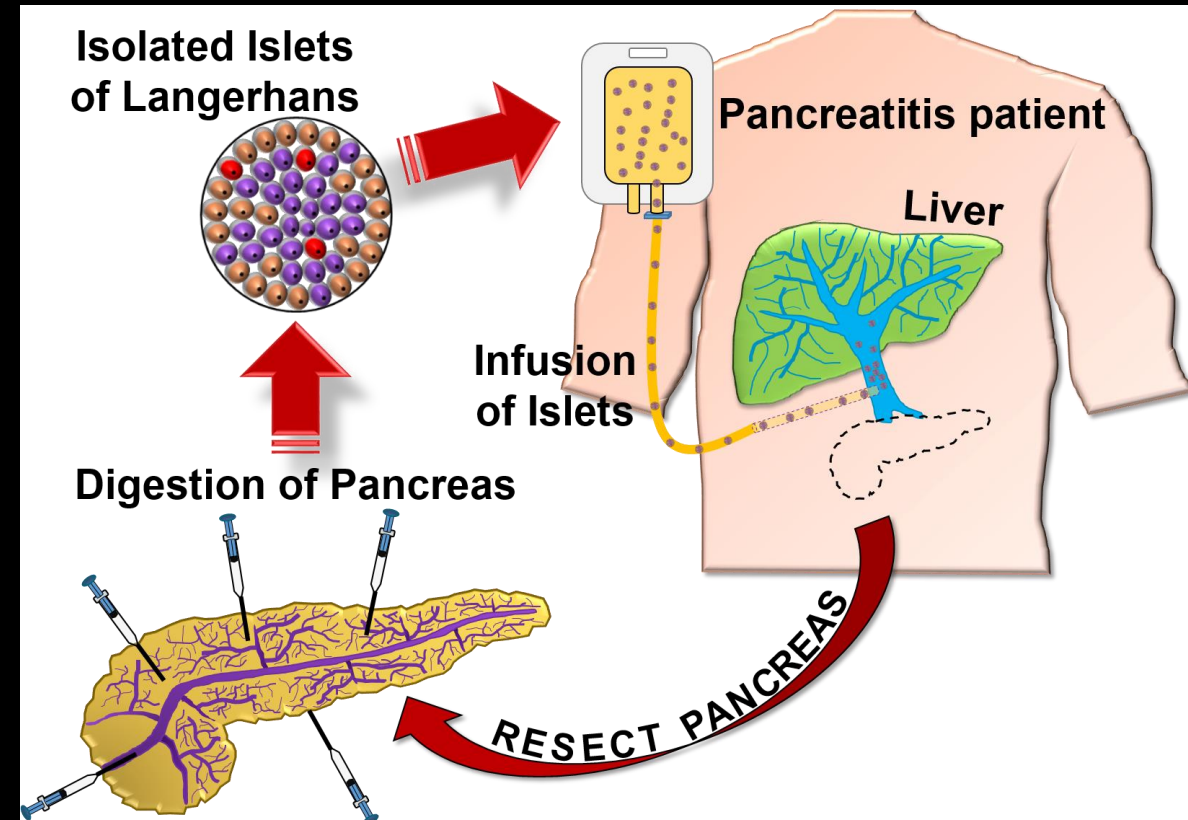
TPIAT

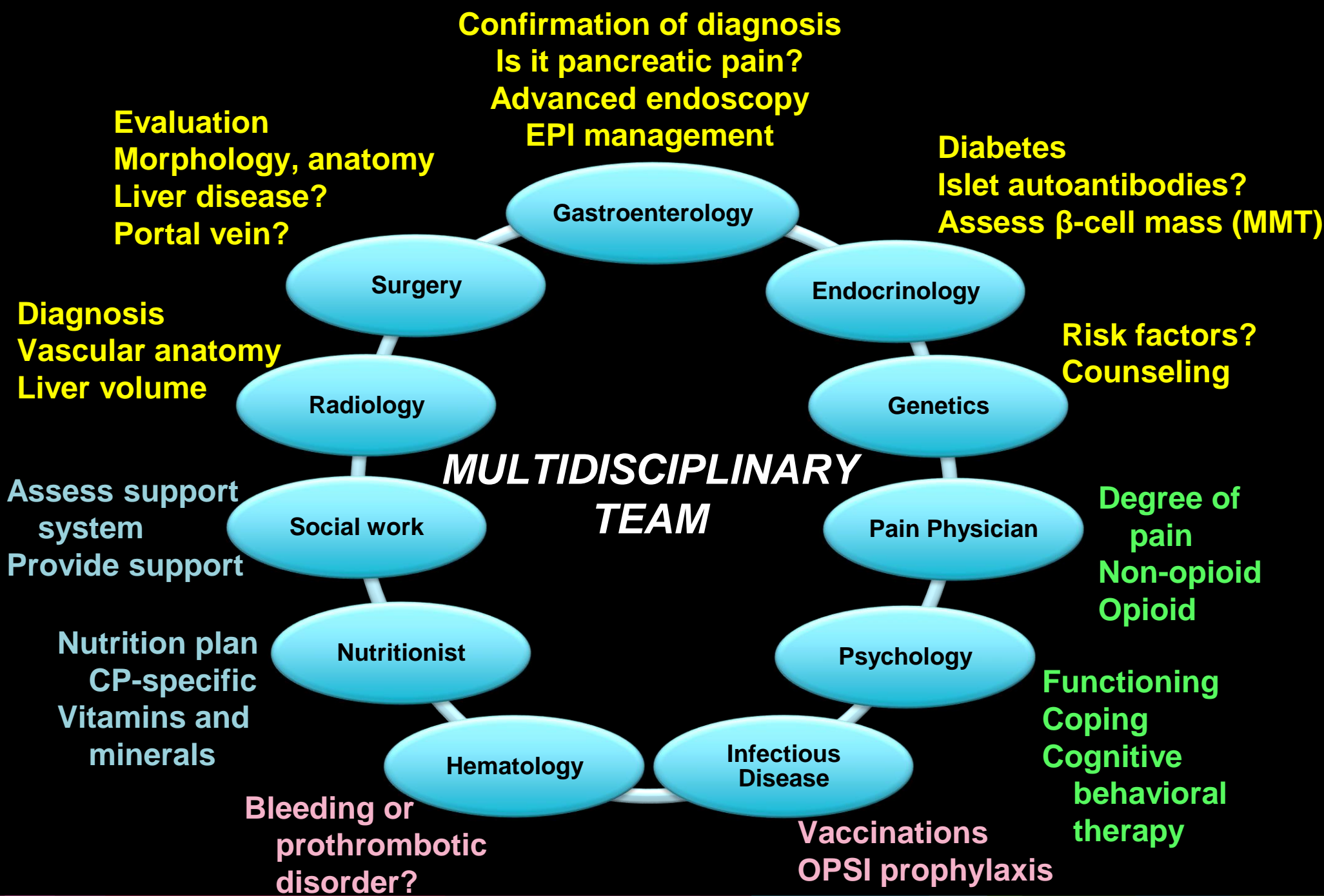
- **Primary goal:**

- Relieve incapacitating pain of chronic pancreatitis or debilitation of acute recurrent pancreatitis in whom all other measures have failed

- **Goal of IAT:**

- Preserve α and β -cell mass and insulin secretory capacity in order to prevent or minimize otherwise inevitable brittle diabetes





TPIAT Pain/QOL Outcomes in Children

- Relief of pancreatitis pain and in severity of pain in 90%¹
 - Elimination of opioid use in 85%
 - Sustained effects over time
- Significant improvement in SF-36 physical health and total scores, SF-10 physical health score by 90 days post-TPIAT²
 - All patients weaned from TPN and significant reduction in need for enteral supplementation by 90 days
- Durability over time
 - Retrospective analysis of 185 adults, 30 children with >10 yr follow-up³
 - Pain was improved in 81.5% at 10 years

¹Chinnakotla et al. Ann Surg 2014;260:56-64.

²Kotagal et al. Am J Transplant 2019;19:1187-1194.

³Bellin et al. J Am Coll Surg 2019;228:329-339.

TPIAT Glycemic Outcomes in Children

- Insulin independence in 41% at 36 months¹
 - Younger children (<12 years) more likely to achieve independence
 - Younger age, no prior Puestow, higher IEQ/kg body weight were associated with higher probability of insulin independence
- Retrospective analysis of 215 patients with >10 yr follow-up²
 - Insulin independence at 10 yrs = 20%; partial function = 32%
 - IEQ/kg > 4000 was strongest predictor of islet graft function
 - Children were more likely to have islet function than adults

¹Chinnakotla et al. Ann Surg 2014;260:56-64.

²Bellin et al. J Am Coll Surg 2019;228:329-339.

Why do young children do better?

- Young children have lower insulin demands

→ Better metabolic milieu for engraftment?

β -Cell Replication Is the Primary Mechanism Subservicing the Postnatal Expansion of β -Cell Mass in Humans

Juris J. Meier,¹ Alexandra E. Butler,¹ Yoshifumi Saisho,¹ Travis Monchamp,² Ryan Galasso,¹ Anil Bhushan,¹ Robert A. Rizza,³ and Peter C. Butler¹ *Diabetes* 57:1584–1594, 2008

- Highest replicatory capacity of β -cells in young children

Severely Fibrotic Pancreases from Young Patients with Chronic Pancreatitis: Evidence for a Ductal Origin of Islet Neogenesis

S.M. Soltani^a, T.D. O'Brien^b, G. Loganathan^a, M.D. Bellin^{a,d}, T. Anazawa^a, M. Tiwari^a, K.K. Papas^a, S.M. Vickers^c, V. Kumaravel^e, B.J. Hering^a, D.E.R. Sutherland^{a,c}, and A.N. Balamurugan^{a,*} *Acta Diabetol.* 2013 October ; 50(5): 807–814.

- Islet neogenesis of ductal origin in response to injury from severe CP

Islet Yield

- Insulin independence correlates¹ with:
islet equivalents (IEQ) per kg body wt
- Relationship between yield and:
 - Imaging (atrophy, calcifications, ductal dilation)²
 - Histopathology (fibrosis, acinar atrophy)³
 - Duration of symptoms⁴

Role in patient selection and timing of TPIAT?

- Ductal drainage procedures and resections reduce yield and decrease probability of insulin independence⁵

Caution in those anticipated to require future TPIAT

¹Chinnakotla et al. Ann Surg 2014;260:56-64.

²Young et al. Pancreas 2016;45:961-966.

³Kobayashi et al. Pancreas 2011;40:193-199.

⁴Takita et al. J Gastrointest Surg 2015;19:1236-1246.

⁵Gruessner et al. J Am Coll Surg 2004;198:559-567.



Timing of Surgery?

- Few studies have examined optimal timing
 - Earlier surgery may be more beneficial by delaying progressive destruction of parenchyma¹
 - Some studies have reported that surgery within 3 years of symptom onset may achieve better pain relief²
 - Because surgery is not uniformly successful in all patients, others advocate “watch and wait” approach

No clear consensus on timing of surgery for CP

¹Nealon et al. Ann Surg 1993;217:458-466.

²Ahmed Ali et al. Cochrane Database Syst Rev 2012.

Clinical Outcome in Relation to Timing of Surgery in Chronic Pancreatitis

A Nomogram to Predict Pain Relief

Arch Surg 2012;147:925-932.

Usama Ahmed Ali, MD; Vincent B. Nieuwenhuijs, MD, PhD; Casper H. van Eijck, MD, PhD;
Hein G. Gooszen, MD, PhD; Ronald M. van Dam, MD, PhD; Olivier R. Busch, MD, PhD;
Marcel G.W. Dijkgraaf, MD, PhD; Femke A. Mauritz, MD; Sjoerd Jens, MD; Jay Mast, MD;
Harry van Goor, MD, PhD; Marja A. Boermeester, MD, PhD; for the Dutch Pancreatitis Study Group

- Cohort study, 266 pts, Dutch Pancreatitis Study Group
- Pancreatic resections and drainage operations for pain relief in CP
- Median follow-up = 62 mos

Table 4. Multivariable Analysis of Risk Factors Associated With Pain Relief

Timing of Surgery	Odds Ratio (95% CI) ^a	P Value
Reported duration of pain \leq 3 y	1.81 (1.02-3.37)	.03
No preoperative opioid use	2.14 (1.23-3.96)	.006
Endoscopic treatments, No. (\leq 5 procedures)	2.46 (1.10-6.27)	.04

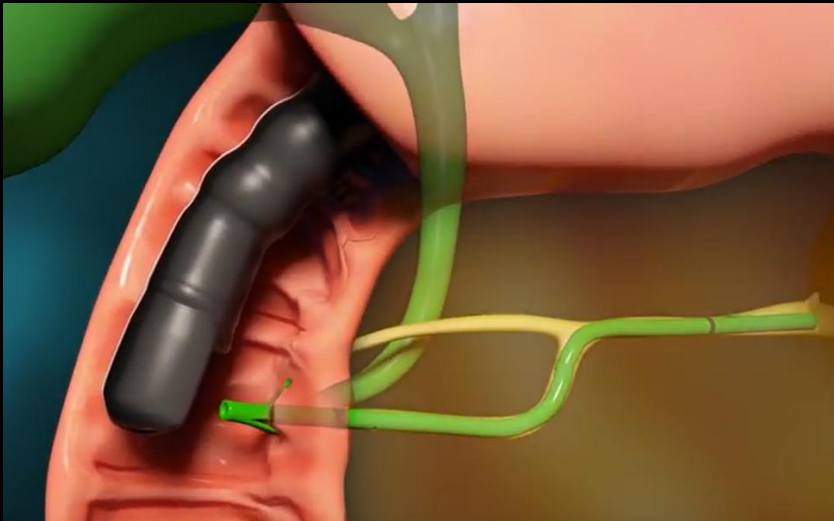
Earlier surgery improves outcomes from painful chronic pancreatitis

Medicine (2018) 97:19(e0651)

Nengwen Ke, MD^a, Dan Jia, MD^b, Wei Huang, MD, PhD^c, Quentin M. Nunes, MRCS, PhD^d, John A. Windsor, MChB, MD, FRACS^e, Xubao Liu, MD, PhD^{a,*}, Robert Sutton, DPhil, FRCS^d

- Retrospective, 297 patients
- Determine whether early surgery (≤ 3 years) offered better pain control and preservation of pancreatic function, compared to late surgery (> 3 years)
- Whipple, Beger, Berne, Frey, Puestow
- Primary endpoint: pain relief by Izbicki pain score (complete, partial, none)
- Pain scores lower in early vs late surgery group
- Complete or partial pain relief higher in early vs late group (92% vs 84%, $p = 0.01$)
- Higher percentage in early group had complete pain relief (69% vs 47%, $p < 0.001$)
- Early surgery associated with lower incidence of exocrine insufficiency (60% vs 80%, $p = 0.005$) and endocrine insufficiency (35% vs 53%, $p = 0.033$)
- Better QOL in early surgery

Endoscopy versus Surgery?



A Prospective, Randomized Trial Comparing Endoscopic and Surgical Therapy for Chronic Pancreatitis

Endoscopy 2003; 35 (7): 553–558

- Prospective RCT, adults with painful obstructive CP
- 140 eligible, 72 randomized
- Endotherapy with sphx/stent and/or stone removal over 12 – 24 mos versus surgery (DPPHR, Whipple, Puestow)

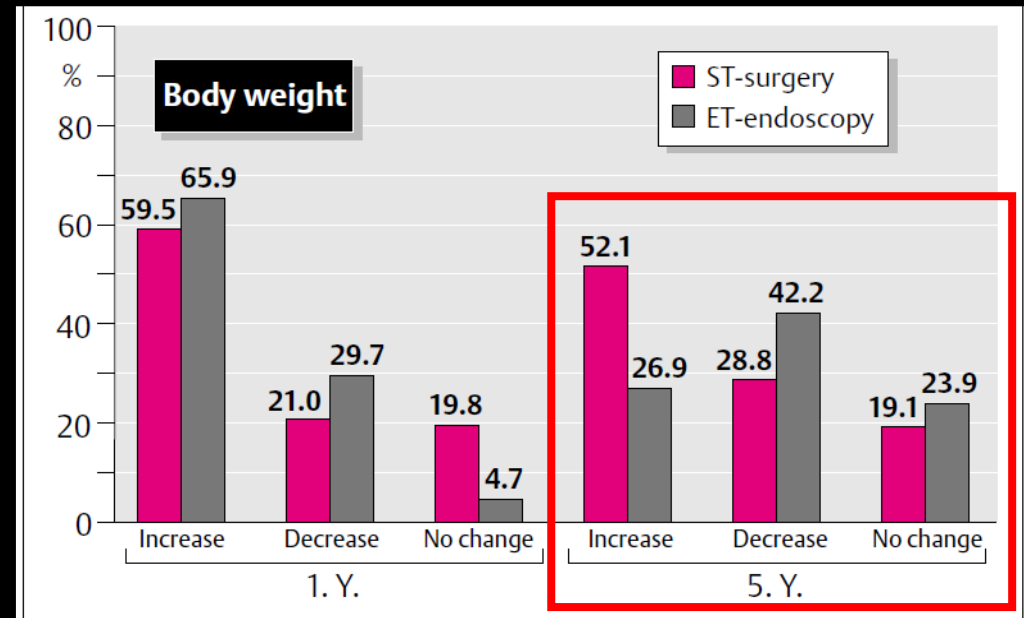
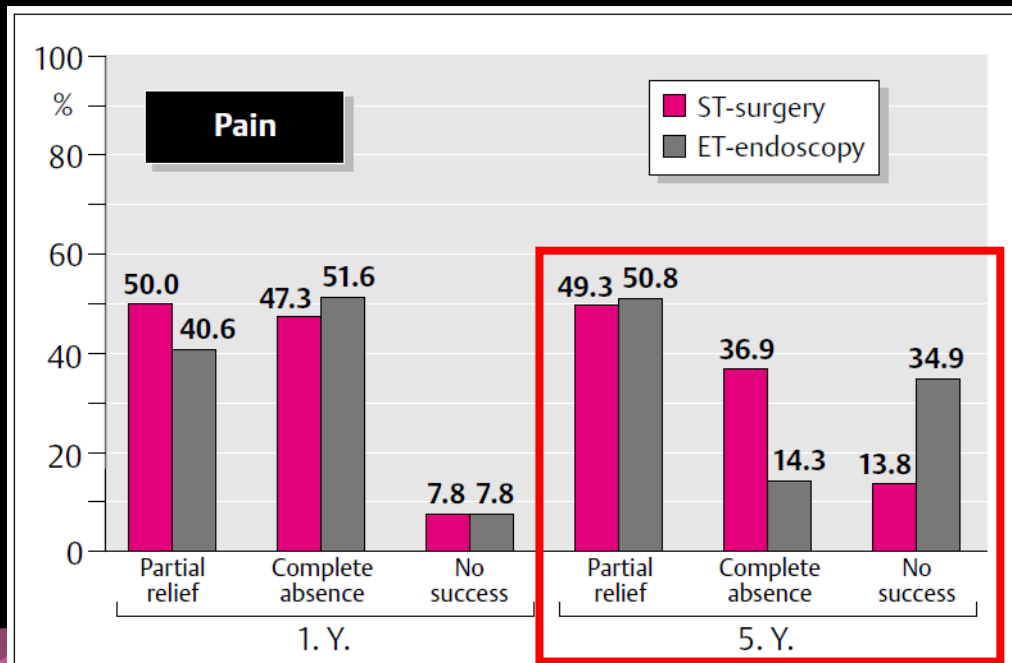


Figure 3 Comparison of the 1-year and 5-year global results for pain and body weight increase >2 kg between endotherapy (ET) and surgery (ST) (results shown only for the total group).

Endoscopic versus Surgical Drainage of the Pancreatic Duct in Chronic Pancreatitis

N Engl J Med 2007;356:676-84.

Djuna L. Cahen, M.D., Dirk J. Gouma, M.D., Ph.D., Yung Nio, M.D., Erik A. J. Rauws, M.D., Ph.D., Marja A. Boermeester, M.D., Ph.D., Olivier R. Busch, M.D., Ph.D., Jaap Stoker, M.D., Ph.D., Johan S. Laméris, M.D., Ph.D., Marcel G.W. Dijkgraaf, Ph.D., Kees Huibregtse, M.D., Ph.D., and Marco J. Bruno, M.D., Ph.D.

- RCT
- Adults with CP and obstructed PD
- Endoscopy with dilation/stent/lithotripsy (n=19) versus operative pancreaticojejunostomy (n=20)

Table 3. Outcomes of Endoscopic and Surgical Treatment after 2 Years of Follow-up.*

Variable	Endoscopy (N=19)	Surgery (N=20)	Endoscopic Results vs. Surgical Results (95% CI)	P Value
Izbicki pain score [†]	51±23	25±15	24 (11 to 36) [‡]	<0.001
Pain relief — no. (%) [§]	6 (32)	15 (75)	-43 (-72 to -15) [¶]	0.007
Complete relief	3 (16)	8 (40)		
Partial relief	3 (16)	7 (35)		
No relief	13 (68)	5 (25)		
Conversion to surgery — no. (%)	4 (21)	NA		
Technical success — no. (%)	10 (53)	20 (100)	-47 (-70 to -25) [¶]	<0.001
Complications — no. (%)	11 (58)	7 (35)	23 (-8 to 53) [¶]	0.15
Major	0	1 (5)		
Minor	11 (58)	6 (30)		
Death — no. (%)	1 (5)	0	5 (-5 to 15) [¶]	0.49
Hospital stay — median no. of days (range)	8 (0-128)	11 (5-59)	-3 (-9 to 4) [¶]	0.13
Hospital readmittance — median no. of patients (range)	1 (0-5)	0 (0-7)		
Procedures — median no. (range)	8 (1-21)	3 (1-9)	5 (2 to 8) [¶]	<0.001
Diagnostic	3 (0-11)	2 (0-8)		
Therapeutic**	5 (1-11)	1 (1-5)		
SF-36 quality-of-life scores ^{††}				
Physical health component	38±9	47±7	-8 (-13 to -3) [‡]	0.003
Mental health component	40±9	45±9	-3 (-8 to 1) [‡]	0.15

- End points at 2 years: pain scores, pain relief, SF-36 QOL, number of procedures
- Surgery patients had lower pain scores, better pain relief, fewer procedures, better physical QOL scores
- No difference in complications, LOS, pancreatic function

Long-term Outcomes of Endoscopic vs Surgical Drainage of the Pancreatic Duct in Patients With Chronic Pancreatitis

GASTROENTEROLOGY 2011;141:1690-1695

DJUNA L. CAHEN,* DIRK J. GOUMA,[§] PHILIPPE LARAMÉE,^{||} YUNG NIO,[¶] ERIK A. J. RAUWS,[‡]
MARJA A. BOERMEESTER,[§] OLIVIER R. BUSCH,[§] PAUL FOCKENS,[‡] ERNST J. KUIPERS,* STEPHEN P. PEREIRA,[#]
DAVID WONDERLING,^{||} MARCEL G. W. DIJKGRAAF,** and MARCO J. BRUNO*

- Long term outcomes after 5 years, 79-month follow-up period
- 68% in endoscopy group required additional drainage, versus 5% in surgery group (p = 0.001)
- Patients in endoscopy group underwent more procedures (median, 12 vs 4, p = 0.001), although hospital stay and costs were comparable
- 47% in endoscopy group eventually underwent surgery
 - But salvage surgery was not very effective
- Surgery superior in terms of pain relief (80% vs 38%, p = 0.042)
- QOL and pancreatic function were comparable

Proper patient selection for optimal outcome of endoscopic therapy: less advanced disease?

ESCAPE Trial

OP004 EARLY SURGERY VERSUS STEP-UP PRACTICE INCLUDING ENDOSCOPY FOR CHRONIC PANCREATITIS: A MULTICENTER RANDOMIZED CONTROLLED TRIAL [ESCAPE TRIAL]

Y. Issa¹, M.A. Kempeneers², M.J. Bruno³, P. Fockens⁴, J.W. Poley⁵, U. Ahmed Ali², T. Bollen⁶, O.R.C. Busch⁷, C.H. Dejong⁸, P. Van Duijvendijk⁹, H. van Dullemen¹⁰, C.H.J. van Eijck¹¹, H.V. Goor, M. Hadithi¹², J.W. Haveman¹³, Y.C.A. Keulemans¹⁴, V. Nieuwenhuijs¹⁵, A.C. Poen¹⁶, E.A.J. Rauws¹⁷, A.C. Tan¹⁴, W.J. Thijs¹⁸, R. Timmer¹⁹, B.J.M. Witteman²⁰, M.G.H. Besselink²¹, J.E. van Hooft², H.C. van Santvoort²², M.G.W. Dijkgraaf^{23,24}, M.A. Boermeester²⁵, Dutch Pancreatitis Study Group.¹

- Multicenter RCT comparing early surgery versus step-up approach in CP patients with dilated PD (≥ 5 mm) and continuous or intermittent pain, who had only recently started on opioids
 - Early surgery arm (n = 44): HOP < 4 cm \rightarrow Puestow or HOP ≥ 4 cm \rightarrow Frey
 - Step-up arm (n = 44): pain meds \rightarrow endoscopy \rightarrow surgery
- Lower mean Izbicki pain score at 18 mos in early surgery group vs. step-up group
- Early surgery group had significantly greater decrease in pain score
- Complete or partial pain relief in 54% in early surgery vs. 33% in step-up (p < 0.001)
- Fewer interventions in early surgery group (1) vs. step-up group (3; p < 0.001)
- Complications, mortality, readmissions, pancreatic function, QOL were comparable

Conclusions

- Surgical approach must be individualized and tailored to anatomy and morphology of disease
- Surgical management of painful obstructive CP likely has better long-term pain relief than endotherapy
- Delaying surgery for CP may result in overall worse pain and QOL outcomes
- In appropriately selected children, TPIAT achieves durable pain relief and improves QOL with manageable glycemic control
- Advanced disease and longer symptom duration negatively impact insulin outcomes after TPIAT
- Comprehensive multidisciplinary team approach is critical to ensure optimal outcomes



Questions?

As long as I have
COURAGE
SUPPORT
STRENGTH
LOVE
I will beat
PANCREATITIS



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