Surgical Interventions for Chronic Pancreatitis in Children

Jaimie D. Nathan, MD
Associate Professor of Surgery and Pediatrics
Surgical Director, Pancreas Care Center
Cincinnati Children’s Hospital Medical Center

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Disclosures

• In the past 12 months, I have had no relevant financial relationships with the manufacturer(s) of any commercial product(s) and/or provider(s) of commercial services discussed in this presentation.
Disclosure: Old General Surgery Adage

*G-rated version*

It's okay to mess with it!

**The Pancreas:**

*Nature's Sugar Daddy*
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**

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

WAIT! HAMMER NO!

QUIET NAIL.

Chronic Pancreatitis

Puestow
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

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**

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
Confirmation of diagnosis
Is it pancreatic pain?
Advanced endoscopy
EPI management

Diabetes
Islet autoantibodies?
Assess β-cell mass (MMT)

Risk factors?
Counseling

Degree of pain
Non-opioid
Opioid

Functioning
Coping
Cognitive
behavioral
therapy

Bleeding or prothrombotic disorder?

Nutrition plan
CP-specific
Vitamins and minerals

MULTIDISCIPLINARY TEAM
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

TPIAT Glycemic Outcomes in Children

- Insulin independence in 41% at 36 months\(^1\)
  - 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-up\(^2\)
  - 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

Why do young children do better?

- Young children have lower insulin demands
  → Better metabolic milieu for engraftment?

- Highest replicatory capacity of \( \beta \)-cells in young children

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

- Insulin independence correlates\(^1\) with:
  \[
  \text{# islet equivalents (IEQ) per kg body wt}
  \]

- Relationship between yield and:
  - Imaging (atrophy, calcifications, ductal dilation)\(^2\)
  - Histopathology (fibrosis, acinar atrophy)\(^3\)
  - Duration of symptoms\(^4\)

  **Role in patient selection and timing of TPIAT?**

- Ductal drainage procedures and resections reduce yield and decrease probability of insulin independence\(^5\)

  **Caution in those anticipated to require future TPIAT**

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\(^2\)Young et al. Pancreas 2016;45:961-966.
Timing of Surgery?

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

No clear consensus on timing of surgery for CP

• 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

<table>
<thead>
<tr>
<th>Timing of Surgery</th>
<th>Odds Ratio (95% CI)(^{\text{a}})</th>
<th>(P) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reported duration of pain (\leq 3) y</td>
<td>1.81 (1.02-3.37)</td>
<td>.03</td>
</tr>
<tr>
<td>No preoperative opioid use</td>
<td>2.14 (1.23-3.96)</td>
<td>.006</td>
</tr>
<tr>
<td>Endoscopic treatments, No. ((\leq 5) procedures)</td>
<td>2.46 (1.10-6.27)</td>
<td>.04</td>
</tr>
</tbody>
</table>
• 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?
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)
RCT
• Adults with CP and obstructed PD
• Endoscopy with dilation/stent/lithotripsy (n=19) versus operative pancreaticojejunostomy (n=20)

• 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 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?
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 → Puestow or HOP ≥ 4 cm → Frey
- Step-up arm (n = 44): pain meds → endoscopy → 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, and LOVE, we will beat PANCREATITIS.

CCHMC Pancreas Care Center