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Review Article

Early surgery versus endoscopic therapy in chronic pancreatitis: toward an evidence-based paradigm shift

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ABSTRACT

Chronic pancreatitis (CP) is a progressive inflammatory disease leading to irreversible pancreatic damage, exocrine and endocrine insufficiency and chronic debilitating pain. Traditional management follows a step-up approach: medical therapy, endoscopic intervention, then surgery for refractory cases. Emerging evidence challenges this sequence, especially for patients with obstructive disease. This review evaluates comparative evidence of endoscopic versus surgical interventions in CP, emphasizing pain relief, durability and timing. Endoscopic therapy including pancreatic duct stenting, stricture dilation and extracorporeal shock wave lithotripsy offers meaningful short-term relief in selected patients with ductal obstruction. However, long-term efficacy is limited; 3–5 years sustained pain relief occurs in only 30–50% of patients, often requiring repeated procedures. In contrast, surgical approaches (pancreaticojejunostomy, Frey or Beger procedures) address both ductal obstruction and inflammatory mass, resulting in more durable outcomes. Randomized trials, including long-term data from the ESCAPE trial (~8-year follow-up), demonstrate superior pain control with early surgery: complete pain relief was achieved in 45% of early surgery patients versus 20% in endoscopy-first patients, with fewer cumulative interventions and higher patient satisfaction. Delayed surgery following repeated endoscopic therapy is associated with reduced efficacy, likely due to central sensitization and neural remodelling. Accumulating evidence supports a paradigm shift toward early, individualized surgical intervention in selected patients with obstructive chronic pancreatitis. While endoscopic therapy retains a role in carefully selected cases, prolonged step-up approaches may compromise long-term outcomes. Timely surgical referral, guided by disease morphology and symptom duration, is critical to optimizing pain relief and quality of life.

Keywords: Chronic pancreatitis, Early surgery, Endoscopic therapy, Obstructive disease, Pain management

INTRODUCTION

CP is a chronic inflammatory disorder characterized by progressive and irreversible structural damage to the pancreas, leading to gradual loss of exocrine and endocrine function.[1,2] Recurrent pancreatic injury promotes fibrosis, ductal distortion, intraductal calculi and parenchymal atrophy, which clinically manifest as exocrine insufficiency and pancreatogenic (type 3c) diabetes mellitus.[2,3] Beyond structural changes, CP imposes a substantial clinical burden. Chronic abdominal pain remains the predominant symptom and primary indication for intervention, significantly impairing quality of life and contributing to repeated healthcare utilization.[4] The global incidence of CP ranges from 5–12 per 100,000 persons per year, with prevalence estimates of 50–100 per 100,000 in Western populations.[5] Alcohol remains the most common etiologic factor worldwide, although smoking has emerged as an independent and synergistic risk factor.[5,6] In addition, genetic mutations

(PRSS1, SPINK1, CFTR), autoimmune mechanisms and idiopathic causes contribute significantly to disease burden, particularly in younger patients.[1,7]

MECHANISMS OF PAIN IN CHRONIC PANCREATITIS

Pain is the most disabling symptom of CP and remains the primary indication for intervention.[4] The pathogenesis is multifactorial and includes ductal hypertension from obstruction, parenchymal ischemia, inflammatory infiltration of intrapancreatic nerves and central sensitization (Table 1).[4,8]

Historically, the "ductal hypertension" theory supported decompressive approaches such as endoscopic stenting or surgical drainage.[8] However, accumulating evidence demonstrates neural remodeling and central pain processing abnormalities in long-standing disease, suggesting that delayed intervention may reduce the likelihood of durable pain relief.[9] These findings provide a mechanistic rationale for reconsidering the traditional step-up treatment strategy.

Traditional step-up management paradigm

Management of painful CP has historically followed a stepwise algorithm beginning with medical therapy (analgesics, pancreatic enzyme replacement), followed by endoscopic therapy for ductal obstruction and reserving surgery for refractory cases.[2,4] Endoscopic techniques including pancreatic sphincterotomy, stricture dilation, stone extraction and stenting are less invasive and have therefore been widely adopted as first-line interventional therapy.[10]

However, randomized and observational data over the past two decades have questioned whether delayed surgery after failed endoscopic therapy compromises long-term outcomes.[11,12] These concerns have catalysed renewed interest in early surgical intervention as a potentially superior strategy in selected patients with obstructive chronic pancreatitis. These data suggest that delayed surgery after prolonged endotherapy may compromise outcomes, possibly due to central sensitization and progressive neural remodeling. Consequently, the timing of surgery has emerged as a critical determinant of long-term pain relief.

This review evaluates the comparative evidence between early surgery and endoscopic therapy in chronic pancreatitis and discusses the implications for contemporary surgical decision-making.

Endoscopic therapy in chronic pancreatitis

Endoscopic therapy has become a cornerstone in the management of painful CP, particularly in patients with obstructive disease characterized by main pancreatic duct (MPD) dilation, strictures or intraductal stones.[10] Owing to its minimally invasive nature and lower immediate morbidity compared with surgery, endoscopic intervention has traditionally been recommended as first-line interventional therapy following failure of medical management.[13]

Indications and patient selection

Endoscopic therapy is primarily indicated in patients with symptomatic CP and evidence of ductal obstruction, especially when the MPD is dilated (>5–7 mm) with a dominant stricture or obstructing calculi.[13] Additional indications include management of pancreatic pseudocysts, biliary strictures secondary to inflammatory head mass and pancreatic duct leaks.[10]

Careful patient selection is essential. Best outcomes are generally observed in patients with a single dominant stricture in the pancreatic head and upstream ductal dilation.[14] In contrast, patients with extensive calcifications, multiple strictures or inflammatory pancreatic head enlargement often experience suboptimal or short-lived benefit.[15]

Endoscopic techniques

Endoscopic approaches aim to relieve ductal hypertension and improve pancreatic drainage. Common techniques include pancreatic sphincterotomy. Stricture dilation with balloon catheters. Placement of plastic stents across dominant strictures. Extraction of intraductal stones using baskets or balloons. Extracorporeal shock wave lithotripsy (ESWL) for large calculi.[16]

ESWL combined with endoscopic extraction is particularly effective for radiopaque stones larger than 5 mm located in the head or body of the pancreas.[16] In selected cases, multiple stent placement or sequential stenting may be required to achieve durable stricture resolution.[14]

Clinical outcomes

Short-term pain relief is achieved in approximately 60–80% of patients undergoing endoscopic therapy; however, sustained long-term relief declines to nearly 30–50% at 3–5 years of follow-up.[17] Reintervention rates remain substantial, with many patients requiring repeated procedures due to stent occlusion, recurrent strictures or stone recurrence.[14]

Randomized data have demonstrated that while endoscopic therapy provides initial symptomatic improvement, long-term pain control may be inferior to surgical drainage in selected patients with obstructive CP.[11,18] Furthermore, repeated endoscopic interventions may delay definitive surgical management, potentially allowing ongoing inflammatory and neural remodeling processes to progress.[18]

Table 1: Mechanisms of pain in chronic pancreatitis.

Mechanism	Underlying pathophysiology	Clinical features	Therapeutic implications
Ductal obstruction and hypertension	Strictures and/or intraductal stones increase intraductal pressure, causing parenchymal distension	Intermittent or persistent deep epigastric pain, often postprandial	Endoscopic decompression, stone clearance, surgical drainage
Parenchymal inflammation and fibrosis	Ongoing inflammation leads to tissue edema, fibrosis and increased intrapancreatic pressure	Constant visceral pain	Anti-inflammatory strategies, decompressive surgery
Neural inflammation and hypertrophy	Inflammatory infiltration and enlargement of intrapancreatic nerves	Severe, often refractory pain	Surgical resection (e.g., head-dominant disease), neuromodulation
Peripheral neuropathic sensitization	Upregulation of nociceptive pathways and altered pain signaling	Burning, neuropathic pain qualities	Neuromodulators (e.g., pregabalin, amitriptyline)
Central sensitization	Sustained nociceptive input alters central pain processing pathways	Pain disproportionate to imaging findings; chronic pain syndrome	Early definitive intervention, multidisciplinary pain management
Extrapancreatic complications	Biliary obstruction, pseudocyst, duodenal stenosis or vascular involvement	Pain with obstructive or compressive symptoms	Targeted endoscopic or surgical management

Complications and limitations

Although less invasive than surgery, endoscopic therapy is not without risk. Complications include post-ERCP pancreatitis, infections, bleeding, perforation and stent-related adverse events.[11] Additionally, repeated procedures contribute to cumulative procedural risk, increased healthcare utilization and economic burden.

Importantly, endoscopic therapy primarily addresses ductal obstruction and does not directly treat inflammatory pancreatic head mass or neuropathic mechanisms of pain, which may explain limited long-term efficacy in certain patient subsets.[18,19]

Surgical management in chronic pancreatitis

Surgical intervention remains the most definitive treatment for CP, particularly in patients with intractable pain, ductal obstruction or complications unresponsive to medical or endoscopic therapy.[18] Surgery not only addresses ductal decompression but can also remove inflammatory pancreatic head mass and reduce neural pain signaling, offering more durable long-term outcomes than endoscopic therapy, potentially preserving pancreatic function.

Indications and patient selection

Indications for surgical management include persistent or severe pain despite optimized medical and endoscopic therapy. Main pancreatic duct obstruction with or without calculi. Large inflammatory pancreatic head mass causing biliary or duodenal obstruction. Complications such as pseudocysts, fistulas or suspicion of malignancy.[18,20] Careful patient selection is crucial. Surgery is most beneficial in patients with a dilated main pancreatic duct, a dominant head lesion or obstructive disease, whereas patients with diffuse small-duct disease may derive limited benefit from resection or drainage procedures.[21]

Surgical approaches

Surgical strategies are broadly classified into drainage procedures and resection or hybrid procedures.

Drainage procedures

Lateral pancreaticojejunostomy (Puestow procedure) is indicated in patients with a dilated duct (>6–7 mm) without a dominant head mass, allowing decompression and improved drainage.[22]

Resection and hybrid procedures

Patients with an inflammatory head mass benefit from partial resection or combined procedures. The Frey procedure combines local head resection with longitudinal pancreaticojejunostomy, whereas the Beger procedure involves duodenum-preserving head resection.[23,24] Total or subtotal pancreatectomy is reserved for diffuse disease or complex complications not amenable to limited resections.[25] Hybrid procedures combine ductal decompression and partial resection, targeting both ductal hypertension and inflammatory mass, addressing the multifactorial nature of pain in chronic pancreatitis (Table 2).[26]

Clinical outcomes

Surgical intervention is associated with superior long-term pain relief compared to endoscopic therapy. Randomized trials and meta-analyses report pain relief rates of 70–90% at 5–10 years, with reduced need for reintervention.[11,18] Additionally, early surgical intervention may preserve pancreatic function better than

delayed surgery following repeated endoscopic procedures.[18]

Complications and considerations

Although more invasive than endoscopic therapy, modern surgical techniques have low perioperative mortality (<5%) in high-volume centers.[20] Complications include pancreatic fistula, delayed gastric emptying and infection. Careful preoperative assessment and selection of procedure type based on ductal morphology, head mass and disease distribution are essential to optimize outcomes.[21]

Surgery addresses not only mechanical obstruction but also inflammatory neural remodeling, explaining its superior efficacy in long-term pain control compared with repeated endoscopic interventions.[11,18]

Comparative evidence from randomized controlled trials

High-quality randomized evidence comparing endoscopic and surgical therapies for CP has reshaped contemporary management paradigms, particularly in patients with obstructive disease and intractable pain.

Early randomized trials

Díte et al trial was among the first to compare surgical with endoscopic management in obstructive CP, demonstrating that surgery provided more durable long-term pain relief and required fewer reinterventions than endoscopic therapy.[11] Similarly, Cahen et al, reported that patients randomized to surgical ductal drainage experienced significantly better pain control compared with an endoscopy-first approach at 2 years follow-up.[12] These early RCTs challenged the traditional step-up approach and highlighted the potential benefits of surgical decompression in selected patients.

ESCAPE trial: short-term outcomes

The multicenter ESCAPE randomized clinical trial subsequently evaluated an early surgery strategy versus an endoscopy-first approach in patients with painful chronic pancreatitis and a dilated main pancreatic duct. In the initial report at 18 months follow-up, early surgery resulted in significantly better pain relief with lower mean Izbicki pain scores as compared with the endoscopy-first strategy. While short-term quality of life and pancreatic function did not differ significantly, early surgery was associated with fewer cumulative interventions and lower pain scores integrated over time.[18]

Long-term follow-up of the ESCAPE trial

The 2025 long-term follow-up of the ESCAPE trial (mean follow-up ~98 months) confirmed the sustained superiority of early surgery over an endoscopy-first strategy in patients with obstructive chronic pancreatitis 27. Early surgery was associated with significantly lower mean Izbicki pain scores (33 vs 51, p=0.03), higher rates of complete pain relief (45% vs 20%, p=0.04) and lower VAS pain scores (29 vs 47, p=0.02).[27] Patient satisfaction and willingness to recommend treatment were also markedly higher in the early surgery group.[27] Patients who required delayed surgery after an initial endoscopy-first strategy experienced less favorable outcomes than those treated with early surgical intervention. Notably, achieving ductal clearance through endoscopic therapy did not translate into sustained long-term pain relief. Although the prevalence of endocrine and exocrine insufficiency and overall quality-of-life measures were comparable between groups at extended follow-up, the endoscopy-first approach was associated with a higher need for subsequent interventions, emphasizing the greater durability and reduced cumulative procedural burden of early surgery.[27]

TOWARDS THE PARADIGM SHIFT

The combined evidence from RCTs consistently demonstrates that surgical therapy provides more durable pain relief, reduces the need for repeated interventions and improves patient satisfaction compared with endoscopic therapy in appropriately selected patients with CP. Early surgical intervention, particularly in patients with obstructive features and dilated ducts, offers sustained superiority over an endoscopy-first strategy in both short and long-term follow-up.[11,12,18,27] These data lend robust support to revisiting the traditional step-up paradigm and considering early surgery as a first-line option in suitable candidates.

Table 2: Surgical procedure for chronic pancreatitis: indications and outcomes.

Procedure	Indication	Key features/technique	Clinical outcomes
Lateral pancreaticojejunostomy (puestow)	Dilated main pancreatic duct (>6–7 mm) without a dominant head mass	Longitudinal duct drainage into a Roux-en-Y jejunal loop	Pain relief in 70–80% of patients; preserves pancreatic tissue.[22]
Frey procedure	Dominant inflammatory head mass with ductal dilation	Local resection of the pancreatic head combined with longitudinal pancreaticojejunostomy	Long-term pain relief 75–90%, reduced reinterventions; preserves duodenum and pancreatic function.[23]
Beger procedure	Large pancreatic head mass with or without ductal dilation	Duodenum-preserving pancreatic head resection	Pain relief 80–90%; excellent long-term outcomes; preserves endocrine/exocrine function.[24]

Continued.

Procedure	Indication	Key features/technique	Clinical outcomes
Total/subtotal pancreatectomy	Diffuse small-duct disease, failed prior interventions or complex complications	Complete or near-complete resection of pancreatic parenchyma	Effective pain control, but high risk of brittle diabetes and exocrine insufficiency.[25]
Hybrid procedures (frey/beger variants)	Obstructive disease with combined ductal dilation and head mass	Combines decompression and partial resection	Optimizes pain control and function preservation; addresses multiple pain mechanisms.[23,24]

Table 3: Indicators favouring early surgical referral in chronic pancreatitis.

Clinical factor	Implication
Dilated duct (>7 mm)	Strong candidate for decompressive surgery
Inflammatory head mass	Consider early Frey or Beger procedure
Pain duration <3 years	Higher likelihood of durable pain relief
Escalating opioid requirement	Avoid prolonged delay
Multiple failed ERCP sessions	Transition to surgical management

Timing of surgery: the window of opportunity

While randomized trials have clarified that surgical therapy provides more durable pain relief than endoscopic management in selected patients, they also raise a more clinically nuanced question: when is the optimal time to operate. CP is a progressive disease in which mechanisms of pain evolve over time. The timing of intervention, therefore, determines whether surgery meaningfully reverses pain or merely addresses its structural component.

Early disease: mechanical pain predominance

In the earlier stages of obstructive CP, pain is largely driven by ductal hypertension and inflammatory head mass–related neural irritation.[4] At this stage, central sensitization mechanisms are thought to be limited and nociceptive signaling remains closely linked to structural abnormalities.[28] Surgical decompression and head resection directly target these biological drivers of pain. The ESCAPE trial specifically enrolled patients with relatively short symptom duration and demonstrated that early surgical intervention resulted in significantly lower pain scores and reduced cumulative procedural burden compared with an endoscopy-first strategy.[11,18,27] Long-term follow-up confirmed the sustained superiority of early surgery over approximately 8 years.[27] These findings support the concept of a therapeutic window, during which correction of anatomical pathology translates into maximal symptomatic benefit.

Late disease: the cost of delay

With prolonged disease duration, persistent nociceptive input may lead to peripheral nerve remodeling and central sensitization.[19] Patients frequently develop hyperalgesia, chronic opioid dependence and pain patterns that are less directly related to ductal obstruction. In such cases, structural correction alone may not fully normalize pain perception. Observational studies have demonstrated that longer preoperative pain duration is associated with inferior postoperative pain outcomes.[29] Patients undergoing surgery after years of unsuccessful endoscopic therapy often achieve less complete pain relief compared with those treated earlier in the disease course. Importantly, the ESCAPE long-term analysis showed that patients who crossed over from endoscopic therapy to surgery experienced worse outcomes than those randomized to early surgery, reinforcing the potential consequences of delayed operative management.[27]

Duration of symptoms as a predictor of outcome

Multiple studies have identified predictors of poorer postoperative pain control, including prolonged pain duration (>3 years), daily opioid use and multiple prior interventions.[29] These findings suggest that extended reliance on repetitive endoscopic therapy may inadvertently reduce the effectiveness of eventual surgical treatment. Thus, timing should not be viewed merely as a sequencing issue but as a determinant of long-term therapeutic success.

Practical clinical implications

Decisions regarding the timing of surgery should integrate morphological and clinical factors, including main pancreatic duct diameter (>7 mm favoring decompression surgery). Presence of an inflammatory pancreatic head mass. Frequency and severity of pain episodes. Escalating opioid requirements. Failure of a limited, well-conducted endoscopic attempt (Table 3).[20,26] A reasonable contemporary approach may include a single trial of endoscopic therapy in selected patients, followed by early surgical referral if symptoms persist. Prolonged and repetitive endoscopic interventions without sustained benefit should be avoided. The emerging paradigm is therefore not “surgery first for all,” but rather “avoid surgery too late.”

Limitation of current evidence

Despite robust randomized data supporting early surgical intervention in selected patients with obstructive chronic pancreatitis, several limitations warrant consideration. Most trials, including the ESCAPE study, enrolled patients treated in high-volume tertiary centers, potentially limiting generalizability to lower-resource.[18,27] Sample sizes remain modest and subgroup analyses are underpowered to definitively guide management in small-duct disease or non-obstructive phenotypes. Pain assessment in chronic pancreatitis is inherently complex and influenced by psychological, social and central sensitization factors that are not fully captured by conventional scoring systems.[28] Additionally, long-term data on endocrine and exocrine function beyond 8–10 years remain limited. Finally, evolving endoscopic and minimally invasive surgical techniques may further influence comparative outcomes in the future. These limitations highlight the need for continued prospective research while supporting individualized, morphology-based decision-making.

FUTURE DIRECTIONS AND CONCLUSION

Toward a personalized, mechanism-based strategy

The management of CP is entering an era that increasingly emphasizes individualized care rather than rigid adherence to a uniform step-up model. Emerging evidence suggests that pain in CP is heterogeneous, with varying contributions from ductal obstruction, inflammatory mass effect, peripheral neural remodeling and central sensitization.[28] Future strategies should incorporate pain phenotyping, morphological assessment and duration of symptoms to guide early decision-making. Advanced imaging modalities, quantitative sensory testing and biomarkers of neural inflammation may help identify patients in whom structural correction is most likely to result in durable pain relief. Such tools could refine selection for early surgery and prevent unnecessary procedural delays.

Evolving surgical strategies

Surgical techniques continue to evolve with improved perioperative safety and functional preservation. Duodenum-preserving pancreatic head resections, such as the Frey and Beger procedures, have demonstrated durable pain control with acceptable preservation of endocrine and exocrine function.[23,24] Minimally invasive and robotic approaches are increasingly being explored in specialized centers, potentially reducing perioperative morbidity while maintaining oncologic and functional principles. For patients with diffuse small-duct disease or refractory pain not amenable to decompression procedures, total pancreatectomy with islet autotransplantation (TP-IAT) has emerged as an important option. Recent contemporary series demonstrate meaningful pain reduction and improved quality of life, with partial preservation of endocrine function in selected patients.[25] Earlier referral for TP-IAT, before prolonged opioid exposure and advanced diabetes, may further optimize outcomes.

Rethinking the step-up paradigm

The traditional management algorithm of medical therapy followed by repeated endoscopic interventions and eventual surgery is increasingly being challenged. Randomized trials, including long-term ESCAPE data, consistently demonstrate superior and more durable pain control with early surgical intervention in appropriately selected patients.[18] Importantly, delayed surgery after prolonged endoscopic therapy appears to yield inferior outcomes compared with early operative management.[27] A contemporary paradigm should therefore emphasize early multidisciplinary evaluation, morphology-based selection. Limited trial of endoscopic therapy when appropriate. Avoidance of repetitive, non-durable interventions. Timely referral for definitive surgical management. The goal is not indiscriminate early surgery, but rather strategic early intervention in patients most likely to benefit.

CONCLUSION

Chronic pancreatitis is a progressive disease in which the timing of intervention significantly influences long-term outcomes. Accumulating randomized evidence demonstrates that surgical therapy provides more durable pain relief and reduces cumulative procedural burden compared with an endoscopy-first strategy in selected patients with obstructive disease. Long-term follow-up data further underscore the importance of early intervention before central sensitization and irreversible neural remodeling predominate. The emerging paradigm is clear: while endoscopic therapy retains an important role, prolonged delay of definitive surgical treatment may compromise outcomes. A shift toward early, individualized and mechanism-based management represents a rational and evidence-supported evolution in the care of chronic pancreatitis. Thus, optimizing the timing and selection of surgical intervention maximizes long-term pain relief and quality of life in chronic pancreatitis, representing a pivotal shift toward evidence-based, individualized care.

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