Leading article

# Chronic pancreatitis – lessons learned

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The therapeutic attitude towards chronic pancreatitis has for years been one of fatalism, even nihilism. However, one of the major reasons favouring conservative treatment, namely the high morbidity and mortality rates associated with pancreatic operations, has become more or less obsolete as a result of significant progress in surgical and interventional techniques. The second major reason for promoting conservative management has been a notion that recurrent pain, the cardinal symptom of chronic pancreatitis, eventually subsides as a consequence of 'burn-out' of the pancreas[1].

That the duration of pain is unpredictable, however, has been shown in more recent reports[2,3], and this has resulted in a therapeutic paradigm shift over the past three decades; conservative 'watchful waiting' is hardly acceptable if pancreatic pain has a morphological basis. However, the optimal treatment of such chronic pain is still controversial. The heterogeneity of patient cohorts, differences in individual pain perception and, frankly, an inadequate insight into the pathophysiology of the matter have hampered studies directed at the optimization of pain management. In the light of this, the American Gastroenterological Association (AGA) produced treatment guidelines in 1998[3], but these, on close inspection, are 'expert opinion' rather than evidence based. This is hardly surprising in view of the paucity of controlled trials comparing different therapeutic approaches in this complex patient population. The first (and only) randomized controlled trial (RCT) had a study population of 72 patients and demonstrated a relative equivalence between surgical and endoscopic therapy in the short term, with surgery having an advantage in terms of durability of pain reduction[4]. No further RCT has been performed to compare conservative therapy limited to non-specific support (non-narcotic analgesics, low-fat diet, alcohol abstinence, suppression of pancreatic secretion) with surgical procedures, endoscopic interventions or nerve block.

The AGA guidelines advocate a 'four phase' concept with: (1) primary non-interventional, supportive treatment; (2) medical therapy, including pancreatic enzymes and acid suppression; (3) endoscopic therapy; and (4) either watchful waiting or surgery. These guidelines ignore two basic aspects. First, in the clinical setting, before 'specific' pain brings the patient to the attention of the pancreatic expert, he or she usually has a long history of 'non-specific' pain. By the time the expert carries out a diagnostic assessment, most patients have severe pathological changes. Second, preliminary prospective data have shown that early operation prevents further functional impairment, or even improves pancreatic endocrine and exocrine function, suggesting that the timing of intervention has an impact not only on functional derangement but also on pain control and quality of life[5,6].

What kind of intervention should be selected? The prerequisite for any customized therapy is a detailed knowledge of the pathological changes. Obstruction of the pancreatic duct, either by stones or by postinflammatory strictures, and an inflammatory cephalic mass are the two principal findings. Although duct dilatation suggests the possibility of abnormally raised ductal and intraparenchymatous pressures, it is doubtful whether duct obstruction alone is responsible for intraparenchymatous hypertension. Several studies have confirmed a correlation between intraparenchymatous pressure and the intensity of pain, leading to the concept of 'retroperitoneal compartment syndrome', but strong evidence of an association between ductal and intraparenchymatous hypertension is lacking.

This matter is clinically important, as it has been argued that in large duct pancreatitis surgical or endoscopic drainage should eliminate pain. However, this disregards the often concomitant cephalic morphological change that has been considered the 'pacemaker' of the disease; any 'limited' surgical therapy (for example, lateral pancreaticojejunostomy) that drains only the distal duct system risks treatment failure. In the authors' experience, an 'extended drainage', encompassing not only ductal decompression but also a duodenum-preserving pancreatic head excision[7] with the extent of resection varying according to the state of the pancreatic gland, represents an approach that may be tailored to the individual patient.

What are the merits of interventional endoscopy? The endoscopic 'door' was opened in 1985 when pancreatic sphincterotomy was performed[8]. Clear indications for

endoscopic intervention as first-line treatment are dominant, single strictures and pancreatic duct stones, as long as there is no other significant pathology. Other possible indications, such as the placement of stents to treat multiple strictures, and the combination of spincterotomy, stenting and lithotripsy for intraparenchymatous stones, are highly debatable.

Consensus exists that complications involving adjacent organs, such as duodenal obstruction, common bile duct (CBD) stenosis and recurrent pseudocyst formation in conjunction with ductal pathology, and problematic internal pancreatic fistulas represent indisputable indications for surgery. Duodenal and CBD obstruction require a more extensive excision of the pancreatic head, which can still be regarded as an extended drainage operation (Hamburg modification of the Frey procedure). Pancreatoduodenectomy should be reserved for patients with irreversible duodenal stenosis irrespective of an extrinsic inflammatory mass, and for those in whom the duodenum cannot be entirely freed from its surrounding scar tissue without damaging its vascular supply. Whether extrahepatic portal hypertension (EPH) of itself in patients otherwise free of pain is an indication for surgery is uncertain. Even though compromised portal flow may be restored by resectional procedures, further progression of EPH after drainage procedures is rare. In addition, the distinctly higher complication rates in patients with EPH[9] hardly favour a 'generous' indication for surgery.

What are the therapeutic options for recurrence of pain after surgery? Treatment failure is reported to occur in 10–40 per cent of patients, and these people require accurate diagnostic assessment. In most instances, either an incomplete resection of an inflammatory cephalic pseudotumour or insufficient drainage of a dilated duct system (or even both) will be found. Second-line salvage procedures should address these individual findings. Surgical rescue options mainly include: (1) excision of a recurrent (or, more likely, residual) inflammatory mass ('redo' duodenum-preserving pancreatic head resection, Whipple procedure, pylorus-preserving pancreaticoduodenectomy) and (2) drainage of a dilated duct system. These operations are aimed at relieving duct strictures localized in the pancreatic body and tail respectively. The final option, which may be considered for patients whose diagnostic imaging fails to reveal any specific underlying pathology, is total pancreatectomy.

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## References

1 Ammann RW, Akovbiantz A, Largiader F. Pain relief in chronic pancreatitis with and without surgery. *Gastroenterology* 1984; **87**: 746–777.
2 Lankisch PG, Happe-Loehr A, Otto J, Creutzfeldt W. Natural course in chronic pancreatitis. Pain, exocrine and endocrine pancreatic insufficiency and prognosis of the disease. *Digest* 1993; **54**: 148–155.
3 Warshaw AL, Banks PA, Fernandez-del Castillo C. AGA technical review: treatment of pain in chronic pancreatitis. *Gastroenterology* 1998; **115**: 765–776.
4 Dite P, Ruzicka M, Zboril V, Novotny I. A prospective, randomized trial comparing endoscopic and surgical therapy for chronic pancreatitis. *Endoscopy* 2003; **35**: 553–558.
5 Nealon WH, Townsend CM Jr, Thompson JC. Operative drainage of the pancreatic duct delays functional impairment in patients with chronic pancreatitis. A prospective analysis. *Ann Surg* 1988; **208**: 321–339.
6 Sidhu SS, Nundy S, Tandon RK. The effect of the modified puestow procedure on diabetes in patients with tropical chronic pancreatitis – a prospective study. *Am J Gastroenterol* 2001; **96**: 107–111.
7 Izbicki JR, Bloechle C, Broering DC, Knoefel WT, Kuechler T, Broelsch CE. Extended drainage *versus* resection in surgery for chronic pancreatitis – prospective randomized trial comparing the longitudinal pancreaticojejunostomy combined with local pancreatic head excision with the pylorus preserving pancreatoduodenectomy. *Ann Surg* 1998; **228**: 771–779.
8 Fuji T, Amano H, Harima K, Aibe T, Asagami F, Kinukawa K *et al*. Pancreatic sphincterotomy and pancreatic endoprosthesis. *Endoscopy* 1985; **17**: 69–72.
9 Izbicki JR, Yekebas EF, Strate T, Eisenberger CF, Hosch SB, Steffani K *et al*. Extrahepatic portal hypertension in chronic pancreatitis: an old problem revisited. *Ann Surg* 2002; **236**: 82–89.