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## PART B: Surgery for chronic pancreatitis: indications and timing of surgery

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### Introduction

With the development of subspecialization in the field of pancreatic diseases over the last two decades, there has been a gradual paradigm shift away from the nihilistic view that other than for complicated disease, surgery has a limited role in the management of pain in patients with chronic pancreatitis (CP), in particular in the alcohol-induced group. In the past, surgery has not enjoyed a good track record because of the morbidity and mortality of major resection operations, the development of exocrine and endocrine insufficiency, and shortened life expectancy. In the 1980s, the conservative school enjoyed further support when the Zurich group introduced the concept of the “pancreatic burn out syndrome.” Their long-term studies on the natural history of CP showed that pain relief developed *pari passu* with the deterioration of pancreatic function and that this followed a predictable pattern [1]. They and others [2] championed the view that by waiting long enough, less patients would require surgery for pain. However, subsequent studies have challenged this concept [3–6]. These showed that at best relief of pain occurred mostly in the subgroup of patients with mild recurrent relapsing pancreatitis and not in the group with severe and persistent pain who required opiates for pain control. In the words of Warshaw [7], *It seems unreasonable to tell a patient to wait an indeterminate number of years in the hope of spontaneous subsidence of pain when surgery can offer a 75% success rate.* Yet, it took some time for the “burn out” concept to be debunked in the context of delaying surgery in suitable cases. In recent times, the advent of endoscopic stenting and extracorporeal shockwave lithotripsy (ESWL) [8] has,

to a certain extent, changed the pattern of referral of patients for surgery.

Subspecialization in pancreatic surgery has significantly improved the results after surgery in CP by virtue of increasingly sophisticated imaging and, refinement of surgical procedures with the emphasis on maximum organ preservation. In addition, improved quality of anesthesia and ICU care and minimally invasive procedures has further reduced post operative morbidity [9]. As a consequence, tailoring of the procedure according to morphological changes of the pancreas has improved and made these much safer operations in the hands of expert pancreatic surgeons. Satisfactory pain relief can now be achieved with acceptable preservation of pancreatic function [10]. Whether these improved results have resulted in an increase in the number of referrals for surgery remains unclear but at least surgery has now assumed an important role in the treatment of patients with persistent and intractable pain who have failed to improve despite receiving adequate conservative treatment.

### Indications for surgery

#### Failure of conservative treatment measures to control intractable pain in uncomplicated disease

Patients should only be considered for invasive interventional procedures once all forms of conservative treatment have been exhausted in order to achieve satisfactory relief of intractable pain over a reasonable period of time. Such a period may vary from patient to patient but it is advisable to err on the conservative side

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unless there is concern about opiate dependency (see Section “Timing of surgery”).

Details of conservative treatment are discussed in Chapters 11 and 14. The reader is also referred to recent published guidelines on CP [11–13].

In summary, the following principles should be adhered to.

#### **i. Multidisciplinary care**

It is imperative that these patients should be managed by a multidisciplinary subspecialist group experienced in the management of patients with CP. At the very least, the team should consist of a medical gastroenterologist, hepatopancreaticobiliary (HPB) surgeon, an experienced endoscopic interventionist, and an HPB radiologist. It is prudent to have further support from a psychiatrist/psychologist, a social worker, a dietician, and a pain management team. Close cooperation between gastroenterologists and surgeons are of paramount importance to avoid unnecessary and prolonged conservative treatment on the one hand and premature intervention on the other (discussed later).

#### **ii. Behaviour modification**

Abstinence from both alcohol [14, 15] and smoking [16] remains the cornerstone of conservative treatment. This can best be achieved with the assistance of an alcohol dependency counselor or psychologist. In many countries, patients with alcohol-induced pancreatitis live in a poor socioeconomic environment. Under these circumstances, the assistance of a social worker is invaluable to provide a holistic approach to patient management.

There are now well-documented pain control regimes based on a sequential step-up approach [11–13, 17]. The mechanisms of pain in CP are poorly understood and may differ among patients and change in the individual patient over a period of time. Two categories mostly seen are those who present with frequent acute attacks of pain requiring hospitalization with pain-free periods in between and those who suffer from severe intractable pain [4–6]. It is important to exclude other causes of pain that may mimic pancreatic pain (i.e., NSAID-induced ulcer disease) and to be aware of the development of possible complications such as pancreatic fluid collections (PFCs), when there is a change in the severity or pattern of the pain.

For all the aforementioned reasons, it is important to monitor the patient’s progress over a reasonable period of time before a decision is taken to intervene.

### **Complications**

The most common complications seen in CP are biliary obstruction and PFCs. Duodenal obstruction and bleeding from segmental portal hypertension or false aneurysms are much less common. Apart from bleeding or secondary infections of PFCs, there is seldom a need for urgent intervention in the other complications and in many instances these can be managed conservatively (see Chapter 16c).

Another important indication for surgery is a strong suspicion of an associated malignancy, which cannot be excluded on preoperative imaging.

### **Timing of surgery**

The decision and timing of both surgery and other interventional procedures remain controversial. It is important to stress that while the indications for less invasive nonoperative procedures are currently the same as for surgery [18], this may change in future with the refinement and further development of minimally invasive techniques.

The main purpose of any interventional procedure is to relieve pain so that patients no longer require opioids, to preserve maximal pancreatic function, and to restore the quality of life (QOL) [19]. There is a fine line between the risks associated with surgery and the problem of addiction to opioids when conservative treatment is unnecessarily prolonged [18]. There is now good evidence that prolonged usage of opioids is one of the important predictors of failure after surgery, both in terms of pain relief and QOL [20–24]. In addition to the problem of opioid dependency, there is evidence to suggest that poor pain outcome after surgery is associated with greater central sensitization and more pronociceptive descending modulation, which results after periods of prolonged pain [25]. It is questionable whether earlier surgery will prevent this phenomenon. Trials on this important issue of timing of intervention are currently being performed. At present, there are no clear guidelines on how long it is safe to keep patients on maintenance opioid therapy before it compromises the results of surgery and other interventional procedures.

On balance, it would seem reasonable to consider some form of intervention when opioids are required for adequate pain control for periods longer than 6 months. However, the decision to intervene early may be delayed by other factors such as the severity of comorbid disease and those with small-duct disease, which often limits the choice of organ-preserving operations.

Prolonged and repeated pancreatic stenting has been identified as a risk factor for failure after subsequent rescue surgery [22]. Apart from the delay in referral for definitive surgery, it is conceivable that stent-induced pancreatitis and a “foreign body” effect may be additional contributing factors. There is now ample evidence that surgical drainage operations afford patients significantly better long-term pain relief and improved QOL when compared with endoscopic drainage of the pancreatic duct [23, 25, 26]. Endoscopic drainage with or without ESWL will continue to play an important role in the management of these patients but it is important to identify those who will benefit most from this less invasive interventional approach. In this regard, guidelines such as those provided by the European Society of Gastrointestinal Endoscopy (ESGED) [27] have been invaluable although further refinement based on level 1 studies are eagerly awaited.

Similarly, guidelines are required for the timing of referral for surgery when endoscopic drainage has failed. The proposed randomized trial by the Dutch Pancreatic Study Group on Early Surgery versus Optimal Step-up Practice for Chronic Pancreatitis (which will include endoscopic drainage) may provide answers to these questions [28]. It is also anticipated that the study will shed more light on the supposition that early drainage surgery preserves or improves pancreatic function [29–31]. This will probably be the most difficult question to answer because progressive deterioration in pancreatic function is usually inevitable in the majority of patients despite successful surgical drainage procedures [10].

## Summary and conclusion

Much of the success in the treatment of patients with CP who have intractable pain depends on a detailed and holistic approach by a multidisciplinary team of experts. It is important to ensure, however, that these patients,

who require considerable support, are not stranded between the various disciplines within the team framework. Ideally, they should primarily be evaluated by and cared for by a medical gastroenterologist in order to establish a rapport with the emphasis on monitoring response to pain control and to adjust medication requirements accordingly. The recent development of guidelines with treatment algorithms are encouraging as are the proposed studies to improve the timing and selection of interventional procedures.

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