HANDS OFF OR HANDS ON FOR PAINFUL CHRONIC PANCREATITIS: CURRENT INDICATIONS FOR SURGERY IN CHRONIC PANCREATITIS

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There is a lack of consensus regarding the best treatment for chronic pancreatitis (CP). The condition usually presents with pain and, as very little can be done to change the natural history of the disease process, our efforts are directed at improving the quality of life of the patients. The most common associated etiological factor is alcohol addiction or abuse. The personality type of many of these patients makes substance abuse common and this significantly impacts on the success of treatment. A nihilistic approach to this condition based on evidence suggesting that the process burns out in approximately 10 years is difficult to accept when one witnesses the suffering of these patients.

Clinicians need to guard against the assumption that they can succeed without significant involvement and commitment by the patient. There is evidence that pollutants or xenobiotics play a role in the pathophysiology of alcoholic CP, and these xenobiotics are often associated with occupations commonly filled by the economically disadvantaged, making rehabilitation more difficult.

Methods to evaluate the extent of the pain are largely qualitative and while being developed as research tools they are not commonly used in clinical practice. There is little standardisation in the reporting of pain and quality of life assessment; therefore comparisons of the efficacy of the many surgical procedures described in the literature are difficult.
DETERMINING OUTCOMES

CP is a benign condition, however we must focus on the outcomes of therapy as for a palliative procedure. Thus durability of pain relief and improved quality of life are essential. Many reports in the literature have relatively short periods of follow up encouraging those who do not favour surgery to be skeptical of its benefits. Apart from pain there are other organ based complications of CP; strictures of the common bile duct, pseudocysts, vascular occlusions and hollow organ obstruction, that require a more aggressive approach due to their potentially life threatening nature.

The relationship between the development of various surgical procedures and our understanding of the pathophysiology of the pain has not always been linear. The understanding is still largely theoretical although exciting developments in this regard are emerging.

Ductal hypertension does not explain the mechanism of pain in all patients\(^4\), this is reflected in the failure of simple duct decompression to relieve the pain in certain cases\(^5,6,7\). Parenchymal hypertension gives rise to a compartment syndrome\(^8,9,10\), which is aggravated by pancreatic stimulation resulting in further ischaemia of the neurons. Disordered neo-proliferation of neurons sensitive to ischaemia produces pain\(^11\).

There is now understanding of noxious agents such as substance P, serotonin, cytokines and other such substances, which stimulate pain receptors on the visceral nerves\(^12,13\). The anatomy of the pain pathways is better understood. The head of the pancreas is regarded as the pacemaker for the pain, based largely on the fact that the majority of the mass of the pancreas is situated in the head. There is immunological evidence that the disease in the head of the pancreas may drive the inflammation process.

TREATMENT

The aim of treatment in CP is multifocal (Table 1). Surgery is not the first port of call in managing CP. The evaluation of the patient requires a multidisciplinary approach, and the central aim is to improve the quality of life.
The initial approach is a non-operative approach. This is a complex treatment algorithm and not one this chapter will deal with. The indications for surgery, with respect to pain, is mainly the failure of medical or other less invasive therapies.

However there are a number of other complications of the CP that require surgery and these may not always be amenable to non-surgical therapy. These include local complications: pseudocysts, obstructive jaundice and biliary strictures, visceral organ outlet obstruction, vascular complications and malignant transformation.

Most patients present with pain but this is often combined with the clinical presentation of the other complications: obstructive jaundice in about a quarter of patients, symptomatic psuedocysts in 15% and a mass in the head of the pancreas in about the same.

**SURGICAL OUTCOMES**

The results from surgery for CP are good. These results have improved with the introduction of the hybrid procedures which require parenchymal resection and duct drainage. These are considered to be parenchymal preserving and duodenal preserving resections of the head of the pancreas (DPPHR) (Table 2). The Pancreateicoduodenectomy (PD) remain popular in many centres.

RCT (comparing the PD with the DPPHR) has demonstrated no real benefit to either\(^{14}\).

There is a lower morbidity with the DPPHR. My operation of choice is the Frey Duodenal preserving head resection with a longitudinal pancreatico-jejunostomy.

The reported results suggest an excellent outcome in 85% with only 2-3% having no improvement in their pain from the surgery. It is very clear today that measuring pain is not adequate and a validated quality of life evaluation should be used. Morbidity remains at approximately 25% but perioperative mortality should be less than 5%.
**Biliary Obstruction**

While only one in six patients present with OJ the natural history of this is of concern. Patients who present with long term OJ have a risk of developing secondary biliary cirrhosis. This is not a common consequence and rarely seen today. The acute complications of OJ are more common. The indications for the management of the OJ has shifted over the last 20 years. Only patients with persistent (> one month) or recurrent OJ should undergo so form of surgical biliary drainage. It is no longer necessary to treat patients with an elevated Alkaline Phosphatase regardless of how long that may have been present\textsuperscript{15}.

The confirmed mechanism of drainage is currently surgical bypass. Endoscopic therapy has not been shown to be durable and requires multiple interventions. The introduction of biodegradable stents and even full covered stents that can be removed is a potential endoscopic solution, but needs further evaluation before it can be recommended as the standard of care. In the presence of an acute complication of OJ such as cholangitis, endoscopic stenting remains the treatment of choice.

The correct approach to the patient who presents with isolated Obstructive jaundice (without pain) is still controversial and ranges from a biliary bypass alone to surgery that addresses the pathological consequence of the CP and may require a pancreas directed operation in addition to the biliary bypass\textsuperscript{16}. The evidence supporting one or other approach to the bypass is also not well defined. In a PD the biliary tree will be resected and reconstructed.

In Duodenal preserving operations the options include draining the biliary tree into the cored out head of the pancreas or a supra-duodenal hepatico-enterosotomy. Our own evidence suggests a reduced recurrence rate in the latter.

**Pseudocysts**

Only symptomatic pseudocysts need to be treated. Neither the size of the cysts nor the duration of the pseudocysts can be considered indications for treatment. However larger cysts are more likely to be symptomatic and as such are more likely to be treated. The evidence supporting a single approach is not available.
The treatment varies from endotherapy, particularly via EUS, including aspiration and cyst enterostomy to surgical management of the CP. The issue is the durability of pseudocyst resolution. The primary pathology resides in the pancreas itself and not the pseudocyst, which may however, be the source of the symptom. As such when open surgery is considered the approach should be directed at the pathology of the chronic pancreatitis and the pathological consequences\textsuperscript{16}.

**Vascular complications**

Vascular complications occur in 15-30%. They range from pseudo-aneurysms to the consequences of venous occlusion due to the inflammatory reaction. The clinical presentation with pseudo-aneurysms includes Haemosuccus pancreas and upper GIT bleeding as well as free intra peritoneal rupture. Acute exacerbation of pain may result from a bleed into an established pseudocyst. After a mucosal lesion in the foregut is excluded a CT angiogram is mandatory and should be followed by a formal angiogram to embolise the artery where possible. There is no evidence indicating whether this procedure should be routinely followed by any intervention to address the CP. It is not considered an indication for definitive surgical treatment in our unit.

In the presence of portal hypertension surgery should be avoided due to an increased morbidity rate as it is very difficult surgery.

Varicose transformation of the portal vein in the porta hepatis is a relative contraindication to surgery. If surgery is going to be required in patients with vascular complications, it should be performed as early as possible in the course of the disease.

**TIMING OF SURGERY**

The presence of PHT raises the question regarding operating on patients with symptomatic CP earlier in the course of the disease. There is a growing body of evidence suggesting that this consideration should be entertained in a number of circumstances.
Pancreatic Function
The prevalence of endocrine and exocrine insufficiency differs in different series. There is however good evidence that there is deterioration in both endocrine and exocrine insufficiency post operatively. The rates differ again with different operations. It is not known if the cause for the deterioration is due to the surgery itself or is an expression of the natural history of the CP which is not halted by the surgery.

In the 1980s and early 1990s Nealon and his coworkers did a small RCT which demonstrated that in early surgery the functional deterioration from the CP was arrested. Unfortunately this evidence was not confirmed in other trials\textsuperscript{17}.

Other evidence suggests that early surgery can improve glycaemic control. While the current evidence does not support a definitive indication for earlier surgery, this issue should be further investigated.

Preoperative Opiate Use
In many patients with CP there is an underlying substance abuse problem and this includes alcohol abuse. There may be an underlying dual psychiatric disorder driving the substance abuse.

The chronic pain may result in a major depression which aggravates the substance abuse, which in return aggravates the alcohol abuse and the progression of the CP. When opiates are introduced as medical management for the pain, as recommended by the WHO pain ladder, the alcohol abused can be swopped for opiate abuse. This seems to be especially true when Pethidine is used for pain control.

There are a number of studies that have shown that there is reduced pain control following surgery in patients who used opiates preoperatively. The severity of the post-operative pain is greater as is the need for opiates in the long-term post-operative period\textsuperscript{18}. This evidence is compelling and suggests that opiates should be avoided in the preoperative period. Should a patient require opiates, earlier surgery should be seriously considered to support a better outcome.
Malignant Transformation
The causal relationship between CP and PDAC is well established. There is a 10-25 fold increase in malignant transformation in sporadic forms of the disease and a 40-70 fold increase in hereditary CP. The role of early surgery in preventing this event is unknown. A recent retrospective review from Japan suggested that the incidence of PDAC was reduced from 5% in patients not receiving surgical therapy, to 0.7% in patients who did have surgery\textsuperscript{19}.

There is a growing body of evidence to support early surgery but at this stage this cannot be adopted as standard of care.

Continued Alcohol Consumption
Should we still be operating on patients who continue to consume alcohol? In other pathologies the data is clearer regarding treatment in the presence of a persistent aetiological agent. In liver cirrhosis and transplant, ongoing substance abuse has been shown to result in a poorer outcome. There has been much debate about the ethics of vascular surgery in patients who continue to smoke.

In CP, due to alcohol abuse, the evidence is not very clear. Some studies have demonstrated an increased relative risk of developing severe pain in patients who stop consuming alcohol\textsuperscript{20}. Our own data confirmed this view\textsuperscript{21}. There have been a number of RCT comparing PD to duodenal preserving head resections and comparing the different duodenal preserving operations. In these relatively small studies there has been very long term follow up to 16 years. These authors clearly showed a statistically significant correlation between ongoing alcohol consumption and worse outcomes regardless of the operation performed.

There is evidence supporting abstinence and stopping to smoke cigarettes with improved outcomes from non-operative management of CP. As the operations do not halt the actual pathological process but rather address the pathological consequences in CP, this supports the view that abstinence is important. In the addiction literature there is a question regarding the extent of the abstinence and I would assume therefore that a similar question would arise in CP.
Employment

The causation of this disease and its prevalence in the working class communities requires that employment rehabilitation is an essential issue in considering the outcome of any therapeutic regime.

The chronic pain and the long duration of pain before surgery is performed, usually results in a poor work history and many of these patients are retrenched. When they are employed post operatively, it is often into high risk occupations.

As such employment rehabilitation is a very difficult outcome to achieve. In addition, in South Africa the nature of the social disability grant often results in a perverse incentive for the patient to report poor outcomes with treatment. As such “employability” as defined by the absence of the requirements to access social grants, is used to measure this outcome. Again, it is possible that operating on patients before these negative circular events are entrenched may improve outcomes.

SUMMARY

The indications for surgery in CP are well defined, however Level 1 evidence is missing in most instances. Medical management of pain is the first line but is complex and requires an MDT. The outcome from surgery should focus beyond pain relief and quality of life should become the standard for reporting treatment outcomes. The timing of surgery is unclear but there is some evidence that suggests we should be operating earlier than later.

Table 1: Aim of Treatment in Chronic Pancreatitis

<table>
<thead>
<tr>
<th>Aim of Treatment</th>
<th>Details</th>
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<tbody>
<tr>
<td>Pain relief</td>
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<tr>
<td>Control of local complications</td>
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<tr>
<td>Preservation of function</td>
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<tr>
<td>Social and occupational rehabilitation</td>
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<tr>
<td>Focus only on pain relief is not always appropriate</td>
<td></td>
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<tr>
<td>Improved quality of life</td>
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<tr>
<td>Exclude malignancy</td>
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Table 2: Duodenal Preserving Pancreatic Head Resections

- Frey DPPHR
- Beger DPPHR
- Izbicki "V" Plasty
- Hamburg modification

REFERENCES


