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Review of Coeliac Plexus Blockade for the Management of Chronic Pancreatitis Pain at Tallaght University Hospital (TUH)

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Abstract

Background: Pain is a major problem for patients suffering from chronic pancreatitis. Unfortunately, medical therapy often fails to adequately control pain. Coeliac plexus block (CPB) is sometimes performed to treat intractable pain in patients with chronic pancreatitis. **Aims:** Our primary objective was to determine the effect of CPB for pain management in a cohort of patients with chronic pancreatitis. We also sought to quantify opioid use in patients with chronic pancreatitis. **Methods:** We reviewed the database of pain referrals for chronic pancreatitis and recorded opioid use for each patient. We interviewed all patients who underwent CPB for chronic pancreatitis at TUH from January 2018-December 2020. Effect of the block, duration of pain relief, analgesia requirements, complications and patient satisfaction were recorded. **Results:** 62 inpatient referrals were made to the pain service over a 3-year period regarding pain management in chronic pancreatitis. 76% of patients referred for chronic pancreatitis pain management require regular long-term opioids. Mean daily oxycodone requirement in this group was 52 mg. 11 of these patients underwent CPB over a 3-year period. Mean age of patients who underwent CPB was 44 years. Effective reduction in pain scores (>50% improvement) was achieved in 7 of 11 patients. The mean NRS pain score decreased from 9.2 (±0.9) to 4.4 (±3.1). Mean duration of pain relief experienced was 69 days. Transient diarrhoea was reported by 1 patient. 4 patients reported a temporary decrease in oral analgesia requirement, while 3 patients reported a sustained decrease in analgesia requirement post CPB. For those who had further CPBs, the effect of repeated interventions was comparable to

the initial procedure. **Conclusion:** High regular opioid consumption is common in patients with chronic pancreatitis. CPB can provide significant improvement in pain control and quality of life in appropriately selected patients. CPB can assist with opioid reduction and containment. It is not effective in all cases and there is high inter-patient variability. The procedure has a good safety profile.

Keywords

Coeliac Plexus Block, Chronic Pancreatitis, Chronic Pain, Opioid Analgesia, Opioid Reduction

1. Introduction

Chronic pancreatitis is a progressive, inflammatory, malabsorptive disease of the pancreas [1]. It is defined as a pathologic fibro-inflammatory syndrome of the pancreas in individuals with genetic, environmental and/or other risk factors, who develop persistent pathologic responses to parenchymal injury or stress [2]. There is progressive destruction of the acinar and islet cells, calcification and formation of scar tissue with resultant deterioration of exocrine and endocrine pancreatic function. Alcohol-related pathology is the predominant aetiology in Ireland and worldwide. Other aetiologies include genetic mutations, hyperlipidaemia, ductal obstruction, cystic fibrosis, hypercalcaemia and autoimmune diseases, while some are "idiopathic" [3]. Life-altering consequences of chronic pancreatitis include osteoporosis, type 3c diabetes and opioid dependency due to the treatment of chronic pain [4] [5]. The natural history of the disease is characterised by intractable pain, malabsorption, malnutrition, periods of symptomatic flare-ups and intermittent remission, reduced quality of life and shorter life expectancy. These contribute to a markedly reduced median survival of 15 - 20 years post-diagnosis [6]. Mean age of diagnosis of the disease is 41 - 45 years [6].

Chronic disease can be described as a progressive medical condition lasting more than three months. Chronic pancreatitis is a chronic disease. It can be treated and managed but not cured. Chronic pancreatitis requires a coordinated long-term response. It carries a significant resource burden due to the length and complexity of treatments with repeated primary care visits, frequent hospital admissions, risks associated with poly-pharmacy and complex co-morbidities. The estimated prevalence of chronic pancreatitis in Ireland ranges from 11.6 per 100,000 population to 13.4 per 100,000 population (in 2009 and 2011 respectively) [7]. Tallaght University Hospital (TUH) is the national centre for the management of chronic pancreatitis in Ireland.

GPs have a major role in treating chronic pain as well as determining the need for escalation of care by providing a conduit between home and hospital [8]. Regarding hospital-based care, the complex nature of the disease means it is best managed by a dedicated multidisciplinary team including surgeons and gastro-

enterologists, with input from other specialities. The goals of treatment include pain management, correction of pancreatic insufficiency and management of complications. Patients require ongoing multidisciplinary follow-up, which should take place at least annually [9].

Chronic pancreatitis typically presents as chronic unrelenting abdominal pain with episodic flares. Pain management in chronic pancreatitis is complex. As a general rule, pain management should proceed in a stepwise approach [10]. This begins with general recommendations involving patient education, reinforcement of lifestyle changes (smoking and alcohol cessation) and dietary intervention. The next step is pancreatic enzyme replacement therapy to suppress pancreatic exocrine secretion and judicious titration of analgesia. However, pharmacologic therapy isn't always adequate for pain control. Patients suffering from severe pain refractory to the above measures may be considered for more invasive therapeutic options such as coeliac plexus block (CPB).

The primary aim of this review was to follow up patients who underwent CPB in order to assess its utility as an intervention for pain management in chronic pancreatitis. Secondary objectives included tabulation of opioid use in patients with chronic pancreatitis and the effects of CPB on opioid requirement in this patient cohort.

2. Methods

The database of referrals to the pain service from January 2018 to December 2020 was reviewed. All referrals relating to pancreatic pain were studied. Referrals relating to pancreatic cancer were excluded. All subjects enrolled had documented chronic pancreatitis and presented with abdominal pain. The average daily analgesic requirement of each referral to the pain service was tabulated using patient notes, medication charts, clinic letters and drug prescriptions. Using an opioid conversion table, the equi-analgesic 24-hour opioid consumption for oxycodone was calculated for each patient who was reviewed by the pain team [10].

All patients who underwent percutaneous CPB at TUH, during 2018-2020, for pain management of chronic pancreatitis were identified. The theatre lists for pain procedures performed at TUH during this time were obtained and compared to the referral database to ensure all cases were identified. The interventional radiology and gastroenterology department databases were also reviewed.

Patients who had undergone CPB were contacted by telephone and underwent a standardised 7-part telephone questionnaire. As no standardised, validated survey exists to evaluate outcomes after CPB, we formulated a 7-part telephone questionnaire using physician expertise. This was designed to target the key elements relevant to CPB experience.

The questionnaire used was as follows:

1) Was there immediate relief? (*i.e.* within <48 hours)

2) Did you experience pain relief > 50% from baseline?

3) How long did the pain relief last?
4) Did you experience any side effects?
5) Did you have a subsequent decrease in oral analgesia requirements?
6) What follow-up did you receive after your procedure?
7) Would you have a CPB performed again?

3. Results

There are 280 patients diagnosed with chronic pancreatitis currently on the register at TUH, as a centre for this orphan disease. A total of 62 inpatient referrals were made to the pain service over a 3-year period (2018-2020 inclusive) regarding pain management for chronic pancreatitis. The overall total number of inpatient referrals to the pain service during this period was 1115 (393 in 2018, 357 in 2019, 365 in 2020). An average of 31 inpatient referrals are made to the pain service each month of which 2 are for chronic pancreatitis management. Of the 62 patients who were referred to the pain service with chronic pancreatitis, 47 use regular daily opioids for chronic pain. Of those using regular daily opioids, the mean equivalent daily oxycodone consumption was 52 mg.

Nineteen patients underwent CPB at TUH from January 2018 to December 2020. Some patients received more than 1 block. In total 24 CPBs were performed during this time. Of the 19 patients who underwent a CPB at TUH, 11 were for chronic pancreatitis, 2 were for pancreatic carcinoma and 6 were for chronic abdominal pain related to upper abdominal organs other than the pancreas. This review focuses solely on the outcomes for patients being treated for chronic pancreatitis.

Eleven patients received CPBs over the 3-year period as an adjunct to pain control for chronic pancreatitis. Mean age of patients who underwent CPB was 44 years (range 20 - 78 years). Regarding the underlying cause of chronic pancreatitis in those who underwent CPB, 6 were secondary to alcohol, 3 were idiopathic, 1 was gallstone-related and 1 was secondary to ERCP (see **Table 1**). Of the group who underwent CPB, all were taking some form of regular daily opioids. The mean equivalent daily oxycodone requirement in this group was 39 mg prior to CPB. There was a small decrease in overall mean equivalent daily oxycodone requirement in the CPB group from 39 mg to 35 mg after the intervention.

From the 11 patients who underwent CPB for chronic pancreatitis, 9 of 11 experienced immediate relief. Immediate relief was defined as an improvement in the severity or characteristic of pain within 48 hours of the block being performed. This is considered a diagnostic block as it gives an indication of the origin of the pain. Seven of 11 experienced pain relief > 50% from baseline (see **Table 2**). Using a simple Numerical Rating Scale (NRS) of 0 - 10, we asked patients to identify the number that best fitted their pain intensity [11] [12]. The mean NRS pain score decreased from 9.2 (±0.9) to 4.4 (±3.1) ($p \leq 0.05$) after CPB. Pain relief lasted on average 69 days from the time of the first block performed on each patient (range 0 - 240 days) (see **Graph 1**).

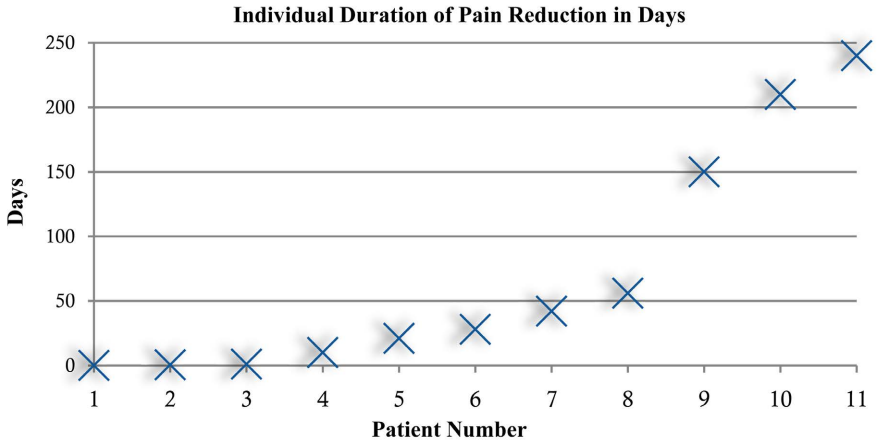
Table 1. Patient demographics.

Patient Number	Age (years)	Gender (Male/Female/Non-binary)	Ethnicity (White/Black/Hispanic)	Aetiology of chronic pancreatitis
1	20	Male	White	Idiopathic
2	48	Female	White	Alcohol
3	60	Male	Hispanic	Alcohol
4	78	Female	White	Gallstones
5	56	Female	White	Post-ERCP
6	21	Female	White	Idiopathic
7	43	Female	White	Alcohol
8	40	Male	White	Idiopathic
9	36	Male	White	Alcohol
10	57	Male	White	Alcohol
11	36	Female	White	Alcohol

Table 2. Results.

Patient Number	Immediate relief (Y/N)	Relief > 50% (Y/N)	Duration of pain reduction (days)	Willing to have repeat CPB (Y/N)	Mean equivalent daily oxycodone requirement pre-CPB (mg)	Mean equivalent daily oxycodone requirement 9 months post-CPB (mg)
1	N	N	0	N	80	80
2	Y	N	1	Y	10	10
3	Y	Y	240	Y	10	0
4	Y	Y	28	Y	10	10
5	Y	Y	150	N	20	20
6	Y	Y	56	Y	40	40
7	Y	Y	210	Y	70	40
8	Y	Y	21	Y	40	30
9	Y	N	42	Y	90	90
10	N	N	10	Y	40	40
11	Y	Y	0	Y	20	20

Six of 11 reported a subsequent decrease in their oral analgesia requirement. One patient noted a brief increased analgesic requirement post block. Of the 6 who reported a decrease in their analgesic requirements, 3 up-titrated their analgesia as the effect of the block weaned and returned to their baseline analgesia doses. Three patients reported a return to an analgesia requirement that was less than their requirement before the block, representing a sustained decrease in daily analgesia requirement (see Table 2).



Graph 1. Individual duration of pain reduction.

Nine of 11 reported that they would be happy to have the block performed again. The side-effect profile from CPB was unremarkable. Patients were questioned specifically about diarrhoea, light-headedness, pain, infection, bleeding, nerve injury, and breathing difficulty. 1 patient reported bilious vomiting on the evening post-procedure. Another patient reported gastrointestinal disturbance and diarrhoea lasting for two days after the procedure but otherwise there were no other reported adverse effects. Follow-up post CPB was variable. Five of 11 were followed up directly by the pain service after CPB, while 6 were followed up by their surgical team alone. Covid-19 was cited as a reason for inability to attend pain service follow-up in 2 cases.

Two patients who had received CPBs went on to receive pulsed radiofrequency ablation (RFA) of the splanchnic nerves. Their initial duration of pain relief after CPB was 2 days and 4 weeks respectively. Their subsequent response to splanchnic nerve RFA was 2 weeks and 10 weeks respectively.

4. Discussion

Pain management in chronic pancreatitis is a complex issue and accordingly represents a significant proportion of the workload of our pain service. 5.6% of the referrals received by the pain team at TUH, during 2018-2020, were related to chronic pancreatitis. The pain may range from occasional postprandial discomfort to debilitating persistent pain associated with nausea, vomiting and weight loss. The pathophysiology of this pain is incompletely understood and pain control can be difficult in some cases. Current concepts in the pathogenesis of pain in chronic pancreatitis include neuronal damage leading to peripheral sensitization and resultant central sensitization, leading to the development of persistent, often refractory pain [13].

The typical pathway involved referral from the General Surgery team either as an inpatient or for outpatient follow-up. Patients were assessed on a case-by-case basis by the pain team. Initial management steps involved offering lifestyle advice and rationalising oral analgesia regimens. The WHO analgesic ladder pro-

vides a logical and consistent framework for the initiation of analgesic medication in the management of pain [14]. Typical oral analgesia regimens included paracetamol, an NSAID (ibuprofen or diclofenac), increasing doses of oral opioids (oxycodone or Targin) and addition of either a tricyclic antidepressant (amitriptyline or nortryptilline) or a gabapentinoid (pregabalin or gabapentin). These were adjusted and titrated based on effect and patient tolerance. Adjuvant therapy with pregabalin has been shown to decrease short-term pain scores and short-term opioid use in people with chronic pain due to chronic pancreatitis, due to the neural origin of the pain [15] [16]. Amitriptyline and nortriptyline have also been shown to reduce daily pain and can help to alleviate co-existent depression and may potentiate the effect of opioids [17]. During episodic flares, short-term hospitalization with the patient kept fasted to minimise pancreatic stimulation is also of benefit in breaking the pain cycle.

Seventy-six per cent of patients referred for pain management secondary to pancreatitis were taking regular long-term opioids. Of these, the average equivalent opioid consumption was 52 mg oxycodone in 24 hours. This demonstrates that high opioid use is a major issue in those suffering with chronic pancreatitis. Opioids are associated with side effects such as nausea and constipation and carry concerns of misuse and dependence. However, chronic opioid analgesia is often required and unavoidable in patients with persistent significant pain. The extent to which patients should be maintained on analgesics before pursuing more aggressive options is a matter of clinical judgment. There may be an argument for earlier use of CPB and further development of RFA to contain opioid prescription given the well-documented concerns with opioid use in chronic conditions. Patients returned to the outpatient clinic to monitor their response to oral analgesia and some were offered CPB.

The coeliac plexus is the main junction for autonomic nerves supplying the upper abdominal organs. It is made up of a dense network of nerve fibres from T5-T12. The plexus includes right and left coeliac ganglia that lie anterolateral to the aorta at the origin of the coeliac trunk on either side of the body of the L1 vertebra, and posterior to the pancreas. The coeliac plexus receives nociceptive impulses transmitted from the pancreas via afferent fibres through the spinal cord to thalamus and cortex of the brain, and this information is perceived as pain. These impulses can be blocked with local anaesthetic or neurolytic techniques for treatment to break the cycle of sympathetically mediated pain associated with pancreatic cancer or pancreatitis [13].

There are a number of different approaches to the block (see **Figure 1**). Both anterior and posterior approaches may be used to access the plexus depending on operator preference and the safest route of access for an individual patient. Posterior approaches include the paravertebral and trans-aortic approaches. Endoscopic Ultrasound (EUS)-guided CPB has been increasingly utilized in clinical practice also. The endoscopic route targets the coeliac plexus from the anterior approach. The advantage of percutaneous technique is that it is less invasive and requires less sedation.

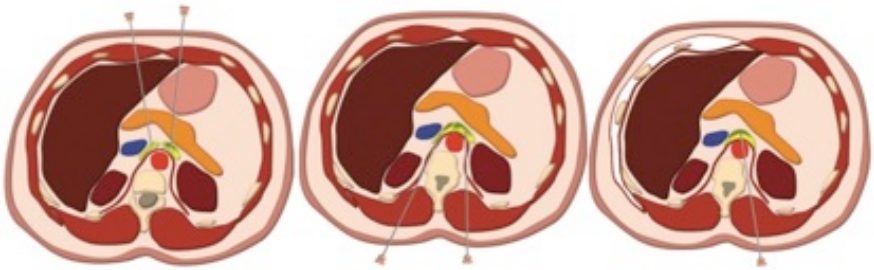


Figure 1. Diagrammatic representation of approaches to the coeliac plexus. From left to right: Anterior approach, bilateral posterior paravertebral approach, posterior trans-aortic approach [18].

The approach primarily adopted at TUH is the posterior paravertebral retrocrural approach (see **Figure 2**). For this approach, the patient is placed in the prone position. The insertion point is just below the tip of the 12th rib approximately 8 cm from the midline. After LA infiltration of the superficial layers, a 100 - 150 mm needle is inserted and directed medially towards the body of the L1 vertebra under image-intensifier guidance. The needle is inserted until it comes into contact with bone. It is then withdrawn, redirected anteriorly and advanced 2 - 3 cm further, taking care to avoid the aorta and IVC. The position is confirmed by the spread of radio-opaque dye. Typically, a needle is also inserted on the contralateral side with half the volume administered by this approach to improve spread (see **Figure 2**). Twenty mls 0.25% plain bupivacaine + 40 mg methylprednisolone are usually injected through each needle around the coeliac plexus, resulting in a total volume of 40 mls of local anaesthetic injected. This blocks nociceptive impulse transmission, interrupting the cycle of pain in chronic pancreatitis. Depending on the spread of injectate visualised by the operator, a single injection technique can be used with half the volume administered. Safe injection technique is used with aspiration before injecting and administration of a test dose. The retrocrural approach employed at TUH has the theoretical advantage of allowing the injectate to diffuse along the splanchnic nerves. In chronic pancreatitis where there is a pain of neuropathic nature without significant anatomical distortion like that seen with invasive pancreatic tumours, it may be that the interruption of splanchnic nerve transmission is an important contributor to the efficacy of our CPBs. Further study of RFA of the splanchnic nerve is required to better understand its' role in chronic pancreatitis pain and a prospective randomised control trial investigating its' effects is needed.

Each patient referred to the pain service was reviewed and those who were deemed appropriate were offered CPB. In total, 11 patients with chronic pancreatitis underwent CPB. All were consuming regular opioids. However, the average opioid consumption in the injection group was not seen to be greater than those who were not offered intervention, indicating that high regular opioid requirement alone was not a sole indication for selection for CPB. Regarding the characteristics of the patients who were selected for CPB, the intervention was

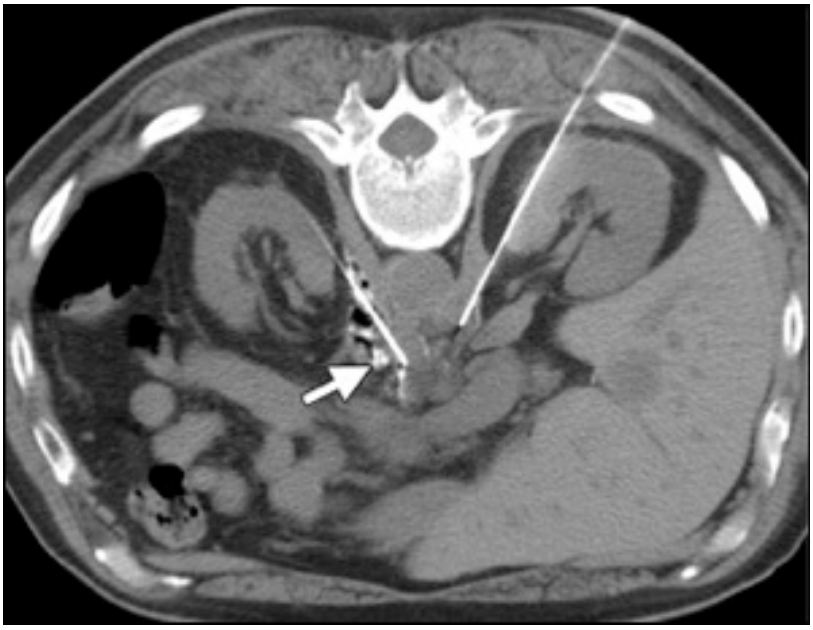


Figure 2. Axial CT showing bilateral posterior paravertebral approach [18].

offered to those who it was felt might benefit most from CPB-typically those who reported reduced quality of life, high pain scores despite repeated trials of oral analgesia, or were intolerant of oral analgesia. All patients selected for CPB were experiencing limitations on their activities of daily living and reduced ability to carry on normal social and work functions and wished to pursue nerve blockade to attempt to manage their pain.

The process of performing a CPB involves arranging a day-case slot on the weekly interventional pain list. A consultant anaesthetist and skilled assistant were present for all blocks. Patients were attached to standard peri-operative monitoring as per AAGBI guidelines with full resuscitation equipment available [19]. The procedure involved intravenous conscious sedation with either midazolam or propofol. Oxygen was administered to all patients undergoing sedation. The block also required a radiographer due to the use of an image intensifier with contrast to confirm correct needle placement. Full aseptic conditions were used for all blocks. Following the procedure, patients were transferred to the recovery room for a 1 to 2 hour period where they were observed for signs of peritonitis or hypotension.

We can see that the impact of CPB as a utility for the management of chronic pancreatitis was variable. Some patients reported little to no benefit from the procedure while others reported improved pain scores for several months afterwards. Possible reasons to account for this include disease variation, anatomical variation and procedural variation. Encouragingly, 3 patients reported a sustained decrease in daily analgesia requirement and opioid reduction. 1 patient achieved complete cessation of opioid use. This may have been attributable to the effects of the block in breaking the pain cycle, but may also represent an overall improvement in their chronic pancreatitis disease progression.

Of patients who received 2 or more CPBs, those who received significant pain relief from their first block were more likely to experience further relief from subsequent blocks. This is consistent with existing literature regarding repeat blocks, where response to subsequent blocks shows association with response to the first CPB [20]. Although our numbers are limited, patients who did not experience significant relief from their first CPB did not benefit more from repeat procedures.

The risks and benefits of the procedure must be balanced carefully. Orthostatic hypotension due to sympathetic blockade is the most common side effect. Diarrhoea can also occur due to sympathetic blockade and unopposed parasympathetic efferent influence. Incorrect needle placement can result in intravascular, intrathecal or epidural injection. Puncture of the aorta, coeliac artery or IVC can cause retroperitoneal haemorrhage. Damage to the kidneys, adrenals or other upper abdominal organs with abscess or cyst formation may occur. Other risks include nerve root injury, sexual dysfunction, paraplegia and local anaesthetic toxicity. Of course, the risk of an unsuccessful block can be considered a complication in itself, and each patient was counselled on this beforehand.

In our patient cohort, complications observed were minimal. Hypotension was rare. This was likely due to adequate hydration pre-procedure, and ongoing monitoring with administration of intravenous crystalloids ± vasopressor boluses if required. All patients had a lying and standing BP recorded before mobilising on the day ward or inpatient ward to prevent orthostatic syncopal episodes. Pain was not reported by any of the patients interviewed. Overall, morbidity associated with the procedure was encouragingly low. CPB can be performed as a day-case and patients were discharged post-procedure provided there were no complications. While it is not without risk and although the outcomes are variable, it shows promise as a safe and effective technique.

There was a high level of patient satisfaction reported regarding the overall experience of the block. Nine of 11 patients reported that they would be happy to undergo the procedure again. 1 patient did not wish the block to be performed again because they did not experience any significant improvement from the block; the other felt their pain was satisfactorily controlled now and that a further block would be unnecessary. Of note, 3 patients who did not experience any long-lasting pain relief from the block expressed willingness to have the block repeated despite the limited impact of their initial CPB.

In centres around the world, percutaneous blocks have been performed both by anaesthesiology/pain specialists and by interventional radiologists [21]. However at TUH this shared practice is not evident. All percutaneous CPBs performed at TUH were undertaken by one of two pain specialists trained in this procedure. EUS-guided CPB has also developed popularity in some centres as a safe alternative that allows for direct visualization and targeting of the coeliac ganglia [21]. Outcomes appear to be similar to percutaneous techniques although evidence is limited in this area [22] [23] [24]. At our institution, EUS-guided CPBs are performed very infrequently, and appear to have fallen out of

favour as a therapeutic intervention. The rare EUS-guided CPBs that have been undertaken here in recent years have been done opportunistically, and at the discretion of individual operators for symptom management, rather than for patients who have been specifically referred for treatment of chronic pancreatitis pain. Due to the low number of EUS-guided CPBs performed at our centre it was not possible to make any meaningful comparison of outcomes versus percutaneous CPBs.

Rhizotomy and RFA of the splanchnic nerves has also been described for control of both malignant and non-malignant chronic abdominal pain. One small single centre study showed encouraging outcomes for patients with chronic pancreatitis pain refractory to medical management who underwent percutaneous RFA of the splanchnic nerves [25]. The number of patients who underwent this procedure at our centre was too small to draw reliable conclusions but the response was encouraging. This is an area for further research to compare outcomes in patients who received traditional CPB versus those who underwent RFA of the splanchnic nerves, to investigate if we should perform a greater frequency of splanchnic nerve ablations in patients with chronic pancreatitis. There is insufficient evidence at present to compare splanchnic nerve RFA to CPB. Given that CPBs only last for an average of 69 days, RFA holds potential as an intervention with longer duration of pain reduction. It should be noted however that this procedure is more technically challenging and carries with it an increased risk of adverse outcomes such as pneumothorax.

This review documents the use of CPB at TUH as a therapeutic intervention for management of pain secondary to chronic pancreatitis. Limitations of this study include small sample size. This is still a relatively uncommon procedure so the number of patients on whom data can be collected was small. This limits the power of our review in drawing conclusions about the overall efficacy of CPB and impacts the external validity. As this study was conducted using retrospectively collected data, there was significant possibility for recall bias where the telephone questionnaire was conducted a significant period of time after the procedure. A prospective study looking at this question would be more informative. Finally, there is no standardised, validated survey that exists for patient follow-up post CPB.

The findings of this single-centre review of CPB practice support the evidence that significant temporary relief is certainly achievable in some patients, while some patients experience minimal or no relief. Prediction of block failure is a challenge. Severity of disease and previous surgery are possible factors in failure of the block. Further study is necessary to help aid patient selection and to identify predictors of block outcome in order to allow more common use in the setting of chronic pancreatitis. In patients who have a good result from a nerve block, the duration of relief is time-limited and showed considerable variability. However, given the limitations of conservative and surgical treatments for chronic pancreatitis pain, CPB should still be considered as part of a multimodal analgesic strategy.

5. Conclusions

High regular opioid consumption is very common in patients with chronic pancreatitis.

Percutaneous CPB can offer an effective option as a time-limited analgesic adjunct in chronic pancreatitis. CPB can assist with opioid reduction and containment. Outcomes are variable with high inter-patient variability.

Considering the overall healthcare burden of chronic pancreatitis, the potential of CPB as an intervention to reduce primary care visits and repeat hospitalisation is significant.

Conflicts of Interest

There were no other competing interests involved in this research. There was no support from any organisation for the submitted work and no other relationships or activities that could appear to have influenced the submitted work.

Availability of Data and Material/Data Transparency

This manuscript is an honest, accurate, and transparent account of the study being reported. No important aspects of the study have been omitted. Any queries should be directed via email to the corresponding author where all collected data is available on request.

Ethics Approval

This study was reviewed and is fully compliant with the ethical guidelines of the SJH/TUH Joint Research Ethics Committee.

Consent to Participate

All participants who participated in telephone interviews during the data collection phase of this study gave their full verbal informed consent for their participation and the anonymous use of their responses in data analysis and reporting.

Consent for Publication

The corresponding author has the right to grant on behalf of all authors and does grant on behalf of all authors, an exclusive licence to the Irish Journal of Medical Science to permit this article (if accepted) to be published in IJMS editions.

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