REVIEW

Bridging clinic: The initial medical management of patients with newly diagnosed pancreatic cancer

Loveena Sreedharan,¹ Bhaskar Kumar,² Anna Jewell,³ Paul Banim,⁴ Andreas Koulouris,⁵ Andrew R Hart⁶

► Additional material is published online only. To view, please visit the journal online (<http://dx.doi.org/10.1136/flgastro-2018-101002>).

¹ST Upper GI Surgery, East of England Deanery, UK

²Upper GI Surgery, Norfolk and Norwich Hospital, Norwich, UK

³Pancreatic Cancer UK, London, UK

⁴James Paget University Hospitals, Great Yarmouth, Norfolk, UK

⁵Academic Clinical Fellow in Gastroenterology, Norfolk and Norwich Hospital, Norwich, UK

⁶Gastroenterology, Norfolk and Norwich Hospital, Norwich, UK

Correspondence to

Miss Loveena Sreedharan, Speciality Trainee General Surgery, East of England Deanery, Norwich NR9 3AW, UK; loveenasree@hotmail.com and Professor Andrew R Hart, University of East Anglia, Norfolk and Norwich Hospital Norwich UK; a.hart@uea.ac.uk

Received 18 April 2018

Revised 11 September 2018

Accepted 12 September 2018

Published Online First

9 October 2018

► <http://dx.doi.org/10.1136/flgastro-2019-101192>

© Author(s) (or their employer(s)) 2019. No commercial re-use. See rights and permissions. Published by BMJ.

To cite: Sreedharan L, Kumar B, Jewell A, et al. *Frontline Gastroenterology* 2019;**10**:261–268.

ABSTRACT

Pancreatic cancer is the 11th most common cancer in the UK and has the worst prognosis of any tumour with minimal improvements in survival over recent decades. As most patients are either ineligible for surgery or may decline chemotherapy, the emphasis is on control of symptoms and management of complications such as poor nutritional status. The time period between informing the patient of their diagnosis and commencing cancer treatments presents a valuable opportunity to proactively identify and treat symptoms to optimise patients' overall well-being. The 'bridging clinic', delivered by a range of healthcare professionals from gastroenterologists to nurse practitioners, can provide this interface where patients are first informed of their diagnosis and second supportive therapies offered. In this article, we provide a structure for instituting such supportive therapies at the bridging clinic. The components of the clinic are summarised using the mnemonic INDASH (Information/Nutrition/Diabetes and Depression/Analgesia/Stenting/Hereditary) and each is discussed in detail below.

INTRODUCTION

Pancreatic cancer (PC) is the 11th most common cancer in the UK and has the worst prognosis of any tumour with minimal improvements in survival over recent decades.^{1 2} The overall 5-year survival rate is <5%.³ Worldwide, PC is the fourth most common cause of cancer-related death with 266 000 annual fatalities. Clinically, patients are classified into those with lesions that are surgically resectable or locally advanced or metastatic, with only 15% presenting at a resectable stage.³ The surgical options are pancreatico-duodenectomy (Whipple's procedure) or a distal pancreatectomy. The management of non-resectable cancer in patients

with a good performance status is usually gemcitabine monotherapy, although recently chemotherapy with combination of FOLinic acid (leucovorin), Fluorouracil, IRinotecan and OXaliplatin has increased the median survival from 6.8 to 11 months.⁴ However, as most patients are either ineligible for surgery or may decline chemotherapy, the emphasis is on control of symptoms including pain and management of medical complications such as poor nutritional status.⁵

The time period between informing the patient of their diagnosis and commencing surgery or palliative treatments presents a valuable opportunity for health professionals to proactively identify and treat symptoms to optimise patients' overall well-being. The 'bridging clinic' can provide this interface where patients are further assessed and supportive therapies offered. In this article, we provide a structure for instituting such supportive therapies at the time of diagnosis. The aim of this clinic is mainly to identify and address the effects of PC sooner in order to alleviate a variety of highly troublesome symptoms that are often overlooked. Depending on local practice, the initial breaking bad news appointment may precede the bridging clinic appointment or may be included in the clinic. Either way the main aim of the bridging clinic is to ensure patients are more amenable both physically and mentally to consider future treatment chemotherapy/surgery at their subsequent consultations with surgeons and oncologists. Recently, the National Institute of Clinical Excellence (NICE) has made up-to-date recommendations on the management of patients with PC.⁶ The components of the bridging clinic closely mirror NICE recommendations and provide a practical structure to its

Box 1 Guidance on information to be given at the bridging clinic appointment

Information

- ▶ Involvement of the Cancer Nurse Specialist from the outset.
- ▶ Ideally inform the patient of their diagnosis at a separate initial consultation.
- ▶ Information should be given at all times with compassion and empathy.
- ▶ Encourage patient to be accompanied by a relative/friend to their appointment.
- ▶ Discuss potential options for their treatment and care.
- ▶ Use clear terminology and avoid medical jargon.
- ▶ Make available written information for patients to review after their appointment.
- ▶ Signposting to organisations providing high-quality, evidence-based information.
- ▶ Telephone advice and comprehensive literature (Pancreatic Cancer UK, Pancreatic Cancer Action and Pancreatic Cancer Scotland).

implementation. These components are summarised using the mnemonic **INDASH** (Information/Nutrition/Diabetes and Depression/Analgesia/Stenting/Hereditary) and each is discussed in detail below.

INFORMATION

The bridging clinic appointment in most cases may follow on from an initial 'breaking bad news' consultation during which, the patient was informed of the diagnosis. The initial consultation may not always be led by a medical gastroenterologist but a variety of medical professionals based in either primary or secondary care depending on local arrangements. A separate initial 'breaking bad news' appointment would allow the patient to deal with the initial shock of the diagnosis and to attend the bridging clinic appointment in a mentally more prepared state and accompanied by a friend(s)/relative wherever possible. The bridging clinic appointment therefore is best incorporated into the cancer pathway after initial consultation. The patient will need to be advised to be accompanied by friend(s)/relative at the bridging clinic appointment. A diagnosis of PC can be devastating, especially as the treatment options may be limited and involvement of the cancer nurse specialist (CNS) in the bridging clinic is essential. The information should always be provided with compassion, empathy and in privacy ([box 1](#)). The way this information is delivered can impact on how patients subsequently feel about their care and healthcare team. The clinician should use clear terminology and avoid medical jargon, which could be misunderstood or misinterpreted. After receiving a diagnosis, it can be difficult for patients to absorb all the complex information. The availability of written information to

review after the appointment is essential. Signposting the patient to organisations providing additional high-quality, evidence-based information is key so that people do not search the internet with no guidance and find alarming or misleading information. Access to high-quality information can empower patients to take part in decisions about their care, to understand their condition and navigate an unfamiliar healthcare system. However, it is vital to understand individuals' preferences for receiving information (eg, verbal and/or written) and to tailor the level of information provided. The relevant charities such as Pancreatic Cancer UK, Pancreatic Cancer Action and Pancreatic Cancer Scotland have telephone advice lines, comprehensive literature and services through which people can meet others with the same diagnosis.

At the bridging clinic, patients must be involved in decision making about their care. Clarity about the care pathway and patient involvement in decision making can help to alleviate future distress and anxiety. To participate effectively patients need to be given clear information about the potential risks and benefits of the different therapeutic options and be given the opportunity to ask questions. They will want to consider how the side effects of the treatment options might impact on their daily life. Importantly as the prognosis can be poor, patients will want to be reassured that treatment will start as soon as possible minimising any waits, and information on appropriate timescales for tests and treatment to start should be provided. The process of effective information giving is especially relevant for the patients who present at an advanced stage who may have undergone a protracted route before a firm diagnosis was established. At the end of the consultation, the patients and carers should feel supported and motivated to discuss the available treatment options in more detail with the relevant specialists. The contact details of their care team must be provided.

NUTRITION

Weight loss

Approximately 80% of patients with PC report weight loss at the time of diagnosis and over a third have lost >10% of their body weight.⁷ The aetiology is multifactorial and includes gastric/biliary obstruction, malabsorption, cachexia and sarcopenia. Early interventions to restore nutritional intake can be successful in increasing body weight and enhancing patients' quality of life. The 'bridging clinic' provides an opportunity to identify and modify these factors that lead to weight loss. A detailed history and examination is the key to identifying the causes, and to deliver the most appropriate and early interventions ([box 2](#)). The clinical assessment should be directed towards the identification of obstructive symptoms, malabsorption, cancer cachexia and sarcopenia.

Box 2 Assessment and management of nutritional issues at the bridging clinic appointment

Nutrition

Assessment

1. Detailed history

Aetiology

- ▶ Gastric obstruction/gastroparesis.
 - ▶ Malabsorption (pancreatic insufficiency)—secondary to pancreatic ductal obstruction.
 - ▶ Sarcopenia—questionnaire.
 - ▶ Cancer cachexia.
2. Baseline body mass index

Management

- ▶ Gastric outlet obstruction: stent vs surgical bypass (gastrojejunostomy).
- ▶ Pancreatic enzyme insufficiency: pancreatic enzyme replacement therapy.
- ▶ Upper gastrointestinal dietitian involvement.
- ▶ Sarcopenia (nutrition, resistance training, etc).

Obstruction

The clinical history will identify obstructive symptoms causing weight loss. Refractory vomiting is the cardinal symptom of gastric outlet obstruction and is invariably due to malignant infiltration of the duodenum or stomach. Evidence of obstruction may be observed on a CT scan. Endoscopically placed self-expanding metal stents (SEMS) in the duodenum are indicated and allow patients to commence oral intake early. Surgical bypass procedures, for example, gastrojejunostomy, may be performed but have largely been replaced by stents as first-choice treatment. Gastroparesis in the absence of an anatomical abnormality on CT is common in PC possibly due to direct cancer infiltration of the autonomic nerve fibres and neurohormonal changes. Here, prokinetics such as erythromycin may be helpful.

Malabsorption

Malabsorption due to pancreatic enzyme insufficiency (PEI) occurs as a result of destruction of the pancreas by the cancer or obstruction of the main pancreatic duct. The prevalence of PEI in PC has been estimated to be as much as 60%.⁸ PC occurring in the head of the pancreas is generally associated with a higher incidence of PEI.^{8,9} PEI presents with symptoms including steatorrhoea, flatus, belching and weight loss. A faecal elastase-1 test measures exocrine pancreatic function but has a low sensitivity. Pancreatic enzyme replacement therapy (PERT) should be considered at diagnosis, even in those without steatorrhoea and weight loss, particularly in patients with cancer of the head of pancreas as most will develop these. Practical measures for successful use of PERT are shown below (box 3). The dose needs to be titrated against symptoms and should be regularly reviewed. Proton pump inhibitors

Box 3 Practical steps in taking pancreatic enzyme supplementation.

Recommendations for initial treatment

- ▶ Initial prescription: 50 000 units lipase with meals/25 000 units with snacks.
- ▶ Prescribe a tablet of a single strength to enhance compliance, eg, 25 000 units tablet (patient takes two tablets with meals, one tablet with snacks).
- ▶ Half the dose (one capsule) to be taken immediately before food and half (one capsule) during the meal.
- ▶ Keep pancreatic enzyme replacement therapy (PERT) in a cool place as heat denatures enzymes.
- ▶ Do not swallow with hot drinks which denatures the enzymes.

Response to PERT

- ▶ Monitor clinical response (weight loss, steatorrhoea) regularly and increase dose if needed.
- ▶ Proton pump inhibitor should be co-administered if malabsorption symptoms do not resolve.
- ▶ Monitor blood glucose which may increase if absorption is improved and dose titrated.
- ▶ Input from specialist dietitian for weight loss which is multifactorial and severe.

may be needed in some patients who are unresponsive to lower enzyme doses as they increase the efficacy of PERT by generating an alkaline environment in the duodenum in which enzymes are more physiologically active.

The cancer cachexia syndrome

Cancer cachexia is defined as involuntary weight loss associated with loss of skeletal muscle mass (sarcopenia)^{10,11} and is increasingly recognised as an important predictor of adverse outcomes in patients with PC. Cancer cachexia often goes undiagnosed particularly in patients with an initial higher body mass index (BMI).¹¹ Assessing the presence of sarcopenia at the first consultation can be difficult, but a crude measure is from the patient description of their muscle mass loss, reduced physical activity and review of muscle mass on the CT scan.¹⁰ One approach to screening for sarcopenia involves the use of questionnaires, such as the Sluggishness, Assistance in walking, Rise from a chair, Climb stairs, Falls, which is a brief 5-item questionnaire with Likert scoring for patient responses.¹² The presence of sarcopenia in the absence of treatable obstructive symptoms and malabsorption require specialist dietitian input that will be able to provide nutritional support therapies. There is at present no standardised care for treating cancer cachexia. The MENAC trial, currently recruiting, is a randomised controlled trial of a Multimodal Intervention (Exercise, Nutrition and Anti-inflammatory Medication) to reduce/reverse the progression of cancer cachexia.¹³ In a recent meta-analysis, the progesterone, megestrol

acetate stimulated appetite and weight gain in patients with cancer cachexia; however, significant side effects including thromboembolic events and oedema were observed.¹⁴

DIABETES AND DEPRESSION

Diabetes

PC may induce new clinical diabetes through both destruction of pancreatic beta cells and increased insulin resistance associated with the production of islet cell amyloid polypeptide.¹⁵ Pancreaticogenic diabetes due to loss of gland function is termed type IIIc diabetes. Furthermore, existing long-term type 2 diabetes, a positive risk factor for PC, may worsen as the cancer progresses.¹⁶ The symptoms of diabetes namely polydipsia, polyuria, lethargy and weight loss can contribute to both impaired physical health and quality of life, which also mimic the symptoms of the cancer itself. In the bridging clinic, plasma glucose should always be measured and if indicated oral hypoglycaemic therapy prescribed. The biguanide metformin is the recommended first-line oral hypoglycaemic drug.¹⁷ Sulfonylureas are less preferable as they may potentially have a mitogenic effect through promoting insulin secretion. However, metformin is contraindicated in patients with significant renal or hepatic impairment, and must be stopped immediately before and after CT scanning in patients with renal impairment. If there is severe hyperglycaemia, insulin therapy is required. Glucose-lowering therapy may not be a clinical priority in patients with rapidly progressive cancer, which is imminently terminal. Following diagnosis, patients' glycaemic status should be regularly monitored as this can be influenced by cancer progression and also treatments (box 4). Hypoglycaemia may occur on glucose-lowering treatment if the patient develops upper intestinal obstruction,

cachexia or steatorrhea, all which may necessitate a dose reduction. Hyperglycaemic states can be precipitated by chemotherapy infusions in dextrose solutions, and steroids such as dexamethasone used for appetite stimulation. Importantly, hyperglycaemia may develop or worsen when PERT is prescribed, which facilitates sugar absorption, emphasising the importance of glucose monitoring.

Depression

Depression is a common symptom in patients with PC with a prevalence of between 33% and 50%,^{18 19} with nearly half developing this prior to cancer diagnosis.²⁰ The cancer itself influences immunological and biochemical processes,²¹ possibly including the release of proteins that stimulate antibody production, which block serotonin receptors.²² Solid tumours are also associated with increased urinary excretion of serotonin leading to its depletion in the body.²³ Furthermore, cancer causes anaemia, hypercalcaemia, acid-base abnormalities and altered neuropeptide synthesis, which all influence mood.¹⁹ These biological mechanisms of depression accentuate the psychological effects of receiving information of the diagnosis, treatments and prognosis.

In the bridging clinic, identifying depression is important, as it is associated with an increased morbidity including pain, anorexia and anxiety, which exacerbates weight loss and impairs patient's quality of life.^{24 25} Early recognition and treatment can lead to an improvement in patient's function and a sense of physical well-being.²⁶ Organic causes of depression should be excluded and treated appropriately (box 5). These include nutritional deficiencies (eg, iron or vitamin B12 deficiency) and drug side effects, particularly chemotherapy-induced depression.²⁷ Generally, at diagnosis patients are not routinely screened for depression. However, a US study of 130 patients with PC used the Beck depression inventory to screen for depression and reported a prevalence of 38%.²⁸ A series of 262 Chinese inpatients with gastrointestinal cancer were assessed with the Hamilton Rating Scale for Depression-24, which documented higher depression scores in those with PC (78%) compared with hepatocellular carcinoma (60%), gastric carcinoma (36%) and colonic cancer (19%).²⁹ An alternative screening tool is the Hospital Anxiety and Depression Scale, which identifies patients who may benefit from further mood assessment.³⁰ This questionnaire focuses on the loss of the pleasure response (anhedonia) rather than somatic symptoms that occur in patients with both cancer and depression, such as anorexia and weight loss. Anhedonia results from a disturbance of neurotransmitter function and is more responsive to antidepressant medication.¹⁷ Although clinicians may choose not to use a formal questionnaire for screening for depression, asking simple questions such as a patient's mood and sleep pattern are useful. If no reversible causes of

Box 4 Practical steps in the assessment and management of diabetes at the bridging clinic

Diabetes

Assessment

- ▶ Assess clinically for polyuria/polydipsia/weight loss.
- ▶ Plasma glucose should always be measured.
- ▶ Urinalysis/haemoglobin A1c.
- ▶ Consider appropriate oral hypoglycaemic therapy.
- ▶ Severe hyperglycaemia may require insulin therapy.
- ▶ Consider causes of hyperglycaemia (chemotherapy infusions in dextrose solutions, steroids/pancreatic enzyme replacement therapy).

Management

- ▶ First-line oral hypoglycaemic=metformin (contraindicated in renal/hepatic impairment).
- ▶ Risk factor modification, eg, high body mass index.
- ▶ Consider referral to a diabetologist.

Box 5 Practical steps in the assessment and management of depression at the bridging clinic

Depression

Assessment

- ▶ Early identification of clinical features of depression.
- ▶ Aetiology.
 - Anaemia.
 - Hypercalcaemia.
 - Acid-base abnormalities.
 - Nutritional deficiencies (eg, iron or vitamin B12 deficiency).
 - Drug side effects, eg, chemotherapy-induced depression.
- ▶ Apply screening tool, eg, Hospital Anxiety and Depression Scale.

Management

- ▶ Antidepressant treatment, eg, mirtazapine (appetite stimulant).
- ▶ Consider referring for counselling and support usually via palliative care services for severe depression.

depression are found, the patient should be considered for antidepressant treatment and if needed counselling and support usually delivered by palliative care services. Pharmacological therapy is dependent on the drug side-effect profile and tricyclic antidepressants are commonly used.²¹ The antidepressant, mirtazapine, has the additional benefit of stimulating appetite and may help weight maintenance.³⁰

ANALGESIA

Approximately 80% of patients with PC develop abdominal pain, with half describing this as severe.^{31,32} Pain is associated with a poor survival (HR for patients with pain compared with those without pain=1.61 (95% CI 1.06 to 2.44) ($p=0.025$)) as well as an impaired performance status,^{33,34} which may then reduce patient's eligibility for chemotherapy. There are two main plausible mechanisms for the development of abdominal pain, first, pancreatic duct obstruction and second pancreatic neuropathy with cancer infiltration of the coeliac plexus. Evidence for the former, is from case series in patients with characteristic abdominal pain and CT radiological appearances of pancreatic duct obstruction whose pain is improved on pancreatic ductal stenting.³⁵ Pancreatic neuropathy leads to alterations in the peripancreatic and endopancreatic microneuroanatomy, neurophysiology and nociception due to chronic, unresolved local inflammation around the tumour microenvironment.³⁶ These changes are an increased nerve density and hypertrophy, perineural infiltration by PC cells, upregulation of nociceptors (transient receptor vanilloid potential-1) and pain neurotransmitters and immune cell infiltration with mast cell predominance.^{36–38}

Box 6 Practical steps in the assessment and management of analgesia at the bridging clinic

Analgesia

Management

- ▶ Pharmacotherapy—first line.
- ▶ WHO analgesic ladder (starting with paracetamol/non-steroidal anti-inflammatory drugs/progressing to weak, and then strong morphine-based opioids).
- ▶ If ineffective—consider methadone and ketamine, two N-methyl-D-aspartate.
- ▶ Requires involvement of palliative care physician.
- ▶ Adjunctive treatments: tricyclic antidepressants and gabapentinoids.
- ▶ Refractory pain—consider endoscopic ultrasound-guided coeliac plexus neurolysis discussed at the multi-disciplinary team (MDT).

Pain management is initially pharmacotherapy, but endoscopic treatments are available if it is refractory to drugs (box 6). The analgesic choice is informed by the WHO analgesic ladder,³⁹ starting with paracetamol and non-steroidal anti-inflammatory drugs and if these are ineffective progressing to weak, and then strong morphine-based opioids. Methadone and ketamine, two N-methyl-D-aspartate, may be prescribed if the above are ineffective, usually by palliative care physicians.⁴⁰ Tricyclic antidepressants and gabapentinoids are adjunctive treatments for pain due to their neuromodulating properties.⁴¹ The many side effects of opiates may limit their use, which include: sedation, constipation, confusion, tolerance and dependence, which impact negatively on quality of life.⁴⁰ In pain refractory to drug therapy, endoscopic ultrasound-guided coeliac plexus neurolysis (EUS-CPN), a procedure that chemical ablates the coeliac ganglia, through which afferent autonomic nerve fibres from the pancreas enter the central nervous system can be considered.³² To date, the only randomised controlled trial assessing EUS-CPN reported that this plus pharmacotherapy if needed, administered to patients with pain at diagnosis gave a 60% greater reduction in pain scores than pharmacotherapy alone at 3 months (95% CI –86.6 to –25.5, $p=0.01$, and 50% lower morphine requirements (95% CI –127.5 to 7.0), $p=0.10$).⁴¹ This trial did not recruit patients with pain developing later after diagnosis or more advanced cancers. Case series of EUS-CPN reported that the most common complications included diarrhoea, orthostatic hypotension and pain, which resolve usually within 48 hours.^{41–44} The most serious complication, documented, in just one case report, was spinal stroke due to alcohol-induced vasoconstriction of a branch of the spinal artery.⁴⁵ For EUS-CPN, specific guidance on patient selection and its timing are lacking. Consequently, the decision for treatment with EUS-CPN in the UK is decided at the multidisciplinary team meetings based on the

experience and expertise of local centres. If chosen this is usually because escalating doses of opiates do not control pain or drug side effects dramatically impair quality of life. Currently, endoscopic pancreatic ductal stenting is not routinely used for pain palliation, although further research on its use is required.

STENTING FOR BILIARY OBSTRUCTION

Jaundice is present in approximately 70% of patients, with intractable pruritus a particularly distressing symptom.⁴⁶ Biliary decompression and stenting can alleviate jaundice and pruritus, allowing bilirubin levels to fall and reducing the risk of toxicity during subsequent chemotherapy.⁴⁶ Endoscopically placed 'through the scope' SEMS have revolutionised the ability to relieve obstructive jaundice and treat pruritus.^{47 48} In a multi-centre randomised controlled trial, routine preoperative biliary drainage in patients undergoing surgery for PC increases the rate of postoperative complications.⁴⁹ Complications such as abscesses, infections, pancreatic fistulae and wound infections have all been shown to be higher.^{49–51} A straight to surgery approach is recommended unless there are logistical delays in which case biliary decompression and stenting should be considered.⁴⁹ A prospective multicentre cohort study showed that SEMS had a lower stent-related complication rate in comparison with plastic biliary stents.⁵² The decision to proceed with biliary stenting should be discussed in a multidisciplinary team setting with medical, surgical, oncology and radiology members present. Palliative patients are best managed by SEMS insertion with endoscopic stent placement preferred over the percutaneous approaches (box 7). Where neither of these is possible, palliative biliary bypass remains an option, although this is now rarely used.

In patients with inoperable cancer, the radiological finding of biliary dilatation in the absence of jaundice represents a clinical dilemma as to whether or not a prophylactic stent should be placed. The rationale for prophylactic stenting is that with biliary duct dilatation

Box 7 Practical steps to consider for stenting at the bridging clinic

Stenting

Assessment

- ▶ Evidence of obstructive jaundice (biochemical/radiological).
- ▶ Inoperable cancer plus biliary dilatation in the absence of jaundice.
- ▶ Prophylactic stent vs watch and wait approach (performance status).

Management

- ▶ MDT discussion.
- ▶ Locally advanced disease/palliative patients: self-expanding metal stents preferred.

Box 8 Practical steps in the assessment and management of hereditary factors at the bridging clinic

Hereditary

Assessment

- ▶ Enquire if there are any first-degree relatives with pancreatic cancer (PC).
- ▶ Checklist of conditions associated with PC: *Peutz-Jeghers syndrome, hereditary pancreatitis, hereditary breast-ovarian cancer syndrome, Lynch syndrome, familial adenomatous polyposis syndromes and BRCA mutations, P16/CDKN2A and PALB2 gene mutations.*

Management

- ▶ If first-degree relatives+for PC then offer referral to medical geneticist and risk factor modification, eg, body mass index.
- ▶ Offer surveillance for PC to people with: Hereditary pancreatitis and a PRSS1 mutation

BRCA1, BRCA2, PALB2 or CDKN2A (p16) mutations, and one or more first-degree relatives with PC.

Peutz-Jeghers syndrome.

- ▶ Consider surveillance for PC for people with:

two or more first-degree relatives with PC, across two or more generations.

Lynch syndrome (mismatch repair gene (MLH1, MSH2, MSH6 or PMS2) mutations) and any first-degree relatives with PC.

- ▶ Consider an MRI/MRCP or EUS for PC surveillance in people without hereditary pancreatitis.
- ▶ Consider a pancreatic protocol CT scan for PC surveillance in people with hereditary pancreatitis and a PRSS1 mutation.

on CT, subsequent jaundice is likely to develop but the decision to proceed as a prophylactic measure should be considered on a case-to-case basis depending on the patient's age and prognosis. Prophylactic stenting may be favoured in a younger patient with a good medical performance status and locally advanced cancer, but probably avoided in the elderly and frail with metastatic disease with a particularly poor prognosis.

HEREDITARY

At the bridging clinic, the history will identify if there is a genetic condition associated with PC or a familial risk due to an unidentified genetic mutation or environmental risk factors shared with affected family members (box 8). Familial PC is defined as at least two first-degree relatives with PC, which accounts for 4%–10% of cases of PC.⁵³ Genetic mutations associated with PC are Peutz-Jeghers syndrome, hereditary pancreatitis (HP), hereditary breast-ovarian cancer

syndrome, Lynch syndrome, familial adenomatous polyposis syndromes and *BRCA* mutations, *P16/CDKN2A* and *PALB2* gene mutations.^{53 54} Families in which there is a clustering of PC also have an increased risk of extra PCs including breast, ovarian and bile duct cancers.⁵³ HP increases the risk by 50-fold compared with the general population.^{55 56} Mutation of the *PRSS1* gene has been implicated for the development of HP. The current European Registry of Hereditary Pancreatitis and Familial Pancreatic Cancer (EUROPAC) trial is a screening study investigating the genetic causes of PC in people with familial PC and HP. This defines HP as two first-degree relatives or at least three second-degree relatives in two or more generations, with chronic pancreatitis for which there is no other aetiology.⁵⁵ When to approach screening with relatives will be difficult, as alarm should not be created at the time of informing the patient of their diagnosis. Relatives with a defined genetic condition should be referred to a medical geneticist. Improvement in lifestyle habits, including smoking cessation and reduction of BMI is recommended for individuals at risk.

SUMMARY

Traditionally, the diagnosis of PC is associated with a dismal prognosis and possibly there is less consideration of supportive medical treatments, which could alleviate symptoms. The bridging clinic provides an opportunity for assessment and instituting interventions that may be highly beneficial. The Bridging clinic checklist for pancreatic cancer can be found in the supplementary file 1. The stepwise approach using the mnemonic *INDASH* may ensure that all relevant areas are systematically addressed to help improve clinical outcomes and possibly enhance patients' suitability for more definitive treatments such as surgery and chemotherapy. The bridging clinic may be deliverable by a variety of healthcare professionals depending on local preferences and working practices. It may be introduced into a patient's cancer pathway following an initial consultation to inform the patient of the diagnosis. Depending on local arrangements, a CNS with appropriate support may run the bridging clinic and the patient's general practitioner can deliver elements of it, for example, dealing with depression. We would recommend discussion at local cancer networks to decide on the best structure of delivery suited to local governance arrangements and practice.

Contributors LS wrote the main content of the article and submitted the study. BK as an upper GI surgeon provided clinical input into the manuscript and provided a structure to the article. AJ provided valuable insights into the information and support needs of people with pancreatic cancer from her experience of providing these services at a national patient organisation. PB wrote the section on depression. AK wrote the section on analgesia. ARH provided the concepts behind the paper as well as writing the section on diabetes.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent Not required.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

- 1 cancer research UK, 2018. Pancreatic cancer survival statistics. <http://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/pancreatic-cancer/incidence>
- 2 Globocan. Estimated cancer incidence, mortality and prevalence worldwide in 2012, 2012. http://globocan.iarc.fr/Pages/fact_sheets_population.aspx.
- 3 Ansari D, Gustafsson A, Andersson R. Update on the management of pancreatic cancer: surgery is not enough. *World J Gastroenterol* 2015;21:3157–65.
- 4 Conroy T, Desseigne F, Ychou M, *et al.* FOLFIRINOX versus gemcitabine for metastatic pancreatic cancer. *N Engl J Med* 2011;364:1817–25.
- 5 Takaori K, Bassi C, Biankin A, *et al.* International Association of Pancreatology (IAP)/European Pancreatic Club (EPC) consensus review of guidelines for the treatment of pancreatic cancer. *Pancreatol* 2016;16:14–27.
- 6 Pancreatic cancer in adults: diagnosis and management. 2018. <https://www.nice.org.uk/guidance/ng85>.
- 7 Witvliet-van Nierop JE, Lochtenberg-Potjes CM, Wierdsma NJ, *et al.* Assessment of Nutritional Status, Digestion and Absorption, and Quality of Life in Patients with Locally Advanced Pancreatic Cancer. *Gastroenterol Res Pract* 2017;2017:1–7.
- 8 Sikkens EC, Cahen DL, de Wit J, *et al.* A prospective assessment of the natural course of the exocrine pancreatic function in patients with a pancreatic head tumor. *J Clin Gastroenterol* 2014;48:e43–6.
- 9 Vujasinovic M, Valente R, Del Chiaro M, *et al.* Pancreatic Exocrine Insufficiency in Pancreatic Cancer. *Nutrients* 2017;9:183.
- 10 Fearon K, Strasser F, Anker SD, *et al.* Definition and classification of cancer cachexia: an international consensus. *Lancet Oncol* 2011;12:489–95.
- 11 Ozola Zalite I, Zyklus R, Francisco Gonzalez M, *et al.* Influence of cachexia and sarcopenia on survival in pancreatic ductal adenocarcinoma: a systematic review. *Pancreatol* 2015;15:19–24.
- 12 Beaudart C, McCloskey E, Bruyère O, *et al.* Sarcopenia in daily practice: assessment and management. *BMC Geriatr* 2016;16:170.
- 13 Solheim TS, Laird BJA, Balstad TR, *et al.* Cancer cachexia: rationale for the MENAC (Multimodal-Exercise, Nutrition and Anti-inflammatory medication for Cachexia) trial. *BMJ Support Palliat Care* 2018;8:258–65.
- 14 Garcia R, V, *et al.* Megestrol acetate for treatment of anorexia-cachexia syndrome. *Cochrane Database Syst Rev* 2013;3:CD004310.
- 15 Andersen DK, Adren-Sandberg Å, Duell EJ, *et al.* Pancreatitis-diabetes-pancreatic cancer: summary of an NIDDK-NCI workshop. *Pancreas* 2013;42:1227–37.
- 16 Liao KF, Lai SW, Li CI, *et al.* Diabetes mellitus correlates with increased risk of pancreatic cancer: a population-based cohort study in Taiwan. *J Gastroenterol Hepatol* 2012;27:709–13.
- 17 Cui Y, Andersen DK. Pancreatogenic diabetes: special considerations for management. *Pancreatol* 2011;11:279–94.
- 18 Joffe RT, Rubinow DR, Denicoff KD, *et al.* Depression and carcinoma of the pancreas. *Gen Hosp Psychiatry* 1986;8:241–5.

- 19 Holland JC, Korzun AH, Tross S, *et al.* Comparative psychological disturbance in patients with pancreatic and gastric cancer. *Am J Psychiatry* 1986;143:982–6.
- 20 Fras I, Litin EM, Pearson JS. Comparison of psychiatric symptoms in carcinoma of the pancreas with those in some other intra-abdominal neoplasms. *Am J Psychiatry* 1967;123:1553–62.
- 21 Makrilia N, Indeck B, Syrigos K, *et al.* Depression and pancreatic cancer: a poorly understood link. *JOP* 2009;10:69–76.
- 22 Brown JH, Paraskevas F. Cancer and depression: cancer presenting with depressive illness: an autoimmune disease? *Br J Psychiatry* 1982;141:227–32.
- 23 Shakin EJ, Holland J. Depression and pancreatic cancer. *J Pain Symptom Manage* 1988;3:194–8.
- 24 Sheibani-Rad S, Velanovich V. Effects of depression on the survival of pancreatic adenocarcinoma. *Pancreas* 2006;32:58–61.
- 25 Jia L, Jiang SM, Shang YY, *et al.* Investigation of the incidence of pancreatic cancer-related depression and its relationship with the quality of life of patients. *Digestion* 2010;82:4–9.
- 26 Passik SD, Breitbart WS. Depression in patients with pancreatic carcinoma. Diagnostic and treatment issues. *Cancer* 1996;78(3 Suppl):615–26.
- 27 Nelson CJ, Nandy N, Roth AJ. Chemotherapy and cognitive deficits: mechanisms, findings, and potential interventions. *Palliat Support Care* 2007;5:273–80.
- 28 Kelsen DP, Portenoy RK, Thaler HT, *et al.* Pain and depression in patients with newly diagnosed pancreas cancer. *J Clin Oncol* 1995;13:748–55.
- 29 Holtom N, Barraclough J. Is the Hospital Anxiety and Depression Scale (HADS) useful in assessing depression in palliative care? *Palliat Med* 2000;14:219–20.
- 30 *Mirtazapine*, in *British National Formulary*, 2009. BMJ Group.
- 31 Koulouris AI, Banim P, Hart AR. Pain in Patients with Pancreatic Cancer: Prevalence, Mechanisms, Management and Future Developments. *Dig Dis Sci* 2017;62:861–70.
- 32 Moore JC, Adler DG. Celiac plexus neurolysis for pain relief in pancreatic cancer. *J Support Oncol* 2009;7:90.
- 33 Müller MW, Friess H, Köninger J, *et al.* Factors influencing survival after bypass procedures in patients with advanced pancreatic adenocarcinomas. *Am J Surg* 2008;195:221–8.
- 34 Moningi S, Walker AJ, Hsu CC, *et al.* Correlation of clinical stage and performance status with quality of life in patients seen in a pancreas multidisciplinary clinic. *J Oncol Pract* 2015;11:e216–e221.
- 35 Sharaiha RZ, Widmer J, Kahaleh M. Palliation of pancreatic ductal obstruction in pancreatic cancer. *Gastrointest Endosc Clin N Am* 2013;23:917–23.
- 36 Ceyhan GO, Bergmann F, Kadihasanoglu M, *et al.* Pancreatic neuropathy and neuropathic pain—a comprehensive pathomorphological study of 546 cases. *Gastroenterology* 2009;136:177–86.
- 37 Hartel M, di Mola FF, Selvaggi F, *et al.* Vanilloids in pancreatic cancer: potential for chemotherapy and pain management. *Gut* 2006;55:519–28.
- 38 Demir IE, Schorn S, Schremmer-Danninger E, *et al.* Perineural mast cells are specifically enriched in pancreatic neuritis and neuropathic pain in pancreatic cancer and chronic pancreatitis. *PLoS One* 2013;8:e60529.
- 39 Hameed M, Hameed H, Erdek M. Pain management in pancreatic cancer. *Cancers* 2010;3:43–60.
- 40 Esin E, Yalcin S. Neuropathic cancer pain: What we are dealing with? How to manage it? *Onco Targets Ther* 2014;7:599–618.
- 41 Wyse JM, Carone M, Paquin SC, *et al.* Randomized, double-blind, controlled trial of early endoscopic ultrasound-guided celiac plexus neurolysis to prevent pain progression in patients with newly diagnosed, painful, inoperable pancreatic cancer. *J Clin Oncol* 2011;29:3541–6.
- 42 Nagels W, Pease N, Bekkering G, *et al.* Celiac plexus neurolysis for abdominal cancer pain: a systematic review. *Pain Med* 2013;14:1140–63.
- 43 Puli SR, Reddy JB, Bechtold ML, *et al.* EUS-guided celiac plexus neurolysis for pain due to chronic pancreatitis or pancreatic cancer pain: a meta-analysis and systematic review. *Dig Dis Sci* 2009;54:2330–7.
- 44 Kaufman M, Singh G, Das S, *et al.* Efficacy of endoscopic ultrasound-guided celiac plexus block and celiac plexus neurolysis for managing abdominal pain associated with chronic pancreatitis and pancreatic cancer. *J Clin Gastroenterol* 2010;44:127–34.
- 45 Mittal MK, Rabinstein AA, Wijdicks EF. Pearls & oysters: Acute spinal cord infarction following endoscopic ultrasound-guided celiac plexus neurolysis. *Neurology* 2012;78:e57–e59.
- 46 Boulay BR, Parepally M. Managing malignant biliary obstruction in pancreas cancer: choosing the appropriate strategy. *World J Gastroenterol* 2014;20:9345–53.
- 47 Wasan SM, Ross WA, Staerke GA, *et al.* Use of expandable metallic biliary stents in resectable pancreatic cancer. *Am J Gastroenterol* 2005;100:2056–61.
- 48 Adams MA, Anderson MA, Myles JD, *et al.* Self-expanding metal stents (SEMS) provide superior outcomes compared to plastic stents for pancreatic cancer patients undergoing neoadjuvant therapy. *J Gastrointest Oncol* 2012;3:309–13.
- 49 van der Gaag NA, Rauws EA, van Eijck CH, *et al.* Preoperative biliary drainage for cancer of the head of the pancreas. *N Engl J Med* 2010;362:129–37.
- 50 Sohn TA, Yeo CJ, Cameron JL, *et al.* Do preoperative biliary stents increase postpancreaticoduodenectomy complications? *J Gastrointest Surg* 2000;4:258–68.
- 51 Pisters PW, Hudec WA, Hess KR, *et al.* Effect of preoperative biliary decompression on pancreaticoduodenectomy-associated morbidity in 300 consecutive patients. *Ann Surg* 2001;234:47–55.
- 52 Tol JA, van Hooft JE, Timmer R, *et al.* Metal or plastic stents for preoperative biliary drainage in resectable pancreatic cancer. *Gut* 2016;65:1981–7.
- 53 Matsubayashi H, Takaori K, Morizane C, *et al.* Familial pancreatic cancer: Concept, management and issues. *World J Gastroenterol* 2017;23:935–48.
- 54 Wang L, Brune KA, Visvanathan K, *et al.* Elevated cancer mortality in the relatives of patients with pancreatic cancer. *Cancer Epidemiol Biomarkers Prev* 2009;18:2829–34.
- 55 Lal A, Lal DR. Hereditary pancreatitis. *Pediatr Surg Int* 2010;26:1193–9.
- 56 Rebours V, Boutron-Ruault MC, Schnee M, *et al.* The natural history of hereditary pancreatitis: a national series. *Gut* 2009;58:97–103.