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

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Abstract

Pancreatic cancer is the 11th commonest cancer in the UK and has the worst prognoses 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 between informing the patient of their diagnosis and commencing surgery or palliative treatments presents a valuable opportunity to proactively identify and treat symptoms to optimise patients' overall wellbeing. The 'Bridging Clinic', delivered by a range of healthcare professionals from gastroenterologists to nurse practitioners, can provide this interface where patients are firstly informed of their diagnosis and secondly 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 pneumonic INDASH (Information / Nutrition / Diabetes & Depression / Analgesia / Stenting / Hereditary) and each is discussed in detail below.

Statements

a. <u>Contributorship Statement</u>

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Introduction

Pancreatic cancer (PC) is the 11th commonest cancer in the UK and has the worst prognoses of any tumour with minimal improvements in survival over recent decades [1,2]. The overall 5-year survival rate is less than 5% [3]. Worldwide, PC is the fourth commonest 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, though recently chemotherapy with FOLFIRINOX (combination of FOLinic acid (leucovorin), Fluorouracil, IRinotecan and OXaliplatin) has increased the median survival from 6.8 months 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 analgesia and management of medical complications such as poor nutritional status [5].

The time 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 wellbeing. 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 which 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) have

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

INFORMATION (*INDASH)*

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 not only deal with the initial shock of the diagnosis but also 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 (Table 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 (e.g. 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 patient 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.

INFORMATION

- Involvement of the Cancer Nurse Specialist (CNS)
- Inform the patient of their diagnosis at 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
- Potential options for their treatment and care discussed
- Use clear terminology and avoid medical jargon
- Written information available for people to review after their appointment.
- Signposting to organisations providing high quality, evidence based information
- Telephone advice & comprehensive literature (Pancreatic Cancer UK, Pancreatic Cancer Action & Pancreatic Cancer Scotland).

Table 1. Guidance on Information to be given at the Bridging clinic appointment.

NUTRITION (*IN*DASH)

Weight loss

Approximately 80% of PC patients report weight loss at the time of diagnosis and over a third have lost more than 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 (Table 2). The clinical assessment should be directed towards the identification of obstructive symptoms, malabsorption, cancer cachexia and sarcopenia.

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 e.g. 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 neuro-hormonal changes. Here, pro-kinetics 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 (FE1) 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 (Table

3). The dose needs to be titrated against symptoms and should be regularly reviewed. Proton pump inhibitors may be a 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.

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 (BMI)**

Management

   - Gastric outlet obstruction: Stent vs. surgical bypass (gastrojejunostomy)
   - PEI: Pancreatic Enzyme Replacement therapy (PERT)
   - Upper GI Dietician involvement
   - Sarcopenia (nutrition, resistance training etc.)

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

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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 e.g. 25 000 units tablet (patient takes 2 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 PERT in a cool place as heat denatures enzymes
- Don't 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 dietician for weight loss which is multifactorial and severe

Table 3. Practical steps in taking pancreatic enzyme supplementation.

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 recognized as an important predictor of adverse outcomes in PC patients. 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 SARC-F (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 dietician 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 randomized 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, megesterol acetate stimulated appetite and

weight gain in patients with cancer cachexia, however significant side effects including thromboembolic events and oedema were observed [14].

DIABETES & DEPRESSION (*INDASH*)

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 recommenced first line oral hypoglycaemic drug [17]. Sulphonylureas 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 (Table 4). Hypoglycaemia may occur on glucose lowering treatment if the patient develops upper intestinal obstruction, cachexia, or steatorrhoea, 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.

DIABETES

Assessment

1. Assess clinically for polyuria / polydipsia / weight loss
2. Plasma glucose should always be measured
3. Urinalysis / HBA1C
4. Consider appropriate oral hypoglycaemic therapy
5. Severe hyperglycaemia may require insulin therapy
6. Consider causes of hyperglycaemia (chemotherapy infusions in dextrose solutions, steroids / PERT)
7. Consider referral to a diabetiologist

Management

1. First line oral hypoglycaemic = metformin (Contraindicated in renal/hepatic impairment)
2. Risk factor modification e.g. High BMI

Table 4. Practical steps in assessment and management of diabetes at bridging clinic.

Depression *(IN**D**ASH)*

Depression is a common symptom in patients with PC with a prevalence of between 33%-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 exacerbate 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 (Table 5). These include nutritional deficiencies (e.g. 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 PC patients used the Beck depression inventory to screen for depression and reported a prevalence of 38% [28]. A series of 262 Chinese in-patients with gastrointestinal cancer were assessed with the Hamilton Rating Scale for Depression-24 which documented higher depression scores in those with PC (78%) compared to: hepatocellular carcinoma (60%), gastric carcinoma (36%) and colonic cancer (19%) [29]. An alternative screening tool is the Hospital Anxiety and Depression Scale (HADS) 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 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].

DEPRESSION

Assessment

- Early identification of clinical features of depression

- Aetiology
  -Anaemia
  -Hypercalcaemia
  -Acid-base abnormalities
  -Nutritional deficiencies (e.g. iron or vitamin B12 deficiency)
  -Drug side-effects, e.g. chemotherapy induced depression

- Apply Screening tool e.g. Hospital Anxiety and Depression Scale (HADS)

Management

- Antidepressant treatment e.g. mirtazapine (appetite stimulant)

> - Consider referring for counselling and support usually via palliative care services for severe depression

Table 5. Practical steps in assessment and management of depression at bridging clinic.

ANALGESIA *(INDASH)*

Approximately 80% of patients with PC develop abdominal pain, with half describing this as severe [31, 32]. Pain is associated with a poor survival [hazard ratio for patients with pain compared to those without pain = 1.61 (95%CI, 1.06 -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, firstly, pancreatic duct obstruction and secondly 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 peri- and endo-pancreatic micro-neuroanatomy, 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 pancreatic cancer cells, upregulation of nociceptors (Transient Receptor Vanilloid Potential-1) and pain neurotransmitters and immune cell infiltration with mast-cell predominance [36-38].

Pain management is initially pharmacotherapy, but endoscopic treatments are available if it is refractory to drugs (Table 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 NMDA (N-methyl-D –aspartate), may be prescribed if the above are ineffective, usually by palliative care physicians [40]. Tricyclic antidepressants (TCAs) 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 commonest 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 multi-disciplinary 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.

ANALGESIA

Management

- Pharmacotherapy – first line
- WHO analgesic ladder (starting with paracetamol/ NSAIDs / progressing to weak, and then strong morphine-based opioids)
- If ineffective – consider methadone and ketamine, two NMDA (N-methyl-D –aspartate)
- Requires involvement of palliative care physician
- Adjunctive treatments: Tricyclic antidepressants (TCAs) and gabapentinoids
- Refractory pain - consider Endoscopic Ultrasound-guided Coeliac Plexus Neurolysis (EUS-CPN) discussed at the MDT

Table 6. Practical steps in assessment and management of analgesia at bridging clinic.

STENTING for BILIARY OBSTRUCTION (*INDASH*)

Jaundice is present in approximately 70% of patients, with intractable pruritis a particularly distressing symptom [46]. Biliary decompression and stenting can alleviate jaundice and pruritis, allowing bilirubin levels to fall and reducing the risk of toxicity during subsequent chemotherapy [46]. Endoscopically placed 'through the scope' self-expandable biliary metal stents (SEMS) have revolutionised the ability to relieve obstructive jaundice and treat pruritis [47, 48]. In a multicentre 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] [50] [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 (Table 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 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.

STENTING

Assessment

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

Management
- MDT discussion
- Locally advanced disease /Palliative patients: Self Expanding Metal Stents preferred

Table 7. Practical steps to consider for stenting at the bridging clinic.

HEREDITARY (*INDASH*)

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 (Table 8). Familial pancreatic cancer is defined as at least 2 first-degree relatives with PC, which accounts for 4-10% of cases of PC [53]. Genetic mutations associated with pancreatic cancer are Peutz-Jeghers syndrome, hereditary pancreatitis, hereditary breast-ovarian cancer syndrome (HBOC), Lynch syndrome, familial adenomatous polyposis (FAP) 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-pancreatic cancers including breast, ovarian and bile duct cancers [53]. Hereditary Pancreatitis (HP) increases the risk by 50 fold compared to the general population [55] [56]. Mutation of the PRSS1 gene has been implicated for the development of HP. The current EUROPAC trial is a screening study investigating the genetic causes of PC in people with familial pancreatic cancer and hereditary pancreatitis. This defines HP as two first-degree relatives or at least 3 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.

HEREDITARY

Assessment

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

Management

- If first degree relatives + for PC then offer referral to medical geneticist & Risk factor modification e.g. BMI

- Offer surveillance for pancreatic cancer to people with:

Hereditary pancreatitis and a PRSS1 mutation

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

Peutz–Jeghers syndrome.

- Consider surveillance for pancreatic cancer for people with:

2 or more first-degree relatives with pancreatic cancer, across 2 or more generations

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

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

Table 8. Practical steps in assessment and management of hereditary factors at bridging clinic.

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 highly beneficial. The stepwise approach using the pneumonic *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 health care 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 Cancer Nurse Specialist with appropriate support may run the bridging clinic and the patient's General Practitioner can deliver elements of it e.g. 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.

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