Palliation of pain and jaundice: An overview

R.C.G. Russell
Department of Surgery, The Middlesex Hospital, London. W1, U.K.

Summary
Between 70 and 90 percent of patients with pancreatic cancer will present with jaundice, and 90% will have pain at some stage of their illness. Resection for cure is possible in less than 5% of patients, thus a palliative approach is of necessity the appropriate management in 95% of patients. A palliative approach demands an attitude of mind which objectively defines relief of symptoms as the end point of treatment. Regional surveys show clearly that the care offered to the pancreatic cancer patient is poor with a high mortality (18%) for both resection and palliative bypass. The evidence that symptoms are managed well is unclear.

The approach to pancreatic pain should follow the stepwise progression advocated by the World Health Organisation with a progression from minor to major analgesics and due attention to control of associated symptoms and mood. Surgery for pain relief is limited to thoracoscopic splanchnicectomy - a technique yet to be fully evaluated or a peroperative coeliac plexus block, which appears to be an important part of palliative surgery. Alternative approaches, such as chemotherapy and radiotherapy have been less well evaluated in terms of symptom control.

The relief of jaundice may provide dramatic but short-lived remission in the patients' well-being - it is a mandatory part of palliation but must be undertaken with minimal disruption to the patients' life. For the majority, an endoscopic stent achieves this goal, but for the minority with a resectable or possibly resectable tumour a surgical bypass is preferable enabling a biliary and gastric bypass and a coeliac plexus block to be performed during the procedure.

Key words: jaundice, pain, palliation, pancreatic carcinoma

Introduction
Of the patients with cancer of the head of the pancreas and the periampullary region 70-90% have jaundice as a result of biliary obstruction [1]. Biliary obstruction aggravates the patients' already poor clinical condition by causing cholangitis, pruritis, nutritional deficiencies through malabsorption, weight loss, and progressive hepatic failure [2]. Surgical resection and reconstruction usually provide an adequate biliary drainage, but only few patients can be treated surgically with an intention to cure [3]. Jaundice is apparent, is measurable, and its treatment has defined end points, yet it is the pain associated with pancreatic cancer which causes the greatest fear of this cancer. A recent survey evaluating 1308 outpatients with mixed tumour types observed that whilst 41% experienced pain only 58% of those with pain received treatment that can be considered appropriate according to accepted standards for cancer pain management [4].

With prominent and debilitating symptoms frequently present at the time of first consultation, and a dismal chance of cure, palliation must be the prime focus of management from the time of diagnosis.

Palliation
Historically, palliative care has been seen as necessary pain and symptom control at the very end of life when 'proper measures' are futile and there is nothing more to be done. Palliative care actually begins at the time the decision is made that the appropriate treatment is not curative. In short, the clinicians who are managing patients with pancreatic cancer are effectively practising palliative care all the time and only a few surgeons are practising potentially curative treatment. A palliative approach is an attitude and quality of practice that manages incurably ill patients sensitively and effectively throughout the illness. As the end point of treatment is not cure but relief of symptoms, a different set of criteria must be used to judge the effectiveness of the management of the patient (Table 1).

<table>
<thead>
<tr>
<th>Table 1. Objectives in palliative care</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Relieve suffering in whatever form it takes</td>
</tr>
<tr>
<td>- Optimise the quality of life</td>
</tr>
<tr>
<td>- Use the patients' time for maximum benefit</td>
</tr>
<tr>
<td>- To help the patient find a meaning in completing their life</td>
</tr>
<tr>
<td>- Ensure the end of life is natural and comfortable</td>
</tr>
</tbody>
</table>

Whatever is necessary to achieve a realistic outcome is a legitimate palliative measure. Thus, there is no conflict between measures which will possibly cure or only palliate - provided that such strategies are centred on the needs and wishes of the patient and family, that there is clear and good reason, that there is a clearly defined goal, and that the clinical situation is reviewed once the defined objective has been met [5].

Palliation for patients with pancreatic cancer demands a different attitude to outcome by the clinician. The emphasis has been on technique, be it radical surgery, palliative surgery, endoprosthesis or nerve blockade, and the end points have been survival, hospital stay, readmission rates and relief of symptoms. However, there has been a woeful lack of assessment of the quality of life achieved by these manoeuvres, and little documentation of how long the patient lived a symptom-free fully active normal life. For example,
the patient who undergoes resection of a pancreatic cancer has a median survival of 12-15 months, yet at three months has a better performance index than the patient who was inoperable and had a lesser procedure. The palliative gain despite the poor prognosis appears worthwhile, but we do not know the limits to which this policy of an aggressive operative approach may be pushed in order still to maintain gain [6].

The disease today

In the United Kingdom, as in other countries, there has been a steady increase in the incidence of pancreatic cancer since the 1960s, but in the last few years there has been a levelling off of its incidence (Figure 1) [7]. The disease occurs in the older age groups; forty-seven percent of patients are now over the age of 75 years, and recently it has become commoner in the female [8]. Many such patients may require minimal intervention to achieve appropriate palliation in view of the other medical problems from which they suffer. Indeed, in practice, this statement is corroborated by Regional data alone [Personal communication, 1998]. In this analysis the incidence of pancreatic cancer was 11.4 per 100 000 population per annum. Fifty-three percent of patients were female. Fifty percent were aged between 60 and 80 years, and 20% were over 80 years. Histological confirmation of the disease was obtained in 36% patients. Only 3.9% (130 of 3278 cases) had a resection, palliative surgery was undertaken in 31% of patients and 54% had no treatment. The mortality rate for resection was 17.7%, which is identical to that of palliative surgery. The overall survival of this large group of patients was poor, with 11% patients alive at one year. Resection improved survival such that 42% were alive at one year compared with 17% who had undergone non-resectional surgery. At two years, 20% of resected patients were alive compared to 5.3% of all other patients. These figures, as do those of the West Midlands study [9], underline the poor prognosis of this condition and emphasise that palliation is the prime concern in over 95% patients.

Alas, palliation is often poorly managed with patients spending prolonged periods in hospitals while various tests and investigations are being arranged, often wasting valuable symptom-free time. A major problem in the case of pancreatic cancer patients is that they present to multiple physicians gastroenterologists, general physicians, geriatricians and oncologists, few of whom have expertise in the patients' care. Palliation demands a team approach by an experienced group who can offer all the modalities of treatment.

Pancreatic pain

Compared with patients with other cancers such as lung, prostate or uterine, the proportion of patients with pancreatic cancer who have significant pain is high [10]. Nineteen studies [11] evaluating the incidence and various features of pain in over 2200 patients found that pain was present at diagnosis in over 50-97% patients, with most studies noting an incidence of 80% or more. Pain occurred in up to 89% patients in those studies in which pain prevalence during the course of the disease was specifically evaluated. In a large surgical series of 340 cases, 60% of the patients undergoing pancreatic resection and 84% of those who were not resected, had moderate to severe pain [12].

Clinical characteristics

The pain is usually abdominal, and mimics that of other conditions (Table 2). Typically it is referred to the epigastric region or the upper abdominal quadrants, but can also involve the lower quadrants or be diffuse. Back pain is associated with abdominal pain in 50-65% of patients, but as few as 5-10% report it as their only complaint. The pain is usually mild, but is already moderate to severe in 20-30% patients at diagnosis. The intensity of the pain fluctuates during the day; it is often exaggerated by the supine position and by food, and may be relieved by changing position. The character of the pain is of a dull aching quality though episodes of colic and ulcer-like pain may occur. A 'full feeling' on the left with 'cramping' is said to be due to pancreatic duct obstruction, although it is rarely as characteristic as that which occurs in obstructive chronic pancreatitis. The impact of pain can be profound, being commonly

Table 2. Pancreatic cancer pain syndromes

<table>
<thead>
<tr>
<th>Direct tumour effects</th>
<th>Neuropathic pain</th>
</tr>
</thead>
<tbody>
<tr>
<td>Visceral</td>
<td>Somatic</td>
</tr>
<tr>
<td>• Involvement of adjacent structures</td>
<td>• Direct retroperitoneal pain</td>
</tr>
<tr>
<td>• Obstruction of bile duct</td>
<td>• Abdominal distension - gas</td>
</tr>
<tr>
<td>• Gallbladder</td>
<td>• Ascites</td>
</tr>
<tr>
<td>• Intestine</td>
<td>• Bone metastases</td>
</tr>
<tr>
<td>• Pancreas</td>
<td>• Radiculopathy from direct spread</td>
</tr>
<tr>
<td>• Ischaemia 2° to thrombosis of portal vein</td>
<td>• Involvement of lumbar plexus</td>
</tr>
<tr>
<td>• Superior mesenteric artery</td>
<td>• Spinal compression</td>
</tr>
</tbody>
</table>
associated with depressed mood and a disinclination to participate in the normal activities of life. Intense depression in the presence of abdominal pain is suggestive of pancreatic cancer [13].

Pain management

Objective assessment of pain relieving treatment is deficient, and thus objective advice to the patient is not possible, most measures being empirical; indeed, despite its frequency, pain relief is not used as a common therapeutic end point.

Surgery

If severe and persistent pain is present, surgical resection is rarely appropriate, and thus resection as a palliative technique is largely disregarded. There is no evidence that patients who have had a resection get less pain in the terminal phases of the disease or have a better quality of life during the terminal phase of their illness, yet there are unsupported statements to this effect; indeed, most surgeons accept this as true.

There is also no evidence that palliative bypass of the bile duct and/or the stomach influences pain unless infection is present. In one survey, less than 10% of patients who underwent a palliative biliary bypass reported any pain relief [12]. Pain relief has been reported following the establishment of pancreatic duct drainage by an endoprosthesis [141, but the relief afforded is temporary and on the basis of experience with chronic pancreatitis, the stents require constant attention. The older experience with 'triple' bypass, in which pancreateojunostomy was added to a biliary and gastric bypass [15] has shown that the procedure offers poor palliation [16]. Thus, surgery as a palliative procedure for pain has nothing to offer, but if surgery is performed, then a surgical or chemical splanchnicectomy is advantageous.

Splanchnicectomy

Surgical. Surgical splanchnicectomy techniques require the plexus to be isolated and the nervous structures resected bilaterally as they originate from the plexus. Apart from the experience of Leger and Dubois [17] in France, there is no other series of this procedure to substantiate its value as a palliative measure. Indeed, experience from the Japanese School of Surgery in the performance of radical splanchnicectomy suggests that the inevitable associated diarrhoea outweighs the benefits of pain relief, thus providing poor palliation. Thoracoscopic. With the development of improved thoracoscopic instruments and the recent enthusiasm for endoscopic surgery [18], there has been a wave of interest in bilateral splanchnicectomy in the supradiaphragmatic position where the nerve is readily visible beneath the pleura. Early reports suggest that the procedure provides good pain relief. If these reports are substantiated by careful follow-up, then this procedure will undoubtedly provide good palliation as it can be done minimally invasively, with a short hospital stay and a low complication rate.

Chemical, intraoperative. The use of intraoperative chemical splanchnicectomy was first introduced by Copping et al in 1969. In their subsequent report of 41 patients in 1978, 88% patients with pain due to pancreatic cancer experienced pain relief postoperatively [11]. Comparison with historical controls suggested benefit. In 1993, the Johns Hopkins group reported the first prospective, randomised, placebo-controlled study [9]. Chemical splanchnicectomy was performed with 20 ml of 50% alcohol, or saline placebo, on each side of the aorta at the level of the coeliac axis. A total of 139 patients were randomised; those receiving alcohol had a significant reduction in pain scores without additional morbidity. It is advised that this procedure is performed on all patients who undergo a palliative surgical procedure.

Percutaneous: The use of percutaneous coeliac plexus nerve block performed under either fluoroscopic or computed tomography-guidance can provide pain relief in 80-90% patients. The relief is effective for up to six months.

Other measures

Radiation therapy. Conventional external beam radiation, intraoperative radiation therapy [IORT] with electrons, IORT with brachytherapy, and IORT with electrons or brachytherapy plus external beam radiotherapy can all produce analgesia [13]. However, studies are limited and characterised by small numbers of patients, the absence of formal pain assessment methods, and short follow-up. Additional studies are required in order for clinicians to give advice which is evidence-based.

Chemotherapy. The potential for favourable palliative effects from systemic chemotherapy is under continuing investigation, and to date studies concentrating specifically on the palliative effect of chemotherapy are limited. Gemcitabine has been given approval in the United States and Europe on the basis of its capacity to ameliorate symptoms [19]. To date, large scale trials determining its value in the palliation of this disease are not available.

Pharmacological pain management. The mainstay of chronic pain management is the use of analgesic medications such as non-steroidal antiinflammatory drugs and opioids with or without adjuvant analgesics. Drug therapy can control pain in 70-90% patients. The treatment of opioid side-effects is an integral part of the therapeutic strategy. Effective management of constipation, nausea and vomiting, delirium, myoclonus and urinary retention enhances comfort and may allow a higher and more efficacious opioid dose.

Jaundice

If untreated, obstructive jaundice will result in progressive liver dysfunction culminating in liver failure and early death. In addition, the pruritus associated with obstructive jaundice can be unbearable and is seldom responsive to medications; further, the jaundiced patient experiences anorexia, nausea, and progressive malnutrition. Therefore, relief of jaundice may provide dramatic, albeit short-term improvement in the patient's well-being. Sarr and Cameron found that biliary bypass was associated with a longer and more comfortable survival (5.4 months) than those patients who only had a diagnostic laparotomy (3.5 months) [20]. There is now no excuse for not attempting relief of jaundice.

Which method to relieve the jaundice is at present the dominant dilemma. The insertion of a stent endoscopically or percutaneously, and the relief of jaundice surgically, offer similar outcomes. In a review of nine studies that included
more than 20 patients in whom stent placement was attempted for malignant bile duct stenosis [21], it was found that the stent was placed successfully in 91%, and was associated with procedure-related complications in approximately 20%, a procedure-related mortality of 1.3% and a 12% 30-day mortality. The median survival in the series was 4.9 months. In five series in which an endoscopically placed stent was randomised against surgical bypass, neither decompensate technique appeared superior to the other with respect to treatment success or survival [21]. In the largest controlled trial, 201 patients were randomised; 101 patients in the surgically treated group and 100 patients in the endoscopic stenting group [22]. Results were analysed on an intention to treat basis. Technical and functional success rates were comparable - 92%, procedure-related mortality was 14% for the surgically treated patients versus 3% for the stented patients. Complications were almost threefold higher in the surgically treated group (29% versus 11%) and there was a statistically significant longer hospitalisation for those treated surgically (26 versus 20 days). However, recurrent jaundice was observed in 7 of 92 surgically treated patients versus 36 of 92 stented patients. Moreover only 7% of the surgically treated patients developed gastric outlet obstruction whereas 17% of the stented patients did so. Approximately one half of the surgically treated group had undergone concomitant gastroenterostomy at the time of biliary bypass. There were comparable median survival times between the two groups. The trial was biased towards stenting, in that the majority of patients were stented in the University Centre, with less than half of the surgical patients so treated, being managed at their referring centre. An increased survival was noted in patients who had undergone surgery when only the survivors of both techniques were compared. The late problems in those who had undergone stenting related to blockage and sepsis, both of which increased early mortality. These studies used plastic prosthetic stents. The availability of metal expanding stents may overcome some of the technical stent problems, while the availability of newly developed duodenal stents will reduce the requirement for late laparotomies for gastric outlet obstruction [23]. Surgery however, has advanced also with recent series suggesting that a mortality rate in surgically treated patients of 2.4% can be achieved [24]. In the series from the Johns Hopkins [25] surgical palliation was accomplished with a 2.5% mortality. Combined biliary and gastric bypass was performed in 75% of the patients. Although perioperative complications were frequent, occurring in 37% patients, most were minor and seldom life-threatening. The mean perioperative hospital stay was 14 days, with patients returning to a regular diet in 10 days. The mean survival was 7.7 months.

The type of biliary bypass performed remains open to personal preference. An anastomosis of the gallbladder is not appropriate as the failure rate is higher, recurrent jaundice occurring in 60% patients so treated [26]. Thus the bile duct is preferable, but whether the more complex choledocho-jejunostomy with Roux-en-Y loop is preferable to the simpler choledocho-duodenostomy is open to debate. I prefer to use the duodenum because of its simplicity and ease of endoscopic access if jaundice recurs.

_Laparoscopic bypass:_ This is an alternative to the open approach, and techniques are available for both biliary and gastric bypass [27] but evidence showing clinical gain is at present lacking.

The palliative approach

Resection offers the only potentially curative approach to pancreatic cancer. The majority of patients are either too old, too ill with coexistent disease, or have a tumour that is undoubtedly inappropriate to resect. Thus for the vast majority an endoprosthesis to relieve the jaundice, and if necessary, to relieve gastric outlet obstruction, is the preferred management. For the remainder, a laparotomy and bypass is preferable as it enables a biliary and gastric bypass to be performed with a splanchic block of the coeliac axis. No imaging modality is sufficiently accurate in the patient with a doubtfully resectable tumour. The preferable bypass is controversial, but the large analyses of published literature suggest that a choledochoenterostomy is preferred with a slight advantage in terms of mortality for a choledocho-duodenostomy [28]. Such a policy is only acceptable if the surgical mortality is less than 5% and the morbidity enables 75% of patients to leave hospital within 18 days. Readmission rates should be lower than for stented patients. Palliative surgery demands surgical excellence which is not the standard achieved at present in most patients with pancreatic cancer.

References

17. Dubois F. Splanchicectomy par voie abdo@rale transhiatale. Presse Med 1977; 6: 2069-70

Correspondence to:
RCG Russell MS FRCS
149 Harley Street
London
WIN 2DE
U.K.