Pancreatic cancer – is an aggressive approach justified?

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ABSTRACT

INTRODUCTION Surgery is the only curative treatment for carcinoma of the pancreas. Resection rates can be low (4.5%), figures of 30% have also been suggested as possible. The approach undertaken in this unit is to consider all patients as potentially resectable unless otherwise proven.

PATIENTS & METHODS 140 patients were studied over 6-year period; 113 underwent palliative treatment (48% distant metastases, 40% local spread, 11% high operative risk); 14 had a triple bypass (14/113 = 12%), 99 were managed conservatively, 43 received palliative chemotherapy. 23/140 (16%) underwent Whipple's procedure (n = 23; 12 females, 11 males; mean age, 60 years); 4/23 had chronic pancreatitis. Distal pancreatectomy was undertaken in 4 patients.

RESULTS Median survival time for patients undergoing a triple bypass was 5 months (range, 0.1–20 months), 3 months for patients treated conservatively (range, 0.1–30 months) and 5 months for patients undergoing palliative chemotherapy (range, 1–30 months). 30-day mortality for Whipple's procedure was 4% (1/23) with median survival rate for patients with carcinoma of 13 months (range, 5–66 months); 31 months for patients with clear resection margins and negative nodes (n = 5).

CONCLUSION This policy allows a resection rate of 19% with increased median survival rate for patients with cancer by 8 months more than those who were not resected. Aggressive staging and pancreatic biopsies allow patients to be entered into chemotherapy trials with improvement in survival and potential future benefits.

KEYWORDS

Pancreatic resection – Whipple's procedure – Pancreatic cancer

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Pancreatic cancer is presently the fourth leading cause of cancer-related deaths in Western countries with an incidence of 8–10 new cases per 100,000 and increasing. It has a poor prognosis with an untreated 1-year survival of less than 20% and 5-year survival of 0%.¹ Since current conservative oncological therapies fail to influence the long-term outcome, curative resection remains the only possibility with a potential for cure.

Postoperative mortality has decreased significantly in the last decade. The contributing factors for this change include improvement in pre-operative staging, surgical technique as well as postoperative care. There is a wide variation between units in the long-term survival as well as the resection rates. The volume of patients with pancreatic cancer seen in a hospital may account for some of these differences as patients managed by higher volume hospitals have been shown to undergo a more aggressive staging and resection.²

Pancreatic resection rates have varied from 2.6% to 99%.^{3,4} These need to be carefully evaluated as the 99% figure was reported by a Japanese study performed in selected centres for tumours less than 2 cm in size while the 2.6% figure was observed in the West Midland region of England and included all patients having pancreatic cancer. A more recent figure from the same region showed a resection rate of 4.8%.⁵ Both Scottish⁶ and Italian⁷ studies have quoted rates of 15–18%. Five-year survival following pancreatic resection has ranged between 5% and 21%.^{8–10}

On the basis of this considerable variety in resection rates and its potential influence on survival, we have looked at the resection rates and management plans in a hospital where all patients with possible pancreatic cancer are seen by one unit – on average, 23 patients per year. The approach has been to consider all patients as potentially resectable and only then exclude those who are not appropriate for 'curative' surgery, rather than assume the opposite.

Figure 1. Treatments in patients presenting with suspected pancreatic cancer.

Patients & Methods

A total of 140 patients with suspected cancer were identified from coding and medical records over a 6-year period. Diagnosis of cancer was based on radiological findings and histology (as much as possible).

If the tumour was found not to be resectable and the patient was fit for further palliative treatment, biopsies were taken to confirm the diagnosis. This was done in 58% of cases before decision about further management was made. Of the biopsies 85% confirmed malignancy.

A lesion was considered resectable if there was no superior mesenteric vessels or portal vein involvement and in the absence of extra-pancreatic spread. Patients' fitness for surgery was determined in conjunction with an anaesthetist and cardiologist. Prior to resection, the appropriate imaging was discussed in a multidisciplinary meeting. With the advent of endoluminal ultrasonography in 2000, those meeting criteria for resection underwent further imaging of vascular involvement with endoluminal ultrasonography. Superior mesenteric artery involvement was considered to make the lesion inoperable as was encasement of superior mesenteric (SMV) or portal vein (PV). If the term 'abut' was used to describe the relationship of tumour to SMV/PV, this did not preclude resection. The 30-day mortality was used as an outcome measure in this study.

Results

Figure 1 shows the overall treatment groups. In total, 19% of patients underwent a pancreatic resection. Overall, 23 patients who presented with jaundice and a pancreatic mass in which cancer could not be excluded had a Whipple's operation. This includes patients undergoing both a Whipple's procedure as well as a pylorus preserving pancreaticoduodenectomy. Four patients underwent a distal pancreatectomy.

The palliative group included 81% of patients: 12% of patients in this group (10% of all patients) had a triple bypass which includes seven patients who had a planned procedure for duodenal obstruction and in seven cases an irresectable tumour was found at laparotomy. The number of triple bypasses has decreased since the introduction of duodenal stenting. 38% of patients in the non-resected group were entered into chemotherapy trials (31% of all patients). The pattern of referral for chemotherapy has also changed over the last few years since current treatment has become less toxic and possibly more effective.¹¹

Computed tomography (CT) accurately predicted resectability of a pancreatic mass in 77% of cases (23/30). Seven patients underwent laparotomy and the tumour was found to be not resectable. This occurred prior to the introduction of the endoluminal ultrasonography. A combination

Figure 2. Distribution of patients who did not undergo resection.

of CT and endoluminal ultrasonography has resulted in 96% accuracy in predicting resectability of a pancreatic mass.

Figure 2 shows the groups not undergoing resection and the reasons for this. These include 48% of patients who had distal metastases on presentation, 40% had local spread involving superior mesenteric vessels, 11% were unfit for surgery based on an anaesthetic and cardiology review, and 1 patient chose not to undergo surgery.

Table 1 gives the overall demographic data. The male-to-female ratio was similar in all groups with a mean age ranging between 60–70 years. The exception was the distal pancreatectomy patients who were all female with a mean age of 52 years. Although small numbers, this could be explained by the unusual pathology found in this group of patients.

Histology from surgical specimens revealed that 4/23 patients who underwent pancreatic resection for suspected cancer had changes consistent with pancreatitis with no evidence of malignancy. Eighteen patients had an adenocarcinoma and one an intraduct papillary neoplasia. Sixteen tumours were pancreatic in origin and three ampullary.

There was one death, giving a 30-day operative mortality for patients undergoing a Whipple's procedure of 4% (1/23). Four distal pancreatectomies were performed – two for endocrine tumours, one for a cystadenocarcinoma and one for a pseudopapillary tumour.

Figure 3 summarises survival details. Median survival time for patients undergoing a triple bypass or chemotherapy was 5 months, 3 months for patients undergoing supportive treatment and 13 months for patients following a Whipple's procedure. Of the 19 patients who underwent resection for confirmed cancer, 5 had clear resection margins with no nodal involvement on histology. When margins and nodes were clear, the survival time increased to 31 months. Clear margins with positive nodes were found in 2 specimens (2/19). Both patients are alive, 31 and 66 months

Table 1 Demographic data

	No. of females	No. of males	Total No.	Mean age (yr)
Supportive treatment	34	40	74	71
Triple bypass	7	7	14	71
Chemotherapy	23	20	43	66
Whipple's procedure	12	11	23	60
Distal pancreatectomy	4	0	4	52

post-surgery. Twelve patients had a positive margin with mean survival time of 16 months (12/19). Four of 18 of patients (22%) who underwent a Whipple's resection for cancer are currently between 3 and 6 years post-resection with no evidence of recurrence (intraduct papillary neoplasia excluded).

Outcome following distal pancreatectomy is difficult to assess since two out of four patients are still alive and one patient died in the postoperative period from a massive pulmonary embolus (25% mortality). This gives an overall mortality for resections of 7%. Clear resection margins with negative nodes were found in two out of four patients.

Postoperative complications include one patient who developed a pancreatic fistula which settled with conservative treatment, one postoperative haemorrhage requiring a second laparotomy and three chest infections.

Discussion

The approach outlined here is that of one unit seeing all patients with a presumptive diagnosis of pancreatic cancer and a policy of assuming resection to be possible unless proven otherwise. This has resulted in a resection rate of 19%, similar to other reports from Europe^{6,7} and higher than reported elsewhere in the UK.^{3,5} Such an approach was associated with an increased median survival time for patients with cancer by 8 months and 26 months for patients who had a complete resection with no nodal involvement. Combined with the resection rates (albeit not great numbers), we have shown a reasonable in-hospital mortality figure for Whipple's procedure of 4% and a 3–6 year disease-free survival of 22% which is comparable with other centres. Aggressive staging and biopsy also allows patients to enter chemotherapy trials with an improvement in survival and potential future benefits.¹¹

The total numbers for time given here are not large. They do, however, indicate that it is possible to achieve a higher than usual resection rate with acceptable outcomes, thus allowing this study, by concentrating patients with pancreatic cancer in one unit. Good outcomes are suggested to depend

Figure 3. Median survival time in months for different groups of patients.

on volume of cases seen² and possibly numbers of resections performed,¹² although, Bachmann *et al.*² found that doctors' or hospitals' surgical volume was not independently associated with operative mortality.

In the re-organisation of pancreatic care services there is much emphasis on the site of resection. We would suggest that perhaps more important is appropriate investigation leading to selection of patients for resection. Before pancreatic cancer services become centralised, considerable care needs to be taken to ensure specialist involvement at all stages of patient care to achieve the results shown both here and in other centres. All patients with pancreatic cancer need to be seen by, or discussed with, the relevant team to avoid selective referral for resection only with a reduction in other treatment options being offered, including best palliative care. It would be a shame if the influence of overall volume of cases were to be lost on the alter of number of resections.

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