

Palliation for carcinoma of head of pancreas

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Summary

Ninety eight consecutive patients with an operative diagnosis of carcinoma of the head of the pancreas are discussed. Recent advances in the preoperative diagnosis and management appear to have failed to make a significant impact in non-specialised units, with 82 patients undergoing palliative procedures with an operative mortality of 25.6% rising to 36% when jaundice was present. Overall median survival was 202 days (range 35–967). Recurrence of jaundice developed in 42 patients and was more common with cholecysto-enteric bypass than in choledocho-enteric bypass. Forty four per cent of patients undergoing biliary bypass alone subsequently had signs of gastric outlet obstruction.

Introduction

In carcinoma of the pancreas, as with all cancers, the aim of treatment must be to obtain a cure if possible and if this is not achievable then to provide effective palliation. Unfortunately the majority of patients with pancreatic cancer present with an advanced tumour which probably precludes any chance of curative surgery. In specialised centres resection rates may be as high as 30% but only one third of the resected specimens show a localised potentially curable lesion (1). The majority of patients have nothing more than palliative treatment.

An appropriate palliative operation should carry a low mortality and little in the way of morbidity enabling early return of the patient to their home. Patients with advanced tumours at the head of the pancreas, however, are frequently jaundiced and surgical procedures in such patients have a reputation for a high mortality and considerable morbidity. This has led many of our colleagues to advocate palliation using radiological or endoscopic techniques (2, 3) thus avoiding operation.

In the last two decades, however, there have been major advances in the investigation and management of these patients which should have improved the prospects for surgical treatment. Investigative techniques using ultrasound, percutaneous cholangiography and computerised tomography may indicate an accurate diagnosis and should enable more appropriate case selection. On the management side it has been suggested that the routine use of vitamin K, antibiotics and measures to prevent renal failure should decrease mortality and morbidity.

If the patient survives the operation it is important that the palliation obtained is effective and that the presenting symptoms do not recur. There is controversy how this is

best achieved and many different forms of bypass procedure are performed, there being relatively little evidence to favour one in particular.

We have reviewed cases of carcinoma of the pancreas in our hospital in an attempt to evaluate the different procedures and also to look at the impact made by recent advances in the investigation and management of these patients.

Patients and methods

The case notes were examined of all patients with a diagnosis of carcinoma of the head of the pancreas admitted to the General and University Hospitals in Nottingham during the four years 1978 to 1981. Follow-up information for all patients was obtained by referral to the case notes, the general practitioner or the Nottingham Cancer Register.

In the series, carcinoma of the head of the pancreas was diagnosed at laparotomy in 98 patients. Biopsy was performed in 33 patients. There were 42 males and 56 females (ratio 1:1.3) with a median age of 68 years (range 41–89). Eight seven patients presented with jaundice of which 25 had been icteric for more than 4 weeks. Gastric outlet obstruction was the presenting feature in 11 patients. Of the jaundiced patients, 46 had a palpable gallbladder. Diabetes mellitus was present in 13 patients with a further 6 patients subsequently developing the condition. Operative mortality is defined as death within 30 days of the operation.

Results

PREOPERATIVE INVESTIGATION

Computerised tomography was not available in Nottingham during the years covered by this study. The 11 patients presenting with gastric outlet obstruction were investigated by barium studies and/or endoscopy prior to laparotomy. The frequency with which ultrasound and transhepatic cholangiography (PTC) were used in the jaundiced patients is shown in Table 1. It is apparent that many surgeons were happy to proceed to a laparotomy without the benefit of preoperative cholangiography.

TABLE 1 *Preoperative investigations*

Year	Number of jaundiced patients	Ultrasound	PTC
1978	17	10	6
1979	31	20	3
1980	22	17	3
1981	17	17	8

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TABLE II Operations performed

Operation	Number of patients
Pancreatico-duodenectomy	1
Cholecysto-enteric by-pass +gastroenterostomy	38
Cholecysto-enteric by-pass alone	28
Choledocho-enteric by-pass +gastroenterostomy	4
Choledocho-enteric by-pass alone	8
Gastroenterostomy alone	4
Laparotomy—no procedure	15

PERIOPERATIVE MANAGEMENT

Preoperative vitamin K was given to all of the jaundiced patients but appropriate antibiotic prophylaxis was used in only 45.

Measures to prevent the development of renal failure were employed in 64 patients, 54 receiving mannitol and 10 receiving a diuretic during the course of the operation. However, in only 26 of these were intravenous fluids given in the immediate preoperative period to ensure adequate hydration.

OPERATIVE PROCEDURES

The operative procedures performed are detailed in Table II. Only one patient underwent resection of the tumour whereas a palliative bypass was performed in 82. There was a marked preference for using the gall bladder for biliary bypass. In 15 patients no procedure was possible. Liver metastases were noted in 31 patients. In only 33 patients was an operative biopsy of the pancreas or metastatic deposit obtained. There was no histological evidence of carcinoma in 7 patients but the remaining patients had proven adenocarcinoma. There were no complications related to the operative biopsy procedure.

OUTCOME

Follow-up is complete with two patients alive at 2 years and 5 years after surgery (in neither of these was positive histology obtained). The rest have all died. Overall operative mortality was 33%. In the 82 patients undergoing palliative bypass the mortality rate was 25.6% and was higher in the jaundiced group (36%) than in the non-jaundiced group (18.2%). Operative mortality in the patients with liver metastases was 48.4%. The use of preoperative hydration, mannitol and antibiotics did not significantly alter the mortality among jaundiced patients in this study (Table III).

The overall median survival of those recovering from operation was 202 days (range 35–1013). Following cholecysto-enteric bypass the median survival was 215 days (range 35–909) but after choledocho-enteric bypass with gastroenterostomy the survival was much longer (median 326 days; range 35–967 days). Patients with liver metastases had a median survival of only 90 days (range 35–399).

TABLE III Operative mortality in jaundiced patients

	Number of patients	Operative mortality
Mannitol/diuretic	64	23 (35.9%)*
No Mannitol/diuretic	23	6 (26.1%)
Preoperative fluids	26	8 (30.8%)*
No preoperative fluids	61	23 (38%)
Antibiotics	45	13 (28.9%)*
No antibiotics	42	18 (44%)

*Chi-square: not significant

Relief of the symptoms was only temporary in many of the patients. Jaundice recurred before death in 42 of the 66 patients in whom the gall bladder was used for the biliary bypass. This significantly contrasts with a recurrence of jaundice in only 2 of the 12 patients who had a bypass to the common hepatic duct (Chi-square $\chi^2=9.1$; $0.01 > P > 0.001$).

In patients undergoing biliary bypass without a gastroenterostomy significant symptoms of gastric outlet obstruction were noted in 11 patients of 25 patients (44%) readmitted to hospital for terminal care. Sixteen patients who underwent double bypass were readmitted and four of these had postprandial vomiting (Chi-square $\chi^2=1.5$; $P > 0.1$).

Discussion

The result of this survey must make depressing reading for any surgeon interested in the management of pancreatic cancer. The main conclusions that can be drawn are:

- 1 Preoperative investigation remains rudimentary in many cases
- 2 The use of antibiotics and measures to prevent renal failure have yet to gain universal acceptance
- 3 Operative assessment of carcinoma of the head of pancreas is good but all cases should have histological or cytological confirmation of the diagnosis
- 4 There is great reluctance to attempt resection for carcinoma in the head of the pancreas
- 5 The operative mortality for malignant obstructive jaundice is unacceptably high
- 6 The palliative procedures used frequently only provide temporary relief of the symptoms.

It might be suggested that much of what is reported is at odds with what would be regarded as 'good practice' in specialised hepatobiliary units. However the patients reported in this study were under the care of 8 surgeons with widely different interests and their management probably reflects the general pattern of practice in British hospitals. It is obvious that the recent advances in diagnosis and management of pancreatic cancer have failed to make any significant impact.

We believe that the major factor influencing the management of these patients is the extremely poor prognosis. Radical resection of the tumour is possible but the operative mortality may be as high as 20% (4-6) and 5 year survival is unlikely to exceed 5%. These figures have led many surgeons to adopt the conservative policy reflected in the practice in Nottingham where only one of the 98 tumours was resected.

If an attempt at resection is unlikely, is extensive investigation justified?

Preoperative diagnosis of pancreatic cancer has been revolutionised by the introduction of ultrasound, percutaneous transhepatic cholangiography, ERCP and computerised tomography with a diagnostic accuracy of over 90% being reported (7,8). In our series there was a progressive increase in the use of ultrasound and in the final year all patients had this investigation. Transhepatic cholangiography was not widely used. It would appear that in many cases the surgeons were happy to accept ultrasound evidence of extrahepatic biliary obstruction and to proceed straight to laparotomy without definite knowledge of the site and cause of the obstruction. Eyre-Brook *et al.* (9) have recently demonstrated that this is probably an acceptable approach although one must have reservations that potentially curable lesions may be missed.

It is evident from our series that the importance of preoperative correction of coagulation defects in jaundiced patients has been accepted into standard surgical practice and all of the jaundiced patients received Vitamin K. Prophylaxis against infection and renal failure has not become routine. In this series only 48% of the patients received antibiotics and in only 74% were measures taken to prevent renal failure. It seems likely that surgeons are

aware that, in patients with bile duct obstruction due to carcinoma of the pancreas, the incidence of infected bile is below 10% (10) and therefore do not consider antibiotic prophylaxis to be essential. Other series have reported a low rate of antibiotic usage in such patients (11,12). Somewhat more surprising is the low priority given to protection of renal function during the perioperative period.

It was in 1965 that Dawson demonstrated the beneficial effect of mannitol (13) but a search of the literature reveals little in the way of large, randomized, controlled trials to confirm this. There is a clear need for such trials as renal impairment may be a contributory factor to death in many of these patients (14). It is hoped that the recent interest in the use of preoperative bile salts (12, 15) to maintain postoperative renal function will lead to appropriate clinical studies. Only when the efficacy of a treatment is proven can we expect its universal application.

The overall operative mortality in this series was 33% but this included 15 patients in whom even palliative surgery was not possible. In patients undergoing palliation the mortality was 25.6% rising to 36% when jaundice was present. Others have reported mortality rates varying from 6–33% with the lower rates usually being achieved in specialist centres (16–18). This raises the question of whether or not all jaundiced patients should be managed by a team with a special interest in biliary tract disease.

Among patients surviving operation it is discouraging to find that a large number developed a recurrence of jaundice. Our study suggests that using the common bile duct for bypass gives longer relief from jaundice and a longer survival than using the gall bladder. However we know of no clinical trials to confirm this and the majority of surgeons appear to favour the simpler operation.

Postprandial vomiting suggestive of gastric outlet obstruction was seen in 11 patients who did not have a double bypass. This represents 44% of patients readmitted to hospital. Other series report a range from 2–50% (18). Further studies such as those of Meinke *et al.* (19) may enable accurate prediction of these patients who require a gastroenterostomy but until this is clarified it would seem sensible to include it with the biliary bypass.

We have shown that in non-specialised units the operative mortality for the palliative treatment of carcinoma of the pancreas remains at a level which is unacceptable and that the palliation achieved is frequently less than ideal. The incidence of this disease appears to be rising (20, 21) and yet surgical practice has made little advance. The scope for further clinical studies is enormous and unless we can improve many aspects of the surgical treatment, it is likely that endoscopists and interventional radiologists will continue to play an increasing role in the management of this distressing condition. At the present time our study shows only too clearly why non-operative means of palliation are being rigorously pursued.

Critical Comment

I am grateful to be allowed to comment on this valuable contribution. The lessons to be learnt are self-evident but merit to be highlighted.

It is sad to note that biopsy of the pancreas was performed in only 33% of patients. In the first place as shown by Phyllis George, as long ago as 1975, it is a perfectly safe procedure (1). Secondly, histological proof is essential in diagnosing a condition which in effect is a death sentence to the patient (2), as clinical assessment can be in error (note two survivors at 2 and 5 years) and finally, the potentially treatable malignant apudoma may be missed.

A triple bypass in patients coming to laparotomy should obviate recurrent jaundice and gastric outlet obstruction. It

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is for this reason a PTC is so valuable in delineating the level of bile duct obstruction and potential cystic duct involvement. Equally, but less clearly, it can be demonstrated on sequential CT scan views or real-time ultrasonography.

But what of the outcome? There are many authoritative papers in the last decade culminating in Mallinson's prospective randomised trial in 1980 to show the value of chemotherapy (3). Likewise, radiotherapy plays a vital role in the palliation of this disease. It seems reasonable on the basis of this survey, which no doubt reflects current British thought and practice in pancreatic cancer, to form a Pancreatic Task Force similar to that formed in 1974 by the late