THE LANCET

Early Diagnosis and Screening for Pancreatic Cancer

ONLY about a third of patients with pancreatic cancer have a palliative bypass for the jaundice, less than 10% have surgical relief of duodenal obstruction, and 3% have a resection of the tumour. So, although the disease has a possible operative treatment, it is no monopoly for surgeons. To achieve the best possible therapeutic results a multidisciplinary approach is necessary, taking into account epidemiology, pathology, staging, number of operations performed, and mortality and survival figures.[1,2] The importance of early diagnosis and screening can only be assesed when the incidence and prevalence of the disease are established, the accuracy and costs of the investigations assessed, and, most importantly, when it is known whether treatment can alter the natural history of the condition. If resection does not alter survival there is no purpose in discovering early disease when the only worthwhile procedure is palliative relief of jaundice or gastric outlet obstruction.

In 1982 there were 5720 deaths from pancreatic cancer in England and Wales, 51% being males. The registration rate was 12·8 per 100 000 for males and 11·2 for females, and median age at presentation was between sixty-five and seventy. 44% of men and 59% of women were over seventy at the time of registration and 75% of all patients were over sixty. The incidence of the disease has increased in every year of this century; England and Wales lie fourth in the international league table, behind Sweden, Denmark, and Scotland, with the USA below them.

In England and Wales in 1979, 1700 bypass operations were done for jaundice and 470 gastrojejunostomies to achieve gastric emptying; these figures represent 34% and 8%, respectively, of the total number of patients. There were only 200 pancreatic resections. Survival data[3] show that one-year survival of 10% fell to 3% at three years and to between 1% and 2% at five years. These overall figures can be improved by surgery,[4] but at the expense of an operation with a postoperative mortality and with bias due to patient selection. Pancreatic resection had an overall mortality in the UK of 14%, but in specialist centres it should be less than 10%. A successful resection should give a 30% one-year survival and a 5% five-year survival,[4] but such patients are highly selected (3% of the total). It is almost unheard of to achieve a five-year survival with cancer of the body of pancreas, but it is possible with carcinoma of the ampulla of Vater. However, ampullary carcinoma is rare; in 1979 there were 5881 pancreatic cancers registered and only 126 carcinomas of the ampulla.

Would earlier diagnosis lead to the discovery of smaller tumours? Do small tumours necessarily have a more favourable staging and would resection of an early cancer prolong life? Attempts to answer these questions have lately been made in a monograph from the Japanese Cancer Association. Among the contributors, Oi[5] studied pancreatic tumours measuring 2 cm or less in a survey by the Pancreatic Cancer Registration Committee of the Japanese Pancreatic Society. In 65 cases (3·2% of the total) 90% could be resected, of which only 38% were thought to be curable resections. Previous assessments,[6,7] which are probably too high, indicated that 15% of all tumours at presentation were stage I and the rest had lymph-node involvement which made them non-resectable. 15% of all pancreatic tumours in England and Wales would be 800, in which case the 200 resections done are theoretically too few; if the true figure for small resectable tumours is only 3%, then the figure of 200 is correct and cannot be increased except by a screening programme to discover earlier disease. Moosa from San Diego, California, a leading proponent of resection, quoted a mean survival time following resection of twenty-three months compared with less than six months for a bypass operation.[4] However, there is no general agreement about whether resection actually prolongs life because it is difficult to stage tumours preoperatively for proper comparison in a prospective controlled trial.

The technology for discovering early tumours is available by means of ultrasonography; computed tomography (CT); radionuclide scanning with either ^{75}Se-selenomethionine or ^{11}C-tryptophan; duodenal drainage studies and cytology; endoscopic retrograde cholangiopancreatography (ERCP) and cytology;

1. Allen-Marsh TG, Earlam RJ. Pancreatic cancer in England and Wales: surgeons look at epidemiology. *Ann R Coll Surg Engl* 1986; **68**: 154–58.
2. Cuschieri A. Carcinoma of the pancreas. *Hospital Update* 1986; 543–48.
3. Cancer Statistics Survival 1971–75. London: OPCS series no 9, 1982.
4. Moosa AR, Cohen DM. Early diagnosis of pancreatic cancer: feasible or worthwhile? In: Inokuchik, ed. Digestive tract tumours. GANN monograph on cancer research no 31 (Japanese Cancer Association). New York: Plenum, 1986: 139–45.
5. Oi I. Early detection of small pancreatic carcinoma. In: Inokuchi K, ed. Digestive tract tumours. GANN monograph on cancer research no 31 (Japanese Cancer Association). New York: Plenum, 1986: 147–49.
6. Nix GAJJ, Schmitz PIM, Wilson JMP, et al. Carcinoma of the head of the pancreas. Therapeutic implications of endoscopic retrograde cholangiography. *Gastroenterology* 1984; **87**: 37–43.
7. Cubilla AL, Fortner J, Fitzgerald PJ. Lymph node involvement in carcinoma of the head of the pancreas. *Cancer* 1978; **41**: 880–87.

coeliac and superior mesenteric angiography; and tumour markers. The individual diagnostic accuracy of ultrasound, CT scanning, and ERCP with cytology is 85–95%. Would the widespread use of these particular tests, either as a screening programme or to investigate patients with symptoms, lead to the discovery of smaller tumours at an earlier stage? Moreover, if such tumours were resected successfully, would the patients live longer? Proper monitoring is required to determine whether the number of tumours measuring 2 cm or less is increasing and whether the number of pancreatic resections in England and Wales has risen above the 1979 figure of 200, given that the overall figures for pancreatic cancer registration are rising. Difficulties are that cancer registration figures tend to have a long lag period and the requisite investigative techniques are new.

Should a screening programme be instituted for diagnosing early pancreatic cancer in symptomless subjects? The overall incidence of the disease is approximately 10 cases per 100 000, which means that in the average sized district of 250 000 inhabitants there will be 25 cases each year of whom about 13 will be over 70 and presumably not always suitable for pancreatic resection. In England and Wales, therefore, with 197 districts and 200 resections, there is 1 pancreatic resection per district per year. In Japan, where screening by endoscopy for gastric cancer is now statutory, the incidence of that disease is more than ten-fold greater—>100 per 100 000. Thus screening a normal population for pancreatic cancer in the UK or any other country would not seem worthwhile.

A more practical solution is to diagnose patients with symptoms, which include jaundice, quickly, easily, and with non-invasive techniques. There are two categories of patient at risk. From centres with experience in treating pancreatic cancer it has been noted that late-onset diabetes mellitus should always be fully investigated and that 10% of those with pancreatic cancer had had a cholecystectomy in the previous two years.[4] It is now clear that a negative barium meal and a negative oral cholecystogram do not constitute adequate investigation either of jaundice or vague upper abdominal symptoms. Ultrasonography should be the next test. A similar case cannot be made for insisting on a CT scan for all patients suspected of having the disease. If the ultrasound scan is abnormal, the patient should be referred to a gastroenterologist for ERCP, biopsy, or cytology. For general practitioners, screening of patients by means of ultrasound and a barium meal would seem to be the best policy; patients with a high clinical or radiological suspicion of pancreatic carcinoma could then be referred for ERCP. Some hospitals have open access endoscopy, but the usual result is overloading of the system; it must be emphasised that gastroduodenoscopy is not equivalent to ERCP.

The message in 1986 must be that a mass screening programme with present techniques cannot be cost-effective because the disease is so rare. However, patients demand a diagnosis as a basis for rational treatment even though it may be symptomatic rather than curative in the majority. The fact that surgery cannot cure pancreatic cancer should not turn us all into therapeutic nihilists.