

Management

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At presentation, more than 85% of patients with ductal adenocarcinoma are unsuitable for resection because of advanced disease. If imaging shows that the tumour is potentially resectable, the patient should be considered for surgical resection, as that offers the only (albeit small) chance of a cure. Every patient with pancreatic cancer should ideally be discussed in a multidisciplinary forum. Comorbidities should be taken carefully into account. Biological rather than chronological age should be the consideration. In patients with locally advanced or metastatic disease the primary objective should be to relieve symptoms, improve quality of life and extend survival, rather than achieve a cure. Patients will broadly fall into four categories. 1 Resectable: these patients should be offered surgery, to be followed by adjuvant chemotherapy. Some centres have begun to suggest that neoadjuvant chemotherapy be used prior to resection, but the evidence is not strong. 2 Borderline resectable (usually because of significant venous occlusion or arterial abutment): these patients may be offered neoadjuvant chemotherapy with/without chemoradiotherapy, to be followed by surgical resection if the disease has been downstaged. Adjuvant therapy should follow. 3 Locally advanced and unresectable: offer systemic chemotherapy. Surgery may subsequently be possible in a small cohort who get downstaged. 4 Metastatic: offer systemic chemotherapy. If a cystic tumour is encountered, no matter how large, surgical resection should be considered as it carries a reasonable chance of cure. Tumours of the ampulla have a good prognosis and should, if at all possible, be resected. Some of the rare tumours and the neuroendocrine lesions should also be resected if at all possible. Surgical resection The standard resection for a tumour of the pancreatic head or the ampulla is a pylorus-preserving pancreatoduodenectomy (PPPD). This involves removal of the duodenum and the pancreatic head, including the distal part of the bile duct. The original pancreatoduodenectomy as proposed by Whipple included resection of the gastric antrum. Preserving the antrum and the pylorus is thought to result in a more physiological outcome with no difference in survival or recurrence rates. The Whipple procedure is now reserved for situations in which the entire duodenum has to be removed (e.g. in FAP) or in which the tumour encroaches on the first part of the duodenum or the distal stomach and a PPPD would not achieve a clear resection margin. Total pancreatectomy is warranted only in situations where the head of the pancreas is too inflamed or too friable to achieve a safe anastomosis with the bowel. The PPPD procedure includes a local lymphadenectomy. Extended lymphadenectomy has not been shown to be beneficial in improving survival and is associated with increased morbidity. - If the tumour is adherent to the portal or superior mesenteric vein but can still be removed by including a patch or a short segment of vein in the resection, with an

appropriate reconstruction of the vessel, then that should be done. This is not associated with an increase in the morbidity or mortality of the procedure and the outcomes are similar. Arterial resections are not recommended unless carried out within the context of a trial. If performed outside a trial, they should be preceded by multidisciplinary discussion and careful counselling of the patient, and be carried out in a specialist unit. For tumours of the body and tail, distal pancreatectomy with splenectomy is the standard. Infiltration of the splenic artery or vein by the tumour is not a contraindication to resection. When resecting the pancreatic tail for a benign lesion, one may attempt to preserve the spleen if possible. When removing the spleen, prior vaccinations against pneumococci, meningococci and Haemophilus influenzae B should be administered, and subsequent antibiotic prophylaxis given (see Chapter 70). While the majority of pancreatic resections continue to be performed via an open approach, minimally invasive approaches – laparoscopic and robotic – are feasible and may yield comparable results. Minimally invasive pancreatic resections are technically challenging, pose additional demands on operating room time and equipment and involve a significant learning curve for the surgeon and the entire team. They should be restricted to specialist centres and surgeons who have experience in doing them. Distal pancreatectomy, especially for smaller tumours, lends itself more easily to the laparoscopic or robotic approach than a pancreatic head resection. Robotic surgery may carry greater ergonomic benefit for the surgeon (see Chapter 10).

Pancreatoduodenectomy

The patient's coagulation screen should be checked preoperatively and adequate hydration ensured. The patient should be aware of the diagnosis, the gravity of the operation and the risks involved. The operation has three distinct phases: exploration and assessment; resection; reconstruction. A cholecystectomy is performed. The bile duct and hepatic artery are exposed, removing the lymphatic tissue in this area. Exposure of the hepatic artery enables division of the gastroduodenal artery and visualisation of the portal vein. The distal part of the gastric antrum is mobilised. The duodenum and right colon are mobilised from the retroperitoneal tissues. The superior mesenteric vein is exposed inferior to the pancreatic head. Careful dissection into the plane between the vein and the pancreatic substance (Figure 72.2) will reveal whether the tumour is adherent to the vein. At this juncture, a decision has to be made whether to proceed to the next phase of resection or not. If resection is to be performed, the fourth part of the duodenum is dissected and freed from the ligament of Treitz so that the upper jejunum can be brought into the supracolic compartment. The jejunum is divided 20–30 cm downstream from the duodenojejunal flexure, and the mesentery of the proximal jejunum is detached. The first part of the duodenum is divided. The neck of the pancreas is divided, and then the uncinate process is separated from the superior mesenteric vein and artery working up towards the upper bile duct, which is divided, releasing the specimen (Figure 72.34). Retroperitoneal lymph nodes within the operative field are completely removed with the specimen. Reconstruction is carried out as in Figure 72.35. The pancreatic stump, the divided bile duct, the jejunum, the stomach, the duodenum and the right colon are anastomosed in the following order. Some surgeons prefer to anastomose the pancreas to the posterior wall of the stomach instead; others prefer to create a separate Roux loop of the jejunum and anastomose the pancreas to that. The operation should take between 3 and 6 hours. Blood loss should be low and transfusion is often not necessary. Patients are usually nursed in a high-dependency area for the first 24–48 hours after surgery. Prolonged nasogastric drainage is unnecessary and early feeding can be commenced. Enhanced recovery after surgery (ERAS) protocols should be applied to pancreatic resections as with other types of gastrointestinal surgery. Resection for pancreatic

cancer should be carried out in specialist units. There is a clear correlation between higher caseload volume and lower hospital mortality and morbidity. PPPD should carry a mortality of no more than 3–5%. The morbidity remains high, with some 30–40% of patients developing a complication in the postoperative period. These complications are usually infective, but a leak from the anastomosis between the pancreas and the bowel is known to occur in at least 10% of patients, and this may give rise to the major complication of a postoperative pancreatic fistula (POPF). Octreotide may be administered in the perioperative period to suppress secretion and reduce the likelihood of a leak, but the evidence for its efficacy is still debatable. Following surgical resection, the pathological tumour-node-metastasis stage should be documented. Adjuvant therapy At the beginning of this century, the reported 5-year survival following resection of a pancreatic adenocarcinoma ranged from 7% to 25% (around 10% for most centres). The median survival was 11–20 months. Considering that, at best, 15% of patients had resectable disease to begin with, this meant only two or three out of 100 patients with this disease could expect to survive to 5 years. Moreover, recurrences could and did show up even beyond the 5-year cut-off. The high recurrence rate following resection inevitably led to the consideration of adjuvant treatments to improve outcome. Starting with the large multicentre European study (ESPAC-1) in 2004, which showed an improvement in median survival after adjuvant chemotherapy with 5-fluorouracil (5-FU) but no advantage with adjuvant radiotherapy, there have been several further studies that have looked at gemcitabine alone, gemcitabine with capecitabine and most recently modified fluorouracil plus leucovorin, oxaliplatin and irinotecan (mFOLFIRINOX). The latter has been associated with disease-free survival of over 21 months and median overall survival of over 54 months. Most patients with resected ductal adenocarcinoma are now offered 6 months of adjuvant chemotherapy with mFOLFIRINOX. Those with a poor functional status or a contraindication to mFOLFIRINOX are offered gemcitabine with/without capecitabine. Some centres continue to offer chemoradiotherapy, particularly in patients with involved (R1) resection margins, and further trials of adjuvant chemoradiation are in progress.

Pancreatic duct Body and tail of pancreas Superior mesenteric artery and vein Jejunum Figure 72.34 Resection of the head of the pancreas in a pylorus-preserving pancreatoduodenectomy. Liver

Stomach Bile duct Choledocho

jejunostomy Pancreato

jejunostomy Pylorus Duodenu

Jejunum Figure 72.35

Reconstruction after a pylorus- preserving pancreatodu odenectomy. m

(c) It should be emphasised, however, that these depressing statistics apply to ductal adenocarcinomas. Patients with resected ampullary tumours have a 5-year survival of 40%, and cystic tumours and neuroendocrine tumours can often be cured by surgical resection. Palliation The median survival of patients with unresectable, locally advanced, non-metastatic pancreatic cancer is 6–10 months and, in patients with metastatic disease, it is 2–6 months. If unresectable disease is found in the course of a laparotomy that was commenced with the intent to resect, a choledochenterostomy and a gastroenterostomy should be carried out to relieve (or pre-empt) jaundice and duodenal obstruction. The bile duct may be anastomosed to the duodenum or to a loop of jejunum. It is preferable to use the bile duct rather than the gallbladder. Cholecystojejunostomy is easier to perform, but the bile must then drain through the cystic duct, which is narrow and, if inserted low into the bile duct, is vulnerable to occlusion by tumour growth. A coeliac plexus block can also be administered. A transduodenal Trucut biopsy of the tumour should be obtained. - In patients found to have unresectable disease on imaging, jaundice is relieved by stenting at ERCP (Figure 72.36a).

Mesh metal stent in bile duct Tumour Endoscope Endoscope Pancreatic tumour Stent in duodenum
duodenum approach Mesh metal stent in bile duct Tumour Figure 72.36
Approaches to biliary and duodenal stenting. (a) Endoscopic retrograde cholangiography and placement of a biliary stent; (b) percutaneous transhepatic cholangiography followed by cannulation of the biliary system and percutaneous placement of a biliary stent (mesh metal in this instance); (c) endoscopic placement of a duodenal stent (mesh metal).

Plastic stents are cheaper but tend to occlude faster and, if the patient is likely to have a longer life expectancy, a metal stent can be used. If the patient is not a suitable candidate for endoscopic biliary stenting, a percutaneous transhepatic stent can be placed (Figure 72.36b). Obstruction of the duodenum occurs in approximately 15% of cases. If this occurs early in the course of the disease, surgical bypass by gastrojejunostomy is appropriate but, if it is late in the course of the disease, then the use of expanding metal stents inserted endoscopically is preferable, as many of these patients have prolonged delayed gastric emptying following surgery (Figure 72.36c). If both biliary and duodenal metal stents are to be placed endoscopically, the biliary one should be placed first. If no operative procedure is undertaken, an EUS-guided or percutaneous biopsy of the tumour should be performed before consideration of chemotherapy or chemoradiation.

Lymphomas of the pancreas are rare and constitute less than 3% of all pancreatic cancers. These respond to chemoradiotherapy and surgical resection is not indicated. For patients with ductal adenocarcinoma who have locally advanced or metastatic disease, mFOLFIRINOX or alternatively gemcitabine plus albumin-bound paclitaxel particles (nab-paclitaxel) should be considered if the functional status is good. However, the 2-5 months' increase in median survival with these regimens has to be offset against the higher toxicity and cost. No long-term cures have been described with chemotherapy or radiotherapy. There is no role for surgical resection if metastases are present at the time of the initial presentation. In a very small proportion of patients who have been deemed unresectable owing to major vascular involvement and do not have metastatic disease, attempts have been made to downstage the tumour with one of the newer combination chemotherapy regimens, sometimes with chemoradiation added in, to try to render them resectable. Such neoadjuvant therapies are only very occasionally successful and should ideally be considered within a clinical trial. Steatorrhea is treated with enzyme supplementation. Diabetes mellitus, if it develops, is treated with oral hypoglycemics or insulin as appropriate, and pain with either analgesics or an appropriate nerve block. Palliation of pancreatic cancer /uni25CF /uni25CF /uni25CF /uni25CF - /uni25CF /uni25CF - -

Relieve jaundice and treat biliary sepsis Surgical biliary bypass Stent placed at ERCP or percutaneous transhepatic cholangiography Improve gastric emptying Surgical gastroenterostomy Duodenal stent Pain relief Stepwise escalation of analgesia Coeliac plexus block Transthoracic splanchnicectomy Symptom relief and quality of life Encourage normal activities Enzyme replacement for steatorrhea Treat diabetes Consider chemotherapy

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