Extended pancreatectomy for pancreatic cancers

Parul J. Shukla · Sujit Vijay Sakpal

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Abstract Pancreatic cancer carries a poor prognosis. A minority of patients are considered for surgical excision. Local extension, lymph node metastasis, poor prognosis with distal spread and the lack of effectiveness of chemo and radiotherapy, have led to a nihilistic approach to this disease. This review outlines the rationale for and technique of extended resections in pancreatic cancer.

Keywords Pancreatic cancer · Extended resections · Local extension

Introduction

Pancreatic cancer is one of the most lethal cancers, and is the fourth leading cause of cancer-related deaths in the United States after malignancies of the lung, colorectal and breast in women or prostate in men [1]. Pancreatic is also second to colorectal in type of digestive tract malignancies [2], and it affects approximately 200,000 people worldwide each year [3]. In India, the incidence rate of pancreatic cancer is low (0.5–2.4 per 100,000 men and 0.2–1.8 per 100,000 women), with highest rates among urban male populations of the western and northern regions. The estimated incidence of pancreatic cancers in the year 2001 was 14,230 cases and time trends reveal a continual increase [4].

The majority (80%–90%) of patients with pancreatic cancers present late with advanced or disseminated disease, which limits their chance for a complete cure. Of all the treatment modalities, surgical resection is the only one with curative potential offering the hope for a disease-free survival in cases of localised and resectable pancreatic cancer. Advent of newer imaging technology with 3-dimensional anatomical reconstruction enables precise visualisation of local advancement of tumours preoperatively. Multi-detector computed tomography (MDCT) evaluates resectability of pancreatic carcinomas with a sensitivity and specificity of 94% and 89%, respectively [5]. Criteria that depict resectability of the pancreatic tumours include—the absence of extrapancreatic or metastatic disease, the patency of the superior mesenteric vein/portal vein (SMV/PV) confluence, and the absence of celiac axis-superior mesenteric artery (SMA) tumour involvement [6]. Precise diagnosis and staging coupled with fine surgical technique make wide excision of pancreatic cancer (R_0) possible, thus prolonging survival. In addition, specialised perioperative care further reduces perioperative morbidity and mortality. However, even in experienced hands it is difficult to achieve R_0 resection since the tumour notoriously spreads into the retroperitoneal neural and lymphatic tissue [3, 6].

P. J. Shukla¹ · S. V. Sakpal²

¹Department of Gastrointestinal & Hepatopancreatobiliary
Surgical Oncology,
Tata Memorial Hospital,
Mumbai, India

²Department of Surgery,
Saint Barnabas Medical Center,
Livingston, New Jersey, USA

P. J. Shukla (✉)
E-mail: pjshukla@hotmail.com

Pancreaticoduodenectomy and distal pancreatectomy are being readily performed due to reduced operative risks. There is now a thrust towards early detection and aggressive surgical therapy to further decrease overall mortality from pancreatic cancers. Radical or extended pancreatectomy entails extensive en bloc resection of the tumour, tumour bed and a wider field of peripheral soft tissue and lymph nodes, and vascular reconstruction if required to achieve increased resectability, tumour-free margins, lower local recurrences and improved disease-free survival. With that aim, numerous innovative surgical techniques are being increasingly performed along side adjuvant therapies to produce promising outcomes.

In pancreatic malignancies, complete resection of tumours with negative histopathological margins and adjuvant treatment offers potential of improved long-term survival. Metastatic spread to regional lymph nodes has been suggested as the most important prognostic factor of overall survival in patients undergoing pancreatic resection with curative intent [1]. Although extensive radical surgery including extended lymph node dissection provides locoregional control with fewer local recurrences and better staging of the disease, improvement in survival rates remains unproved [3, 6–10]. Radical resection is not indicated if extrapancreatic nerve plexus around the superior mesenteric or celiac artery is invaded since dissection around these mesenteric vessels to harvest distant lymph nodes disrupts the plexuses resulting in severe diarrhoea postoperatively [9, 10]. Also, most studies reveal no survival benefit and increased morbidity and mortality with total pancreatectomy over pancreaticoduodenectomy and distal pancreatectomy [11, 12]. However, in rare situations including a soft pancreas with risk of a leak from pancreatoenterostomy, or if positive margins on sequential frozen sections are obtained while resection is carried out into the pancreatic tail, or if there are papillomatous changes or dysplasia throughout the pancreatic duct, or if a family history of multicentric disease exists total pancreatectomy should be considered [13].

While total pancreatectomy and extended lymphadenectomy may be of limited benefit, Nakao et al [14] suggested that vascular resection is indicated when in need to obtain a carcinoma-free surgical margin. PV resection for pancreatic masses with venous involvement has been a long established technique [15]. Although primary closure with partial excision of the vein wall is possible, autologous venous graft or synthetic prosthesis, PTFE, for vascular reconstruction is preferable (see Fig. 1). However, the infectious risks of pancreaticoduodenectomy make autologous tissue ideal were it not for the extra time and surgical procedure required for harvest [16, 17]. Studies have demonstrated that segmental venous resection and subsequent reconstruction is the ideal means of managing tumours adherent to the SMV and PV, and can achieve survival equivalent to any margin-negative pancreaticoduodenectomy [17]. It is worth noting that the efficacy of arterial resection is much lesser

than venous resection, and histologically confirmed tumour infiltration into the vascular tunica media is associated with no significant benefit in long-term survival [13, 14].

Locally-advanced pancreatic adenocarcinoma depicts poor survival despite chemotherapy or chemoradiation therapy, or both, and survival is even dismal without resection. Katz et al [18] have defined a new category of patients with pancreatic adenocarcinomas—borderline resectable. Patients in this category either have tumours that about the portomesenteric circulation offering an opportunity for vascular reconstruction, or have undiagnosed but suggested metastases, or possess suboptimal performance status to undergo resection. Out of the 160 categorised patients, 66 underwent neoadjuvant chemotherapy or chemoradiation therapy, or both prior to surgical resection with resultant improvement in median survival (40 months) and 5-year survival rates (36%) in comparison to those who did not undergo surgery. Long-term survival in patients with pancreatic cancer is severely impeded by local advancement and recurrence, and depends on en bloc resection [1, 19]. In a series of 357 patients that underwent pancreaticoduodenectomy for malignant disease, a negative margin (R_0) was associated with a greater overall survival compared with positive margins (R_1 or R_2) [1].

Organ-preserving resections have also evolved over the years for pancreatic malignancies, and they distinctly predict the quality of life postoperatively. Central pancreatectomy (see Fig. 2) with pancreaticogastrostomy has been introduced as an advantageous option over Roux-en-Y pancreaticojejunostomy for pancreatic tumours [20]. This novel technique coupled with the natural anatomy allows for a tension-free anastomosis between the remnant distal pancreas and a well-vascularised posterior stomach wall, thus reducing the risk of pancreatic leaks. Also, the technique avoids bowel manipulation and reduces the number

Fig. 1 Intra operative photograph shows an interposition vascular graft, PTFE, sutured between the portal vein (PV) and superior mesenteric vein (SMV) during a pancreatectomy performed at Tata Memorial Hospital.

Fig. 2 Intra operative photograph from a central pancreatectomy performed at Tata Memorial Hospital. Photo shows residual oversewn proximal pancreas (PP) and distal pancreas (DP) prior to creating a pancreato-enteric anastomosis. Inset shows the resected central pancreas (CP) containing the tumor (encircled).

of anastomosis, and spares the islet-concentrated distal pancreas decreasing the risk of endocrine insufficiency. Isaji and Kawarada [21] introduced pancreatic head resections with second-portion duodenectomy for early stage periampullary to middle bile duct and gall bladder carcinomas to achieve complete lymph node dissection. In doing so the third portion of the duodenum is preserved by conserving the anterior inferior pancreaticoduodenal artery. Also, the technique enables resection of part of the pancreatic head nerve plexus responsible for pain in chronic pancreatitis. In another series of 54 patients that underwent R_0 resection with either Billroth I (27/54) or Billroth II (27/54) reconstruction for pancreatic ductal adenocarcinoma, the disease-free and overall survival did not differ [19]. However, patients that underwent Billroth II may have had some advantage in terms of postoperative oral ingestion and avoiding palliative procedures.

Surgery for pancreatic cancer is a highly complex procedure since it involves multiple anastomoses, dissection along major intra-abdominal organs, and may also include vascular reconstruction. Hence, the surgical management of pancreatic cancer is exemplified in demonstrating superior outcome of high-volume institutions in recent times supporting the concept of centralisation of surgery. However, we believe that adopting the healthcare delivery system of advanced, high-volume centres—teaching surgeons-in-training to develop surgical expertise and adopt treatment patterns; multidisciplinary teams to provide global perioperative management; and patient education to develop knowledge of self's disease and its treatment—can produce comparable or better outcomes.

In conclusion, an aggressive surgical approach for pancreatic cancers including total pancreatectomy, extended lymphadenectomy and arterial resection do not appear to improve survival above pancreaticoduodenectomy and standard lymph node dissection, and are likely to be as-

sociated with greater morbidity. On the contrary, portal or mesenteric venous resection poses no additional morbidity and may actually prolong survival if performed to achieve disease-free margins in advanced local disease. Also, organ-preserving procedures may complement better outcomes. Hence, “extended pancreatectomy” if considered must justify its feasibility, and its efficacy in terms of lower morbidity-mortality rates, enhanced disease-free long-term survival, reduced recurrences, pain relief, and primarily improved quality of life.

Conflict of interest The authors do not have any disclosable interest

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