Is there a role for arterial reconstruction in surgery for pancreatic cancer?

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Abstract

Surgery remains the only potentially curative treatment for patients with pancreatic cancer. Locally advanced pancreatic cancer with vascular involvement remains a surgical challenge because high perioperative risk and the uncertainty of a survival benefit. Whilst portal vein resection has started to gather momentum because the perioperative morbidity and long term survival is comparable to standard pancreatectomy, there isn’t yet a consensus on arterial resections. There have been various reports and case series of arterial resections in pancreatic cancer, with mixed survival results. Mollberg et al. have appraised the heterogeneous published literature available on arterial resection in pancreatic cancer in an attempt to compare this to standard pancreatectomy. In this article, we discuss the results of this systematic review and meta-analysis, and the limitations associated with analysing results from heterogeneous data. We have outlined the important features in surgery for pancreatic cancer and specifically to arterial resections, and compared arterial resections to the published literature on venous resections.

Key words: Arterial resection; Pancreatic cancer; Vascular resection; Hepatic artery; Coeliac axis; Pancreatectomy

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COMMENTARY ON HOT TOPICS

The systematic review and meta-analysis on arterial resection during pancreatectomy by Mollberg et al. is a very timely and current paper. They report perioperative and survival outcomes associated with arterial resection during pancreatectomy for pancreatic cancer, compared to pancreatectomy alone.

Worldwide, pancreatic cancer is the 13th most common cancer, but the eighth most common cause of cancer death with little improvement in survival over the last few decades. Surgical resection remains the only hope for cure in these patients. However, many of these patients are diagnosed at a late stage because of the nature of the disease and surgical resection with a curative intent is rarely possible. Fortner, first described a “regional pancreatectomy” involving total pancreatectomy, radical lymph node clearance, combined portal vein resection (Type 1) and/or combined arterial resection and reconstruction (Type 2). This was found to be associated with unacceptably high morbidity and mortality rates, and was abandoned. More lately, pancreatectomy with portal vein resection and reconstruction has began to gather momentum as studies demonstrated acceptable morbidity and long term survival rates comparable to standard pancreaticoduodenectomy (PD). In recent years, the morbidity and mortality rates between standard PD and pancreatico-duodenectomy with vascular resection have been similar. Isolated venous involvement
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is no longer a contraindication to PD when performed by experienced surgeons at high volume centers as part of a multidisciplinary approach to localized pancreatic cancer[9] arterial resection, however, has remained highly controversial. Current oncological guidelines suggest that pancreatic tumours invading arterial structures render these cancers inoperable[9]. Nevertheless, attempts at resection involving reconstruction of the main arteries such as the coeliac axis, hepatic artery and superior mesenteric artery (SMA) have been reported, albeit in small case series[6,13-18].

The study population for the meta-analysis is the largest in the published literature despite the unsurprising heterogeneity of the 26 studies that met inclusion criteria; a limitation acknowledged by the authors. In total, 366 patients underwent pancreatectomy with concomitant arterial resection (AR) out of a total of 2609 patients that were included in the study. All data were non-controlled, collected retrospectively, over a prolonged study period (1973-2010), with a high proportion of procedures performed pre-2000, and with a high risk of bias in 22/26 studies. In addition, as the authors point out, the median number of patients per study is 12.5, suggesting a pooled analysis may be a more suitable method of data evaluation[1].

There was considerable heterogeneity in the types of surgical procedures performed across the studies included in Mollberg’s systematic review, including cases where arterial resection was performed in combination with venous resection and/or extended lymphadenectomy. Mollberg et al[8] found that perioperative morbidity was significantly increased in patients undergoing concomitant AR compared to those undergoing pancreatectomy alone (OR = 2.17, 95%CI: 1.26-3.75, P = 0.006; I² = 35%), with a significantly higher re-operation rate (OR = 3.28, 95%CI: 1.68-6.41, P < 0.001; I² = 33%) and with a 5 times greater perioperative mortality risk in the AR group (OR = 5.04, 95%CI: 2.69-9.4, P < 0.0001; I² = 24%). This can be explained by the complexity and technical challenge associated with an arterial resection including the risk of bowel ischaemia. They also found a greater perioperative mortality rate amongst patients undergoing arterial resection in comparison to venous resection in their subgroup analyses (OR = 8.87, 95%CI: 3.4-23.13, P < 0.0001; I² = 5%).

There was no significant difference in the incidence of lymph node metastases between patients undergoing pancreatectomy with and without AR (OR = 1.39, 95%CI: 0.85-2.27, P = 0.19; I² = 0%). There was also no difference found in R0 resection rates between the 2 groups when analysing 209 patients in 15 studies who provided this data. However, the exclusion of a study by Boggi et al[20] by sensitivity analysis indicated a lower R0 resection rate in the AR group with low heterogeneity. However, the role of resection margin status as a prognostic indicator remains controversial due to the lack of uniformity of pathology reporting for pancreatic cancer[1,18].

Median survival at 1, 3 and 5 years for patients undergoing AR during pancreatectomy was 49.1%, 8.3% and 0%, respectively. Meta-analysis of survival data demonstrated that there was a significantly lower chance of long term survival for patients undergoing pancreatectomy with concomitant AR compared to pancreatectomy. This is in contrast to survival outcomes for patients with pancreatic cancer involving the portal vein where the overall survival is similar in the resection groups (with and without vein resection) and significantly greater than patients having a palliative bypass[3,5,19,21]. The median 1-, 3- and 5-year survival rates for patients with AR were significantly reduced. This persisted even after excluding the study by Boggi et al[14] for heterogeneity following a sensitivity analysis. The authors therefore compared AR to palliative non-surgical therapy, which was reported in 6 studies. This showed a significantly higher 1- and 2-year survival for patients undergoing AR after excluding a study by Wang for heterogeneity. However, as explained by the authors, the non-controlled nature of these studies could have meant that the patients who did not undergo resection could have had an inherently worse prognosis, with more advanced tumours, compared to those undergoing AR.

This study is a very comprehensive analysis of the data that are currently available concerning arterial resection during pancreatectomy. It demonstrates significantly increased peri-operative morbidity and mortality, combined with significantly poorer survival outcomes at 1, 3 and 5 years. The authors conclude that the need for arterial resection in itself is the actual risk factor for increased perioperative death. However, they also suggest that in the absence of other treatment for tumours involving the SMA, with careful patient selection, arterial resection may be justified in a small cohort of patients. In addition, the authors also suggest a prospective registry to allow accurate analysis of outcome data for patients undergoing an arterial resection. We would augment this idea by suggesting a protocol detailing patient eligibility for arterial resection as a first step towards determining the suitability of this highly complex procedure, which may only be relevant to a specific subset of patients.

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