controversial topics in surgery

Portal vein resection during pancreaticoduodenectomy for cancer

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Pancreaticoduodenectomy is the treatment of choice for adenocarcinoma of the head of the pancreas. However, this treatment is applicable only to a minority with the disease. Approximately one-third present with locally advanced, non-metastatic disease. In view of the close anatomical proximity between the head of the pancreas and the portal/superior mesenteric vein confluence, it is logical for surgeons to seek to expand the pool of patients who may benefit from pancreaticoduodenectomy by undertaking *en bloc* resection of the vein. However, portal vein resection during pancreaticoduodenectomy is controversial. Unresolved issues remain about the terminology (as partial circumference excision may be classified as portal vein resection), indications and outcome.

Given these variations and the small proportion of patients having pancreatic cancer surgery who undergo portal vein resection, it is difficult to construct a suitably designed randomised trial to address this question. Under these circumstances, surgeons will continue to base their practice on summative evidence from case series and the two articles presented here summarise the arguments for and against portal vein resection during pancreaticoduodenectomy.

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Pancreaticoduodenectomy for peri-ampullary malignancy: the case for portal vein resection

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Resection and reconstruction of the portal vein or superior mesenteric vein is not new, but rather an integral part of pancreatic resectional surgery; venous invasion of mesenterico-portal system should be seen as a function of tumour location rather than an indicator of aggressive tumour biology. Pancreatic head cancer remains a dismal disease with over 7000 new cases diagnosed each year in the UK.¹ Apart from surgery, other treatments have little effect on outcome. Therefore, all surgical techniques to achieve an R₀ resection should be given consideration. The *sine qua non* of surgery is first do no harm. The current literature suggests the addition of a venous resection does not cause an increase in morbidity and mortality over a standard pancreaticoduodenectomy. Importantly, the data indicate that portal vein resection can lead to similar survival outcomes in same-stage tumours. In this article, we briefly review the principles of portal vein resection and then summarise current evidence.

The intimate relationship between the pancreatic head and the uncinate process to the superior mesenteric vein and portal vein results in around 30% of all pancreatic head tumours being considered as locally advanced.^{2,3} Advances in cross-sectional imaging now allow precise examination of the pancreatic venous interface, but the extent of the disease can be underestimated even with the combination of multidetector computed tomography, endoscopic ultrasound and magnetic resonance imaging.⁴ We use the criteria proposed by the MD Anderson Cancer Center when considering resectability based on imaging.⁵ We believe pancreatic head tumours to be potentially resectable when there is a patent superior mesenteric vein/portal vein confluence and there is absence of tumour extension into the superior mesenteric artery, coeliac axis and common hepatic artery. Locally advanced, unresectable tumours include encasement of the adjacent arteries and or occlusion of the superior mesenteric vein/portal vein confluence.⁶

Various methods are currently used for portal vein reconstruction. Adequate mobilisation of the liver and small bowel can allow a 3-cm segment to be bridged and an end-to-end direct repair performed. Various conduits for reconstruction can also be used including, bovine pericardium, autologous saphenous, internal jugular or left renal vein.⁷ We prefer mobilisation with end-to-end anastomosis. However, when the venous involvement is over 3 cm, we perform hepatic mobilisation and use a left renal vein graft, preferring this conduit since it is autologous and located in the same operating field.

Currently, there is no randomised control trial or meta-analysis assessing the potential benefit of the addition of venous resection to pancreaticoduodenectomy. However, there are numerous large case series and a systematic review⁸ supporting venous resection. Performing a randomised control trial of venous resection may be difficult since most fit patients with a borderline resectable tumour will undergo a trial of dissection and the extent of disease is only fully determined when committed to resection. All contemporary large series support venous resection at the time of pancreaticoduodenectomy. Yekebas *et al.*⁹ recently reported on 585 patients undergoing pancreaticoduodenectomy between 1994 and 2005 and compared patients undergoing venous resection with those undergoing a standard pancreaticoduodenectomy on an intention-to-treat analysis. They found comparable median survival rates (15 months versus 16 months; $P = 0.086$) with no difference in peri-operative morbidity and mortality and concluded that venous resection at the time of pancreaticoduodenectomy can be offered with similar morbidity and mortality and offers these patients longer survival times than palliative chemotherapy. Similarly Riediger *et al.*¹⁰ analyzed 165 patients undergoing pancreaticoduodenectomy and reported similar postoperative morbidity (23% versus 35%) and mortality (3.5% versus 4.1%) rates for patients undergoing pancreaticoduodenectomy without and with the need for venous resection. Long-term survival was not influenced by the need for portal or superior mesenteric vein reconstruction in any of the tumour groups.¹⁰ Tseng *et al.*¹¹ reported similar long-term survival in patients undergoing pancreaticoduodenectomy with venous reconstruction from the MD Anderson Cancer Center. A total of 141 patients underwent venous reconstruction at the time of pancreaticoduodenectomy. Superior mesenteric-portal vein resections included tangential resection with vein patch ($n = 36$), segmental resection with primary anastomosis ($n = 35$), and segmental resection with autologous interposition graft ($n = 55$). Pancreaticoduodenectomy was performed for pancreatic adenocarcinoma in 291 patients; standard pancreaticoduodenectomy was performed in 181 and venous reconstruction in 110. Median survival was 23.4 months in the group which required venous reconstruction and 26.5 months in the group which underwent standard pancreaticoduodenectomy ($P = 0.177$). They concluded that properly selected patients who require venous reconstruction have a similar survival to those

undergoing standard pancreaticoduodenectomy and better survival by comparison to historical data reporting survival of patients treated non-operatively.¹¹

All surgeons undertaking pancreaticoduodenectomy should be able to undertake venous resection and reconstruction since, occasionally, the requirement for this may be unexpected. Despite the lack of randomised control trials, large series from major pancreatic centres demonstrate that, when venous resection is performed, it can be done safely and appears to give similar survival. A randomised, controlled trial to compare pancreaticoduodenectomy and venous resection against palliative chemotherapy for locally advanced pancreatic cancers would be ideal but may be difficult to undertake. The management paradigm for pancreatic cancer is evolving and neo-adjuvant treatments may make portal vein resection more commonplace.

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Vascular reconstruction in pancreatic resections: the case against

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Surgical resection is the only potentially curative treatment for pancreatic carcinoma. Despite advances in chemotherapy and surgery, 5-year survival remains less than 5%. Survival following surgical resection and adjuvant treatment has improved slightly with the centralisation of pancreatic surgery into high-volume units and 5-year survival of up to 20% has been reported. Outcome after resection is affected by tumour size, extrapancreatic disease, lymph nodes status and vascular involvement.

The option of arterial or venous resection with reconstruction may increase the number of patients offered surgery. Intuitively, vascular infiltration implies advanced, unresectable cancer with high probability of lymph node involvement and a greater potential for R_1 resection. In order to be considered a viable adjunct, it must be shown that pancreatic resection with vascular reconstruction can be done as safely as resection alone, with a reasonable chance of achieving an R_0 resection, following which a survival advantage is evident compared to palliative treatment.

Arterial resection

The superior mesenteric artery is in direct contact with lymphatic tissue and the nerve plexus relating to the pancreas. Evidence in favour of arterial resection is scant and confined to small, mostly retrospective series. One recent study reported 13 patients undergoing hepatic or superior mesenteric arterial resection, with one-third of the patients surviving beyond 2 years.¹ A small series of 23 patients from Japan who underwent pancreatic resection with arterial reconstruction, described a 91% R_0 resection rate with zero mortality, with an estimated 5-year survival rate of 42%.² These are impressive figures but focus on a select group of patients with distal pancreatic tumours. The majority of published series conclude that arterial involvement is a contra-indication to resection, as there is a high rate of operative morbidity, a high R_1 resection rate and doubtful survival benefit.

Portal vein/superior mesenteric vein resection

The techniques involved in venous resection associated with pancreatic cancer surgery were first described 35 years ago.³ Regional pancreatectomy with *en bloc* venous

resection was shown to be feasible, but was associated with high rates of morbidity and mortality and poor long-term survival. The technique has become more established during the last decade with several series reporting postoperative complication rates of a level similar to pancreatic resection without venous resection.^{1,4} There are, however, no prospective studies comparing pancreatic resection with and without venous resection which makes interpretation of the available data difficult. In addition, the incidence of venous resection in large series from centres in the US varies widely (3–38%), which indicates that there is a considerable difference of opinion between centres regarding the wisdom of, and indications for, pancreatic resection with venous resection.⁵

Concerns remain regarding the increased operating time, higher blood loss and greater transfusion requirements associated with pancreatic resections including venous resection compared to resections without venous resection. In addition, there is little evidence regarding the outcomes of pancreatic resection with venous resection from centres within the UK, with only one joint Anglo-French paper published to date.⁶ A recent informal survey of UK surgical practice regarding venous resection in pancreatic surgery had a poor response and revealed little useful information (Richard Hall, President of Pancreatic Society of UK and Ireland, personal communication). The overall view appears to be that pancreatic resection with venous resection has evolved into a safe procedure with zero operative mortality reported in some series.^{6,7} There remain, however, on-going concerns regarding venous resection including a high R_1 resection rate and positive lymph node status, poor outlook for patients with actual invasion into the vein and limited survival benefit.

A recent meta-analysis has shown that pancreatic resection with venous resection is associated with a 40% R_1 resection rate and a 70% incidence of lymph node involvement.⁸ Both are recognised adverse prognostic factors after pancreatic resection and few patients will survive beyond 2 years. Large tumour size is also known to be a poor prognostic indicator after pancreatic resection and increased median tumour size in pancreatic resections with venous resection compared to resections without has been reported.⁹ Perineural invasion, another adverse prognostic factor after pancreatic resection, has also been shown to be present more

Figure 1 Pre-operative contrast-enhanced computed tomography scan showing a 3-cm pancreatic tumour abutting the right side of the superior mesenteric vein. There is a clear plane between the tumour and the superior mesenteric artery and R0 resection was possible with vascular resection of the lateral wall of the superior mesenteric vein.

often after pancreaticoduodenectomy with venous resection compared to the same operation without venous resection.¹⁰

The key question is whether this association of adverse prognostic features with pancreaticoduodenectomy with venous resection, correlates with poor long-term survival after surgery. Some studies have shown that survival after pancreaticoduodenectomy with venous resection is poor compared to survival in patients who did not require venous resection.^{10,11} However, the published data are not consistent and several recent studies have shown that there is no difference in tumour size, R_1 incidence, nodal status and long-term survival between patients having pancreatic resections either with or without venous resection.^{1,4,5} In patients undergoing pancreaticoduodenectomy with venous resection, the R status plays a vital role in determining survival, with R_0 patients having a 57% 2-year survival compared to 0% in the R_1 group in one recent study.⁷ These data suggest that venous resection may be indicated in cases where adoption of the technique allows an R_0 resection where this would otherwise not be possible.

The presence of actual invasion of tumour into the vein wall is reported to be an independent predictor of survival after pancreatic resection with venous resection.^{10,12} Accurate pre-operative staging is, therefore, vital to identify patients who may be suitable for resection with venous resection, with a chance of R_0 resection and long-term survival.

Pancreatic tumours elicit a marked desmoplastic response and pre-operative prediction of vessel wall invasion can be inaccurate, as can intra-operative assessment of the same question during attempted resection. Initial staging is usually undertaken with a contrast-enhanced CT scan which provides useful information regarding the relationship between the tumour and the portal vein/superior mesenteric vein and superior mesenteric artery. Patients with a clear plane between the superior mesenteric artery and the tumour may be candidates for trial dissection and, potentially, resection with venous resection (Fig. 1).

If initial staging suggests venous involvement, a more detailed assessment of the degree of venous narrowing may help to identify patients suitable for trial dissection. Magnetic resonance angiography (MRA) and endoscopic ultrasound (EUS) have superseded angiography as the investigations of choice, with both modalities offering reasonable degrees of specificity and sensitivity in the assessment of venous invasion.¹⁵ There is, however, no large comparative data sets looking at each modality or their impact on the clinical outcome following venous resection and non-venous resection operations.

Selecting patients who will benefit from venous resection from those in whom it is either excessive or futile remains a challenge. Many patients undergoing venous resection with curative intent may not actually require it to achieve R_0 resection, as demonstrated by the wide variation (26–85%) from published series in the incidence of portal vein wall invasion.¹ In addition, the need to assess pre-operative vein wall invasion has been questioned over the past few years by several series which have shown that survival after pancreatic resection with venous resection is equivalent in the presence of actual venous invasion, compared to those without.^{1,5,7}

Conclusions

There is now clear evidence that, in many centres, pancreatic resection with venous reconstruction can be performed safely. Questions remain, however, regarding whether this technique should be widely adopted or reserved for use in selected cases involving small tumours in a difficult anatomical location in which there is a chance that venous resection will facilitate an R_0 resection. Many recent studies have shown equivalent survival after resection with venous resection or without it, provided an R_0 resection is achieved. The incidence of venous resection in series is very variable, as is the incidence of actual vein wall invasion, which, in turn, makes data interpretation difficult. The lack of data from UK centres is a cause of concern and there is a clear need for an overview of UK practice in this regard. The forthcoming AUGIS National HPB audit may provide invaluable data to guide our views regarding the safety and appro-

priateness of venous resection as part of attempted curative resection of pancreatic tumours.

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