Impact of portal vein infiltration and type of venous reconstruction in surgery for borderline resectable pancreatic cancer

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Background: The International Study Group of Pancreatic Surgery (ISGPS) recommends operative exploration and resection of pancreatic cancers in the presence of reconstructable mesentericoportal axis involvement. However, there is no consensus on the ideal method of vascular reconstruction. The effect of depth of tumour invasion of the vessel wall on outcome is also unknown.

Methods: This was a retrospective cohort study of pancreaticoduodenectomy with vein resection for T3 adenocarcinoma of the head of the pancreas across nine centres. Outcome measures were overall survival based on the impact of the depth of tumour infiltration of the vessel wall, and morbidity, in-hospital mortality and overall survival between types of venous reconstruction: primary closure, end-to-end anastomosis and interposition graft.

Results: A total of 229 patients underwent portal vein resection; 129 (56.3 per cent) underwent primary closure, 64 (27.9 per cent) had an end-to-end anastomosis and 36 (15.7 per cent) an interposition graft. There was no difference in overall morbidity (26 (20.2 per cent), 14 (22 per cent) and 9 (25 per cent) respectively; $P = 0.82$) or in-hospital mortality (6 (4.7 per cent), 3 (3 per cent) and 2 (6 per cent); $P = 0.80$) between the three groups. One hundred and six patients (47.5 per cent) had histological evidence of vein involvement; 59 (26.5 per cent) had superficial invasion (tunica adventitia) and 47 (21.1 per cent) had deep invasion (tunica media or intima). Median survival was 18.8 months for patients who had primary closure, 27.6 months for those with an end-to-end anastomosis and 13.0 months among patients with an interposition graft. There was no difference in median survival between patients with and without histological vein involvement (20.9 *versus* 22.8 months; $P = 0.48$). Venous tumour infiltration was not associated with decreased overall survival on multivariable analysis.

Conclusion: In this study, there was no difference in morbidity between the three modes of venous reconstruction, and overall survival was similar regardless of tumour infiltration of the vein.

+A: Introduction

Pancreatic cancer remains a leading cause of cancer death worldwide and is one of the few cancers associated with an increasing mortality[1]. Resectability remains a matter of debate, particularly where the tumour involves vascular structures. A tumour with CT findings of venous distortion, including short segment occlusion with sufficient length for reconstruction, is classified as borderline resectable[2]. As such, the consensus statement from the International Study Group of Pancreatic Surgery (ISGPS) has recommended primary operative exploration and resection in the presence of reconstructable portomesenteric venous axis involvement[3]. Indeed, in the past decade several studies[4–7] have confirmed that portal vein resection in patients undergoing pancreaticoduodenectomy for pancreatic cancer has comparable survival to standard resection and is a safe procedure when performed in specialized pancreatic centres.

Although venous resection should today be regarded as the standard of care in patients with involvement of the portomesenteric venous axis, there is no consensus on the ideal method of vascular reconstruction. Tangential resection with primary closure, and segmental resection with primary end-to-end anastomosis or an interposition graft are the commonest types of venous reconstruction (*Fig. 1*)[5]. A similar classification was also suggested by the ISGPS but, to date, the correlation between different surgical techniques and perioperative risk and the impact on overall survival has not been established.

The effect of depth of tumour invasion of the vessel wall on clinical outcome is also unclear. Portal venous tumour invasion has been shown to be a negative prognostic factor[8,9] and the depth of tumour invasion to be associated with inferior survival[10]. Conversely, others[5,6,11] have suggested that histological involvement of the segment of vein resected does not seem to affect survival.

In line with the ISGPS consensus statement recommendation on borderline resectable pancreatic cancer[3], the aim of this study was to assess the impact of the depth of tumour infiltration of the vessel wall on survival; and to compare morbidity, in-hospital mortality and overall survival between those receiving the different types of venous reconstruction.

+A: Methods

This UK multicentre retrospective cohort study included consecutive patients with T3 adenocarcinoma of the head of the pancreas only undergoing pancreaticoduodenectomy with vein resection between December 1998 and January 2012. The inclusion criteria for the study were borderline resectable disease based on CT and no evidence of metastatic disease. Patients with cholangiocarcinoma, ampullary tumours, intraductal papillary mucinous neoplasms and neuroendocrine tumours were excluded.

Patients were identified from prospectively compiled unit databases or from hospital pathology department records. Data not available from databases were obtained from electronic patient records or patient notes. Dates of death were obtained from electronic records, national registries or the patient's general practitioner; for patients who were still alive, the last follow-up outpatient visit was considered the last follow-up date. National ethical approval was obtained for the study (REC reference 11/LO/0312) and nine high-volume UK centres contributed data.

+B: Preoperative evaluation

All patients underwent contrast-enhanced CT as routine preoperative evaluation. MRI, endoscopic ultrasound imaging and laparoscopy were performed on an individual basis, and the preoperative decision to resect was made after discussion at a multidisciplinary team meeting with surgeons, radiologists and oncologists in attendance. Only patients with tumours deemed resectable or borderline resectable on preoperative assessment were included. Patients with arterial involvement were excluded. Portal vein resection was performed when the pancreatic tumour was found to be inseparable from the portal vein during the operation, and surgery was undertaken with the intention of obtaining R0 resection margin status. Patients with portal vein occlusion and those with metastatic disease were excluded.

+B: Perioperative data

Pancreaticoduodenectomy was performed as a classical Whipple operation or a pylorus-preserving

procedure. Portal vein resection was defined as resection of the superior mesenteric vein (SMV) or main portal vein. Vascular resections were carried out as partial venous excision with primary closure of the vein (ISGPS type 1 or 2[3]), segmental venous resection with end-to-end anastomosis (ISGPS type 3[3]), or segmental resection and reconstruction with an interposition graft (ISGPS type 4[3]) (*Fig. 1*). The graft was sourced from the patient's jugular vein, long saphenous vein or renal vein, or from a suitable stored cadaveric donor vessel. No patient had a concurrent arterial resection. None of the patients received neoadjuvant therapy.

Pancreatic fistula was defined by a drain amylase concentration of more than three times the serum amylase level on the third postoperative day, irrespective of grade (A, B or C)[12], and delayed gastric emptying by the requirement for a nasogastric tube for more than 10 days after operation and/or intolerance of food intake for longer than 2 weeks[13]. Other complications recorded were postoperative bleeding as defined by the ISGPS[14], non-pancreatic anastomotic leak, portal vein thrombosis and need for a relaparotomy.

+B: Histology

Data collected included tumour size, grade, presence of lymphovascular and perineural invasion, and resection margin status. Histological assessment of the resected specimen was based on the standards and minimum data set published by the Royal College of Pathologists in 2002 and updated in 2010[15,16]; this defined the resection margin status as positive if it was within 1 mm of the tumour, and recommended more extensive sampling of the circumferential resection margin when the pancreatic frozen section is positive. Portal vein invasion was subdivided histopathologically into superficial (invasion to the tunica adventitia) and deep (invasion to the tunica media or intima).

+B: Statistical analysis

Baseline demographic and clinical characteristics, and postoperative complications, are described using proportions and median (range), as appropriate. Univariable comparisons of these characteristics in groups defined by the type of venous reconstruction and the degree of histological vein involvement were performed using χ^2 test for categorical variables and Mann–Whitney *U* test

for continuous data. Kaplan–Meier plots were used to describe overall survival patterns in the various groups. Cox proportional hazards regression models was used for univariable and multivariable survival analyses in the groups defined by type of venous reconstruction and degree of histological vein involvement, before and after adjustment for possible confounders. Potential confounders considered were factors that had been demonstrated to be associated with mortality in previous analyses of the data set[4,17]: resection type, nodal status and perineural invasion in primary analyses, and delayed gastric emptying, anastomotic leak and receipt of blood transfusions in sensitivity analyses. All tests were two-tailed and statistical significance set at $P < 0.050$. SAS® software version 9.3 (SAS Institute, Cary, North Carolina, USA) was used for statistical analysis.

+A: Results

Two-hundred and twenty-nine patients underwent vein resection and reconstruction (*Table 1*). There were 115 men and the median age at surgery was 66 years. Median ICU stay was 0 (range 0–40) days and median hospital stay was 13 (0–90) days. Some 143 patients (62.4 per cent) had an R1 resection. Delayed gastric emptying was the most common complication (25 patients,10.9 per cent). Seventeen patients (7.4 per cent) needed a relaparotomy, in eight instances for postoperative bleeding. Of these eight patients, five had a primary closure, two an end-to-end anastomosis and one had an interposition graft. Ten patients developed portal vein thrombosis after surgery. Ten patients (4.4 per cent) died in hospital. Postoperative anticoagulation was not administered routinely, and protocols were highly variable among units and surgeons. There was a tendency to use anticoagulation in patients having an interposition graft, with intravenous heparin in the postoperative period. Patients who received an interposition graft underwent Doppler ultrasound imaging on the day after surgery. Median follow-up was 1.3 (0–11.3) years.

+B: Type of venous resection and reconstruction

In total, 129 patients (56.3 per cent) had underwent primary closure of the vein, 64 (27.9 per cent) an end-to-end anastomosis and 36 (15.7 per cent) had an interposition graft (*Table 2*). In only two patients was a polytetrafluoroethylene (PTFE) interposition graft used. Patients having an

interposition graft had a longer ICU stay than those undergoing primary closure or end-to-end anastomosis (median 1 (range 1–28), 0 (0–25) and 0 (0–40) days respectively; $P < 0.001$), but venous resection type had no impact on the length of hospital stay.

No significant difference was found in tumour size, lymph node yield or nodal status between the three groups. However, lymphovascular and perineural invasion was more prevalent in patients having interposition graft reconstruction. Similarly, these patients were more likely to have R1 resections.

There was no difference between the primary closure, end-to-end anastomosis and interposition graft groups in overall morbidity (26 (20.2 per cent), 14 (22 per cent) and 9 (25 per cent respectively; $P = 0.82$) or in-hospital mortality (6 (4.7 per cent), 3 (3 per cent) and 2 (6 per cent; $P = 0.80$). Patients with an interposition graft or an end-to-end anastomosis were more likely to develop portal vein thrombosis than those who underwent primary closure. Five patients were found to have portal vein thrombosis during the hospital stay (4 end-to-end anastomosis, 1 interposition graft). Two of these (both end-to-end anastomosis) required a relaparotomy for portal vein thrombosis, one of whom died at 3 months after surgery from an unknown cause; the second remained alive after 37 months of follow-up. Another patient who developed immediate portal vein thrombosis died in hospital. Of the five patients who developed portal vein thrombosis after discharge, none required intervention or died as a consequence of the thrombosis. All five patients died from local recurrence, and portal vein thrombosis was identified on routine follow-up imaging.

Neither the risk of postoperative bleeding nor the need for blood transfusion differed significantly between the three groups.

+B: Histology and venous tumour infiltration

Details of histological vein involvement were available for 223 patients (*Table 3*). One hundred and six patients (47.5 per cent) had histological evidence of vein involvement, of whom 59 (26.5 per cent) had superficial invasion limited to the tunica adventitia and 47 (21.1 per cent) had deep invasion into the tunica media or intima. Patients with vein involvement were more likely to have

lymphovascular invasion, which was present in 38 of 47 patients with deep invasion and 42 of 59 with superficial invasion, compared with 63 of 117 patients with no vein involvement ($P = 0.002$). An involved resection margin was more common among those with vein involvement: 34 of 47 patients with invasion into the tunica media or intima, 42 of 59 with invasion into the tunica adventitia and 62 of 117 patients with no vein involvement had an R1 resection ($P = 0.02$). Patients with vein involvement were also more likely to have a positive SMV groove margin. There were no differences between the three venous involvement groups in tumour size, lymph node yield, perineural invasion or nodal status.

The extent of venous infiltration was also similar for the three types of venous reconstruction ($P = 0.79$). For the primary closure group, 68 of 127 patients (53.5 per cent) had no invasion, 30 (23.6 per cent) had superficial invasion and 29 (22.8 per cent) had deep involvement. In the end-to-end anastomosis group, 33 of 64 patients (52 per cent) had no invasion, 20 (31 per cent) had superficial invasion and 11 (17 per cent) had deep invasion. Among 32 patients in the interposition graft group, 16 (50 per cent) had no invasion, nine (28 per cent) had superficial and seven (22 per cent) had deep invasion.

+B: Survival

Median survival was 18.8 months in patients who had primary closure, 27.6 months among those with an end-to-end anastomosis and 13.0 months in those with an interposition graft, with no significant difference between the groups (*Fig. 2*). There was also no difference in survival between patients with and without histological vein involvement; median survival was 20.9 *versus* 22.8 months respectively ($P = 0.48$, log rank test; adjusted hazard ratio (HR) 0.95, $P = 0.84$) (*Fig. 3*).

Multivariable analysis using an adjusted Cox proportional hazards regression model showed that R1 resection (adjusted HR 1.56, 95 per cent c.i. 1.11 to 2.20; $P = 0.01$), pN1 nodal status (adjusted HR 1.84, 1.14 to 2.96; $P = 0.01$), relaparotomy (adjusted HR 3.71, 2.11 to 6.55; $P < 0.001$) and receipt of blood transfusion (adjusted HR 1.65, 1.17 to 2.32; $P = 0.005$) were

independently associated with overall survival. Histological evidence of venous tumour infiltration was not associated with decreased overall survival.

In further analyses of type of reconstruction, there was no difference in overall survival between primary closure and either end-to-end anastomosis (adjusted HR 0.85, 0.57 to 1.37; P = 0.48) or interposition graft (adjusted HR 0.88, 0.51 to 1.52; P = 0.64). Similarly, the lack of effect of vein involvement on overall survival persisted in analyses of no involvement *versus* superficial involvement (adjusted HR 0.74, 0.48 to 1.13; P = 0.16) and no involvement *versus* deep involvement (adjusted HR 1.18, 0.77 to 1.81; P = 0.44).

+A: Discussion

This study demonstrated no differences in morbidity between the three modes of venous reconstruction after surgery for borderline resectable pancreatic cancer, and similar overall survival regardless of whether tumour had infiltrated the vein. The results compare well with those of other studies[3,5,6,10,18–21] regarding methodology and patient characteristics, with the added benefit of a large cohort size and comparison of both venous tumour infiltration and type of venous resection.

A descriptive analysis of the types of vascular reconstruction was reported previously in a series of 110 patients with borderline resectable pancreatic cancer, but no attempt was made at a statistical correlation with perioperative complications[20]. In the present study, the type of venous reconstruction did not influence the short- or long-term outcomes. Perioperative bleeding and the number of patients requiring blood transfusion were similar between the three groups. In a retrospective study of 28 patients, Stauffer and colleagues[21] reported a median blood transfusion of 6.5 units, mostly in patients having interposition grafts.

The portal vein thrombosis rate of 4.4 per cent in the present series is comparable to that in other reports[7,18,20]. One study[21] reported a portal vein thrombosis rate of 10 per cent, being highest in those having an end-to-end anastomosis. Another series[22], with a similar predominance of primary closure (45 per cent), reported no significant difference in the incidence of portal vein thrombosis between the three groups, and an overall rate of 17 per cent. Conversely, in the present

study, interposition graft reconstruction was associated with an increased risk of developing portal vein thrombosis, perhaps related to the greater technical complexity of this reconstruction. Early portal vein thrombosis might be the result of a technical failure, whereas late thrombosis has been associated with local recurrence[23–25]. Furthermore, an immune-mediated phenomenon in interposition graft reconstruction with cadaveric veins cannot be excluded. The evidence for use of postoperative anticoagulation in the event of portal vein reconstruction is equivocal. Patients having a PTFE graft are more likely to receive postoperative anticoagulation[26]. A systematic review[26] found that the use of anticoagulation after venous resection had no effect on the rate of early portal vein thrombosis, morbidity and mortality.

The type of venous reconstruction did not affect long-term survival in this study, suggesting that the appropriate surgical technique should be applied with the intention to perform a radical resection, regardless of the technical complexity[27]. Tumour infiltration into the wall of the vein was found in 47.5 per cent of patients, in keeping with published rates of histopathological vascular invasion ranging from 26 to 85 per cent[5,7,28–30]. However, this did not have a negative impact on overall survival (20.9 *versus* 22.8 months in patients with and without histological vein involvement respectively; $P = 0.48$). Although some other studies[6,31] have also shown no correlation between venous tumour involvement and overall survival, others[8–10,20,32] have demonstrated venous tumour invasion to be a negative prognostic indicator associated with poorer overall survival. In a retrospective analysis[9] of 100 patients who underwent portal vein resection, 77 with venous tumour infiltration and 23 without, median survival was 15 and 16 months respectively; however, no differentiation of the depth of involvement was made. Only five cohort studies[10,20,29,30,32] have reported on the significance of the depth of portal vein invasion, with some suggesting decreased overall survival with deep invasion into the tunica media/intima. One study[32] reported that any tumour invasion into the tunica intima of the vein was associated with significantly poorer survival (9 months *versus* 14 months in those with no vein involvement; $P < 0.050$), despite advocating an attempt at aggressive surgical resection because of a low proportion of patients (21.1 per cent)

without true histological vascular infiltration. Another study[10] reported a non-significant decrease in 1-year survival in patients with deeper tumour invasion. Similarly, in the present study, there was a trend towards worse survival in patients with deep involvement of the tunica media and intima, but no significant difference in median survival between the three groups. A retrospective analysis[30] of 101 patients suggested that lack of histological invasion was associated with better outcome, but failed to demonstrate a survival difference according to the degree of invasion.

Lymphovascular and perineural invasion as well as R1 resections were more frequent in patients having an interposition graft, and those with tumour invasion into the tunica adventitia and intima/media. The SMV groove was also more likely to be positive in these patients and this may be related to a greater area of venous involvement requiring a larger resection. The tumour size was no different, in keeping with the postulate that venous involvement is a matter of topography and not an indicator of more aggressive tumour biology[4,6,18,31].

Some 139 patients (60.4 per cent) in the present cohort received adjuvant chemotherapy. This treatment was introduced as standard practice only after completion of ESPAC-1 in 2004. The initial results from the Alliance Trial[34] using neoadjuvant chemoradiation reported that the disease progressed in six of 23 patients during treatment. Of the 15 patients who underwent resection, 12 required a portal vein resection and four required an arterial resection; R0 resection was achieved in 14 of the 15 patients[34]. The present ISGPS guidelines[3] recommend primary exploration with a view to resection of borderline resectable pancreatic cancer in the absence of conclusive data on the potential benefit of neoadjuvant therapy. Trials that are currently recruiting, such as ESPAC-5, the Alliance Trial and the NEOPA (Neoadjuvant Treatment in Resectable Pancreatic Cancer) Trial, may provide further evidence on this.

The main limitation of this study is its retrospective nature, with potentially less reliable data on the incidence of specific postoperative complications and R1 rate in the early years of the study, as ISGPS definitions and the minimum histopathological reporting standards were published in

2005–2007 and 2002 respectively. None of the present patients received neoadjuvant treatment, which is increasingly being used in the treatment of borderline resectable pancreatic cancers.

+A: Disclosure

The authors declare no conflict of interest.

+A: References

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Fig. 1 Venous reconstruction procedures: **a** primary closure, **b** end-to-end anastomosis and **c** interposition graft. PV, portal vein; SplV, splenic vin, SMV, superior mesenteric vein; IJ, ??

Fig. 2 Survival in relation to type of venous reconstruction

Fig. 3 Survival in relation to type of venous invasion

Table 1 Demographic and clinical characteristics

	No. of patients* (*n* = 229)
Age (years)†	66 (43–80)
Sex ratio (M : F)	115 : 114
Endoscopic ultrasonography	38 (16.6)
MRI	8 (3.5)
Preoperative biliary drainage	112 (48.9)
Bilirubin (mg/dl)†	38.5 (4–798)
Haemoglobin (g/dl)†	12.2 (4.7–17.0)
Albumin (g/l)†	38 (15–49)
Creatinine (μmol/l)†	75 (41.0–183.0)
Length of hospital stay (days)†	13 (0–90)
Length of ICU stay (days)†	0 (0–40)
Type of PD	
Whipple	125 (54.6)
PPPD	104 (45.4)
Pancreatic anastomosis	
Pancreaticogastrostomy	102 (44.5)
Pancreaticojejunostomy	127 (55.5)
Type of vein reconstruction	
Primary closure	129 (56.3)
End-to-end anastomosis	64 (27.9)
Interposition graft	36 (15.7)
Tumour size (mm)†	30 (10–90)
Lymph node yield†	18 (4–50)
Lymphovascular invasion	149 (65.1)
Perineural invasion	179 (78.2)
Resection margin status	
R0	85 (37.3)
R1	143 (62.7)
Missing	1
Resection margin-positive	
Anterior	40 (17.9)
Posterior	71 (31.6)
SMV	82 (36.3)
SMA	24 (10.8)
Nodal status	
N0	42 (18.3)
N1/N2/Nx	187 (81.7)
Depth of venous invasion	
No invasion	117 (52.5)
Superficial	59 (26.5)
Deep	47 (21.1)
Unknown	6
Pancreatic fistula	15 (6.6)
Delayed gastric emptying	25 (10.9)

Non-pancreatic anastomotic leak	10 (4.4)
Relaparotomy	17 (7.4)
Postoperative bleeding	12 (5.2)
Patients receiving blood transfusion	72 (31.4)
Amount transfused (units)† All patients Patients receiving transfusion	 0 (0–9) 2 (1–9)
Portal vein thrombosis	10 (4.4)
In-hospital death	10 (4.4)

*With percentages in parentheses unless indicated otherwise; †values are median (range). PD, pancreaticoduodenectomy; PPPD, pylorus-preserving pancreaticoduodenectomy; SMV, superior mesenteric vein; SMA, superior mesenteric artery.

Table 2 Demographic and clinical characteristics according to type of venous reconstruction

	Primary closure (*n* = 129)	End-to end-anastomosis (*n* = 64)	Interposition graft (*n* = 36)	*P*†
Age (years)*	65 (43–80)	66 (45–80)	65 (44–75)	0.47‡
Sex ratio (M : F)	67 : 62	29 : 35	19 : 17	0.65
Length of hospital stay (days)*	12 (0–82)	14.5 (4–90)	14 (7–34)	0.56‡
Length of ICU stay (days)*	0 (0–25)	0 (0–40)	1 (1–28)	< 0.001‡
Type of PD				< 0.001
Whipple	57 (44.2)	55 (86)	13 (36)	
PPPD	72 (55.8)	9 (14)	23 (64)	
Pancreatic anastomosis				< 0.001
Pancreaticogastrostomy	45 (34.9)	53 (83)	4 (11)	
Pancreaticojejunostomy	84 (65.1)	11 (17)	32 (89)	
Tumour size (mm)*	30 (13–90)	30 (10–70)	31 (15–65)	0.62‡
Lymph node yield*	18 (5–50)	16 (4–40)	20 (8–47)	0.20‡
Lymphovascular invasion	83 (64.3)	31 (48)	35 (97)	< 0.001
Perineural invasion	103 (79.8)	41 (64)	35 (97)	< 0.001
Resection margin status				< 0.001
R0	44 (34.4)	37 (58)	4 (11)	
R1	84 (65.6)	27 (42)	32 (89)	
Missing	1	0	0	
Resection margin-positive				
Anterior	18 (14.5)	17 (27.0)	5 (14)	0.09
Posterior	37 (29.4)	20 (31.8)	14 (39)	0.56
SMV	42 (33.1)	26 (41.3)	14 (39)	0.51
SMA	16 (13.0)	2 (3.2)	6 (17)	0.06
Nodal status				0.12
N0	23 (17.8)	16 (25)	3 (8)	
N1	106 (82.2)	48 (75)	33 (92)	
Pancreatic fistula	10 (7.8)	12 (10.1)	3 (8)	0.42
Delayed gastric emptying	13 (10.1)	8 (13)	4 (11)	0.88
Non-pancreatic anastomotic leak	7 (5)	2 (3)	1 (3)	0.67
Relaparotomy	9 (7.0)	3 (5)	5 (14)	0.23
Postoperative bleeding	7 (5.4)	4 (6)	1 (3)	0.75
Patients receiving blood transfusion	42 (32.6)	19 (30)	11 (31)	0.89
Any complication	26 (20.2)	14 (22)	9 (25)	0.82
In-hospital death	6 (4.7)	2 (3)	2 (6)	0.81
Portal vein thrombosis	2 (1.6)	5 (8)	3 (8)	0.04

Values in parentheses are percentages unless indicated otherwise; *values are median (range). PD, pancreaticoduodenectomy; PPPD, pylorus-preserving pancreaticoduodenectomy; SMV, superior mesenteric vein; SMA, superior mesenteric artery. †χ^2 test, except ‡Mann–Whitney *U* test.

Table 3 Demographic and clinical characteristics according to degree of histological vein involvement

	No invasion (*n* = 117)	Invasion into tunica adventitia (*n* = 59)	Invasion into tunica media/intima (*n* = 47)	*P*†
Age (years)*	66 (43–80)	65 (43–80)	68 (51–78)	0.53‡
Sex ratio (M : F)	57 : 60	30 : 29	24 : 23	0.95
Type of vein reconstruction				0.79
Primary closure	68 (58.1)	30 (51)	29 (62)	
End-to-end anastomosis	33 (28.2)	20 (34)	11 (23)	
Interposition graft	16 (13.7)	9 (15)	7 (15)	
Tumour size (mm)*	30 (10–70)	31 (15–70)	30 (15–90)	0.28‡
Lymph node yield*	17.5 (4–50)	18.5 (4–45)	16 (7–47)	0.17‡
Lymphovascular invasion	63 (53.9)	42 (71)	38 (81)	0.002
Perineural invasion	85 (72.6)	48 (81)	40 (85)	0.16
Resection margin status				0.02
R0	54 (46.6)	17 (29)	13 (28)	
R1	62 (53.4)	42 (71)	34 (72)	
Missing	1	0	0	
Resection margin-positive				
Anterior	17 (14.9)	13 (22.8)	10 (21.7)	0.37
Posterior	29 (25.4)	23 (39.7)	18 (38.3)	0.10
SMV	19 (16.5)	32 (55.2)	28 (59.6)	< 0.001
SMA	12 (10.5)	3 (5.4)	6 (13.0)	0.39
Nodal status				0.32
N0	24 (20.5)	7 (12)	10 (21)	
N1	93 (79.5)	52 (88)	37 (79)	

Values in parentheses are percentages unless indicated otherwise; *values are median (range). SMV, superior mesenteric vein; SMA, superior mesenteric artery. †χ^2 test, except ‡Mann–Whitney *U* test.