Portal vein reconstruction using primary anastomosis or venous interposition allograft in pancreatic surgery

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ABSTRACT

Objective: Superior mesenteric vein/portal vein (SMV/PV) resection and reconstruction during pancreatic surgery are increasingly common. Several reconstruction techniques exist. The aim of this study was to evaluate characteristics of patients and clinical outcomes for SMV/PV reconstruction using interposed cold-stored cadaveric venous allograft (AG+) or primary end-to-end anastomosis (AG−) after segmental vein resections during pancreatic surgery.

Methods: All patients undergoing pancreatic surgery with SMV/PV resection and reconstruction from 2006 to 2015 were identified. Clinical and histopathologic outcomes as well as preoperative and postoperative radiologic findings were assessed.

Results: A total of 171 patients were identified. The study included 42 and 71 patients reconstructed with AG+ and AG−, respectively. Patients in the AG+ group had longer mean operative time (506 minutes [standard deviation, 83 minutes] for AG+ vs 420 minutes [standard deviation, 91 minutes] for AG−; $P < .01$) and more intraoperative bleeding (median, 1000 mL [interquartile range (IQR), 650-2200 mL] for AG+ vs 600 mL [IQR, 300-1000 mL] for AG−; $P < .01$). Neoadjuvant therapy was administered more frequently for patients in the AG+ group (23.8% vs 8.5%; $P = .02$). Patients with AG+ had a longer length of tumor-vein involvement (median, 2.4 cm [IQR, 1.6-3.0 cm] for AG+ vs 1.8 cm [IQR, 1.2-2.4 cm] for AG−; $P = .01$), and a higher number of patients had a tumor-vein interface >180 degrees (35.7% for AG+ vs 21.1% for AG−; $P = .02$). There was no difference in number of patients with major complications (42.9% for AG+ vs 36.6% for AG−; $P = .51$) or early failure at the reconstruction site (9.5% for AG+ vs 8.5% for AG−; $P = 1$). A subgroup analysis of 10 patients in the AG+ group revealed the presence of donor-specific antibodies in all patients.

Conclusions: The short-term outcome of SMV/PV reconstruction with interposed cold-stored cadaveric venous allografts is comparable to that of reconstruction with primary end-to-end anastomosis. Graft rejection could be a contributing factor to severe stenosis in patients reconstructed with allograft. (J Vasc Surg: Venous and Lym Dis 2017;■:1-9.)

Numerous studies have supported the safety and feasibility of combining pancreatectomy with resection of the superior mesenteric vein/portal vein (SMV/PV). The procedure is currently considered standard of care for patients with pancreatic tumors with limited involvement of the SMV/PV. Consequently, focus on development of an optimal reconstruction technique of the SMV/PV is pivotal. Several reconstruction techniques have been described, and primary repair with end-to-end anastomosis or venorrhaphy is most frequently reported.[1] For patients in whom a tension-free anastomosis cannot be achieved, the use of various interposition grafts has been described: venous and arterial allografts, autologous veins, synthetic grafts, and grafts made from parietal peritoneum or bovine pericardium.[1-4]

Existing literature concerning venous allograft for SMV/PV reconstruction during pancreatic surgery is limited.[4-8] Furthermore, long-term results on patency at the reconstruction site are not always reported.[8] Moreover, differences in the definition of adequate patency and the measurement of stenosis at the reconstruction site make published data troublesome to interpret. The aim of this study was to evaluate characteristics of patients and clinical outcomes for SMV/PV reconstruction during pancreatic surgery using interposed cold-stored cadaveric venous allograft (AG+) and primary end-to-end anastomosis (AG−). Also, donor-specific alloantibodies (DSAs) were investigated in patients receiving AG+ in an attempt to prove the hypothesis that an allogeneic immune response directed against the graft tissue could play a role in late graft stenosis.[6]

METHODS

Study population

We performed a retrospective review of all patients undergoing pancreatic surgery with venous resection and reconstruction at Oslo University Hospital between

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Author conflict of interest: none.

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The editors and reviewers of this article have no relevant financial relationships to disclose per the Journal policy that requires reviewers to decline review of any manuscript for which they may have a conflict of interest.

2213-333X

https://doi.org/10.1016/j.jvsv.2017.09.003

January 2006 and December 2015. Hospital records and pathology reports were reviewed. The type of procedure, venous reconstruction technique, duration of operation, intraoperative blood loss, and presence of severe complications were registered. Length of stay was defined as the day of surgery until discharge. End of data collection was set at June 30, 2016. Data from 37 of the patients in the AG+ group have been published previously.[6]

Study ethics

The Hospital Review Board approved the study (2015/18135) according to the general guidelines provided by the Regional Ethics Committee. The subgroup analysis of DSAs was approved by the Regional Ethics Committee (2016/1409/REK South East), and all patients analyzed for DSAs gave written informed consent. The manuscript was completed in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology statement.[9]

Definitions

Complications. Postoperative complications were assessed according to the Clavien-Dindo classification.[10] Major complications were defined as Clavien-Dindo grade ≥III, which are complications requiring surgical, endoscopic, or radiologic intervention as well as single or multiorgan dysfunction or death.

Patency. Preoperative and postoperative computed tomography (CT) images were evaluated in a blinded setting by an experienced staff radiologist (A.E.B.). Preoperative workup included multidetector CT with an optimized pancreatic protocol and a chest CT. Preoperative images were evaluated for tumor-vein circumferential interface (TVI) as described by Tran Cao et al[11] and for the length of tumor-vein involvement. SMV/PV diameter was measured in preoperative and postoperative axial images on portal venous-phase CT images, taken at a thickness of 1.5 to 3 mm. To eliminate the confounding effect of initial SMV/PV diameter, the change in diameter was calculated as the percentage postoperative reduction compared with preoperative SMV/PV diameter at the most narrow site, as described by others[12] (Fig 1). The degree of SMV/PV diameter change was classified as grade A (0%-49% reduction in diameter), grade B (50%-69% reduction), and grade C (≥70% lumen reduction) change. Complications associated with anastomotic stenosis of the portal venous system, including refractory ascites, hepatic encephalopathy, and gastrointestinal bleeding, have been found to occur in patients with stenosis ≥70%.[13] A grade C change was therefore regarded as severe stenosis and included fully occluded or thrombosed anastomoses. The causes and clinical implications of severe stenosis were retrieved from postoperative CT images and hospital records. Local recurrence was defined as soft tissue formation that increased in size over time in the resection area or along the cardinal visceral vessels around the pancreatic bed, as proposed by Heye et al.[14] Early failure at the reconstruction site was defined as the presence of thrombosis or no flow or low flow within the first 30 days after surgery.

ARTICLE HIGHLIGHTS

- **Type of Research:** Retrospective cohort study
- **Take Home Message:** In 113 patients who underwent superior mesenteric vein/portal vein reconstruction during pancreatic surgery with either primary end-to-end anastomosis or cold-stored interposition cadaveric allografts, there were no differences in complications or early outcomes between the two groups. Donor-specific antibodies developed in 10 allograft patients.
- **Recommendation:** The authors suggest both primary anastomosis and allograft reconstruction of superior mesenteric and portal veins during pancreatic surgery, although graft rejection could be a contributing factor to severe stenosis in the long term.

Patient management and operation technique

All patients were preoperatively evaluated in a multidisciplinary setting. Pylorus-preserving or classic pancreatoduodenectomy and subtotal or total pancreatoduodenectomy were performed. Since 2012, patients with preoperative findings consistent with borderline resectable pancreatic cancer, as defined by Callery et al,[15] were treated with at least four cycles of neoadjuvant chemotherapy. Reassessment with a new CT study was than performed to identify patients with resectable disease. The type of venous resection and reconstruction technique was based on intraoperative findings and the surgeon's preference. All SMV/PV resections and reconstructions were performed by experienced abdominal transplant surgeons. For patients with AG+, iliac veins removed during multiorgan harvesting procedures by the transplantation unit were used as interposition grafts. Immediately after harvesting, grafts were stored in University of Wisconsin solution at 4°C and matched to recipients according to blood group. Rejection drugs were not used for AG+ patients because of suspicion of cancer at the time of surgery and the risk of accumulating complications. Grafts stored for >14 days were discarded. All PV reconstructions were performed with polypropylene 5-0 or 6-0 running suture. A primary end-to-end anastomosis was obtained for patients in the AG− group. Perioperative use of heparin before vein resection was administered on a routine basis to all patients. Ultrasound of the reconstructed vein on postoperative day (POD) 1 was considered standard of care from 2012 onward. Patients were discharged home or to their local hospital as soon as the postoperative course was without suspicion of adverse events. Anticoagulation therapy varied throughout the study

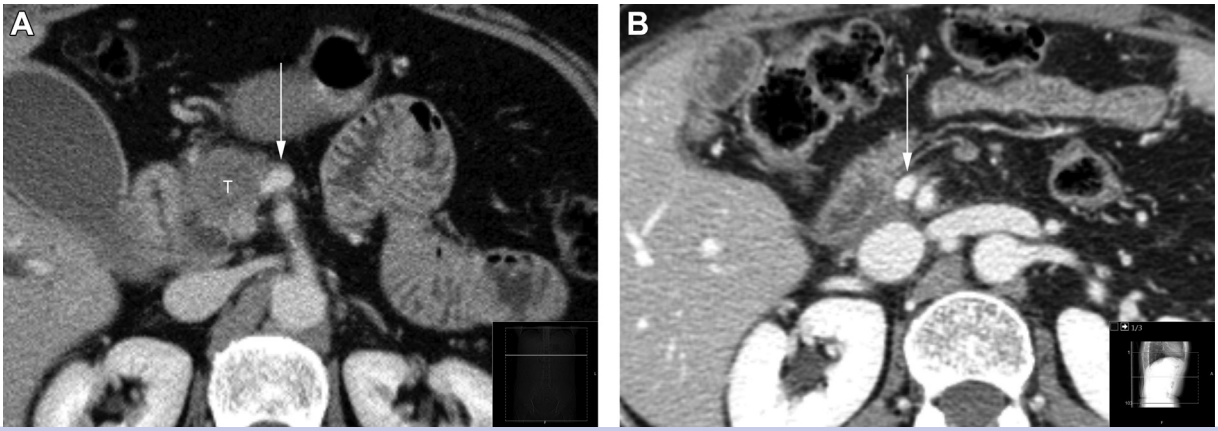

Fig 1. Assessment of patency. The axial diameter in this patient was 8 mm before **(A)** vs 6 mm after **(B)** surgery. The percentage postoperative reduction compared with preoperative diameter was (100 × (8-6)/8) = 25% (ie, a grade A stenosis). The *arrows* show the SMV/PV. *T,* Tumor.

period. Prophylaxis consisted of half-dose or full-dose low-molecular-weight heparin (LMWH). Lifelong aspirin at 75 mg daily was prescribed at the surgeon's discretion. Only prophylaxis given within 30 days after surgery was analyzed. Patients who were given standard prophylaxis (half-dose LMWH) but subsequently converted to extended prophylaxis (full-dose LMWH) during the first 30 days after surgery were recorded as "extended." Because of differences in histopathologic diagnosis, follow-up regimens varied.

Pathology assessment

Histopathologic characteristics, recurrence patterns, and overall survival were recorded for patients with pancreatic ductal adenocarcinoma. Until 2007, resection margins were reported positive (R1) if tumor cells were present at the surface (clearance = 0 mm). From 2008, the definition was changed to 1-mm clearance.

Allosensitization

A subgroup analysis of patients reconstructed with an allograft was performed by screening native blood sera for immunoglobulin G antibodies against human leukocyte antigen (HLA) class I and class II molecules with LABScreen Mixed assay (One Lambda, Thermo Fisher, Canoga Park, Calif). Positive samples (normalized background ratio ≥2.5) were further tested with LABScreen Single Antigen assays (beads coated with single recombinant HLA molecules; One Lambda) and analyzed with HLA Fusion 3 software (One Lambda). Antibodies with a mean fluorescence intensity ≥1000 (baseline normalized value) were defined as positive.

Statistical analysis

Continuous variables were expressed as mean or median (with standard deviation or interquartile range [IQR]). Differences in continuous variables were analyzed with independent samples *t*-test or Mann-Whitney *U* test based on distribution of data. Differences in proportions were analyzed with χ^2 test or Fisher exact test where appropriate. Overall and recurrence-free survival for patients with ductal adenocarcinoma was analyzed using the Kaplan-Meier method. *P* values of ≤ .05 were considered statistically significant. All analyses were performed using SPSS version 24 for Microsoft Windows (IBM Corp, Armonk, NY).

RESULTS

During the study period, a total of 857 patients underwent open pancreatic surgery, of whom 171 (20%) had vascular resection and reconstruction. The study included 42 patients with AG+ reconstruction and 71 patients with AG− reconstruction. Fifty-eight patients were reconstructed with other techniques and were therefore excluded from the study. Perioperative and postoperative characteristics are listed in Table I. A significantly higher proportion of patients in the AG+ group received neoadjuvant chemotherapy (10/42 [23.8%] for AG+ vs 6/71 [8.5%] for AG−; $P = .02$). Furthermore, there was a significantly longer operative time in the AG+ group (mean, 506 minutes [standard deviation, 83 minutes] for AG+ vs 420 minutes [standard deviation, 91 minutes] for AG−; $P < .01$). Estimated blood loss during surgery was also higher in the AG+ group, with a median of 1000 mL (IQR, 650-2200 mL) vs 600 mL (IQR, 300-1000 mL) for the AG− group ($P < .01$). There were no differences in postoperative morbidity, mortality, or length of stay between the groups.

Management of early failure at reconstruction site.

Four patients in the AG+ group and six patients in the AG− group had early failure at the reconstruction site. In the AG+ group, two patients had thrombosis on POD 11 and POD 22, respectively. Both patients underwent successful reoperation with thrombectomy. Two patients were reoperated on because of no or low flow at the reconstruction site on POD 1 (detected by routine

Table I. Demographic, clinical, and intraoperative characteristics of the study population

	AG+ (n = 42)	AG− (n = 71)	*P* value
Age, years, mean (SD)	61.6 (12.5)	65.3 (9.8)	.08
Sex ratio (M/F)	24 (57.1)/18 (42.9)	31 (43.7)/40 (56.3)	.16
ASA class			.59
1	3 (7.1)	3 (4.2)	
2	20 (47.6)	30 (42.3)	
3	19 (45.2)	38 (53.5)	
Diagnosis			.35
Pancreatic ductal adenocarcinoma	26 (61.9)	50 (70.4)	
Common bile duct cancer	5 (11.9)	11 (15.5)	
Intraductal papillary mucinous neoplasia	1 (2.4)	0 (0)	
Pancreatic neuroendocrine tumor	6 (14.3)	6 (8.5)	
Pancreatitis	2 (4.8)	4 (5.6)	
Microcystic serous cystadenoma	1 (2.4)	0 (0)	
Leiomyosarcoma	1 (2.4)	0 (0)	
Tumor size,[a] cm, median (IQR)	3.5 (2.7-5.5)	3.5 (3-4)	.34
Neoadjuvant therapy	10 (23.8)	6 (8.5)	.02[d]
Operative time,[b] minutes, mean (SD)	506 (83)	420 (91)	<.01[e]
Blood loss, mL, median (IQR)	1000 (650-2200)	600 (300-1000)	<.01[f]
Type of procedure			.06
PPPD	15 (35.7)	41 (57.7)	
cWP	13 (31)	18 (25.4)	
TPD	9 (21.4)	10 (14.1)	
DP	5 (11.9)	2 (2.8)	
Planned reconstruction	27 (64.3)	41 (57.7)	.49
Concomitant arterial resection	6 (14.3)	9 (12.7)	.80
Major complications[c]	18 (42.9)	26 (36.6)	.51
Length of stay, days, median (IQR)	13 (8-19)	9 (7-17)	.10
Ninety-day mortality	2 (4.8)	4 (5.6)	1
Early failure at the reconstruction site	4 (9.5)	6 (8.5)	1
Anticoagulation therapy			.79
Standard prophylaxis	8 (19)	15 (21.1)	
Extended prophylaxis	34 (81)	56 (78.9)	
Lifelong aspirin, yes/no	24 (57.1)	41 (57.7)	.95

AG, Allograft; *ASA*, American Society of Anesthesiologists; *cWP*, classic Whipple procedure; *DP*, distal pancreatectomy; *IQR*, interquartile range; *PPPD*, pylorus-preserving pancreatoduodenectomy; *SD*, standard deviation; *TPD*, total pancreatectomy.
Values are reported as number (%) unless otherwise indicated.
[a]Pancreatitis excluded from analysis.
[b]Data were incomplete for n = 1 in AG+ group and n = 8 for AG− group.
[c]Clavien-Dindo ≥IIIa.
[d]*P* value determined using Chi-square test.
[e]*P* value determined using independent sample *t*-test.
[f]*P* value determined using Mann-Whitney *U* test.

ultrasound examination) and POD 4, respectively. In one of these patients, low flow was due to kinking of the graft. Both patients had a new reconstruction with AG+.

In the AG− group, two patients underwent thrombectomy on POD 1 and POD 3, respectively. One patient in whom the splenic vein was reimplanted during the primary procedure developed splenic vein thrombosis. This was conservatively managed with no further complications. One patient with a pancreatic fistula underwent reoperation on POD 16 because of clinical deterioration and unsuccessful drainage. Relaparotomy revealed PV thrombosis but no signs of intestinal edema. A new reconstruction was considered too dangerous in the contaminated area, and the PV was ligated. This patient was discharged 46 days after the primary operation with no further complications related to the occluded PV. Two patients were reoperated on because of thrombosis (detected on routine ultrasonography) on POD 1, and

Table II. Preoperative and postoperative imaging

	AG+ (n = 42)	AG− (n = 71)	*P* value
Preoperative imaging			
TVI			.02
No TVI	0 (0)	4 (5.6)	
TVI ≤180 degrees	23 (54.8)	51 (71.8)	
TVI >180 degrees	15 (35.7)	15 (21.1)	
SMV/PV occlusion	4 (9.5)	1 (1.4)	
Length of tumor-vein involvement, cm, median (IQR)	2.4 (1.6-3.0)	1.8 (1.2-2.4)	.01[c]
Postoperative imaging[a]			
Grade of stenosis[b]	(n = 42)	(n = 66)	<.01[d]
A (0%-49%)	10 (23.8)	40 (60.6)	
B (50-69%)	6 (14.3)	13 (19.7)	
C (≥70% or occlusion or thrombus)	26 (61.9)	13 (19.7)	
Causes of SMV/PV grade C stenosis	(n = 26)	(n = 13)	.93
Locoregional recurrence	19 (73.1)	10 (76.9)	
Postoperative changes without recurrence	4 (15.4)	2 (15.4)	
Thrombosis	3 (11.5)	1 (7.7)	
Complications of SMV/PV grade C stenosis	(n = 26)	(n = 13)	
Gastroesophageal varices	16 (61.5)	11 (84.6)	.15
Hepaticojejunostomy varices	17 (65.4)	8 (61.5)	1
Ascites	10 (38.5)	9 (69.2)	.05
Postoperative bleeding requiring gastroscopy	4 (15.4)	5 (38.5)	.12
Postoperative SMV/PV stent placement	2 (7.7)	3 (4.3)	1
Time to last CT, months, median (IQR)	310 (32-1708)	246 (9-2522)	.54

AG, Allograft; *CT*, computed tomography; *IQR*, interquartile range; *SMV/PV*, superior mesenteric vein/portal vein; *TVI*, tumor-vein interface.
Values are reported as number (%) unless otherwise indicated.
[a]Two patients from the AG− group were reoperated on and underwent reconstruction of the SMV/PV with cold-stored cadaveric vein allograft. Hence, these patients were included in the AG+ group for the analysis of "postoperative imaging" results.
[b]The change in SMV/PV diameter was used to calculate the degree of stenosis. A reduction in the postoperative luminal diameter of ≥70% compared with the preoperative diameter or the presence of thrombosis was considered not patent. Data missing on four patients.
[c]*P* value determined using Mann-Whitney *U* test.
[d]*P* value determined using Chi-square test.

reoperation was performed with a new reconstruction with an AG+.

Preoperative and postoperative imaging. The distribution of TVI on preoperative CT images and the grade of stenosis at last available CT are shown in Table II. The length of tumor-vein involvement was larger in the AG+ group (median, 2.4 cm [IQR 1.6-3.0 cm]) than in the AG− group (median, 1.8 cm [IQR, 1.2-2.4 cm]; $P = .01$). The proportion of patients with TVI >180 degrees was higher in the AG+ group than in the AG− group (15/42 [35.7%] vs 15/71 [21.1%]; $P = .02$).

Postoperative imaging was not available for two patients in the AG+ group (one patient with benign histologic features and consequently no radiologic follow-up and one patient who died on POD 11). Both patients from the AG− group who were reoperated on and received an allograft on POD 1 were included in the AG+ group for analysis of the results of postoperative imaging. Hence, 42 patients remained available for analysis of postoperative imaging in the AG+ group. In the AG− group, one patient died on POD 36, and there was no postoperative CT scan available for review. Furthermore, one patient had a postoperative CT scan without intravenous administration of contrast material that was not suitable for measurement of the degree of stenosis at the reconstruction site. Last, the patient with PV ligation at POD 16 was excluded. Overall, 66 patients were available for analysis of postoperative imaging in the AG− group.

The proportion of patients with grade C stenosis at last available CT scan was significantly higher in the AG+ group (26/42 [61.9%] vs 13 of 66 [19.7%] for AG−; $P < .01$). On evaluating the causes of SMV/PV stenosis in patients with grade C stenosis, the presence of a thrombus was found in three patients in the AG+ group and in one patient in the AG− group. Local recurrence was considered to be the main cause of severe stenosis for both groups, and there was no difference in the presence of local recurrence in patients with grade C stenosis

Table III. Histopathologic tumor characteristics and disease recurrence in patients with pancreatic ductal adenocarcinoma

Characteristics	AG+ (n = 26)	AG− (n = 50)	*P* value
Tumor size, cm, median (IQR)	3.5 (3-3.5)	3.5 (3-4.1)	.54
T stage			.51
T1	0 (0)	2 (4)	
T2	2 (7.7)	2 (4)	
T3	24 (92.3)	46 (92)	
Resection margin			.20
R0	8 (30.8)	9 (18)	
R1	18 (69.2)	41 (82)	
pN stage			.32
N0	9 (34.6)	12 (24)	
N1	17 (65.4)	38 (76)	
Microvascular infiltration	18 (69.2)	41 (82)	.20
Perineural invasion	23 (88.5)	48 (96)	.33
Tumor differentiation[a]			.14
High	3 (15)	7 (15.2)	
Moderate	15 (75)	39 (84.8)	
Poor	2 (10)	0 (0)	
Disease recurrence[b]	(n = 25)	(n = 47)	
Patients with recurrence	21 (84)	30 (63.8)	.12
Site of recurrence			.54
Local	11 (52.4)	12 (40)	
Distant	3 (14.3)	7 (23.3)	
Local and distant	7 (33.3)	11 (36.7)	
Follow-up, months, median	11.5 (2.1-53.6)	10.7 (3.5-57.9)	.44
Recurrence-free survival, months, median	12.2 (8.9-15.5)	13.1 (9.7-16.5)	.31
Overall survival, months, median	18.6 (8.8-28.4)	20.5 (14.7-26.3)	1

AG, Allograft; *IQR*, interquartile range.
Values are reported as number (%) unless otherwise indicated.
[a]Patients receiving neoadjuvant therapy were excluded.
[b]Four patients who died within 90 days of surgery were excluded.

(73.1% for AG+ vs 76.9% for AG−; $P = .93$). Gastroscopy was performed under the indication "anemia" or "hematemesis" with verification of the bleeding site in the upper gastrointestinal tract in nine patients with grade C stenosis (four in the AG+ group and five in the AG− group). The bleeding source was identified as being related to portal hypertensive gastropathy (n = 1), esophageal and gastric varices and ulcers (n = 3), and gastroenterostomy varices and ulcers (n = 5). Finally, two patients in the AG+ group and three patients in the AG− group had a stent inserted for the treatment of SMV/PV stenosis.

Oncologic outcomes in patients with pancreatic ductal adenocarcinoma. Pancreatic ductal adenocarcinoma was the most common histologic diagnosis in both groups (26/42 [61.9%] for AG+ and 50/71 [70.4%] for AG−). There was no difference in R0 resection rates between the groups, with R0 resection being achieved in eight and nine patients (30.8% and 18%) with AG+ and AG−, respectively ($P = .20$; Table III). There was no significant difference in estimated median recurrence-free or overall survival between groups, with an estimated median overall survival of 18.6 months for AG+ and 20.5 months for AG− (Figs 2 and 3).

Allosensitivity. We collected blood samples from 13 patients who received venous allografts, and these were subjected to Luminex analysis. All these patients had HLA-specific antibodies, and HLA typing of 10 of the donors revealed that the antibodies were donor specific (Table IV).

DISCUSSION

Exploration and resection in case of pancreatic tumor involvement of the mesentericoportal venous axis are increasingly common and have become an integral part of routine surgical treatment.[16-19] Therefore, identification of the optimal reconstruction technique is important. This study retrospectively evaluated SMV/PV reconstruction using primary end-to-end anastomosis or interposed cold-stored cadaveric vein allograft after

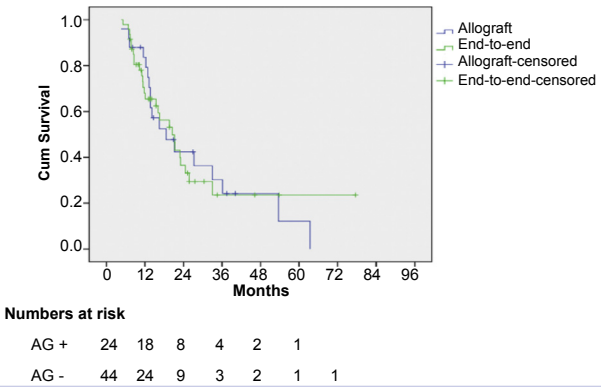

Fig 2. Overall survival in patients with pancreatic ductal adenocarcinoma undergoing reconstruction with allograft (*AG+*) or primary end-to-end anastomosis (*AG−*).

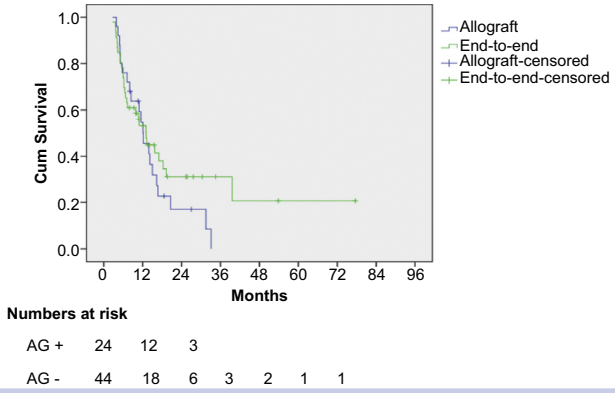

Fig 3. Recurrence-free survival in patients with pancreatic ductal adenocarcinoma undergoing reconstruction with allograft (*AG+*) or primary end-to-end anastomosis (*AG−*).

Table IV. Donor-specific antibodies (*DSAs*) in patients transplanted with venous allograft

Patient No.	DSAs, HLA class I molecules	DSAs, HLA class II molecules
1		DR17, DQ2
2	A11	
3	B8	DR17, DR52, DQ2
4	A2, A23, B7, B44	DR12, DR15, DQ7
5		DR17, DR52
6	A24, A26, B44, B55	
7	A3, A24, B35	DR9, DR53 DQ9
8	B62	DR1, DR4, DR53
9	A2, A24, B60	
10	A1, B7, B8	DR15, DQ2

HLA, Human leukocyte antigen.

segmental resections. DSAs were detected in a subgroup of patients reconstructed with AG+. Graft rejection could be a contributing factor to severe stenosis in the long term for these patients. However, no differences in major morbidity or mortality were observed.

This study shows that reconstruction of the SMV/PV with allograft is associated with longer operative time and more perioperative bleeding compared with primary end-to-end anastomosis. These findings are consistent with observations from a previous study that compared primary end-to-end anastomosis with prosthetic interposition grafts for SMV/PV reconstruction.[2] Preoperative images revealed that AG+ reconstruction was performed in patients in whom a longer segment of the vein was affected by tumor. Furthermore, a higher proportion of patients in the AG+ group had >180-degree TVI on preoperative CT imaging, even though the tumor size did not differ from that in the AG− group. These preoperative findings could reflect the fact that the patients requiring interposed allograft had a tumor—and tumor-associated fibroinflammatory reaction—that was located closer to the SMV/PV. Undoubtedly, resection in these patients was technically more challenging, which may account for the longer operative time and more extensive perioperative bleeding. Importantly, however, perioperative morbidity, mortality, and early failure at the reconstruction site did not differ between the two patient groups. This indicates that interposed allografts provide a safe alternative for reconstruction in the short term. Kang et al[12] have recently investigated the clinical consequences of PV stenosis after pancreatoduodenectomy. The authors found that gastric or hepaticojejunostomy varices occurred in 21 of 162 patients (13%) with >75% PV stenosis. Furthermore, they reported that 5 of 162 patients (3%) with PV stenosis or occlusion developed fatal recurrent gastrointestinal variceal bleeding. In this study, the presence of gastroesophageal and hepaticojejunostomy varices was higher, and overall nine patients (8%) underwent gastroscopy because of bleeding. Furthermore, PV stent placement for recurrent ascites or bleeding was performed in five patients, which confirms that PV stenosis can have considerable clinical consequences.

We found a significantly higher proportion of patients with severe stenosis in the group reconstructed with interposed allograft compared with primary anastomosis. However, interpretation of these findings must be done with some caution. First, as previously mentioned, preoperative radiology showed a longer length of tumor-vein involvement as well as a higher number of patients with TVI >180 degrees in the AG+ group. This illustrated the need for a more extensive venous resection that likely influenced the type of reconstruction technique chosen by the individual surgeon. Second, this is a retrospective study. Postoperative CT scans were not taken according to a standardized protocol, which likely influenced interpretation. Last, our method of calculating stenosis is based on the

preoperative diameter mainly because the retrospective nature of the study precluded acquisition of the immediate postoperative diameter after reconstruction. Ultrasound on POD 1 included only direction and speed of flow and the presence or absence of a thrombus but no routine measurement of diameter.

It is known that vascular endothelium expresses HLA class I and class II antigens.[20] The fact that all AG+ patients with HLA-typed donors in this study had DSAs confirms a previous report on a high rate of donor-specific allosensitization after allogeneic venous transplantation for peripheral occlusive vascular disease.[21] Because of the lack of representative biopsy material, investigation of the exact immunologic reaction and histopathologic changes in allogeneic venous transplants is not straightforward. However, investigation of PV transplantation in mice revealed within the first postoperative week full-thickness infiltration of the vascular wall with mononuclear cells and moderate destruction of the endothelium and tunica media. Even though the lumen was intact 4 weeks after transplantation, it was significantly reduced in size, and there was marked intimal thickening.[22] Thus, it cannot be excluded that an allogeneic rejection process in the venous graft could be a contributing factor to severe stenosis.

Histologic assessment of microscopic tumor invasion in the resected vein wall was not routinely performed for all patients. The significance of true SMV/PV wall invasion has recently been investigated, and it has been suggested that histopathologically confirmed venous wall invasion is associated with shorter median disease-free survival, predominantly owing to local recurrence.[23] Furthermore, detection of tumor growth along and around the PV on preoperative imaging correlates well with histopathologic tumor infiltration of the PV.[24] Tran Cao et al,[11] on the basis of a series of 277 patients with pancreatic ductal adenocarcinoma in the pancreatic head, reported that histopathologic evaluation could confirm tumor infiltration of the vein in 80% of patients with TVI >180 degrees who underwent SMV/PV resection. In this study, the proportion of patients with TVI >180 degrees was higher in the AG+ group. However, we found no significant difference in recurrence-free survival for patients who were resected for ductal adenocarcinoma. Furthermore, the type of reconstruction technique did not seem to influence overall survival for these patients, as has been reported by others.[25]

The limitations of this study lie in its retrospective design. Because of the different types of histologic diagnoses, there was heterogeneity in patient follow-up procedures. Postoperative CT protocols used to evaluate recurrence and stenosis were not standardized. This, together with the lack of an immediate postoperative diameter of the reconstructed vein, suggests that interpretation of long-term results on patency must be done with caution. Furthermore, the decision as to which reconstruction technique was used in the individual patient was based on intraoperative findings and the surgeon's preference. Planned venous resection was undertaken in only approximately 60% of the patients in both groups, indicating that the choice of reconstruction technique could have been discussed preoperatively in more patients. Even though long segmental SMV/PV resection and reconstruction without the use of interposition graft have been reported previously,[26,27] the availability of an alternative technique is important in case a primary end-to-end anastomosis cannot be performed safely because of tension.

CONCLUSIONS

This study shows that the short-term outcome of SMV/PV reconstruction with interposed cold-stored cadaveric venous allografts is comparable to that of reconstruction with primary end-to-end anastomosis. Graft rejection could be a contributing factor to severe stenosis in patients reconstructed with allograft.

The authors would like to thank Dr Kristoffer W. Brudvik for his contribution to the design of this study and transplant coordinator Hans Inge Birkeland for his support and help with data collection on patients receiving allografts.

AUTHOR CONTRIBUTIONS

Conception and design: DK, IG, PL, KL
Analysis and interpretation: DK, AB, MS, CV, CN, IG, KL
Data collection: DK, AB, MS, CV, CN, SH, PL, KL
Writing the article: DK, KL
Critical revision of the article: DK, AB, MS, CV, CN, SH, IG, PL, KL
Final approval of the article: DK, AB, MS, CV, CN, SH, IG, PL, KL
Statistical analysis: DK, AB, MS, CV, CN, SH, IG, PL, KL
Obtained funding: Not applicable
Overall responsibility: KL

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Submitted Apr 25, 2017; accepted Sep 7, 2017.