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RESEARCH

Portal vein reconstruction with bovine pericardium: a comparative analysis of postoperative outcomes in pancreatic surgery

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Abstract

Purpose Extended pancreatic resections with venous reconstruction are increasingly performed for borderline resectable pancreatic cancer. Various venous reconstruction techniques have been described. At our center, reconstruction is performed using bovine pericardium patches. So far, few studies reported outcomes using this technique in the field of pancreatic surgery.

Methods Data of consecutive pancreatoduodenectomies between January 1st 2015 and December 31st 2023 were analyzed retrospectively. Postoperative complications were graded by the Clavien-Dindo Classification, Comprehensive Complication Index (CCI) and complications specific to pancreatic resections as recommended and published by the International Study Group of Pancreatic Surgery (ISGPS).

Results Pancreatoduodenectomy included portal vein resection (PVR) in 23 patients compared to 95 patients without PVR. Patient age and comorbidities were similarly distributed between groups. Pancreatic adenocarcinoma was more prevalent in the PVR-group compared to no-PVR (87% vs. 58%, $p=0.009$). Operation time and blood loss were both increased with PVR (median: 416 min vs. 315 min and 300 ml vs. 150 ml, $p<0.001$ for both comparisons). Within ISGPS defined complications, grade B delayed gastric emptying and grade A postoperative hemorrhage were increased with PVR ($N=22$ vs. $N=1$, $p=0.001$ and $N=13$ vs. $N=0$, $p=0.007$). All other ISGPS complications, overall complications, CCI, 30-day and 90-day mortality were similar between groups. Out of 23 patients with PVR, early and late thrombosis occurred in one patient each.

Conclusion Portal vein reconstruction with bovine pericardium is feasible with comparable overall morbidity and mortality compared to pancreatoduodenectomy without PVR.

Keywords Pancreatoduodenectomy · Bovine pericardium · Portal vein reconstruction · Pancreatic cancer · Pancreatic resection

Introduction

The gold standard of care for resectable pancreatic cancer is surgical resection followed by adjuvant chemotherapy. According to the National Cancer Institute, only 12% of pancreatic cancer patients are diagnosed at a localised stage, when the cancer is still confined to the pancreas and resectable. Neoadjuvant therapy has been evaluated in recent years, showing a survival benefit in the setting of borderline resectable pancreatic cancer [1]. Today, the five-year survival rate for node-negative localised pancreatic cancer is 43.9%. However, this decreases to 16% with lymphatic spread and further declines to just 3.1% for patients with distant metastases [2–8].

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Local resectability of pancreatic cancer depends primarily on vascular involvement. It is determined by the extent of involvement of the portal vein, superior mesenteric artery, hepatic artery, and celiac trunk. Based on vascular involvement, pancreatic cancer is classified as resectable, borderline resectable or locally advanced [9]. In recent years, venous and, less frequently, arterial resections and reconstructions have been performed in experienced centers with acceptable morbidity rates. Today, portal vein reconstruction in pancreatic cancer is an established procedure that improves prognosis by increasing resectability rates [10–13]. Various techniques for portal vein reconstruction have been described, including primary suture, prosthetic allografts, cryopreserved allografts and autologous vein transplants. So far, no gold standard has been established. Poral vein reconstruction with tailored bovine pericardium patches offers the advantage of being readily available without prior harvesting or complex storage and being easily adaptable to various portal vein diameters [14].

The aim of the present study is to evaluate the feasibility and outcomes of portal vein resection and reconstruction using bovine pericardium patches compared to pancreatoduodenectomy without vascular resection.

Materials and methods

Patient population

Our retrospective database includes 118 consecutive patients, aged≥18 years, undergoing pancreatoduodenectomy for suspected or confirmed neoplasia between March 1st, 2015, and December 31st, 2023, at the Cantonal Hospital Baden. The period was selected to encompass our complete experience with bovine pericardium patch reconstruction in the context of pancreatoduodenectomy. The patient cohort was divided in two groups. The first group included 23 patients who underwent venous resection and reconstruction (PVR group), while the second group consisted of 95 patients who underwent pancreatoduodenectomy without vascular resection (no-PVR group). To improve comparability between groups, patients who underwent arterial reconstructions or other pancreatic resections were excluded. Patient and tumour characteristics including comorbidities, cancer stage, cancer type and neoadjuvant therapy were compared between the two groups. Peri- and postoperative variables included operation time, blood loss, length of intensive care (ICU) and hospital stay. Postoperative complications were reported using established grading scores like the Clavien-Dindo (CD) classification and the Comprehensive Complication Index (CCI) [15]. Complications specific to pancreatic resections were reported and graded as recommended and published by the International Study Group of Pancreatic Surgery (ISGPS) [16–19].

Portal venous patency after portal venous reconstruction was evaluated by duplex ultrasound or computed tomography (CT) either in the setting of postoperative complications or within regular postoperative tumour surveillance. The study was approved by the local ethics committee (IRB No. 2022 − 00665).

Portal vein reconstruction

All pancreatic resections were conducted as open procedures by two surgeons from the Department of General-, Visceral- and Vascular Surgery. To address the limited exposure of the pancreas team to vascular reconstruction while minimizing vessel clamping time, all portal vein reconstructions were performed by a vascular surgeon. Depending on the local tumour extension either pancreatoduodenectomy (PD) or pylorus preserving pancreatoduodenectomy (PPPD) was performed. Variations of portal vein resections and reconstructions were classified according to Krepline and colleagues into tangential resection with patch repair (VR1), segmental resection with splenic vein division and either primary anastomosis (VR2) or graft interposition (VR3) and segmental resection with splenic vein preservation and either primary repair (VR4) or graft interposition (VR5) (Fig. 1) [20].

Statistical analysis

Statistical analysis was performed using SPSS software (Version 24; IBM, Armonk, NY). Categorical variables were compared using the Chi-Square- or Fisher exact test, as applicable. Dichotomous data was expressed as frequency and percentages. To compare means and standard deviations of normally distributed continuous variables, the unpaired t-test was applied. The Mann-Whitney-U test was used to analyse differences in rank numbers of non-normally distributed variables presented as median values and interquartile range. P-values of <0.05 were considered statistically significant.

Results

Patient demographics

The characteristics of all 118 patients are summarised in Table 1. Gender distribution was balanced and comparable between the groups. The proportion of female patients was 61% in the PVR group, compared to 41% in the no-PVR group ($p=0.086$). Similarly, no significant differences were

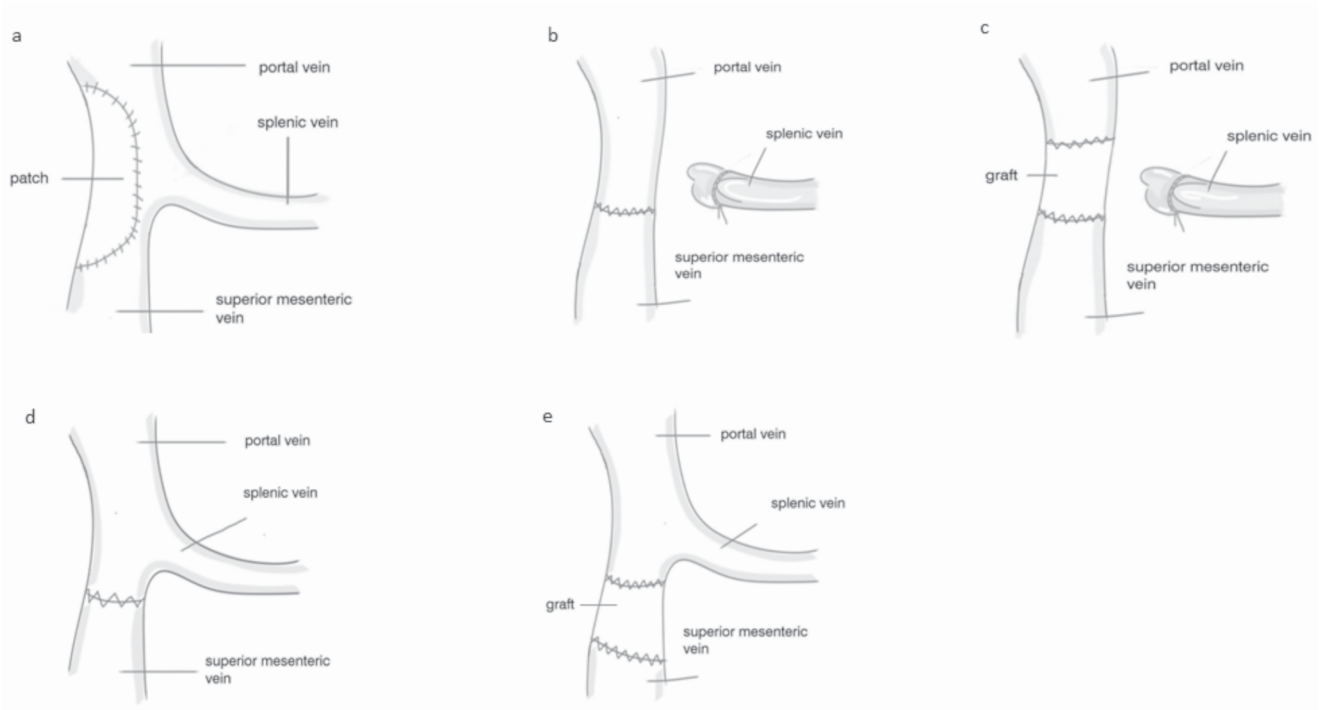

Fig. 1 Variations of Portal Vein Reconstructions According to Krepline and Colleagues
a Tangential resection with patch repair (VR1)
b Segmental resection with splenic vein division and either primary anastomosis (VR2)
c Graft interposition (VR3)
d Segmental resection with splenic vein preservation and either repair (VR4)
e Segmental resection with splenic vein preservation and graft interposition (VR 5)

Table 1 Patient characteristics. BMI (body mass index), ECOG (Eastern cooperative oncology Group), ASA (American Society of Anesthesiologists)

Variable	PV resection *N* = 23	No PV resection *N* = 95	*P* value
Female, N (%)	14 (61)	39 (41)	0.086
Age, years, mean (SD)	68 (65–81)	72 (65–76)	0.445
BMI subgroups. N (%)			
BMI < 18.5	0	2 (2)	1.0
BMI >/=18.5–30	22 (96)	84 (88)	0.456
BMI > 30	1 (4)	7 (7)	1.0
ECOG score, N (%)			
0 − 1	21 (91)	89 (94)	0.653
>/= 2	2 (9)	6 (6)	
Age Adjusted Charlson Comorbidity Score, median (interquartile range)			
Liver disease, N (%)	1 (4)	2 (2)	0.481
Chronic heart failure, N (%)	0	1 (1)	1.0
Chronic kidney disease, N (%)	0	4 (4)	1.0
Chronic obstructive pulmonary disease, N (%)	0	9 (10)	0.202
Diabetes, N (%)	4 (17)	9 (9)	0.278
Active smoking, N (%)	3 (14)	24 (26)	0.226
Previous smoking, N (%)	6 (27)	45 (47)	0.080
ASA classification, N (%)			
ASA 1–2	15 (65)	50 (53)	0.276
ASA 3–4	8 (35)	45 (47)	
Weight loss before surgery in % body weight, median (interquartile range)	4 (0–13)	3 (0–9)	0.398
Nutrition risk score, median (interquartile range)	4 (3–5)	4 (3–5)	0.912

observed in age distribution (median age of 68 vs. 72 years) and BMI (Table 1). For BMI-analysis, patients were subdivided into three BMI-groups (group 1: BMI < 18,5 group 2: BMI >/=18.5–30, group 3: BMI > 30). The majority of patients had a BMI of >/=18.5–30 (PVR: 96% vs. no-PVR: 88%). Most patients had an Eastern Cooperative Oncology Group Scale (ECOG) score of 0–1 (PVR: 91% vs. no-PVR: 94%). The rate of preoperative diabetes was not different between groups (17% vs. 9%, $p = 0.278$). Age adjusted Charlson Comorbidity Score, American Society of Anesthesiologists Classification (ASA) and Nutrition Risk Score (NRS) were similar between groups (Table 1).

Tumour entities and surgical procedures

Regarding tumour histopathology, the majority of patients in the PVR-group had a pancreatic adenocarcinoma (87% compared to 58% in the no-PVR group; $p < 0.009$, Table 2). Accordingly, tumour marker CA19-9 was increased in the PVR group (median 484 U/ml vs. 84 U/ml, $p = 0.003$). Neuroendocrine tumours were equally distributed in both groups (4% vs. 5%, Table 2). The frequency of distal cholangiocarcinoma showed a trend towards higher percentage in the no-PVE group (4% vs. 16%). Other malignant neoplasia were infrequent and similarly distributed between groups. Benign neoplasia like intraductal papillary mucinous neoplasms were more common in the no-PVR group (0 vs. 16%, $p = 0.04$). Preoperative biliary drainage was most commonly achieved via endoscopic retrograde cholangiopancreatography (ERCP) in 47% in the PVR-group and in 37% in the no-PVR group.

Neoadjuvant therapy was performed in one patient without PVR (Table 2). Regarding the surgical procedures, classic Whipple resection was performed in 48% of patients in the PVR group compared to 30% in the no-PVR group. Conversely, pylorus-preserving pancreatoduodenectomy (PPPD) was more frequently performed in the no-PVR group, accounting for 70% of cases, compared to 52% in the PVR group. Median operation time was longer with PVR compared to no-PVR (416 min vs. 315 min, $p < 0.001$). Mean blood loss was increased with PVR (300 ml vs. 150 ml, $p = 0.001$, Table 2). Microscopic residual tumour at margin (R1) was more frequently found with PVR compared to no-PVR (41% vs. 18%, $p = 0.042$).

Table 2 Surgical and histopathological characteristics. CA 19−9 (Carbohydrate-Antigen 19−9), CEA (Carcinoembryonic Antigen), NET (Neuroendocrine Tumour), Tis (Carcinoma in situ)

Metric	PV resection $N=23$	No PV resection $N=95$	*P* value
Pancreatic adenocarcinoma, N (%)	20 (87)	55 (58)	**0.009**
Distal cholangiocarcinoma, N (%)	1 (4)	15 (16)	0.192
Neuroendocrine tumour, N (%)	1 (4)	5 (5)	1.0
Other maligne neoplasia, N (%)	1 (4)	5 (5)	1.0
Benigne neoplasia, N (%)	0 (0)	15 (16)	**0.040**
Preoperative biliary drainage, N (%)			
ERCP	13 (57)	45 (47)	0.431
PTCD	0	5 (5)	0.582
Tumour marker (only adenocarcinoma)			
CA 19−9 level, U/ml), median (interquartile range)	484 (85–741)	84 (14–252)	**0.003**
Neoadjuvant therapy, N (%)	0	1 (1)	1.0
Surgical procedure, N (%)			
Classic pancreatoduodenectomy (Whipple)	11 (48)	28 (30)	0.093
Pylorus preserving pancreatoduodenectomy	12 (52)	67 (70)	
Operation time, min, median, range	416 (361–480)	315 (276–360)	**<0.001**
Blood loss ml, mean (SD)	300 (200–700)	150 (100–300)	**<0.001**
Pathologic tumour stage, N (%) (only adenocarcinoma and NET, $N=81$)			
pT0-Tis	0	0	
pT1-2	0	14 (26)	0.057
pT3-4	14 (100)	40 (74)	0.057
pNx / N0	3 (13)	38 (40)	**0.015**
pN1-2	20 (87)	57 (60)	
pM1	0	1 (1)	1.0
Margin status (not benigne), N (%)			
Complete resection (R0)	13 (59)	73 (82)	**0.042**
Microscopic residual tumour at margin (R1)	9 (41)	16 (18)	

Portal vein reconstruction outcomes

Portal vein resection was performed in 23 of 118 patients (19%). Venous resections and reconstructions were categorised according to Krepline et al. and are presented in Table 3. Bovine pericardium was used for all reconstructions not amenable to direct suture. Among the 23 patients, 8 underwent direct venous repair, while 15 required reconstruction using bovine pericardium. For the 8 patients who underwent direct repair, one patient received a segmental resection with splenic division (VR2), while the remaining 7 patients underwent resection and primary anastomosis without splenic vein division (VR4).

In the 15 patients requiring bovine pericardium reconstruction, different techniques were used based on the extent of resection: Tangential resection with vein patching (VR1) in 5 patients; segmental resection with splenic vein division and graft interposition (VR3) in 7 patients and segmental resection with splenic vein preservation interposition grafting (VR5) in 4 patients.

Early graft thrombosis, within 30 days after surgery, occurred in one patient 8 days after PPPD and PVR with direct suture (VR4). Interestingly, none of the patients who underwent PVR and bovine pericardium reconstruction experienced early graft thrombosis. In contrast, late graft thrombosis, as defined by 30 days or longer after surgery [21], was found in one patient 134 days after PPPD and PVR with pericardium tube graft reconstruction and splenic vein division (VR3). After three months of oral anticoagulation, no further signs of portal thrombosis were noticed and anticoagulation was discontinued. In addition, one patient after PPPD and PVR with direct suture (VR4) developed portal vein narrowing without thrombosis 730 days postoperatively. No intervention was required.

Postoperative outcomes

Postoperative complications were categorised according to the Clavien-Dindo (CD) classification. Moderate complications (Grade 1–2) were found in 44% of patients in the PVR- compared to 63% in the no-PVR-group ($p=0.085$). Severe complications (grade 3–5) were noted in 39% of the PVR-group and 23% of the no-PVR group ($p=0.118$, Table 4).

Cumulative complications were assessed using Comprehensive Complication Index (CCI) showing comparable outcomes between the groups with median scores of 30 in the PVR- vs. 21 in the no-PVR-group ($p=0.411$). There were no cases of 30-day mortality in either group. However, 90-day mortality was observed in 2 patients in the

Table 3 Portal vein resection types and patency at follow-up all grafts were bovine pericardium patches. N/A (not applicable), PD (pancreatoduodenectomy), PPPD (pylorus preserving pancreatectomy), VR (venous resection)

Patient No	Age	Type of resection	Type of venous resection VR1– VR5	Thrombosis (days after surgery)	Status of portal vein patency at last contact	Last follow-up (days after surgery; death or last contact)
1	82	PD	VR3	N/A	open	66
2	67	PPPD	VR3	N/A	open	85
3	68	PPPD	VR3	134	open	1265
4	69	PPPD	VR1	N/A	open	177
5	73	PD	VR1	N/A	open	265
6	59	PPPD	VR1	N/A	open	1661
7	82	PD	VR5	N/A	open	359
8	63	PPPD	VR5	N/A	open	581
9	68	PPPD	VR4	N/A	stenosis	730
10	61	PD	VR3	N/A	open	22
11	74	PD	VR4	N/A	open	26
12	65	PPPD	VR3	N/A	open	101
13	65	PPPD	VR 4	N/A	open	1007
14	68	PD	VR2	N/A	open	115
15	87	PD	VR3	N/A	open	115
16	65	PD	VR1	N/A	open	319
17	78	PPPD	VR5	N/A	open	40
18	80	PPPD	VR4	8	thrombosis	69
19	58	PPPD	VR5	N/A	open	696
20	81	PD	V4	N/A	open	104
21	78	PD	VR1	N/A	open	145
22	74	PPPD	VR4	N/A	open	277
23	81	PD	VR4	N/A	open	148

Table 4 Postoperative outcomes. ICU (intensive care unit), ECOG (Eastern cooperative oncology Group), ASA (American Society of Anesthesiologists)

Variable	PV resection $N=23$	No PV resection $N=95$	*P* Value
Hospital length of stay (after surgery), days, median, (interquartile range)	24 (14–32)	18 (14–26)	0.098
ICU stay, days, median (interquartile range)	2 (1–6)	0 (0–2)	**0.009**
International study group of pancreatic surgery (ISGPS) complications			
Postoperative pancreatic fistula (POPF), N (%)			
Biochemical leak	3 (13)	15 (16)	1.0
Grade B fistula	1 (4)	3 (3)	1.0
Grade C fistula	0	6 (6)	0.596
Delayed gastric emptying, N (%)			
Grade A	1 (4)	19 (20)	0.118
Grade B	5 (22)	1 (1)	**0.001**
Grade C	0	4 (4)	1.0
Bile leakage, N (%)			
Grade A	0	1 (1)	1.0
Grade B	1 (4)	2 (2)	0.481
Grade C	0	1 (1)	1.0
Postpancreatectomy hemorrhage, N (%)			
Grade A	3 (13)	0	**0.007**
Grade B	0	0	
Grade C	0	6 (6)	0.596
Chyle leak, N (%)			
Grade A	2 (9)	3 (3)	0.250
Grade B	0	0	
Grade C	0	0	
Postpancreatectomy acute pancreatitis, N (%)			
POH	4 (17)	22 (23)	0.549
Grade B	0	0	
Grade C	0	0	
Complication graded by Clavien Dindo (CD), N (%)			
CD1-2	10 (44)	60 (63)	0.085
CD3-5	9 (39)	22 (23)	0.118
Comprehensive complication index, median (interquartile range)	30 (9–46)	21 (9–31)	0.411
30-day mortality	0	0	
90-day mortality	2 (9)	1 (1)	0.097

PVR-group and in 1 patient in the no-PVE group (9% vs. 1%, $p=0{,}097$).

Complications specific to pancreatic resections were categorised and graded according to the criteria established by the ISGPS. Postoperative pancreatic fistula (POPF) of Grade B severity had similar occurrence in both groups, with one case in the PVR-group and 3 cases in the no-PVR, However, Grade C POPF was observed exclusively in the no-PVR group, affecting six patients (Table 3).

Delayed gastric emptying of Grade B severity was significantly more common after PVR (22% vs. 1%, $p=0.001$). Grade A postoperative hemorrhage was observed in 3 patients in the PVR-group whereas no cases were found in the no-PVR group (13% vs. 0%, $p=0.007$). In contrast, Grade C postoperative hemorrhage occurred exclusively in the no-PVR group, affecting six patients (0% vs. 6%, $p=0.597$).

In the evaluation of post-pancreatectomy acute pancreatitis, postoperative hyperamylasemia was found in 4 patients in the PVR- and in 22 patients in the no-PVR group ($p=0.549$, Table 4). Bile leak and chyle leak were infrequent and similarly distributed across both groups (Table 4).

Discussion

The present study compares the outcomes of pancreatoduodenectomy with and without portal vein reconstruction primarily using bovine pericardium grafts. We found a high vein patency rate with no additional morbidity and mortality in patients undergoing PVR. These findings suggest that portal vein resection with bovine pericardium repair is a viable option for vascular reconstruction in pancreatic resections.

Bovine pericardium patch grafts are readily available, require no prior harvest and can be easily adapted to different portal vein diameters offering practical advantages over other techniques [14]. Our results indicate that bovine pericardium patch plasty for portal vein reconstruction is a safe technique, yielding comparable short- and long-term outcomes to more commonly used methods such as autologous vein reconstruction. A systematic review by Labori and colleagues evaluated the safety and feasibility of different grafts used for superior mesenteric/portal vein reconstruction in partial pancreatectomy, covering studies published between 2000 and 2020. The review included 34 studies, each of which reported on a minimum of five patients and focused on graft thrombosis rates [21].

Autologous venous grafts were utilised in 14 studies, covering a total of 239 patients. Early graft thrombosis was found in 5.6% of patients, with an overall thrombosis rate of 11.7%. In comparison, our study demonstrated no early graft thrombosis and an overall thrombosis rate of 7% with bovine pericardium reconstruction.

Similarly, a U.S. study analysing outcomes of 99 patients who underwent portal vein resection and reconstruction using different techniques– including autologous vein, cryopreserved allograft and bovine pericardium– reported an early thrombosis rate of 6.6% [22]. Notably, in their study, early thrombosis occurred exclusively in patients with patch plasty or interposition graft repair, whereas we observed early thrombosis only in a patient who underwent direct portal vein repair. Compared to autologous vein and bovine pericardium patch reconstruction, synthetic grafts exhibited higher thrombosis rates, with early thrombosis occurring in 7.5% of cases and overall thrombosis reaching 16.4%. Interestingly, the study by Labori and colleagues reported more favourable outcomes with cadaveric allografts, demonstrating lower early and overall thrombosis of 2.5% and 4.3%; respectively, based on data from 161 patients across 9 studies. Few studies have reported exclusively on bovine pericardium patch plasty for vein reconstruction [14]. A Swiss study published their experience with bovine pericardium patch reconstruction in 15 patients undergoing pancreatectomy with venous resection. Among these patients, bovine pericardium patches were used for tube reconstruction in 12 cases and for patch plasty in 3 cases, with a reported thrombosis rate of 7%, which aligns with our findings [23].

Postoperative hemorrhage is a well-recognised and dreaded complication following pancreatic resection. In our study, 3 patients (13% of PVR cases) experienced ISGPS type A postoperative hemorrhage, characterised by a drop of haemoglobin without any intervention required. In contrast, a retrospective analysis found postoperative hemorrhage rates of 9% with a patent portal vein and 23% in cases of portal vein thrombosis after reconstruction [24]. Similarly, a study from the UK reported a postoperative haemorrhage rate of 5% following pancreatic resection with PVR [25]. However, the degree of hemorrhage severity was not specified in those studies.

Operation time and blood loss were both significantly higher in the PVR group, a fact that was previously reported with other PVR techniques [26, 27]. Despite this, in our study, the majority of the pancreatectomy-specific complications were similarly distributed between patients with and without PVR. Additionally, both mild and severe complications, as well as 90-day mortality rate, did not differ significantly between the two groups.

A study from a high-volume German center, reported an increased morbidity- and a 90 day-mortality rate of 6,3% in patients with PVR. However, most other studies have not found an association between PVR and increased postoperative morbidity and mortality [28–30]. The higher complication rates in the German study may be attributable to the inclusion of all types of pancreatic resections, potentially introducing a disproportionate number of more complex procedures such as extended vascular resections or total pancreatectomies in the PVR group. Moreover, in the German study, outcomes were categorized according to the type of portal vein resection with a substantial increase in complication rate and hospital stay with portal vein reconstruction by graft inter-position resulting in two anastomoses. In the present study, due to statistical constraints because of the limited patient numbers in the PVE group, conducting a subgroup analysis was considered inappropriate.

A limitation of our study lies in the diverse nature of the patient population, which presents challenges for direct comparisons in certain aspects. Our primary aim was to enhance the growing body of knowledge regarding the feasibility and safety of bovine pericardium reconstruction by sharing our experiences with this technique. Due to the limited data currently available in the literature, a broader analysis was essential to encompass the full range of outcomes. Focusing narrowly on a specific histological subgroup would have constrained the scope of our findings and excluded a significant portion of the study population. Furthermore, the PVE group's limited size encourages a careful and nuanced interpretation of the findings.

Conclusion

In this study, portal vein reconstruction using bovine pericardium emerged as a feasible and effective approach, demonstrating favorable graft patency rates. The technical advantages, such as ease of adaptation and ready availability, position it as a promising alternative for vascular

reconstruction in pancreatic surgery. Nonetheless, additional research is necessary to validate this concept.

Author contributions Silvan Patalong, Andrea Wirsching and Antonio Nocito contributed to the study conception and design. Materi-al preparation, data collection and analysis were performed by Silvan Patalong, Annatina Weber, Elena Krombholz, Michael Frey, Dominique Sülberg and Andrea Wirsching. The first draft of the manuscript was written by Silvan Patalong and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Data availability No datasets were generated or analysed during the current study.

Declarations

Consent for publication All authors reviewed the final version of the manuscript and approved its submission.

Competing interests The authors declare no competing interests.

Conflict of interest /Competing interests.
All authors of this manuscript declare no conflicts of interest.

Ethics approval The local ethics committee approved the current study.
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Consent to participate Patients consent was waived as approved by the local ethics committee.

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