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ORIGINAL ARTICLE

Results of portosystemic shunts during extended pancreatic resections

Florian Oehme[1] · Marius Distler[1] · Benjamin Müssle[1] · Christoph Kahlert[1] · Jürgen Weitz[1] · Thilo Welsch[1]

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Abstract

Purpose Patients with borderline resectable pancreatic cancer are increasingly explored after neoadjuvant treatment protocols. A complete resection, then, frequently includes the resection of the mesentericoportal axis. Portosystemic shunting for advanced tumours with infiltration of the splenic vein or cavernous transformation of the portal vein can enable complete tumour resection and prevent portovenous congestion of the intestine. The aim of this study was to report the results of this technique for selected patients.

Methods Patients operated for pancreatic cancer at our department between September 2012 and December 2017 using intraoperative portosystemic shunting were included in this retrospective analysis.

Results Some 11 patients with pancreatectomy and simultaneous portosystemic shunting were included. The median age was 65.1 years. A distal splenorenal shunt and a temporary mesocaval shunt were accomplished in 5 and 4 cases, respectively. Two patients were operated using persistent mesocaval shunts (from the coronary, splenic or inferior mesenteric veins). The median operating time was 9.43 h. All but one patient were resected with tumour-negative resection margins; 5 patients had relevant complicated postoperative courses. There was one case of in-hospital mortality but no further 30- or 90-day mortality or graft-associated complications. Five patients were alive after a median follow-up of 24.6 months. The median postoperative survival was 12 months.

Conclusion Portosystemic shunting at the time of extended pancreatectomy is technically challenging but feasible and enables complete tumour resection in cases in which standard vascular reconstruction is limited by cavernous transformation or to prevent sinistral portal hypertension with acceptable morbidity in selected cases. Considering the limited overall survival, the potential individual patient benefit needs to be weighed against the considerable morbidity of advanced tumour resections.

Keywords Pancreatic cancer · Pancreatectomy · Mesocaval shunt · Portosystemic · Venous reconstruction

The study took place at the Department for Visceral, Thoracic and Vascular Surgery, University Hospital Dresden. Supervision lead surgeons are Prof. Welsch and Prof. Weitz.

None of the information, neither in part nor the complete manuscript, has been published elsewhere. This manuscript is furthermore neither in part nor as complete manuscript under consideration for publication in any other journal.

Florian Oehme, Marius Distler, and Benjamin Müssle contributed equally to this work.

✉ Thilo Welsch
thilo.welsch@uniklinikum-dresden.de

Florian Oehme
florian.oehme@uniklinikum-dresden.de

Marius Distler
marius.distler@uniklinikum-dresden.de

Benjamin Müssle
benjamin.muessle@uniklinikum-dresden.de

Christoph Kahlert
christoph.kahlert@uniklinikum-dresden.de

Jürgen Weitz
juergen.weitz@uniklinikum-dresden.de

[1] Department of Visceral, Thoracic and Vascular Surgery, University Hospital Carl Gustav Carus, Technische Universität Dresden, Fetscherstrasse 74, 01307 Dresden, Germany

Introduction

Recent trials investigating the multimodal treatment of pancreatic ductal adenocarcinoma (PDAC) have resulted in a 5-year survival of 40% if complete surgical tumour resection (R0) is achieved and the operation is followed by adjuvant chemotherapy. Even for borderline resectable tumours, neoadjuvant treatment resulted in resectability rates of 60% [1, 2]. These advances support the radical resection of pancreatic malignancies, even in cases of borderline resectable stages and vascular involvement of the mesentericoportal axis [3]. Resection of the superior mesenteric vein (SMV) or portal vein (PV) during pancreatoduodenectomy (PD) for tumour infiltration is the current standard at specialized centres if tumour-free segments of the PV cranial to the tumour and the SMV or jejunal/ileal branches caudal in the mesenteric rout are accessible for vascular anastomosis or graft interposition [4–6]. Reconstruction of the splenic vein (SV) confluence with the SMV in cases in which this segment is involved by the tumour is challenging because of the critical design of the anastomosed vein segment and the risk of kinking or stenosis with subsequent intestinal congestion or vein thrombosis. This problem can be solved by ligation of the SV, which might lead to sinistral portal hypertension, especially if the left gastric vein is not preserved.

Moreover, PV anastomoses can be safely performed only if simultaneous intestinal decompression is guaranteed (e.g., competent inferior mesenteric vein, which depends on the entry into the SV or SMV) or if temporary congestion of the intestine is compensated during PV anastomosis. If there is cavernous transformation of the PV due to tumour infiltration or occlusion, a safe anastomosis often requires prior bypassing of the portal blood flow from the intestine and tumour resection.

Technically, both the sinistral portal and the intestinal portal system can be decompressed using portosystemic shunt procedures. Whereas distal splenorenal shunting (DSRS) decompresses the left portal system, a temporary mesocaval shunt (MCS) drains the intestinal portal blood flow and allows subsequent reconstruction. The feasibility and first results of these complex shunt procedures were reported in 2013 in 11 patients [7]. Here, we present our experience and outcome of extended pancreatic cancer resection with intraoperative DSRS or MCS.

Materials and methods

Patients

All patients who were operated for pancreatic cancer at our department between September 2012 and December 2017 were retrospectively identified from our database. Patients were eligible for inclusion if their operation included either a temporary MCS, DSRS [8] or splenocaval shunt [9]. All patients were discussed preoperatively by an interdisciplinary tumour board to establish the individual treatment plan. The study was approved by the institutional review board at the Technische Universität Dresden (decision number: EK 469112918).

Surgical technique and pathological analysis

Our standard surgical technique of pancreatic cancer resection with PV reconstruction was described recently [10, 11]. Briefly, venous reconstructions were performed with 5–0 Prolene running sutures. The left internal jugular vein segments were harvested using a 4- to 5-cm cervical incision along the sternocleidomastoid muscle.

Microscopic resection status was classified as R1 if tumour cells were detected at the circumferential resection margin (CRM). Cases without direct CRM invasion (R0) but with tumour cells ≤ 1 mm from the CRM were classified as R0 CRM+.

Surgical morbidity included intra-abdominal abscess, postoperative bile leak, delayed gastric emptying, postoperative pancreatic fistula, postoperative postpancreatectomy haemorrhage and surgical site infection. The complications delayed gastric emptying [12], postoperative pancreatic fistula [13] and postpancreatectomy haemorrhage [14] were defined and graded according to the international consensus definitions of the International Study Group of Pancreatic Surgery. All complications were categorized using the Clavien-Dindo classification [15].

Statistical analysis

The R software package (R version 3.1.3, The R Foundation for Statistical Computing; http://www.R-project.org/) was used for statistical calculation and obtaining data plots. The follow-up time was defined from surgery to death or the last patient contact.

Results

During the study period, 11 patients underwent tumour resection plus either an intraoperative temporary or persistent MCS or a DSRS (Table 1). The median age of the patients was 65 years (interquartile range, 57–73.5 years), and the median time period between diagnosis and operation was 5.67 months for the neoadjuvant chemotherapy group and 2.2 months for patients operated without neoadjuvant chemotherapy (interquartile range, 1–7 months). Four of the 9 patients in the PDAC group received preoperative chemotherapy (combined with radiation in one patient) with a median duration of

Table 1 Patient and operative characteristics

Case	1	2	3	4	5	6	7	8	9	10	11	Median (SD)*
Patients												
Age (years)	53	68	75	69	72	49	75	82	46	66	61	65.1 (11.6)
Sex	F	F	M	F	F	F	F	F	M	M	F	
ASA	3	3	3	3	3	3	2	2	1	3	2	
Neoadjuvant treatment	No	No	No	Yes	Yes	Yes	Yes	No	No	No	No	
Operation												
Resection	PD	TP	PPPD	TP	TP	TP	PD	PPPD	PPPD	PPPD	PD	
Venous resection	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	
Arterial resection	No	Yes	No	Yes	Yes	No	Yes	No	No	No	Yes	
Type of arterial resection	NA	CHA	NA	AHD	CHA	NA	CHA	NA	NA	NA	CHA	
Shunt	SV-LRV	VC-IMV; VC-LGV	tMCS	tMCS	tMCS	tMCS	SV-LRV	SV-LRV	SV-ICV	SV-LRV	SV-LRV	
Graft	None	None	LJV	Bovine	LJV	LJV	None	None	None	None	None	
Blood loss (mL)	1600	2000	3200	3300	1100	1700	NA	NA	NA	600	800	1787.5 (1016.2)
OR time (hh:mm)	09:08	07:56	11:11	12:15	14:05	10:13	07:53	09:18	07:05	06:34	07:36	9.23 (2.42)

TP, total pancreatectomy; PPPD, pylorus-preserving pancreatoduodenectomy; PD, pancreatoduodenectomy; CHA, common hepatic artery; AHD, right hepatic artery; tMCS, temporary mesocaval shunt; SV-LGV, splenic to coronary vein; SV-LRV, splenic to renal vein; VC-LGV, inferior caval vein to coronary vein; LJV, left jugular vein; NA, not applicable

6 cycles (three received FOLFIRINOX; one received gemcitabine [alone]). Reasons not to perform a neoadjuvant treatment for borderline tumours in the remaining cases were based on an interdisciplinary consensus of the tumour board panel ($n = 3$), severe cholestasis with liver function impairment ($n = 2$), direct referral from another centre after intraoperative exploration ($n = 1$) and patient refusal of chemotherapy ($n = 1$). Complete sets of CA 19–9 values were available in only two of the 4 patients with neoadjuvant treatment. Whereas a significant decline (600 to 188 U/ml) was observed in one patient during chemotherapy, the other patient had a moderate increase (392 to 476 U/ml). The median preoperative CA 19–9 level of all 11 patients was 3083 U/ml (interquartile range, 188–4483 U/ml).

The American Society of Anesthesiologists (ASA) score was 2 or 3 in 10 patients and 1 in a single patient. The reasons for ASA 3 classification were a high cardiac risk situation (2 patients), an insulin-dependent diabetes mellitus with recurrent glycaemic dysbalances reinforced by a substantial weight loss (2 patients), a limited pulmonary function with chronic obstructed pulmonary disease (2 patients) and a history of colon cancer with a complicated postoperative course and reduced fitness (1 patient).

Total pancreatectomy (TP), a pylorus preserving pancreatoduodenectomy (PPPD) and a classic PD procedure were performed in 4, 4 and 3 cases, respectively. Five patients received a classic DSRS (two during PPPD and three during classic pancreatico-duodenectomy; Fig. 1a–e), whereas one patient underwent a splenocaval shunt and one patient received a combined shunt (shunt between the left gastric vein and the inferior vena cava in combination with a shunt between the inferior mesenteric vein and the inferior cava vein; Fig. 2). In three cases of TP and in one case of PPPD, a temporary MCS was performed, using the left internal jugular vein (Fig. 3a–d), whereas a bovine pericardium patch was used in one case.

Reconstruction of the mesentericoportal blood flow after temporary MCS was achieved either by using the internal jugular vein as an interposition graft or by an end-to-end anastomosis without graft. Synchronous segmental resection of the hepatic artery was performed in 5 patients; among those, an interposition graft from either the splenic artery or the inferior mesenteric artery was applied in two patients.

The median operating time was 566 min (9.43 h; interquartile range, 456–671 min). The operations with a temporary MCS lasted longer compared with operations with permanent established shunt (e.g., Warren shunt) (724 vs. 475 min, $P < 0.001$). The median tumour size was 5.4 cm (interquartile range, 3.2–8.6 cm), and a microscopically complete tumour (R0) resection was achieved in 10 patients.

The median intraoperative blood loss was 1800 ml (interquartile range, 525–3075 ml). Five patients developed a relevant postoperative morbidity with a complication grade ≥ III.

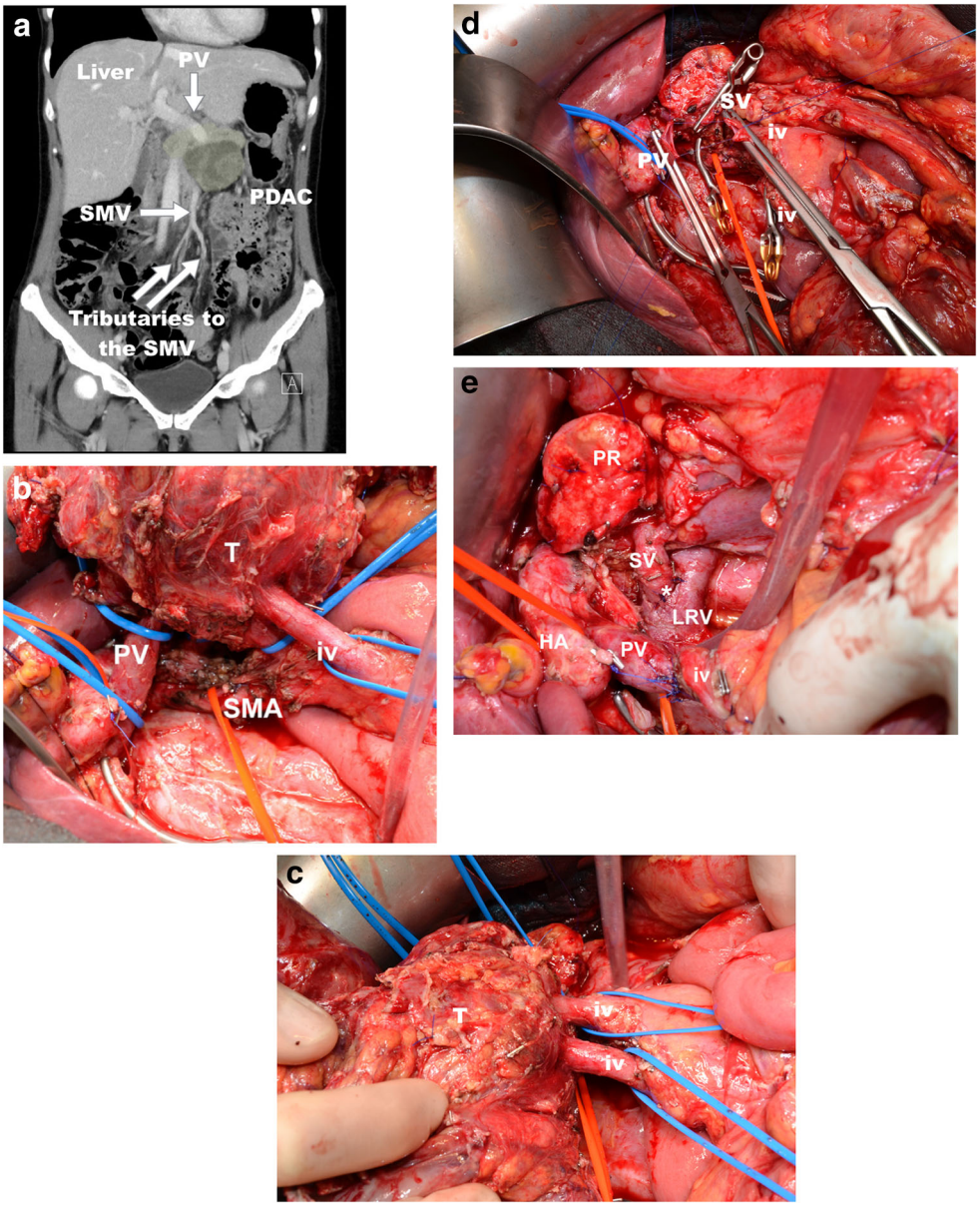

Fig. 1 Case 1. (**a**) Local advanced pancreatic cancer (T) with tumour infiltration at the level of the superior mesenteric vein (SMV) and portal vein (PV) confluence. The ileal veins (iv) that join into the SMV are dilated caudal to the tumour. The splenic vein (SV), entering at the same level in the tumour, is not displayed. The ileal veins (iv) caudal to and the PV cranial to the tumour showed no signs of infiltration and were suitable for a primary anastomosis. (**b**,**c**) The tumour (T) encased the confluence of the SMV and PV, and two ileal veins (iv) could be dissected in the mesenteric root. The superior mesenteric artery (SMA) was not invaded by the tumour. (**d**) Reconstruction of the mesentericoportal axis was accomplished by end-to-end anastomosis of one of the ileal veins (iv) to the portal vein (PV). The other ileal vein was ligated. The splenic vein (SV) is clamped at that time. (**e**) Because of a relevant congestion of the stomach, a distal splenorenal shunt (*) was performed anastomosing the SV to the left renal vein (LRV). The hepatic artery (HA) was tagged with a vascular loop. Later during the procedure, the pancreatic remnant (PR) with its tumour-free margin was anastomosed to the first jejunal loop

Two patients underwent relaparotomy because of postoperative haemorrhage or leakage of the gastrojejunostomy. Computed tomography (CT)-guided drainage of abdominal fluid collection was indicated in two other cases. There was one in-hospital mortality (sepsis following bowel ischemia on postoperative day 20), but no further 30-day or 90-day mortality. In total, 7 patients were recommended to undergo adjuvant chemotherapy, while only 4 patients actually received adjuvant chemotherapy.

In 8 of the 11 patients, at least one postoperative contrast-enhanced CT-imaging study was available during the postoperative course and demonstrated patency of the venous anastomoses and shunts in all cases. All patients with a temporary MCS further had a patent SMV-PV anastomosis after a 3-month follow-up. Another two patients who obtained a splenorenal shunt showed vascular patency in follow-up CT scans at 6 and at 12 months, respectively. One patient that received an anastomosis of the coronary vein and the ICV in combination with an anastomosis between the IMV and the ICV showed no signs of occlusion after 12 months. Ultimately, one patient who received an anastomosis between the splenic vein and the ICV had one follow-up CT scan at six months postoperative which proved patency of the employed shunt.

The pathohistological tumour characteristics are displayed in Table 2. At the last follow-up in August 2018, 5 patients were deceased because of the progression of tumour growth (4 patients with a PDAC and 1 with a pleomorphic carcinoma), with a median postoperative survival of 9.6 months (range, 7–12 months). Five patients were alive after a median follow-up

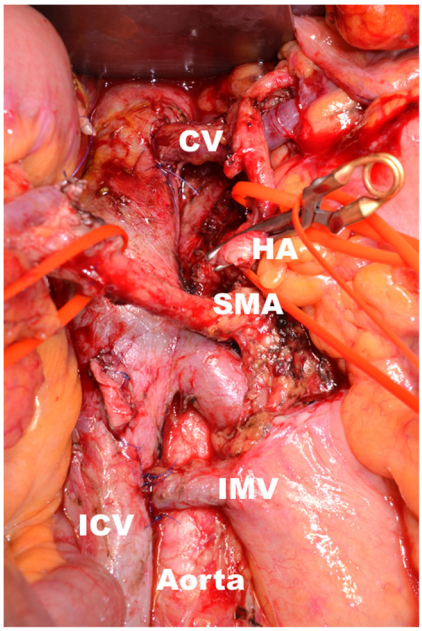

Fig. 2 Case 2. During tumour resection (including right colectomy), venous congestion of the remaining large bowel occurred. Consequently, an intraoperative anastomosis between the IMV and the ICV for decompression of the colon was performed. Thus, retrograde decompression of the left-sided portal system via IMV was no longer possible, and venous congestion of the stomach occurred. Therefore, an anastomosis from the coronary vein (CV) to the ICV was performed, which led to sufficient decompression

of 24.6 months (range, 22–26 months), of whom two patients developed tumour recurrence (after 6 and 12 months, respectively). The median estimated postoperative survival of the 11 patients was 12 months.

Discussion

Pancreatic cancer is one of the most lethal solid malignancies with a high level of metastatic growth and a high resistance toward available chemotherapeutic agents. Besides the aggressive tumour biology and poor prognosis, major radical surgery (i.e., pancreatic resections with or without vascular resections) is indicated because the multimodal treatment including complete tumour resection offers the best survival chances.

During the past decade, borderline resectable PDAC has been increasingly treated according to neoadjuvant protocols to enable potentially curative resection. This approach yielded some remarkable results, especially in comparison with patients treated with upfront resection [16].

Once the indication for tumour resection is set, the surgical approach must aim for tumour-free resection margins, although the intraoperative situation can necessitate vascular resection. Vascular resection at the portovenous axis can lead to left-sided hypertension (LSH) at least if the SV is ligated during reconstruction for SMV-PV and the inferior mesenteric vein (IMV) enters directly into the SMV [17]. The value of LSH has been discussed intensively, with some authors arguing that LSH does not necessarily lead to gastrointestinal haemorrhage, which can be explained by sufficient drainage via the Arc of Barkow [18]. Ono et al. presented a retrospective analysis showing that a considerable portion of patients developed a postoperative sinistral hypertension after SV ligation, but only a minority (about 2 of 27) developed postoperative haemorrhage [18]. In our own experience, the efficiency of shunting for LSH depends on the following two influencing factors: First, portal hypertension should be treated only if it leads to obvious intraoperative venous congestion of the stomach. This regularly occurs if the left gastric vein is resected during tumour resection and no venous retrograde drainage via IMV is possible (as in case in which IMV enters the ICV directly). The short gastric vessels usually are the main cause for venous congestion of the stomach, as the blood flow (at least if retrograde drainage is not possible) is from the sinistral system via the short gastric vessels directly to the PV [18]. Second, whenever the need for a vascular anastomosis is present based on the venous congestion due to LSH, we favour the DSRS, because a venous anastomosis of the SV to the reanastomosed SMV/PV axis often results in a kinking or stenosis of the SMV-PV anastomosis.

On the other hand, temporary MCS can be indicated if complex tumours with encasement of the portomesenteric axis or the hepatoduodenal ligament endanger uncontrolled venous bleeding or congestion of the small bowel. One first manoeuver to minimize or avoid venous congestion of the small bowel during SMV/PV resection is temporary clamping of the SMA. In our own practice, this is regularly done if no further venous outflow of the small bowel can be preserved at the time of reconstruction. However, Evans et al. showed that this might be not sufficient to reduce venous congestion during resection of the SMV-PV segment but potentially could lead to both increased intraoperative bleeding with increased postoperative morbidity [19] and inoperability.

In cases in which preoperative imaging suggests venous congestion or intraoperative congestion can be anticipated, we plan for intraoperative temporary employment of a mesentericocaval shunt and discuss this with the patients preoperatively. The technique requires a surgical team with experience in vascular surgery. Once the portosystemic drainage/decongestion is established, a controlled complex tumour resection becomes feasible and safe. As complete tumour resection is mandatory to ensure long-term survival, a temporary MCS can be the key to ensure negative resection margins [20]. In general, the internal jugular vein is the preferred autologous graft for interposition, as reported earlier [7]. Advantages of the internal jugular vein are the optimal vessel diameter and length, long-term patency and the

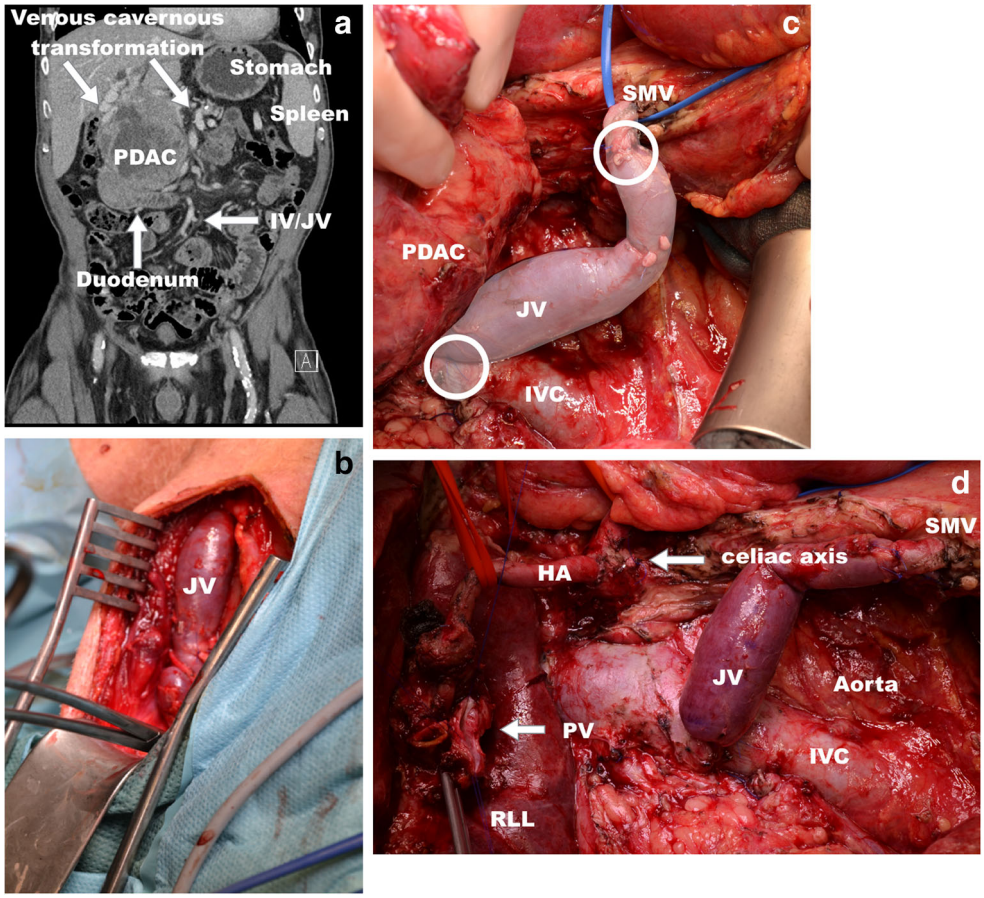

Fig. 3 Case 3. (**a**) Coronary computed tomography displaying the PDAC of the pancreatic head. The tumour encased the SMV-PV confluence, resulting in venous cavernous transformation, as seen at the level of the ileal and jejunal vein (IV/JV). At the level of the hepatoduodenal ligament, close to the tumour, venous cavernous transformation was obvious. The PDAC itself does show signs of regression due to local necrosis at the central part of the PDAC. (**b**) During resection, the decision for a temporary mesocaval shunt (tMCS) was made. Thus, the left-sided internal jugular vein (JV) with sufficient calibre for a tMCS was used. (**c**) The established tMCS from the SMV to the ICV (whitish area). The circles point to the anastomosis between both the SMV/JV and the JV/SMV (both sutured with Prolene 5–0 in a running single row fashion). (**d**) Tumour resection was performed, allowing exposure of the celiac axis and the hepatic artery (HA) as well as resection of the SMV-PV confluence. The tMCS was taken down after complete resection with primary anastomosis of the SMV-PV. Because of the resection of the SV (not displayed), the SMV was without tension mobilized and anastomosed to the PV (as the SMV was no longer tethered to the SV).

possibility of using the autologous graft for the final reconstruction of the portomesenteric axis. This can be advantageous to prevent graft infection by bacterial, bile or pancreatic juice contamination during the postoperative course. The authors have not observed any complications from the cervical harvest site, and the harvest procedure can be safely performed in less than 10–15 min.

A further indication for a permanent mesocaval shunt can be venous congestion of the stomach because of sacrification of the CV and/or TP with splenectomy. Here, subtotal resection of the stomach or an anastomosis between the CV and the ICV is a valid option. An additional vascular anastomosis naturally bears additional risks for postoperative morbidity but enables preservation of the stomach. The authors prefer the organ-preserving vascular shunts when oncologically adequate and technically feasible.

The extent of such radical and complex operations needs to be critically discussed with the selected patients before surgery. The present data clearly show that the underlying tumours, in which extended resections were indicated, exhibited an aggressive tumour biology, resulting in a median survival of only 12 months. The complexity of the operation is demonstrated in the long operating time and high blood loss, which are comparable to findings of a previously published report of simultaneous shunts [17]. However, the latter article did not report on survival or long-term outcome data. To compare, the median 1-year survival after pancreatectomy with arterial resection is only 49.1% [21]. In particular, the postoperative quality of life (QoL) needs to be highlighted with such a limited period of remaining lifetime. Thus, the QoL for patients who are scheduled for resection of locally advanced PDAC must be an integral

Table 2 Pathohistological outcome

Case	1	2	3	4	5	6	7	8	9	10	11	Median (SD)*
Tumour	Dediff.	PDAC	Pleomorphic	PDAC	PDAC	PDAC	PDAC	PDAC	PDAC	PDAC	PDAC	
Size (cm)	6.8	2.7	13	7.2	5.8	3.6	4	3.7	2.4	7.3	3.8	5.48 (3.06)
T/N/M	3/0/1	2/0/0	3/0/0	3/1/0	3/1/0	3/0/0	3/1/0	3/1/0	2/1/1	3/1/0	3/1/0	
Ln resected	28	16	27	28	25	15	29	10	24	27	17	23.18 (5.33)
LN positive	0	0	0	2	2	0	1	3	3	4	10	2.27 (2.94)
Minimal resection margin (mm)	4	1	> 10	1	5	2	1	1	1	0	1	2.7 (2.95)
R	0	0	0	0	0	0	0	0	0	1	0	
CRM	–	+	–	+	+	–	+	+	+	+	–	
pPV invasion	–	+	–	+	+	+	+	+	–	+	+	
pHA invasion	–	–	–	+	–	–	–	–	–	–	–	

CRM, circumferential resection margin; dediff, dedifferentiated; LN, lymph node; R, resection status; PDAC, pancreatic ductal adenocarcinoma; pHA invasion, pathohistological hepatic artery tumour invasion; pPV invasion, pathohistological portal vein/superior mesenteric vein tumour invasion

factor influencing the decision process. Several trials revealed that in the early postoperative course (between 14 days and 1 month), QoL is significantly impaired [4, 5]. Recovery of QoL and recovery of preoperative values are seen after 3 to 6 months [5, 20], which should be taken into consideration. The patients should be informed that only a subselection may significantly benefit from an ultra-radical treatment approach for pancreatic cancer. Unfortunately, routine data on the pre- and postoperative QoL of the patients were not available for the present analysis.

The present study and its conclusions are limited because of the retrospective design and the small cohort size. Further, the heterogeneity of our patients limits the generalizability of the conclusions. Especially the combination of TP with, for example, pylorus-preserving resections might distort the results significantly.

Conclusion

In conclusion, we present the results on the technique of mesocaval shunting during pancreatic surgery for locally advanced pancreatic cancer. So far, the literature on this technique with additional information on the postoperative course is rare, and there is only one other report with no long-term outcome [17]. With the present results, we open the discussion on a very sophisticated, highly demanding surgical approach for selected patients with pancreatic cancer. Nevertheless, this technique can be used as a rescue manoeuvre for intraoperative complications during standard pancreatic resection.

Author's Contributions Study conception and design: TW, MD, and JW. Acquisition of data: FO, BM, and CK. Analysis and interpretation of data: FO, BM, CK, TW, MD, and JW. Drafting of the manuscript: FO, BM, CK, TW, MD, and JW. Critical revision of the manuscript: TW, MD, and JW.

Compliance with ethical standards

Conflict of interest The authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria, educational grants, participation in speakers' bureaus, membership, employment, consultancies, stock ownership, or other equity interest, and expert testimony or patent-licencing arrangements) or non-financial interest (such as personal or professional relationships, affiliations, knowledge, or beliefs) in the subject matter or materials discussed in this manuscript.

Human and animal rights and informed consent All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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