

Postoperative Outcomes of Tangential *versus* Segmental Resection and End-to-end Reconstruction of the Superior Mesenterico-Portal Vein During Pancreatoduodenectomy for Pancreatic Adenocarcinoma: A Single-Center Experience

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Abstract. *Background/Aim:* The impact of venous resections and reconstruction techniques on morbidity after surgery for pancreatic cancer (PDAC) remains controversial. *Patients and Methods:* A total of 143 patients receiving pancreatoduodenectomy (PD) for PDAC between 2013 and 2018 were identified from a prospective database. Morbidity and mortality after PD with tangential resection versus end-to-end reconstruction were assessed. *Results:* Fifty-two of 143 (36.4%) patients underwent PD with portal venous resection (PVR), which was associated with longer operation times [398 (standard error (SE) 12.01) vs. 306 (SE 13.09) min, $p < 0.001$]. PVR was associated with longer intensive-care-unit stay (6.3 vs. 3.8 days, $p = 0.054$); morbidity (Clavien-Dindo classification (CDC) grade IIIa-V 45.8% vs. 35.8%, $p = 0.279$) and 30-day mortality (4.1% vs. 4.2%, $p > 0.99$) were not different. Tangential venous resection was associated with similar CDC grade IIIa-IV (42.9% vs.

50.0%, $p = 0.781$) and 30-day mortality rates (3.5% vs. 4.1%, $p = 0.538$) as segmental resection and end-to-end venous reconstruction. *Conclusion:* Both tangential and segmental PVR appear feasible and can be safely performed to achieve negative resection margins.

Pancreatic ductal adenocarcinoma (PDAC) is one of the most aggressive gastrointestinal tumors and associated with dismal prognosis. PDAC is expected to be in the top three causes of cancer-related deaths by 2030 (1-4). Five-year overall survival rates are as low as 6% for all PDAC patients (5). Surgical resection remains the only curative treatment, and tumors of the pancreatic head undergo pancreatoduodenectomy (PD) (1-3). About 20% of patients with PDAC are unresectable at the time of initial diagnosis presenting with distant metastasis or major arterial involvement (1, 2). While arterial resections during PD are associated with increased morbidity and mortality (3), resection of the superior mesenterico-portal vein (SMPV) has become a standard procedure (4). The guidelines of the National Comprehensive Cancer Network (NCCN) define involvement of the SMPV as borderline resectable PDAC if safe reconstruction is deemed feasible (5-7). Large studies of PD for PDAC reported PVR rates of about 30% (2, 3). Although PVR is increasingly considered a standard procedure at "high-volume" centers of pancreatic surgery, heterogeneous results have been reported regarding perioperative morbidity and mortality (4, 8) as well as long-term outcomes (4, 9-12). Venous resections can be performed as tangential or segmental resections with end-to-end

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reconstruction. The impact of the venous resection technique on postoperative outcomes is controversial.

The aim of this study was to analyze postoperative morbidity and mortality after PD with PVR for PDAC and to evaluate the impact of PVR technique (tangential *versus* segmental resection and end-to-end reconstruction).

Patients and Methods

Patients, operations and standard postoperative care. The study was approved by the ethics committee of the University of Luebeck (#17-118A). All patients underwent pancreatic surgery for pancreatic head cancer at the Department of Surgery, University Hospital Schleswig-Holstein, Campus Lübeck between 2013 and 2018. Patients received a pylorus-preserving PD and a reconstruction with pancreatogastrostomy (PG) or pancreatojejunostomy (PJ). No neoadjuvant therapy was performed. Arterial resections were excluded from the study. Further exclusion factor was distant metastasis. PVR was performed in case of tumor adherence or suspected invasion of the SMPV. Borderline resectability was defined by the NCCN 1.2020 version. Briefly, borderline resectability criteria included tumors involving more than 180° of the circumferences of the superior mesenteric artery (AMS) or celiac trunk and tumors in contact with the inferior vena cava (IVC). Total portal vein occlusion was considered a contraindication for resection. Decisions to perform PVR were made by the surgical team based on preoperative imaging as well as intraoperative tumor-vein adhesion. Vascular prostheses or vein grafts were used if a Cattle Braasch maneuver was not sufficient to bridge the resected segment of the vein. Further intraoperative parameters were operation time and pancreatic texture evaluated by the surgeon (hard *versus* soft).

PVR was performed as either tangential or segmental resection. After tangential resection, the SMPV was reconstructed by running suture with prolene 5-0. Segmental resection was followed by end-to-end reconstruction with running sutures with prolene 5-0. To facilitate reconstruction, a Cattle Braasch maneuver is routinely performed mobilizing the liver ligaments to allow for safe reconstruction of the PV. Homologous grafts were used in two cases. During PD a standardized lymphadenectomy is carried out. This involves lymph node sampling along the hepatoduodenal ligament, common hepatic artery, portal and superior mesenteric vein and along the right aspect of the superior mesenteric artery. Two soft silicon drains were placed near the pancreatic anastomosis and routinely removed on day 5 when no postoperative pancreatic fistula (POPF) occurred. Two additional drains were placed next to the hepaticojejunostomy. Partial thromboplastin time (PTT) guided anticoagulation (PTT: 40-50 s) was measured for 5 days after PVR. All patients received subcutaneous prophylactic low-dose heparin therapy.

Pancreas-specific postoperative complications, such as postoperative pancreatic fistula (POPF), delayed gastric emptying (DGE) and post-pancreatectomy hemorrhage (PPH) were described according to the International Study Group of Pancreatic Surgery (ISGPS) definition (13-15). Severity of all surgical postoperative complications were classified according to the Clavien-Dindo classification (CDC) (10).

Specimen workup and histopathologic parameters. The following baseline parameters were included in the statistical analysis: Age,

gender, body mass index (BMI), American Society of Anesthesiologists (ASA), weight loss, diabetes mellitus, preoperative jaundice, pancreatic texture. Histopathological parameters were T stage, N stage, the lymph node ratio (LNR), tumor grading (G) and resection margin status (R status). All tissue samples were histologically examined for tumor cell presence at the resection margins. Each resection margin was considered separately. R status was evaluated according to the UICC/AJCC criteria (conventional R status) as R0 if no tumor cells were detected at the resection margin, *versus* R+ if tumor cells were present at the resection margin. TNM staging was performed according to the 8th edition of the American Joint Committee on Cancer (AJCC) (16). Primary tumor stage was dichotomized as T1-2 *vs.* T3-4, nodal stage as N0 *vs.* N+, LNR according to the median LNR value, and tumor grading as G1-2 *vs.* G3-4. In case of portal vein resection, the portal vein labeled by the surgeon was embedded in relation to the tumor and its resection margins allowing detailed pathological workup of the complete contact surface between the pancreatic tumor and the vein. Histopathological tumor cell invasion to the portal vein (PVI) was defined as the presence of tumor cells in the vascular tunica media (smooth muscle) or intima. In order to analyze the postoperative course, the following parameters were assessed: Operation time, overall hospital stay, re-operations, postoperative complications according to CDC, occurrence of postoperative pancreatic fistula (POPF), postpancreatectomy hemorrhage (PPH), delayed gastric emptying (DGE), intraabdominal abscess, anastomotic leaks of the biliodigestive anastomosis and gastroenteric anastomosis, surgical site infections, burst abdomen and ICU stay. POPF, PPH and DGE were dichotomized as grade 0 and A *versus* clinically relevant grade B and C complications according to the ISGPS Guidelines (13, 14, 15). Overall survival was defined from the day of surgery until death.

Statistical analysis. Data analysis was performed using IBM SPSS Statistics for Windows, Version 25.0 (developer: IBM, Chicago, Illinois, United States). Scale variables were expressed as median and range, categorical parameters as absolute count and percentage. Dichotomized independent variables were examined by Chi-squared tests and metrical variables by *t*-tests. Overall survival analyses were performed with Kaplan-Meier method and Cox proportional hazard model. Statistical significance was set to $p < 0.05$ (two-sided). All confidence intervals (CI) evaluated are 95% confidence intervals.

Results

Baseline parameters. A total of 143 patients underwent PD for PDAC from 2013 to 2018. Fifty-two patients (36.4%) had a venous resection. Eighty (55.9 %) patients were male and 63 (44.1 %) were female. The median age was 68 years, ranging from 41 to 85. The median body mass index (BMI) was 30 kg/m². Thirty-six (25.2%) patients had a history of weight loss, 21 (14.7%) presented with preoperative jaundice and 41 (28.7%) had diabetes mellitus.

Histopathology. A total of 113 (86.3%) patients presented with stage T3/T4 tumors, and 85 (59.4%) had positive lymph nodes with a median lymph node ratio (LNR) of 0.3. Tumor

Table I. Baseline, histopathology and postoperative course.

Parameter	Condition	n or median	% or range/SE
		n	143
Demography and operations			
Age	68	41-85	
Gender	Female	63	44.1%
	Male	80	55.9%
BMI	<30 kg/m ²	122	85.3%
	>30 kg/m ²	21	14.7%
ASA	I-II	65	45.5%
	III-IV	78	54.5%
Weight loss	No	107	74.8%
	Yes	36	25.2%
Diabetes mellitus	No	102	71.3%
	Yes	41	28.7%
Preoperative Jaundice	No	122	85.3%
	Yes	21	14.7%
Pancreatic Texture	Hard	79	61.7%
	Soft	49	38.3%
Histopathology			
T stage	T1/2	18	13.7%
	T3/4	113	86.3%
N Stage	N0	58	40.6%
	N+	85	59.4%
LNR		0.3	0.0-1.0
Tumor Grading	G1/2	107	74.8%
	G3/4	36	25.2%
R Status	R0	95	66.4%
	R+	48	33.6%
Postoperative course			
Operation time		340	11.45
ICU stay		4.5	1.23
OHS		20.8	5-53
Reoperation		32	22.4%
Clavien-Dindo Classification	0-II	87	60.8%
	IIIa-IV	56	39.2%
CDC V		6	4.2%

BMI: Body mass index; ASA: American Society of Anesthesiologist classification; T stage: tumor stage; LNR: lymph node ratio; ICU: intensive care unit; OHS: overall hospital stay; CDC: Clavien-Dindo classification; SE: standard error.

grade G1/2 was found in 107 (74.8%) patients. Forty-eight patients (33.6%) had positive resection margins (Table I).

Postoperative parameter. The median operation time was 340 min (SE=11.45). Thirty-two (22.4%) patients had a reoperation. Median intensive care unit stay (ICU) was 4.5 days (standard error (SE) 1.243) and median overall hospital stay (OHS) was 20.8 days (SE 2.278). Eighty-seven (60.8%)

patients developed mild postoperative complications according to CDC I-II and 56 (39.2%) patients had serious complications (CDC IIIa-IV). 30-day mortality in all patients was 4.2%.

Morbidity and mortality of patients with and without PVR. In a total of 143 patients, 52 patients (36.4%) underwent PVR and 91 patients (63.6%) did not. Although PD with PVR was associated with longer operation times (median 398 (SE 12.01) vs. 306 (SE 13.09), $p<0.001$) than in patients without PVR, there was no difference in surgical morbidity (CDC grade IIIa-V 45.8% vs. 35.8%, $p=0.279$) as well as 30-day mortality rates (4.1% vs. 4.2%, $p>0.999$) (Table II).

The incidence of pancreas-specific postoperative complications was equivalent for both patients with and without PVR. Patients with PVR had a similar rate of clinically relevant POPF grade B/C (8.3% vs. 10.5%, $p=0.774$), PPH grade B/C (10.4% vs. 15.8%; $p=0.453$), DGE grade B/C (14.6% vs. 10.5%, $p=0.585$), surgical site infection (SSI) (18.8% vs. 14.9%, $p=0.632$), re-operation (20.8% vs. 23.2%, $p=0.834$), as well as intrabdominal abscesses (8.3% vs. 8.4%, $p>0.999$) and anastomotic leaks of the gastro-enteric and biliodigestive anastomosis (2.1% vs. 2.1%, $p>0.999$ and 4.2% vs. 7.4%, $p=0.718$). In patients with PVR, ICU stay was prolonged (median 6.3 vs. 3.8 days, $p=0.054$) but length of overall hospital stay (OHS) (20 days vs. 18 days; $p=0.542$) was comparable to patients without PVR. No mesenteric vein thrombosis, portal hypertension or bleeding were observed in relation to portal vein resection. 30-day mortality was 4.1% (2.1% surgical mortality) in patients with PVR and 4.2% in patients without PVR ($p>0.999$).

Morbidity and mortality of patients with PVR depending on the type of resection. Fifty-two patients after PD with PVR for PDAC were divided into two groups with regard to type of portal vein reconstruction: 28 (53.8%) patients received tangential resection and 24 (46.2%) patients underwent segmental PVR with end-to-end anastomosis. There was no difference in operation time between PD with tangential resection associated with a median operation time of 378 min and segmental PVR and end-to-end reconstruction with an operation time of a median of 426 min ($p=0.162$). The incidences of pancreas-specific postoperative complications such as clinically relevant POPF (grade B/C), PPH B/C, DGE B/C and other surgical complications (intrabdominal abscess, anastomotic leaks, SSI, burst abdomen) were similar in both resection groups (Table III). Postoperative OHS, reoperation rate as well as severe postoperative complications (CDC IIIa-V) were similar for both groups. Type of venous reconstruction had no impact on 30-day mortality rates (tangential resection 3.5% vs. segmental resection 4.1%, $p=0.538$). The tangential resection group

Table II. Postoperative complications by patients with and without portal vein resection.

Parameter condition	Total		No PVR		PVR		p-Value	
	n or median	%/range/SE	n or median	%/range/SE	n or median	%/range/SE		
n	143		91 (63.6%)		52 (36.4%)			
Operation time	340	11.45	306	13.09	398	12.01	0.001	
Perioperative complications								
CDC	0-II	87	60.8%	58	64.2%	29	54.2%	0.279
	IIIa-V	56	39.2%	33	35.8%	23	45.8%	
POPF	no/BL	129	90.2%	81	89.5%	48	91.7%	0.774
	B/C	14	9.8%	10	10.5%	4	8.3%	
PPH	0/A	123	86.0%	77	84.2%	46	89.6%	0.453
	B/C	20	14.0%	14	15.8%	6	10.4%	
DGE	0/A	126	88.1%	81	89.5%	45	85.4%	0.585
	B/C	17	11.9%	10	10.5%	7	14.6%	
Intraabdominal abscess		12	8.4%	8	8.4%	4	8.3%	>0.999
BDA Leak		9	6.3%	7	7.4%	2	4.2%	0.718
GE Leak		3	2.1%	2	2.1%	1	2.1%	>0.999
SSI		23	16.2%	14	14.9%	9	18.8%	0.632
Burst Abdomen		8	5.6%	4	4.2%	4	8.3%	0.442
Re-op		32	22.4%	22	23.2%	10	20.8%	0.834
Other		23	16.1%	15	15.8%	8	16.7%	>0.999
ICU stay		4.5	1.243	3.8	1.369	6.3	1.531	0.054
OHS		20.8	2.278	18	2.320	20	2.250	0.542
CDC V		6	4.2%	4	4.2%	2	4.1%	>0.999

CDC: Clavien-Dindo classification; POPF: postoperative pancreatic fistula; PPH: postpancreatectomy hemorrhage; DGE: delayed gastric emptying; BDA: biliodigestive anastomosis; GE: gastro-entero anastomosis; SSI: surgical site infection; Re-op: reoperation; ICU: intensive care unit; OHS: overall hospital stay; SE: standard error. Significant p-Values are shown in bold.

showed prolonged ICU stay in comparison with the segmental PVR group (median 7.9 vs. 5.8 days; $p=0.012$). The median overall survival for all PVR patients was 21.5 months. There was no difference in overall survival when comparing tangential resection to segmental PVR (20.2 vs. 23.4 months, $p=0.786$).

Discussion

Complete surgical resection is the only curative option in pancreatic cancer (PDAC), and the main goal of pancreatic surgery is to achieve negative resection margins (R0) (17, 18). R status remains one of the most important prognostic factors in PDAC and should be aimed for whenever feasible (19). Over the past decades, radical oncological surgery for PDAC has become possible, and postoperative mortality decreased due to advanced postoperative care and ICU management (8). As a result of improvements in operation technique and perioperative care as well as centralization of procedures at high-volume centers, postoperative mortality has decreased to less than 5% in recent studies (20-24). Despite a considerable reduction of postoperative mortality, postoperative morbidity remains high, ranging from 30 to

60% (25-28). The main contributors to high postoperative morbidity are the occurrence of postoperative pancreatic fistula (POPF) and further pancreas-specific complications (29-31).

PDAC is characterized by early loco-regional spread and besides lympho-vascular and perineural invasion local tumor involvement of the SMPV is common in PDAC. Over the past years, PVR has become a feasible option to achieve complete oncological resection. PDAC tumors with adhesion, abutment or encasement of the SMPV are considered borderline resectable (32, 33). While resection is technically possible, these patients are at increased risk of margin positive resection as compared to PDAC patients without any tumor-vessel contact. Besides a higher risk of incomplete resection in PVR patients, the impact of these resections on postoperative morbidity and mortality are controversially discussed. PVR remains a high-risk procedure associated with potential hemorrhagic or thrombotic complications that require expertise in vascular surgery, specialized perioperative care and close postoperative monitoring at high volume centers. Over the past years, the rate of PD with PVR for PDAC is as high as 30% at specialized high-volume centers (8, 9, 34).

Table III. Postoperative complications depending on the type of portal vein resection.

Parameter condition	Total		Tangential PVR		End-to-end PVR		p-Value	
	n or median	% or range/SE	n or median	% or range/SE	n or median	% or range/SE		
n	52		28 (53.8%)		24 (46.2%)			
Operation time	398	12.01	378	13.1	426	14.2	0.162	
Perioperative complications								
CDC	0-II	28	53.8%	16	57.1%	12	50.0%	0.781
	IIIa-V	24	46.2%	12	42.9%	12	50.0%	
POPF	no/BL	47	90.4%	24	85.7%	23	95.8%	0.358
	B/C	5	9.6%	4	14.3%	1	4.2%	
PPH	0/A	45	86.5%	23	82.1%	22	91.7%	0.430
	B/C	7	13.5%	5	17.9%	2	8.3%	
DGE	0/A	44	84.6%	22	78.6%	22	91.7%	0.262
	B/C	8	15.4%	6	21.4%	2	8.3%	
Intraabdominal abscess		5	9.6%	3	10.7%	2	8.3%	>0.999
BDA Leak		3	5.8%	2	7.1%	1	4.2%	>0.999
GE Leak		2	3.8%	2	7.1%	0	0.0%	0.493
SSI		10	19.2%	4	14.3%	6	25.0%	0.483
Burst Abdomen		5	9.6%	3	10.7%	2	8.3%	>0.999
Re-op		12	23.1%	6	21.4%	6	25.0%	>0.999
Other		9	17.3%	4	14.3%	5	20.8%	0.716
ICU stay		6.7	2.095	7.9	2.095	5.8	2.095	0.012
OHS		20.7	4.173	20.6	4.203	20.8	4.143	0.727
CDC V		2	4.1	1	3.5%	1	4.1%	0.538

CDC: Clavien-Dindo classification; POPF: postoperative pancreatic fistula; PPH: postpancreatectomy hemorrhage; DGE: delayed gastric emptying; BDA: biliodigestive anastomosis; GE: gastro-entero anastomosis; SSI: surgical site infection; Re-op: reoperation; ICU: intensive care unit; OHS: overall hospital stay; SE: standard error. Significant *p*-Values are shown in bold.

The current study conducted at a high-volume center specialized in pancreatic surgery demonstrated that PVR is not associated with higher postoperative morbidity or 30-day mortality as compared to PD without PVR. Despite equivalent postoperative complication rates, PVR patients had a prolonged ICU stay mirroring a standard protocol of close postoperative surveillance after a potentially high-risk vascular surgery procedure. Equivalent postoperative outcomes of patients with and without PVR were confirmed in other large cohort studies. The American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) gathered patient data from 43 USA institutions and reported that pancreatic surgery involving vascular resection has similar overall morbidity and mortality rates as the standard procedure (35). Siriwardana *et al.* reviewed a total of 6,333 patients and reported that 1,646 (26%) of them underwent PV/SMV resection with a postoperative morbidity rate of 42% and postoperative mortality of 5.9% as compared to 5.2% in non-PVR patients (36). Zettervall *et al.* could not detect an increase in postoperative mortality or morbidity in patients with PVR as compared to those without PVR (37). Callejas *et al.* also failed to find an association between resections of the portal

vein, the superior mesenteric vein or the venous confluents and patient morbidity (38). Ramacciato *et al.* reported that the use of preoperative biliary drainage was related to postoperative morbidity but PVR was not (39).

While the majority of current studies show no increase in postoperative morbidity or mortality following PVR, long-term overall survival rates of PVR patients are still subject to debate. In the current study, median overall survival rates of PVR patients were non-inferior to patients without PVR. While several studies confirm equivalent overall survival rates in PVR and non-PVR patients (4, 40, 41), other studies show worse prognosis after PVR (42, 43). It was recently demonstrated that the subgroup of PVR patients who show definite histo-pathological invasion of the SMPV experience reduced overall survival rates as compared to those with mere tumor-vein adhesions (9, 44). A recent study from our group demonstrated features of more aggressive tumor biology leading to loco-regional tumor spread in patients with actual tumor invasion to the SMPV wall (45).

Comparative studies on postoperative outcome in different types of SMPV resections are still lacking. The current study found no difference in postoperative morbidity and mortality following tangential *versus* segmental PVR.

Grafts were rarely used for end-to-end reconstruction in this cohort, instead, extensive mobilization of the venous ends was achieved by Cattle-Braasch maneuvers. Graft interposition may increase the risk of thrombosis (46), and the Cattle-Braasch maneuver can bridge a segmental resection of up to 10 cm. Other studies confirm equivalent outcomes in patients with tangential *versus* segmental PVR. Tseng *et al.* reported on 141 patients who underwent venous reconstruction at the time of pancreaticoduodenectomy. PVR included tangential resection with vein patch (n=36), segmental resection with primary anastomosis (n=35), and segmental resection with autologous interposition graft (n=55). Postoperative morbidity and long-term outcomes were similar in all three subgroups. Serenari *et al.* performed a study in 99 patients with PD comparing outcomes of tangential *versus* segmental PVR (47). The authors could not find differences in terms of CDC complications grade IIIA or higher or 30-day and 90-day postoperative mortality.

A limitation of this study is its retrospective nature with the potential for selection and reporting bias. Because patient data were derived from a prospectively maintained database, the limitations of a retrospective study are reduced but cannot be completely eliminated. Furthermore, patients in this cohort did not receive neoadjuvant therapy. Neoadjuvant therapy can achieve a downstaging in borderline resectable tumors and thus improve resectability and reduce the rates of portal vein resections (48). Future studies are warranted to determine postoperative outcomes of PD with PVR following neoadjuvant treatment.

In summary, we present a large single-center cohort study of patients with PD and PVR for PDAC. PD with PVR was associated with prolonged operation time and ICU stay but not with higher postoperative morbidity and 30-day mortality as compared to patients not undergoing PVR. Both tangential and segmental PVR are feasible procedures and can be safely performed to achieve negative resection margins.

Conflicts of Interest

The Authors have no conflicts of interest related to this study.

Authors' Contributions

H.L., T.S., U.F.W. and L.B. participated in the design of the study. N.P., E.P., K.H., R.B., S.D. and D.R. provided data that were analyzed by T.S. and L.B. H.L., T.S., N.P., B.K., J.H., T.K., D.B. and L.B. drafted the article, which was reviewed and finally approved by all Authors.

References

- Hidalgo M: Pancreatic cancer. *N Engl J Med* 362(17): 1605-1617, 2010. PMID: 20427809. DOI: 10.1056/NEJMra0901557
- Zhou B, Xu JW, Cheng YG, Gao JY, Hu SY, Wang L and Zhan HX: Early detection of pancreatic cancer: Where are we now and where are we going? *Int J Cancer* 141(2): 231-241, 2017. PMID: 28240774. DOI: 10.1002/ijc.30670
- Mollberg N, Rahbari NN, Koch M, Hartwig W, Hoeger Y, Büchler MW and Weitz J: Arterial resection during pancreatotomy for pancreatic cancer: a systematic review and meta-analysis. *Ann Surg* 254(6): 882-893, 2011. PMID: 22064622. DOI: 10.1097/SLA.0b013e31823ac299
- Lapshyn H, Bolm L, Kohler I, Werner M, Billmann FG, Bausch D, Hopt UT, Makowiec F, Wittel UA, Keck T, Bronsert P and Wellner UF: Histopathological tumor invasion of the mesenterico-portal vein is characterized by aggressive biology and stromal fibroblast activation. *HPB (Oxford)* 19(1): 67-74, 2017. PMID: 27825542. DOI: 10.1016/j.hpb.2016.10.002
- Toomey P, Hernandez J, Morton C, Duce L, Farrior T, Villadolid D, Ross S and Rosemurgy A: Resection of portovenous structures to obtain microscopically negative margins during pancreaticoduodenectomy for pancreatic adenocarcinoma is worthwhile. *Am Surg* 75(9): 804-9; discussion 809-10, 2009. PMID: 19774952. DOI: 10.1177/000313480907500911
- Kato K, Yamada S, Sugimoto H, Kanazumi N, Nomoto S, Takeda S, Kodera Y, Morita S and Nakao A: Prognostic factors for survival after extended pancreatotomy for pancreatic head cancer: influence of resection margin status on survival. *Pancreas* 38(6): 605-612, 2009. PMID: 19629002. DOI: 10.1097/MPA.0b013e3181a4891d
- Tseng JF, Raut CP, Lee JE, Pisters PW, Vauthey JN, Abdalla EK, Gomez HF, Sun CC, Crane CH, Wolff RA and Evans DB: Pancreaticoduodenectomy with vascular resection: margin status and survival duration. *J Gastrointest Surg* 8(8): 935-49; discussion 949-50, 2004. PMID: 15585381. DOI: 10.1016/j.gassur.2004.09.046
- Riediger H, Makowiec F, Fischer E, Adam U and Hopt UT: Postoperative morbidity and long-term survival after pancreaticoduodenectomy with superior mesenterico-portal vein resection. *J Gastrointest Surg* 10(8): 1106-1115, 2006. PMID: 16966029. DOI: 10.1016/j.gassur.2006.04.002
- Lapshyn H, Bronsert P, Bolm L, Werner M, Hopt UT, Makowiec F, Wittel UA, Keck T, Wellner UF and Bausch D: Prognostic factors after pancreatoduodenectomy with en bloc portal venous resection for pancreatic cancer. *Langenbecks Arch Surg* 401(1): 63-69, 2016. PMID: 26739620. DOI: 10.1007/s00423-015-1363-2
- Dindo D, Demartines N and Clavien PA: Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg* 240(2): 205-213, 2004. PMID: 15273542. DOI: 10.1097/01.sla.0000133083.54934.ae
- MOORE GE, SAKO Y and THOMAS LB: Radical pancreatoduodenectomy with resection and reanastomosis of the superior mesenteric vein. *Surgery* 30(3): 550-553, 1951. PMID: 14866700.
- Fortner JG: Regional resection of cancer of the pancreas: a new surgical approach. *Surgery* 73(2): 307-320, 1973. PMID: 4265314.
- Bassi C, Marchegiani G, Dervenis C, Sarr M, Abu Hilal M, Adham M, Allen P, Andersson R, Asbun HJ, Besselink MG, Conlon K, Del Chiaro M, Falconi M, Fernandez-Cruz L, Fernandez-Del Castillo C, Fingerhut A, Friess H, Gouma DJ,

- Hackert T, Izbicki J, Lillemoe KD, Neoptolemos JP, Olah A, Schulick R, Shrikhande SV, Takada T, Takaori K, Traverso W, Vollmer CR, Wolfgang CL, Yeo CJ, Salvia R, Buchler M and International Study Group on Pancreatic Surgery (ISGPS): The 2016 update of the International Study Group (ISGPS) definition and grading of postoperative pancreatic fistula: 11 Years After. *Surgery* 161(3): 584-591, 2017. PMID: 28040257. DOI: 10.1016/j.surg.2016.11.014
- 14 Wente MN, Bassi C, Dervenis C, Fingerhut A, Gouma DJ, Izbicki JR, Neoptolemos JP, Padbury RT, Sarr MG, Traverso LW, Yeo CJ and Büchler MW: Delayed gastric emptying (DGE) after pancreatic surgery: a suggested definition by the International Study Group of Pancreatic Surgery (ISGPS). *Surgery* 142(5): 761-768, 2007. PMID: 17981197. DOI: 10.1016/j.surg.2007.05.005
- 15 Wente MN, Veit JA, Bassi C, Dervenis C, Fingerhut A, Gouma DJ, Izbicki JR, Neoptolemos JP, Padbury RT, Sarr MG, Yeo CJ and Büchler MW: Postpancreatectomy hemorrhage (PPH): an International Study Group of Pancreatic Surgery (ISGPS) definition. *Surgery* 142(1): 20-25, 2007. PMID: 17629996. DOI: 10.1016/j.surg.2007.02.001
- 16 Kamarajah SK, Burns WR, Frankel TL, Cho CS and Nathan H: Validation of the American Joint Commission on Cancer (AJCC) 8th edition staging system for patients with pancreatic adenocarcinoma: a surveillance, epidemiology and end results (SEER) analysis. *Ann Surg Oncol* 24(7): 2023-2030, 2017. PMID: 28213792. DOI: 10.1245/s10434-017-5810-x
- 17 Lillemoe KD, Yeo CJ and Cameron JL: Pancreatic cancer: state-of-the-art care. *CA Cancer J Clin* 50(4): 241-268, 2000. PMID: 10986966. DOI: 10.3322/canjclin.50.4.241
- 18 Bell R, Ao BT, Ironside N, Bartlett A, Windsor JA and Pandanaboyana S: Meta-analysis and cost effective analysis of portal-superior mesenteric vein resection during pancreatoduodenectomy: Impact on margin status and survival. *Surg Oncol* 26(1): 53-62, 2017. PMID: 28317585. DOI: 10.1016/j.suronc.2016.12.007
- 19 Butturini G, Stocken DD, Wente MN, Jeekel H, Klinkenbijl JH, Bakkevold KE, Takada T, Amano H, Dervenis C, Bassi C, Büchler MW, Neoptolemos JP and Pancreatic Cancer Meta-Analysis Group: Influence of resection margins and treatment on survival in patients with pancreatic cancer: meta-analysis of randomized controlled trials. *Arch Surg* 143(1): 75-83; discussion 83, 2008. PMID: 18209156. DOI: 10.1001/archsurg.2007.17
- 20 Merath K, Mehta R, Tsilimigras DI, Farooq A, Sahara K, Paredes AZ, Wu L, Ejaz A and Pawlik TM: In-hospital mortality following pancreatoduodenectomy: a comprehensive analysis. *J Gastrointest Surg* 24(5): 1119-1126, 2020. PMID: 31292889. DOI: 10.1007/s11605-019-04307-9
- 21 de Wilde RF, Besselink MG, van der Tweel I, de Hingh IH, van Eijck CH, Dejong CH, Porte RJ, Gouma DJ, Busch OR, Molenaar IQ and Dutch Pancreatic Cancer Group: Impact of nationwide centralization of pancreatoduodenectomy on hospital mortality. *Br J Surg* 99(3): 404-410, 2012. PMID: 22237731. DOI: 10.1002/bjs.8664
- 22 McPhee JT, Hill JS, Whalen GF, Zayaruzny M, Litwin DE, Sullivan ME, Anderson FA and Tseng JF: Perioperative mortality for pancreatotomy: a national perspective. *Ann Surg* 246(2): 246-253, 2007. PMID: 17667503. DOI: 10.1097/01.sla.0000259993.17350.3a
- 23 Gleeson EM, Shaikh MF, Shewokis PA, Clarke JR, Meyers WC, Pitt HA and Bowne WB: WHipple-ABACUS, a simple, validated risk score for 30-day mortality after pancreatoduodenectomy developed using the ACS-NSQIP database. *Surgery* 160(5): 1279-1287, 2016. PMID: 27544541. DOI: 10.1016/j.surg.2016.06.040
- 24 Castleberry AW, White RR, De La Fuente SG, Clary BM, Blazer DG 3rd, McCann RL, Pappas TN, Tyler DS and Scarborough JE: The impact of vascular resection on early postoperative outcomes after pancreatoduodenectomy: an analysis of the American College of Surgeons National Surgical Quality Improvement Program database. *Ann Surg Oncol* 19(13): 4068-4077, 2012. PMID: 22932857. DOI: 10.1245/s10434-012-2585-y
- 25 Ding J, Zhang C, Huang D and Zhang Y: The state of minimally invasive pancreatoduodenectomy in Chinese mainland: A systematic literature review. *Biosci Trends* 13(6): 488-501, 2020. PMID: 31875583. DOI: 10.5582/bst.2019.01278
- 26 Boggi U, Amorese G, Vistoli F, Caniglia F, De Lio N, Perrone V, Barbarello L, Belluomini M, Signori S and Mosca F: Laparoscopic pancreatoduodenectomy: a systematic literature review. *Surg Endosc* 29(1): 9-23, 2015. PMID: 25125092. DOI: 10.1007/s00464-014-3670-z
- 27 Corcione F, Pirozzi F, Cuccurullo D, Piccolboni D, Caracino V, Galante F, Cusano D and Sciuto A: Laparoscopic pancreatoduodenectomy: experience of 22 cases. *Surg Endosc* 27(6): 2131-2136, 2013. PMID: 23355144. DOI: 10.1007/s00464-012-2728-z
- 28 Winter JM, Cameron JL, Campbell KA, Arnold MA, Chang DC, Coleman J, Hodgins MB, Sauter PK, Hruban RH, Riall TS, Schulick RD, Choti MA, Lillemoe KD and Yeo CJ: 1423 pancreatoduodenectomies for pancreatic cancer: A single-institution experience. *J Gastrointest Surg* 10(9): 1199-210; discussion 1210-1, 2006. PMID: 17114007. DOI: 10.1016/j.gassur.2006.08.018
- 29 Chen JS, Liu G, Li TR, Chen JY, Xu QM, Guo YZ, Li M and Yang L: Pancreatic fistula after pancreatoduodenectomy: Risk factors and preventive strategies. *J Cancer Res Ther* 15(4): 857-863, 2019. PMID: 31436243. DOI: 10.4103/jcrt.JCRT_364_18
- 30 Nahm CB, Connor SJ, Samra JS and Mittal A: Postoperative pancreatic fistula: a review of traditional and emerging concepts. *Clin Exp Gastroenterol* 11: 105-118, 2018. PMID: 29588609. DOI: 10.2147/CEG.S120217
- 31 Lapshyn H, Petruch N, Thomaschewski M, Sondermann S, May K, Frohneberg L, Petrova E, Zemskov S, Honselmann KC, Braun R, Keck T, Wellner UF and Bolm L: A simple preoperative stratification tool predicting the risk of postoperative pancreatic fistula after pancreatoduodenectomy. *Pancreatol* 21(5): 957-964, 2021. PMID: 33775565. DOI: 10.1016/j.pan.2021.03.009
- 32 Tempero MA, Malafa MP, Chiorean EG, Czito B, Scaife C, Narang AK, Fountzilias C, Wolpin BM, Al-Hawary M, Asbun H, Behrman SW, Benson AB, Binder E, Cardin DB, Cha C, Chung V, Dillhoff M, Dotan E, Ferrone CR, Fisher G, Hardacre J, Hawkins WG, Ko AH, LoConte N, Lowy AM, Moravek C, Nakamura EK, O'Reilly EM, Obando J, Reddy S, Thayer S, Wolff RA, Burns JL and Zuccarino-Catania G: Pancreatic adenocarcinoma, Version 1.2019. *J Natl Compr Canc Netw* 17(3): 202-210, 2019. PMID: 30865919. DOI: 10.6004/jnccn.2019.0014
- 33 Bockhorn M, Uzunoglu FG, Adham M, Imrie C, Milicevic M, Sandberg AA, Asbun HJ, Bassi C, Büchler M, Charnley RM,

- Conlon K, Cruz LF, Dervenis C, Fingerhutt A, Friess H, Gouma DJ, Hartwig W, Lillemoie KD, Montorsi M, Neoptolemos JP, Shrikhande SV, Takaori K, Traverso W, Vashist YK, Vollmer C, Yeo CJ, Izbicki JR and International Study Group of Pancreatic Surgery: Borderline resectable pancreatic cancer: a consensus statement by the International Study Group of Pancreatic Surgery (ISGPS). *Surgery* 155(6): 977-988, 2014. PMID: 24856119. DOI: 10.1016/j.surg.2014.02.001
- 34 Murakami Y, Satoi S, Motoi F, Sho M, Kawai M, Matsumoto I, Honda G and Multicentre Study Group of Pancreatobiliary Surgery (MSG-PBS): Portal or superior mesenteric vein resection in pancreatoduodenectomy for pancreatic head carcinoma. *Br J Surg* 102(7): 837-846, 2015. PMID: 25877050. DOI: 10.1002/bjs.9799
- 35 Beane JD, House MG, Pitt SC, Zarzaur B, Kilbane EM, Hall BL, Riall TS and Pitt HA: Pancreatoduodenectomy with venous or arterial resection: a NSQIP propensity score analysis. *HPB (Oxford)* 19(3): 254-263, 2017. PMID: 28038967. DOI: 10.1016/j.hpb.2016.11.013
- 36 Siriwardana HP and Siriwardana AK: Systematic review of outcome of synchronous portal-superior mesenteric vein resection during pancreatectomy for cancer. *Br J Surg* 93(6): 662-673, 2006. PMID: 16703621. DOI: 10.1002/bjs.5368
- 37 Zettervall SL, Ju T, Holzmacher JL, Huysman B, Werba G, Sidawy A, Lin P and Vaziri K: Arterial, but not venous, reconstruction increases 30-day morbidity and mortality in pancreaticoduodenectomy. *J Gastrointest Surg* 24(3): 578-584, 2020. PMID: 30945084. DOI: 10.1007/s11605-019-04211-2
- 38 Callejas GH, Concon MM, Rezende AQM, Chaim EA, Callejas-Neto F and Cazzo E: Pancreatoduodenectomy with venous resection: an analysis of 30-day morbidity and mortality. *Arq Gastroenterol* 56(3): 246-251, 2019. PMID: 31633719. DOI: 10.1590/S0004-2803.201900000-46
- 39 Ramacciato G, Nigri G, Petrucciani N, Pinna AD, Ravaioli M, Jovine E, Minni F, Grazi GL, Chirletti P, Tisone G, Napoli N and Boggi U: Pancreatectomy with mesenteric and portal vein resection for borderline resectable pancreatic cancer: multicenter study of 406 patients. *Ann Surg Oncol* 23(6): 2028-2037, 2016. PMID: 26893222. DOI: 10.1245/s10434-016-5123-5
- 40 Zhang XM, Zhang J, Fan H, He Q and Lang R: Feasibility of portal or superior mesenteric vein resection and reconstruction by allogeneic vein for pancreatic head cancer-a case-control study. *BMC Gastroenterol* 18(1): 49, 2018. PMID: 29661201. DOI: 10.1186/s12876-018-0778-y
- 41 Xie ZB, Li J, Gu JC, Jin C, Zou CF and Fu DL: Pancreatoduodenectomy with portal vein resection favors the survival time of patients with pancreatic ductal adenocarcinoma: A propensity score matching analysis. *Oncol Lett* 18(5): 4563-4572, 2019. PMID: 31611964. DOI: 10.3892/ol.2019.10822
- 42 Okabayashi T, Shima Y, Iwata J, Morita S, Sumiyoshi T, Kozuki A, Saisaka Y, Tokumaru T, Iiyama T, Noda Y, Hata Y and Matsumoto M: Reconsideration about the aggressive surgery for resectable pancreatic cancer: a focus on real pathological portosplenomesenteric venous invasion. *Langenbecks Arch Surg* 400(4): 487-494, 2015. PMID: 25940756. DOI: 10.1007/s00423-015-1305-z
- 43 Rebelo A, Michalski C, Ukkat J and Kleeff J: Pancreatic cancer surgery with vascular resection: current concepts and perspectives. *Journal of Pancreatology* 2(1): 1-5, 2021. DOI: 10.1097/JP9.0000000000000013
- 44 Fukuda S, Oussoultzoglou E, Bachellier P, Rosso E, Nakano H, Audet M and Jaeck D: Significance of the depth of portal vein wall invasion after curative resection for pancreatic adenocarcinoma. *Arch Surg* 142(2): 172-9; discussion 180, 2007. PMID: 17309969. DOI: 10.1001/archsurg.142.2.172
- 45 Lapshyn H, Bolm L, Kohler I, Werner M, Billmann FG, Bausch D, Hopt UT, Makowiec F, Wittel UA, Keck T, Bronsert P and Wellner UF: Histopathological tumor invasion of the mesenterico-portal vein is characterized by aggressive biology and stromal fibroblast activation. *HPB (Oxford)* 19(1): 67-74, 2017. PMID: 27825542. DOI: 10.1016/j.hpb.2016.10.002
- 46 Dua MM, Tran TB, Klausner J, Hwa KJ, Poultsides GA, Norton JA and Visser BC: Pancreatectomy with vein reconstruction: technique matters. *HPB (Oxford)* 17(9): 824-831, 2015. PMID: 26223388. DOI: 10.1111/hpb.12463
- 47 Serenari M, Ercolani G, Cucchetti A, Zanello M, Proserpi E, Fallani G, Masetti M, Lombardi R, Cescon M and Jovine E: The impact of extent of pancreatic and venous resection on survival for patients with pancreatic cancer. *Hepatobiliary Pancreat Dis Int* 18(4): 389-394, 2019. PMID: 31230959. DOI: 10.1016/j.hbpd.2019.06.004
- 48 Kurahara H, Shinchi H, Ohtsuka T, Miyasaka Y, Matsunaga T, Noshiro H, Adachi T, Eguchi S, Imamura N, Nanashima A, Sakamoto K, Nagano H, Ohta M, Inomata M, Chikamoto A, Baba H, Watanabe Y, Nishihara K, Yasunaga M, Okuda K, Natsugoe S and Nakamura M: Significance of neoadjuvant therapy for borderline resectable pancreatic cancer: a multicenter retrospective study. *Langenbecks Arch Surg* 404(2): 167-174, 2019. PMID: 30649607. DOI: 10.1007/s00423-019-01754-5

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