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The Role of Vascular Resection in Pancreatic Cancer Treatment

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Abstract

Currently, porto-mesenteric vein resection is a standard procedure at high-volume pancreatic centers. Experience in vascular surgery is indispensable for a modern pancreatic surgeon. Nowadays, only arterial resections still are a controversial issue. Nevertheless, attempts at resection involving reconstruction of the main arteries such as the coeliac axis, hepatic artery, and superior mesenteric artery (SMA) have been reported, although in small case series. An overview of the historical and contemporary methods for surgical management of superior mesenteric/portal vein involvement as well as arterial involvement by pancreatic cancer is presented. We compare the data from the literature with our data based on the examination and long-term follow-up of more than 300 radical pancreatic resections. Seventy-two of the presented patients underwent pancreatic resection with simultaneous vascular resection—SMPV in 65 cases (44 with resection of the portal vein, 15 with resection of the superior mesenteric vein, 6 with resection of the porto-mesenteric confluence), arterial in 2 and partial resections of IVC in 5 cases. Combined vascular resections were done in three cases. Both groups PVR and PR showed similarly close results in complication rates, mortality, and morbidity. Three and 5 years survival rates were 42 and 38% in PD group and 28 and 19% in the PVR group. The vascular resection must be performed only upon carefully selected patients with data for presence of resectable tumors or tumors with borderline resectability from the preoperative imaging studies. The prompt management of pancreatic cancer with vascular involvement should involve multidisciplinary consultation in high-volume centers.

Keywords: pancreatic cancer, vascular resections, borderline resectability, venous reconstruction

1. Introduction

Nowadays, radical surgical treatment remains the only potentially curative treatment for patients with pancreatic cancer. Radical surgical resection followed by adjuvant chemotherapy can be performed in about 20% of all pancreatic ductal adenocarcinoma (PDAC) patients by the time of diagnosis and quite often is the only chance for long-term survival of the patients, with an average 5-year survival of 20–25% [1, 2]. More than 80 % of them are unresectable at the moment of diagnosis due to invasion of retroperitoneal tissue, portal vein (PV)/superior mesenteric vein (SMV), invasion of mesenteric artery, presence of liver or peritoneal metastases, or inability to sustain major surgical resection. As a result of the development of surgical techniques and technologies, extended operations, including vascular resections, have become more frequently performed in specialized centers [3]. This has led to a significant change in pancreatic surgery and has enlarged the border of resectability and ensured the possibility to achieve a curative surgical approach combined with neoadjuvant and adjuvant treatment strategies in patients with pancreatic cancer. Pancreatic carcinoma is characterized with high biological activity and early involvement of retroperitoneal tissue, lymph nodes, and peripancreatic blood vessels. The majority of pancreatic cancers are diagnosed at an advanced stage. Between 30 and 35% of them are classified as unresectable because of the isolated involvement of superior mesenteric/portal vein (**Figure 1**) [4]. For the first time the idea for resection of the portal vein for the sake of complete removal of the tumor was presented systematically by Fortner [5]. Currently, porto-mesenteric vein resection is a standard procedure at high-volume pancreatic centers. Experience in vascular surgery is indispensable for a modern pancreatic surgeon. Nowadays, only arterial resections are still a controversial issue. Nevertheless, attempts at resection involving reconstruction of the main arteries such as the coeliac axis, hepatic artery, and superior mesenteric artery (SMA) have been reported, although in small case series [6].

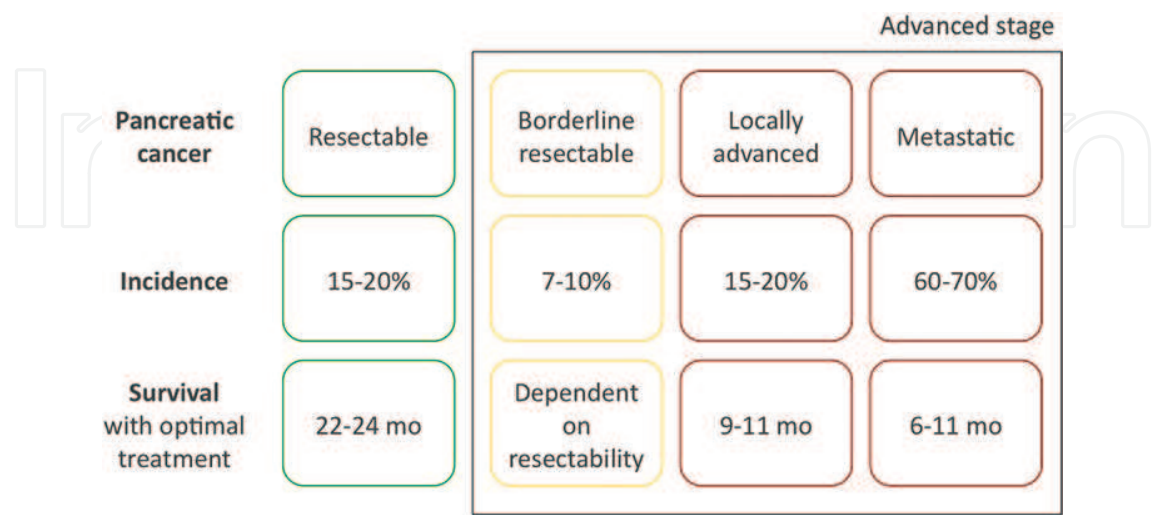


Figure 1. Resectability of pancreatic cancer patients at the time of initial diagnosis [4].

2. History

Moore et al. performed the first superior mesenteric vein (SMV) resection and reconstruction, thus making the base for the treatment of locally advanced pancreatic cancer with aggressive surgery [7]. Twelve years later (1963), Asade et al. published their results, followed by Fortner who first described a "regional pancreatectomy" involving total pancreatectomy, radical lymph node clearance, combined portal vein resection (Type 1), and/or combined arterial resection and reconstruction (Type 2) [6, 8]. These surgical interventions carried a greater morbidity and mortality than conventional surgery, so lately they were abandoned. Fuhrman et al. were the first to report that infiltration of the portal vein/SMV was not a function of the biological aggressiveness of the tumor but of the proximity of the tumor to the pancreatic head [9].

With the improvement of surgical technique, anesthesia, and critical care support, the interest in vascular resection in cases with isolated involvement of the portal vein (PV) and/or superior mesenteric vein (SMV) in locally advanced pancreatic cancer has gradually been renewed during the last decade (**Figure 2**) [3]. There are numerous reports on portal vein resection in locally advanced pancreatic cancer in the last decade, but still the results are conflicting [10–17]. Nowadays, it is accepted that the pancreatoduodenectomy with vein resection does not increase the postoperative risk, but there are still no reliable proofs that it significantly improves survival.

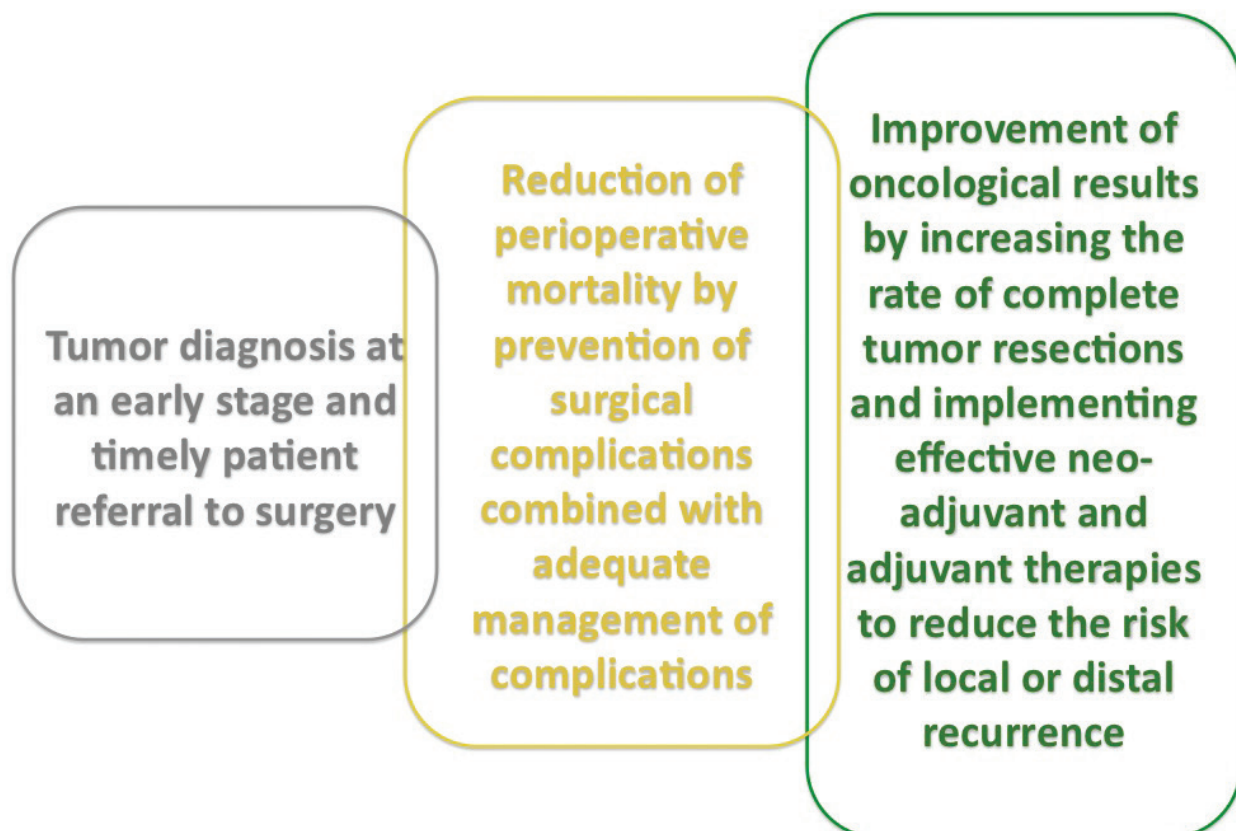


Figure 2. Improvement of surgical results for pancreatic cancer [3].

3. Rationale in vascular resections

3.1. Pro

Surgeons have gradually pushed the boundaries in surgical resection thanks to the advancements in oncology and critical care. Unfortunately, PDVR has not yet been generally accepted and applied as surgical management of patients with locally advanced adenocarcinoma of the head of the pancreas, despite of the growing evidence.

3.2. Cons

Pancreatic carcinoma is characterized with high biological activity and early involvement of retroperitoneal tissue, lymph nodes, and peripancreatic blood vessels. Vascular involvement is frequently combined with invasion in neural plexus so clear resection margin could not be achieved. Vascular resections especially arterial ones add an additional level of complexity to the usually difficult pancreatic surgery without clear impact on the long-term survival rates.

4. Indications for vascular resection

Extended surgical approaches, such as vascular and multivisceral resections, have become commonly performed in PDAC due to the improvement of surgical technique and intensive care, as well as the exact complications management [18].

Combined portal vein resection with pancreatectomy should be considered in order to achieve clear resection margins on the basis of preoperative imaging in cases susceptible of invasion of the portal vein rather than making the decision purely on operative findings. All patients should undergo contrast-enhanced tomography (CT) as routine preoperative work up. The development of multislice multidetector computed axial tomography allows imaging of the whole pancreas in peak contrast intensification. Additionally, the information from the CT may be processed for acquiring of three-dimensional images and visualization of different view planes. Spiral computed axial tomography with i.v. contrast and technique for thin sections may accurately assess the relations of tumor formation with low density to the celiac trunk, superior mesenteric artery, and superior mesenteric-portal vein confluence. Magnetic resonance imaging (MRI), endoscopic ultrasound scans (EUS), and laparoscopy should be performed on an individual patient basis depending on the multidisciplinary team (MDT) discussion. MRI is usually recommended when there is a suspicion of liver metastases present.

According to Ishikawa et al. and Nakao and coworker, the indications are limited to unilateral ($<180^\circ$) segmental vascular involvement [19, 20]. Attention was especially paid to the exclusion of the cases with deep retroperitoneal invasion, defined by the absence of intact connective tissue between the tumor and the right lateral side of the superior mesenteric artery. Isolated arterial involvement is not accepted as an absolute contraindication. Endoscopic ultrasonography (EUS) at this stage is more reliable regarding detection of invasion in the porto-mesenteric system and is a standard procedure in the specialized medical

centers. Tumors with simultaneous involvement of several blood vessels or massive retroperitoneal invasion are treated as resectable only in the case of sensitivity to neoadjuvant chemotherapy.

Preoperative evaluation of resectability should be based on a computed tomography (CT) scan with a pancreas-specific protocol, for example, a “hydropancreas” CT, according to these recommendations. Three grades of resectability can be defined for localized PDAC—“resectable,” “borderline resectable,” and “unresectable” [21]. A tumor is defined as resectable when no vascular attachment (no distortion of the venous structures and clearly preserved fat planes toward the arteries) is present. The resectability is accepted as borderline when distortion/narrowing/occlusion of the mesentericoportal veins with a technical possibility of reconstruction on the proximal and distal margin of the veins or a semicircumferential abutment ($\leq 180^\circ$) of the superior mesenteric artery (SMA) or an attachment at the hepatic artery without the celiac axis is diagnosed—see below. The locally advanced, surgically unresectable tumors are defined as those with infiltration of celiac trunk and/or superior mesenteric artery or as tumors involving the superior mesenteric vein, portal vein, or their confluence. The term “encasement” indicates that the tumor is undistinguishable from the blood vessel for more than 180° of the circumference of the latter. A tumor is defined as unresectable when it presents with the presence of distant metastases, greater than 180° SMA encasement, any celiac abutment, unreconstructible SMV/portal vein, aortic/IVC invasion or encasement, or metastases to lymph nodes beyond the field of resection.

Despite the development of pancreatic imaging, distinguishing between the resectable (stage I and II) and locally advanced (stage III) disease may be difficult and these cases are named with the term “borderline resectability.” Vascular resections are usually required in cases often described as with “borderline resectable” findings.

The definition of borderline resectable carcinoma according to an expert consensus statement from 2009 [22] includes short SMV/PV involvement with free proximal and distal venous segments, permitting secure reconstruction and $\text{SMA} < 180^\circ$ or short hepatic artery involvement with intact truncus coeliacus. The difference from the M. D. Anderson Group classification is in considering tumors, encasing or abutting (depending on the degree of tumor-vessel interface) the SMV/PV borderline but not resectable [23].

Effected vessel	AHPBA/SSAT/SSO/NCCN [1]	MD Anderson [2]	Alliance [3]
SMV/PV	Abutment, impingement, encasement of the SMV/PV or short segment venous occlusion	Occlusion	Tumor-vessel interface $\geq 180^\circ$ of vessel wall circumference, and/or reconstructable occlusion
SMA	Abutment	Abutment	Tumor-vessel interface $< 180^\circ$ of vessel wall circumference
HA	Abutment or short segment encasement	Abutment or short segment encasement	Reconstructable short segment interface of any degree between tumor and vessel wall
CA	Uninvolved	Abutment	Tumor-vessel interface $< 180^\circ$ of vessel wall circumference

Table 1. CT criteria for borderline resectable pancreatic cancer.

The TVI-classification of Tran Cao et al. [24] considers the radiographic tumor-vein circumferential interface and its value as a predictive factor for concomitant vessel resection.

A consensus statement standardizing the definition of the term “borderline resectability” in accordance with the guidelines of the National Comprehensive Cancer Network (NCCN) as well as the definition of extended resections published by the International Study Group for Pancreatic Surgery (ISGPS) (**Table 1**) [21–23].

The approach should be different when borderline findings in venous and arterial vessel involvement are diagnosed. No neoadjuvant treatment is recommended in venous borderline resectability. Upfront surgery should be performed and, if the intraoperative finding matches the presumed borderline situation as defined above, completed as an en bloc tumor removal with venous replacement [21]. In contrast, palliative treatment should be regarded as the standard of care when suspected arterial borderline resectability is intraoperatively confirmed as a true arterial involvement. Stratification and recognition of the patients with borderline findings who do not benefit from extended resections could be done with the neoadjuvant treatment. Patients with a clear tumor progression under neoadjuvant treatment should be excluded from secondary exploration.

Vascular resection must be performed only upon carefully selected patients with data for presence of resectable tumors or tumors with borderline resectability from the preoperative computed axial tomography.

5. Arterial resections

Arterial resection is usually performed in cases of advanced tumors that infiltrate the retroperitoneal nerve plexus and are related with poor prognosis. Some studies doubted the question whether performing of arterial resection in patients with pancreatoduodenectomy is necessary because the procedure itself is a technical challenge. They confirmed that the arterial resection is possible, but there were not enough data in favor, and that is why it is applied in the context of randomized controlled trials (RCTs) [25].

Neoadjuvant treatment should be evaluated to achieve a better local tumor control in case of arterial tumor infiltration. It can be performed following different study protocols and is not standardized yet [26]. Following the restaging, patients should be subjected to surgical exploration as long as no signs of systemic tumor spread are visible. Further mobilization of the pancreatic head could be performed. First an incision of the peritoneal layer at the ligament of Treitz from the left side is made and then is continued with clearing of the tissue along the artery down to the origin from the aorta via this access. This preparation is used for confirmation or ruling out of the tumor infiltration, so that further needed procedures could be determined.

As a whole, arterial resections and reconstructions are limited to the common hepatic artery or resections (with or without any reconstruction) of the right or left hepatic artery in the presence of aberrant hepatic arterial anatomy. Segmental resections of the common hepatic artery may be considered in isolated involvement usually in the area of branching of

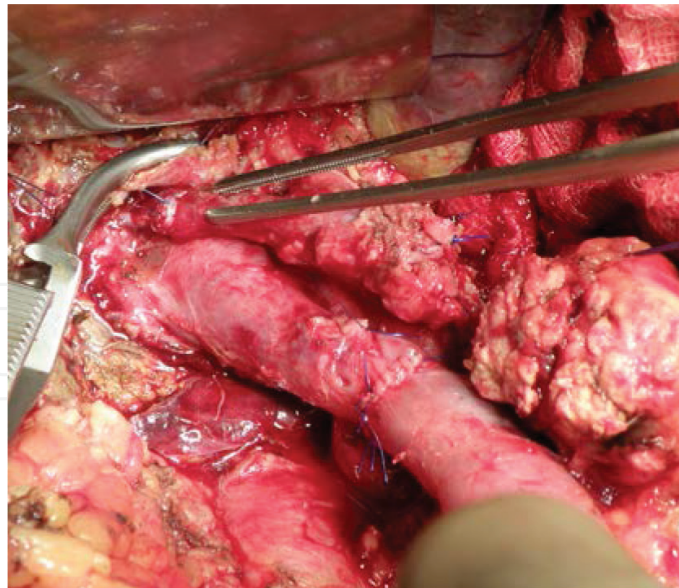


Figure 3. Combined resection of the common/proper hepatic artery with T-T anastomosis, along with segmental portal vein resection with T-T anastomosis.

gastrooduodenal artery [6]. The transition between the common and proper hepatic artery is usually long enough and makes primary anastomosis possible, when the area of gastrooduodenal artery is resected (**Figure 3**). The use of an interpositional graft from reversed saphenous vein is sometimes required. Due to the communication of the right and left hepatic artery inside the liver, ligation of the right hepatic artery is well tolerated, on providing that normal levels of the serum bilirubin and normal blood flow through the portal vein are maintained. Despite that, revascularization of these blood vessels is usually required

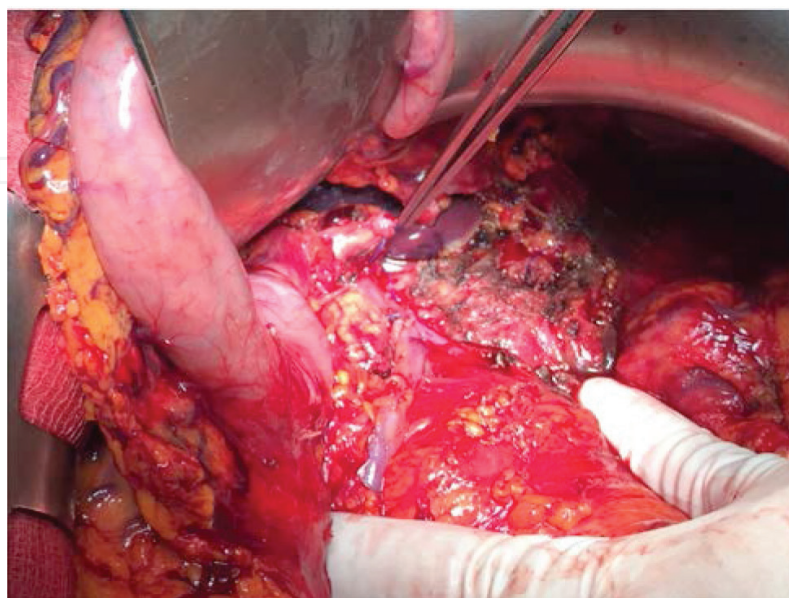


Figure 4. Distal spleno-pancreatectomy with resection of the celiac trunk and segmental resection of SMV. Ligated common hepatic artery is pointed by the forceps.

because the proximal hepatic duct receives almost all of its arterial blood flow from the right hepatic artery after interruption of the blood flow from the right gastric artery. The aberrant right hepatic artery may be infiltrated by the tumor, when the latter reaches the celiac trunk (upon early bifurcation and low position of the left hepatic artery) or when the artery branches from the superior mesenteric artery. Replaced right hepatic artery, branching from the superior mesenteric artery, in contrast to the accessory hepatic arteries, represents the only direct arterial branch toward the right lobe of the liver. When the right hepatic artery, branching from the superior mesenteric artery is infiltrated along the postero-lateral border of the head of pancreas, the pancreatoduodenal resection does not frequently require removal of these blood vessels, because the larger part of these tumors are localized more in front of the head of pancreas and uncinate process of pancreas. The whole common hepatic artery may rarely branch from the superior mesenteric artery (type IX), no identification of that anatomical variant and inattentive ligation of the hepatic artery requires performing of reconstruction.

A high rate of complete resection and favorable prognosis (estimated overall 5-year survival rate of 42%) could be observed in selected patients with distal pancreatectomy with en bloc coeliac axis resection for locally advanced pancreatic body cancer (**Figure 4**) [27, 28].

6. Venous resections

The tumor invasion in the porto-mesenteric system depends on the tumor localization and has no relation to the long-term survival and recurrence. This is not a prognostic factor, but it is an indicator of the biological aggressiveness of the tumor [9]. Invasion of the tumor process in the mesenteric portal blood vessels was considered as a contraindication for radical surgery until recently. Nowadays, this opinion has changed and vascular resections are considered justified if achievement of clear resection margins is possible. Radical resection may be performed in approximately 25–30% of the patients with preoperative diagnostic imaging data for invasion in the porto-mesenteric system [1]. Superior mesenteric/portal vein resections are quite well studied in clinical trials and large series demonstrate equivalence in short-term outcome and long-term survival of the pancreatoduodenectomies combined with venous resections.

Absence of dissemination of the process toward superior mesenteric artery and celiac trunk, which is the prerequisite for achieving of clear resection lines, is the main principle in resections of portal vein in the course of one duodenopancreatic resection [21]. The Japanese, as well as European and American experience, clearly demonstrate that positive resection lines are a prerequisite for recurrent lesions, as well as for lower survival. The level of infiltration of the tumor toward the porto-mesenteric vein is finally determined along the course of surgical operation by mobilization of the specimen from the surrounding tissues and its left repositioning to hang only from the growth. Resection of the vein and recovery of its integrity is the next step. It could be partial or segmental (**Figure 5**). Vein integrity is recovered by one of the following four methods:

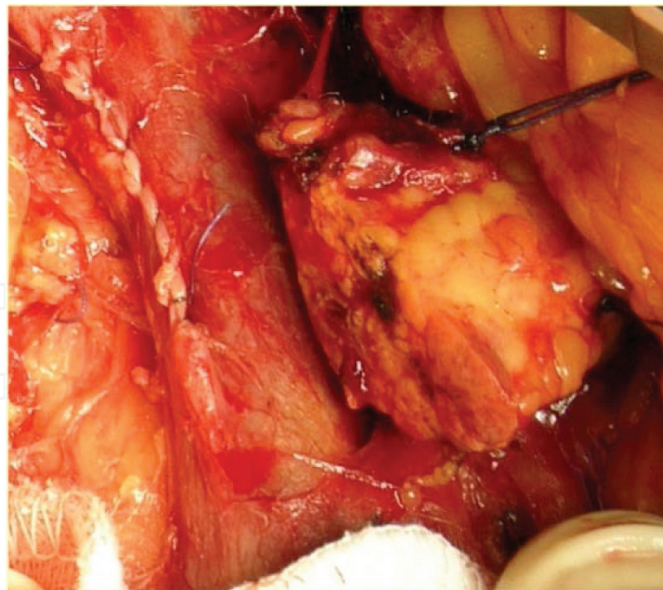


Figure 5. Partial tangential resection of the portal vein sutured longitudinally.

1. Partial tangential resection of no more than one-third of circumference of the vein with suture or placing of venous patch.
2. Segmental resection with termino-terminal veno-venous anastomosis.
3. Segmental resection with venous prosthesis from autologous vein.
4. Segmental resection with synthetic venous prosthesis.

The ISGPS proposes a classification of porto-mesenteric resections according to the type of venous reconstruction [21]:

Type 1: Partial excision of venous wall with a suture closure.

Type 2: Partial excision of venous wall with a patch closure.

Type 3: Segmental venous resection with termino-terminal anastomosis.

Type 4: Segmental venous resection with a conduit and at least two anastomoses.

More recent classification by Tseng et al. takes in general consideration the management of splenic vein along with the type of reconstruction [29]:

V1—Tangential resection with saphenous vein patch.

V2—Segmental resection with splenic vein ligation and primary anastomosis.

V3—Segmental resection with splenic vein ligation and interposition graft.

V4—Segmental resection without splenic vein ligation and primary anastomosis.

V5—Segmental resection without splenic vein ligation and interposition graft.

Shibata et al. divided SMV/PV resections into another four types being guided mainly from the localization of the resection line [30]:

1. Above and below the level of the splenic vein.
2. Above the level of the splenic vein.
3. Below the level of the splenic vein.
4. Tangential resection.

It seems that the management of the splenic vein plays a crucial role during the reconstruction of the SMV/PV confluence [31]. The classical technique of segmental venous resection includes transection and ligation of the splenic vein. In technical aspect, this maneuver allows complete presentation of the superior mesenteric artery medially to the superior mesenteric vein, and elongation of the superior mesenteric vein and portal vein (because the latter blood vessels are not adducted by the splenic vein) for performing of primary venous anastomosis after segmental venous resection. The retroperitoneal dissection ends with cutting by sharp manner of soft tissues anteriorly to the aorta and on the right side of the so presented superior mesenteric artery. As a result of that the specimen remains fixed only to the superior mesenteric-portal vein confluence.

Extensive 2–3 cm segment of the superior mesenteric-portal vein confluence may be resected without any need for interposition of a venous graft, if the splenic vein is cut. The venous resection is always performed with occlusion of the incoming through superior mesenteric vein blood flow and heparinization before its interruption. Upper gastrointestinal tract bleeding could be observed due to the left-side portal hypertension after ligation of the splenic vein, inferior mesenteric vein, and left gastric veins. The mobilization of the neck of the pancreas frequently leads to ligation of the left gastric veins. If the blood flow of

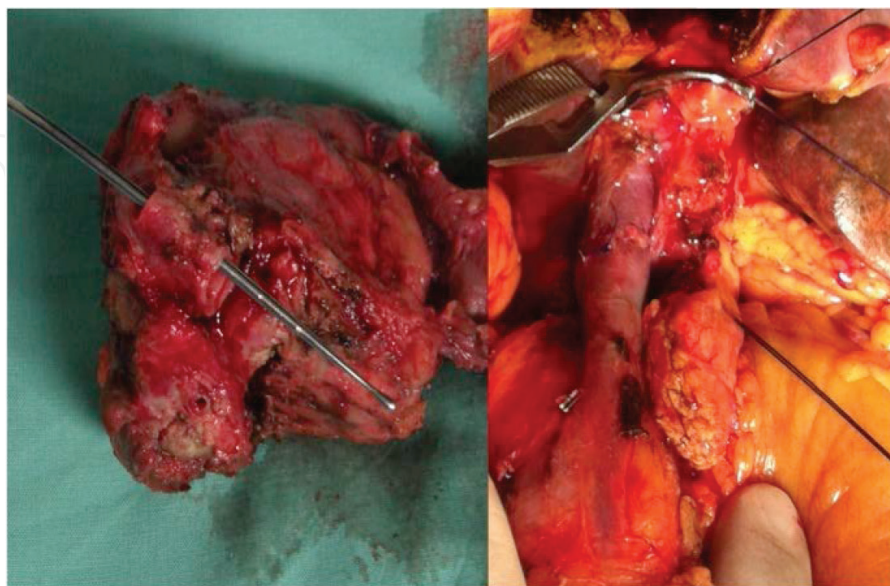


Figure 6. Segmental resection of portal vein with T-T venous anastomosis.

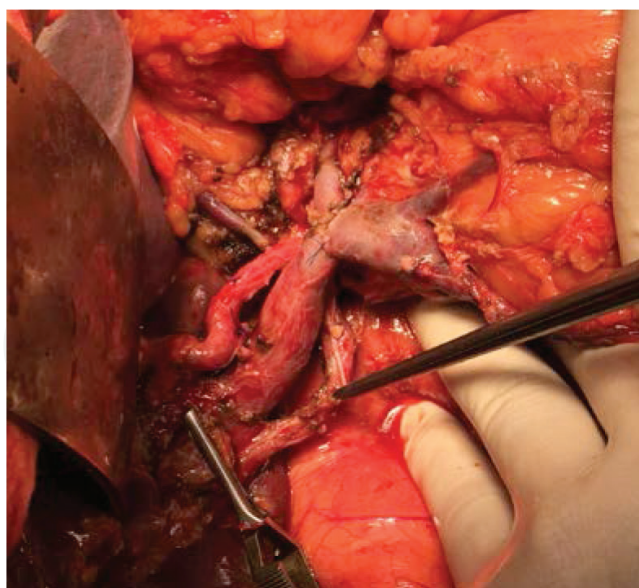


Figure 7. Segmental resection of SMV with T-T reconstruction. Replaced right hepatic artery is pointed by the forceps.

the inferior mesenteric vein runs into the segment of the superior mesenteric vein, which is to be resected, the former vein must also be cut. Upon running of superior mesenteric vein into the splenic vein a way of collateral venous flow is ensured (after interruption of the splenic vein) in retrograde direction and the cutting of splenic vein in this situation is usually well tolerated. Of course, it is recommendable the splenic-portal vein confluence to be preserved if possible, especially when ligation and cutting of inferior mesenteric vein is required. Preservation of the splenic vein is possible, only when the tumor invasion of the superior mesenteric vein or portal vein does not include the confluence with the splenic vein. Preservation of the splenic-superior mesenteric-portal vein confluence significantly limits the mobilization of the portal vein and preserves the primary anastomosis of superior mesenteric vein (following segmental resection of superior mesenteric vein), except in cases when the segmental resection is limited up to 2 cm or less. On account of the latter an interpositional graft should be placed after resection of the superior mesenteric vein with preservation of splenic vein in most of the patients.

Reconstruction of portal vein and superior mesenteric vein after Cattell-Braasch maneuver is usually possible without creating of considerable pressure on the venous anastomosis (**Figures 6 and 7**), at the same time the latter event could be avoided by implanting of a venous graft.

Segmental resection along a great extent of the porto-mesenteric vein makes impossible the reconstruction with termino-terminal anastomosis. In these cases a prosthesis (graft) is used, which may be an autologous one (most frequently internal jugular vein) or an artificial venous prosthesis.

Various types of autogenous veins have been used. Jugular, external iliac vein, great saphenous vein, left renal, and umbilical veins, as well as synthetic grafts could be used as substitutes for portal vein reconstruction. Fleming et al. reported that the superficial

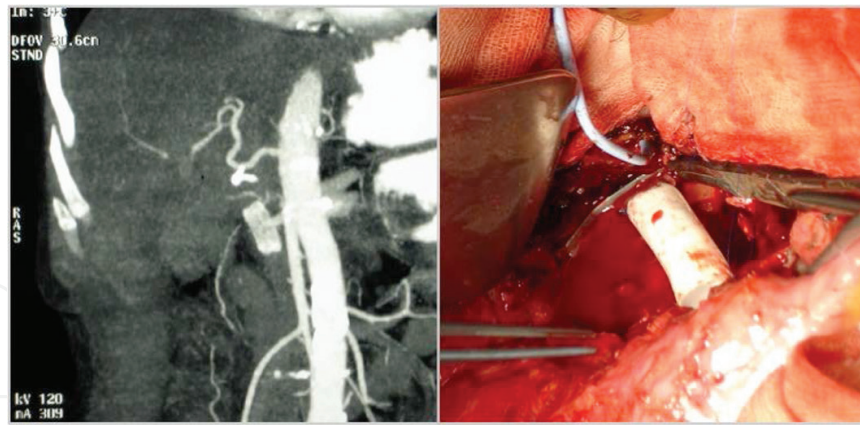


Figure 8. Large resection of the portal vein with PTFE prosthesis replacement.

femoral vein is an excellent size-matched conduit for reconstruction of the SMV or PV without serious complications associated with venous insufficiency in the leg [32]. The patency of reconstruction of the PV or SMV using superficial femoral vein (GSV) reported by Lee et al. was 88% at mean follow-up of 5 months with only a few patients developing mild lower leg edema. Chiba University's team [33] first reported the use of a left renal vein graft for reconstruction of the portal vein. No obvious left kidney dysfunction has been diagnosed after the removal of left renal vein graft [34]. This technique has the following advantages compared with other substitutes:

1. No additional skin incision because the vein is in the same operative field.
2. Usually harvesting takes only 5–10 min.
3. Vein size is often suitable for the portal vein to be reconstructed.

Chiba et al. reported a 100% patency rate in a cohort of 35 patients using a left renal vein graft for portal vein reconstruction, even at long-term follow-up. Suzuki et al. [34] also demonstrated that reconstruction of the inferior vena cava (IVC) or PV with the left renal vein is a durable and safe method without adverse effects on early and long-term renal function. Other veins with smaller diameters like external jugular vein also could be used. The vein is customized by cutting longitudinally and suturing it into a sheet or tube-like graft in order to overcome size discrepancy.

Its recommended synthetic grafts need to be avoided because many resections may involve contaminated bile and postoperative infectious complications could occur. On the other hand, the placement of autologous graft prolongs operative time, which is a prerequisite for postoperative complications. Use of artificial vascular prosthesis also bear risks from thrombosis, as well as infectious complications, which is the main reason for it not to be preferred by most of the medical specialists, although it decreases up to the minimum by the time of clamping of the portal blood flow and is completely justified in critical situation, according to us (**Figure 8**). No difference is observed regarding the hepatic function and hemodynamics of the portal blood flow in the postoperative period, compared to other patients.

Subacute or chronic thrombosis of the graft with the formation of collaterals are observed in long-term follow-up of patients with prosthesis of the porto-mesenteric vein. This process, however, is of minor clinical significance, because it does not influence the liver function or the pressure on the system of portal vein. Recently, a multicenter analysis reported of synthetic graft reconstruction after portal vein resection in pancreaticoduodenectomy. The overall graft patency rate after 36 procedures was 76%. Portal vein thrombosis within 30 days after surgery occurred in 9.1%. Based on the data obtained from this study, it may be recommended that synthetic graft should not be selected as a portal vein substitute if an autogenous vein graft is available. Synthetic graft could be used as an intraoperative temporary portal vein shunt, followed by its removal after tumor excision combined with portal vein resection [35].

7. Operative techniques

Pancreaticoduodenectomy with or without vein resection should be performed in resectable cases. A classical Whipple procedure or a pylorus preserving pancreaticoduodenectomy (PPPD) could be carried out. The preferred access is through bi-subcostal incision. The whole abdominal cavity is consecutively examined—the liver is palpated and intraoperative ultrasonography is performed for excluding metastatic lesions. The area around the celiac trunk is inspected for the presence of metastatic lymph nodes or local invasion. The parietal and visceral peritoneum are carefully examined for carcinosis. Mobilization of duodenum with Kocher maneuver ensures inspection of the head of pancreas and retroperitoneum in the area of the inferior vena cava. This is followed by dissection of the hepatoduodenal ligament. The suspected lesions are sent for express histological examination. Resectability is technically assessed based on the local status of the tumor and its relation to major blood vessels. If resectable, radical resection is undertaken. The type of the latter is determined by the anatomical localization of the process. If all resection margins are free of tumor invasion, the surgical operation is performed according to the standard approach, but if invasion is suspected, the course of operation may be changed by freeing the easier for dissection parts of the anatomical specimen at first, and proceeding to the most difficult for dissection areas at the end.

Vascular resections could be finished by primary closure of the vein, end-to-end anastomosis, or a segmental resection and reconstruction with interposition graft. Venous resections can be performed differently depending on the location and length of tumor adherence. In cases when the tumor infiltration reaches the vein from the right circumference and can be excised with a small patch and direct closure of the defect directly without a hemodynamically relevant stenosis, latero-tangential resection of the portal vein could be done [31, 36, 37].

The mesenteric root should be mobilized completely by resolving the attachment of the right hemicolon to the retroperitoneal adhesions in cases when tangential vein resection is not possible [38]. In such a way, a greater flexibility of the mesenteric vein is achieved and this almost always allows approximation of the distal and proximal resection margins of the vein without any critical tension. A vascular graft needs to be inserted when the resected venous length

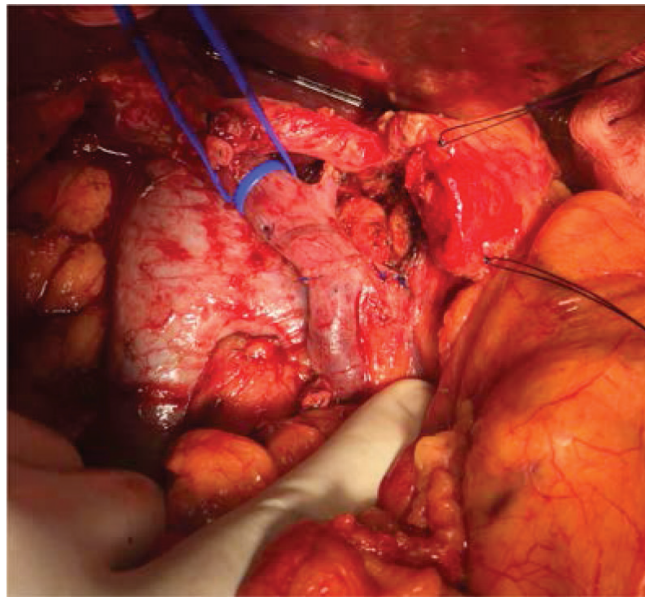


Figure 9. Resection of SMV/PV confluence with ligation of the splenic vein with preservation of the left gastric and inferior mesenteric veins.

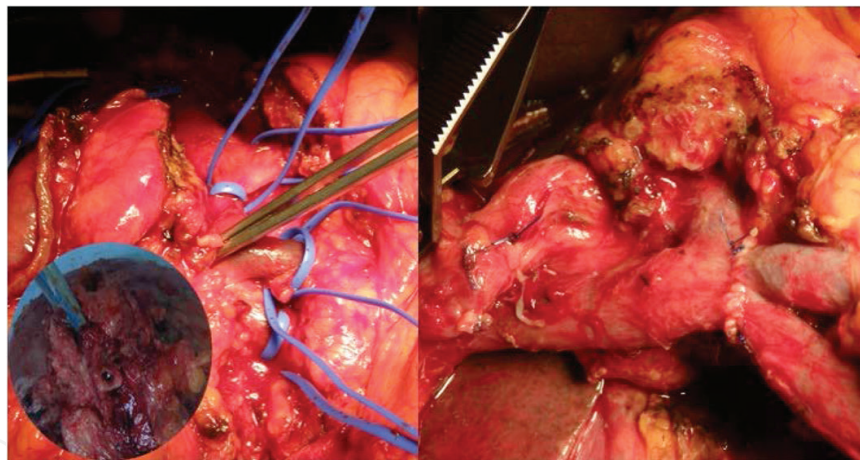


Figure 10. Resection of the proximal part of the superior mesenteric vein followed by difficult anastomosis between portal vein and trifurcation of the distal superior mesenteric vein.

cannot be bridged by the direct anastomosis. A study, including a series of 110 patients undergoing venous resection with different reconstruction techniques, revealed that no differences in surgical outcome were observed when different types of venous reconstruction (venorrhaphy, end-to-end anastomosis, or graft insertion) were performed [38].

Venous resection is also hampered by the need for preservation of the splenic vein, because this makes the direct approach to the most proximal 3–4 cm of the superior mesenteric artery

much more difficult. Venous resection and reconstruction may be performed either before the separation of the specimen from the right lateral wall of the superior mesenteric artery, or after the accomplishment of the mesenteric dissection by separation of the superior mesenteric artery at first. Both techniques require significant pancreatic surgery experience and must be performed only by surgeons who have enough experience in vascular resections and reconstructions during pancreatoduodenal resections. The patency of the venous gastric drainage is a special aspect in venous resections that has to be respected in certain situations. The splenic vein can be closed during venous resection as the stomach is usually drained sufficiently via the coronary vein (if preserved) and collaterals via the short gastric veins (**Figure 9**).

A plan for reconstruction must be preliminarily drawn if the proximal part of superior mesenteric vein at the site where the three major veins join is involved. Major postoperative complications may result from the ligation of veins with no adequate collateral draining. Use of interpositional graft may become necessary for ensuring the possibility of lateral implantation of collaterals if reconstruction of more than one vein is needed. The first jejunal vein, which passes behind the superior mesenteric artery, could usually be ligated with no consequences. Despite that, every larger vein must at first be clamped for checking of presence of adequate collateral blood draining (**Figure 10**).

The temporary interruption of the portal blood flow could additionally damage the usually cholestatic liver. Data analysis shows a tendency for significant increase of the liver enzymes in patients with vascular resections, which is due to the clamping of the portal blood flow during the resection. However, this is observed only during the early postoperative period and does not influence liver function afterwards. The direct termino-terminal reconstruction requires fast performing of the anastomosis, independently from the clamping of the superior mesenteric vein. In cases of isolated involvement of superior mesenteric vein, the latter may be clamped proximally below the confluence with the splenic vein, which allows performing of anastomosis upon partially preserved portal blood flow through the splenic vein with intact inferior mesenteric vein. Portal blood flow is fully recovered through the created anastomosis after the specimen removal. Upon resection of the spleno-portal confluence, the splenic vein could be anastomized termino-laterally to the portal vein, while usually partial lateral clamping of the latter is performed. Avoidance of splanchnic stasis is exceptionally important upon performing of pancreatoduodenal resection combined with venous resection. The consequent intestinal and pancreatic edema hampers accomplishing of surgery and may have negative consequences regarding the digestive anastomosis.

Assessment of the specimen based on anatomical pathology is of considerable significance regarding size of the tumor, grade of invasion in the venous wall, as well as achievement of clear resection margins. Tumors' diameter is measured most precisely after its removal from the abdominal cavity. Resection lines are assessed during surgery with express histological examination after separation of 3–4 mm of the resection margin of pancreas. The presence of tumor cells in the vein, as well as growth of the process into the adventitia or media layer of venous wall reveals vascular infiltration.

8. Outcome

The overview of literature revealed that the resection and reconstruction of porto-mesenteric vein in case of pancreatoduodenal resection does not change the percentage of complications and mortality compared to the standard surgical operation. By excluding the first series with regional pancreatectomy, vein resection does not have prognostic significance regarding the survival. Large series with radical surgical resection showed that surgical morbidity and mortality rates are comparable to standard pancreatic head resections [38–40]. Comparable complication rates between standard pancreaticoduodenectomy (PD) and pancreaticoduodenectomy with vascular resection (PDVR) were reported by some studies [12, 13]. Tseng et al. from the MD Anderson Centre, found no survival difference in patients undergoing PD and PDVR [29]. Yekebas et al. found similar postoperative morbidity and mortality rates between PD and PDVR [41]. There are also studies that have reported increased morbidity with no survival benefit in PDVR [38]. The analysis of our data showed that the total level of complications in both groups of patients does not show statistical difference, while the present one is due mainly to patients with venous resection and interposition of artificial graft. In patients with vascular resection there is higher rate of early and late bleeding and a tendency for more frequent need for hemotransfusions. This is especially emphasized in patients with segmental resection and reconstruction with an artificial prosthesis. This fact is explained with the advanced stage of the disease, involving a larger portion of the vein and the more technically difficult destructive stage of surgical operation, related with higher volume of blood loss. The rate of relaparotomies in patients with vascular resections is not greater as compared to patients with no vascular resections. Regarding the porto-mesenteric invasion, the analysis of the literature and our experience leads to the following conclusions:

1. Involvement of superior mesenteric artery or celiac trunk usually means mesenteric nerve plexus involvement, which makes impossible the achievement of clear resection lines.
2. In portal and mesenteric venous resections there is no increase of the morbidity or mortality rates, compared to those of standard pancreatoduodenectomy.
3. The survival of patients with resection of portal vein does not differ significantly from that of patients with standard pancreatoduodenectomy.

Ishikawa et al. reported of 3-year survival in 59% of the cases with unilateral invasion and 18-month survival in patients with bilateral invasion of the process [19]. A systematic review by Siriwardena suggested that PDVR was associated with a high rate of nodal metastases and low survival rates [42]. There is also some evidence of better survival outcomes with PDVR over palliative treatment [36–38]. Recently, a meta-analysis by Zhou et al. [43] compared 19 studies and 661 patients with venous resections during PDAC with 2247 patients undergoing similar operation but without vessel resection. The surgical outcome of the two groups was comparable. No difference in overall survival between both patient groups was found, the 5-year survival rate being 12.3%—superior compared with palliative treatment. Bachellier et al. reported 22% and 2-year survival in 31 patients with pancreatoduodenectomy and resection of porto-mesenteric vein, which is close to the 24% reported for the conventional surgical

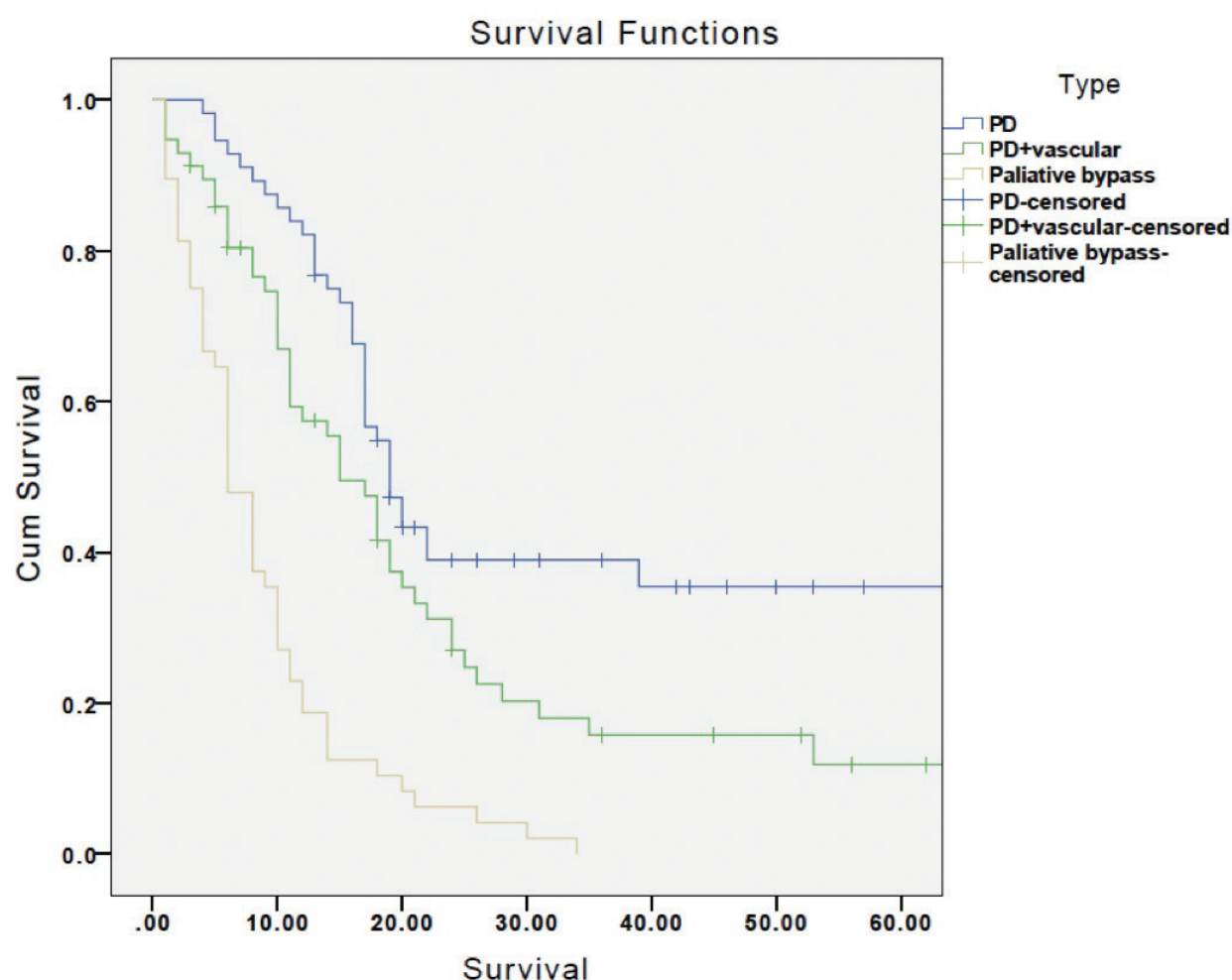


Figure 11. Survival rates depending on the type of intervention.

operation [35]. Nakagohri et al. reported absence of significant difference in the survival of 33 patients with porto-mesenteric venous resection compared to 48 conventional pancreatoduodenectomies (15 vs. 10 months; $p > 0.05$) [44]. Other researchers present similar results: Leach et al.—average survival of 20 vs. 22 months, Harrison et al.—average survival of 13 vs. 17 months, Tseng et al.—average survival of 23.43 vs. 26.5 months, and Hartel et al.—5-year survival of 22 vs. 24%. Moreover, in cases of resection of the vein and absence of histological verification of invasion, improvement of survival was observed, but these observations of Nakagohri and Hartel are still not confirmed and remain controversial [44].

Based on our experience with 356 patients with pancreatic cancer radically operated in our department for a 10-year period (2006–2016)—285 pancreatoduodenectomies and 71 distal pancreatectomies, we could point the level of combined vascular resections of 20.2%. Seventy-two of the presented patients underwent pancreatic resection with simultaneous vascular resection—SMPV in 65 cases (44 with resection of the portal vein, 15 with resection of the superior mesenteric vein, 6 with resection of the porto-mesenteric confluence), arterial in 2 and partial resections of IVC in five cases. Combined vascular resections were done in three

cases. Twenty-eight segmental (21 end-to-end anastomosis and seven interposition grafts) and 37 partial wedge venous resections of SMPV were done. Both groups PVR and PR showed similarly close results in complication rates, mortality, and morbidity. Three- and 5-year survival rates were 42 and 38% in the PD group and 28 and 19% in the PVR group (**Figure 11**).

9. Tips and tricks

- CT with intravenous enhancement is the proper imaging modality for operative planning, MRI is better for searching of liver metastasis;
- Venous resection should be done at the end of resection to decrease the time of liver ischemia;
- Prolene 5/0 is the most used suture material;
- In cases with segmental resection direct anastomosis is the preferred method for reconstruction;
- Left renal vein is the ideal graft;
- Routine use of heparin is controversial—it could be changed by subcutaneous application of 40 mg enoxaparine twice daily.

10. Conclusions

At present, it is accepted that pancreatoduodenectomy with resection of the vein does not increase the postoperative risk and significantly improves survival compared with drainage procedures, this being supported by the results obtained from our study too. Most of the published series include mainly patients with exceptionally invasive tumors or patients, in which the infiltration of the vein is found lately during the operation with inability for discontinuing of the pancreatic resection. That is why the comparison of the results with standard pancreatectomy is not completely correct. Vascular resection must be performed only upon carefully selected patients with data for presence of resectable tumors or tumors with borderline resectability from the preoperative imaging studies. The prompt management of pancreatic cancer with vascular involvement should involve multidisciplinary consultation in high-volume centers.

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References

- [1] W. Hartwig, T. Hackert, U. Hinz et al., Pancreatic cancer surgery in the new millennium: better prediction of outcome. *Annals of Surgery* 2011, 254(2): 311–319.
- [2] T. Schnelldorfer, A. Ware, M. Sarr et al., Long-term survival after pancreatoduodenectomy for pancreatic adenocarcinoma is cure possible. *Annals of Surgery* 2008, 247(3): 456–462.
- [3] W. Hartwig, J. Werner, D. Jäger, J. Debus and MW Büchler, Improvement of surgical results for pancreatic cancer. *Lancet Oncology* 2013, 14: e476-85.
- [4] V. Heinemann, M. Haas and S. Boeck, Neoadjuvant treatment of borderline resectable and non-resectable pancreatic cancer. *Annals of Oncology* 2013, 0: 1–8.
- [5] J. Fortner, Regional resection of cancer of the pancreas: a newsurgical approach. *Surgery* 1973, 73(2): 307–320.
- [6] N. Mollberg, N. Rahbari, M. Koch, W. Hartwig, Y. Hoeger, MW Büchler, J. Weitz, Arterial resection during pancreatectomy for pancreatic cancer: a systematic review and meta-analysis. *Annals of Surgery* 2011, 254: 882–893.
- [7] G. Moore, Y. Sako, L. Thomas, Radical pancreaticoduodenectomy with resection and reanastomosis of the superior mesenteric vein. *Surgery* 1951, 30: 550–553.
- [8] S. Asada, H. Itaya, K. Nakamura, T. Isohashi and S. Masuoka, Radical pancreatoduodenectomy and portal vein resection. *Archives of Surgery* 1963, 87:93–97.
- [9] G. Fuhrman, S. Leach, Ch. Staley, J. Cusack, D. Evans et al., Rationale for En Bloc vein resection in the treatment of pancreatic adenocarcinoma adherent to the superior mesenteric-portal vein confluence. *Annals of Surgery* 1996, 223(2): 154–162.
- [10] L. Harrison, D. Klimstra and M. Brennan, Isolated portal vein involvement in pancreatic adenocarcinoma: a contraindication for resection? *Annals of Surgery* 1996, 224(3): 242–348.
- [11] M. Hartel, M. Niedergethmann, M. Farag-Soliman et al., Benefit of venous resection for ductal adenocarcinoma of the pancreatic head. *European Journal of Surgery* 2002, 168(12): 707–712.
- [12] H. Riediger, F. Makowiec, E. Fischer, U. Adam and U. Hopt, Postoperative morbidity and long-term survival after pancreaticoduodenectomy with superior mesenterico-portal vein resection. *Journal of Gastrointestinal Surgery* 2006, 10(8): 1106–11.
- [13] M. Ouaiissi, C. Hubert, R. Verhelst et al., Vascular reconstruction during pancreatoduodenectomy for ductal adenocarcinoma of the pancreas improves resectability but does not achieve cure. *World Journal of Surgery* 2010, 34(11): 2648–2661.
- [14] V. Banz, D. Croagh, C. Coldham et al., Factors influencing outcome in patients undergoing portal vein resection for adenocarcinoma of the pancreas. *European Journal of Surgical Oncology* 2012, 38(1): 72–79.

- [15] Y. Murakami, K. Uemura, T. Sudo et al., Benefit of portal or superior mesenteric vein resection with adjuvant chemotherapy for patients with pancreatic head carcinoma. *Journal of Surgical Oncology* 2013, 107(4): 414–421.
- [16] R. Ravikumar, C. Sabin, M. Hilal et al., Portal vein resection in borderline resectable pancreatic cancer: a United Kingdom multicenter study. *Journal of the American College of Surgeons* 2014, 218(3): 401–411.
- [17] B. Kulemann, J. Hoepfner, U. Wittel et al., Perioperative and long-term outcome after standard pancreaticoduodenectomy, additional portal vein and multivisceral resection for pancreatic head cancer. *Journal of Gastrointestinal Surgery* 2015, 19(3): 438–444.
- [18] T. Hackert, C. Tjaden, and MW Buchler, Developments in pancreatic surgery during the past ten years. *Zentralblatt für Chirurgie* 2014, 139(3): 292–300.
- [19] O. Ishikawa, H. Ohgashi, S. Imaoka, T. Iwanaga et al., Preoperative indications for extended pancreatectomy for locally advanced pancreas cancer involving the portal vein. *Annals of Surgery* 1992, 215(3): 231–236.
- [20] T. Kaneko, A. Nakao, S. Inoue, H. Takagi et al., Intraportal endovascular ultrasonography in the diagnosis of portal vein invasion by pancreatobiliary carcinoma. *Annals of Surgery* 1995, 222(6): 711–716.
- [21] M. Bockhorn, F. G. Uzunoglu, M. Adham et al., Borderline resectable pancreatic cancer: a consensus statement by the International Study Group of Pancreatic Surgery (ISGPS). *Surgery* 2014, 155(6): 977–988.
- [22] M. Callery, KJ Chang, E. Fishman, M. Talamonti, L. William Traverso et al., Pretreatment assessment of resectable and borderline resectable pancreatic cancer: expert consensus statement. *Annals of Surgical Oncology* 2009, 16(7): 1727–1733.
- [23] G. Varadhachary, E. Tamm, J. Abbruzzese, H. Wang, J. Lee et al., Borderline resectable pancreatic cancer: definitions, management, and role of preoperative therapy. *Annals of Surgical Oncology* 2006, 13(8): 1035–1046.
- [24] H. Tran Cao, A. Balachandran, H. Wang, Evans D et al., Radiographic tumor-vein interface as a predictor of intraoperative, pathologic, and oncologic outcomes in resectable and borderline resectable pancreatic cancer. *Journal of Gastrointest Surg* 2014, 18(2): 269–278.
- [25] P. Bachellier, E. Rosso, I. Lucescu, D. Jaeck et al., Is the need for an arterial resection a contraindication to pancreatic resection for locally advanced pancreatic adenocarcinoma? A case-matched controlled study. *Journal of Surgical Oncology* 2011, 103: 75–84.
- [26] D. Evans, P. Ritch, B. Erickson, Neoadjuvant therapy for localized pancreatic cancer. *Annals of Surgery* 2015, 261–271.
- [27] Y. Yamamoto, Y. Sakamoto, D. Ban, K. Shimada et al., Is celiac axis resection justified for T4 pancreatic body cancer? *Surgery* 2012, 151: 61–69.

- [28] W. Pratt, Sh. Maithel, Ts. Vanounou, Clinical and economic validation of the International Study Group of Pancreatic Fistula (ISGPF) Classification Scheme. *Annals of Surgery* 2007, 245(3): 443–451.
- [29] J. Tseng, Ch. Raut, J. Lee, JN Vauthey, E. Abdalla et al., Pancreaticoduodenectomy with vascular resection: margin status and survival duration. *Journal of Gastrointestinal Surgery* 2004, 8(8): 933–950.
- [30] C. Shibata, M. Kobari, T. Tsuchiya, T. Yamazaki et al., Pancreatectomy combined with superior mesenteric-portal vein resection for adenocarcinoma in pancreas. *World Journal of Surgery* 2001, 25: 1002–1005.
- [31] M. Shoup, K. Conlon, D. Klimstra, and M. Brennan, Is extended resection for adenocarcinoma of the body or tail of the pancreas justified? *Journal of Gastrointestinal Surgery* 2003, 7(8): 946–952.
- [32] J. Fleming, C. Barnett, G. Clagett, Superficial femoral vein as a conduit for portal vein reconstruction during pancreaticoduodenectomy. *Arch Surg* 2005; 140: 698–702.
- [33] M. Miyazaki, H. Itoh, T. Kaiho et al. Portal vein reconstruction at the hepatic hilus using a left renal vein graft. *J Am Coll Surg* 1995, 180: 497–498.
- [34] T. Suzuki, H. Yoshidome, F. Kimura, H. Shimizu et al. Renal function is well maintained after use of left renal vein graft for vascular reconstruction in hepatobiliary-pancreatic surgery. *J Am Coll Surg* 2006, 202:87–92.
- [35] P. Bachellier, E. Rosso, P. Fuchshuber, P. Addeo, P. David, E. Oussoultzoglou et al. Use of a temporary intraoperative mesentericoportal shunt for pancreatic resection for locally advanced pancreatic cancer with portal vein occlusion and portal hypertension. *Surgery* 2014, 155: 449–456.
- [36] J. Weitz, P. Kienle, J. Schmidt, H. Friess, and MW Buchler, Portal vein resection for advanced pancreatic head cancer. *Journal of the American College of Surgeons* 2007, 204(4): 712–716.
- [37] A. Sasson, J. Hoffman, E. Ross et al. En bloc resection for locally advanced cancer of the pancreas: is it worthwhile? *Journal of Gastrointestinal Surgery* 2002, 6(2): 147–158.
- [38] S. Muller, M. Hartel, A. Mehrabi et al. Vascular resection in pancreatic cancer surgery: survival determinants. *Journal of Gastrointestinal Surgery* 2009, 13(4): 784–792.
- [39] P. Kim, A. Wei, E. Atenafu et al. Planned versus unplanned portal vein resections during pancreaticoduodenectomy for adenocarcinoma. *British Journal of Surgery* 2013, 100(10): 1349–1356.
- [40] R. Martin II, C. Scoggins, V. Egnatashvili, C. Staley, K. McMasters and D. Kooby, Arterial and venous resection for pancreatic adenocarcinoma operative and longterm outcomes. *Archives of Surgery* 2009, 144(2): 154–159.

- [41] E. Yekebas, D. Bogoevski, G. Cataldegirmen et al. En bloc vascular resection for locally advanced pancreatic malignancies infiltrating major blood vessels: perioperative outcome and long-term survival in 136 patients. *Annals of Surgery* 2008, 247(2): 300–309.
- [42] H. Siriwardana and A. Siriwardena, Systematic review of outcome of synchronous portal-superior mesenteric vein resection during pancreatectomy for cancer. *British Journal of Surgery* 2006, 93(6): 662–673.
- [43] Y. Zhou, Z. Zhang, Y. Liu, B. Li and D. Xu, Pancreatectomy combined with superior mesenteric vein-portal vein resection for pancreatic cancer: a meta-analysis. *World Journal of Surgery* 2012, 36(4): 884–891.
- [44] T. Nakagohri, T. Kinoshita, M. Konishi et al., Survival benefit of portal vein resection for pancreatic cancer. *Am J Surg* 2003, 186: 149–153.