Venous Resections in Pancreatic Head Carcinoma - 15 Years Experience with Survival and Prognostic Factor Analysis

Nikola Vladov, Tsvetan Trichkov*, Vassil Mihaylov, Ivelin Takorov, Tsonka Lukanova, Radoslav Kostadinov, Stefan Marvakov

HPB Surgery and Transplantology, Military Medical Academy, Sofia, Bulgaria

*Corresponding author:

Tsvetan Trichkov, M.D.
Clinic of HPB Surgery and
Transplantology
Military Medical Academy, Sofia
Bulgaria
Sv. Georgi Sofiyski Street No.3,
floor 14, 1606 Sofia, Bulgaria
E-mail: cvetantrichkov@gmail.com

Abbreviations:

PDR: pancreatoduodenal resection,
VR: briefly from pancreatoduodenal
venous resection,
PP: palliative procedure,
PDAC: pancreatic ductal adenocarcinoma,
ChT: chemotherapy,
ISGPS: International Study Group of
Pancreatic Surgery,
NCCN: National Comprehensive Cancer
Network,
SMV: superior mesenteric vein,
SMA: superior mesenteric artery,
PMVA: portomesenteric venous axis,
BRPC: borderline resectable pancreatic
cancer,
POPF: postoperative pancreatic fistula,
POBF: postoperative biliary fistula,
AJCC: American Joint Committee of
Cancer

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Rezumat

Rezecții venoase în carcinomul de cap de pancreas - 15 ani de experiență în analiza factorilor de supraviețuire și prognostic

Context: Prezentăm o analiză comparativă a supraviețuirii, a complicațiilor și a factorilor de risc major la pacienții cu intervenție chirurgicală pentru carcinomul de cap de pancreas.

Metode: Acesta este un studiu retrospectiv, unicentric, care evaluează caracteristicile clinice, chirurgicale și anatomo-patologice a 467 de pacienți cu intervenții chirurgicale radicale pentru carcinomul de cap de pancreas, în perioada septembrie 2004 - octombrie 2019. Studiul include 88 de pacienți (18.8%) cu rezecții venoase pentru adenocarcinom pancreatic la limita rezecabilității.

Rezultate: Ratele de supraviețuire estimate au fost semnificativ diferite din punct de vedere statistic, cu 19.3 luni în rezecțiile venoase pancreatoduodenale (RV) și 26.9 luni în rezecțiile pancreatoduodenale (RPD), respectiv ($p=0.047$). Pe de altă parte, ratele de supraviețuire la unu, trei și cinci ani de 46.6%, 17.6% și 8.3% în RV și 53.6%, 20.8%, 14.9% în RPD nu au prezentat diferențe semnificative statistic ($p=0.13$, 0.5 și 0.11 respectiv). Ratele de supraviețuire în RPD, RV și procedurile paliative (PP) între cele trei grupuri diferă semnificativ statistic ($p<0.05$). Complicațiile postoperatorii relevante clinic în rezecțiile venoase (13.6%) față de 14.8% în RPD nu au prezentat diferențe semnificative statistic ($p=0.77$). Hemoragia postoperatorie și reintervenția ($p<0.05$) sunt factori de prognostic independenți pentru rezultate mai slabe. Nu a existat o relație semnificativă statistic între supraviețuire și prezența invaziei vasculare ($p=0.581$).

Concluzii: Atunci când sunt efectuate de chirurghi experimentați în centre specializate cu volum mare, rezecțiile pancreatico-duodenale combinate cu rezecția venoasă și reconstrucția sunt proceduri chirurgicale fiabile și sigure.

Cuvinte cheie: adenocarcinom ductal pancreatic, rezecție pancreatoduodenală, rezecție venoasă

Abstract

Background: We present a comparative analysis of survival, complications and major risk factors in patients who underwent surgery for pancreatic head carcinoma.

Methods: This is a single-centre retrospective study aimed to evaluate clinical, surgical and pathoanatomical features of 467 patients who underwent radical surgery for pancreatic head carcinoma between September 2004 and October 2019. The series includes 88 patients (18.8%) with venous resections for borderline resectable pancreatic adenocarcinoma.

Results: The estimated median survival rates were statistically significant with 19.3 months in pancreatoduodenal venous resections (VR) and 26.9 months in pancreatoduodenal resections (PDR), respectively ($p=0.047$). On the other hand, one, three, and five-year survival rates of 46.6%, 17.6% and 8.3% in VR, and 53.6%, 20.8%, 14.9% in PDR were not statistically significant ($p=0.13$, 0.5 and 0.11 respectively). Survival rates comparison in PDR, VR, and palliative procedures (PP) between the three groups showed statistical significance ($p<0.05$). The clinically relevant postoperative complications in venous resections (13.6%) vs. 14.8% in PDR were not statistically significant ($p=0.77$). Postoperative bleeding and reoperation ($p<0.05$) are independent prognostic factors for worse outcomes. There was no statistically significant relationship between survival and presence of vascular invasion ($p=0.581$).

Conclusions: When performed by experienced surgeons at specialized high-volume centres, pancreatoduodenal resections combined with venous resection and reconstruction are reliable and safe surgical procedures.

Key words: pancreatic ductal adenocarcinoma, pancreatoduodenal resection, venous resection

Introduction

Over the last decades pancreatic ductal adenocarcinoma (PDAC) has established itself as one of the most lethal digestive tract tumours. It constitutes 90% of all pancreatic neoplasm, with 5-year survival rate of only 7-8% (1). PDAC is the fourth leading cause of cancer-related mortality in industrially developed countries and expected to become the second leading cause of cancer-related death by the end of 2030 (2). At present the only curative option for PDAC patients is radical surgical resection (3). Unfortunately, only 15% to 20% of patients qualify for upfront surgery (4,5), as over 50% of them present with distant

metastases and 35% with locally advanced disease at the time of diagnosis (6,7).

Preoperative disease staging is essential for selection of patients eligible for surgery (8). The conventional approach in resectable disease is performance of surgery followed by adjuvant chemotherapy (ChT). The neoadjuvant approach in the treatment of PDAC is increasingly being recommended over recent years. Three grades of resectability can be defined for localized PDAC which are termed as resectable, borderline resectable, and irresectable (5). Resectable tumours are characterized by a clean connective-tissue margin along the superior mesenteric artery (SMA). Borderline resectability is defined as

compression or occlusion of the portomesenteric venous axis (PMVA), with a technical possibility of reconstruction on the proximal and distal margin of the veins. Furthermore, tumours with abutment ($\leq 180^\circ$) of the SMA, or at the hepatic artery, are also regarded as borderline resectable. Irresectability is defined as an encasement of the SMA ($>180^\circ$) or no technical possibility for venous resection and reconstruction. Tumour involvement of major blood vessels is present in approximately 50% of the patients (9). With the improvement in modern imaging and surgical techniques the number of patients diagnosed with borderline resectable pancreatic cancer (BRPC) is growing (5,10). Nevertheless, the borderline concept is not well defined yet, with a lot of differences in international definitions, complicating its interpretation. In some highly specialized centres VR is performed in up to 20-25% of patients (3,11-13). The main aim of the procedure is achievement of a clear resection margin. This aggressive surgical approach of vascular resection and reconstruction is the only chance for longer survival of patients with borderline resectable pancreatic cancer (3,14).

There are four known techniques of vein reconstruction, namely: tangential resection with suture (*Fig. 1*); tangential resection with patch angioplasty (*Fig. 2*); segmental resection with end-to-end anastomosis (*Fig. 3*) and segmental resection with graft (*Fig. 4*) (15-17).

The grafts can be either autologous (from renal or saphenous vein) (18) or synthetic vascular prosthesis for venous segment "bridging". However, the use of synthetic grafts is associated with risks of complications as infection or anastomotic leakage (19).

A situation of a synthetic graft in combination with a postoperative pancreatic fistula (POPF) should be regarded as a high-risk constellation for postoperative haemorrhage or difficult to treat long-lasting graft infection. Direct venous reconstructions, without use of patch or graft, have demonstrated fewer thrombotic complications (20), while the use of synthetic prostheses is associated

Figure 1. Tangential resection of the portal vein
PV – portal vein; PS – pancreatic stump

with four-fold higher risk of early thrombosis and worse survival outcome (21).

To most surgeons, arterial invasion is an absolute contraindication for surgical resection (22-25), while according to others it should be performed only in strictly selected cases after careful benefit-risk assessment (19,26-30). Artery resection as a routine procedure is not recommended by the ISGPS guidelines. The „artery-first“ approach is a useful procedure for assessment of suspected retroperitoneal involvement of SMA (31).

Figure 2. Tangential resection and reconstruction with peritoneal patch from the falciform ligament
AP – autologous patch (falciform ligament); PV – portal vein; SMV – superior mesenteric vein; SV – splenic vein; PS – pancreatic stump

Figure 3. Segmental resection of the portal vein with end-to-end anastomosis, as well as reconstruction of replaced right hepatic artery from SMA
PV – portal vein; rRHA – replaced right hepatic artery

Material and Method

This is a single-centre retrospective study evaluating clinical, surgical and pathoanatomical features of 467 patients with performed pancreatoduodenal resection during the period between September 2004 and October 2019. The series includes only patients who underwent surgery for pancreatic head adenocarcinoma and excludes all benign diseases. To

compare survival, a representative group of 120 randomly selected patients who underwent palliative procedures (exploration or bypass anastomoses) was included. All patients underwent contrast-enhanced CT as a routine preoperative work-up. Magnetic resonance imaging, endoscopic ultrasound scan, and laparoscopy were performed on an individual basis based on the multidisciplinary team discussion. The final operative decision lay with the surgeon at the procedure. The preferred operative approach was bilateral subcostal laparotomy. Jejunum was exclusively used for the anastomosis to the pancreas (duct to seromuscular type, two layers) and for bile reconstruction successively. In 88 patients (18.8%) was performed venous resection for borderline resectable pancreatic adenocarcinoma. The conducted comprehensive statistical analysis included various factors and parameters as postoperative complications, perioperative mortality (30 days), short- and long-term survival, as well as different histological characteristics. Categorical data were compared using χ^2 test and confidence interval (95%). P-value < 0.05 was adopted as statistically significant. For statistical analysis of the parameters was used SPSS® Statistics, Version 26.0 of IBM®.

Figure 4. Segmental resections and reconstructions with grafts: Left – reconstruction of the portal vein with synthetic prosthesis (PTFE); Right – autologous reconstruction of the SMV (Left renal vein)
CHD – common hepatic duct; SVP – synthetic vascular prosthesis; AG – autologous graft; PV – portal vein; SMV – superior mesenteric vein; SV – splenic vein; SMA – superior mesenteric artery; PS – pancreatic stump

Results

In *Tables 1, 2* and *3* are presented clinical, surgical and pathoanatomical parameters, as well as a comparison of complications between the two target groups. The differences in some values are clearly statistically significant, while others are with borderline significance. The median survival rates of 19.3 months in 88 VR patients and 26.9 months in patients with PDR were statistically significant ($p=0.047$, *Table 1*). On the other hand, 1-, 3- and 5-year survival rates of 46.6%, 17.6% and 8.3% in VR and 53.6%, 20.8% and 14.9% in PDR were statistically insignificant ($p=0.13$, 0.5 and 0.11 respectively, *Table 1*). Kaplan-Maier survival comparison in PDR (26.9 mo), VR (19.3 mo) and PP (8.4 mo) showed statistically significant differences between all three groups ($p<0.05$). The observed perioperative 30-day mortality rate of 12.5% in VR was markedly significant compared to 3.2% in standard procedures ($p<0.05$, *Table 1*). The data show, that the incidence of clinically relevant postoperative complications graded in accordance with the Clavien-Dindo classifi-

cation (III+IV) was not statistically significant - 13.6% in VR vs. 14.8% in PDR ($p=0.77$, *Table 2*). On the other hand, the rate of certain complications was statistically significant. Besides being significant in both patient groups, postoperative bleeding ($p<0.05$) and reoperation ($p<0.05$) are independent prognostic factors for worse outcomes. 44.3% of vascular resections required intra- or postoperative blood transfusions compared to only 19.8% in the standard procedures group ($p<0.05$, *Table 1*). Compared to PDR, a significantly higher percentage of G3-carcinomas ($p=0.045$), as well as more frequent achievement of R0-resections ($p=0.039$), was typical in VR (*Table 2*). In 10 cases (11.4 %) in VR and 73 (19.3 %) in PDR it was not possible to identify the resection margins (R) due to learning curve of the pathologist or inaccuracy in the processing of the specimens (*Table 3*). The same goes to vascular and perineural invasion status. For this reason, these cases are excluded from the statistical survival comparison. No statistically significant relationship was found between survival and vascular invasion status in the VR group ($p=0.58$).

Table 1. Clinical parameters

Parameters	PDR	VR	P	95% CI	χ^2 test
Gender					
Male	246 (64.9%)	47 (53.4%)	0.045	0.295 to 22.836	4.031
Female	133 (35.1%)	41 (46.6%)	0.045	0.295 to 22.836	4.031
Age (average)	59.5	60.5	0.362	-1.155 to 3.155	-
Jaundice	331 (82.6%)	63 (71.6%)	0.020	1.669 to 21.750	5.499
Pain	121 (31.9%)	42 (47.7%)	0.005	4.577 to 27.047	7.833
Previous jaundice operations	35 (9.2%)	7 (8.0%)	0.723	-6.783 to 6.455	0.126
Bile duct stenting	245 (64.6%)	52 (59.1%)	0.335	-5.369 to 16.930	0.931
Type of operation					
PPPD	306 (80.7%)	57 (64.8%)	0.001	5.785 to 26.930	10.399
Whipple procedure	69 (18.2%)	23 (26.1%)	0.094	-1.168 to 18.549	2.813
Total pancreatectomy	4 (1.1%)	8 (9.1%)	0.000	3.288 to 15.865	17.960
Blood transfusion	75 (19.8%)	39 (44.3%)	0.000	13.682 to 35.539	23.179
Average hospital stays (days)	16.6	17.1	0.576	-1.257 to 2.257	-
Average survival (months)	26.9	19.3	0.047	-15.094 to -0.106	-
Annual survival					
1-year	53.6%	46.6%	0.128	-2.548 to 20.111	2.312
3-years	20.8%	17.6%	0.501	-6.804 to 11.074	0.453
5-years	14.9%	8.3%	0.105	-1.705 to 12.328	2.633
30-day mortality	12 (3.2%)	11 (12.5%)	0.000	3.456 to 17.919	13.094

PDR – pancreaticoduodenal resections; VR – vascular resections; P – p-value; 95% CI – Confidence interval (95%); χ^2 test – Chi-squared test

Table 2. Surgical complications

Parameters	PDR	VR	P	95% CI	χ^2 test
Dindo-Clavien IIIA/IIIB/IV	56 (14.8%)	12 (13.6%)	0.774	-8.074 to 8.082	0.082
Bleeding	47 (12.4%)	19 (21.6%)	0.026	1.005 to 19.325	4.970
Reoperation	48 (12.7%)	20 (22.7%)	0.017	5.721 to 20.229	5.721
POPF	45 (11.9%)	6 (6.8%)	0.168	-2.715 to 10.260	1.903
POBF	17 (4.5%)	4 (4.5%)	1.000	-3.768 to 6.760	0.000
Sepsis	10 (2.6%)	8 (9.1%)	0.004	1.594 to 14.426	8.185
DGE	36 (9.5%)	5 (5.7%)	0.257	-3.600 to 8.475	1.284
Abscess	25 (6.6%)	9 (10.2%)	0.242	-1.993 to 11.940	0.119

PDR – pancreaticoduodenal resections; VR – vascular resections; P – p-value; 95% CI – Confidence interval (95%); χ^2 test – Chi-squared test

Table 3. Pathological parameters

Parameters	PDR	VR	P	95% CI	χ^2 test
Average tumour size (cm)	3.08	3.26	0.193	-0.091 to 0.451	-
Perineural invasion					
Pn+	215 (56.7%)	57 (64.8%)	0.166	-3.401 to 18.558	1.922
Pn-	71 (18.7%)	10 (11.4%)	0.104	-1.760 to 13.914	2.651
Pnx	93 (24.5%)	21 (23.9%)	0.906	-10.083 to 9.554	0.014
Degree of differentiation					
G1	62 (16.4%)	7 (7.95%)	0.045	0.162 to 14.183	4.034
G2	231 (60.9%)	52 (59.1%)	0.756	-9.096 to 13.285	0.097
G3	86 (22.7%)	29 (32.95%)	0.045	0.263 to 21.324	4.033
Lymph nodes					
N+	187 (49.3%)	40 (45.5%)	0.521	-7.717 to 14.985	0.412
N-	146 (38.5%)	32 (36.4%)	0.715	-9.361 to 12.644	0.133
Nx	46 (12.1%)	16(18.2%)	0.129	-1.515 to 15.875	2.307
Resection margin					
R1	32 (8.4%)	5 (5.7%)	0.398	-4.644 to 7.272	0.715
R0	274 (72.3%)	73 (83.0%)	0.039	0.573 to 18.668	4.275
Rx	73 (19.3%)	10 (11.4%)	0.081	-1.181 to 14.540	3.038

PDR – pancreaticoduodenal resections; VR – vascular resections; P – p-value; 95% CI – Confidence interval (95%); χ^2 test – Chi-squared test.

Discussion

PMVA invasion per se is not a contraindication for surgery (13,18,32–34). One of the main aims of the intervention is achievement of clear resection margins (16,35,36). When performed by a skilled surgical team, VR becomes a routine procedure for radical removal of the tumour (37–39). The decision for vascular resection is important and depends primarily on perioperative assessment and patient selection. However, there is no recommendation consensus yet for either initial resection or neoadjuvant treatment approach. In most cases with BRPC, we have performed upfront surgery. Neoadjuvant ChT followed by resection was performed in single patients only, but their limited number does

not allow for a conclusive judgement of treatment efficacy yet.

Many studies do not demonstrate survival differences in patients with PDR compared to those with VR (3,16,18,23,32–34,40–47). Other authors report worse survival in vascular resections attributable to more aggressive tumour characteristics (48–51). The results from our study show a significant difference in survival in favour of PDR – 26.9 months vs. 19.3 months in VR (*Table 1*). Nevertheless, 1-, 3- and 5-year survival rates were not statistically significant ($p=0.128$, 0.501 and 0.105 respectively). A similar correlation in 5-year survival rates has been reported by Siriwardana as far back as in 2006 (52). On the other hand, 30-day mortality in the VR group was considerably higher compared with

the PDR group ($p=0.0003$). Similar results have also been reported in a recent meta-analysis by Peng (53). Survival rates comparison in PDR, VR and PP shows significantly lower survival in palliative procedures compared with venous resections ($p<0.05$, *Graph 1*). This provides grounds for the conclusion that performance of VR in borderline resectable tumours is a justified procedure aiming at better survival in patients who would otherwise be deemed inoperable. This relationship has also been established by other authors over the years (16,44,47,54).

In *Table 2* are listed the clinically relevant postoperative complications, graded according to Clavien-Dindo (55) and ISGPS (56) classifications. There was no significant difference in Grades IIIa, IIIb and IV complications ($p=0.774$). Similar correlations of postoperative complications have also been found in a number of other studies (11-13,18,27,32-34,42,43,47,57,58). On the other hand, the rates of postoperative bleeding and reoperations were significantly higher in the VR group ($p=0.026$ and $p=0.017$ respectively).

These two parameters are also independent prognostic factors for worse survival ($p<0.05$, *Graphs. 2 and 3*). The incidence of septic complications in vascular resections was also higher ($p=0.004$), probably due to the large wound area and trauma associated with such surgical volume. There was no significant difference between the two groups in the incidence of POPF ($p=0.168$) or postoperative biliary fistula (POBF, $p=1$). The increased rate of POBF in vascular resections demonstrated in a meta-analysis by Peng has led to speculations about a possible hepatoduodenal ligament blood flow disturbance in the course of extended surgery (53). Although many series report similar postoperative complications in PDR compared to VR, some other authors have demonstrated higher complications rates in vascular resections (49-51,59).

The observed incidence of blood transfusions in VR (44.3%) was much higher and markedly significant than that in standard procedures (19.8%, $p<0.0001$). This could also be attributed to the higher incidence of reoperations in vascular resections. One of the most common

Graph 1. The comparison of long-term survival in PDR, VR and PP groups
Kaplan-Meier survival comparison in PDR, VR and PP showed statistically significant differences between all three groups ($p<0.05$)

Graph 2. The comparison of survival in postoperative bleeding
Comparison of survival in cases with (POB+) and without (POB-) postoperative bleeding – statistically significant ($p < 0.05$)

Graph 3. The comparison of survival in reoperation
Comparison of survival in cases with (ROP+) and without (ROP-) reoperations – statistically significant ($p < 0.05$).

series complications reported by Ravikumar in 2014 were blood transfusion requirements during the early postoperative period (47).

Regarding the type of surgical procedures

performed in the two groups, pylorus-preserving resections were more frequent in the PDR group ($p = 0.001$), while in the VR group were performed more total pancreatectomies ($p < 0.0001$). The

latter is attributed to the more extensive resections in vascular procedures.

The average hospital stay was half a day longer in VR compared to PDR (16.6 vs. 17.1), without statistical significance ($p=0.576$). Such correlation has been reported by other authors as well (47). The meta-analysis by Peng (53) demonstrates longer hospital stay in vascular resections.

The average tumour size was 16 mm larger in VR, however far below the significance level ($p=0.193$, *Table 3*). Ravikumar has found that the average size of blastomas observed in vascular resections is insignificantly larger than those in standard procedures (47). VR opponents on the other hand argue that because of vascular invasion BRPC are generally larger and have a worse prognosis (27,60-62). According to Peng, the average size of tumours in vascular resections is larger compared to those in standard pancreatoduodenal procedures (53). Furthermore, some series demonstrate that the lack of significant histological differences between the two groups shows that vascular invasion is rather due to

topographic factors than to the histological aggressiveness of the tumour (50,63,64).

No significant differences were found in the lymphovascular and perineural invasion status ($p>0.05$). A certain correlation in the degree of tumour differentiation was observed, with G1 carcinomas being more common in PDR ($p=0.045$) compared to a higher percentage of G3 tumours in VR ($p=0.045$). No statistically significant differences were found about moderately differentiated blastomas. Michalski reports longer survival rates after vascular resection in patients with G1 and G2 tumours compared to patients with G3 neoplasms (65). The same statistically significant correlation was found in our study ($p=0.006$, *Graph 4*).

The percentage of R0-resections observed in vascular procedures was higher (83%) and statistically significant compared to PDR (72.3%, $p=0.039$). There were no significant differences between the two groups regarding the rate of R1-resections ($p=0.398$). According to publications by Peng (53) and Ravikumar (47), R1-resections prevail in the VR group. In

Graph 4. The comparison of survival at degrees of differentiation
Longer survival rates after VR in G1/G2 group compared to patients with G3 ($p=0.006$)

Graph 5. The comparison of survival in resection margins
R0-resections are associated with better survival compared to R1 group ($p=0.011$)

addition, R0-resections are associated with better survival compared to R1-resections ($p=0.011$, *Graph 5*). Carrere confirms that achievement of an R0-resection is a major prognostic factor, therefore venous involvement is not a contraindication for pancreaticoduodenal resection (66). Other series have also demonstrated that R0-resection is a favourable prognostic marker for longer survival (67-70). In contrast, the results from several studies performed during the past decade show that R1-resection status has no impact on long-term survival (18,27,41,71).

PDR are associated with higher onset incidence of jaundice manifestations ($p=0.02$) while vascular resections are characterized by higher onset manifestations of pain ($p=0.005$). This is explained by the tumour localization and the presence of either bile duct infiltration or involvement of retroperitoneal nerve plexuses and PMVA.

In *Table 4* are listed the performed vascular resections. In addition to 88 venous resections, were performed 5 arterial and 6 inferior vena cava resections. One of the most common localizations was the portal vein

Table 4. Vascular resections

Type of resection	Tangential n=41 (46.6%)	Segmenta n=47 (53.4%)		Total
		End-to-End n=36 (40.9%)	Graft n=11 (12.5%)	
PV	25 (28.4%)	20 (22.7%)	5 (5.7%)	50 (56.8%)
SMV	14 (15.9%)	9 (10.2%)	3 (3.4%)	26 (29.5%)
Confluence	2 (2.3%)	7 (8.0%)	3 (3.4%)	12 (13.7%)
IVC				6
SMA				5

PV – portal vein; SMV – superior mesenteric vein; IVC – inferior vena cava; SMA – superior mesenteric artery

(n=50, 56.8%), followed by the SMV (n=26, 29.5%). 41 tangential (46.6%) and 47 segmental resections (53.4%) were performed, 36 of which were done with end-to-end vascular anastomosis (40.9%), and 11 with grafts (12.5%, 7 synthetic prostheses and 4 autologous grafts). No statistical relationship between the type of resection and the documented postoperative complications was observed even in cases with prosthetic reconstructions ($p>0.05$). In their series Hackert, Schneider and Büchler point out that the use of such synthetic grafts may lead to higher incidence of complications as infection or anastomotic leakage (19). The specific situation of a synthetic graft in combination with a pancreatic fistula must be regarded as a high-risk constellation for postoperative haemorrhage or difficult to treat long-lasting graft infection.

According to different authors, histologically confirmed vascular invasion is observed in 21% to 70% of patients (80,86–88). In our series, histological venous infiltration (V+) was present in 43.2% (n=38) of patients with

performed vascular resection, but absent (V-) in 26.1% (n=23) of patients. The histological status of the remaining 30.7% (n=27) was classified as Vx, i.e. their vascular status could not be determined due to pathological limiting factors. There were no significant differences in the survival rates between patients with V+ and V- status ($p=0.581$, *Graph 6*). The same outcomes have been reported by a number of other authors (11,16,18,27). On the other hand, Nakagohri points out that negative vascular infiltration status (V-) is associated with better survival (75). Mierke has reported important findings of higher incidence of development of metachronous liver metastases consistent with histologically confirmed venous infiltration (V+) (76). The median survival in those patients was 11.9 months vs. 16.1 months in patients without vascular infiltration. The median survival in our study was 18 months in patients from the V- group and 16 months in the V+ group ($p>0.05$).

The limited number of inferior vena cava (n=6) and SMA resections (n=5) did not provide conclusive evidence of the benefits and

Graph 6. The comparison of survival regarding the presence of venous invasion
No significant differences in the survival rates regarding the venous status ($p=0.581$)

disadvantages of this type of vascular procedures. Mollberg has reported higher incidence of complications (53.6%) and perioperative mortality (11.8%) in patients who underwent arterial resection as compared with standard PDR procedures (26). In addition, arterial resections are associated with worse 1-year and median survival (21). Nevertheless, there is also an opinion that arterial resections can be carried out safely in experienced hands but at this stage cannot be recommended as a standard procedure (13). Del Chiaro have even demonstrated an advantage of arterial resections in terms of survival comparable to that in palliative procedures (77).

In conclusion, median survival rates observed in VR were lower than that in PDR. Nevertheless, 1-, 3- and 5-year survival rates were fully comparable statistically. Among patients with vascular resections was observed significant perioperative mortality. The comparison of long-term outcomes in PDR, VR and PP showed worse survival in vascular resections relative to standard procedures, yet significantly higher than that in palliative procedures. The total percentage of clinically relevant complications in the two groups was fully comparable, except for higher incidence of postoperative bleeding and reoperations in VR, both being independent prognostic factors for survival. In consequence, the percentage of blood transfusions in vascular resections was much higher. The average size of tumours in VR was slightly larger compared with that in standard procedures but without statistically significant differences. On the other hand, the percentage of poorly differentiated tumours in vascular resections was significantly higher. R0-resections, associated with better long-term outcomes than R1-resections, were achieved more frequently in the VR group. The most common clinical manifestation of disease onset in the PDR group was jaundice, while in vascular resection the most common symptom was pain. There was no evidence that the presence or absence of venous infiltration in the group with vascular resections has significant impact on survival.

One of the limitations of our study is its retrospective design. In addition, long-term postoperative follow-up for quality-of-life assessment was not practically possible in all patients. Another shortcoming was the impossibility to determine resection margins, vascular and perineural invasion status in a certain percentage of histologically examined specimen. In addition, for determination of resection margins were used different criteria.

Conclusion

Vascular resections in pancreatic cancer remain a great challenge for all surgeons. The decision for their performance should not be impulsive but based on strict patient selection after careful benefit-risk assessment. Compared with palliative procedures vascular resections are associated with better survival outcomes almost comparable to those in standard procedures. The performed analysis shows that pancreatoduodenal procedures in combination with venous resections are reliable and safe but only when performed by surgeons with long-term experience in high-volume centres of excellence.

Conflicts of Interest and Source of Funding

No funding to declare.

Ethics Approval

Ethical approval was waived by the local Ethics Committee of Military Medical Academy - Sofia (Bulgaria) in view of the retrospective nature of the study and all the procedures being performed were part of the routine care.

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