Pancreatic malignancies are difficult objects for diagnosis and surgical treatment. Radical surgery is impossible (distant metastases, advanced local spread) in large proportion of patients by the moment of diagnosis while this question is controversial in the others.

According to the data published in the book «The state of oncological care in Russia in 2017», firstly-diagnosed pancreatic head malignancies were observed in 16188 patients (without posthumous ones) while stage IV was confirmed in 58.3% of cases. Mortality rate within 1 year after diagnosis was 68.2%. Radical treatment was completely carried out in 2061 (12.7%) cases among those with firstly-diagnosed cancer, curative measures will be continued in 1247 (7.7%) of them [1]. Thus, only 20.4% of patients with firstly-diagnosed pancreatic cancer underwent radical surgery.

The one of the reasons to refuse radical procedure is great vessels involvement - superior mesenteric artery and celiac trunk pool, mesenteric-portal veins (MPV). State of these vessels is one of the most complex and extremely important tasks of preoperative diagnosis. Surgical dissection of these vessels and resection of mesenteric-portal veins are very difficult in case of their involvement and solid attachment to the tumor.

For the first time, the American surgeon Bernard Sigel successfully performed pancreaticoduodenectomy followed by mesenteric-portal vein resection and autovenous replacement on December 14, 1962 [2]. This procedure was considered exclusive and rarely performed at that time. In 1977 J. Fortner et al. [3] reported 18 total pancreaticoduodenectomies followed by MPV resection (regional pancreatectomy): mortality was 16.6%, annual survival - 62%. However, pancreatic malignancies involving MPV have been considered unresectable for a long time. Currently, pancreaticoduodenectomy followed by MPV resection is performed in well-experienced pancreatic centers with satisfactory results. There is common sense concept considering retroperitoneal spread of tumor followed by impossible R0-resection as the main cause of unsatisfactory survival after pancreaticoduodenectomy followed by MPV resection besides biologically determined aggressiveness of ductal adenocarcinoma [4].

The search for objective criteria of radiological diagnosis and reasonable surgical approach for pancreatic head malignancies involving MPVs remains one of the most urgent problems.

Aim — to evaluate the outcomes of pancreaticoduodenectomy with mesenteric-portal vein resection for pancreatic head cancer.

Material and methods. Retrospective analysis included 124 patients with pancreatic head cancer for the period 2010—2017. Mesenteric-portal vein (MPV) invasion was diagnosed in 37 (29.8%) patients, tumor contact with superior mesenteric artery as a borderline resectable state was noted in 11 cases. All patients underwent pancreaticoduodenectomy with mesenteric-portal vein resection.

Results. Vein invasion was histologically confirmed in 19 (51.3%) out of 37 patients. At the same time, arterial invasion was absent in 11 patients with a borderline resectable tumor. CT-associated overdiagnosis of venous wall invasion was 6.4%, intraoperative overdiagnosis - 87.5%. R0-resection was achieved in 88.5% after conventional pancreaticoduodenectomy and in 78.4% after pancreaticoduodenectomy followed by MPV resection. Median survival was 17 months, 2-year survival — 41%. Among 11 patients with a borderline resectable tumor median survival was 11 months. Pancreaticoduodenectomy without vein resection was followed by 2-year survival near 68.1%. Differences were significant (p=0.02).

Conclusion. Pancreaticoduodenectomy followed by MPV resection as the first stage of combined treatment of pancreatic head cancer is absolutely justified if circumferential involvement of the vein and contact with superior mesenteric artery or celiac trunk do not exceed 50%. Vein resection can provide R0-surgery in these cases.

Keywords: pancreatic cancer, vein invasion, pancreaticoduodenectomy, vein resection, borderline resectable tumor.
tures of diagnosis and surgical treatment of patients with pancreatic malignancies and MPV invasion.

**Material and methods**

There were 450 pancreatic procedures for various disease of pancreas, terminal common bile duct and duodenum performed in the 1st abdominal department in 2010—2017 (275 pancreaticoduodenectomies, 162 distal pancreatectomies and 13 total pancreaticoduodenectomies). Great vein resection was required in 48 (10.7%) cases.

X-ray examination data and surgical outcomes of 124 patients with pancreatic head cancer were analyzed. These patients did not have invasion of superior mesenteric and hepatic arteries, as well as distant metastases. All patients underwent pancreaticoduodenectomy. MPV resection was performed in 37 (29.8%) patients.

Contrast-enhanced computed tomography was performed in all patients 16 days prior to surgery on the average. Involvement of MPVs, celiac trunk and superior mesenteric artery pools was carefully examined. Marinelli’s criteria were applied to assess peripancreatic vascular invasion [5]. Typical variants of tumor contact with great vessels are shown in Fig. 1.

Blood clotting was preoperatively evaluated in all patients. Hospitalization 2—4 days prior to surgery was preferred in case of coagulopathy for correction up to normal values. Prophylactic dose of low-molecular-weight heparin was administered 12 hours prior to surgery in all patients. Intraoperative monitoring of hemostasis was achieved using activated blood coagulation time (ABC) and thromboelastography data. Continuous infusion of heparin was used to maintain ABC within 180—200 s at the vascular surgical stage and in postoperative period. ABC values were controlled prior to surgery, just before vascular stage, during vascular reconstruction, 30 min after vascular stage and at the end of surgery. ABC has been assessed every 3 hours within the 1st postoperative day and then every 12 hours. Since the 2nd day after surgery low-molecular-weight heparin therapy combined with anti-platelet agents (aspirin) was used to achieve ABC time 160—180 s. Subsequent therapy included rivaroxaban combined with aspirin during 3 months.

Prevention of postoperative pancreatitis was administered in all patients. Complex preventive therapy included synthetic analogues of somatostatin (octreotide 200 mcg 3 times daily intravenously), nonsteroidal anti-inflammatory drugs (xefocam 8 mg 2 times daily intravenously), proton-pump inhibitors (nexium 40 mg daily intravenously). Initial dose of the drugs was administered 1 hour prior to surgery (skin incision). Duration of preventive treatment was 5 days including the day of surgery.

Pancreatoduodenal complex was mobilized after preliminary ligation of vessels supplying pancreatic head and duodenum [6]. Technical peculiarity of pancreaticodudenumectomy in case of suspected MPVs invasion is mandatory preliminary dissection of certain vascular segment for subsequent resection. In this regard, portal, superior mesenteric and splenic veins were circularly dissected from surrounding fatty tissue after intersection of pancreatic isthmus. The veins were exposed for placing the tapes at least 1 cm from the area of suspected invasion without lumen compression. Small veins of mesenteric-portal pool were ligated and intersected. Then venous wall was dissected from pancreatic head and uncinate process. Sharp scissors with closed branches or monopolar electrode without cautery were applied for this purpose. This approach was useful to avoid advanced bleeding in case of venous wall injury due to possible rapid cessation of blood flow in certain vascular segment.

Advanced intension was not necessary during venous wall dissection if true invasion was absent. The last was confirmed if the vein could not be separated under these conditions.

MPVs resection was performed by a vascular surgeon (A.F. Kharazov). Heparin 2500 - 5000 units were intravenously administered prior to cross-clamping of the vein depending on ABC values. Anastomosis in end-to-end fashion was formed if advanced tension of both venous ends was absent. Replacement using PTFE prosthesis...
Pancreaticoduodenectomy with MPV resection was performed in 37 (29.8%) out of 124 patients who underwent pancreaticoduodenectomy. Circular resection of superior mesenteric vein below splenic vein ostium was carried out in 19 patients, tangential (within lower contour of splenic vein ostium) — in 3 cases. Circular resection of MPV confluence was performed in 7 patients. This procedure was followed by ligation of splenic vein stump in 4 cases, its implantation into vascular prosthesis in 3 cases, tangential resection of the right contour of the confluence — in 6 cases. Two patients underwent tangential resection of the portal vein (along upper contour of splenic vein ostium). Variants of MPV resection are presented (Fig. 2).

Pancreaticoduodenectomy with MPV resection was followed by advanced time of surgery (395 vs. 359 min, \( p_{\text{medi}} = 0.021 \)) and greater blood loss (830 vs. 320 ml, \( p_{\text{medi}} < 0.00001 \)) compared with operations without resection. This was caused by more difficult mobilization of the complex and lymph node dissection in case of venous invasion while heparin administration at the vascular stage increased blood loss and time of haemostasis.

Postoperative morbidity after pancreaticoduodenectomy with/without MPV resection was similar (48.7 and 36.7%, respectively). Postoperative hospital-stay was also similar (22 vs. 17; \( p_{\text{medi}} = 0.077 \)). Thrombosis of prosthesis of the vein developed in 3 out of 10 patients that resulted in hepatic insufficiency and death of 2 patients. Thrombosis after anastomosis of the vein in end-to-end fashion occurred in 1 out of 16 patients. There were no cases of thrombosis after tangential resection. Three (8.1%) patients died after pancreaticoduodenectomy with MPV resection, 3 (3.4%) patients — after pancreaticoduodenectomy alone (n=87). Differences were not significant due to small sample size.

Histological examination confirmed various morphological variants of pancreatic head cancer (Table 1). Vein invasion was histologically confirmed in 19 (51.3%) out of 37 patients. R0-resection was made in 88.5% after conventional pancreaticoduodenectomy and in 78.4% after that followed by MPV resection. However, significant differences were absent.

Median survival after pancreaticoduodenectomy with MPV resection was 17 months, 2-year survival — 41%. Median survival was 11 months among 11 patients with conditionally resectable tumor. Pancreaticoduodenectomy without MPV resection was associated with 2-year survival near 68.1%. Differences were significant (\( p=0.02 \)) (Fig. 3).

**Discussion**

Pancreaticoduodenectomy is the main component of the combined treatment of resectable pancreatic head cancer. The main criterion for assessing the resectability of tumor is relationship with superior mesenteric artery, celiac trunk pool and mesenteric-portal veins. MPV invasion is considered as T3-stage and not contraindication for pancreaticoduodenectomy with resection of the vessel [7]. In our opinion, the position of Anderson Cancer Center (Houston, USA) that MPV invasion is primarily indicative of topography rather spread of the tumor is doubtful [8]. Accordingly, vein resection may be followed by R0-resection if invasion of retropancreatic tissues and arteries is absent.

Systematic review of H. Siriwardana et al. [9] included 52 trials of 1646 patients with pancreatic cancer and MPV invasion who underwent surgery in 1965—2003. Pancreaticoduodenectomy with MPV resection was performed in 952 (71.4%) patients, total pancreatectomy — in 321 (24.1%), subtotal pancreatectomy — in 30 (2.2%), distal pancreatectomy — in 31 (2.3%) patients. Type of surgery was unknown in 312 patients. Median survival was 13 months that was comparable with life expectancy of non-operated patients. The main reason of these results...
was high incidence of R1-procedures (39.8%). In view of these data an assumption of overestimated resectability of tumor prior to surgery may be supposed.

J. Tseng et al. [10] from the Anderson Cancer Center reported pancreaticoduodenectomy in 572 patients with MPV resection in 126 (22%) of them in 1990—2002. The operation was only performed if invasion of retropancreatic tissues, superior mesenteric artery and celiac trunk was absent. Median survival after vascular resection was 23.4 months, incidence of R0-resection - 78% that did not differ from the outcomes after pancreaticoduodenectomy without vein resection. Perhaps, so good results were obtained due to strict selection of patients and comprehensive evaluation of tumor resectability.

Table 1. Morphological types of pancreatic head cancer

<table>
<thead>
<tr>
<th>Morphological type of pancreatic head cancer</th>
<th>Pancreatectoduodenectomy, n=87</th>
<th>Pancreatectoduodenectomy with MPV resection, n=37</th>
</tr>
</thead>
<tbody>
<tr>
<td>Poorly differentiated ductal adenocarcinoma</td>
<td>17</td>
<td>7</td>
</tr>
<tr>
<td>Moderately differentiated ductal adenocarcinoma</td>
<td>44</td>
<td>20</td>
</tr>
<tr>
<td>Highly differentiated ductal adenocarcinoma</td>
<td>9</td>
<td>3</td>
</tr>
<tr>
<td>Mucinous adenocarcinoma</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Undifferentiated carcinoma with osteoclast-like giant cells</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>Undifferentiated (anaplastic) ductal cancer</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Neuroendocrine cancer</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>IPMN - adenocarcinoma</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>Mixed variant of the structure (colloid, acinar and neuroendocrine)</td>
<td>1</td>
<td>—</td>
</tr>
</tbody>
</table>

Fig. 2. MPV resection modes. 1. Tangential resection of MPV within confluence followed by lateral suture (a); patch repair (b). 2. Circular resection of MPV with replacement and restoration of splenic vein ostium. 3. Circular resection of superior mesenteric vein with end-to-end anastomosis.
Tumor contact with lateral wall of the vein does not always indicate true invasion [11]. Six X-ray classifications have been developed since 1996 in order to evaluate the probability of vascular invasion [5]. The following criteria are used as reference standards:

1. Proximity of tumor and vessel (presence of fatty tissue or pancreatic tissue with normal characteristics, as well as the shape of the contact contour - convex, concave or irregular)
2. Length of the contact (mm)
3. Coverage of the vessel (degrees)

MPV invasion is indisputable in case of circular involvement of the vessel, thrombosis/occlusion of the vein can indirectly indicate arterial invasion even in the absence of CT-visible contact [12].

Marinelli’s classification has the highest diagnostic value (sensitivity 96% and specificity 100%) [5] (Table 2).

In our opinion, Klauss’s classification is less convenient for practice [5]. According to our experience, we can confidently say that the value of CT significantly exceeds intraoperative assessment of vein invasion probability. Accurate preoperative diagnosis of superior mesenteric artery and celiac trunk invasion is the key to determining the optimal treatment strategy and for long-term outcomes.

In our opinion, various additional factors should be considered regarding oncologic indications for pancreateoduodenectomy with vein resection: 1) «mellow» pancreas calls into question the possibility of MPV resection since postoperative pancreatitis and pancreatic fistula is likely to be associated with vein thrombosis or bleeding; 2) patients who are scheduled for MPV resection should be anticipatorily hospitalized to examine blood coagulation system; 3) vascular surgeon should perform vascular repair in multi-field hospitals especially in case of advanced vascular reconstruction. We tried to preserve the ostium of splenic vein during superior mesenteric and portal veins resection if this did not contradict oncological requirements, tangential resection of MPV veins was applied. Anastomosis of prosthesis with splenic vein in end-to-side fashion was formed if circular resection of MPV with orifice of splenic vein was required. In our opinion, this type of vascular repair should be preferred. We believe that preserved blood flow through splenic vein into portal system reduces the likelihood of thrombosis of the prosthesis due to advanced blood flow and subsequently prevents hypertension in gastric veins. However, there is no clear opinion on this matter. Y. Ono reported long-term complications due to segmental (left-sided) portal hypertension in 3 out of 43 patients (7%) after pancreateoduodenectomy and MPV resection followed by splenic vein ligation. Surgical treatment including splenectomy in 2 cases was required [13]. At the same time, Hattori and colleagues reported similar early and long-term outcomes in 81 patients after pancreateoduodenectomy with splenic vein ligation and 60 patients without vein occlusion [14]. H. Tanaka et al. [15] obtained similar results.

Prevention of postoperative pancreatitis is obligatory after pancreatectomy especially in case of vein resection. Somatostatin analogues administration is still debatable.

**Fig. 3.** Kaplan—Meier curve, postoperative survival.

![Fig. 3. Kaplan—Meier curve, postoperative survival.](image)

**Table 2.** Marinelli’s criteria (2014) for assessing mesenteric-portal invasion

<table>
<thead>
<tr>
<th>Grade (likelihood of vascular invasion)</th>
<th>Tumor contact with vessel*</th>
<th>Length of tumor contact with vessel, mm</th>
<th>Circumferential vein involvement (°)</th>
<th>Stenosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (no)</td>
<td>A—B</td>
<td>0</td>
<td>0</td>
<td>No</td>
</tr>
<tr>
<td>2 (probably no)</td>
<td>C</td>
<td>&lt;5</td>
<td>0—90</td>
<td>No</td>
</tr>
<tr>
<td>3 (probably yes)</td>
<td>C—D</td>
<td>&gt;5</td>
<td>0—90</td>
<td>Flattened</td>
</tr>
<tr>
<td>4 (yes)</td>
<td>D</td>
<td>&gt;5</td>
<td>90—180</td>
<td>Occlusion</td>
</tr>
<tr>
<td>E—F</td>
<td>—</td>
<td>&gt;180</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Note: * — Loyer’s criteria (1996). Type A — fat plane separates tumor and/or normal pancreatic parenchyma from adjacent vessels; Type B — normal parenchyma separates tumor from adjacent vessels; Type C — hypodense tumor is inseparable from adjacent vessels, points of contact form a convexity against vessels; Type D — Hypodense tumor is inseparable from adjacent vessels, points of contact form a concavity against vessels; Type E — Hypodense tumor encircles adjacent vessels; Type F — Tumor occludes vessels.

---
issue of surgical pancreatology. Metaanalysis of 21 trials and 2348 patients confirmed significantly less incidence of postoperative complications in group of somatostatin analogues administration [16]. On the other hand, there are data about no effect of these drugs on the occurrence of pancreatic fistula. So, further trials are necessary to determine the role of synthetic somatostatin analogues [17].

Recent metaanalyses reported worse immediate and long-term outcomes of pancreaticoduodenectomy with MPV resection compared with isolated pancreaticoduodenectomy. F. Giovinazzo et al. [18] has analyzed 27 trials and 9005 patients with pancreatic cancer, 1587 of them underwent MPV resection. Postoperative mortality (3.9% vs. 3.0%) and incidence of non-radical operations (37% vs. 30.9%) were significantly higher in vein resection group.

Median survival was also worse in this group (14.3 vs. 19.5 months; p = 0.063). R. Bell et al. [19] reported similar conclusions in analysis of 4145 patients after pancreaticoduodenectomy for pancreatic head cancer; MPV resection was required in 1207 cases. Postoperative mortality (6% vs. 4%) and incidence of non-radical operations (37% vs. 32%) were higher while 5-year survival (3% vs. 8%; p = 0.002) was significantly lower in vein resection group.
The search of optimal treatment strategy for pancreatic head cancer with vein invasion and close adherence of tumor to celiac trunk and superior mesenteric artery was realized within the concept of «borderline resectable pancreatic cancer» based on CT-data. For the first time this proposal was announced at the Anderson Cancer Center (USA) [21]. Later, advanced criteria for borderline resectable pancreatic cancer were developed by American Hepato-Pancreato-Biliary Association (AHPBA) in collaboration with Society of Surgical Oncology and Society for Surgery of the Alimentary Tract. These criteria were also independently determined by National Comprehensive Cancer Network (Fig. 4).

The concept of «borderline resectable pancreatic cancer» suggests selection of patients with unclear CT-data of retroperitoneal invasion but high likelihood of this event. At the same time, acceptable deadline for CT is 4 weeks prior to surgery. Neoadjuvant therapy is supposed for borderline resectable pancreatic cancer with following surgery if growth of tumor is absent [7].

Validity of this postulate has not been yet proved. R. Casadei et al. [22] and H. Golcher et al. [23] compared immediate surgery and preoperative neoadjuvant chemotherapy for resectable pancreatic cancer in randomized trials. Significant differences were absent in these groups and trials were prematurely terminated.

E. Versteijne et al. [24] in metaanalysis analyzed 38 retrospective trials and 3484 patients with borderline resectable pancreatic cancer. In overall group of patients who received neoadjuvant therapy alone or in combination with surgical treatment median survival was 18 months. Neoadjuvant chemotherapy was followed by surgery in 66% of patients, median survival was 26.1 months. Median survival was 15 months in the group of primary surgical treatment.

**Conclusion**

Combined treatment of patients with pancreatic head cancer followed by MPV invasion and borderline resectable cancer requires further intensive study. Primary pancreaticoduodenectomy with MPV resection in patients with pancreatic head cancer is absolutely justified if circular involvement of the vein, tumor contact with superior or mesenteric artery or celiac trunk over half of circumference of the vessel are absent. Vein resection may be advisable to achieve R0-resection.

**REFERENCES**

7. Под ред. Дьямова М.Н. «Онкология. Клинические рекоменда- ции» НИИ РОНЦ им. Блохина РАМН. С.680.

TO CITE THIS ARTICLE: