https://doi.org/10.33878/2073-7556-2024-23-4-57-64

Postoperative outcomes of pancreatoduodenaectomy with colon resection

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ABSTRACT *AIM: to assess early results of pancreatoduodenalectomy with colon resection for cancer.*
PATIENTS AND METHODS: a retrospective cohort two-center controlled study included 927 patients. The first group included 95 patients after pancreatoduodenalectomy with colon resection. The second group included 832 patients who underwent pancreatoduodenalectomy without resection of adjacent organs. The first group was divided into two subgroups: the first subgroup is patients with malignant neoplasms of the colon — 42, the second subgroup is patients with malignant neoplasms of other sites — 53.
RESULTS: the group of patients with pancreatoduodenalectomy and colon resection was significantly more often assessed according to the ECOG 2–3 and ASA 3 (52/95 (54.7%) vs 63/669 (9.4%), p < 0.001 and 25/95 (26.3%) vs 104/669 (15.5%), respectively). The postoperative morbidity rate, as well as their class according to Clavien-Dindo, was homogeneous in both groups. The postoperative mortality rate was higher in the group of pancreatoduodenalectomy with colon resection (13/42 (31.0%) vs 49/832 (5.9%), p = 0.004). When comparing with subgroups, the postoperative mortality rate was comparable between patients after pancreatoduodenalectomy with colon resection for colon cancer and pancreatoduodenalectomy without resection of adjacent organs (3/42 (7.1%) vs 49 / 832 (5.9%), p = 0.7), and was significantly higher in the pancreatoduodenalectomy with colon resection (10/53 (18.9%) vs 49/832 (5,9%), p < 0.001).
CONCLUSION: patients in the pancreatoduodenalectomy with colon resection group are clinically more severe, and the operation itself is accompanied by a high rate of postoperative morbidity, but a comparable with pancreatoduodenalectomy in a standard volume, without resection of adjacent organs. Pancreatoduodenalectomy with colon resection for colon cancer is also associated with a comparable rate of postoperative mortality with standard pancreatoduodenalectomy, while pancreatoduodenalectomy with colon resection for cancer of other locations is characterized by a significantly higher level of postoperative mortality.

KEYWORDS: *pancreatoduodenectomy, colorectal cancer, pancreatic cancer, multivisceral surgery, postoperative morbidity*

CONFLICT OF INTEREST: *the authors declare no conflict of interest*

FOR CITATION: Egorov V.I., Kotelnikov A.G., Patyutko Yu.I., Akhmetzyanov F.Sh., Podluzhny D.V. Valiev N.A., Polyakov A.N., Kudashkin N.E., Kuzmichev D.V. Postoperative outcomes of pancreatoduodenaectomy with colon resection. *Koloproktologia.* 2024;23(4):57–64. (in Russ.). https://doi.org/10.33878/2073-7556-2024-23-4-57-64

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Received — 20.08.2024 *Revised — 05.09.2024* *Accepted for publication — 01.11.2024*

INTRODUCTION

Pancreatoduodenal resection (PDR) is the main type of surgery for patients with malignant neoplasms of the periampular zone [1]. This procedure is traumatic and is accompanied by a high rate of postoperative morbidity, reaching 63%, and a mortality rate of 3–6% [2,3]. PDR can also be performed as part of multivisceral procedure, when, in addition to removing the pancreatoduodenal complex, the operation is combined with resection and/or removal of other organs not included in the standard intervention [4,5]. Colorectal resection is often found in the structure of multivisceral procedures (MVO) with PDR, in its various volumes: right hemicolectomy, resection of the

transverse colon, segmental atypical colorectal resection and others [6,7]. Indications for MVO, including PDR with colorectal resection, may be local advanced colorectal cancer with involvement of the duodenum and/or the head of the pancreas (PH); tumors of the periampular zone or beyond with in growth into the colon or its mesentery; primary-multiple synchronous tumors (PMST), when neoplasmsin the periampular zone and large intestine are combined [7–9].

PDR with colorectal resection is a great threat to the patient, as it is accompanied by a higher rate of postoperative morbidity and mortality, reaching 73% and 25%, respectively [10,11].

Colorectal cancer, with which there is a need for MVO with PDR, is often accompanied by intestinal obstruction, colo-duodenal fistula, abscess, intoxication, anemia, bleeding, perforation [12,13]. Complications of the tumor significantly worsens the patient's condition, often requires urgent admission in order to stop these clinical manifestations and make it difficult or impossible for neoadjuvant antitumor drug therapy [14]. In this regard, surgery for these patients is often seen as the only and main option for the first stage of specialized treatment [15].

THE AIM OF THE STUDY

To assess early results of pancreatoduodenal resection with colorectal resection.

PATIENTS AND METHODS

The retrospective cohort two-center study included 95 patients with PDR and colorectal resection (January 2011 — April 2024). The control group was selected for the same period, in whom PDR without resection of adjacent organs was performed — 832 cases. Thus, a total of 927 patients were included in the study. Additionally, the group of patients who had undergone PDR with colorectal resection was divided into subgroups depending on the tumor site: the first subgroup consisted of patients with colorectal cancer — 42 cases, the second subgroup consisted of patients with other tumors — 53 people.

The clinical and demographic indicators of patients (gender, age, age category according to WHO, BMI, ECOG, ASA), comorbidities, morbidity from the primary tumor, indicators of the early postoperative period, morbidity were analyzed. The 30-day postoperative mortality was assessed as well.

Statistical analysis

The statistical analysis was carried out using the StatTech v. 4.3.3 program (Stattech LLC, Russia). Categorical data were described with absolute values and percentages. Quantitative data were described using median (Me) and lower and upper quartiles (Q1-Q3). The comparison of the two groups by quantitative indicators was performed using the Mann-Whitney U-test. The comparison of percentages in the analysis of four-field conjugacy tables was performed using Pearson's c^2 test (for values of the expected phenomenon greater than 10), Fisher's exact test (for values of the expected phenomenon less than 10).

The comparison of percentages in the analysis of multi-field conjugacy tables was performed using Pearson's c^2 test. The differences in the indicators were considered statistically significant at the level of $p < 0.05$.

RESULTS

Colorectal procedures were performed: right hemicolectomy — 62, other colorectal procedures — 33. A comparative analysis of the main clinical and demographic indicators of patients is presented in Table 1.

As follows from Table 1, the following significant differences were revealed — in the group of patients with colorectal resection there were more elderly patients (*16.8% vs. 5.9%, p < 0.001*). However, when assessing the median age, there were no differences: *63 (54–72) years* versus *62 (55–67) years, respectively, (p = 0.21)*; Also, patients in this group were more often rated 2–3 points by ECOG

Table 1. *Analysis of clinical and demographic indicators of patients*

Indicators	PDR with colorectal resection N = 95	PDR without resection of adjacent organs N = 832	*p*-value
Gender Male Female	51 (53.7) 44 (46.3)	376 (45.2) 456 (54.8)	0.12
Age groups according to the WHO classification Young aged (18–44 years old) Middle aged (45–59 years) Elderly aged(60–74 years old) Senile aged (75–89 years old)	8 (8.4) 33 (34.7) 38 (40.0) 16 (16.8)	63 (7.6) 266 (32.0) 454 (54.6) 49 (5.9)	**< 0.001**
ECOG, points 0–1 2–3	43 / 95 (45.3) 52 / 95 (54.7)	606 / 669 (90.6) 63 / 669 (9.4)	**< 0.001**
ASA, class 1–2 3	70 / 95 (73.7) 25 / 95 (26.3)	565 / 669 (84.5) 104 / 669 (15.5)	**0.009**
Obesity (BMI > 30)	10 (10.5)	131 (15.7)	0.18
DM is not IC	15 (15.8)	93/661 (14.1)	0.65
DM is IC	7 (7.4)	42/661 (6.4)	0.7
IHD: AP	26 (27.4)	122/661 (18.5)	**0.041**
IHD:PICS	5 (5.3)	33/661 (5.0)	0.9
IHD: CA	12 (12.6)	47/660 (7.1)	0.06
CVA	2 (2.1)	22/661 (3.3)	0.52
Hypertonia	55 (57.9)	368/660 (55.8)	0.7
Tumor complications	80 (84.2)	607 (73.0)	**0.018**
Anemia	56 (58.9)	85 (10.2)	**< 0.001**
Tumor stenosis	28 (29.5)	21 (2.5)	**< 0.001**
Intoxication/abscess	18 (18.9)	5 (0.6)	**< 0.001**
Jaundice	34 (35.8)	578 (69.5)	**< 0.001**

Note: DM — diabetes mellitus, IHD — ischemic heart disease, AP — angina pectoris, PICS — post-infarction cardio-sclerosis, CA — cardiac arrhythmia, CVD — cerebrovascular disease, HT — hypertension, IC — insulin-consuming

scale (*54.7% vs. 9.4%, p < 0.001*), and were more often class 3 on the ASA scale (*26.3% vs. 15.5%, p = 0.009*), they were more likely to have anemia (*58.9% vs. 10.2%, p < 0.001*) and ischemic heart disease (IHD): CA (*27.4% vs. 18.5%, p = 0.04*), more often there were tumor complications — tumor stenosis (*29.5% vs. 2.5%, p < 0.001*), intoxication/abscess (*18.9% vs. 0.6%, p < 0.001*). The groups were comparable in the other clinical and demographic features.

As can be seen in Table 2, the groups of patients did not significantly differ in the rate of postoperative morbidity and their class according to Clavien-Dindo (class 1–2 versus class 3 or more). In the group of patients with colorectal resection, intestinal fistula was significantly more common (*6.3% vs. 2.5%, p = 0.039*), intraperitoneal abscess (*9.5% vs. 4.1%, p = 0.019*), pneumonia (*7.4% vs. 3.2%, p = 0.043*) and gastrostasis were less common (*26.3% vs. 37.9%, p = 0.027*). PDR with colorectal resection were significantly more often accompanied by postoperative mortality (*13.7% vs. 5.9%, p = 0.004*).

PDR with colorectal resections were longer (*median 320 (250–410) minutes vs 300 (240–325), p = 0.004*). Blood loss between the first and second groups was insignificant (*600 (250–1500) ml versus 500 (250–1000), p = 0.416*).

Postoperative mortality was assessed in subgroup analysis. The first subgroup included 42 (44.2%) patients, of whom 36 (85.7%) had locally advanced colorectal cancer with involvement of duodenum and/or pancreas head, and 6 (14.3%) patients had primary multiple synchronous

Table 2. *Early outcomes of surgeries*

Indicators	PDR with colorectal resection N = 95	PDR without resection of adjacent organs N = 832	*p*-value
Clavien-Dindo Class 1–2 Class ⩾ 3	25 (26.3) 39 (41.1)	274 (32.9) 307 (36.9)	0.4
Early morbidity	64 (67.4)	581 (69.8)	0.6
PDA leakage	14 (14.7)	120 (14.5)	0.9
BDA leakage	8 (8.4)	63 (7.6)	0.7
Pancreatonecrosis	2 (2.1)	24 (2.9)	0.6
Intestinalfistula	6 (6.3)	21 (2.5)	**0.039**
Intra-abdominal abscess	9 (9.5)	34 (4.1)	**0.019**
Bleeding from the surgery site	7 (7.4)	57 (6.9)	0.8
Bleeding from gastrointestinal ulcers	4 (4.2)	49 (5.9)	0.4
Pancreatic fistula BL Type B Type C	 4 (4.2) 14 (14.7) 7 (7.4)	 21 (2.5) 189 (22.7) 28 (3.4)	0.07
Relaparotomy	9 (9.5)	51 (6.1)	0.2
Pneumonia	7 (7.4)	27 (3.2)	**0.043**
Diabetes mellitus	7 (7.4)	58 (7.0)	0.8
Gastrostasis	25 (26.3)	315 (37.9)	**0.027**
Mortality	13 (13.7)	49 (5.9)	**0.004**

Note: PDA — pancreadigestive anastomosis, BDA — biliodigestive anastomosis, GIT — gastrointestinal tract

tumors: periampular malignancies combined with colorectal cancer. The second subgroup included 53 (55.8%) patients with cancer of different sites, with involvement of the colon or its mesentery. Of the 53 patients who underwent PDR with colorectal resection with cancer of different sites, 28 (52.8%) patients had PH ductal cancer, six (11.3%) ones had secondary malignancy of the pancreas head, three (5.7%) ones had cancer of the large duodenal papilla (LDP), five (9.4%) ones had gastric MNs, four (7.5%)ones hadmalignancy in duodenum, two (3.8%) ones had a neuroendocrine tumor of the pancreas head, two (3.8%) ones had cancer of the distal choledochus, two (3.8%) ones had gallbladder cancer, and one (1.9%) patient had kidney cancer. A comparative analysis is presented in Table 3.

As can be seen from Table 3, the patients were comparable in most parameters. Patients with colorectal cancer compared to the group of patients with a different sites were significantly more likely to be rated 2–3 points by ECOG scale (*78.6% vs. 35.8%, p < 0.001*), they were significantly more likely to have hypertonia (*67.9% vs. 45.2%, p = 0.026*), anemia as a tumor morbidity (*78.6% vs. 43.4%, p < 0.001*), intoxication/abscess (*35.7% vs. 5.7%, p < 0.001*). Mechanical jaundice was more common in the subgroup of patients with other malignancies (*56% vs. 9.5%, p < 0.001*), which is rather due to the fact that patients with tumors of the pancreas head and periampullary zone prevailed in this subgroup.

When analyzing the operation time, intraoperative blood loss in the subgroups with colorectal cancer and malignancies of another sites, it was not possible to reveal significant differences (*285 (242–380) minutes versus 330 (260–420), p = 0.14 and 550 (250–1475) ml versus 600 (300–1500), p = 0.6*, respectively).

As shown in Table 4, there were no significant differences in the immediate results between the two subgroups. However, it should be noted that the mortality rate in the subgroup of another localization was almost 3 times higher than in the subgroup of colon cancer (*18.9% vs. 7.1%, p = 0.13*). It also draws attention to the fact that the rate of PDA, BDA leakage, pancreatic necrosis, pancreatic fistula, including fistula C, intra-abdominal

Table 3. *Analysis of clinical and demographic indicators of patients*

Indicators	Tumor site		*p*-value
	Colorectal cancer, N = 42	Malignancy of a different sites, N = 53	
Gender			0.8
Male	23 (54.8)	28 (52.8)	
Female	19 (45.2)	25 (47.2)	
Age group			0.6
Up to 69 years old	29 (69.0)	34 (64.2)	
Over 70 year sold	13 (31.0)	19 (35.8)	
Obesity (BMI > 30)	6 (14.3)	4 (7.5)	0.3
ECOG			**< 0.001**
0-1	9 (21.4)	34 (64.2)	
2-3	33 (78.6)	19 (35.8)	
ASA			0.6
1-2	30 (71.4)	40 (75.5)	
3	12 (28.6)	13 (24.5)	
DM is not IC	5 (11.9)	10 (18.9)	0.4
DM is IC	2 (4.8)	5 (9.4)	0.4
IHD: AP	14 (33.3)	12 (22.6)	0.2
IHD: PICS	1 (2.4)	4 (7.5)	0.3
IHD: CA	5 (11.9)	7 (13.2)	1.0
CVA	0 (0.0)	2 (3.8)	0.5
HT	19 (45.2)	36 (67.9)	**0.026**
Tumor morbidity	37 (88.1)	43 (81.1)	0.4
Anemia	33 (78.6)	23 (43.4)	**< 0.001**
Tumor stenosis	16 (38.1)	12 (22.6)	0.10
Intoxication/Abcess	15 (35.7)	3 (5.7)	**< 0.001**
Mechanical jaundice	4 (9.5)	30 (56.6)	**< 0.001**
Number of combinations			0.7
PDR + 1 organ	2 (76.2)	42 (79.2)	
PDR + ⩾ 2 organs	10 (23.8)	11 (20.8)	

abscess, postoperative bleeding in the surgical area was higher in the subgroup of patients with malignancies of another sites, although the differences turned out to be insignificant.

In an intergroup comparison, the chances of postoperative mortality in the subgroup of patients with malignancies of a different sites were 3.7 times higher, compared with the group of patients who underwent standard PDR, the differences were significant (*18.9% vs. 5.9%, p < 0.001*). Mortality in the group of patients who underwent standard PDR and PDR with colorectal resection for colon cancer was comparable (*5.9% vs. 7.1%, p = 0.7*).

As can be seen from Table 5, the main cause of mortality was morbidity from the pancreatic stump, in particular, the leakage of pancreodigestive anastomosis, which occurred only in the subgroup of patients with malignancies of a different site (6 out of 10 cases — 60%).

In the group of deceased patients after PDR with colorectal resection for non-colon cancer, the risk factors for postoperative mortality were morbidity from the pancreatic stump (leakage of pancreodigestive anastomosis, pancreonecrosis, bleeding from the area of surgery, pancreatic fistula type C), the fact of relaparotomy and pneumonia (Table 6). At the same time, the analysis of mortality depending on gender, age, and BMI showed no significant differences.

DISCUSSION

One of the problems of assessment the results of PDR with colorectal resection, including for colorectal cancer, is that almost all studies have a small sample (with rare exceptions). The maximum is slightly more than two dozen cases, and therefore a comprehensive trial of the early and late

Table 4. *Early outcomes of operations*

Indicators	Tumor site		*p*-value
	Colorectal cancer, N = 42	Malignancy of a different site, N = 53	
Clavien-Dindo Class 1–2 Class ⩾ 3	11 (26.2) 13 (31.0)	14 (26.4) 26 (49.1)	0.11
Early morbidity	24 (57.1)	40 (75.5)	0.05
PDA leakage	4 (9.5)	10 (18.9)	0.2
BDA leakage	2 (4.8)	6 (11.3)	0.2
Pancreatonecrosis	0 (0.0)	2 (3.8)	0.5
Pancreatic fistula	7 (16.7)	18 (34.0)	0.057
Intestinal fistula	3 (7.1)	3 (5.7)	1.0
Intra-abdominal abscess	1 (2.4)	8 (15.1)	0.07
Bleeding from the surgical site	1 (2.4)	6 (11.3)	0.12
Bleeding from gastrointestinal ulcers	1 (2.4)	3 (5.7)	0.6
Pancreatic fistula BL Type B Type C	 2 (4.8) 5 (11.9) 0 (0.0)	 2 (3.8) 9 (17.0) 7 (13.2)	0.07
Relaparotomy	2 (4.8)	7 (13.2)	0.2
Pneumonia	1 (2.4)	6 (11.3)	0.12
Diabetes mellitus	3 (7.1)	4 (7.5)	1.00
Gastrostasis	10 (23.8)	15 (28.3)	0.6
Postoperative mortality	3 (7.1)	10 (18.9)	0.13

Table 5. *Causes of postoperative mortality in a group of patients with colon resection*

Cause	n	%
PDA leakage	6	46.1
Acute myocardial infarction	3	23.1
Gastric perforation	1	7.7
DIC syndrome, bleeding	1	7.7
Multipleorgan failure	1	7.7
Thrombosis of mesenteric vessels	1	7.7
Total	**13**	**100**

Table 6. *Analysis of postoperative mortality in the group*

Indicators	Postoperative mortality		*p*-value
	Yes, N = 10	No, N = 43	
Early morbidity	10 (100.0)	30 (69.8)	0.09
PDA leakage	5 (50.0)	5 (11.6)	**0.014**
Pancreatonecrosis	2 (20.0)	0 (0.0)	**0.033**
Pancreatic fistula	6 (60.0)	12 (27.9)	0.07
Intestinal fistula	1 (10.0)	2 (4.7)	0.4
Intra-abdominal abscess	5 (50.0)	3 (7.0)	**0.004**
Bleeding in the surgical site	5 (50.0)	1 (2.3)	**< 0.001**
Pancreatic fistula BL Type B Type C	 0 (0.0) 0 (0.0) 6 (60.0)	 2 (4.7) 9 (20.9) 1 (2.3)	**< 0.001**
Relaparotomy	5 (50.0)	2 (4.7)	**0.002**
Pneumonia	5 (50.0)	1 (2.3)	**< 0.001**

results is not possible [4–11]. That is why we combined the experience of two large Russian oncological institutions, which allowed us to assemble the largest group of patients to study the results of PDR with colorectal resection in both colorectal cancer and malignancies of other sites.

PDR, even without resection of adjacent organs, is accompanied by a high rate of postoperative morbidity and mortality: 63% and 3–6%, respectively [2,3]. The combination of PDR with colorectal resection can significantly increase the risks of morbidity and mortality, which can reach 25% [10]. In this regard, some authors very cautiously conclude that it is advisable to perform such procedures [10]. In this study, we obtained an overall postoperative mortality rate of 13.7% among all patients after PDR with colorectal resection. Also, it was found that the mortality in the group of patients with colorectal cancer was the same as the mortality in the group of patients after PDR without resection of adjacent organs (*7.1% vs. 5.9%, p = 0.738, 95% CI: 0.367–4.119*). This allows us to recommend these procedures, both the local advanced colorectal cancer with involvement of duodenum and/or pancreas, as well as with PMST when colorectal cancer is combined with malignancy of the periampular area.

It is believed that the ASA is fundamental for predicting morbidity [16,17]. The groups and subgroups of patients with colorectal resection compared with each other were comparable in ASA points. At the same time, when compared with the group of patients who had undergone PDR without resection of adjacent organs, the latter were significantly less likely to be assessed according to the degree of risk of ASA 3 (*15.5% vs. 26.3%, p = 0.009, 95% CI: 1,174–3,206*).

Treatment of local advanced tumors is recommended to begin with perioperative drug antitumor therapy [18,19]. However, patients who need

to perform PDR with colorectal resection often have a tumor complication, which requires urgent admission and surgical treatment [14,15]. In this situation, neoadjuvant therapy is barely impossible. This study showed that in the group of patients who underwent PDR with colorectal resection, patients had significantly worse ECOG status, which is primarily due to the fact that these patients were significantly more likely to have tumor complication as bleeding, anemia, intoxication/abscess, intestinal obstruction. Neoadjuvant chemotherapy was started only in 5 (5.3%) of 95 patients.

The obtained differences in ASA and ECOG indicate that patients who need MVO with PDR with colorectal resection are initially poor.

The main complication after PDR is pancreatic fistula, the rate of which can exceed 30% [20,21]. In the comparative analysis, we showed that there were no significant differences in both the rate of PF and its types in both groups. An additional analysis revealed that in the subgroup of patients with PDR with colorectal resection for malignancies of a different sites, compared with the group who underwent PDR without resection of adjacent organs, pancreatic fistula type C developed more often (*13.2% vs. 3.4%, p = 0.004*), the difference was significant. Complications of the pancreatic stump, including pancreatic fistula type C, were a negative prognostic factor of mortality.

The mortality rate in the group of patients who underwent PDR with colorectal resection for malignancies of different sites was 18.9%. The difference in mortality was significant when compared with the PDR group without resection of adjacent organs. In a detailed analysis in this group, we found that the main independent risk factor for postoperative mortality was complication of the pancreatic stump, which occurred in 60% of deceased patients. Relaparotomy in this group was a factor of mortality. At the same time, there were no fatal cases associated with complication of the pancreatic stump in the group of patients with colorectal cancer.

CONCLUSION

Patients requiring PDR with colorectal resection are clinically poor, and the surgery is accompanied by a high rate of postoperative morbidity, but a comparable level compared to the standard PDR without resection of adjacent organs. PDR with colorectal resection for colorectal cancer is followed by a comparable level of postoperative mortality compared to PDR without resection of adjacent organs.

PDR with colorectal resection for the so-called malignancies of different sites (not colorectal cancer) is characterized by a significantly higher level of postoperative mortality, primarily against the background of a significantly high rate of morbidity from the pancreatic stump.

AUTHORS CONTRUBUTION

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