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Clinical and Functional Characteristics of Patients Undergoing Multivisceral Surgery With Pancreaticoduodenectomy

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ABSTRACT

BACKGROUND: Multivisceral procedures involving pancreaticoduodenectomy are associated with postoperative complications that worsen the general condition of patients, hinder specialized treatment initiation, and increase treatment-related risks.
AIM: To investigate the clinical and functional characteristics of patients undergoing multivisceral surgery with pancreaticoduodenectomy.
MATERIAL AND METHODS: The study included 251 patients who underwent multivisceral resection with pancreaticoduodenectomy (group 1) for tumors of various localizations between January 2011 and April 2024 at two institutions: National Medical Research Center of Oncology, named after N.N. Blokhin, and Republican Clinical Oncological Dispansery, named after Prof. M.Z. Sigal. The control group comprised 832 patients who underwent standard-volume pancreaticoduodenectomy (group 2) at the same institutions during the same period. The patients' sex, age, ECOG performance status, ASA physical status classification, body mass index, comorbidities, tumor-related complications, and characteristics of the pancreatic remnant, which are major determinants of postoperative complications, were evaluated. Continuous variables are described using the median and lower and upper quartiles (Q1–Q3). Categorical variables are presented as absolute numbers and percentages. The continuous variables of the two groups were compared using the Mann–Whitney U test. Comparison of percentage distributions in 2×2 contingency tables was performed using Pearson's χ^2 test. Differences were considered significant at p <0.05.
RESULTS: Group 1 had a significantly higher proportion of patients with ECOG scores of 2 (30.3 vs. 8.7%, p <0.001) and 3 (4.4 vs. 0.7%, p <0.001), a lower prevalence of obesity (8.8 vs. 15.7%), and fewer elderly patients (38.6 vs. 54.6%). Anemia (38.2 vs. 10.2%, p <0.001), tumor-related stenosis (19.5 vs. 2.5%, p <0.001), and enteric fistula or peritumoral abscess (10.4 vs. 0.6%, p <0.001) were significantly more common in group 1, whereas obstructive jaundice was more frequent in group 2 (47.8 vs. 69.5%, p <0.001). The pancreatic duct diameter was significantly smaller in group 1 (0.3 mm [0.2–0.4] vs. 0.4 mm [0.2–0.5], p <0.001), whereas pancreatic parenchymal density did not significantly differ between the groups.
CONCLUSION: Patients undergoing multivisceral surgery that includes pancreaticoduodenectomy represent a clinically more complex cohort with poorer overall functional status compared with those undergoing standard pancreaticoduodenectomy without adjacent organ resection.

Keywords: multivisceral surgery; pancreaticoduodenectomy; pancreatic cancer; anesthetic risk.

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ОРИГИНАЛЬНОЕ ИССЛЕДОВАНИЕ
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Клинико-функциональные особенности пациентов, перенёсших мультивисцеральную операцию с панкреатодуоденальной резекцией

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АННОТАЦИЯ

Актуальность. Мультивисцеральные операции с панкреатодуоденальной резекцией часто сопровождаются осложнениями, что значительно ухудшает общее состояние больных и затрудняет в целом начало любого специализированного лечения и несёт риски в процессе его проведения.

Цель. Изучение клинико-функциональных особенностей больных, перенёсших мультивисцеральную операцию с панкреатодуоденальной резекцией.

Материал и методы. Включены все пациенты (251 больной), которые перенесли мультивисцеральную операцию с панкреатодуоденальной резекцией (1-я группа) по поводу опухолей различных локализаций с января 2011 г. по апрель 2024 г. в двух учреждениях: НМИЦ онкологии им. Н.Н. Блохина и ГАУЗ «РКОД МЗ РТ им. проф. М.З. Сигала». Для группы контроля выбрана когорта из 832 пациентов, перенёсших в указанный период панкреатодуоденальную резекцию в стандартном объёме (2-я группа) в указанных клиниках. Оценивали: пол, возраст, состояние по шкале ECOG, шкале риска ASA, индекс массы тела, сопутствующие заболевания, осложнения опухоли, а также характеристики культи поджелудочной железы в значительной степени определяющие послеоперационные осложнения. Количественные показатели описывали с помощью медианы (Me) и нижнего и верхнего квартилей (Q1–Q3). Категориальные данные описывали с указанием абсолютных значений и процентных долей. Сравнение двух групп по количественному показателю выполняли с помощью U-критерия Манна–Уитни. Сравнение процентных долей при анализе четырёхпольных таблиц сопряжённости производили с помощью критерия хи-квадрат Пирсона. Различия показателей считали статистически значимыми при уровне p <0,05.

Результаты. Достоверное различие выявлено по следующим параметрам: в 1-й группе больные чаще имели оценки по шкале ECOG 2 (30,3 против 8,7%, p <0,001) и ECOG 3 (4,4 против 0,7%, p <0,001); ожирение отмечалось реже (8,8 против 15,7%); доля лиц пожилого возраста была ниже (38,6 против 54,6%). В 1-й группе достоверно чаще встречалась анемия (38,2 против 10,2%, p <0,001), опухолевый стеноз (19,5 против 2,5%, p <0,001), внутренний кишечный свищ/параканкрозный абсцесс (10,4 против 0,6%, p <0,001), во 2-й группе чаще наблюдалась механическая желтуха (47,8 против 69,5%, p <0,001). Диаметр панкреатического протока был достоверно меньше в 1-й группе [0,3 мм (0,2–0,4) против 0,4 мм (0,2–0,5), p <0,001], в то время как плотность железы значимо не различалась в обеих группах.

Заключение. Пациенты, которым проводили мультивисцеральную операцию, включающую панкреатодуоденальную резекцию, представляют собой контингент клинически более тяжёлых больных по общему физическому состоянию по сравнению с больными после панкреатодуоденальной резекции без резекции смежных органов.

Ключевые слова: мультивисцеральная операция; панкреатодуоденальная резекция; рак поджелудочной железы; анестезиологический риск.

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BACKGROUND

Multivisceral resection (MVR) with pancreatoduodenectomy (PD) is a complex and traumatic surgical procedure for malignant hepatobiliopancreatoduodenal neoplasms and tumors located outside this anatomically and functionally unified system [1–5].

The main indication for MVR with PD is the extent of the tumor process that does not preclude potentially radical surgery in cases of primary chemoresistant tumors or exhausted chemotherapy options. Additionally, it may be indicated in cases of complicated progression of advanced malignancy or synchronous primary multiple tumors [6]. MVR with PD is often performed for tumors of the pancreas, right-sided colon, stomach, duodenum, extrahepatic bile ducts, and gallbladder and less commonly for tumors of the kidney and retroperitoneal space [2–5, 7–10].

Owing to its extent and the need to resect or remove organs beyond the standard scope of PD, MVR with PD carry additional risks for the patient and is accompanied by high postoperative complication and mortality rates, reaching 73% and 15%, respectively [11, 12].

Tumors requiring MVR with PD are often accompanied by various complications [13]. The most common include obstructive jaundice; bleeding; posthemorrhagic anemia; tumor-induced stenosis of the gastric outlet, duodenum, or colon; internal intestinal fistulas at the site of tumor disintegration involving the duodenum and colon; peritumoral abscess; and purulent intoxication [13]. These complications impair the patient's functional status, hindering or rendering impossible the administration of full-scale antitumor pharmacotherapy. In such cases, controlling tumor bleeding, draining a peritumoral abscess, or closing a fistula is unachievable without tumor removal [13, 14].

In these circumstances, surgery remains the only feasible initial stage of specialized treatment, which also aims to eliminate tumor-related complications [14].

In addition to tumor-related complications, decreased functional status may result from comorbidities, which increases postoperative complication and mortality risks [15].

This study aimed to identify and investigate the clinical and functional characteristics of patients who underwent multivisceral surgery with PD.

MATERIAL AND METHODS

This retrospective, two-center, controlled cohort study included patients who underwent MVR with PD (group 1) for tumors of various localizations between January 2011 and April 2024 at the N.N. Blokhin National Medical Research Center of Oncology (Ministry of Health of the Russian Federation) and Republican Clinical Oncological Dispensary named after Prof. M.Z. Sigal (Ministry of Health of the Republic of Tatarstan). The control group (group 2) comprised patients who had standard PD for malignant neoplasms (MNs) of the periampullary region without resection of adjacent organs during the same period at the same institutions.

Indications for MVR with PD included local tumor invasion of adjacent organs and tissues requiring en bloc resection of the tumor conglomerate, metastatic liver nodules, and synchronous primary tumors (i.e., coexisting malignancies of the periampullary region and other organs). Table 1 presents the tumor localizations for which the surgeries were performed.

In both groups, the most common tumor localization was MN of the pancreatic head (50.9% in group 1 and 66.5% in group 2) (Table 1). In group 1, tumors located outside the periampullary region accounted for 28.3% (71/251).

Among the 251 patients in the study group, MVR with PD was performed for primary multiple synchronous tumors in 18 patients (7.2%). In these cases, a tumor of the periampullary region was combined with an MN of the colon in six cases and with an MN of the stomach in three cases.

In group 1, the tumor stages according to the TNM classification (8th edition) were distributed as follows: stage 1, 18 cases (7.2%); stage 2, 84 cases (33.5%); stage 3, 80 cases (31.9%); and stage 4, 69 cases (27.5%). The proportion of stage 4 tumors is relatively high because in some patients, the indication for MVR with PD was the presence of metastatic tumors (e.g., pancreatic neuroendocrine tumors, secondary pancreatic tumors, and oligometastatic pancreatic cancer).

The evaluated parameters were sex, age (classified according to the World Health Organization [WHO]), performance status (assessed using the Eastern Cooperative Oncology Group [ECOG] scale), surgical risk (evaluated using the American Society of Anesthesiologists [ASA] classification), body

Table 1. Characteristics of patient groups by tumor localization

Tumor localization	Group 1 MVR with PD		Group 2 PD	
	n	%	n	%
MN of the pancreatic head	128	50.9	553	66.5
MN of the colon	36	14.3	—	—
MN of the Vater ampulla	26	10.4	157	18.9
MN of the stomach	24	9.6	—	—
MN of DU	17	6.8	36	4,3
MN of the distal common bile duct	9	3.6	84	10.1
MN of the gallbladder	5	2	—	—
MN of the kidney	3	1.2	—	—
MN of the bile ducts (excluding the common bile duct)	2	0.8	2	0.2
MN of the retroperitoneal space	1	0,4	—	—
Total	251	100	832	100

Note: MN, malignant neoplasm; DU, duodenum; MVR, multivisceral resection; PD, pancreatoduodenectomy.

mass index (BMI), comorbidities, tumor-related complications, and pancreatic remnant characteristics that influence postoperative complication risk. The diameter of the pancreatic duct and firmness of the pancreatic remnant were intraoperatively assessed by the surgeon via visual inspection and palpation, respectively.

Statistical analysis was performed using StatTech software, version 4.4.1 (StatTech LLC, Russia). Quantitative variables were described using the median and interquartile range (Q1–Q3). Categorical variables were presented as absolute numbers and percentages. The two groups for quantitative variables were compared using the Mann–Whitney U test. The Pearson chi-squared test was utilized to compare proportions in 2 × 2 contingency tables when the expected cell frequency exceeded 10. $p < 0.05$ indicated significant differences.

RESULTS

The study included 1083 patients. Group 1 comprised 251 patients who underwent MVR with PD for MNs of various localizations. Group 2 included 832 patients who underwent standard PD without resection of adjacent organs for MNs of the periampullary region (Table 1).

Table 2 summarizes the clinical and demographic characteristics of the patients in the comparative group analysis.

The median number of neoadjuvant chemotherapy courses was significantly higher in group 1 [6 (5–8) vs 5 (4–6), $p = 0.038$], whereas the median number of adjuvant chemotherapy courses did not significantly differ between the two groups [4 (3–6) vs 5 (4–6), $p = 0.253$].

The immediate outcomes for both groups was compared. No significant differences were found in the incidence of postoperative complications of Clavien–Dindo grade 3 or higher [97 (38.6%) vs 307 (36.9%), $p = 0.194$] and mortality rates [18 (7.2%) vs 49 (5.9%), $p = 0.460$]. In 9 (50%) of the 18 deceased patients, death occurred following surgery due to a type C postoperative pancreatic fistula: three patients died from sepsis, two from peritonitis, one from erosive bleeding, one from renal failure, one from acute myocardial infarction, and one from pulmonary artery thromboembolism. In the remaining 9 (50%) deceased patients, type C fistula was not observed. The causes of death in these patients included four cases of acute myocardial infarction and one case each of disseminated intravascular coagulation with bleeding, mesenteric thrombosis, pneumonia with sepsis, multiple-organ failure, and gastric perforation with peritonitis.

The median duration of surgery in Groups 1 and 2 was 295 (240–372) min and 300 (240–352.5) min, respectively ($p = 0.42$); intraoperative blood loss was 600 (250–1500) mL and 500 (250–1,000) mL, respectively ($p = 0.078$); and the median postoperative hospital stay was 19 (14–26) and 19 (15–27) days, respectively ($p = 0.49$).

The assessment of immediate outcomes following MVR with PD should consider multiple factors, including vascular resection and the number of resected or removed organs in addition to PD, extent of surgery on adjacent organs, presence and nature of tumor-related complications, and patient's functional status. These aspects will be analyzed in future studies.

DISCUSSION

PD is performed for MNs of the periampullary region and tumors of other organs located in close anatomic and topographic proximity to the pancreatoduodenal system. PD is a combined multivisceral procedure when performed for tumor pathology of non-periampullary organs—that is, along with pancreatoduodenal complex removal and tumor-affected organ resection or removal [3, 4]. This significantly increases the extent of surgery and intraoperative and postoperative risks [16, 17]. In the present study, MVR with PD was performed for MNs of non-periampullary origin in 28.3% of cases.

Currently, treatment strategies for patients with MNs are influenced by nosological indicators and the assessment of physical status using the ECOG performance scale. Along with tumor-related complications, it determines the feasibility of neoadjuvant chemotherapy [18, 19]. The present study shows that patients who underwent MVR with PD were in poorer physical condition, as reflected by higher ECOG scores, compared with those in group 2.

The impaired physical condition in group 1 was associated with the complicated course of the tumor process.

Comparative analysis revealed that the overall incidence of tumor-related complications did not significantly differ between the two groups [192/251 (76.5%) vs 607/832 (73%), $p = 0.264$]. However, the structure of complications markedly differed. Patients in group 1 more frequently experienced tumor-related bleeding of varying severity with posthemorrhagic anemia; tumor-induced stenosis of the stomach, duodenum, or colon; and internal intestinal fistula caused by tumor breakdown involving the colon and duodenum, often complicated by paracancerous abscess formation. These complications contributed to the deterioration of the patients' overall condition and higher ECOG performance status scores.

Notably, the abovementioned complications are considered indications for urgent hospital admission and their relief [20]. Moreover, despite advances in minimally invasive surgery, these complications can be managed only by eliminating all tumor manifestations. Unlike obstructive jaundice, such tumor-related complications prevent the possibility of chemotherapy [21, 22].

A higher incidence of bleeding, tumor-induced stenosis, and intestinal fistula with peritumoral abscess may be associated with tumor localization. Table 1 reveals that 23.9% of patients in group 1 had malignant neoplasms of the stomach and colon, for which such complications are more characteristic [20].

Furthermore, the more advanced stage of disease in the MVR group may have affected the patients' overall functional status.

Table 2. Clinical and demographic characteristics of patients in both groups

Parameters	Comparison groups		p
	Group 1 (*n* = 251)	Group 2 (*n* = 832)	
Sex, abs (%):			
Male	125 (49.8)	376 (45.2)	0.199
Female	126 (50.2)	456 (54.8)	
Age group, abs (%):			
≤69 years	202 (80.5)	677 (81.4)	0.751
>70 years	49 (19.5)	155 (18.6)	
WHO age category, abs (%):			
Young	35 (13.9)	63 (7.6)	$p_{(elderly)}$
Middle-aged	95 (37.8)	266 (32.0)	< 0.001
Elderly	97 (38.6)	454 (54.6)	
Senile	24 (9.6)	49 (5.9)	
Obesity, abs (%):			
(BMI >30)	22 (8.8)	131 (15.7)	0.005
ECOG, abs (%):			
0	22 (8.8)	88 (13.2)	
1	142 (56.6)	518 (77.4)	$p_{(ECOG2)}$ < 0.001
2	76 (30.3)	58 (8.7)	$p_{(ECOG3)}$ < 0.001
3	11 (4.4)	5 (0.7)	
ASA, abs (%):			
1	9 (3.6)	15 (2.2)	
2	201 (80.1)	550 (82.2)	0.488
3	41 (16.3)	104 (15.5)	
Controlled DM, abs (%)	28 (11.2)	93 (14.1)	0.247
Insulin-dependent DM, abs (%)	13 (5,2)	42 (6.4)	0.506
CAD, abs (%)	79 (31.5)	183 (27.7)	0.259
CAD with SA, abs (%)	51 (20.3)	122 (18.5)	0.522
CAD with prior MI, abs (%)	6 (2.4)	33 (5.0)	0.083
CAD with cardiac arrhythmias, abs (%)	23 (9.2)	47 (7.1)	0.301
CVD, abs (%)	8 (3,2)	22 (3.3)	0.915
HTN, abs (%)	123 (49.0)	368 (55.8)	0.068
Tumor-related complications, abs (%)	192 (76.5)	607 (73.0)	0.264
Hemorrhage/anemia, abs (%)	96 (38.2)	85 (10.2)	< 0.001
Tumor-related stenosis, abs (%)	49 (19.5)	21 (2.5)	< 0.001
Intestinal fistula/abscess/intoxication, abs (%)	26 (10.4)	5 (0.6)	< 0.001
Obstructive jaundice, abs (%)	120 (47.8)	578 (69.5)	< 0.001
Management of jaundice:			
Percutaneous transhepatic biliary drainage	51 (42.5)	256 (44.3)	$p_{(biliodigestive\ anastomosis)}$
Biliodigestive anastomosis	32 (26.7)	53 (9.2)	< 0.001
Biliary stenting	24 (20.0)	152 (26.3)	$p_{(cholecystostomy)}$ < 0.001
Cholecystostomy	10 (8.3)	115 (19.9)	
Nasobiliary drainage	3 (2.5)	2 (0.3)	
Pancreatic duct diameter (cm), Me (Q1–Q3)	0.3 (0.2–0.4)	0,4 (0.2–0.5)	< 0.001
Pancreatic texture, abs (%)			
Soft	134 (53.4)	399 (48.0)	0.132
Firm	117 (46.6)	433 (52.0)	
NACT, abs (%)	24 (9.6)	200 (24)	< 0.001
ACT, abs (%)	120 (47.8)	482 (57.9)	0.005

Note: DM, diabetes mellitus; CAD, coronary artery disease; SA, stable angina; MI, myocardial infarction; CVD, cerebrovascular disease; HTN, hypertension; NACT, neoadjuvant chemotherapy; ACT, adjuvant chemotherapy; BMI, body mass index; WHO, the World Health Organization.

The ASA Physical Status Classification System is widely accepted for predicting surgical outcomes, including postoperative complications. A higher ASA class is associated with an increased risk of complications [23]. In the current study, ASA class 3 was observed in 16.3% and 15.5% of patients in Groups 1 and 2, respectively, and no differences were found ($p = 0.488$).

The diameter of the main pancreatic duct and texture (firmness) of the pancreatic stump parenchyma are independent negative prognostic factors of postoperative pancreatic fistula [24]. Our study showed that patients in group 1 had a significantly smaller pancreatic duct diameter, whereas gland texture did not significantly differ. The median diameter of the pancreatic duct was 0.3 cm in group 1 and 0.4 cm in group 2. It has been found that the risk of pancreatic fistula is high when the duct diameter is <0.3 cm [25].

CONCLUSION

The clinical and functional characteristics of patients who underwent multivisceral surgery with PD indicate that these patients have significantly poorer general physical status, assessed using the ECOG scale, than those who underwent PD without resection of adjacent organs. This markedly complicates the administration of perioperative antitumor pharmacotherapy, making surgical intervention the only feasible initial specialized cancer treatment.

ADDITIONAL INFORMATION

Author contributions: V.I.E.: conducting the study, working with data, writing the draft; A.G.K.: revising and editing the manuscript; Yu.I.P.: revising and editing the manuscript, F.Sh.A.: working with data; D.V.P.: working with data. All authors approved the version of the manuscript to be published and agreed to be accountable for all aspects of the work, ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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ДОПОЛНИТЕЛЬНАЯ ИНФОРМАЦИЯ

Вклад авторов: В.И.Е. — проведение исследования, работа с данными, написание черновика; А.Г.К. — пересмотр и редактирование рукописи; Ю.И.П. — пересмотр и редактирование рукописи, Ф.Ш.А. — работа с данными; Д.В.П. — работа с данными. Все авторы одобрили рукопись (версию для публикации), а также согласились нести ответственность за все аспекты работы, гарантируя надлежащее рассмотрение и решение вопросов, связанных с точностью и добросовестностью любой её части.

Этическая экспертиза. Неприменимо.

Согласие на публикацию. Все пациенты, перед прохождением лечения, подписывали информированное согласие об использовании медицинских данных для использования в исследованиях. Рукопись не содержит персональных данных.

Источники финансирования. Отсутствуют.

Раскрытие интересов. Авторы заявляют об отсутствии отношений, деятельности и интересов за последние три года, связанных с третьими лицами (коммерческими и некоммерческими), интересы которых могут быть затронуты содержанием статьи.

Оригинальность. При создании настоящей работы авторы не использовали ранее опубликованные сведения (текст, иллюстрации, данные).

Доступ к данным. Редакционная политика в отношении совместного использования данных к настоящей работе не применима, новые данные не собирали и не создавали.

Генеративный искусственный интеллект. При создании настоящей статьи технологии генеративного искусственного интеллекта не использовали.

Рассмотрение и рецензирование. Настоящая работа подана в журнал в инициативном порядке и рассмотрена по обычной процедуре. В рецензировании участвовали два внешних рецензента, член редакционной коллегии и научный редактор издания.

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