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# Retroperitoneal pancreas transplantation with a Roux-en-Y duodenojejunostomy for exocrine drainage

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## Abstract

**Background** Pancreatic transplantation is the only definitive surgical treatment for diabetes mellitus. Currently, most transplant centers use enteric exocrine drainage of pancreatic secretions; however, experts disagree on which part of the gastrointestinal tract is preferable for enteric anastomosis. We analyzed the outcomes of retroperitoneal pancreatic transplantation with enteric drainage of pancreatic secretions.

**Materials and methods** We evaluated the outcomes of 60 simultaneous retroperitoneal pancreas-kidney transplantations. Based on the type of enteric anastomosis, the patients were divided into two groups: the study group consisted of 10 patients who underwent enteric drainage via Roux-en-Y duodenojejunostomy, and the control group included 50 patients who underwent exocrine drainage via duodenoduodenal anastomosis. No statistically significant differences were observed between the groups in terms of the main parameters.

**Results** The rate of surgical complications did not differ significantly between the groups ( $p > 0.05$ ). Clavien IVb complications occurred only in the control group ( $n = 4.8\%$ ). The in-hospital pancreatic graft survival rate in both groups was 80%, whereas the recipient survival rates were 90% and 84%, in the study and control groups, respectively ( $p < 0.05$ ).

**Conclusion** Retroperitoneal pancreatic transplantation with exocrine drainage via a Roux-en-Y duodenojejunostomy is an effective alternative technique that reduces the rate of severe surgical complications.

**Keywords** Pancreas transplantation, Simultaneous pancreas-kidney transplantation, Duodenojejunal anastomosis, Duodenoduodenal anastomosis, Surgical complications, Pancreatic graft survival, Recipient survival

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## Introduction

Diabetes mellitus (DM) has been recognized by the World Health Organization as an epidemic of non-infectious etiology and is a real challenge for the medical community worldwide. According to the International Diabetes Federation Report, there are over 463 million people with DM worldwide in 2021 [1]. According to the Data Registry, 4.8 million patients with DM were registered in Russia in 2021, and 265,400 of them had type 1 DM [2, 3]. Diabetic nephropathy (DN) is the most threatening complication of type 1 DM, exacerbating its course in 25.9% of patients [4]. These patients demonstrated the lowest survival rates when renal replacement therapy is used. In the opinion of the professional medical community, simultaneous pancreas and kidney transplantation (SPKT) is the best treatment option for this group of patients [5, 6]. The initial ideological goal of pancreas transplantation (PTx) is kidney graft nephroprotection, which contributes to a fold increase in graft survival [7, 8]. In addition to a significant improvement in quality of life, SPKT increases the long-term survival of patients with stage 4–5 chronic kidney disease originating from DN.

Conceptually, PTx allows lost endocrine function of the pancreas to be replaced; however, the exocrine parenchyma of the pancreas graft (PG) is the main cause of most non-vascular complications. Historically, the issue with the most significant impact on PTx outcomes was PG exocrine drainage. Various surgical techniques have been used, including ligation [9] and duct injection with synthetic polymers [10, 11], performing cutaneous graft duodenostomy [12], open-duct drainage [13] and urinary drainage [14–16]. Currently, 95% of all PTxs are performed with enteric drainage, which has been proven to be the most physiological method [17, 18]. Some authors report the use of the small intestine to form an interintestinal anastomosis, placing the graft in the peritoneal cavity. This is often associated with prolonged intestinal paresis and septic complications [16]. Others report retroperitoneal PG placement and drainage of pancreatic secretions into the recipient's duodenum [19, 20] with the peritoneal cavity remaining intact. With this approach, in case of complications, the pathology focus is located outside the peritoneal cavity and is often amenable to minimally invasive treatment. When using this technique, the incidence of interintestinal anastomosis failure is 5–20% [21], and the mortality in such cases is 78% [22].

We implemented an PTx technique that uses the advantages of retroperitoneal graft placement and obviates the main disadvantage of duodenal drainage.

## Materials and methods

### Recipients

The study was included 60 patients who underwent retroperitoneal SPKT between 2011 and 2022 and was single-center, prospective study with historical control group. Patients inclusion criterion was type 1 diabetes mellitus with unsatisfactory glycemic control, complicated by stage 5 chronic kidney disease resulting in diabetic nephropathy. The exclusion criteria were terminal conditions, uncorrectable dysfunctions of vital organs, untreatable systemic and local infections (AIDS, replication of hepatitis viruses, active tuberculosis, etc.), septic conditions, malignant neoplasms, developmental defects accompanying diabetes mellitus that cannot be corrected, narcotic and/or alcohol addiction, psychosocial factors. The study group comprised 10 patients who underwent PTx with modified Roux-en-Y duodenojejunostomy. The control group included 50 patients who underwent PTx with exocrine drainage via a duodenoduodenal anastomosis. The study was approved by the Institutional Review Board at the N.V. Sklifosovsky Research Institute for Emergency Medicine (№1–22 from 11.01.2022).

### Surgical technique

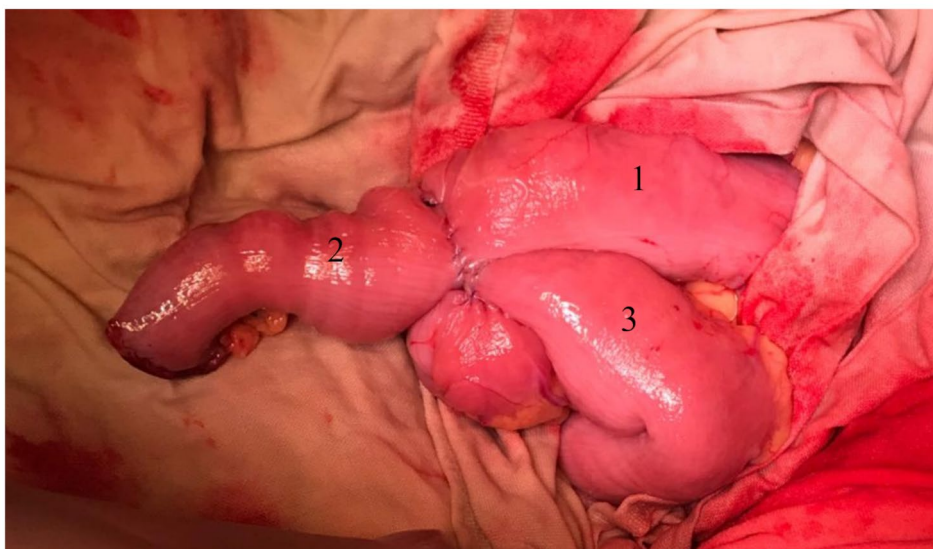
In the study group, the small intestine was divided at a distance of 40–60 cm from the ligament of Treitz using a linear stapler. Next, a side-to-side anti-peristaltic interintestinal anastomosis was performed between the two ends of the native jejunum using the linear staple technique (Fig. 1a).

Roux-en-Y, excluding the small intestinal loop, was drawn through the parietal peritoneal foramen under the recipient's ascending colon into the retroperitoneal space to the duodenal stump of the pancreaticoduodenal graft. A side-to-side duodenojejunal anastomosis was formed in the retroperitoneal space between the stump of the donor duodenum and the Roux-en-Y-excluded loop of the recipient jejunum (Fig. 1b).

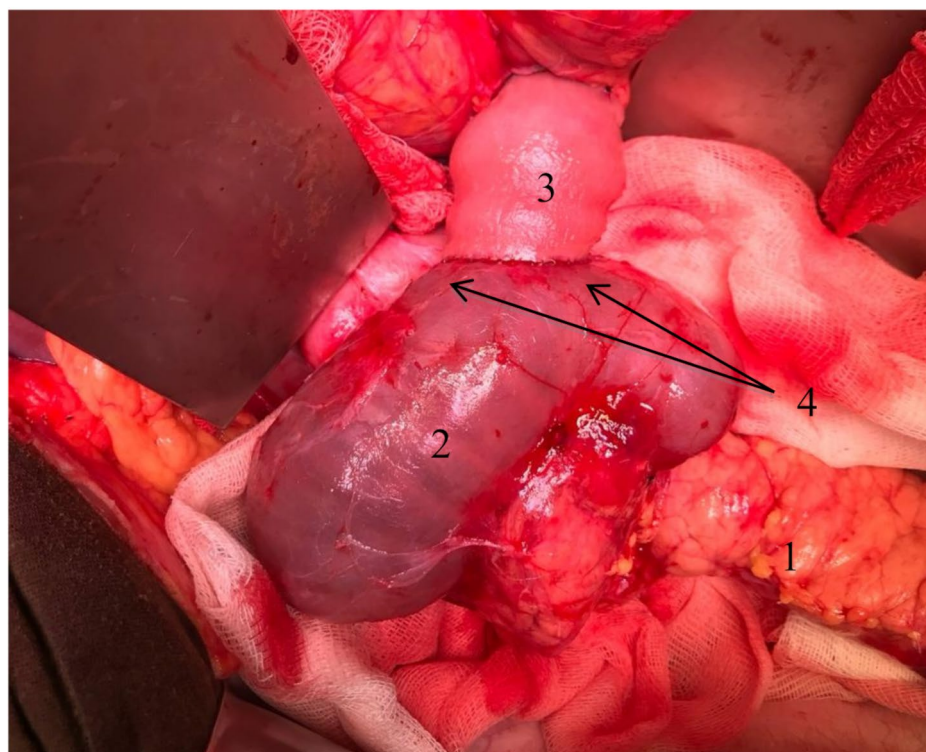
In the parietal peritoneal foramen, the peritoneum was fixed with interrupted sutures to the excluded loop of the jejunum, isolating the pancreatic graft from the peritoneal cavity (Fig. 2).

In the control group, the duodenum was isolated, and a side-to-side hand-sewn duodenoduodenal anastomosis was performed using a two-layer uninterrupted intestinal suture (Figs. 3 and 4).

The kidney graft cold ischemia time varied from 5 to 12.5 h and from 5 to 14 h in the study and control groups, respectively, the respective medians [0.25;0.75 percentile] being 7.3 [7; 7.8] h and 7.75 [6.6;9.5] h. The pancreatic graft cold ischemia time varied from 7 to 10 h and from 6.5 to 13 h in the study and control groups, respectively, with median values of 9 [8.6;9.4] h and 9 [8.1;11] h, respectively.



**Fig. 1a** Enteric side-to-side anastomosis. 1, the afferent part of the small intestine; 2, the Roux-en-Y small intestine loop; 3, the efferent part of the small intestine



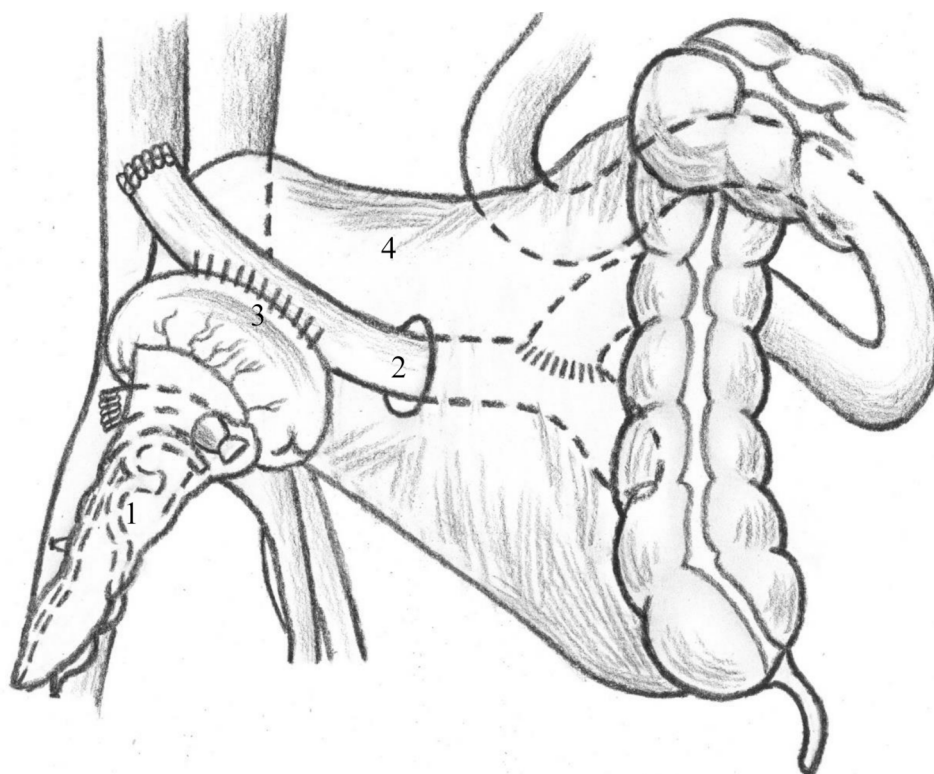
**Fig. 1b** Roux-en-Y duodenojejunal anastomosis. 1, pancreas graft; 2, donor duodenum; 3, recipient Roux-en-Y excluded small intestinal loop; 4, duodenojejunal anastomosis

#### Immunosuppressive therapy

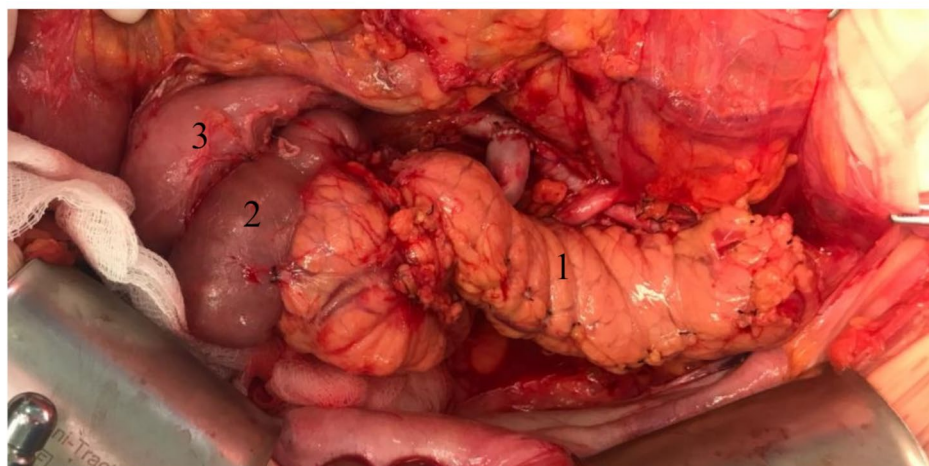
Induction immunosuppressive therapy administered to patients in both groups included methylprednisolone 750 mg intraoperatively, then 250 mg on postoperative day 1 and 2, basiliximab 20 mg intraoperatively, and on postoperative day 4. Triple maintenance

immunosuppressive therapy included tacrolimus, mycophenolic acid, and methylprednisolone. The target values for tacrolimus blood concentrations were 8–9 ng/ml in the early postoperative period and 6–7 ng/ml in the distant period.





**Fig. 2** Scheme of retroperitoneal pancreas transplantation with Roux-en-Y duodenojejunal anastomosis. 1, pancreas graft; 2, Roux-en-Y small intestine loop; 3, duodenojejunal anastomosis; 4, peritoneum



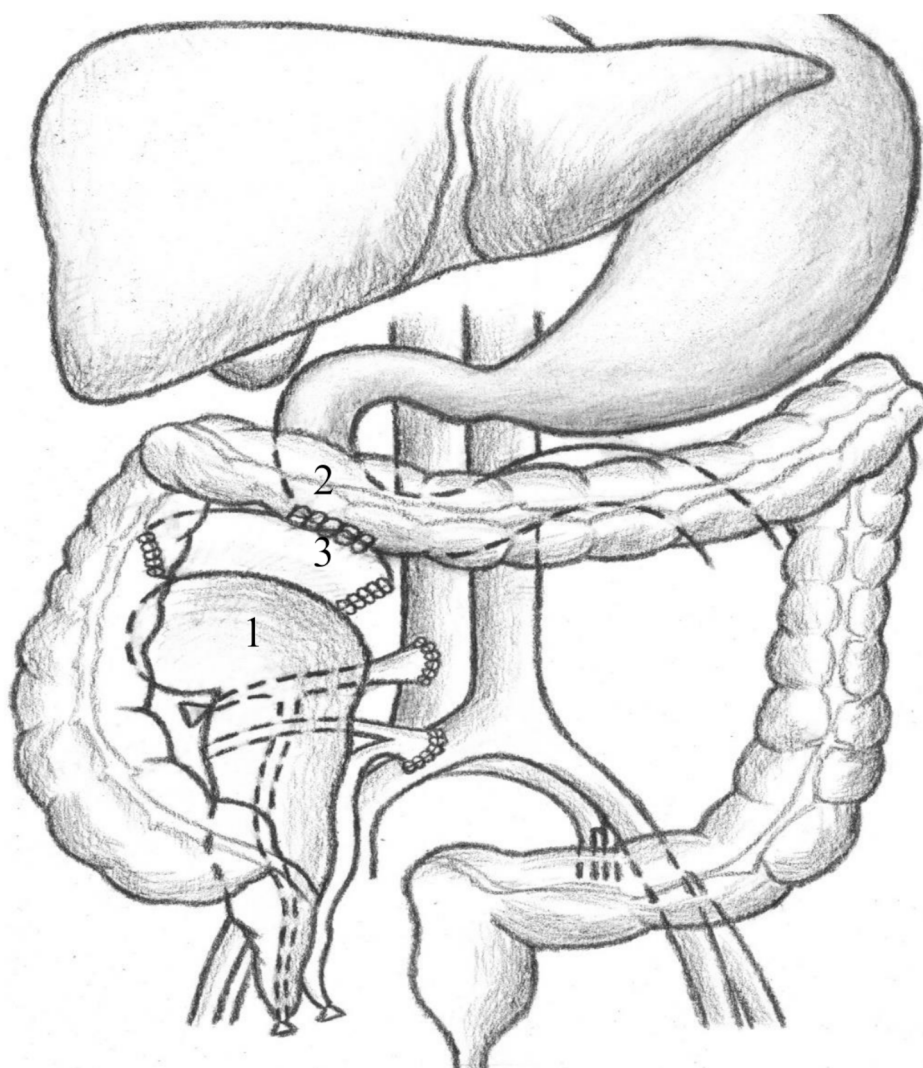
**Fig. 3** Duodenoduodenal anastomosis. 1, pancreas graft; 2, donor duodenum; 3, recipient duodenum

#### Prophylactic antibiotic therapy

Perioperative antibiotic prophylaxis in both groups was administered using 1000 mg meropenem twice daily for 7 days, 500 mg 3 times a day for 10 days, and 500 mg vancomycin once daily for 5 days.

#### Antisecretory therapy

For antisecretory therapy, octreotide was administered via an infusion pump at a dose of 1200  $\mu\text{g}/24\text{ h}$  for 5 days. On postoperative day 5, the antisecretory therapy was converted from intravenous to subcutaneous octreotide administration at a dose of 300  $\mu\text{g}$  3 times a day with the dose tapering down with complete withdrawal after blood amylase level returned to normal. The therapeutic



**Fig. 4** Scheme of retroperitoneal pancreatic transplantation with duodenoduodenal anastomosis. 1, pancreas graft; 2, recipient duodenum; 3, duodenoduodenal anastomosis

treatment protocols employed in our clinic are standardised and did not differ between patients in the two groups.

#### Assessment of surgical complications

Surgical complications were graded according to the Clavien-Dindo Classification modified by Grochowiecki [23].

#### Statistical analyses

Statistical analyses were performed using IBM SPSS Statistics version 24 software (IBM Corp, Armonk, NJ, USA). Quantitative parameters were assessed for compliance with normal distribution using the Shapiro–Wilk test. Comparison of two groups in terms of a quantitative parameter having a normal distribution, provided that the variances were equal, was performed using Student's

t-test. Comparison of the two groups in terms of a quantitative parameter, the distribution of which differed from the normal distribution, was performed using the Mann–Whitney U test. Percentage comparisons in the four-field contingency tables were performed using Fisher's exact test (with expected phenomenon values lower than 10). To assess the statistical significance of the differences between two or more relative parameters, Pearson's chi-square test was used. The Kaplan–Meier method was used to calculate patient and graft survival rates. Differences were considered statistically significant at  $p < 0.05$ .

#### Results

##### Recipient characteristics

The detailed characteristics of the patients in the study and control groups are presented in Table 1.

**Table 1** Demographic data of recipients in the study and control groups

Parameter	Study group (n = 10)	Control group (n = 50)	p
Men/women, n/n	2/8	19/31	0.47 <sup>1</sup>
Age, years*	36 [32;39]	35 [33;36]	0.55 <sup>2</sup>
BMI, kg/m <sup>2</sup> *	21 [19;22]	21 [20;23]	0.41 <sup>3</sup>
RRT duration, years*	3 [1;4]	2 [1;4]	0.67 <sup>3</sup>
History of diabetes, years*	26 [23;28]	24 [20;29]	0.74 <sup>3</sup>

\*Median [0.25;0.75 percentile]; <sup>1</sup> Fisher's exact test; <sup>2</sup> Student's t test; <sup>3</sup> Mann-Whitney U test; BMI, body mass index; RRT, renal replacement therapy

**Table 2** Donor characteristics in the study and control groups

Parameter	Study group (n = 10)	Control group (n = 50)	R
Men/women, n/n	7/3	44/6	0.16 <sup>1</sup>
Age, years*	29 [25;32]	28 [26;29]	0.64 <sup>2</sup>
TBI/CVA, n/n	6/4	32/18	1.0 <sup>1</sup>
PG cold ischemia time, h*	9 [8.625;9.375]	9 [8;125;11]	0.41 <sup>3</sup>
Donor total blood amylase, U/L*	61 [54;109]	73 [57;117]	0.66 <sup>3</sup>
Bacteriology study of perfusate: positive/negative result, n/n	1/9	3/47	0.53 <sup>1</sup>

\* Median [0.25;0.75 percentile]; <sup>1</sup> Fisher's exact test; <sup>2</sup> Student's t-test; <sup>3</sup> Mann-Whitney U test; TBI, traumatic brain injury; CVA, cerebrovascular accident; PG, pancreas graft

### Donor characteristics

Organs donated after ascertaining brain death from deceased standard criteria donors were used for transplantation (Table 2).

There was a high degree of HLA antigen incompatibility in the donor-recipient pairs in the study and control groups: six [6;6] and five [4;6] antigen mismatches, respectively.

### Immunological complications

In the study group, one patient (10%) experienced a rejection crisis, which was successfully treated with pulse therapy comprising methylprednisolone for a period of three days. In the control group, acute rejection crises were diagnosed in 16 patients (32%). Of these patients, six (37.5%) experienced a recurrent episode of transplant rejection. In 21 cases (95.5%), pulse therapy with methylprednisolone was employed as a therapeutic measure for rejection crises. In 10 cases (45.5%), ATGAM was additionally administered, while in one case (4.5%), Timoglobulin was incorporated. In one case (4.5%), only ATGAM was utilized as the primary therapeutic agent. In 13 cases (59.1%), plasmapheresis sessions were added to the main therapy. No significant differences were observed in the treatment of rejection crises ( $p > 0.05$ ).

**Table 3** Comparison of surgical complications in the study and control groups

Complication	Study group (n = 10)	Control group (n = 50)	p*
Severity grade IIIa			
Peripancreatic abscess, n (%)	1 (16.7%)	2 (5.3%)	> 0.05
Peripancreatic infection, n (%)	1 (16.7%)	6 (15.8%)	
PPFC, n (%)	1 (16.7%)	13 (34.2%)	
Intestinal bleeding, n (%)	0	2 (5.3%)	
Severity grade IIIb			
Intestinal bleeding, n (%)	1 (16.7%)	1 (2.6%)	> 0.05
Peripancreatic abscess, n (%)	0	1 (2.6%)	
Peripancreatic infection, n (%)	0	1 (2.6%)	
Bleeding (venous/arterial), n (%)	0	1 (2.6%)	
Severity grade IVa			
Occlusive arterial thrombosis, n (%)	1 (16.7%)	2 (5.3%)	> 0.05
Occlusive venous thrombosis, n (%)	1 (16.7%)	2 (5.3%)	
Interintestinal anastomosis failure, n (%)	0	2 (5.3%)	
Clinically significant stenosis of the splenic artery, n (%)	0	1 (2.6%)	
Severity grade IVb			
Interintestinal anastomosis failure + peri- pancreatic infection, n (%)	0	4 (10.5%)	> 0.05
Total complications	6	38	

\*Fisher's exact test; PPFC, peripancreatic fluid collection

### Surgical complications

The postoperative course was uneventful in 24 patients; 36 patients developed 44 complications. The incidences of early surgical complications were 30% and 66% in the study and control groups, respectively ( $p = 0.08$ ). A comparative description of surgical complications in the groups is presented in Table 3.

Intestinal obstruction occurred in 2 patients of the study group and in 1 patient of the control group. This complication did not require surgical intervention and was resolved conservatively.

There was one category IIIa complication in the study group, represented by a parapancreatic collection complicated by infection. Treatment consisted of drainage tubes and daily lavage with 1% dioxidine solution until the flow of contents through the drains was stopped. In the control group, category IIIa complications ( $n = 23$ ) occurred in 19 patients (38%). Abscess formation ( $n = 1$ ), parapancreatic collections complicated by an infectious process ( $n = 3$ ) and uncomplicated ( $n = 10$ ) were found. There were also cases of severe pancreatic necrosis ( $n = 3$ ). As in the study group, sanation-aspiration methods of treatment with de-escalation antibacterial



therapy were used, which led to cure of the patients. In one case, failure of the inter-intestinal anastomosis was noted. In this case, percutaneous drainage of the anastomotic defect allowed the defect to heal on its own without surgical intervention. There were also intestinal haemorrhages ( $n=2$ ) which were successfully managed by endoscopic intervention.

Category IIIb complications were observed in one (10%) and four (8%) cases in the study and control groups, respectively. In the study group, one case of intestinal bleeding was observed, which was successfully treated with endoscopic intervention. However, there were indications for a revision of the graft. In the control group, four cases of complications were diagnosed: one case of intestinal bleeding, one case of severe parapancreatic infection, one case of formed abscess, and one case of bleeding from the graft vascular anastomosis. All complications required repeated surgical intervention to correct them.

One patient (10%) in the study group experienced complications of category IVa, manifested as arterial and venous thrombosis of the graft. This adverse event necessitated a transplant removal procedure, after which the patient was discharged in a satisfactory condition. In the control group, five patients (12%) experienced this complication. Among the complications observed, there were occlusive venous thrombosis ( $n=2$ ), occlusive arterial thrombosis ( $n=1$ ), failure of interintestinal anastomosis with arterial thrombosis ( $n=1$ ) and without arterial thrombosis ( $n=1$ ). All patients underwent graft removal. However, two patients with interintestinal anastomosis failure developed an infection in the area of the removed graft, which subsequently led to a fatal outcome.

Consequently, category IVb complications were observed in a total of four patients (8%) within the control group. In addition to the two patients described above, two further patients developed parapancreatic infection, one of whom also developed interintestinal anastomosis failure. These complications were fatal. It should be noted that the presence of an infectious process at the development of interintestinal anastomosis failure ( $n=3$ ) in patients with duodenal drainage resulted in a lethal outcome in 100% of cases. Conversely, no correlation was identified between arterial thrombosis and interintestinal anastomosis failure ( $p=0.190$ ). No complications of this category occurred in the patients of the study group.

The total number of complications per patient was 0.6 and 0.8 in the study and control groups, respectively. A comparative analysis showed no statistically significant effect of the type of pancreatic exocrine secretion drainage on the incidence of surgical complications ( $p>0.05$ ).

### Surgical outcomes

The length of hospital stay was significantly shorter in the study group (21 [14;30] days) than in the control group (41 [29;63] days) ( $p=0.03$ ). The overall in-hospital pancreatic graft survival rate was 81.7%. The death-censored pancreaticoduodenal graft survival rate was 83.3%. Death-censored in-hospital pancreatic graft survival was 90% and 80% in the study and control groups, respectively. One-year pancreas graft survival rate was 76% in the control group and 90% in the study group. The overall in-hospital survival rate was 85%. The in-hospital recipient survival rates showed no statistically significant differences between the groups, with 90% in the study group and 84% in the control group ( $p>0.05$ ). One-year survival of patients were 82% and 90% in the control and study groups, respectively. Following discharge, no recipients in either group were readmitted to hospital within a one-year period. In the study group, there was one case of a lethal outcome due to cardiological complications unrelated to the transplantation procedure. In the control group, the presence of parapancreatic infection and inter-intestinal anastomosis failure (two cases, representing 4% of the total) resulted in a 100% fatality rate. In instances where graft removal was necessary due to the presence of parapancreatic infection (three cases, representing 6% of the total), the lethal outcome was also observed in 100% of cases. In the early postoperative period, seven graftectomies were performed (14%), with one additional graftectomy carried out in the distant postoperative period. Of these, three cases resulted in the patient's demise. Overall, in this group, there were eight fatal outcomes in the early postoperative period and one additional fatal outcome in the distant postoperative period.

### Discussion

Surgical treatment of diabetes mellitus currently includes simultaneous kidney and pancreas transplantation, pancreas after kidney and pancreas transplant alone. With improvements in surgical technique, postoperative management and immunosuppressive therapy, pancreas graft survival has improved and now matches graft survival rates of kidney and liver transplant. Thus, the current survival rates for patients and transplants exceed 90% after 1 year [23].

The first pancreas transplant was performed in 1966. Then William D. Kelly and Richard C. Lillehei performed a pancreas transplantation with main pancreatic duct ligation [24]. Subsequently, surgeons used various methods of drainage of pancreatic secretions: drainage into the abdominal cavity, filling of the duct of Wirsung, drainage into the bladder and own ureter. Currently about two thousand pancreas transplantations are performed annually worldwide, and enteric drainage of pancreatic secretions is currently performed in 95% of transplant centers

[25]. Some centers perform intraperitoneal transplantation by forming a duodenojejunal anastomosis, whereas others prefer the retroperitoneal pancreatic transplantation technique with formation of a duodenoduodenal anastomosis. Some authors describe successful attempts at gastric drainage [26]. However, the number of surgical complications still remains high and reaches 55% [27, 28]. Despite the fact that sufficient international experience has accumulated in pancreas transplantation, there is currently no standardized drainage option [29, 30]. On the one hand, an undoubted advantage is the retroperitoneal location of the PG, in which the abdominal cavity remains relatively intact and there is the possibility of minimally invasive treatment methods. However, if PG is placed retroperitoneally duodenal drainage is used which increases the risk of severe surgical complications. High recipient mortality rates have been reported in cases of duodenoduodenal anastomosis incompetence and the development of infectious complications requiring graft removal. When using this technique, the incidence of interintestinal anastomosis failure is 5–20% [21], and the mortality in such cases is 78% [22]. On the other hand, small intestinal drainage is a technically simpler and safer method for forming an anastomosis, but the intra-abdominal location carries the risk of severe complications due to the lack of delimitation of the graft from the abdominal cavity.

In the present study, we describe the results of a transplant series using a technique that combines the advantages of retroperitoneal graft placement and enteric drainage and obviates the main disadvantage of duodenal drainage [31–33]. The overall incidence of early surgical complications and graft and recipient survival rates did not differ significantly with regard to the method of graft pancreatic secretion drainage. Severe Clavien–Dindo grade IVb surgical complications occurred only in the control group. It is important that the occurrence of interintestinal anastomosis failure and peripancreatic infection (four cases) led to death in 100% of cases in patients with duodenoduodenal anastomosis formation. This fact indicates more severe management of patients with surgical complications after transplantation with duodenal drainage. Also length of hospitalization of patients in study group was significantly shorter. This is due to fewer severe surgical complications in these patients. The results obtained in this study suggest that this surgical technique is an effective alternative for pancreatic transplantation.

Limitations in this study are those inherent to any retrospective and prospective analysis of a database with various biases. The retrospective nature of the control group inherently limits the ability to establish causality. Such designs are more prone to biases and confounding factors that cannot be controlled as effectively as in fully

prospective studies. The sample size for the groups is small due to the surgery's rarity, which can limit the statistical power to detect effects. The required sample size for the one-sided alternative hypothesis was calculated based on a power of 80%, a genus I error rate of 10%, a ratio  $n_c/n_s$  of 5, and the assumption that the correlation coefficients  $\rho_c$  and  $\rho_s$  are 0.75 and 0.15. Estimates of the required sample size:  $n_c = 50$ ,  $n_s = 10$ . Given the retrospective study design and the specific patient population from a single geographic region, the results cannot be generalised to all pancreas transplant recipients. The study may not have taken into account all potential confounding factors, such as variations in immunosuppressive therapy regimens, patient comorbidities, and lifestyle factors that may affect treatment outcomes. The selection criteria for SPKT may vary from center to center, inducing a selection bias. Experience with retroperitoneal pancreas transplantation is still not matured in many centers, which may have impacted the adverse outcomes. In the study group, transplants were performed by different surgical teams, thereby ensuring that the experience of the surgeons in each case was approximately equivalent. Recently, future research will be needed to examine that question.

## Conclusion

Retroperitoneal pancreatic transplantation with enteric drainage of pancreatic secretions by forming a duodenojejunal anastomosis on the Roux-en-Y-excluded small intestine loop is an effective alternative transplantation technique that reduces the number of severe surgical complications.

## Acknowledgements

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## Author contributions

M. Sh. Khubutiya: Concept/design, Critical revision of article, Approval of article. I. V. Dmitriev: Concept/design, Critical revision of article, Approval of article. N. S. Zhuravel: Concept/design, Data analysis/interpretation, Statistics, Data collection. A. G. Balkarov: Critical revision of article, Approval of article. R. V. Storozhev: Data analysis/interpretation, Data collection. Yu. A. Anisimov: Data analysis/interpretation, Statistics, Data collection. A. S. Kondrashkin: Data analysis/interpretation. N. V. Shmarina: Data analysis/interpretation.

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## Data availability

we affirm that we had full access to all the study's data. The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.



## Declarations

### Ethics approval and consent to participate

The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The trial was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Institutional Review Board at the N.V. Sklifosovsky Research Institute for Emergency Medicine (№1–22 from 11.01.2022) and informed consent was taken from all individual participants. Patients were informed about all details of the surgical technique of pancreas transplantation, as well as warned about the risks associated with the new technique.

### Consent for publication

not applicable.

### Conflict of interest

The authors have no conflicts of interest to declare.

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