https://doi.org/10.23873/2074-0506-2021-13-3-220-234

Analysis of the results of pancreas transplantation in one transplant center in Russia

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Abstract

Introduction. *The total number of pancreas transplantations performed in Russia by the end of 2019 had been 176. There are no detailed reports on the number and results of pancreas transplantation in Russia with analysis of factors that statistically significantly affect outcomes.*

Material and methods. *This article presents a retrospective analysis of 60 pancreas transplantation results, which had been performed from*

January 2008 to July 2019 at the N.V. Sklifosovsky Research Institute for Emergency Medicine. In addition, the assessment of factors that statistically significantly affect the outcomes of pancreas transplantations was performed.

Results. *17 intra-abdominal pancreas transplantations with duodenoejunoanastomosis and 43 retroperitoneal pancreas transplantations with interduodenal anastomosis were performed. In 52 patients, the pancreas graft after vascular reconstruction with a Y-shaped vascular prosthesis was used; in other 8 patients, the pancreas graft with isolated blood flow through the splenic artery was used. The rates of immunological and surgical complications were 23.3% and 56.7%, respectively. In-hospital and 1-year recipient, kidney and pancreas graft survival rates were 88.3%, 86.4%, 83.3% and 86.6%, 84.8%, and 81.7%, respectively. The factors that significantly affected the outcomes of pancreas transplantation were the conversion of the dialysis therapy modality, the development of parapancreatic infection, repeated open surgical interventions, surgical complications of IIIb-IVa severity grades by Clavien-Dindo Classification, some features of basic and induction immunosuppressive therapy.*

Conclusion. *The results of pancreas transplantation at the N.V. Sklifosovsky Research Institute for Emergency Medicine are comparable to the outcomes of pancreas transplantation in most world transplant centers.*

Keywords: pancreas transplantation, complications, recipient survival rate, kidney graft survival, pancreas graft survival, results, factors

Conflict of interests Authors declare no conflict of interest

Financing The study was performed without external funding

For citation: Dmitriev IV, Shchelykalina SP, Lonshakov DV, Anisimov YuA, Kazantsev AI, Pinchuk AV. Analysis of the results of pancreas transplantation in one transplant center in Russia. *Transplantologiya. The Russian Journal of Transplantation.* 2021;13(3):220–234. (In Russ.). https://doi.org/10.23873/2074-0506-2021-13-3-220-234

CVA, cerebrovascular accident

ATGAM, equine antithymocyte immunoglobulin

BMI, body mass index

CAPD, continuous ambulatory peritoneal dialysis

CI, confidence interval

DDA, duodenoduodenoanastomosis

DEA, duodenojejunoanastomosis

ESRD, end-stage chronic renal disease

GFR, glomerular filtration rate

HD, hemodialysis

HLA, human leukocyte antigen

ISABS, isolated splenic artery blood supply

IST, immunosuppressive therapy

MOF, Multiple Organ Failure

PG, pancreas graft

PGNF, primary graft nonfunction

PIPPG, primarily infected pancreatic graft

PIRAG, primary infected renal allograft

PPFC, parapancreatic fluid collection

RAG, renal allograft

RRT, renal replacement therapy

SA, splenic artery

SPKT – simultaneous pancreas-kidney transplantation

SMA, superior mesenteric artery

T1DM, type 1 diabetes mellitus

TBI, traumatic brain injury

TMA, thrombotic microangiopathy

PTx – pancreas transplantation

PT – pancreas transplant

Introduction

Simultaneous kidneys and pancreas transplantation (SKaPT) is the best medical option for achieving stable euglycemia and true insulin independence in patients with stage 5 chronic kidney disease in the outcome of type 1 diabetes mellitus (T1DM) [1, 2]. Due to the critical shortage of donor organs and the strict criteria for the selection of pancreas graft (PG), the number of transplantations annually performed in the United States does not exceed 860-1200 [3]. Despite the more than 50-year history of clinical pancreas transplantation (PTx) the first successful transplantation in our country was performed only at the end of 2005 [4]. Since then, the total number of PTx in Russia as of the end of 2019 has made 176, of which 62 (35.2%) have been performed in our center. In world medical literature, there are many articles analyzing the results of PT performed in various transplant centers. This article presents the results of one Russian center that performed the largest number of PT in Russia.

Material and methods

In the period from January 2008 to June 2019, 60 PT were performed on the base of our department: 59 SPKT and 1 PT after previous kidney transplantation.

Recipients

The recipient group consisted of 60 patients with T1DM complicated by stage 5 chronic kidney disease in the outcome of diabetic nephropathy. The characteristics of the recipients are presented in Table 1.

Table 1. Characteristics of recipients

Age Me Me[25%;75%] (min;max), years	34[30.75;39] (22;51)
Gender, male, n (%)/female, n(%)	27 (45)/33 (55)
BMI Me[25%;75%] (min;max), kg/m^2	20.8[19.5;22.6] (16.8;43.2)
RRT, n (%)	56 (93)
HD, n (%)	35 (62.5)
CAPD, n (%)	15 (26.8)
HD+CAPD, n (%)	6 (10.7)
Without RRT, n (%)	4 (6.7)
RRT timing Me[25%;75%] (min;max), years	2[1;4] (0;18)
Period of T1DM manifestations Me[25%;75%] (min;max), years	10[8.8;13] (1;35)
Duration of T1DM by the time of transplantation Me [25%; 75%] (min; max), years	24.5[20;29] (4;40)
Recipient distribution by blood group	
0(I), n (%)	26 (43.3)
A(II), n (%)	23 (38.3)
B(III), n (%)	10 (16.7)
AB(IV), n (%)	0

Notes: HD; hemodialysis; RRT: renal replacement therapy, BMI: body mass index, CAPD: continuous ambulatory peritoneal dialysis, T1DM: type 1 diabetes mellitus

The absolute majority of patients (n=58, 97%) underwent primary organ transplantation. Only 2 patients had a history of a postmortem donor kidney allotransplantation; one of them lost the transplanted kidney due to an acute rejection during the initial 14 days after transplantation, the second patient had a functioning kidney for 8 years that was lost for an unknown reason.

Donors

Organs for transplantation were obtained in the course of multi-organ removal exclusively from donors with confirmed brain death. The characteristics of the donor pool are presented in Table 2.

Table 2. Characteristics of donors

Age Me [25%; 75%] (min; max), years	27 [23;32] (18;45)
Gender male, n (%) / female, n (%)	53 (88.3)/7 (11.7)
TBI (%) / CVA (%)	42 (70)/18 (30)
Creatinine, Me [25%; 75%] (min; max), μmol/L	94[74;109] (50;180)
Urea, Me [25%; 75%] (min; max), mmol/L	4.95[3.8;6.8] (1.4;11.2)

Notes: CVA, cerebrovascular accident, TBI, traumatic brain injury

According to the results of perfusate microbiology study, 9 cases showed the presence of pathological flora in clinically significant titers: staphylococcal flora (S. Aureus or S. Epidermidis) in 5 cases (8%), Klebsiella pneumoniae in 2 (3%), Escherichia coli and Pseudomonas aeruginosa in 1 case each.

The characteristics of surgical interventions are presented in Table 3.

Table 3. Characteristics of surgical interventions

Intra-abdominal PT with DEA, n (%)	17 (28.3)
Retroperitoneal PT with DDA, n (%) − including those with the stumpless technique, n (%)	43 (71.7) 2 (3.3)
Y-shaped graft, n (%)	52 (86.7)
ISABS, n (%)	8 (13.3)
Systemic venous outflow, n (%)	47 (78.3)
Portal venous outflow, n (%)	13 (21.7)
RAG preservation period, Me [25%; 75%] (min; max), hour	7[5.5;8.8] (1.5;14)
PG preservation period, Me [25%; 75%] (min; max), hour	9[8;10.7] (5.5;16)
HLA matches	
1 match, n (%)	23 (38.3)
2 matches	11 (18.3)
3 matches	3 (5)
4 matches	3 (5)
5 matches	0
6 matches	0
No matches	19 (31.7)

Notes: DDA - duodenoduodenoanastomosis, DEA, duodenojejunoanastomosis; RAG, renal allograft; PG, pancreas graft; ISABS, isolated splenic artery blood supply; HLA, human leukocyte antigen

Immunosuppressive therapy

A three-component basic immunosuppressive therapy (IST) with calcineurin inhibitors, mycophenolic acid agents, and prednisolone was used (Table 4). Monoclonal antibodies or polyclonal antibodies were used as an IST induction in 42 patients (70%), and in 18 patients (30%), respectively.

Table 4. Characteristics of immunosuppressive therapy

Immunosuppressive therapy	
Baseline	
Calcineurin inhibitors	
Tacrolimus, n (%)	53 (88)
Cyclosporine, n (%)	3 (5)
Drug conversion, n (%)	4 (7)
Induction	
Monoclonal antibodies	
Daclizumab, n (%)	1 (2)
Basiliximab, n (%)	41 (68)
Polyclonal antibodies	
Anti-thymocyte rabbit immunoglobulin (thymoglobulin), n (%)	9 (15)
Equine antithymocyte immunoglobulin (ATGAM), n (%)	9 (15)

Surgical complications: The Clavien–Dindo classification was used to assess the severity of surgical complications.

Statistical data processing was performed using statistical programming in the R language. Quantitative comparisons were made using the Mann-Whitney U-test. The influence of a qualitative binary attribute on the outcome was evaluated using the odds ratio, risk ratio, and Fisher's exact test. Differences were considered statistically significant at $p<0.05$. Overall survival and functional graft survival were analyzed using the Kaplan-Meier estimator. The endpoints of functional survival were considered the resuming to continuous insulin therapy for PG, and the return to dialysis for kidney graft. When evaluating the RAG functional survival, the female patient who underwent pancreas

transplantation after previous kidney transplantation was excluded from the analysis.

Results

Kidney graft function

Primary RAG function was observed in 52 patients, the time of serum creatinine normalization ranged from 1 to 30 days, the median being 3 days. A delayed graft function was seen in 7 patients, and the blood creatinine normalization was noted in 4 of them on days 3, 8, 20, and 47. At the stage of graft function recovery, these patients needed from 1 to 19 HD or hemodiafiltration sessions, the median number being 6. One patient developed a primary kidney graft non-function (PGNF).

Pancreas graft function

All patients had PG primary function with a true insulin independence from the first hours of graft reperfusion.

Immunological complications

The development of immunological complications was noted in 14 patients (23.3%). Ten of them were diagnosed with a single episode of rejection in the early postoperative period, 3 had 2 episodes of rejection, and one had 3 episodes of rejection. An isolated kidney graft rejection was observed in 7 recipients, an isolated PG rejection was observed in 4 patients, and a combined rejection of both grafts was observed in 3 patients. Pulse therapy with corticosteroids was performed in 3 patients for the purpose of anti-crisis therapy, which had a positive effect. In 5 patients, pulse therapy did not lead to a clinical effect, so anti-crisis therapy was enhanced with polyclonal antibodies and plasmapheresis sessions. In 6 patients, the anti-crisis therapy included using polyclonal antibodies and plasmapheresis sessions from its initiation.

Surgical complications

An uneventful postoperative course was seen in 26 patients (43.3%); and 52 complications developed in 34 patients (56.7%). The incidence, severity, and structure of surgical complications are presented in Table 5.

Table 5. Surgical complications after pancreas transplantation

Surgical complications	
Number of complications, n	52
The number of patients with a complicated postoperative period, n (%)	34 (56.7)
Number of patients with 1 complication, n (%)	22 (64.7)
Number of patients with 2 complications, n (%)	7 (20.6)
Number of patients with 3 complications, n (%)	4 (11.8)
Number of patients with 4 complications, n (%)	1 (2.9)
Severity degree:	
I, n (%)	12 (23)
II, n (%)	7 (13.5)
IIIa, n (%)	16 (30.8)
IIIb, n (%)	8 (15.4)
IVa, n (%)	4 (7.7)
IVb, n (%)	5 (9.6)
Complications	-
Occlusive arterial thrombosis, n	2
Occlusive thrombosis of the superior mesenteric artery (SMA), n	8
Hemodynamically significant splenic artery (SA) stenosis, n	1
Non-occlusive venous thrombosis (portal or splenic vein) or non-occlusive SA thrombosis, n	3
Bleeding (venous or arterial), n	2
Intestinal bleeding, n	4
Clinically significant pancreatic necrosis, n	5
Parapancreatic fluid collection (PPFC), n	11
Parapancreatic fistula +/- abscess, n	1
Parapancreatic infection, n	7
Incompetence of the interintestinal anastomosis, n	4
Paralytic / adhesive small bowel obstruction / gastrostasis / intestinal paresis, n	6

Fifty one recipients were discharged with a functioning kidney graft (Table 6). The mean blood creatinine and urea levels at the time of

discharge were 98.5 [87.5; 122.3] mmol/L and 6.9 [5.1; 8] mmol/L, respectively. The mean glomerular filtration rate (GFR) was 62 [47; 85] mL/min. There were 6 cases of in-hospital RAG removal. In the long-term postoperative period, there was 1 case of RAG removal and 2 cases of RAG function loss and the patients' return to RRT.

Table 6. Outcomes for renal allograft

Functioning RAG, n (%) 51 (86.4)		51 (86.4)
Creatinine Me [25%; 75%], μmol / L 98 [87; 122]		98 [87;122]
Urea Me [25%; 75%], mmol/L		6.9 [5.1;8]
In-hospital* losses of RAG function, n (%)		8 (13.6)
Patient No.	Timing, days	The cause, if known
3	54	PGNF
27	14	Acute rejection of RAG, retransplantation
29	10	Uncontrollable acute humoral rejection of RAG, RAG removal
52	9	PIRAG, sepsis, RAG removal on vital indications
57	33	Total necrosis of the RAG ureter and pelvis, RAG removal
58	28	RAG dysfunction, RAG removal for vital indications in order to cancel IST
23	3	Fatal outcome with a functioning RAG
26	29	
Loss of RAG function* in the long-term, n		7
Patient No.	Timing, months	The cause, if known
16	104	Persistent chronic pyelonephritis, recurrent ESRD
18	100	Chronic humoral rejection, recurrent ESRD
60	4	RAG TMA, RAG removal for vital indications
2	4	Fatal outcome with a functioning RAG
9	98	
11	63	
43	25	

* - uncensored by death.
Note: PIRAG, primary infected renal allograft; ESRD, end-stage chronic renal failure; TMA, thrombotic microangiopathy.

The RAG survival rate is shown in Figure 1.

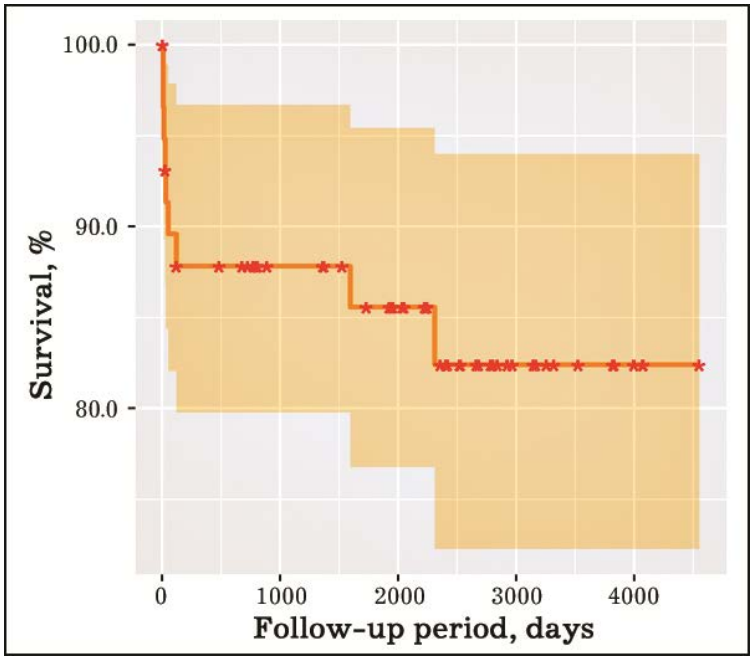

Fig. 1. The renal allograft survival rates (1- and 3-year survivals 88% (95% CI 80-97), 5-year survival 86% (95% CI 77-95), 7 - and 10-year survivals 82% (95% CI 72-94)

Fifty patients were discharged with functioning PG. The PG function parameters, as well as the cases of early and long-term PG loss are presented in Table 7.

Table 7. Outcomes for pancreatic graft

Functioning PG, n (%) 50 (83.3)		50 (83.3)
Total amylase, Me [25%; 75%] (min; max), U/L		117[85;169](36;269)
Pancreatic amylase, Me [25%; 75%] (min; max), U/L		100[66;159](21;245)
Lipase, Me [25%; 75%] (min; max), U/L		81[51;152](2;588)
Free insulin, Me [25%; 75%] (min; max), μIU/mL		13.7 [6.6;17](2;32.7)
C-peptide, Me [25%; 75%] (min; max), ng/mL		4[2.9;4.8](2;8.4)
Glycosylated hemoglobin, Me [25%; 75%] (min; max),%		5.3 [4.8;5.6]
In-hospital* loss of PG function, n 10		10
Patient No.	Timing, days	Cause, if known
1	57	Arrosive bleeding due to fungal infection of the graft arteries
29	10	Uncontrollable acute humoral rejection of PG

42	1	Occlusive arterial thrombosis of PG
52	5	PIPPG, sepsis
57	40	Occlusive thrombosis of the single PG splenic artery
58	28	Infected PPFC, MOF
3	58	Fatalities with functioning PG
23	3	
26	29	
27	52	
Loss of PG function in the long-term*, n		11
Patient number	Timing, months	Cause, if known
4	79	Cause unknown
5	83	Cause unknown
9	97	Breast cancer, chemotherapy
18	9	Chronic humoral rejection
36	34	Cause unknown
45	121	Cause unknown
46	12	Cause unknown
60	4	PG TMA, interintestinal anastomosis incompetence, recurrent bleeding from the wall of the duodenal stump, an increase in intoxication syndrome
2	4	Fatalities with functioning PG
11	63	
43	25	

* - uncensored by death.

Notes: PIPPG, primary infected PG, MOF, multiple organ failure.

The PG survival rate is shown in Figure 2.

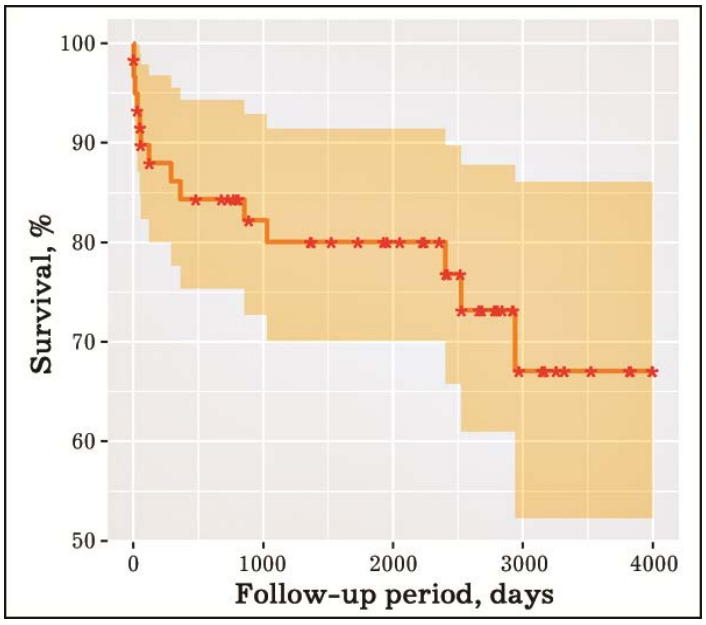

Fig. 2. Pancreas graft survival rates (1-year survival 84% (95% CI 75-96), 3- and 5-year survivals 80% (95% CI 70-91), 7-year survival 73% (95% CI 61–88), 10-year survival 67% (95% CI 52–86)

The time and causes of patient mortality are presented in Table 8.

Table 8. Patient survival after simultaneous kidney and pancreas transplantation

Recipients discharged, n 53		53
In-hospital survival, %		88.3
Death in hospital, n		7
Patient No.	Timing, days	Cause, if known
3	58	Catheter sepsis, MOF
23	3	Acute cardiovascular failure
26	29	IST complications, MOF
27	52	IST complications, MOF
52	21	PIPPG, sepsis, MOF
57	96	Sepsis, MOF
58	53	Infected PPFC, sepsis, MOF
A 1-year survival rate,%		86.6
Death in the long-term postoperative period, n		5
Patient No.	Timing, months	Cause, if known
2	17	Cytomegalovirus pneumonia
9	98	Breast cancer, cancer intoxication
11	63	Cause unknown
43	25	Cause unknown
60	4	TMA, MOF

The recipient survival rates are graphically, presented in Figure 3.

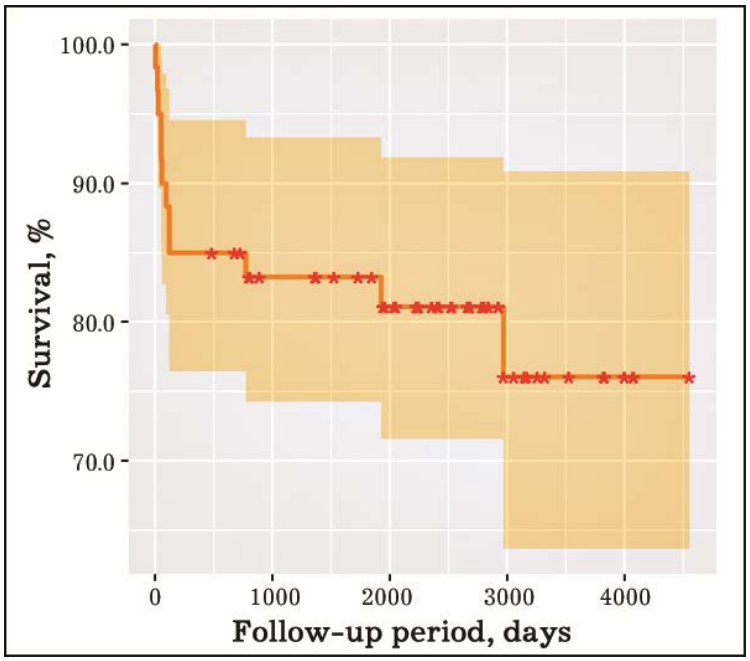

Fig. 3. Recipient survival rates (1-year survival 86.7% (95% CI 76-95), 3- and 5-year survivals 83% (95% CI 74-93), 7-year survival 81% (95% CI 72-92), 10-year survival 76% (95% CI 64-91)

Fifty three patients were discharged from hospital, including 50 patients with both grafts functioning, 2 patients with only RAG functioning, no patients with only PG functioning, and 1 patient with both grafts non-functioning.

Seven people died in the early postoperative period (during the first hospitalization).

One patient having both grafts functioning died, no patients with functioning only RAG died, 3 patients with only PG functioning died, and 3 people died with both grafts non-functioning.

At the end of the follow-up period, 48 patients were still alive. Of these, 38 patients had both grafts functioning, 6 patients had only kidney

graft functioning, 1 patient had only RAG functioning, and 2 patients with both graft non–functioning.

Thus, 5 patients died in the long-term postoperative period. Of these, there were 3 patients with both grafts functioning, 1 patient with only RAG functioning, none with only PG functioning, and 1 patient with both grafts non-functioning.

Factors that have a statistically significant impact on the outcome of pancreas transplantation

1. Kidney transplant function.

Patients who lost RAG in the early postoperative period had had a longer time on RRT prior to transplantation compared to the patients with a functioning RAG at discharge (4.5 [4;7.25] (0;18) years versus 2 [1;3] (0; 10) years, respectively (p=0.013)); the same trend was observed in respect of RAG loss in the long term (4.5 [2;6.5] (0; 18) years versus 2 [1; 3] (0; 10) years, respectively, (p=0.03)). The group of patients with in-hospital RAG removal statistically significantly differed in RRT duration from the patients without such removal; their RRT period was significantly higher (4.5 [4; 6.5] (4; 18) years compared to 2 [1; 3] (0; 10) years in patients who did not have their RAG removed in hospital, respectively (p=0.003)); moreover, they had had longer duration of diabetes by the time of transplantation: 24 [20; 29] (4; 40) and 29 [28.3; 30.5] (27; 35), p=0.038). The group of patients who returned to RRT in the long-term differed in the RRT terms by the time of transplantation: their RRT terms were statistically significantly longer than in patients with functioning RAG (4.5 [4; 5.75] (1; 18) years versus 2 [1; 3] (0; 10) years, respectively (p=0.035)).

The factors that have a statistically significant impact on PT outcomes with regard to RAG are presented in Table 9.

Table 9. Factors statistically significantly affecting the outcomes for renal allograft

Factor	RR	95% CD	p	OR	95% CD	p
Early RAG function (up to 90 days)						
CAPD-HD conversion	0.55	0.25–1.23	0.028	0.1	0.016–0.66	0.028
Parapancreatic infection	–	–	–	0.14	0.025–0.82	0.046
Repeated open surgery	–	–	–	0.063	0.01–0.38	0.0045
RAG removal in the early postoperative period						
CAPD-HD conversion	8.83	2.27–34.4	0.011	16.7	2.3–120.7	0.0011
ATGAM as a component of induction IST	6.38	1.55–26.3	0.028	9.6	1.5–60.8	0.028
Surgical complications IVa	6.88	1.76–29.8	0.048	12.8	1.4–116	0.048
Parapancreatic infection	7.43	1.85–29.9	0.018	12.3	1.84–81.7	0.018
Repeated open surgery	7.43	1.85–29.9	0.018	12.3	1.84–81.7	0.018
RAG function in the long-term postoperative period						
CAPD-HD conversion	–	–	–	0.13	0.02–0.81	0.032
Surgical complications IIIb	–	–	–	0.15	0.03–0.72	0.02
Parapancreatic infection	–	–	–	0.095	0.016–0.56	0.009
Repeated open surgery	–	–	–	0.095	0.016–0.56	0.009

2. Pancreas graft function.

The patients with functioning PG at the time of discharge and at the end of the follow-up period had statistically significantly shorter periods of pre-transplant RRT than the patients with removed PG: (2 [1; 3] (0; 10) years versus 4 [2.5; 6.5] (0; 18) years, respectively (p=0.027)). In addition, the patients in the group with non-functioning PG by the end of the follow-up period had statistically significantly lower GFR at discharge 47 [42; 64] (16; 86) ml/min versus 68.8 [52.8; 88.5] (38.5; 155) ml/min (p=0.01), and higher urea levels (7.8 [6.1; 16] (4.6; 31) versus 6.6 [4.8; 7.6] (3.5; 14.5) mmol/L (p=0.04), total amylase 180 [144; 228] (89; 269) U/L versus 115 [74.6; 139.5] (36; 230) U/L (p=0.004), pancreatic

amylase 161 [110; 195.6] (56; 245) U/L versus 95.6 [53; 129] (21; 182) U/L (p=0.009) and lipase 161 [122.5; 206.4] (29; 588) U/L versus 66 [43.5; 114.5] (2; 236) U/L (p=0.009), respectively.

Table 10 presents the factors that statistically significantly affect the outcomes of PT with regard to PG.

Table 10. Factors statistically significantly affecting the outcomes for pancreatic graft

Factor	RR	95% CI	p	OR	95% CI	p
Functioning PG at discharge from hospital						
Parapancreatic infection	–	–	–	0.096	0.017–0.54	0.012
Repeated open surgery	–	–	–	0.096	0.017–0.54	0.012
In-hospital PG removal						
Blood group - A (II)	8.04	1.002–64.58	0.027	10	1.09–92.1	0.027
ATGAM as a component of induction IST	5.67	1.35–23.8	0.038	8	1.31–48.95	0.038
Surgical complications IVa	28	7.2–109.2	0.00003	–	–	–
Parapancreatic infection	15.1	3.4–68.1	0.001	34	4.3–266.3	0.001
Functioning PG in the long-term						
Surgical complications IIIb	–	–	–	0.053	0.006–0.47	0.002
Tacrolimus as a component of the baseline IST	–	–	–	5.78	1.01–33	0.045
Repeated open surgery	–	–	–	0.066	0.007–0.59	0.006
Return to insulin therapy						
Blood group - A (II)	2.9	1.1–7.57	0.03	4.11	1.2–14.5	0.03
Surgical complications IVa	5.6	3.2–9.8	0.002	–	–	–
Parapancreatic infection	5.6	2.8–11.5	0.0003	33.8	3.6–319	0.0003

According to the data obtained, the development of parapancreatic infection had reduced the probability of PG functioning by more than half by the time of discharge. The development of IVa surgical complications and parapancreatic infection increases the risk of PG early removal by 28 and 15 times, respectively.

3. Patient survival rate.

The group of patients who died during the early postoperative period in hospital was characterized by longer RRT periods before transplantation compared to survived patients (4 [4; 7.5] (0; 18) years versus 2 [1; 3] (0; 10) years, respectively, (p=0.028)).

Table 11 shows the factors that statistically significantly affect the early and long-term mortality of patients.

Table 11. Factors statistically significantly affecting the patient survival

Factor	RR	95% CI	p	OR	95% CI	p
Patient being alive on the day of discharge from hospital						
CAPD-HD conversion	-	-	-	0.08	0.012–0.53	0.017
Parapancreatic infection	-	-	-	0.11	0.018–0.67	0.029
Repeated open surgery	-	-	-	0.045	0.007–0.3	0.002
Patient being alive at the moment of writing this article						
CAPD-HD conversion	-	-	-	0.09	0.014–0.56	0.012
Surgical complications IIIb	-	-	-	0.09	0.018–0.48	0.006
Parapancreatic infection	-	-	-	0.06	0.01–0.38	0.002
Repeated open surgery	-	-	-	0.06	0.01–0.38	0.002
In-hospital fatal outcome						
CAPD-HD conversion	6.75	1.96–23.25	0.017	12.5	1.9–83.3	0.017
Parapancreatic infection	5.7	1.6–20.3	0.029	9.2	1.50–56.2	0.029
Repeated open surgery	10.1	2.8–36	0.002	22.2	3.3–148	0.002
Long-term fatal outcome						
Surgical complications IIIb	11.75	2.43–56.74	0.008	22.5	2.65–190.7	0.008
Parapancreatic infection	8.17	1.88–35.54	0.04	15.3	1.57–150.1	0.04
All-cause fatal outcome						
CAPD-HD conversion	4.5	1.92–10.57	0.012	11.5	1.8–73.6	0.012
Surgical complications IIIb	4.64	1.94–11.1	0.006	10.7	2.1–55.1	0.006
Parapancreatic infection	5.41	2.35–12.45	0.002	16.43	2.65–101.7	0.002
Repeated open surgery	5.41	2.35–12.45	0.002	16.43	2.65–101.7	0.002

Discussion

To date, the need for PT is not decreasing and, despite the performed transplantations, the "waiting lists" for PT are not being reduced. Thus, in the United States in 2018, 1485 new candidates were included in the "waiting list" for PT, and 962 patients had been on the list [5]; in the Russian Federation in 2019, 14 people were included in the "waiting list" for PT for the first time, and 100 patients had been on the list [6].

One-, 5-, and 10-year recipient survival rates, as reported by transplant centers, range from 82% to 100%, from 81% to 95%, and from 67 to 83%, respectively; those of kidney grafts range from 80% to 98%, from 63% to 94%, and from 57% to 81%, respectively; those of pancreas grafts range from 71% to 95%, from 59% to 94%, and from 53% to 71%, respectively [7-16]. The results we have obtained correspond to the results of world transplant centers.

According to M. Bodro et al., and A. Marcacuzco et al., repeated open surgical interventions significantly reduce the PG survival (Bodro: OR 4.7 (2.4-9.4) p=0.001; A. Marcacuzco: HR 2.99 (1.,39–6.43) p=0.005) [17, 18]. F. Messner et al. reported on a statistically significant impact of surgical complications of IIIb or higher severity on PG survival (HR 2.96 (1.95-4.5) p<0.01) [19], Y.M.Venstrom et al. reported on the statistically significant impact of post-transplant complications on the recipient survival rates (RR 1.45 (1.19-1.75) p=0.001) [20].

Serrano et al. published the data showing that the use of anti-T cell induction (HR 0.9 (0.82-0.98) p=0.019) and tacrolimus as a calcineurin inhibitor in the baseline IST was a protective factor for PG survival [21]. In turn, S. Parajuli et al. spoke on a statistically significant reduction in the risk of death when using T-cell-depleting drugs as induction (HR 0.63 (0.41-0.96) p=0.03) [22].

As a result of our study, we noted a statistically significant impact of such factors as peripancreatic infection, IIIb and IVa surgical complications, repeated open surgery, the dialysis therapy conversion from peritoneal dialysis to HD, as well as the use of T-cell-depleting agents as an induction IST component and tacrolimus a baseline IST component on the survivals of recipients, RAG, and PG

Thus, all the cases of the transplanted organ rejections were successfully cured. Polyclonal antithymocyte antibodies were administered as part of the combined anti-crisis therapy in most cases (11 patients (78.6%)). The incidence of early surgical complications after pancreatic transplantations was 56.7%, however, the majority of complications (82.7%) were mild or moderate (Clavien–Dindo categories I–IIIb). Meanwhile, the renal allograft in-hospital, 1-, 3-, 5-, 7-, and 10-year survival rates were 86.4%, 88%, 88%, 86%, 82% and 82%, respectively. The pancreas graft in-hospital, 1-, 3-, 5-, 7-, and 10-year survival rates were 83.3%, 84%, 80%, 80%, 73%, and 67%, respectively. A recipient in-hospital, 1-, 3-, 5-, 7-, and 10-year survival rates were 88.3%, 86.7%, 83%, 83%, 81%, 76%, respectively.

Our study has a number of objective shortcomings, including the lack of randomization and an insufficient number of cases for conducting a multivariate analysis. After the required number of pancreas transplantations has been performed, we shall make a multivariate analysis to assess more objectively the factors that statistically significantly affect the outcome of this surgery.

Conclusions

1. The incidence of early immunological complications after pancreatic transplantations was 23.3%. In most cases, an isolated rejection of a renal allograft or pancreatic graft occurred (78.6%).

2. The factors that significantly affect the renal allograft survival rate in the early postoperative period were recognized the following: the conversion of renal replacement therapy from peritoneal dialysis to hemodialysis (RR 8.83 (2.27–34.4) p=0.011), peripancreatic infection and the need for repeated open surgery (RR 7.43 (1.85–29.9) p=0.018), the development of IVa surgical complications according to the Clavien–Dindo classification (RR 6.88 (1.76–29.8) p=0.048), and the administration of antithymocyte polyclonal antibodies (ATGAM) in the induction immunosuppressive therapy (RR 6.38 (1.55–26.3) p=0.028).

3. The factors that significantly increased the probability of in-hospital removal of the pancreas graft were the following: IVa surgical complications according to the Clavien–Dindo classification (RR 28 (7.2–109.2) p=0.00003), the development of peripancreatic infection (RR 15.1 (3.4–68.1) p=0.001), the administration of antithymocyte polyclonal antibodies (ATGAM) in the induction immunosuppressive therapy (RR of 5.67 (1.35–23.8) p=0.038).

4. The factors that statistically significantly reduced the in-hospital survival of patients undergoing pancreas transplantation were the need for repeated open surgery (RR 10.1 (2.8–36) p=0.002), the conversion of renal replacement therapy from peritoneal dialysis to hemodialysis (RR 6.75 (1.96–23.25) p=0.017) and the development of peripancreatic infection (RR of 5.7 (range: 1.6 to 20.3) p=0.029).

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The article was received on February 15, 2021;
approved after reviewing March 24, 2021;
accepted for publication June 30, 2021