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The influence of intraoperative hemodynamic parameters on the results of combined kidney and pancreas transplantation

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Abstract

Introduction. *Reperfusion syndrome has been proven to impact the early results of simultaneous pancreas and kidney transplantation. The optimal values of hemodynamic parameters at the moment of reperfusion of the kidney graft and the pancreas graft have been the subject of discussion in relation to possible early complications and outcomes of simultaneous*

pancreas and kidney transplantation. This issue needs additional research.

The objective *was to evaluate how the intraoperative hemodynamic parameters may influence early results of simultaneous pancreas and kidney transplantation*

Material and methods. *The retrospective study was conducted to analyze the impact of intraoperative hemodynamic parameters on the early results of treatment in 83 patients who underwent simultaneous pancreas and kidney transplantation in the N.V. Sklifosovsky Research Institute for Emergency Medicine in the period from 2008 to 2023. Given the primary ROC analysis results, we allocated the patients into 2 groups, according to their mean arterial pressure (MAP) values at reperfusion. Group I consisted of patients with MAP<90 mmHg (n=21), group II included patients with MAP≥90 mmHg (n=62). The characteristics of donors and recipients were comparable between the groups (p>0.05). The intraoperative hemodynamic parameters of the recipients (MAP, central venous pressure, heart rate) were analyzed at the beginning of surgery, at reperfusion stages, at the time of making the interintestinal anastomosis, and on surgery completion; the incidence of postoperative complications was studied; the primary functions of the kidney and pancreas grafts were evaluated; the in-hospital graft and recipient survival rates were calculated.*

Results. *The median values of MAP (mm Hg) were significantly lower in group I compared to those in group II at all stages of surgery, except for the surgery beginning: 87 (86;87) mmHg versus 101 (97;104) mmHg at the time of the kidney graft reperfusion; 89 (83;95) mmHg versus 97 (93;102) mmHg at the time of the pancreatic graft reperfusion; 91 (85;95) mmHg versus 97 (89;99) mmHg at the time of making interintestinal anastomosis; 90 (82;100) mmHg and 103 (90;116) mmHg*

on surgery completion, respectively (p<0.05). The remaining hemodynamic parameters had no statistically significant differences between the groups (p>0.05). There were no statistically significant differences between the groups in the incidence of postoperative complications, either (p>0.05). The rate of primary kidney graft function was significantly higher in group II (96.8%; n=60) compared to group I (42.9%; n=11) (p<0.05). All recipients displayed a primary pancreatic graft function. The median hospital length of stay in group I days was statistically significantly longer compared to that of the patients in group II, making 45 (28.5;72) versus 34.5 (25;60) days, respectively (p<0.05). The hospital survival rates of kidney grafts, pancreas grafts and recipients were significantly higher in patients of group II compared to those in patients of group I: 93.5% (n=58), 87.1% (n=54), and 96.8% (n=60) versus 57.1% (n=12), 57.1% (n=12), and 66.7% (n=14), respectively (p<0.05).

Conclusion. *MAP≥90 mmHg at the timepoint of reperfusion is a factor that has a statistically significant effect on the primary function of a kidney graft in the early postoperative period, associates with the increase in hospital survival rates of grafts and recipients at early stages after simultaneous pancreas and kidney transplantation.*

Keywords: simultaneous pancreas and kidney transplantation, intraoperative hemodynamic parameters, mean arterial pressure, graft hospital survival, recipient hospital survival

Conflict of interests Authors declare no conflict of interest

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BMI, body mass index
CETA, combined endotracheal anesthesia
CETA+EA, combined endotracheal anesthesia in combination with epidural anesthesia
CI, confidence interval
CVP, central venous pressure
DM 1, type I diabetes mellitus
ESRD, end-stage (chronic) renal disease
HLA, human leukocyte antigens
HR, heart rate
MAP, mean arterial pressure
PG, pancreas graft
RAG, renal allograft
ROC analysis, receiver operating characteristic curve analysis
SPKT, simultaneous pancreas and kidney transplantation

Introduction

Simultaneous pancreas and kidney transplantation (SPKT) is recognized as the “gold standard” for the treatment of patients with type 1 diabetes mellitus (DM 1) complicated by end-stage chronic renal disease (ESRD) [1–3]. Improvements in surgical techniques and the optimization of immunosuppressive therapy observed over the past two decades have contributed to significant improvements in the life expectancy and the quality of life in this patient population [4–8]. Despite such encouraging results, SPKT is still associated with a high risk of developing surgical and immunological complications and, as a consequence, a high risk of a graft loss and recipient mortality [9–13, 14]. Among the factors influencing SPKT outcomes, it is customary to distinguish between donor-associated and recipient-dependent factors, as well as transplantation factors [15]. Donor-associated factors include the body mass index (BMI), age, donor gender, donor type (a confirmed brain-dead donor or a non-heart-beating donor), and the cause of death; the recipient-dependent factors are the recipient age and gender, type and duration of

diabetes mellitus, type and duration of renal replacement therapy, comorbid pathology [16, 17]. Transplantation factors include immunological incompatibility of HLA antigens in the donor-recipient pair, the pancreatic secretion drainage from the pancreas graft, the time period of graft preservation, immunosuppressive therapy type, the nature of the initial graft function, and the development of surgical and immunological complications [15]. Most of them cannot be changed or corrected at the time of organ donation procurement, but currently the available medical literature contains some studies on the effect of intraoperative hemodynamics on early and long-term outcomes of SPKT [18–20]. According to these sources, maintaining adequate perfusion of transplanted organs during surgery has a favorable prognostic value in relation to outcomes [20, 21]. Mean arterial pressure (MAP) is one of the main intraoperative parameters of parenchymal organ perfusion, which is used in clinical practice as an indirect sign of adequate perfusion of transplanted organs [22, 23]. Due to the lack of a mechanism for the autoregulation of the blood flow in the renal allograft (RAG) and pancreatic graft (PG), maintaining MAP within physiological limits is of particular importance, and for this reason this parameter has been given increased attention [18–20, 24]. The impact of the MAP parameter at reperfusionon the function of kidney and pancreas grafts in SPKT, as well as on the results of the operation, has been little studied and requires additional research [18, 20, 25].

The study objective was to evaluate the influence of intraoperative hemodynamic parameters on the early results of combined kidney and pancreas transplantation.

Material and methods

A retrospective analysis of the impact of intraoperative hemodynamics on early treatment outcomes was performed in 84 recipients who underwent SPKT in the Kidney and Pancreas Transplantation Department of the N.V. Sklifosovsky Research Institute for Emergency Medicine of the Moscow Health Department from January 1, 2008, to December 31, 2023.

Inclusion criteria for the study were SPKT in patients with DM 1 complicated by stage 5 chronic kidney disease as a result of diabetic nephropathy.

Non-inclusion criteria were isolated kidney transplantation, pancreas transplantation after previous kidney transplantation.

Exclusion criteria were patients with insufficient or missing data on intraoperative hemodynamic parameters and outcomes.

Initially, a “receiver operating characteristic analysis” (ROC analysis) was made to assess the prognostic accuracy and determine the optimal values of mean arterial pressure at the time of reperfusion, allowing the classification of recipients into two groups with regard to the graft primary function. According to the results of that analysis, the recipients were allocated into groups: group I included the recipients with the mean arterial pressure lower than 90 mm Hg at the time of reperfusion, group II consisted of the recipients with mean arterial pressure equal or higher than 90 mm Hg at the time of reperfusion.

Demographic and clinical characteristics of donors included age, gender, cause of donor death, serum creatinine and urea levels, total amylase, and length of stay in the Intensive Care Unit.

Demographic and clinical characteristics of recipients included such data as the age, gender, BMI, type and duration of renal replacement therapy, duration of diabetes, and the presence of cardiac comorbidities.

Transplantation factors included the number of incompatible genes according to the human leukocyte antigen (HLA) system, cold ischemia time of the RAG and PG, surgical technique for draining pancreatic secretions, bacteriological examination of perfusate i.e. the preservative solution for transplanted organs.

Intraoperative data included the surgery duration, anesthesia type (combined endotracheal anesthesia (CETA) or combined endotracheal anesthesia in combination with epidural anesthesia (CETA+EA)), the surgical blood loss volume, warm ischemia time for the RAG and PG, the volume of intravenous infusion-transfusion therapy, and the vasopressor administration rate.

To assess hemodynamic parameters during SPKT, the following data were collected and analyzed: central venous pressure (CVP), MAP, and heart rate (HR) at the surgery start, at the time of RAG and PG reperfusion, on completion of the intestinal anastomosis, and on surgery completion.

We analyzed postoperative complications that arose in recipients after SPKT, including a delayed RAG function, an acute RAG and PG rejection crisis, surgical and infectious complications, repeated operations and the hospital length of stay assessed in bed-days.

The initial kidney graft function was considered primary if there was no need for renal replacement therapy with hemodialysis during the first 7 days of the postoperative period after transplant surgery.

If there was a need for a hemodialysis session in the first week after transplantation and a delay in recovery of water and nitrogen excretory functions, the delayed initial function of the transplanted kidney was recorded.

If the blood glucose level was normalized during the first day after transplantation without administering the exogenous insulin, the PG

function was qualified as immediate. If exogenous insulin administration in an amount exceeding 30 U/day was needed in the first week after transplantation, the PG initial function was considered as delayed.

Induction immunosuppressive therapy was performed using mono- or polyclonal antibodies. Maintenance immunosuppressive therapy included calcineurin inhibitors (tacrolimus or cyclosporine), mycophenolic acid agents, and glucocorticosteroids. There were no statistically significant differences between the groups in the main components of the immunosuppressive therapy regimens ($p>0.05$).

General anesthesia was induced by intravenous propofol, fentanyl, and cisatracurium; anesthesia was maintained by administering an inhalation agent (isoflurane, sevoflurane, or desflurane) in the form of oxygen-air mixture with bolus administration of fentanyl and cisatracurium depending on the surgery stage and the time factor. In addition to standard monitoring, invasively measured arterial pressure and central venous pressure were continuously monitored. Dopamine was used as a vasopressor during surgery in all patients in dosages that ensured the optimal hemodynamics at the stages of graft reperfusion: systolic blood pressure over 140 mm Hg, mean arterial pressure over 70 mm Hg. The fluid therapy was performed with crystalloid solutions, including balanced ones. In case of intraoperative bleeding at a volume of more than 500 ml, a fresh frozen plasma transfusion was undertaken; if the hemoglobin level was below 70 g/L, a transfusion of washed erythrocytes was performed.

The endpoint of the study was in-hospital PG and RAG survival, as well as in-hospital recipient survival. The loss of PG function was defined as the insulin therapy resumption, the pancreas graft removal, retransplantation, or in-hospital death. The loss of RAG function was

defined as the need for dialysis (return to dialysis), the kidney graft removal, retransplantation, or in-hospital death.

Quantitative parameters were assessed for compliance with normal distribution by using the Shapiro–Wilk test. Quantitative parameters with normal distribution were expressed as arithmetic means and standard deviations. In absent normal distribution, the quantitative data were described as median (Me) and the lower and upper quartiles (Q1;Q3). Categorical data were expressed in absolute values and percentages. The inter-group comparison of a quantitative parameter with normal distribution, provided that variances were equal, was performed using Student's t-test. The inter-group comparison of a quantitative parameter with a non-normal distribution was performed using the Mann–Whitney U-test. Comparison of percentages in the analysis of four-field contingency tables was performed using Fisher's exact test (for expected event values less than 10). The Kaplan–Meier method was used to calculate the patient and graft survival rates. To assess the significance of the odds ratio, the upper and lower limits of the 95% confidence interval (CI) were calculated. Differences were considered statistically significant at $p<0.05$. Graphic design editor software of Microsoft Office v. 16.16.27, SPSS v. 27.0, and Startech v. 2.8.8 were used to create diagrams and graphs.

Results

The initial ROC analysis showed a correlation between the primary kidney graft function and the mean arterial pressure values during reperfusion. The resulting ROC curve is shown in Fig. 1.

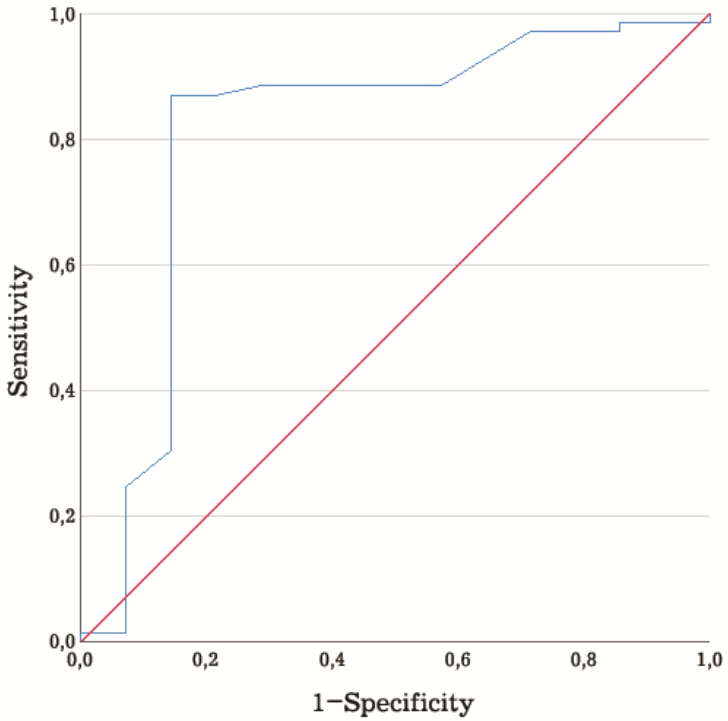

Fig. 1. ROC curve characterizing the relationship of the primary graft function to the mean arterial pressure values at reperfusion

The resulting ROC curve was characterized by an AUC of 0.81±0.08; 95% CI [0.66–0.96]. The model was statistically significant ($p<0.001$).

The mean arterial pressure at the cut-off point was 90 mm Hg: at mean arterial pressure up to 90 mm Hg during reperfusion, a higher risk of delayed kidney graft function was noted, whereas at mean arterial pressure of 90 mm Hg and higher, the risk of delayed kidney graft function was considered low. The sensitivity and specificity of the model at the selected threshold value of the mean arterial pressure were 85.5% and 85.7%, respectively.

Since in our study, a 100% primary PG function was achieved in all recipients, only the mean arterial pressure values during kidney graft reperfusion were used to construct the ROC curve for the model.

Thus, recipients were divided into two groups with regard to the mean arterial pressure during the kidney graft reperfusion: group I included recipients with the mean arterial pressure under 90 mm Hg and group II included those with the mean arterial pressure equal or higher than 90 mm Hg.

The main demographic and clinical characteristics of the two groups were compared and presented in Table 1.

Table 1. Baseline original demographic, clinical and pathological characteristics of donors and recipients, transplantation factors in the study groups

Parameters	Group I (n=21)	Group II (n=62)	p
Donors:			
Age, full years, M±SD	29.2±7.66	28.1±5.97	0.462*
Gender, male/female, n (%)	18 (85.7%)/3 (14.3%)	52 (83.9%)/10 (16.1%)	0.958**
Traumatic brain injury, n (%)	15 (71.4 %)/6 (28.6%)	39 (62.9%)/23 (37.1%)	0.600**
Acute cerebrovascular accident, n (%)	6 (28.6%)/15 (71.4%)	23 (37.1%)/39 (62.9%)	0.600**
Blood creatinine (μmol/L), Me(Q1;Q3)	94 (74;104)	91.1 (73;108)	0.822***
Blood urea (mmol/L), Me(Q1;Q3)	5.5 (4.2;7.4)	4.7 (3.9;6.3)	0.214***
Blood total amylase (mmol/L), Me(Q1;Q3)	73 (62;156.2)	60.5 (47.3;161)	0.599***
Donor's hospital length of stay, days, Me(Q1;Q3)	2 (2;3)	2 (1;2,5)	0.235***
Recipients:			
Age, full years, M±SD	35.57±5.9	34.84±5.52	0.607*
Gender, male/female, n (%)	10 (47.6%)/11 (52.4%)	22 (35.5%)/40 (64.5%)	0.437 **
BMI, kg/m^2, Me(Q1;Q3)	21.4 (20.1;22.7)	20.7 (19.3;22.2)	0.164***
Duration of diabetes mellitus, full years, Me(Q1;Q3)	28 (23;31)	24 (20;28)	0.129***
Duration of renal replacement therapy, full years, Me(Q1;Q3)	4 (1;6)	2 (1;4)	0.241***
Associated cardiac pathology:			
Hypertension, n (%)	8 (38%)	17 (27.4%)	0.566**
Ischemic heart disease, n (%)	2 (9.5%)	12 (19.3%)	0.311**
Transplantation factors:			
Number of incompatible antigens in HLA system, Me(Q1;Q3)	5 (4;6)	5 (4;6)	0.794***
Cold ischemia time, full hours:			
- *RAG*, Me(Q1;Q3)	7 (5;9)	7.5 (6;10)	0.334***
- *PG*, Me (Q 1;Q 3)	8.5 (7;9)	9 (8;10.5)	0.081***
Surgical technique to drain pancreatic secretions:			

- *Duodenoduodenoanastomosis formation*, n (%)	12 (57.1%)	38 (61.3%)	0.799**
- *Duodenojejunostomy*, n (%)	6 (28.6%)	17 (27.4%)	1.000**
- *Duodenojejunostomy on Roux-en-Y excluded intestinal loop (retroperitoneal location)*, n (%)	3 (14.3%)	7 (11.3%)	0.663**
Positive result of perfusate bacteriology culture, n (%)	4 (19%)	5 (8.1%)	0.221**

Notes: Differences in parameters between the groups are considered statistically significant at p<0.05; *Student's t-test; ** Fisher's exact test; *** Mann–Whitney U -test

As one can see in Table 1, the main baseline characteristics of donors and recipients in both groups were similar; no statistically significant differences were obtained for any of the parameters. Differences in transplantation factors between the groups were statistically insignificant, either.

Table 2 shows the general intraoperative data in the two compared groups and their statistical significance.

Table 2. General intraoperative data in the study groups

Parameter	**Group I** (n=21)	**Group II** (n=62)	**p**
Surgery duration, minutes, M±SD	581.2±111.8	531.8±97.3	0.056*
Anesthesia type, CETA/CETA+EA, n (%)	12 (57.1%)/9 (42.9%)	36 (58.1%)/26 (41.9%)	1.000**
Blood loss volume, ml, Me(Q1;Q3)	400 (300;500)	300 (200;500)	0.204***
Warm ischemia time, minutes:			
RAG, M±SD	37.5±7.3	35.9±8.1	0.321*
PG, M±SD	42.5±8.7	46.1±5.2	0.441*
Total infusion volume, ml, Me(Q1;Q3)	3500 (2700;4500)	3305 (2550; 4050)	0.540***
FFP, ml, M±SD	715±119.6	580±216.8	0.552*
Washed erythrocytes, ml, M±SD	295±37.0	298±27.8	0.893*
Dopamine infusion rate, mcg/kg/min, Me(Q1;Q3)	4 (2;5)	3 (2;5)	0.144***

Notes: Differences in parameters between the groups are considered statistically significant at p<0.05; *Student's t-test; ** Fisher's exact test; *** Mann–Whitney U -test

Table 2 shows that the surgery duration in Group 1 was longer than in Group 2 (581.2±111.8 minutes and 531.8±97.3 minutes, respectively), but these differences were statistically insignificant (p=0.056). The remaining intraoperative parameters did not differ statistically significantly between the groups, either.

Table 3 presents intraoperative hemodynamic parameters: CVP, MAP, and HR at the beginning of surgery, at the time of graft reperfusion, at the time of the intestinal anastomosis completion, and on surgery completion.

Table 3. Intraoperative hemodynamic parameters in the studied groups

Parameter	Group I (n=21)	Group II (n=62)	p
CVP, mm Hg			
At the beginning of surgery, Me(Q1;Q3)	7 (4;8)	6 (4;9)	0.806***
At RAG reperfusion, Me(Q1;Q3)	9 (7.5;10)	7 (7;9)	0.098***
At PG reperfusion, Me(Q1;Q3)	9.5 (7;11.5)	8 (7;9)	0.193***
On completing the intestinal anastomosis, Me(Q1;Q3)	10 (7.5;11)	8 (7;10)	0.170***
On surgery completion, Me(Q1;Q3)	6 (6;8.5)	7 (7;8)	0.381***
Mean arterial pressure, mm Hg			
At the beginning of surgery, Me(Q1;Q3)	100 (87;120)	111 (105;119)	0.058***
At RAG reperfusion, Me(Q1;Q3)	87 (86;87)	101 (97;104)	<0.001***
At PG reperfusion, Me(Q1;Q3)	89 (83;95)	97 (93;102)	<0.001***
On completing the intestinal anastomosis, Me(Q1;Q3)	91 (85;95)	97 (89;99)	0.021***
On surgery completion, Me(Q1;Q3)	90 (82;100)	103 (90;116)	0.003***
Heart rate, beats per minute			
At the beginning of surgery, Me(Q1;Q3)	75 (65;86)	79 (72;89)	0.253***
At RAG reperfusion, Me(Q1;Q3)	70 (67;75)	72 (66;80)	0.653***
At PG reperfusion, Me(Q1;Q3)	73 (67;77)	74 (70;88)	0.368***
On completing the intestinal anastomosis, Me(Q1;Q3)	76 (66;85)	80 (74;88)	0.253***
On surgery completion, Me(Q1;Q3)	88 (77;97)	86 (79;98)	0.680***

Notes: Differences in parameters between the groups are considered statistically significant at p<0.05;

*Student's t-test; ** Fisher's exact test; *** Mann–Whitney U -test

Table 3 shows that the hemodynamic parameters at the beginning of the operation did not differ statistically significantly between the groups. However, the mean arterial pressure values in recipients in Group I at all other stages of surgery were statistically significantly lower compared to the data in patients in Group II: 87 (86;87) mm Hg versus 101 (97;104) mm Hg at the moment of RAG reperfusion, respectively ($p<0.001$); 89 (83;95) mm Hg versus 97 (93;102) mm Hg at the moment of PG reperfusion, respectively ($p<0.001$); 91 (85;95) mm Hg versus 97 (89;99) mm Hg at the stage of completing the intestinal anastomosis, respectively ($p=0.021$); and 90 (82;100) mm Hg versus 103 (90;116) mm Hg, on surgery completion, respectively ($p=0.003$). At all stages of surgery, the CVP values did not differ statistically significantly between the groups. The heart rate was higher in group II compared to that in group I at all stages of surgery; however, that difference did not rich a statistical significance. Intraoperative hemodynamic parameters demonstrating the dynamics of mean arterial pressure, central venous pressure, and heart rate in both groups at all stages of surgery are clearly shown in the form of graphs in Fig. 2, 3, 4.

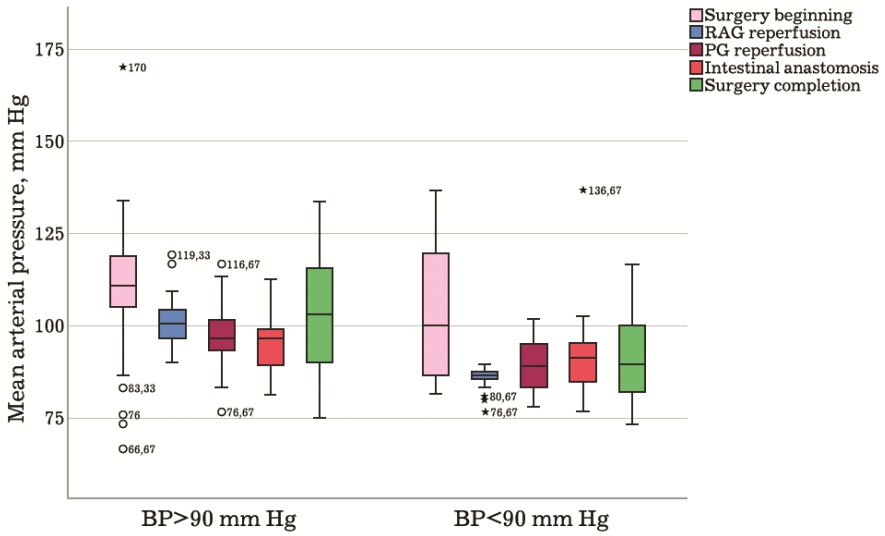

Fig. 2. Mean arterial pressure at the stages of surgery in the study groups

As one can see in Fig. 2, a decrease in the medians and quartiles of MAP took place in the group of patients with BP lower than 90 mm Hg at all stages of surgery except for the first one. At the first stage, these values were comparable.

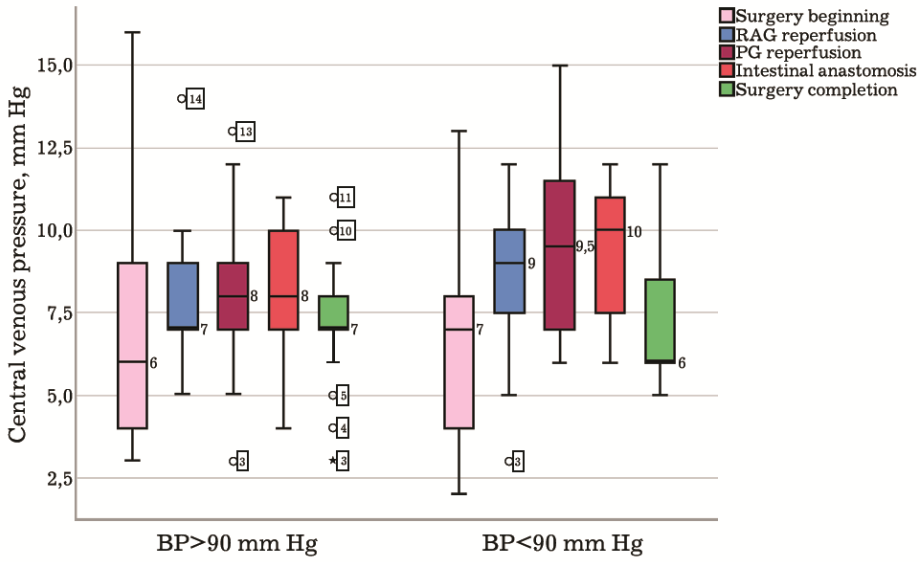

Fig. 3. Central venous pressure at the stages of surgery in the study groups

In Fig. 3, which shows box plots of medians and quartiles of CVP in two groups by stage of surgery, one can see that the two groups were comparable in this parameter, having no statistical differences from each other.

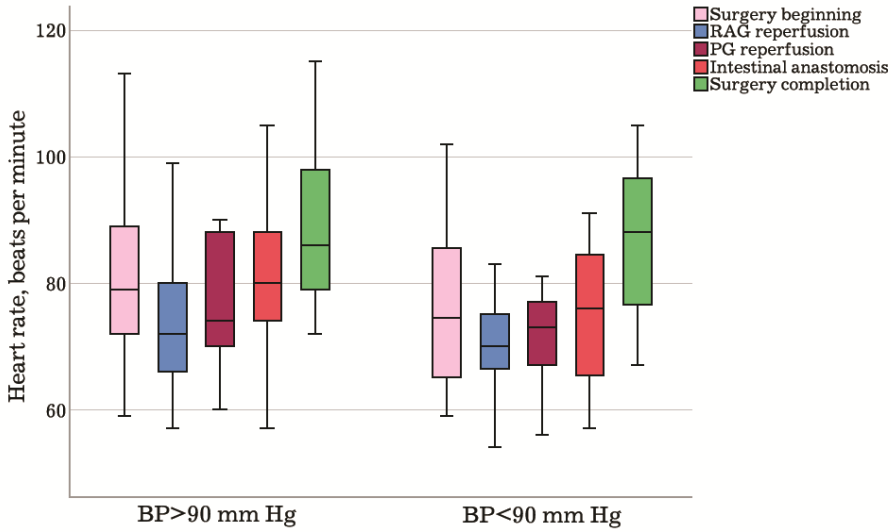

Fig. 4. Heart rate at the stages of surgery in the study groups

Fig. 4 presenting the graph of the heart rate dynamics in the patient groups at all stages of surgery demonstrated that the median heart rate was lower in the group of patients with BP lower than 90 mm Hg than this parameter in the compared group. However, these differences were statistically insignificant.

Postoperative complications studied in both groups are presented in Table 4.

Table 4. Postoperative complications in recipients after simultaneous pancreas and kidney transplantation

Parameter	Group I (n=21)	Group II (n=62)	p
Delayed RAG function, n (%)	12 (57.1%)	2 (3.2%)	<0.001**
Acute rejection crisis:			
Kidney graft, n (%)	3 (14.31%)	16 (27.2%)	0.436**
PG, n (%)	5 (23.8%)	18 (29%)	0.781**
Surgical complications:			
Occlusive arterial thrombosis, n (%)	1 (4.8%)	2 (3.5%)	1,000**
Occlusive thrombosis of superior mesenteric artery, n (%)	2 (9.5%)	14 (24.6%)	0.210**
Parapancreatic fluid collections, n (%)	3 (14.3%)	14 (24.6%)	0.537**
Intestinal anastomotic failure, n (%)	1 (4.8%)	7 (12.3%)	0.437**
Bleeding, n (%)	2 (9.5%)	7 (12.3%)	0.103**
Pancreatic necrosis, n (%)	2 (9.5%)	4 (6.8%)	0.650**
Infectious complications, n (%)	6 (28.6%)	7 (12.3%)	0.100**
Repeated surgery, n (%)	5 (23.8%)	6 (10.3%)	0.150**
Hospital length of stay, bed-days, Me (Q1;Q3)	45 (28.5;72)	35 (25;60)	0.029***

Notes: differences in parameters between the groups are considered statistically significant at p <0.05; *Student's t-test; ** Fisher's exact test; *** Mann–Whitney U -test

Delayed kidney allograft function in group I recipients took place in 12 cases with an incidence of 57.1% compared to that in recipients in group II where only 2 cases (3.2%) were recorded. This difference was statistically significant (p<0.001). There were no cases of primary renal graft non-function in both groups. Also, all patients in both groups displayed a primary PG function.

The median hospital stay of recipients from group I was statistically significantly longer than the median hospital stay in group II: 45 (28.5;72) versus 35 (25;60) days, respectively (p=0.029). No statistically significant difference was found for the remaining parameters of postoperative complications.

Fig. 5 clearly shows the hospital length of stay in the recipients with regard to the mean arterial pressure level.

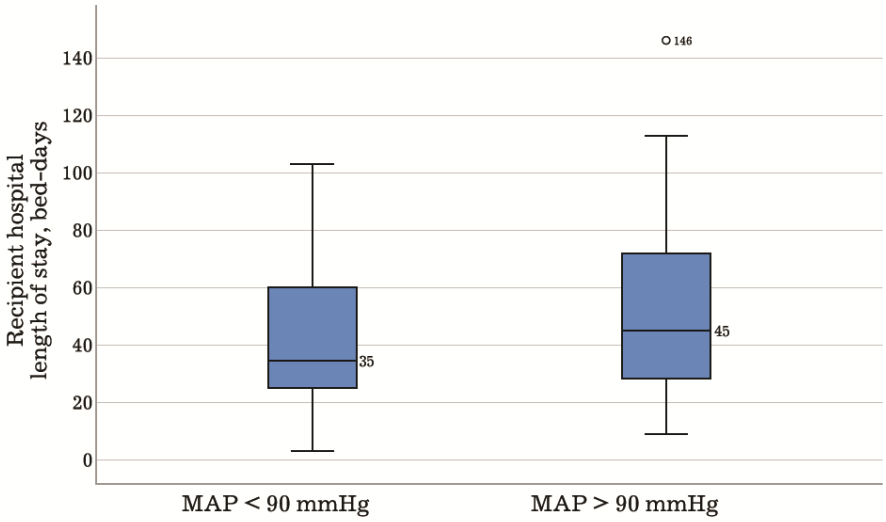

Fig. 5. The hospital length of stay in recipients after simultaneous pancreas and kidney transplantation, with regard to the mean arterial pressure at reperfusion

As one can see in Fig. 5, the median hospital length of stay in the group of recipients with BP lower than 90 mm Hg was obviously longer compared to this parameter in the compared group. These differences were statistically significant (p=0.029).

The endpoint of the study – the in-hospital pancreas and kidney graft survivals, as well as the recipient survival after SPKT is shown in Table 5.

Table 5. In-hospital graft and recipient survival rates after simultaneous pancreas and kidney transplantation

Parameter	Group I (n=21)	Group II (n=62)	p	Odds ratio; [95% CI]
In-hospital survival:				
RAG, n (%)	12 (57.1%)	58 (93.5%)	< 0.001*	10.9 [2.87–41.2]
PG, n (%)	12 (57.1%)	54 (87.1%)	0.009*	5.1 [1.62–15.8]
In-hospital survival:				
Recipients, n (%)	14 (66.7%)	60 (96.8%)	<0.001*	15 [2.8-80.1]

Notes: Differences in parameters between the groups are considered statistically significant at $p<0.05$;

* Fisher's exact test

When comparing the in-hospital RAG survival rates with regard to the mean arterial pressure in recipients, the statistically significant differences were obtained ($p<0.001$). In Table 5, one can see that the in-hospital RAG survival made 58 (93.5%) of 62 recipients in group II versus 12 (57.1%) of 21 recipients in group I. The chances of RAG functioning at discharge in group II increased by 10.9 times (95% CI [2.87–41.2]). A relatively strong Kramer's V correlation was noted between the compared variables ($V=0.435$).

When comparing the in-hospital survival rate with regard to the mean arterial pressure in recipients, the statistically significant differences were also obtained ($p=0.009$). The in-hospital PG survival rate was 54 cases (87.1%) among the recipients of group II versus 12 cases (57.1%) among the recipients of group I. The chances of PG functioning at discharge from the hospital increased by 5.1 times (95% CI [1.62–15.8]) in the recipients whose mean arterial pressure was more than 90 mm Hg at the time of reperfusion. An average Kramer's V correlation was noted between the compared variables ($V=0.323$).

In-hospital recipient survival rates in the group with MAP equal or higher 90 mm Hg was also statistically significantly higher compared to the other group of recipients: 60 cases (96.8%) versus 14 cases (66.7%),

respectively. The odds of recipient survival by the end of hospital stay were 15 times higher (95% CI [2.8–80.1]) provided the MAP at reperfusion was higher 90 mm Hg.

Figure 6 clearly shows the in-hospital RAG, PG and recipient survival rates.

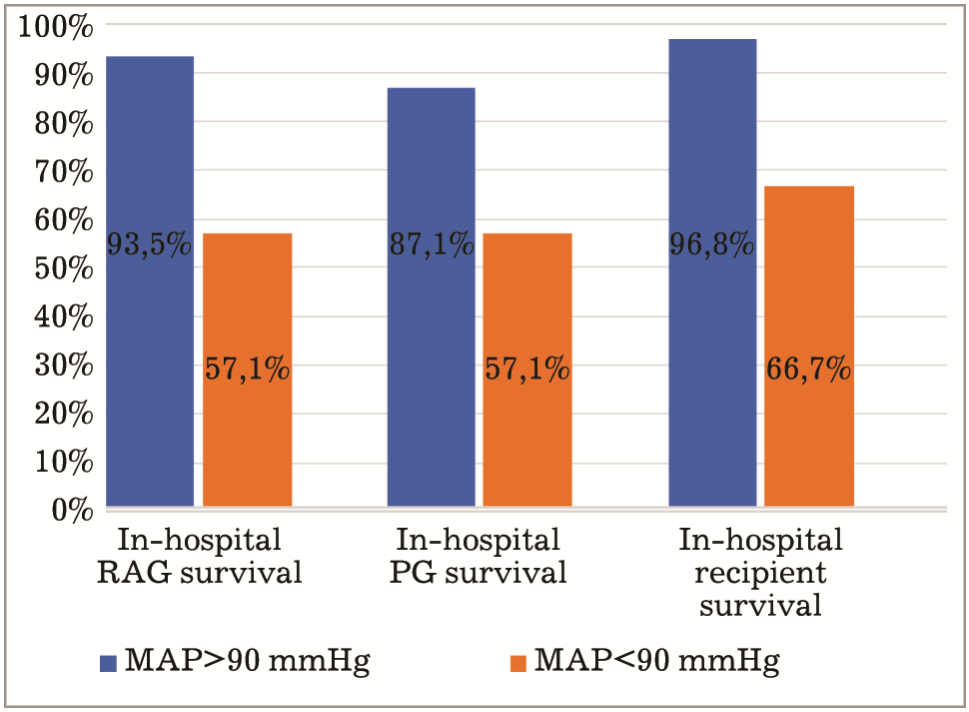

Fig. 6. Grafts and recipients survival rates in hospital after simultaneous pancreas and kidney transplantation

Discussion

A success of SPKT surgery is determined by a combination of several factors [13, 25, 26]. An important role among these factors belongs to the optimization of intraoperative hemodynamic parameters in patients. In this regard, the key point is normovolemia and normotension at the stage of graft reperfusion as the factor of preventing hypoxia and preventing a dysfunction of transplanted organs, which has a direct impact on survival and long-term outcomes [27–29].

According to a number of studies, the MAP and CVP levels at the stage of the graft reperfusion can affect both the early and long-term results of SPKT. The MAP below 70 mm Hg and CVP below 8 mm Hg at RAG reperfusion were shown to be associated with the occurrence of its delayed function [19, 21, 24]. In turn, an intraoperative increase in MAP above 95 mm Hg and maintaining CVP above 12 mm Hg were associated with immediate kidney graft function and better long-term survival [30, 31]. In a 2022 study, R. Sucher et al. indicated that an appropriate blood pressure level at reperfusion was a strong independent predictor of the increased long-term PG survival and a decreased incidence of delayed function of both PG and the RAG functions [26].

Our study was retrospective. We analyzed the early treatment results of 84 recipients who underwent SPKT over a 15-year period: from 2008 to 2023. The chosen design is a limitation of the study, reducing its value, but the results of our work confirm the data obtained in the studies by foreign colleagues. Calculated by using the ROC analysis, the mean arterial pressure of 90 mm Hg and higher recorded at kidney graft reperfusion was associated with a statistically significant increase in the in-hospital kidney and pancreas graft and recipient survival rates. In addition, this parameter statistically significantly influenced the reduction in the incidence of delayed kidney graft function in the early postoperative period of recipients after SPKT.

According to numerous literature sources, delayed kidney graft function can occur due to various factors, including pathophysiological characteristics of donors and recipients, transplantation factors, and intraoperative factors [15, 26]. Our study demonstrates the correlation between such hemodynamic parameter as the mean arterial pressure (especially at the time of graft reperfusion) and the delayed kidney graft function. Meanwhile, in all patients who underwent SPKT, we achieved a

primary PG function regardless of the mean arterial pressure level at the time of PG reperfusion. This may be due to the initially low blood flow velocity in the pancreas, so this parameter is not as critical as in the blood supply to the kidney graft.

The median hospital stay of patients in the group with a mean arterial pressure of at least 90 mm Hg was 34.5 (25;60) bed-days, which is statistically significantly shorter than the median hospital stay of 45 (28.5;72) bed-days in the recipients with a mean arterial pressure of lower than 90 mm Hg ($p=0.029$). This result also emphasizes the undoubted importance of adequate hemodynamic status of patients during surgery. In this context, the use of invasive hemodynamic monitoring, CVP monitoring are necessary components in ensuring intraoperative control of the patient. In the literature, these techniques in SPKT have shown their efficacy and have been used routinely to assess the intravascular fluid status and response to fluid therapy [26, 32]. It is known that fluid therapy under the guidance of CVP has been a traditional approach in kidney transplantation [19, 32].

However, the results of a number of studies have shown that CVP in values from 5 to 15 mm Hg as a tool for assessing fluid therapy efficiency is not always a reliable indicator of postoperative kidney graft function [32, 33]. In our study, we did not obtain statistically significant differences in CVP values between the study groups at the surgery stages. Meantime, the median CVP values in the group of recipients with a mean arterial pressure of at least 90 mm Hg were lower compared to the median values in the group of recipients with a mean arterial pressure of less than 90 mm Hg (see Table 3). The medians of the total fluid therapy volume did not differ statistically between the groups, nor did the median dopamine administration rates (see Table 2). This emphasizes the

importance of further studying the issue of adequate volume status in recipients and improving the methods for its assessment [24, 26].

Conclusion

Maintaining an optimal level of mean arterial pressure at the main stages of surgery SKPT is crucial for the successful functioning of the kidney and pancreas grafts in the early postoperative period.

In conclusion we can state the following:

1. Mean arterial pressure of at least 90 mm Hg at the renal allograft reperfusion is a factor that statistically significantly ($p<0,001$) reduces the incidence of delayed renal allograft function in recipients in the early postoperative period after simultaneous pancreas and kidney transplantation. Delayed renal allograft function in the recipients in group I occurred in 12 cases with an incidence of 57.1% compared to the recipients in group II, where 2 cases (3.2%) were recorded.

2. The mean arterial pressure of at least 90 mm Hg at the stages of reperfusion is a factor that statistically significantly increases the in-hospital kidney and pancreas graft survival rates. The in-hospital renal allograft survival in recipients of group II was 93.5% versus 57.1% in group I ($p<0.001$), the in-hospital pancreas graft survival in group II was 87.1% versus 57.1% in group I ($p<0.001$).

3. The in-hospital recipient survival in group II was statistically significantly higher compared to the recipient data of group I: 96.8% versus 66.7%, respectively ($p<0.001$). The chances of survival of these patients at the end of hospital stay were 15 times higher (95% CI [2.8–80.1]) provided that the MAP at reperfusion was at least 90 mm Hg.

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