

The impact of pulmonary hypertension on the risk of early graft dysfunction in related kidney transplantation

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Abstract

Introduction. Pulmonary hypertension is a common complication among patients with end-stage renal disease and has a significant impact on the outcome of kidney transplantation, including during kidney transplantation from a living related donor.

Objective. To study the prevalence of pulmonary hypertension among patients with end-stage renal disease and to determine its impact on the development of early renal graft dysfunction.

Material and methods. The study was based on the analysis of treatment results in 650 patients who underwent kidney transplantation from a living related donor. Depending on the graft function, 2 groups of patients were identified: group I consisting of patients with early renal graft dysfunction (n=82); group II (n=79) that included the patients with a primary graft function who were selected by demographic and clinical laboratory data statistically comparable to patients of group I (p>0.5). This allowed us to equalize the chances of achieving the study endpoint (early graft dysfunction). Transthoracic echocardiography was

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performed in all patients, with the calculation of the mean pulmonary artery pressure. The relative risk of early renal graft dysfunction was calculated depending on the presence of pulmonary hypertension and its severity.

Results. Among group I patients, pulmonary hypertension was detected in 97.56% of cases (mean pulmonary artery pressure 48.26 ± 18.63 mmHg), versus 86.08% in patients with a primary graft function (mean pulmonary artery pressure 31.92 ± 16.11 mmHg) (p<0.001). The presence of mild pulmonary hypertension increased the relative risk of early graft dysfunction by 2.58 times (95% CI [0.698-9.547]; p=0.174), moderate by 3.18 times (95% CI [0.860-11.764]; p=0.064), severe by 5.91 times (95% CI [1.644-21.241]; p<0.001) compared with patients without pulmonary hypertension.

Conclusions. When performing kidney transplantation from a living donor, the presence of severe pulmonary hypertension in the recipient is associated with an increased risk of early graft dysfunction. This suggests that pulmonary hypertension may be one of the modifiable risk factors for this complication.

Keywords: kidney transplantation from a living related donor, pulmonary hypertension, early kidney graft dysfunction

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BMI, body mass index CKD, chronic kidney disease

CVD, cardiovascular disease
EGD, early (renal) graft dysfunction
ESRD, end-stage renal disease
KT, kidney transplantation
MPAP, mean pulmonary artery pressure
PAP, pulmonary artery pressure
PGF, primary graft function
PH, pulmonary hypertension
PHD, program hemodialysis
RAP, right atrium pressure
RHC, right heart catheterization
RR, relative risk
TTEchoCG, transthoracic echocardiography

Introduction

Kidney transplantation (KT) is recognized as the gold standard treatment for end-stage chronic renal disease (ESRD), providing significant benefits compared to dialysis in terms of both patient quality of life and healthcare costs. Progress achieved over the past decades in immunosuppressive therapy has significantly improved the long-term results of surgery. Thus, the median survival rate of recipients increased from 8.2 years in the period of 1995–1999 to 11.7 years in 2014–2017 for cadaveric transplantation, and from 12.1 years to approximately 19.2 years during the same period after transplantation from a living donor [1].

Meanwhile, as soon as in the early stages of chronic kidney disease (CKD), there is an increased risk of developing cardiovascular diseases (CVDs). A large meta-analysis of 85 clinical studies found that the threshold value of glomerular filtration rate, below which a steady increase in CVD occurrence and relative mortality is observed, approximated to 75 ml/min/1.73/m² reaching a maximum in patients in the end-stage of CKD [2]. In patients with CKD, stages I-IIIb, the mortality risk due to cardiovascular events is 5–10 times higher than the

probability of their surviving to the end stages of renal diseases, since 90% of patients in this group die from cardiovascular pathology [3].

In recent years, there has been a steady increase in the number of studies examining pulmonary hypertension (PH) in ESRD, which is explained by the high prognostic value of PH in stratifying the risk of developing various complications for both patients with CKD and kidney transplant recipients [4–9].

The prevalence of PH in the population of patients with ESRD according to various authors varies from 13% to 77%. Significant disagreements in these figures can be explained by differences in the choice of parameters and methods for measuring the pulmonary artery pressure (PAP), and determining its threshold value (PAP above 25–45 mmHg) chosen by the study authors to determine PH [6–9].

Right heart catheterization (RHC) is the preferred method for diagnosing PH, but the invasiveness of the method does not allow its routine use in real clinical practice. Most studies on PH in CKD have been based on measuring mean PAP (MPAP) using transthoracic echocardiography (TTEcoCG), which is part of the preoperative diagnostic standards for potential kidney transplant recipients.

Studying the prevalence and risk factors for the PH development among potential kidney transplant recipients, as well as its impact on the graft function, is a topical scientific and practical trend in current nephrotransplantology, helping to expand the opportunities for improvements of transplantation results.

The objective was to study the prevalence of pulmonary hypertension among patients with end-stage chronic kidney disease in the perioperative period of kidney transplantation from a living related donor, to determine its significance in the development of delayed renal graft function.

Material and methods

The study was based on a retrospective analysis of the treatments results from 650 patients with ESRD who underwent KT from a living related donor at the Great Vessel Surgery and Kidney Transplantation Department of V. Vakhidov Republican Specialized Scientific and Practical Medical Center for Surgery in the period from January 2018 to August 2022.

The study cohort was dominated by young people (18–44 years old), n=543; 83.54%; their median age was 33 (27; 39) years. There was also a predominance of males: 476 (73.23%), there were 174 females (26.7%). Body mass index (BMI) was calculated using the formula: body weight (kg)/height (m²). The median BMI was 22.7 (20.2; 25.3) kg/m². Renal replacement therapy by using program hemodialysis (PHD) was given to 565 (86.92%) patients. Vascular access was achieved through either an arteriovenous fistula (n=507; 89.73%) or a central venous catheter (n=58; 10.27%). In 85 (13.08%) patients, KT was performed at the pre-dialysis stage of the disease.

In our study, the structure of nosological forms of kidney diseases that were the cause of the ESRD development is presented in Fig. 1. As can be seen from the presented diagram, in the vast majority of cases, the cause of the ESRD development in the study cohort of patients was chronic glomerulonephritis (n=554; 85.23%). Among other pathologies there were 3 (0.46%) cases each of diabetic and gouty nephropathy; 2 cases each (0.31%) of neurogenic bladder, interstitial nephritis of pregnancy, lupus nephritis. In one patient, the CKD was caused by the Alport syndrome.

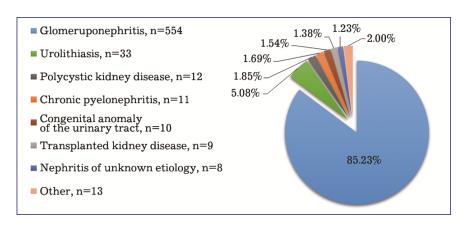


Fig. 1. The structure of nosological forms of kidney diseases

The examination of patients was performed in the outpatient clinic and at hospital stages of preparation for KT surgery in accordance with the approved National Examination Protocol for KT candidates (the Ministry of Health of the Republic of Uzbekistan Order No. 179 dated June 27, 2022, Appendix No. 2 "List of tests for medical examination of a living donor and recipient").

The selection of a related donor-recipient pair was made taking into account histocompatibility based on the determination of HLA class I and II antigens; and a lymphocytotoxic test was also performed. Determinations of markers of hepatitis B, C, HIV, TORCH complex, biochemical and hematological studies were performed in the Laboratory of V. Vakhidov Republican Specialized Scientific and Practical Medical Center for Surgery using the automatic analyzers BC-5300 (Mindray, China), Vitros-350 (G&G, USA), Maglumi-800 (China).

Instrumental test methods included electrocardiography, TTEchoCG, multislice spiral computed tomography of the chest, and the abdominal ultrasound examination.

Echocardiographic examination was performed using GE LOGIQ P6 ultrasound scanners (General Electric HealthCare, USA), Philips HD11 XE (Philips Healthcare, USA), Toshiba Xario 200 (Toshiba Medical Systems Corp., Japan) using sectoral sensors 3-5 MHz. The

standard TTEchoCG study Protocol was followed according to the Guidelines of the American Society of Echocardiography and the European Association of Cardiovascular Imaging [10]. In patients treated with PHD, the study was performed primarily on the day after the hemodialysis procedure, and thus leveled the volume overload factor associated with the interdialytic increase in extracellular fluid volume.

As a result of measurements from parasternal, apical, subcostal approaches, in M- and B-modes, the structural and geometric characteristics, the parameters of systolic function of the heart, and the assessment of the valve system status (using pulse-wave, constant-wave Doppler mode) were determined.

To diagnose the PH, the MPAP was calculated based on registering the pulmonary regurgitation (PR) flow using continuous wave Doppler scanning mode with the measurement of flow velocity and pressure gradient at the beginning of diastole. The data obtained were used in the formula for calculating the MPAP based on the modified Bernoulli equation:

$$MPAP = 4 \times V^{2}_{PR(bd)} + RAP,$$

where $V_{PR(bd)}$ is the PR flow velocity at the beginning of diastole, RAP is the pressure in the right atrium as measured based on the size and level of the inferior vena cava collapse at a distance of 2 cm from the place of its entry into the right atrium (RA).

The currently generally accepted clinical classification of PH was recommended by the European Society of Cardiology (ESC) and the European Respiratory Society (ERS) Guidelines in 2022 [11]. Based on similar pathophysiological mechanisms, clinical manifestations, hemodynamic characteristics, and therapeutic treatment, 5 main groups of PH-associated clinical conditions were distinguished:

- Pulmonary arterial hypertension;
- PH due to the left heart pathology;

- PH due to lung diseases and/or hypoxia;
- Chronic thromboembolic PH:
- PH due to unclear or multifactorial mechanisms.

Pulmonary hypertension in CKD is classified by experts as group 5 clinical conditions due to the multifactorial pathophysiological mechanism of development. According to the presented Guidelines, PH is defined when MPAP increases by more than 20 mmHg at rest. According to the MPAP level, the following stages of PH have been distinguished: Stage I (mild PH) with MPAP 20–39 mm Hg; Stage II (moderate) with MPAP 40–59 mm Hg, Stage III PH (severe) with MPAP lower than 60 mm Hg.

Delayed graft function was defined as the need for dialysis within the first 7 days after KT (n=48; 7.38%). Delayed function was determined by a 2-fold increase in plasma creatinine during the first 5 days after KT (n=34; 5.23%). These patients made up study group I (n=82) with early renal graft dysfunction (EGD). Patients with a primary graft function (PGF) (n=539) were adjusted for basic clinical and demographic parameters in order to exclude the influence of these parameters on the graft function. As a result, 79 patients with PGF were selected to form group II of the study.

In 9 patients (1.38%), an acute kidney transplant rejection was noted, and therefore these patients were excluded from the further study sample, since the main cause of this complication was immunological factors. Other 12 patients (1.85%) who had infectious and surgical complications leading to graft dysfunction or loss were not included in the study, either.

Statistical processing was performed using parametric and nonparametric analysis methods. Accumulation, adjustment, systematization of the initial information and the visualization of the results obtained were made in Microsoft Office Excel 2016 spread sheets.

Statistical analysis was carried out using the IBM SPSS Statistics software, v.26 (developed by IBM Corporation, USA).

The correspondence of quantitative variables to normal distribution was assessed using the Kolmogorov–Smirnov test. In case of describing the variables that had a normal distribution, the data obtained were presented in the form of the arithmetic mean (M) and standard deviation (SD); the variables whose distribution differed from normal were described using the median values (Me) and the lower and upper quartiles (Q1;Q3). Nominal data were described as absolute values and percentages.

When comparing mean values in normally distributed sets of quantitative data, the Student's t-test was calculated; in cases without signs of normal distribution, the Mann–Whitney U-test was used.

Comparisons of nominal data were made using Pearson's χ^2 test. In case of analyzing four-field tables with an expected phenomenon of less than 10, we calculated the χ^2 criterion with the Yates correction, which allowed us to reduce the likelihood of type 1 error. In cases where the number of expected events was lower than 5, the Fisher's exact test was used to assess the level of significance of the differences.

As a quantitative measure of the effect when comparing relative indicators, we used the relative risk value (RR), which reflected how many times the risk of outcome (EGD) in the presence of a risk factor (PH) is higher than the risk of outcome in the absence of a risk factor. In order to extrapolate the obtained RR values onto the general population, we calculated the limits of the 95% confidence interval [95% CI]. Statistical significance of differences in variables was recognized at p<0.05.

Results

During the initial examination of ESRD patients (n = 650), the PH incidence was 80.15%. PH was detected in 97.56% of patients in the EGD

group, and in 86.08% in the PGF group. The distribution of patients according to the PH severity is presented in Fig. 2.

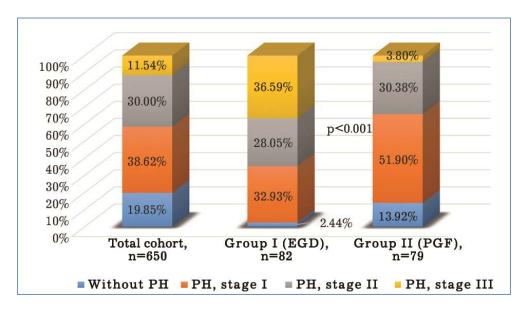


Fig. 2. Prevalence of pulmonary hypertension among patients with end-stage chronic kidney disease

As seen on Fig.2, Stage III PH was statistically significantly more common in patients with EGD; one can also note a smaller number of patients without PH compared to patients with PGF.

Patients with EGD and PGF were ranked by gender, age, BMI, experience of dialysis therapy, residual diuresis, and the renal anemia severity. The results obtained are presented in Table 1.

As can be seen from Table 1, in a comparative analysis, the groups were comparable in age, gender, BMI, and the length of dialysis therapy (p>0.05). At the same time, statistically significant differences were obtained in the degree of diuresis reduction, and the renal anemia severity (p<0.05). These factors also had a significant impact on the function of the kidney graft. Thus, with diuresis decrease, the relative risk of developing EGD increased from 1.8 times with diuresis up to 1500 mL/day to 3.1 times with anuria, compared with patients with residual diuresis of more than 1500 mL/day. Among patients with severe

anemia, the relative risk of EGD was 2.2 times higher than in patients without anemia. In addition, the relative risk of EGD was higher among male patients (RR 1.493; 95% CI [0.891–2.501]). With dialysis experience of up to 24 months, the relative risk of developing EGD was 2 times higher, and with dialysis experience of more than 2 years, it was 1.5 times higher compared with patients at the pre-dialysis stage.

Table 1. The main clinical and demographic parameters and their impact on kidney transplant function

Parameter	Group I (n=82) (EGD)		Group II (n=539) (PGF)		р	RR	[CD]			
Age (Me; Q1;Q3), years	32.5	27;38	33	27;39	0.807					
Men (n, %)	66	80.49%	390	72.36%	0.121	1.493	[0.891–			
Women (n, %)	16	19.51%	149	27.64%		1.473	2.501]			
BMI (M±SD)	22.99	3.41	23.01	4.18	0.632					
		od on dialy								
Before dialysis (n, %)	6	7.32%	76	14.1%						
Up to 12 months (n, %)	51	62.20%	302	56.0%	0.085	1.975	[0.877– 4.443]			
For 12–24 months (n, %)	17	20.73%	95	17.6%	0.148	2,074	[0.855 – 5.032]			
Over 24 months (n, %)	8	9.76%	66	12.2%	0.630	1.477	[0.538– 4.060]			
		Residual d	iuresis							
Anuria (n, %)	18	21.95%	69	12.8%	0.003	3.103	[1.414– 6.809]			
For up to 500 mL/day (n, %)	41	50.00%	249	46.2%	0.034	2.121	[1.025 - 4.388]			
500–1500 mL/day (n, %)	15	18.29%	109	20.2%	0.147	1.815	[0.799– 4.122]			
More than 1500 mL/day (n, %)	8	9.76%	112	20.8%						
Renal anemia										
Patients without anemia (n, %)	8	9.76%	70	13.0%						
Mild degree (n, %)	22	26.83%	162	30.1%	0.855	1.166	[0.543– 2.504]			
Medium degree (n, %)	26	31.71%	220	40.8%	0.894	1.030	[0.487– 2.182]			
Severe degree (n, %)	26	31.71%	87	16.1%	0.024	2.243	[1.072– 4.693]			

In accordance with the study objective set up, we leveled the patients from the comparison group in order to exclude the influence of the factors described above on the development of EGD (Table 2).

Table 2. The main clinical and demographic indicators and their impact on kidney transplant function (after adjusting for the group II)

Parameter	Group I (n=82) (EGD)		Group II (n=79) (PGF)		p	RR	[CD]			
Age (Me; Q1;Q3)	32.5	27;38	33	26;37.5	0.907					
Men (n, %)	66	80.49%	63	79.75%	0.908	1.023	[0.696–			
Women (n, %)	16	19.51%	16	20.25%	0.908	1.023	1.504]			
BMI (M±SD)	22.99	3.41	22.51	3.41	0.384					
	Pe	riod on dial	lysis ther	apy						
Before dialysis (n, %)	6	7.32%	7	8.86%						
For up to 12 months (n, %)	51	62.20%	41	51.90%	0.741	1.201	[0.649– 2.222]			
For 12–24 months (n, %)	17	20.73%	15	18.99%	0.925	1.151	[0.588– 2.252]			
Over 24 months (n, %)	8	9.76%	16	20.25%	0.445	0.722	[0.320 – 1.632]			
		Residual	diuresis							
Anuria (n, %)	18	21.95%	17	21.52%	0.964	0.90	[0.516– 1.570			
Up to 500 mL/day (n, %)	41	50.00%	34	43.04%	0.904	0.96	[0.581– 1.575]			
500–1500 mL/day (n, %)	15	18.29%	22	27.85%	0.455	0.71	[0.390 – 1.291]			
More than 1500 mL/day (n, %)	8	9.76%	6	7.59%						
	Renal anemia									
Patients without anemia (n, %)	8	9.76%	10	12.66%						
Mild degree (n, %)	22	26.83%	19	24.05%	0.713	1.21	[0.669– 2.177]			
Medium degree (n, %)	26	31.71%	28	35.44%	0.786	1.08	[0.603– 1.947]			
Severe degree (n, %)	26	31.71%	22	27.85%	0.670	1.22	[0.683– 2.173]			

As seen in Table. 2, the 79 PGF patients we had selected were comparable to the main group in terms of demographic characteristics,

the experience of dialysis therapy, degree of diuresis reduction, and the anemia severity.

The comparative analysis of preoperative TTEchoCG data between the study groups is presented in Table 3.

Table 3. Comparative analysis of transthoracic echocardiography results in patients with regard to kidney transplant function

Parameters		up I (n=82) (EGD)	Gro	p	
EDV, mL (M±SD)	170.74	41.97	154.51	44.76	0.016
ESV, mL (Me; Q1;Q3)	79	59;99	64	46.5;89	0.002
SV, mL (M±SD)	87.77	23.42	84.70	21.82	0.362
EF, % (M±SD)	51.35	10.45	56.05	8.08	0.002
IVSTh, cm (Me; Q1;Q3)	1.5	1.3;1.8	1.4	1.2;1.6	0.060
LVPWTh, cm (Me; Q1;Q3)	1.5	1.3;1.8	1.4	1.2;1.65	0.058
RWTi (Me; Q1;Q3)	0.52	0.41;0.6	0.52	0.42;0.62	0.450
LVMMI (Me; Q1;Q3)	245.13	184.79;325.33	197.28	150.49;265.95	0.001
EDD (M±SD)	5.92	0.87	5.39	0.96	< 0.001
ESD (Me; Q1;Q3)	4	3.5;4.5	3.7	3.3;4.2	0.009
MVI II, III (n, %)	47	57.32%	28	35.44%	0.04
TVI II, III (n, %)	41	50.00%	15	18.99%	0.011
AVI II (n, %)	3	3.66%	1	1.27%	0.378
MPAP, mm Hg, (M±SD)	48.26	18.63	31.92	16.11	< 0.001

Notes: EDV, end-diastolic volume; ESV, end-systolic volume; SV, stroke volume; EF, ejection fraction; IVSTh, interventricular septum thickness, LVPWTh, left ventricular posterior wall thickness; RWTi, relative wall thickness index; LVMMI, left ventricular myocardial mass index; EDD, end-diastolic dimension; ESD, end-systolic dimension; MVI, mitral valve insufficiency; TVI, tricuspid valve insufficiency; AVI, aortic valve insufficiency

As seen in Table 3, the analysis of preoperative TTEchocardiography data revealed statistically significant differences in almost all linear and volumetric parameters characterizing the left ventricle (LV) function (with the exception of SV, LVPWTh, LV RWTi), the presence of damage to the valve system, and MPAP. Patients with

EGD were more commonly characterized by LV dilatation, decreased myocardial contractility, the left ventricular hypertrophy severity, and the incidence of detecting the mitral and tricuspid valve insufficiency. In the EGD group, MPAP was 48.26 mmHg compared to 31.92 mm Hg in the PGF patient group (p<0.001).

Calculation of a quantitative measure of the effect of PH showed that its presence increases the risk of developing EGD in the post-transplant period by 2.58 times in PH, stage I, (95% CI [0.698–9.547]), by 3.18 times in PH, stage II, (95% CI [0.860–11.764]), 5.91 times in PH, stage III, (95% CI [1.644–21.241]). At the same time, statistical significance of the differences was obtained only for PH, stage III, (Table 4).

Table 4. Risk of early renal graft dysfunction depending on the pulmonary hypertension stage

PH		Group I =82) (EGD)	Group II (n=79) (PGF)		χ^2	р	RR	95% CI
St. I (n, %)	27	32.93%	41	51.90%	1,850	0.174	2.58	[0.698- 9.547]
St. II (n, %)	23	28.05%	24	30.38%	3.437	0.064	3.18	[0.860- 11.764]
St. III (n, %)	30	36.59%	3	3.80%	21.685	<0.001	5.91	[1.644- 21.241]

Discussion

According to a number of studies investigating the PH effect on the course of the post-transplant period, we found that the risk of overall mortality and achieving the transplant-related endpoints among patients with PH was higher than among patients without PH [4, 5, 8]. However, the proportion of kidney transplant recipients from a living related donor in the presented studies was relatively small, which could have influenced the results obtained.

Determination of MPAP by TTEchoCG is not as accurate as the RHC being the "gold standard" in diagnosing PH, while current Guidelines suggest considering TTEchoCG as a screening method for verifying this pathology among potential kidney transplant recipients. To obtain the most reliable results of TTEchoCG, it is recommended to conduct the study when the patient reaches the "dry weight", namely, the day after the dialysis therapy session [12]. A special role is played by such advantages of TTEchoCG as its non-invasive nature, relative ease of implementation, and an availability of the method for most modern surgical clinics.

The simultaneous use of color Doppler scanning makes it possible to assess the nature of the propagation of the LR flow and correctly position the ultrasound beam cursor, which makes it possible to make more accurate measurements of the LR velocity and, accordingly, more accurately determine the MPAP.

Nevertheless, the search for an optimal method for non-invasive diagnosis of PH among the population of ESRD patients remains a topical issue.

In a recent study conducted by M.Sh. Khubutia et al., the prognostic value of determining the LV myocardial deformation using the speckle-tracking EchoCG method was studied in the diagnosis of PH among patients with ESKD. The authors found a statistically significant relationship between the parameters of general LV circumferential strain and systolic pressure in the pulmonary artery (r=0.488 (p<0.001) and r=0.545 (p<0.001), respectively). The authors also found an increase in the risk of death by 1.13 times (95% CI [1.05–1.22]; p<0.002) with an increase in MPAP by 1 mm Hg. [13].

Currently, there are no randomized clinical trials examining the treatment of PH in patients with ESRD. Typically, this group of patients

is excluded from studies of various therapeutic treatments due to the increased risk of drug toxicity, which often makes it difficult to implement existing guidelines in the general population.

Also unresolved are the issues of tactics for managing kidney transplant recipients with concomitant PH, which persists at various times after transplantation in 17–48% of patients [14].

According to the results of our study, PH defined as an increase in MAP to more than 20 mm Hg, was detected in 97.56% of cases among recipients with EGD and in 86.08% of cases with PIIF (p<0.001). It is noteworthy that these values were obtained, among other things, after leveling the groups according to demographic (gender, age), anthropometric (BMI), and clinical parameters (dialysis experience, residual diuresis, the renal anemia severity), which can influence both the PH prevalence and the risk of EGD development.

A statistically significant increase in the risk of EGD development was detected in the presence of a concomitant PH, stage III, in a potential recipient of a kidney graft (MPAP more than 60 mm Hg) (RR 5.91; 95% CI [1.64–21.24]; p<0.001).

Conclusion

The widespread prevalence of pulmonary hypertension among patients with end-stage chronic renal disease identified according to the results of our study, allows us to consider pulmonary hypertension as a modifiable risk factor for the development of a delayed function of the kidney graft from a living related donor.

Identifying pulmonary hypertension among potential recipients of living related donor kidney transplantation is important for preoperative comorbidity assessment to reduce the risk of postoperative complications. There is no doubt the need for further studying the pulmonary

hypertension among kidney transplant candidates, aimed at improving diagnostic and treatment tactics; and that requires multicenter randomized clinical trials.

Based on our study results, we can make the following conclusions

- 1. Pulmonary hypertension is widespread among patients with end-stage chronic kidney disease and, according to the results of our study, was detected in 80.15% of patients. Pulmonary hypertension was detected in 97.56% of cases in the group of patients with early graft dysfunction, and in 86.08% of cases among those with a primary graft function.
- 2. A comparison of the main clinical and demographic parameters showed that the age and gender of patients did not have a statistically significant effect on the development of early renal graft dysfunction. However, a statistically significant effect was exerted by a decrease in diuresis less than 500 mL/day (OR 2.12; 95% CI [1.03–4.39]; p=0.034), the development of anuria (OR 3.1; 95% CI [1, 41–6.81]; p=0.003), and severe anemia (RR 2.24; 95% CI [1.07–4.69]; p=0.024).
- 3. When comparing preoperative echocardiography parameters, we found that patients with early renal graft dysfunction were more commonly characterized by left ventricular dilatation (p=0.016), decreased myocardial contractility (p=0.002), the severity of left ventricular hypertrophy (p=0.001), and the incidence of the mitral valve and tricuspid valve insufficiency (p=0.04 and p=0.011, respectively) (statistically significant in all cases).
- 4. The risk of early graft dysfunction during kidney transplantation from a living related donor is also associated with the presence of severe pulmonary hypertension in the recipient (RR 5.91; 95% CI [1.64–21.24]; p<0.001).

References

- 1. Poggio ED, Augustine JJ, Arrigain S, Brennan DC, Schold JD. Long-term kidney transplant graft survival-making progress when most needed. *Am J Transplant*. 2021;21(8):2824–2832. PMID: 33346917 https://doi.org/10.1111/ajt.16463
- 2. Vanholder R, Massy Z, Argiles A, Spasovski G, Verbeke F, Lameire N. Chronic kidney disease as cause of cardiovascular morbidity and mortality. *Nephrol Dial Transplant*. 2005;20(6):1048–1056. PMID: 15814534 https://doi.org/10.1093/ndt/gfh813
- 3. Tonelli M, Wiebe N, Culleton B, House A, Rabbat C, Fok M, et al. Chro-nic kidney disease and mortality risk: a systematic review. *J Am Soc Nephrol*. 2006;17(7):2034–2047. PMID: 16738019 https://doi.org/10.1681/ASN.2005101085
- 4. Goyal VK, Solanki SL, Baj B. Pulmonary hypertension and post-operative outcome in renal transplant: a retrospective analysis of 170 patients. *Indian J Anaesth*. 2018;62(2):131–135. PMID: 29491519 https://doi.org/10.4103/ija.IJA_529_17
- 5. Frost AE, Moore LW, Valdivia E, Alvarado M, Obi C, Graviss EA, et al. The echocardiographic course of pretransplant pulmonary hypertension following kidney transplantation and associated outcomes. *Pulm Circ.* 2022;12(1):e12030. PMID: 35506107 https://doi.org/10.1002/pul2.12030
- 6. Travers A, Farber HW, Sarnak MJ. Pulmonary hypertension in chronic kidney disease. *Cardiol Clin.* 2021;39(3):427–434. PMID: 34247755 https://doi.org/10.1016/j.ccl.2021.04.004
- 7. Sabirov IS, Murkamilov IT, Fomin VV, Sabirova AI, Mamytova AB. Pulmonary hypertension in the pre-dialysis stages of chronic kidney disease: prevalence and risk factors. *The Scientific Heritage*. 2021;66–2(66):28–38. (In Russ.). https://doi.org/10.24412/9215-0365-2021-66-2-28-38
- 8. Brinza C, Covic A, Stefan AE, Floria M, Popa IV, Scripcariu DV, et al. Pulmonary arterial hypertension and adverse outcomes after kidney transplantation: a systematic review and meta-analysis. *J Clin Med.* 2022;11(7):1944. PMID: 35407552 https://doi.org/10.3390/jcm11071944
- 9. Rudenko TE, Vasilyeva MP, Bobkova IN. Pulmonary hypertension and chronic kidney disease: prevalence, potential mechanisms and treatment. *Consilium Medicum*. 2018;20(12):55–60. (In Russ.). https://doi.org/10.26442/20751753.2018.12.000034

- 10. Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *Eur Heart J Cardiovasc Imaging*. 2015;16(3):233-270. PMID: 25712077 https://doi.org/10.1093/ehjci/jev014
- 11. Humbert M, Kovacs G, Hoeper MM, Badagliacca R, Berger RMF, Brida M, et al. 2022 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension. *Eur Respir J.* 2023;61(1):2200879. PMID: 36028254 https://doi.org/10.1183/13993003.00879-2022
- 12. Chadban SJ, Ahn C, Axelrod DA, Foster BJ, Kasiske BL, Kher V, et al. Summary of the Kidney Disease: Improving Global Outcomes (KDIGO) clinical practice guideline on the evaluation and management of candidates for kidney transplantation. *Transplantation*. 2020;104(4):708–714. PMID: 32224812 https://doi.org/10.1097/TP.00000000000003137
- 13. Khubutiya MSh, Shuvalova EV, Khamidova LT, Ivannikov AA, Balkarov AG, Dmitriev IV, et al. Echocardiographic assessment of left ventricular myocardial strain, as a non-invasive method for diagnosing pulmonary hypertension in patients with end-stage chronic kidney disease. *Transplantologiya*. *The Russian Journal of Transplantation*. 2023;15(4):439–449. (In Russ.). https://doi.org/10.23873/2074-0506-2023-15-4-439-449
- 14. Lentine KL, Lam NN, Caliskan Y, Xiao H, Axelrod DA, Costa SP, et al. Incidence, clinical correlates, and outcomes of pulmonary hypertension after kidney transplantation: analysis of linked US Registry and Medicare billing claims. *Transplantation*. 2022;106(3):666–675. PMID: 33859148 https://doi.org/10.1097/TP.00000000000003783

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