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Early and long-term outcomes of primary infected kidney transplantation

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Abstract

Introduction. The transplantation of primary infected grafts poses a significant challenge in the field of kidney transplantation. This issue is not adequately addressed in the existing medical literature. In our country, no systematic studies of the results of such transplants have been conducted.

Objective. To evaluate the frequency of primary infected kidney transplants and the types of microorganisms isolated from

positive bacterial cultures of perfusates; to study the frequency of clinically significant infectious complications in this category of patients and their outcomes; to identify factors that had a statistically significant impact on the outcomes.

Material and methods. Between 1 January 2015 and 31 December 2024, 1,923 kidney transplants from deceased donors were performed. The study group consisted of 87 patients who tested positive for bacterial perfusion culture. Of these, 42 (48.3%) were men and 45 (51.7%) were women. The average age of the patients was 47±11.9 years. Patients were divided into two groups to assess the impact of clinically significant infectious complications on treatment outcomes: group I consisted of 15 patients with such complications and group II consisted of 72 patients without. Patients in both groups were comparable in terms of key characteristics.

Results. The frequency of initially infected kidney transplants was 4.5%. The microorganisms causing perfusion contamination were as follows: 88 bacterial strains and one fungal strain. Of these bacteria, 51 were Gram-positive, 36 were Gram-negative and one was anaerobic. Clinically significant infectious complications occurred in 17.2% of cases, with a median time to development of 9 (4;12) days. The development of infectious complications significantly reduced kidney transplant survival. Significant factors included clinically significant infectious complications, the detection of Klebsiella pneumoniae in the perfusate and type 2 diabetes mellitus in patients.

Conclusion. The frequency of primary infected kidney transplants, as well as the frequency of clinically significant infectious complications, is consistent with data from other transplant centers. Algorithms for diagnosing and treating infectious

complications enabled fatal outcomes to be avoided in this patient group.

Keywords: primary infected kidney transplant, significant infectious complications, transplant outcomes, kidney transplant survival, recipient survival, statistically significant factors

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BMI, body mass index

CAKUT, Congenital Anomalies of the Kidney and Urinary Tract

CAPD, Continuous Ambulatory Peritoneal Dialysis

CKD, chronic kidney disease

CVA, cerebrovascular accident

HD, hemodialysis

IC, infectious complication

IST, immunosuppressive therapy

KT, kidney transplantation

miss-match, the degree of mismatch across 6 HLA antigens in a donor-recipient pair

m-TOR inhibitors, mammalian target of rapamycin

NFGNB, non-fermenting gram-negative bacteria

PD, peritoneal dialysis

PGNF, primary graft non-function

RAG, renal allogeneic graft

RRT, renal replacement therapy

TBI, traumatic brain injury

Introduction

The issue of effective treatment of chronic kidney disease (CKD) remains relevant due to the pronounced socioeconomic nature of this disease. The global prevalence of CKD in the general population averages 13.4% and is widely recognized as one of the leading causes of death worldwide [1, 2]. Furthermore, CKD remains a significant financial burden on global healthcare [2–4].

Dialysis methods of renal replacement therapy (RRT) allow patients to survive while waiting for kidney transplantation (KT), which remains the best treatment option for this category of patients, contributing to the achievement of the maximum possible life expectancy and quality of life, as well as the level of medical and social rehabilitation [5]. In 2023, 1817 KTs were performed in the Russian Federation, including 1620 from deceased donors and 197 from living related donors [6]. Despite the quantity and increase in the number of KTs performed annually, the volume of operations performed does not meet the need for this type of treatment. At the present stage, the median survival rate of renal allogeneic grafts (RAG) in many centers exceeds 10 years, and the 1-, 3-, 5-, and 10-year survival rates vary in the range of 84–97%, 87–89%, 78–92%, 74–83%, respectively [7–11].

Infectious complications (ICs) arising in the post-transplant period in immunocompromised recipients significantly reduce RAG survival. ICs may originate from surgical intervention, reactivation of a latent infection, the addition of a new infection, or may be donor-derived infection transmissions [12]. The IC development depends on the immunosuppressive status of the patient and the epidemiological

environment. According to J. A. Fishman, infections at early post-transplant stages usually originate from the donor or recipient, but may also result from technical complications of the operation [13–14].

According to scientists, the proportion of infectious events associated with the donor-associated infection transmissions varies between 0.13% and 2% [15–17]. It is known that the organ preservation fluid, due to its biochemical properties, can support the life of microorganisms and also promote their growth [18]. Currently, no guidelines offer recommendations on the optimal clinical approach to the management of patients with positive bacterial cultures of perfusate [19, 20].

An analysis of articles covering the KT results, where microbiological culture of the perfusate revealed the presence of bacterial or fungal flora, showed no consensus regarding the incidence of contamination, the structure of pathogens, timing of clinically significant IC developments, and outcomes. According to world scientists, the incidence of perfusate contamination can vary from 5% to over 90%, however, the rates of detecting the pathogenic flora are in the range of 10 – 21% [21–24].

Most studies have shown that the most common contaminants in perfusate are coagulase-negative staphylococci and enterococci, most of which are low-virulence bacteria [25–27]. Coagulase-negative staphylococci are the most common microorganisms detected in perfusate cultures, but recent studies have increasingly emphasized the role of enterobacteria, which are more virulent and most often multidrug-resistant [21, 25].

Considering the above and the lack of systematic reports from homeland centers regarding the rates of transplanting primarily infected RAGs, the profile of microorganisms, the CI incidence in these patients and an analysis of outcomes, we decided to conduct the present study.

The aim of the study was to assess the rates of transplanting primarily infected kidney grafts, specify the profile of microorganisms isolated from the perfusate, determine the incidence and timing of clinically significant infectious complication developments, and identify factors that significantly affect the treatment outcomes in this category of patients.

Material and methods

Study design. Inclusion and exclusion criteria

A retrospective, non-randomized, single-center study was conducted. The outcomes of primarily infected RAG transplants between January 1, 2015, and December 31, 2024 were analyzed.

Inclusion criteria were successful transplantation from a deceased donor, recipient age 18 years or older, positive perfusate culture. Non-inclusion criteria were simultaneous transplantation of other organ (pancreas, liver, heart), transplantation from a living related donor, technically unsuccessful transplantation. Exclusion criteria: none.

Recipients

The study group consisted of 87 patients with stages 4–5 CKD resulting from various diseases. Detailed characteristics of the recipients are presented in Table 1.

Table 1. General characteristics of patients

Parameter	Parameter value
Age*, years	47±11.9 [44.5–49.6] (18;73)
Male gender, n (%) Female gender, n (%)	42 (48.3) 4 5 (51, 7)
BMI*, kg/ m^2	24.6 ±5 [23.6 – 25.7] (15.5;39.3)
Diseases leading to CKD stage 4–5, n (%):	

• Chronic glomerulonephritis • Polycystic kidney disease • Hypertensive nephroangiosclerosis • Chronic pyelonephritis • Nephropathy of unknown etiology • Congenital anomaly of the urinary system • Type 1 diabetes mellitus • Type 2 diabetes mellitus • Vasculitis • Amyloidosis • Periodic disease • Systemic lupus erythematosus	42 (48.2) 12 (13.8) 8 (9.2) 5 (5.7) 5 (5.7) 4 (4.6) 4 (4.6) 4 (4.6) 3 (3.4) 2 (2.3) 1 (1.1) 1 (1.1)
RRT, n (%) • GD, n (%) • PD, n (%)	75 (86.2) 59 (67.8) 16 (18.4)
Without RRT, n (%)	12 (13.8)
O (I), n (%)	37 (42.5)
A (II), n (%)	34 (39.1)
B (III), n (%)	11 (12.6)
AB (IV), n (%)	5 (5.7)

Notes: * M ± SD [95% CI] (min; max); BMI, body mass index; CKD, chronic kidney disease; RRT, renal replacement therapy; HD, hemodialysis; PD, peritoneal dialysis

Donors

Organs for transplantation were obtained from deceased donors. The characteristics of the donor group are shown in Table 2.

Table 2. Characteristics of donors

Parameter	Parameter value
Donor age*, years	51 (41.5;56) (22;67)
Male gender, n (%) Female gender, n (%)	67 (77) 20 (23)
Donors with confirmed brain death, n (%): • CVA • TBI Non-heart-beating donors, n (%)	 57 (65.5) 28 (32.2) 2 (2.3)
Length of stay in the Intensive Care Unit*,	1 (0;3) (0;9)

days	
Azotemia levels at time of removal* • Serum creatinine, mmol/L • Blood urea, mmol/L	 90 (76;128) (39;243) 6.7 (4.7;7.9) (1.7;25.2)
Blood leukocytes*, $x10^9$ /L	9.5 (6.2;13.6) (3.8;32.5)

Notes: * Me (Q_1;Q_3) (min; max); CVA, cerebrovascular accident; TBI, traumatic brain injury

Surgical technique of kidney transplantation

KT was performed using an identical surgical technique. Reperfusion of the RAG was achieved by anastomosing its artery/arteries with the recipient's external iliac artery (less commonly, the internal or common iliac artery), and the RAG vein with the recipient's external iliac vein. Adequate urine flow was achieved by creating an antireflux neoureterocystostomy according to Witzel-Sampson-Litch on an internal ureteral. Cold ischemia time for the RAG varied from 7 to 27 hours and made mean of 15.2±4.1 [14.3–16.1] hours.

Immunosuppressive therapy (IST)

Patients received an induction and three-component baseline IST. The induction IST was performed by infusion of mono- and polyclonal antibodies. Baseline IST included calcineurin inhibitors, antimetabolites or proliferative signal inhibitors (m-TOR inhibitors), and glucocorticosteroids. Detailed characteristics of IST are presented in Table 3.

Table 3. Characteristics of immunosuppressive therapy

Induction IST	
Monoclonal antibodies (basiliximab), n (%)	48 (55.2)
Polyclonal antibodies, n (%): • Antithymocyte rabbit immunoglobulin, n (%) • Equine antithymocyte immunoglobulin, n (%)	26 (29.9) 19 (21.8) 7 (8.1)
Without mono- and polyclonal antibodies, n (%)	13 (14.9)
Basic IST	
Tacrolimus, n (%)	65 (74.7)
Cyclosporine, n (%)	22 (25.3)
Mycophenolic acid preparations	85 (97.7)

m-TOR inhibitors	2 (2.3)

Notes: IST, immunosuppressive therapy; m-TOR inhibitors, mammalian target of rapamycin

Antibacterial therapy

For the prevention of bacterial ICs, from 2015 to February 2022, patients received ceftriaxone at a dose of 2 g daily from the time of surgery for 7 days and vancomycin at a dose of 0.5 g intravenously once before surgery, then co-trimoxazole at a dose of 480 mg once a day for 6 months. From February 2022, ceftriaxone was used at a dose of 2 g twice a day for a 7-day course without glycopeptides, then also co-trimoxazole at a dose of 480 mg once a day for a 6-month course. After receiving the results of the microbiological culture of the perfusate, broad-spectrum antibiotics from the carbapenem group were administered until the sensitivity of microorganisms had been determined: meropenem at a dose of 1 g intravenously by drip 3 times a day for a course of 7-10 days. After receiving the results of antibiotic susceptibility testing, the antibacterial therapy was adjusted.

Antifungal therapy

Prophylactic antifungal therapy was not used in the practice of our clinical department. When fungi were identified in the RAG perfusate, medications with fungicidal action were administered at therapeutic doses based on susceptibility testing results.

Microbiological culture methodology

Obtaining, storing, and transporting clinical material samples for microbiological testing were performed in accordance with Guidelines 4.2.203905 "Technique for collecting and transporting biomaterial to microbiological laboratories." At the stage of pre-transplantation RAG processing, the perfused Custodiol® solution (Dr. F. Kohler Chemie,

GmbH, Germany) was sampled in the amount of 5-10 ml for microbiological examination, under sterile conditions upon opening the internal transport package; in the microbiological laboratory the delivered material was cultured on Petri dishes with dense nutrient media, and in thioglycollate broth, which were incubated for 24-48 hours in a thermostat at 35°C. Microorganisms species were identified using a WalkAway 40 automatic microbiological analyzer (Beckman Coulter, USA) or classical microbiological methods. Since November 2020, identification has been performed using a VITEK MS mass spectrometer; sensitivity has been determined using VITEK-2 Compact (bioMerieux, France). When isolating multiple microorganisms from a single clinical sample, for a subsequent analysis, all etiologically significant pathogens were considered. Etiologically significant pathogens were identified in accordance with generally accepted standards [28].

Distribution of patients into study groups

Based on the development of ICs, patients were divided into two groups: Group I consisted of patients who developed ICs (n=15), Group II consisted of patients without ICs (n=72). Patients in both groups were comparable in terms of basic characteristics (see Table 4).

Table 4. Comparative characteristics of patients in groups I and II

Parameter	Group I (n=15)	Group II (n=72)	p
Recipient-dependent factors			
Age*, years	43 (33;51)	46 (42;54.5)	0.14
Male gender, n (%) Female gender, n (%)	4 (26.7) 11 (73.3)	38 (52.8) 34 (47.2)	0.07
BMI*, kg/m^2	24 (18.5;26.7)	24.7 (21;28.3)	0.25
Diseases leading to CKD stage 4–5, n (%): Chronic glomerulonephritis	7 (46.7)	32 (44.4)	0.88

Hypertensive nephroangiosclerosis	2 (13.3)	6 (8.3)	0.55
Polycystic kidney disease	1 (6.7)	11 (15.3)	0.39
Chronic pyelonephritis	1 (6.7)	4 (5.6)	0.88
Type 2 diabetes mellitus	1 (6.7)	3 (4.2)	0.69
Nephropathy of unknown etiology	1 (6.7)	3 (4.2)	0.69
Nephropathy of combined genesis	0 (0)	5 (6.9)	0.30
CAKUT	0 (0)	4 (5.6)	0.36
Type 1 diabetes mellitus	2 (13.3)	2 (2.8)	0.08
Vasculitis	0 (0)	3 (4.2)	0.43
Rapidly progressive glomerulonephritis	0 (0)	3 (4.2)	0.43
Amyloidosis	0 (0)	2 (2.8)	0.53
Periodic disease	0 (0)	1 (1.4)	0.67
Systemic lupus erythematosus	0 (0)	1 (1.4)	0.67
Nephropathy in the outcome of preeclampsia	0 (0)	1 (1.4)	0.67
HD, n (%):	11 (73.3)	48 (66.7)	0.62
CAPD, n (%):	4 (26.7)	12 (16.7)	0.37
Without RRT, n (%)	0 (0)	12 (16.7)	0.09
O (I), n (%)	5 (33.3)	32 (44.4)	0.43
A (II), n (%)	7 (46.7)	27 (37.5)	0.51
B (III), n (%)	2 (13.3)	9 (12.5)	0.94
AB (IV), n (%)	1 (6.7)	4 (5.6)	0.88
Donor-related factors			
Male gender, n (%) Female gender, n (%)	14 (93.3) 1 (6.7)	53 (73.6) 19 (26.4)	0.10
Donor age*, years	49 (36;56)	51 (41.5;57.5)	0.55
Donors with confirmed brain death, n (%): • CVA • TBI Non-heart-beating donors, n (%)	 8 (53.3) 7 (46.7) 0 (0)	 49 (68.1) 21 (29.2) 2 (2.8)	 0.28 0.19 0.53
Donor's bed-days of hospital stay*, n (%):	1 (1;2)	1 (1;3)	0.49
Donor serum creatinine*, μmol/L	90 (81;136)	89 (75;127)	0.66
Donor blood urea*, mmol/L	7.3 (4.8;8.3)	6.6 (4.6;7.9)	0.72
Donor blood leukocytes*, $x10^9$ /L	12.4 (11.4;18.8)	13 (10;18)	0.72
KT factors			
CIT*, hours	12.5 (11;18)	15 (12;18)	0.16
Miss-match*, n	3 (3;4)	3 (3;4)	0.96
Induction IST			
Monoclonal antibodies (basiliximab), n (%)	9 (60)	39 (54.2)	0.69

Polyclonal antibodies, n (%): • Antithymocyte rabbit immunoglobulin, n (%) • Equine antithymocyte immunoglobulin, n (%)	 1 (6.7) 1 (6.7)	 18 (25) 6 (8.3)	 0.12 0.84
Without mono- and polyclonal antibodies, n (%)	4 (26.7)	9 (12.5)	0.17
Basic IST			
Tacrolimus, n (%)	10 (66.7)	55 (76.4)	0.44
Cyclosporine, n (%)	5 (33.3)	17 (23.6)	0.44
Mycophenolic acid preparations, n (%)	15 (100)	70 (97.2)	0.53
m-TOR inhibitors, n (%)	0 (0)	2 (2.8)	0.53

Notes: * Me (Q_1;Q_3); BMI, body mass index; CAKUT, Congenital Anomalies of the Kidney and Urinary Tract; HD, hemodialysis; CAPD, Continuous Ambulatory Peritoneal Dialysis; CVA, acute cerebrovascular accident; TBI, traumatic brain injury; KT, kidney transplantation; CIT, cold ischemia time; miss-match, the degree of mismatch across6 HLA antigens in the donor-recipient pair; m-TOR inhibitors, mammalian Target of rapamycin

Evaluation criteria for primary infected renal graft

Given that organ removal is performed using standard techniques under sterile conditions and a sterile preservative solution, perfusate culture should be negative. If the perfusate culture was positive, the RAG was considered to be primarily infected.

Criteria for assessing renal transplant function

Primary initial RAG function is characterized by the absence of the need for RRT dialysis methods during the first 7 days after KT, whereas in case of a delayed initial function there is a need for at least one RRT procedure during the first 7 days after KT. The RAG dysfunction is usually considered when the level of serum creatinine increases by at least 20% from its baseline level and(or) the emergence of severe proteinuria (protein content in daily urine of at least 1 g/day). A primary graft non-function (PGNF) is usually defined as the RAG with no function since KT, but preserving blood supply confirmed by

instrumental examination methods (ultrasound, computed tomography). To establish this diagnosis, a histological examination of RAG is necessary in order to exclude other causes of its function loss [29].

Study endpoints

Cases of return to RRT dialysis methods, repeated pre-dialysis KT, and deaths with a functioning RAG were classified as events of uncensored loss of RAG.

Statistical data processing

Statistical processing was carried out using the Statistics for Windows statistical package, v. 10.0, StatSoft Inc. (USA); StatTech software, v. 4.8.1 (developer: Stattech LLC, Russia), statistical programming in the R language and using the Microsoft Office Excel 2018 software, Microsoft (USA). Normality of distribution was tested using the Shapiro–Wilk test. Quantitative parameters with a normal sampling distribution were described using arithmetic means (M) and standard deviations (SD). The boundaries of the 95% confidence interval [95% CI] were indicated as a measure of representativeness for mean values. In the absence of a normal distribution of quantitative data, the median (Me), lower and upper quartiles (Q_1;Q_3) and, if necessary, the maximum and minimum values (min; max) were presented. Categorical data were described using absolute values and percentages. The 95% CI for percentages was calculated using the Clopper–Pearson method. When comparing groups by qualitative characteristics, the Pearson Chi-square test was used; the two-tailed Fisher exact test was used for qualitative binary characteristics. In cases where statistically significant differences in complication rates were identified in the study groups, pairwise comparisons were performed using Fisher's exact test. The overall

survival and functional survival of RAG were analyzed using the Kaplan–Meier estimator. Differences were considered statistically significant at $p<0.05$.

Ethical aspects of the study conduct

Given the retrospective nature of the study, its implementation did not require approval from the local ethics committee (Protocols No. 3-13 of July 22, 2013, No. 4-22 of April 26, 2022). The study was conducted in accordance with the principles of the Declaration of Helsinki of the World Medical Association [30].

Results

The incidence of primarily infected RAG transplants was 4.5% (87/1923). Microorganisms that contaminated the perfusates included 88 bacterial strains and one fungal species. Of the 88 bacteria isolated, 51 were gram-positive, 36 were gram-negative, and one was anaerobic. One bacterial culture was isolated from the RAG perfusate in 85 patients, and two bacterial cultures were isolated from two patients.

The profile of pathogens isolated from RAG perfusates is presented in Table 5.

Table 5. The profile of pathogens isolated from renal graft perfusates

Microorganism	**n**	**%**
Staphylococcus	33	
Staph. Coagulase Negative Group	31	37.1
Staphylococcus aureus	2	
Klebsiella pneumonia	22	24.7
Enterococcus spp	6	6.7
Escherichia coli	6	6.7
Polymorphic gram-positive rods	4	4.5
Acinetobacter spp	3	3.4
Micrococcus spp	3	3.4
Enterobacter spp	2	2.2
Pseudomonas aeruginosa	2	2.2

Streptococcus spp	1	1.1
NGONB	1	1.1
Candida albicans	1	1.1
Achromobacter denitrificans	1	1.1
Bacillus simplex	1	1.1
Bacillus species	1	1.1
Kocuria palustris	1	1.1
Lactobacillus jensenii	1	1.1
Total	89	

Note: NFGNB, non-fermenting gram-negative bacteria

Clinically significant infectious complications

The incidence of clinically significant ICs after transplantation of primarily infected RAG was 17.2%. The time of the onset varied from 3 to 120 days, with a median of 9 (4;12) days. The structure of these complications is presented in Table 6.

Table 6. Infectious complications in patients after transplantation of a primarily infected kidney graft

Infectious complication	Timing of the occurrence of complications, days
Neoureterocystomotic failure of infectious origin*	3
Neoureterocystomotic failure of infectious origin*	3
Venous thrombosis of infectious origin	4
Sepsis	4
Phlegmon of the RAG bed and anteromedial surface of the right hip. Sepsis	5
Inflammatory infiltrate of the right hip and shin. Systemic inflammatory response	6
RAG bed phlegmon	7
Neoureterocystomotic failure of infectious origin (No. 2). Pelvic abscess. Systemic inflammatory response	9
RAG acute pyelonephritis	10

Lesions of RAG infectious-necrotic, vascular anastomoses, external iliac artery and external iliac vein with the formation of the RAG bed hematoma	10
Neoureterocystoanastomosis failure of infectious origin	11
RAG ureteral stricture of infectious origin	12
Urinary tract infection	23
Abscess formation in the RAG bed. Diffuse purulent peritonitis. Systemic inflammatory response	27
RAG ureteral stricture of infectious origin	120

Note: * – complications that arose at the same time in two different patients

Outcomes of transplantation of primarily infected kidney grafts

Early outcomes

A total of 78 patients (89.7%) were discharged with a functioning RAG, including 59 (67.8%) with adequate RAG function and 19 (21.8%) with RAG dysfunction. The serum creatinine, blood urea, and glomerular filtration rate values in patients in these two subgroups were 141 (120;191) μmol/L, 10 (7.6;14.3) mmol/L, and 48.3 (41.7;66) mLmin, respectively. Two patients (3.5%) were discharged with a nonfunctioning RAG to continue RRT with program HD at the outpatient stage of treatment. One of them underwent repeat KT from a deceased donor a year later and was discharged with satisfactory RAG function. Seven patients (8.1%) underwent in-hospital RAG removal. The structure of the reasons for RAG removal is presented in Table 7.

Table 7. The reasons for in-hospital removal of renal grafts in patients with a primarily infected renal graft

Reasons for RAG removal	Timing of graft removal, days

Sepsis	4
RAG thrombosis of infectious genesis	4
Phlegmon of the RAG bed and hip, RAG septic necrosis, pneumonia, sepsis	5
Hip phlegmon	6
Phlegmon of the RAG bed	7
Recurrent neoureterocystoanastomotic failure of infectious origin, pelvic abscess	9
Necrosis of RAG vessels, recipient iliac vessels	10

Thanks to the timely diagnosis and treatment equivalent to the clinical situation, there were no fatal outcomes in the study group of patients.

Long-term outcomes

As of April 1, 2025, there were 75 living patients in the study group; the follow-up period was 29.4 (11.7–106.2) months. Sixty-five of these patients had functioning RAG, while 10 patients had lost their RAG function (7 at in-hospital stage, and 3 in the later period). Eight patients died in the long-term postoperative period: seven with functioning RAG at the time of death, and one with the RAG removed during the in-hospital stage.

Overall kidney graft and recipient survival rates

The diagrams of overall recipient survival rates, death-censored and death-uncensored RAG survival are presented in Fig. 1.

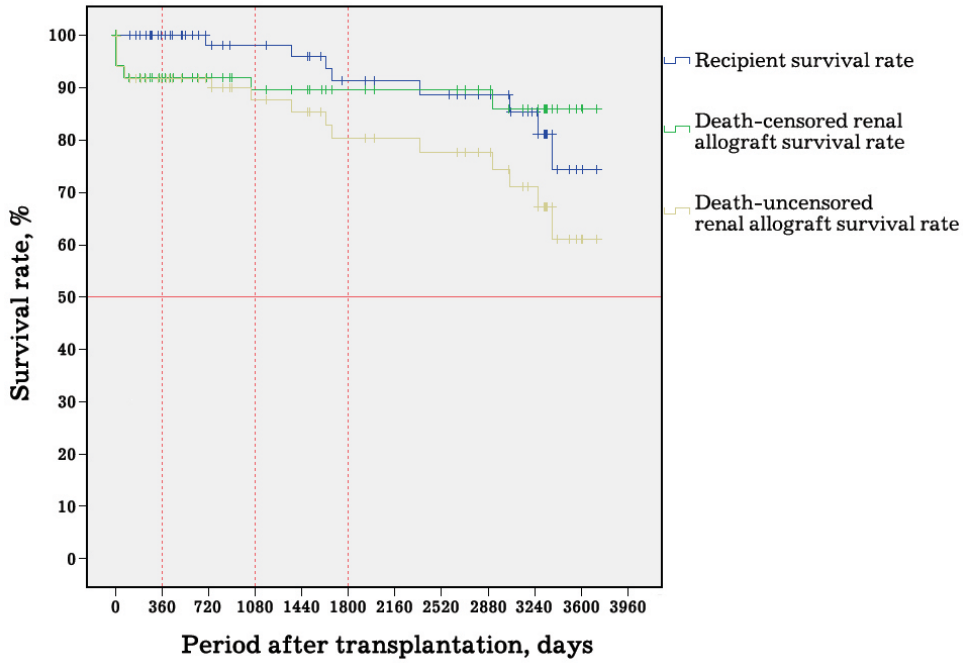

Fig. 1. Diagrams of overall recipient survival, death-censored and death-uncensored renal allograft survival rates. The half-life is indicated by the horizontal red line. The vertical dotted lines indicate the periods of 1 year, 3 years, and 5 years after kidney transplantation

The impact of clinically significant infectious complications on the outcomes of primarily infected renal graft transplants

The profile of microorganisms isolated from patients of groups I and II is presented in Table 8.

Table 8. The profile of pathogens isolated from renal transplant perfusates in patients of groups I and II

Microorganism	Group I (n=15)	Group II (n=72)	p
Staphylococcus spp	3 (20)	30 (41.7)	0.12
Klebsiella pneumonia	6 (40)	16 (22.2)	0.15
Enterococcus spp	0 (0)	6 (8.3)	0.25
Escherichia coli	2 (13.3)	4 (5.6)	0.29

Polymorphic gram-positive rods	1 (6.7)	3 (4.2)	0.69
Acinetobacter spp	1 (6.7)	2 (2.8)	0.47
Micrococcus spp	0 (0)	3 (4.2)	0.43
Enterobacter spp	2 (13.3)	0 (0)	**0.002**
Pseudomonas aeruginosa	0 (0)	2 (2.8)	0.53
Streptococcus spp	0 (0)	1 (1.4)	0.67
NGONB	0 (0)	1 (1.4)	0.67
Candida albicans	0 (0)	1 (1.4)	0.67
Achromobacter denitrificans	1 (6.7)	0 (0)	**0.03**
Bacillus simplex	0 (0)	1 (1.4)	0.67
Bacillus species	0 (0)	1 (1.4)	0.67
Kocuria palustris	0 (0)	1 (1.4)	0.67
Lactobacillus jensenii	0 (0)	1 (1.4)	0.67

Note: NFGNB – non-fermenting gram-negative bacteria

In group I, the microorganisms significantly more frequently cultured in the perfusate were Enterobacter spp. (p=0.002) and Achromobacter denitrificans (p=0.03).

Early and late outcomes of primarily infected RAG transplants in the study groups are presented in Table 9.

Table 9. Early and long-term outcomes for patients in groups I and II

Outcomes	Group I (n=15)	Group II (n=72)	p
Initial RAG function			
Primary RAG function, n (%)	8 (53.3)	44 (61.1)	0.58
Delayed RAG function, n (%)	7 (46.7)	28 (38.9)	0.58
RAG function at the time of discharge from hospital			
Satisfactory RAG function, n (%)	6 (40)	53 (73.6)	**0.012**
RAG dysfunction, n (%)	3 (20)	15 (20.8)	0.91
Serum creatinine*, μmol/L	145 (91;214.5)	143 (123;201)	**0.004**
Blood urea*, mmol/L	9.5 (4.6;23.8)	10.2 (7.7;14.8)	**0.007**
RAG non-function, n (%)	6 (40)	3 (4.2)	**0.0000**
Removed RAG, n (%)	6 (40)	1 (1.4)	**0.000001**
RAG function as of 01.04.2025			
Number of patients available for follow-up	14**	69**	
Patient alive, n (%)	12	63	0.52
Alive, RAG is functioning, n (%)	6 (40)	59 (81.9)	**0.0004**

Alive, RAG non-functioning, n (%)	6 (40)	4 (5.6)	**0.0001**
Fatal outcome, n (%)	2	6	0.52
Died with a functioning RAG, n (%)	1 (6.7)	6 (8.3)	0.85
Died with non-functioning RAG, n (%)	1 (6.7)	0 (0)	**0.03**

Notes: * Me (Q_1;Q_3); RAG, renal allogeneic graft; ** number of patients available for evaluation of long-term outcomes (1 patient from group I and 3 patients from group II changed their permanent place of residence and were unavailable for contact)

In addition, significant differences were noted in the overall uncensored (Fig. 2) and death-censored (Fig. 3) survival of RAG in the study groups.

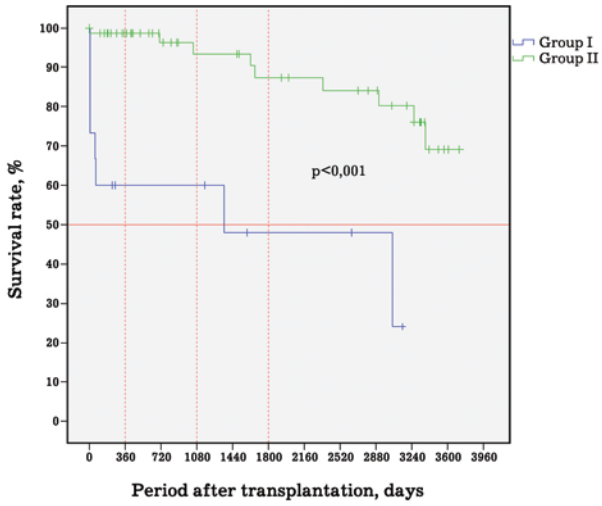

Fig. 2. Diagrams of overall death-uncensored renal allograft survival in patients of Group I and Group II. The half-life is indicated by the horizontal red line. The vertical dotted lines indicate the periods of 1, 3, and 5 years after kidney transplantation

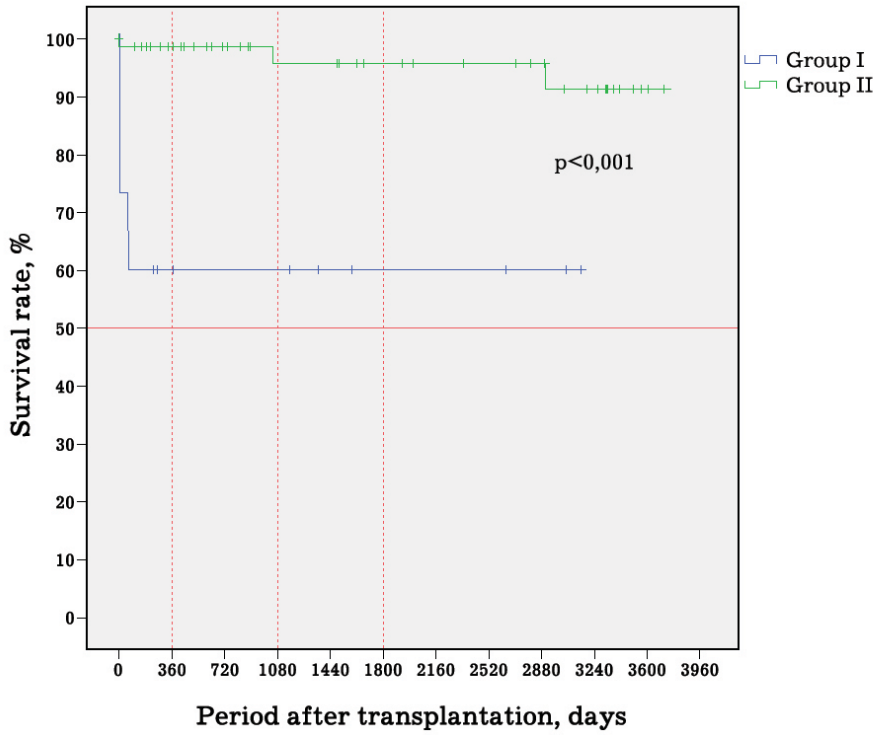

Fig. 3. Diagrams of overall death-censored renal allograft survival in patients in Group I and Group II. The half-life is indicated by the horizontal red line. The vertical dotted lines indicate the periods of 1, 3, and 5 years after kidney transplantation

According to our study data, the IC developments did not significantly affect a 1-year recipient survival rate, which was 100% in both groups. Figure 4 shows the overall recipient survival rate in the study groups.

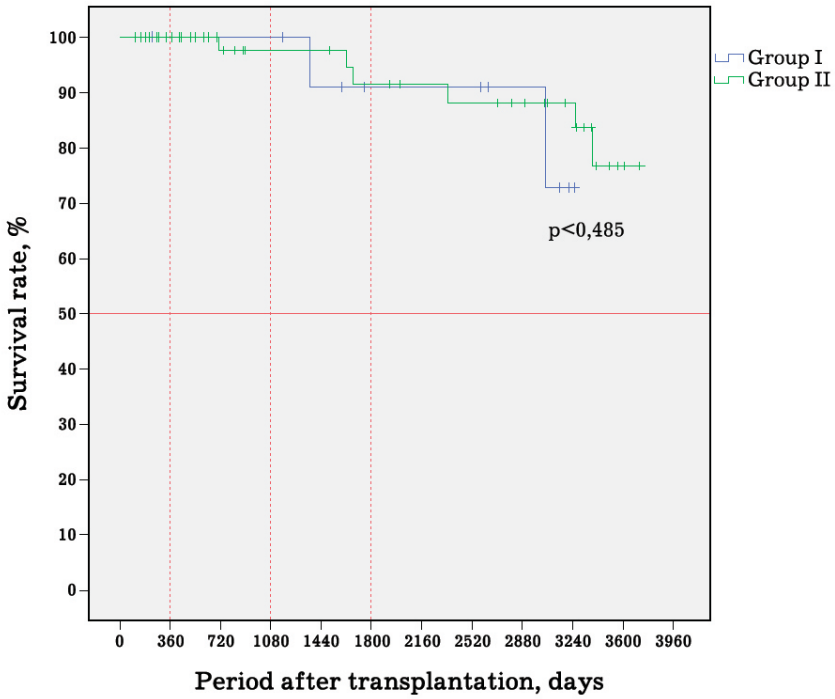

Fig. 4. Diagrams of overall patient survival rates for patients in Group I and Group II. The half-life is indicated by the horizontal red line. The vertical dotted lines indicate the periods of 1 year, 3 years, and 5 years after kidney transplantation

Discussion

Currently, there remains a discrepancy between the availability of transplantation and the demand for this type of treatment. This naturally contributes to an increased number of patients on waiting lists, which predictably leads to an increase in mortality rates in this patient category [31–34]. Despite improvements in transplantation techniques and postoperative management algorithms, the emergence of new immunosuppressive and antibacterial drugs, and a significant increase in recipient and graft survival rates, these rates are far from ideal.

The overall IC incidence after KT can reach 58% in some centers, with the incidence of mycoses ranging from less than 5% to 16.7% and bacterial infection rates exceeding 7.3% [35–39]. The continuing challenges in diagnosing and treating ICs are due to the constantly

changing epidemiology of infections, increasing antimicrobial resistance, and suboptimal methods of microbiological screening of organ donors [13, 40]. Early postoperative infections remain a significant cause of recipient morbidity and mortality, and death with a functioning graft becoming the most common form of the graft loss [41–46].

Unreasonably little attention has been paid in the available medical literature to the problem of ICs resulting from the infection transmitting from donors. A donor-acquired infection is defined as an infection present in the donor that is transmitted to one or more recipients. Significant difficulties remain in diagnosing donor infections, and there are no generally accepted treatment guidelines [3]. A distinction is generally made between expected and unexpected transmission of the pathogen from a donor to a recipient [47]. To detect pathogen transmission, many centers have introduced routine microbiological testing of perfusate [48–49]. However, even if the pathogen is identified, proving the donor origin of the infection remains a difficult and expensive task.

Donor infections remain one of the major problems in current solid organ transplantation. A few studies have reported that favorable outcomes can be achieved in patients who developed donor-associated infections after transplantation of primarily infected RAG by using an appropriate antimicrobial therapy [50, 51]. However, most scientists agree that donor-associated infections are accompanied by significantly higher morbidity and mortality in recipients [52, 53]. It is known that, due to the characteristics of its composition, perfusate often supports the life of microorganisms and promotes their growth [18]. The frequency of detection of positive microbiological cultures of perfusates varies widely from 5 to 90%, but the incidence of donor-associated infections in this category of patients ranges from 0.13–10%, while mortality can reach

40% [54]. According to our data, the frequency of transplanting a primarily infected RAG in a Kidney and Pancreas Transplantation Department in the period from 01.01.2015 to 31.12.2024 was 4.52%.

Unfortunately, even today, difficulties in identifying and treating donor-associated infections persist, as do relatively high mortality rates. There is still no consensus regarding the profile of pathogens contaminating kidney perfusates [54, 55]. Among the microorganisms isolated from the renal perfusates in our study, there were 88 bacterial strains and one fungal strain. Bacteria were represented by 51 gram-positive bacteria, 36 gram-negative bacteria, and one anaerobic bacteria. Most often (n=85), a monoculture was isolated; in 2 patients, two bacterial cultures were isolated. More than 75% of the isolated microorganisms were represented by staphylococci, Klebsiella, enterococci, and Escherichia coli spp.

Among other things, there is no consensus regarding the list of factors that significantly influence the frequency of perfusate contamination and the development of donor-associated infection, as well as the early and long-term KT outcomes. Among such factors, it is customary to highlight the antibiotics use and ICs in the donor, the advanced age of the donor, contamination with pathogens of the ESKAPE group (a collective term based on the first letters of the pathogens *Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa, and Enterobacter species*), intestinal perforation during organ retrieval, multi-organ retrieval, use of a perfusion machine, recipient age, and their comorbidity level [22, 26, 44].

The incidence of clinically significant ICs in patients of the study group was 17.2%, the median time of occurrence was 9 (4;12) days (Table 6). Complications included failure of neoureterocystostoma (n=4),

with formation of a RAG bed abscess and diffuse purulent peritonitis (n=1) or pelvic abscess (n=1); RAG bed phlegmon (n=2), with the formation of hip phlegmon in one of them; the ureteral stricture formation (n=2); infectious-necrotic lesion of the RAG vessels, vascular anastomoses and iliac vessels of the recipient (n=1); in addition, there was 1 case each of RAG acute pyelonephritis, RAG vein thrombosis, inflammatory infiltrate of the right hip and lower leg, as well as the severe urinary infection development. They were accompanied by a systemic inflammatory response in 3 recipients, and by the sepsis development in 2 other recipients.

Despite the relatively high incidence of clinically significant ICs, the diagnostic and treatment algorithms used enabled satisfactory clinical outcomes. Of the 87 recipients of primarily infected RAG, 78 (89.7%) were discharged with satisfactorily functioning RAG. The nitrogenous waste products (serum creatinine, blood urea) and glomerular filtration rate (GFR) levels in these patients were 141 (120; 191) μmol/L, 10 (7.6;14.3) mmol/L, and 48.3 (41.7;66) mL/min, respectively. The PGNF incidence in the study group was 3.5%. Seven patients underwent a life-saving RAG removal during the in-hospital period (Table 7). As of April 1, 2025, the information on 83 patients was available: 75 were alive, and 65 of them had a functional RAG. In the long-term postoperatively, the RAG function loss was reported in 3 recipients. The late mortality rate was 9.6%; however, we should note that 7 of the 8 deceased patients had functional renal allograft at the time of death. Therefore, a one-year recipient survival rate was 100%, and RAG survival was 92%.

Distributing the patients into groups based on the presence/absence of clinically significant ICs enabled to study their impact on the early and long-term outcomes of primarily infected RAGs. Thus, the development of ICs significantly reduced the likelihood for the recipients to have a

functioning RAG at discharge and the likelihood of having a functioning RAG in the late postoperative period, and also increased the likelihood of in-hospital RAG removal. Factors that significantly affected early and long-term outcomes were identified. These included the development of clinically significant ICs, type 2 diabetes mellitus as the underlying disease that led to the development of stage 5 CKD in recipients of the study group.

Conclusions

1. The incidence of transplanting primarily infected kidney grafts was 4.52%. The predominant microorganisms were staphylococci, Klebsiella, enterococci, and E. coli (a total of 75%).

2. The incidence of clinically significant infectious complications was 17.2%. Their development significantly reduced the early ($p<0.001$) and late ($p<0.001$) kidney graft survival, but did not affect the recipient survival.

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