Chirurgia (2024) 119: 572-579
No. 5, September - October

http://dx.doi.org/10.21614/chirurgia.3018

Cold Ischemia Time as a Risk Factor for Graft Dysfunction Types in Kidney Transplant Recipients

Teodor Căluși[1]*, Bogdan Sorohan[2,3], Alexandru Iordache[4], Florea Purcaru[5]

[1]Intensive Care Unit, Department 2, Fundeni Clinical Institute, Bucharest, Romania
[2]Department of Nephrology, Carol Davila University of Medicine and Pharmacy, Bucharest, Romania
[3]Department of Kidney Transplantation, Fundeni Clinical Institute, Bucharest, Romania
[4]Department of Urology, Fundeni Clinical Institute, Bucharest, Romania
[5]Craiova University of Medicine and Pharmacy, Craiova, Romania

***Corresponding author:**
Teodor Căluși, M.D.
Intensive Care Unit, Department 2
Fundeni Clinical Institute
Fundeni Street No 258, District 2
Bucharest, Romania, Zip Code 022328
E-mail: calusiteodor@yahoo.com

Abbreviations:
CIT: cold ischemia time;
SGF: slow graft function;
DGF: delayed graft function;
IGF: immediate graft function;
KT: kidney transplants;
ESRD: end-stage renal disease;
HLA: human leukocyte antigen;
ATG: anti-thymocyte globulin;
TAC: tacrolimus;
MPA: mycophenolic acid;
MPA: mycophenolate sodium or mofetil;
ATP: adenosine triphosphate;
ATPase: enzymecatalyze decomposition of ATP;
IQR: interquartile range.

Received: 29.07.2024
Accepted: 24.09.2024

Rezumat

Timpul de ischemie rece ca factor de risc pentru diferite tipuri de disfuncție de grefa la receptorii transplantați renal

Introducere: Timpul de ischemie rece (CIT) ar putea aduce informații în ceea ce priveşte probabilitatea funcției lente a grefei (SGF) sau a funcției întârziate a grefei (DGF). Ne propunem să determinăm incidența diferitelor tipuri de disfuncție a grefei şi asocierea cu timpul de ischemie.
Material şi Metode: Am efectuat un studiu prospectiv pe 54 de adulți beneficiari de transplant renal, transplantați între 1 ianuarie 2019 şi 31 decembrie 2019. Grefa a fost definită şi clasificată în trei categorii: funcția de grefă imediată (IGF), funcția de grefă lentă (SGF) şi funcția de grefă întarziată (DGF). Am utilizat modelul de regresie Cox în identificarea factorilor de risc pentru disfuncția grefei. Printre cei 54 de beneficiari de transplant renal, incidența disfuncției grefei (SGF şi DGF) a fost de 24,07%. Mediana timpului de ischemie rece a fost semnificativ mai mare la pacienții cu oricare disfuncție de grefă decât la cei cu funcție imediată a grefei [600 minute (82,5-1005) vs 150 minute (45-540), p = 0,03].
Rezultate: Conform analizei multivariate de regresie Cox, s-a observat că timpul de ischemie rece [HR = 1,004, 95% CI = 1,001-1,007, p = 0,007] a fost un factor de risc independent pentru apariția disfuncției grefei, în timp ce donatorul în moarte cerebrală [HR = 11,94, 95% CI = 0,73-194,94, p = 0,08] şi diabetul [RR = 2,71, 95% CI = 0,083-8,80, p = 0,09] au avut o tendință de asociere cu rezultatul urmărit. În două modele separate de analiză multi-

variată am constatat că timpul de ischemie rece a fost un factor de risc independent pentru DGF [HR = 1,003, 95% CI = 1,001-1,006, p = 0,01], dar nu şi pentru SGF.
Concluzie: În concluzie, am constatat că diferitele tipuri de disfuncție ale grefei renale sunt asociate cu un timp de ischemie rece ridicat şi timpul de ischemie rece a fost un factor de risc important pentru DGF, dar nu si al SGF la beneficiarii de transplant renal.

Cuvinte cheie: transplant renal, timp de ischemie rece, funcția de grefa

Abstract
Introduction: Cold Ischemia time (CIT) could be informative regarding the possibility of slow graft function (SGF) or delayed graft function (DGF). We aim to determine the incidence of graft dysfunction types and the association with ischemia time.
Material and Methods: We performed a prospective study on 54 adults KT recipients, transplanted between 1 of January 2019 and 31 of December 2019. Graft was defined and classified into three categories: immediate graft function (IGF), SGF, and DGF. Cox regression analysis has been used to identify risk factors for graft dysfunction.
Results: According to multivariate Cox regression analysis, it was observed that CIT [HR = 1.004, 95%CI = 1.001-1.007, p = 0.007] was an independent risk factor for the occurrence of graft dysfunction, while the brain death donor [HR = 11.94, 95%CI = 0.73-194.94, p = 0.08] and diabetes [HR = 2.71, 95%CI = 0.083-8.80, p = 0.09] had a trend of association with the followed outcome. In two separate models of multivariate we found that CIT was an independent risk factor for DGF [HR = 1.003, 95%CI = 1.001-1.006, p = 0.01], but not for SGF.
Conclusion: In conclusion we found that kidney graft dysfunction types are associated with high CIT and CIT was an important risk factor for DGF, but no SGF in KT recipients.

Key words: kidney transplant, cold ischemia time, graft function

Introduction

Kidney transplantation is considered the optimal renal replacement therapy in patients with end-stage renal disease (ESRD) (1,2,3). Despite the increase of survival rate of the kidney graft in the first-year post-transplant, the risk of graft loss remains significantly higher in the case of deceased donors (4). An important indicator of long-term graft survival is the immediate kidney graft function. There are two major graft dysfunction types associated with negative outcomes: slow graft function (SGF) and delayed graft function (DGF)(1). DGF represents the need for dialysis in the first week after KT. SGF is an intermediate phenotype for a slow and unsatisfactory decline of serum creatinine after KT, but without need for hemodialysis (5). There are many factors described in the literature that are associated with an increased risk of graft dysfunction, including cold ischemia time (CIT). Although we know more about the link between prolonged cold ischemic time and DGF, there is a lack of information about the link with SGF (5).

Aim of the Study

We intend to evaluate the incidence of graft dysfunction types and to analyze the incidence between graft dysfunction types and ischemia time in KT recipients.

Material and Methods

Study Design and Population

We performed a prospective, observational, study in 54 kidney transplant recipients who underwent a kidney transplantation in Fundeni Clinical Institute, Center for Uronephrology and Kidney Transplantation, between 1st of January 2019 and 31st of December 2019.

Inclusion Criteria

Patient selected for kidney transplantation, age > 18 years, patient signed inform consent, functional renal graft.

Exclusion Criteria

Age < 18 years, patient's refusal to participate. The study protocol was approved by the Ethical Committee of Fundeni Clinical Institute (registration number: 21189).

Variables and Definitions

Data were collected preoperatively, during surgical intervention, and in the first seven postoperative days. Recipient, donor, and transplant variables were recorded. The graft function was evaluated based on serum creatinine and estimated based on CKD-EPI 2021 formula. Graft function is classified into three categories: immediate graft function (serum creatinine < 3 mg/dl at day 5 after KT), slow graft function (serum creatinine ≥ 3 mg/dl at day 5 or ≥ 2.5 mg dl at day 7 after KT), and delayed graft function (the need for at least one dialysis treatment in the first week after kidney transplantation).

Protocol

Induction of anesthesia was made with: Propofol 1-2 mg/kg/c, Fentanyl 1-3 mcg/kg/cc, Atracurium 0.4-0.6 mg/kg, maintenance was achieved with Sevoflurane, Fentanyl, Atracurium and hydro, electrolytic and acid-base equilibrium was maintained with crystalloids, colloids, albumin and sodium bicarbonate. All patients were evaluated with ASA anesthesia score III-IV and received general anesthesia. After the kidney was removed from donor patient, it was preserved in an ice-cold solution to keep the kidney cells viable (*Fig. 1*). Even with all precaution measures taken, hypoxia – induced cell damage cannot be completely prevented. These injuries, together with those induced by the reperfusion of an ischemic kidney, after the anastomosis is performed (*Fig. 2*), can manifest as SGF or DGF and can decrease the lifespan of the kidney graft. All these complications start from an increased ischemia time, so it is reasonable to appreciate that an increased ischemia time increases the risk of graft dysfunction (4).

HLA typing for HLA-A, -B, -C, -DR, -DP and DQ and pre-KT anti-HLA donor specific antibodies evaluation was performed in all patients. Induction of immunosuppression consisted of an anti-interleukin 2 receptor antibody (basiliximab) administered intravenously on day 0 (20 mg) and day 4 (20 mg) or anti-thymocyte globulin (ATG) in a total cumulative dose of 3-5 mg/kg, divided over 3-5 days, in combination with intravenous methylprednisolone (500 mg - day 0 and day 1, 250 mg - day 2, 125 mg - day 3). Choosing between basiliximab and ATG was based on

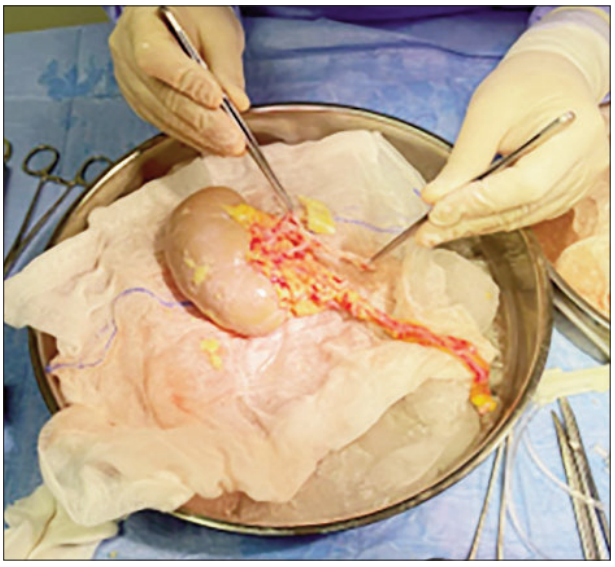

Figure 1. Kidney preserved in an ice-cold solution and prepared for grafting.

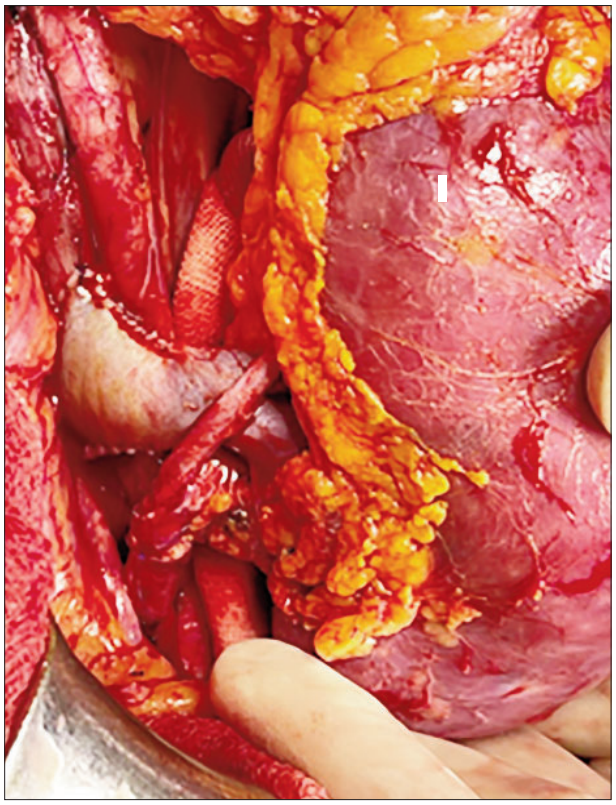

Figure 2. Kidney graft after the anastomosis is performed.

the immunological risk. Maintenance of immunosuppression consisted of tacrolimus (TAC), mycophenolic acid (MPA), and prednisone. TAC (immediate-release or prolonged-release) was started with 0.2 mg/kg/day, adjusted then to achieve the target levels. MPA (mycophenolate sodium or mofetil) doses were 1440 mg or 2000 mg twice daily, followed by tapering to 360 mg twice daily at 3 months post-KT. Oral prednisone was started on day 4 post-KT according to the protocol of the center.

Statistical Analysis

Data were reported as percentages for categorical variables, mean with standard deviation for continuous parametric variables and median with interquartile range (IQR) for continuous non-parametric ones. For group comparison, Chi-square or Fisher exact test were used as appropriate for categorical data, t student test for continuous parametric data and Mann-Whitney U form continuous non-parametric data. Cox regression analysis was used to evaluate risk factors for kidney graft dysfunction types. Three separate models were performed to identify the factors for DGF or SGF (model A), DGF (model B), and SGF (model C) respectively. For multivariate models, we used the backward elimination method. A p-value < 0.05 was considered statistically significant. The statistical analysis was performed with SPSS version 26 (SPSS Inc, Chicago, IL, USA).

Results

General characteristics of the patient were presented in *Table 1*. In the 54 KT recipients, mean age was 38.5 ± 12.3 years, 59.3% of patients were male, 55.5% received a graft form a deceased donor (DD), and the donor mean age was 40.2 ± 14.8 years. The main causes of CKD were HTN (29.6%), DKD (22.2%), and glomerulonephritis (14.8%). Most patients (92.6%) received basiliximab as induction immunosuppression and all received triple therapy with TAC, MPA, and prednisone as maintenance immunosuppression. Regarding ischemia time, median cold ischemia time (CIT) was 300 (60-600) minutes, mean warm ischemia time (WIT) was 26.9 ± 7.9 minutes. Mean serum creatinine at the moment of KT was 7.8 ± 2.4 mg/dL and at 1 week after KT was 2.4 ± 1.8 mg/dL, respectively 2.7 ± 1.2. Deceased donor KT was performed in 55.5% of patients (*Fig. 3*). The mean donor age was 40.2 ± 14.8 years. SGF or DGF were found in 13 patients (24.1%).

Characteristics of Patients with SGF or DGF

Patients with SGF or DGF had significantly higher values of CIT [600 (82.5-1005) vs 150 (45-540) minutes, [p = 0.03], higher values of creatinine at day 7 (4.4 ± 2.0 vs 1.8 ± 1.2 mg/dl $p \leq 0.001$) respectively at 1 year (2.4 ± 1.7 vs 1.6 ± 0.9 mg/dl p = 0.03) than patients with IGF. No association was observed between graft disfunction and normal graft function in

Table 1. Characteristics of patients enrolled. Global analysis

Variables	Entire cohort (N= 54)	SGF or DGF (N= 13)	IGF (N=41)	P value
Age (years, mean)	38.5 ± 12.3	42.7 ± 14.3	37.1 ± 11.4	0.16
Gender (%)				0.12
Male	32 (59.3%)	10 (76.9%)	22 (53.7%)	
Female		3 (23.1%)	19 (46.3%)	
Diabetes (%)	12 (22.2%)	5 (38.5%)	7 (17.1%)	0.12
Obesity (%)	16 (29.6%)	5 (38.5%)	11 (26.8%)	0.43
Dialysis before KT (%)	49 (90.7%)	12 (92.3%)	37 (90.2%)	0.82
CKD cause (%)				0.17
HTN	16 (29.6%)	4 (30.8%)	12 (29.3%)	
DKD	12 (22.2%)	5 (38.5%)	7 (17.1%)	
Glomerulonephritis	8 (14.8%)	3 (0%)	8 (19.5%)	
Others	6 (11.1%)	1 (7.7%)	5 (12.2%)	
Unknown	12 (22.2%)	3 (23.1%)	9 (22.0%)	
CIT (mins, median)	300 (60 - 600)	600 (82.5 - 1005)	150 (45 - 540)	0.03
WIT (mins, mean)	26.9 ± 7.9	28.6 ± 6.0	26.5 ± 7.3	0.37
Creatinine at day 0 (mg/dL, mean)	7.8 ± 2.4	7.1 ± 2.9	8.0 ± 2.3	0.24
Creatinine at day 7 after KT (mg/dL, mean)	2.4 ± 1.8	4.4 ± 2.0	1.8 ± 1.2	<0.001
Creatinine at 1 year after KT (mg/dL, mean)	2.7 ± 1.2	2.4 ± 1.7	1.6 ± 0.9	0.03
Donor type (%)				0.24
DD	30 (55.5%)	9 (69.2%)	21 (51.2%)	
LD	24 (44.5%)	4 (30.8%)	20 (48.8%)	
Donor age (years, mean)	40.2 ± 14.8	42.5 ± 10.7	38.6 ± 12.5	0.12
Donor gender (Male, %)	30 (55.5%)	8 (61.5%)	22 (53.7%)	0.61
Immunouppression				
Induction				1
Basiliximab	50 (92.6%)	12 (92.3%)	38 (92.7%)	
ATG	4 (7.4%)	1 (7.7%)	3 (7.3%)	
Methylprednisolone	100 (100%)	13 (100%)	41 (100%)	1
Maintenance				
ER-TAC	22 (40.7%)	6 (46.2%)	16 (39.0%)	0.64
IR-TAC	32 (59.3%)	7 (53.8%)	25 (61.0%)	
Mycophenolate sodium	100 (100%)	13 (100%)	41 (100%)	1
Prednisone	100 (100%)	13 (100%)	41 (100%)	1

N - number; % - percentage; SBP - systolic blood pressure; ICU - intensive care unit; CIT - cold ischemia time; WIT - warm ischemia time; $HCO3^-$ - bicarbonate; $NaHCO3^-$ - sodium bicarbonate; BE - base excess; IGF - immediate graft function; SGF - slow graft function; DGF - delayed graft function; DD - deceased donor; LD - living donor; ATG - anti-thymocyte globulin; KT - kidney transplantation

the following groups: donor age, gender and type, presence or absence of diabetes or obesity of the recipient, dialysis initiated or not before KT, CKD causes, transplant immunosuppression and WIT (*Table 1*).

Univariate and multivariate Cox regression analysis were used to identify the risk factor for graft dysfunction types. (*Tables 2-4*).

In model A (*Table 2*), according to univariate Cox analysis, CIT was a risk factor for kidney graft dysfunction [HR = 1.002, 95% CI = 1.001-1.004, p = 0.009]. In the multivariate analysis, it was observed that CIT [HR = 1.004, 95%CI = 1.001-1.007, p = 0.007] was an independent risk factor for the occurrence of graft dysfunction, while the deceased donor type [HR = 11.94, 95%CI = 0.73-194.94, p = 0.08] and diabetes [HR = 2.71, 95%CI = 0.083-8.80, p = 0.09] presented a trend of association with the followed outcome.

In model B (*Table 3*) univariate Cox regression analysis showed that recipient age [HR = 1.09, 95%CI = 1.05-1.20, p = 0.04] was a risk factor for SGF. In the multivariate analysis, recipient age [HR = 1.11, 95%CI = 1.01-1.21, p = 0.02] was also an independent risk factor

Table 2. Cox regression analysis to identify risk factors for graft disfunction

	Univariate analysis			Multivariate analysis		
	HR	95%CI	P value	HR	95%CI	P value
Recipient age	1.04	0.98 - 1.09	0.14	-	-	-
Recipient male gender	2.32	0.63 - 8.43	0.20	-	-	-
Diabetes	2.35	0.76 - 7.20	0.13	2.71	0.83-8.80	0.09
CKD cause (hypertension)	1.03	0.31 - 3.36	0.95	-	-	-
Donor type (cadaveric)	1.96	0.60 - 6.37	0.26	11.94	0.73-194.94	0.08
Donor age	1.08	0.97 - 1.10	0.16	-	-	-
CIT	1.002	1.001 - 1.004	0.009	1.004	1.001-1.007	0.007

Table 3. Slow Graft Function

	Univariate analysis			Multivariate analysis		
	HR	95%CI	P value	HR	95%CI	P value
Recipient age	1.09	1.05 - 1.20	0.04	1.11	1.01 - 1.21	0.02
Recipient male gender	0.23	0.03 - 1.96	0.19	-	-	-
Donor male gender	0.43	0.08 - 2.24	0.32			
ER-TAC	7.14	0.86 - 59.63	0.07	8.71	0.99-72.87	0.05
CIT	1.00	0.99 -1.003	0.27	-	-	-

Table 4. Delayed graft function

	Univariate analysis			Multivariate analysis		
	HR	95%CI	P value	HR	95%CI	P value
Diabetes	3.41	0.68 -16.90	0.13	-	-	1
Donor type (cadaveric)	4.11	0.48 - 35.20	0.19	-	-	-
Induction type (ATG)	6.44	1.17 - 35.27	0.03	-	-	-
WIT	1.05	0.98 - 1.13	0.11	-	-	-
CIT	1.004	1.001 - 1.008	0.02	1.003	1.001-1.006	0.01

for the occurrence of SGF. ER-TAC [HR = 8.71, 95% CI = 0.99-72.87, p = 0.05] was associated with SGF at the limit of statistical significance.

In model C (*Table 4*), according to univariate Cox regression analysis, CIT [HR = 1.004, 95%CI = 1.001-1.008, p = 0.02] and induction type (ATG) [HR = 6.44, 95% CI = 1.17-35.27, p = 0.03] were risk factors for DGF. But, by multivariate analysis CIT [HR = 1.003, 95% CI = 1.001-1.006, p = 0.01] was the only risk factor for DGF.

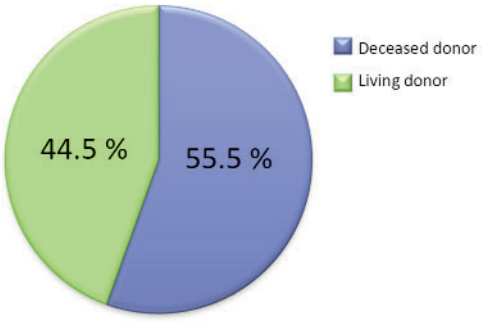

Figure 3. Donor type

Discussion

We presented a prospective study in which we enrolled 54 patients and followed the outcome in terms of the association between graft dysfunction and a series of risk factors, especially CIT. SGF/DGF appeared at a percentage of 24.07% with a higher incidence of SGF (*Fig. 4*), something that correlates with current literature.We showed that increased CIT is a risk factor for DGF, but not for SGF. Results were like that finding in many other studies in the case of DGF (6-15), this further supporting the hypothesis of a correlation between DGF and cold ischemia time. In the

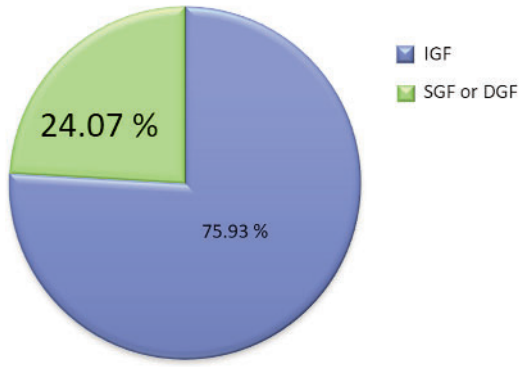

Figure 4. Incidence of IGF and SGF or DGF

case of SGF, our study does not indicate an association between SGF and CIT, while in the current literature, although less studied than DGF, SGF seems to be associated with CIT (16,17).

Cold ischemia causes a cascade of harmful effects that are amplified once reperfusion is restored. After surgical removal the kidney is set in a cold solution to preserve viable cells as much as possible. Reactive oxygen species are produced in the mitochondria in response to hypoxia. Intracellular acidosis occurs because of the anaerobic glycolysis necessary to produce ATP, whose synthesis decreases as the glycolytic substrate is exhausted. As the generation of ATP decreases, the activity of the Na/K ATPase pump is affected, affecting the balance between intracellular K ions and extracellular Naions, having as a direct effect cellular swelling. Accentuation of inflammation and oxidative destruction appear together with the perfusion of the ischemic kidney, a phenomenon known as ischemic reperfusion lesions, all these changes additionally affecting the integrity of the renal graft (18). The intensity of these changes seems to be serious enough to be especially associated with DGF, a more problematic disfunction than SGF.

SGF and DGF, both are associated with an older recipient in the current literature, but in our study, recipient age seems to correlate well only with SGF (19,20).

We also observed that patients who developed SGF or DGF had a significantly higher creatinine at 7 days and one year respectively. The strength of the study is its prospective manner. However, our study has some limitations represented by the small sample size and single center recruitment. The single-center nature of the study limits the generalizability and reproducibility of these results to other cohorts.

Conclusion

In conclusion, our study showed that high CIT was associated with graft dysfunction phenotypes. Particularly, we found that high CIT was an independent risk factor for DGF, but not for SGF.

Conflicts of Interest and Source of Funding

The authors declare no conflict of interest. This research receives no funding.

References

1. Csaba P. Kovesdy Epidemiology of chronic kidney disease: an update 2022. Kidney Int Suppl (2011). 2022;12(1):7-11.
2. Abecassis M, Bartlett ST, Collins AJ, Davis CL, Delmonico FL, Friedewald JJ, et al. Kidney Transplantation as Primary Therapy for End-Stage Renal Disease: A National Kidney Foundation/Kidney Disease Outcomes Quality Initiative (NKF/KDOQI™) Conference. Clin J Am Soc Nephrol. 2008;3(2): 471-480.
3. Axelrod DA, Schnitzler MA, Xiao H, Irish W, Tuttle-Newhall E, Chang SH, et al. An economic assessment of contemporary kidney transplant practice. Am J Transplant. 2018;18(5):1168-1176.
4. Nieto-Ríos JF, Ochoa-García CL, Serna-Campuzano A, Benavides-Hermosa B, Calderón-Puentes LL, Aristizabal-Alzate A et al. Time of Cold Ischemia and Delayed Graft Function in a Cohort of Renal Transplant Patients in a Reference Center; Indian J Nephrol. 2019;29(1):8-14.
5. Humar A, Ramcharan T, Kandaswamy R, Gillingham K, Payne WD, Matas AJ. Risk factors for slow graft function after kidney transplants: a multivariate analysis. Clin Transplant. 2002;16(6):425–9.
6. Lauronen J, Peräsaari JP, Saarinen T, Jaatinen T, Lempinen M, Helanterä I. Shorter Cold Ischemia Time in Deceased Donor Kidney Transplantation Reduces the Incidence of Delayed Graft Function Especially Among Highly Sensitized Patients and Kidneys From Older Donors. Transplant Proc. 2020;52(1):42-49.
7. Debout A, Foucher Y, TrébernLaunay K, Legendre C, Kreis H, Mourad G, et al. Each additional hour of cold ischemia time significantly increases the risk of graft failure and mortality following renal transplantation. Kidney Int. 2015;87(2):343-9.
8. Lum EL, Homkrailas P, Abdalla B, Danovitch GM, Suphamai Bunnapradist; Cold Ischemia Time, Kidney Donor Profile Index, and Kidney Transplant Outcomes: A Cohort Study. Kidney Med. 2022;5(1):100570.
9. Husain SA, Khanna S, Yu M, Adler JT, Cron DC, King KL, et al. Cold Ischemia Time and Delayed Graft Function in Kidney Transplantation: A Paired Kidney Analysis. Transplantation. 2024;108(9):e245-e253.
10. Peters-Sengers H, Houtzager JHE, Idu M, Heemskerk M, van Heurn ELW, Homan van der Heide JJ, et al. Impact of Cold Ischemia Time on Outcomes of Deceased Donor Kidney Transplantation: An Analysis of a National Registry. Transplant Direct. 2019;5(5):e448.

11. Requião-Moura LR, de Souza Durão Junior M, Carvalho de Matos AC, Pacheco-Silva A. Ischemia and reperfusion injury in renal transplantation: hemodynamic and immunological paradigms. Einstein (Sao Paulo). 2015; 13(1):129-35. English, Portuguese
12. Gorayeb-Polacchini FS, Caldas H, Fernandes IMM, Sperto Ferreira Baptista MA, Ravazzi Gauch C, Abbud-Filho M. Impact of Cold Ischemia Time on Kidney Transplant: A Mate Kidney Analysis. Transplant Proc. 2020;52(5): 1269-1271.
13. van de Laar SC, Lafranca JA, Minnee RC, Papalois V, Dor FJMF. The Impact of Cold Ischaemia Time on Outcomes of Living Donor Kidney Transplantation: A Systematic Review and Meta-Analysis. J Clin Med. 2022; 11(6):1620.
14. Saat TC, van den Akker EK, Jzermans JNM, Dor FJMF, de Bruin RWF. Improving the outcome of kidney transplantation by ameliorating renal ischemia reperfusion injury: lost in translation? J Transl Med. 2016;14:20.
15. Ghioldiș AC, Sârbu V, Pundiche M, Dan C, Butelchin C, Olteanu C, et al. Clostridium Difficile Infection in Rectal Cancer Patients after Diverted Loop Ileostomy Closure. Chirurgia (Bucur). 2024;119(1):36-43.
16. Peeters P, Vanholder R. Therapeutic interventions favorably influencing delayed and slow graft function in kidney transplantation: mission impossible? Transplantation. 2008;85(7 Suppl):S31-7.
17. Humar A, Ramcharan T, Kandaswamy R, Gillingham K, Payne WD, Matas AJ. Risk factors for slow graft function after kidney transplants: a multivariate analysis. Clin Transplant. 2002;16(6):425-9.
18. Ponticelli CE. The impact of cold ischemia time on renal transplant outcome. Kidney Int. 2015;87(2):272-5.
19. Veroux M, Sanfilippo F, Roscitano G, Giambra M, Giaquinta A, Riccioli G, et al. Prevention of Delayed Graft Function in Kidney Transplant Recipients through a Continuous Infusion of the Prostaglandin Analogue Iloprost: A Single Center Prospective Study. Biomedicines. 2024;12(2):290.
20. Johnston O, O'Kelly P, Spencer S, Donohoe J, Walshe JJ, Little DM, et al. Reduced graft function (with or without dialysis) vs immediate graft functiona comparison of long-term renal allograft survival. Nephrol Dial Transplant. 2006;21(8):2270-4.