Influence of deceased donor hemodynamic factors in transplant recipients renal function

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ABSTRACT

Introduction: The incidence of delayed graft function (DGF) and unsatisfactory creatinine clearance (UCC) after renal transplantation is significantly higher in Brazil, when compared with that observed in United States or Europe. Deceased donor (DD) characteristics should directly influence the occurrence of these two outcomes. **Objective:** This study aim to evaluate the influence of DD characteristics on DGF and UCC incidence in Brazil. **Methods:** DD clinical and laboratory variables were correlated with outcome's incidence. **Results:** We evaluated 787 DD whose organs were transplanted in 1298 patients. We noted a high prevalence of vasoactive drugs use (90.2%), hypernatremia (66.6%) and renal dysfunction (34.8%). The incidence of DGF and UCC was 60.6% and 55.2%, respectively. We observed a progressive increase in DGF risk for age groups over 30 years and for cold ischemia time (CIT) greater than 24 hours. DGF risk was two times higher in recipients of donor kidney final serum creatinine (Cr) over than 1.5 mg/dl. Hypertension and CIT over 36 hours was associated with an increasing of 82% and 99% in UCC risk, respectively. Donor age above 40 years was associated with a progressive increase in UCC risk. **Conclusion:** DD age, renal function, hypertension and prolonged CIT were associated with increased risk DGF and UCC.

Keywords: creatinine, delayed graft function, donor selection, kidney transplantation.

INTRODUCTION

The need to increase the supply of kidneys for transplantation because of the high number of patients registered on the waiting list has demanded a more widespread use of organs from borderline deceased donors, which were previously discarded.[1,2] Since the superiority of renal transplantation compared to dialysis was proven, it became necessary to use these organs.[3-6]

However, the increased use of borderline kidneys from deceased donors has been associated with an increased incidence of complications after transplantation, among them: delayed graft function (DGF), which occurs when there is a need for renal replacement therapy in the first week after transplantation, and poor kidney function (PKF), defined as serum creatinine above 1.5 mg/dL six months or one year after the transplant.[2,7]

The negative association between DGF and PKF and graft survival is well established. DGF patients have lower survival, lower graft function after recovery and higher incidence of acute rejection.[8] Unsatisfactory renal function six months after transplantation was associated with a relative risk for graft loss being twice the risk of patients with serum creatinine lower than this value.[9,10]

For these reasons, it is necessary to identify the risk factors for DGF and PKF in order to develop interventions to reduce the occurrence of these outcomes and prevent complications.

Characteristics related to the deceased donor leading to higher incidences of these two outcomes have been thoroughly investigated.[11] Factors related to hemodynamic and electrolytic maintenance prior to multiple organ extraction, in addition to demographic characteristics, are

associated with increased risk for the development of DGF and PKF.[9,12-15]

In Brazil, the incidence of DGF is significantly higher than the U.S. incidence (57.3% *vs.* 23.5%),[2,16] and there is a lower graft survival after one year of the transplant.[1,2] We still need to investigate the factors related to the deceased donor that determine a worse outcome of kidney transplantation in this country.

This study aimed at assessing the characteristics of deceased donors, associated with the incidence of DGF and PKF in a large transplant center in Brazil.

Methods

This is a retrospective study using a sequential cohort of deceased donors identified by the Organs and Tissues Search Service of the Paulista School of Medicine (SPOT-EPM) from January 1998 through December 2008. This study was approved by the local Ethics in Research Committee.

We removed from this analysis those deceased donors whose kidneys were transplanted at another transplant center; recipients aged less than 18; second kidney transplant recipients and recipients of another organ combined. The characteristics of deceased donors were extracted from the "Information About the Deceased Donor" form, completed by the SPOT-EPM and transferred to the State Transplant Central. The data about the kidney transplant recipients was obtained from medical records.

The aim of the study was to identify deceased donor risk factors associated with the development of delayed graft function (DGF) or poor kidney function (PKF) six months after transplantation. DGF was defined as the need for dialysis during the first week after transplantation. PKF six months after transplantation was defined as creatinine clearance less than or equal to 50 ml/min/1.73m^2, calculated using the Cockcroft-Gault.[17] Follow-up loss was defined as the definitive transfer of the recipient for monitoring in another service. Graft loss was defined as return to dialysis or retransplantation.

Statistical Analysis

The categorical variables were presented as absolute and relative frequencies and the numerical variables as means and standard deviations. To analyze the PKF outcome in the sixth month we used an imputation method for missing values, as follows: (1) those patients who lost the graft before the sixth month were assigned a value of zero for creatinine clearance; (2) for patients who died or lost the follow-up we used the last reading made (creatinine) ("Last observation carried Forward") for the calculation of creatinine clearance in the sixth month.

The characteristics of the deceased donor assessed against the outcomes were: age, gender, ethnicity, cause of brain death, hypertension, diabetes mellitus, active infection, use of vasoactive drugs, length of stay in the intensive care unit, cardiac arrest during hospitalization, serum creatinine on the day of assessment (creatinine final), glutamic oxaloacetic transaminase (GOT), glutamic pyruvic transaminase (GPT), creatine phosphokinase, serum sodium, serology for hepatitis B (HBsAg), serology for hepatitis C (anti-HCV) and cold ischemia time. The association between donor characteristics and DGF and PKF outcomes were assessed using the chi-square or Fisher's exact test for categorical variables and the *Student t*-test for the continuous variables. In order to find the donor variables independently associated with the DGF and PKF outcomes, we used logistic regression. The adequacy of fit of this model was verified using the Hosmer and Lemeshow test. For all the statistical tests we used a significance level of 5%, with $p < 0.05$. We used the SPSS version 17.0 (SPSS Inc., Chicago, IL, USA) software used for analysis.

Results

During the study period, we found 1,085 deceased donors whose kidneys were transplanted into 1,646 recipients in our service. We excluded 298 donors whose kidneys were allocated to 223 recipients under the age of 18 years and 125 recipients of second or third kidney transplant. We then analyzed 787 deceased donors and 1,298 kidney transplant recipients.

The average age of deceased donors was 40.2 years and stroke was the leading cause of death (54.9%). The donor maintenance parameters analysis shows that 90.2% received a vasoactive drug at the time of evaluation and 15% had had a cardiac arrest reversed (Table 1). In addition, 70% had hypernatremia (Na > 145 mEq/l); 66.6% had elevated creatinine phosphokinase and 34.8% had kidney failure (creatinine > 1.5 mg/dl) (data not shown). The kidneys were transplanted within a mean cold ischemia time of 23.2 (Table 1).

Table 1 Demographic, clinical and laboratorial characteristics of the deceased donors

Donor	Total (n = 787)
Age, mean ± DP (years)	40.2 ± 14.9
Age range, n (%)	
≤ 10 years	18 (2.3)
11-20 years	78 (9.9)
21-30 years	127 (16.1)
31-40 years	134 (17.0)
41-50 years	218 (27.7)
51-60 years	159 (20.2)
≥ 61 years	53 (6.8)
Gender, n (%)	
Males	434 (55.1)
Females	353 (44.9)
Ethnicity, n (%)	
Black	75 (9.5)
Not black	571 (72.6)
No information	141 (18.0)
Brain death cause, n (%)	
Stroke	432 (54.9)
Head injury	315 (40.0)
Neoplasia	11 (1.4)
Anoxic encephalopathy	23 (3.0)
Others	6 (0.8)
Systemic arterial hypertension, n (%)	201 (25.6)
Diabetes Mellitus, n (%)	21 (2.7)
Final creatinine, mean ± SD (mg/dL)	1.5 ± 1.0
≤ 0.8 mg/dL	167 (23.0)
0.8-1.5 mg/dL	306 (42.2)
> 1.5 mg/dL	252 (34.8)
No information	62
Active infection, n (%)	245 (31.2)
Use of vasoactive drug, n (%)	710 (90.2)
Cardiac arrest, n (%)	118 (15.0)
B Hepatitis virus, n (%)	2 (0.2)
C Hepatitis virus, n (%)	2 (0.2)
Days in the ICU, mean ± SD	5.4 ± 4.4
Sodium, mean ± SD (mEq/L)	154.6 ± 15.4
TGO, mean ± SD (U)	107.1 ± 302.7
TGP, mean ± SD (U)	75.4 ± 159.3
CPK, mean ± SD (U/L)	1706 ± 4262
≤ 250 U/L	191 (33.6)
250-1000 U/L	186 (32.7)
> 1000 U/L	192 (33.7)
No information	218
TIF, mean ± SD (h)	23.2 ± 7.2
≤ 12h	49 (6.4)
13-18h	152 (19.6)
19-24h	255 (33.2)
25-30h	192 (24.9)
31-36h	94 (12.4)
≥ 37h	27 (3.5)
No information	18

Recipients had a mean age of 46.1 years; 80.4% had hypertension, and 13.8% had diabetes mellitus. The incidence of DGF was 60.6% and the incidence of PKF was 55.2%. The mean creatinine level was 1.6 mg/dl and creatinine clearance was 46.1 ml/min/1.73m^2 in the sixth month of transplantation. The receiver survival rate was 93% and graft survival was 90.6% six months after transplantation (Table 2).

Table 2 Demographic, clinical and laboratorial characteristics of recipients of deceased kidney donors

Recipient	Total (n = 1298)
Age, mean ± SD (years)	46.1 ± 12.1
Weight, mean ± SD (kg)	62.7 ± 13.7
Gender, n (%)	
Males	729 (56.2)
Females	569 (43.8)
Ethnicity, n (%)	
Black	138 (10.6)
Not Black	922 (71.0)
No information	238 (18.3)
Cause of CKD, n (%)	
Diabetes	176 (13.6)
Hypertension	248 (19.1)
Glomerulonephritis	168 (12.9)
Undetermined	472 (36.4)
Others	234 (18.0)
Hypertension, n (%)	1044 (80.4)
Diabetes Mellitus, n (%)	179 (13.8)
B Hepatitis virus, n (%)	46 (3.5)
C Hepatitis virus, n (%)	172 (13.3)
Delayed graft function, n (%)	787 (60.6)
Creatinine (6 months), mean ± SD (mg/dl)	1.6 ± 0.7
Creatinine clearance (6 months), mean ± SD (ml/min/1.73 m^2)	46.1 ± 23.7
Poor kidney function (6 months), n (%)	717 (55.2)
Graft loss, n (%)	122 (9.4)
Death, n (%)	91 (7)
Loss of follow up, n (%)	8 (0.6)

Delayed graft function (DGF)

The patients who developed DGF received kidneys from donors with higher mean ages (41.5 *vs.* 38.3 years, $p < 0.001$), higher final creatinine mean levels (1.6 *vs.* 1.3 mg/dl, $p < 0.001$) and longer mean cold ischemia time (23.9 *vs.* 22.2 hours, $p < 0.001$). The

rate of hypertensive donors was higher in the group with DGF (28.5% *vs.* 21.1%, $p = 0.003$), respectively (Table 3). After the logistic regression analysis with multiple variables, we observed a progressive increase in the risk of developing DGF from age greater than 30 years, with the final creatinine valuesabove 1.5 mg/dl and cold ischemia times longer than 24 hours (Table 4).

Poor kidney function six months after kidney transplantation

Recipients with PKF in the sixth month after transplantation received kidneys from deceased donors with higher mean age (43.7 *vs.* 35.9 years, $p < 0.001$), with a higher number of females (49.1% *vs.* 39.8%, $p = 0.001$), non-black ethnicity (75.2% *vs.* 69.4%, $p = 0.044$), with stroke as a cause of brain death (60.8% *vs.* 47.5%, $p < 0.001$) and associated hypertension (33.6% *vs.* 15.7%, $p < 0.001$). The mean cold ischemia time was almost one hour higher on the recipients with PKF (23.6 *vs.* 22.7 hours, $p = 0.028$). On the other hand, CPK levels were higher in patients without PKF (1444.4 *vs.* 20005.5 U/l, $p = 0.051$) in the sixth semester of transplantation (Table 5). After logistic regression analysis with multiple variables, we observed a progressive increase in the risk of developing PKF from age greater than 40 years, with arterial hypertension and cold ischemia times greater than 36 hours (Table 6).

Discussion

The most important observation of this study was the high incidence of outcomes assessed. In our sample,

Table 3 Comparison of demographic, clinical and laboratorial characteristics of deceased donors in function of developing or not delayed graft function (DFG)

	With DGF (n = 787)	Without DGF (n = 511)	*p*-value
Age, mean ± SD (years)	41.5 ± 14.3	38.3 ± 15.7	< 0.001
Gender, n (%)			0.459
Males	440 (55.9)	275 (53.8)	
Females	347 (44.1)	236 (46.2)	
Ethnicity, n (%)			0.445
Black	79 (10.0)	45 (8.8)	
Not Black	575 (73.1)	367 (71.8)	
No information	133 (16.9)	99 (19.4)	
Brain death cause, n (%)			0.106
Stroke	453 (57.6)	259 (50.7)	
Head injury	295 (37.5)	224 (43.8)	
Neoplasia	12 (1.5)	7 (1.4)	
Anoxic encephalopathy	23 (2.9)	15 (2.9)	
Others	4 (0.5)	6 (1.2)	
Arterial hypertension, n (%)	224 (28.5)	108 (21.1)	0.003
Diabetes Mellitus, n (%)	22 (2.8)	13 (2.5)	0.785
Active infection. n (%)	234 (31.8)	152 (30.3)	0.599
Use of vasoactive drugs, n (%)	694 (90.1)	458 (90.3)	0.904
Cardiac arrest, n (%)	118 (15.3)	74 (14.6)	0.721
B hepatitis virus, n (%)	3 (0.4)	0 (0.0)	0.162
C hepatitis virus, n (%)	2 (0.3)	0 (0.0)	0.522
ICU stay in days, mean ± SD	5.5 ± 4.5	5.2 ± 4.4	0.442
Sodium, mean ± SD (mEq/L)	155.3 ± 15.3	153.6 ± 15.6	0.085
TGO, mean ± SD (U)	110.9 ± 327.3	102.2 ± 267.9	0.662
TGP, mean ± SD (U)	74.7 ± 148.8	76.2 ± 172.1	0.884
CPK, mean ± SD (U/L)	1655 ± 3412	1772 ± 5160	0.676
Final creatinine, mean ± SD (mg/dL)	1.6 ± 1.1	1.3 ± 0.8	< 0.001
Cold ischemia time, mean ± SD (h)	23.9 ± 7.5	22.2 ± 6.8	< 0.001

Table 4 Risk variables associated with delayed graft function

Variable	Univariate		Multivariate	
	OR (CI 95%)	*p*	OR (CI 95%)	*p*
Age range				
≤ 10 years (ref.)	1.00	-	1.00	-
11-20 years	1.19 (0.4-3.7)	0.771	1.00	Ns
21-30 years	1.14 (0.4-3.5)	0.822	1.00	Ns
31-40 years	2.36 (0.8-7.2)	0.132	1.67 (1.2-2.4)	0.007
41-50 years	2.67 (0.9-8.0)	0.082	2.09 (1.5-2.9)	< 0.001
51-60 years	2.18 (0.7-6.7)	0.172	1.68 (1.2-2.4)	0.004
≥ 61 years	2.23 (0.7-7.3)	0.186	1.70 (1.0-2.8)	0.037
Gender				
Males	1.23 (0.9-1.7)	0.234		
Females (ref.)	1.00	-		
Ethnicity				
Blacks	0.81 (0.5-1.3)	0.418		
Not blacks (ref.)	1.00	-		
No information	0.95 (0.7-1.4)	0.769		
BD cause				
Stroke (ref.)	1.00	-		
Head injury	0.85 (0.6-1.3)	0.413		
Neoplasia	1.16 (0.3-4.0)	0.818		
Anoxic encephalitis	2.24 (0.8-6.4)	0.132		
Others	1.57 (0.3-8.2)	0.589		
Arterial Hypertension	1.22 (0.8-1.8)	0.289		
Diabetes Mellitus	0.80 (0.4-1.7)	0.565		
Final Cr	2.51			
≤ 0.8 mg/dL (ref.)	1.00	-		
0.8-1.5 mg/dL	1.18 (0.8-1.7)	0.399		
> 1.5 mg/dL	2.51 (1.6-3.9)	< 0.001	2.09 (1.6-2.7)	< 0.001
Active infection	0.96 (0.7-1.3)	0.811		
VAD use	1.04 (0.6-1.8)	0.898		
Cardiac arrest	1.17 (0.7-1.8)	0.507		
Days in the ICU	1.01 (1.0-1.0)	0.436		
Sodium	1.01 (1.0-1.0)	0.268		
TGO	1.00 (1.0-1.0)	0.563		
TGP	1.00 (1.0-1.0)	0.535		
CPK	1.00 (1.0-1.0)	0.436		
TIF				
≤ 12h (ref.)	1.00	-	1.00	-
13-18h	1.08 (0.4-2.8)	0.872	1.00	ns
19-24h	1.19 (0.5-3.0)	0.714	1.00	ns
25-30h	2.10 (0.8-5.4)	0.120	1.56 (1.2-2.0)	0.001
31-36h	1.60 (0.6-4.2)	0.341	5.10 (2.1-12.4)	< 0.001

Table 5 Comparison of demographic, clinical and laboratorial characteristics of deceased donors in function of the presence or absence of poor kidney function (PFK) in the sixth month of transplant

	With PKF (n = 712)	Without PKF (n = 581)	*p*-value
Age, mean ± SD (years)	43.7 ± 14.5	35.9 ± 14.3	< 0.001
Age range, n (%)			
Gender, n (%)			0.001
Males	365 (50.9)	350 (60.2)	
Females	352 (49.1)	231 (39.8)	
Ethnicity, n (%)			0.044
Black	66 (9.2)	58 (10.0)	
Not black	539 (75.2)	403 (69.4)	
No information	112 (15.6)	120 (20.7)	
Brain death cause, n (%)			< 0.001
Stroke	436 (60.8)	276 (47.5)	
Head injury	242 (33.8)	277 (47.7)	
Neoplasia	11 (1.5)	8 (1.4)	
Anoxic encephalopathy	22 (3.1)	16 (2.8)	
Others	6 (0.8)	4 (0.7)	
Hypertension, n (%)	241 (33.6)	91 (15.7)	< 0.001
Diabetes Mellitus, n (%)	22 (2.8)	13 (2.5)	0.358
Active infection, n (%)	217 (32.1)	169 (30.1)	0.443
Use of vasoactive drug, n (%)	637 (90.2)	515 (90.2)	0.984
Cardiac arrest, n (%)	108 (15.3)	84 (14.7)	0.813
HBV, n (%)	1 (0.1)	2 (0.3)	0.505
HCV, n (%)	2 (0.3)	0 (0.0)	0.505
Days in the ICU, mean ± SD	5.6 ± 4.5	5.1 ± 4.4	0.097
Sodium, mean ± SD (mEq/L)	153.9 ± 14.3	155.4 ± 16.6	0.122
TGO, mean ± SD(U)	100.3 ± 335.2	115.1 ± 260.2	0.451
TGP, mean ± SD(U)	71.8 ± 149.6	79.5 ± 169.9	0.459
CPK, mean ± SD (U/L)	1444 ± 3249	2005 ± 5169	0.051
Final creatinine, mean ± SD (mg/dL)	1.5 ± 1.0	1.5 ± 1.1	0.931
Cold ischemia duration, mean ± SD (h)	23.6 ± 7.3	22.7 ± 7.1	0.028

in which 22.7% of deceased donors were classified as extended, the incidence of DGF was 60.6%. This incidence is much higher than that in the U.S., in which 15.8% of the transplants were performed with kidneys from donors with cardiac arrest - a group of donors with worse outcomes.[2] PKF incidence in this population was 55.2%; analyzing only the group of kidney recipients of expanded criteria donor, 70.9% had DGF. Comparing to the United States, where 28.9% of recipients had creatinine clearance below 60 ml/min six months after transplantation, this percentage is quite high.[2]

In fact, the high incidence of outcomes may have hindered the emergence of other characteristics associated with hemodynamic maintaining of deceased donors as a risk factor for DGF and PKF. Furthermore, the high prevalence of laboratory abnormalities and severe hemodynamic disorders in this study population, as described above, also masked the impact of other characteristics on outcomes. The average length of ICU stay until multiple organ extraction was 5 days, 90% of them were using vasoactive drugs at the time of evaluation and 69% were being treated for an infection. The mean serum sodium was 156.1 mg/dl and creatinine was 1.5 mg/d, valueswhich were higher than normal reference ranges. This high incidence of outcomes and risk factors analyzed reflects the poor maintenance of deceased donors in Brazil.

In this study, age over 30 years, cold ischemia time greater than 24 hours and final creatinine above

Table 6 Risk variables associated with poor kidney function

Variable	Univariate		Multivariate	
	OR (CI 95%)	*p*	OR (CI 95%)	*p*
Age range				
≤ 10 years (ref.)	1.00	-	1.00	-
11-20 years	0.44 (0.1-1.3)	0.148	1.00	ns
21-30 years	0.56 (0.2-1.6)	0.291	1.00	ns
31-40 years	0.69 (0.2-2.0)	0.496	1.00	ns
41-50 years	1.07 (0.4-3.1)	0.897	1.84 (1.4-2.4)	< 0.001
51-60 years	1.80 (0.6-5.3)	0.286	2.77 (2.0-3.9)	< 0.001
≥ 61 years	2.72 (0.8-8.8)	0.095	3.84 (2.2-6.7)	< 0.001
Gender				
Males	0.82 (0.6-1.1)	0.235		
Females (ref.)	1.00	-		
Black ethnicity				
Blacks	0.67 (0.4-1.1)	0.117		
Not blacks (ref.)	1.00	-		
No information	0.84 (0.6-1.2)	0.371		
BD cause				
Stroke (ref.)	1.00	-		
Head injury	1.00 (0.7-1.5)	0.995		
Neoplasia	1.00 (0.3-3.6)	0.995		
Anoxic encephalopathy	2.07 (0.8-5.5)	0.147		
Others	0.78 (0.2-4.2)	0.770		
High blood pressure	2.14 (1.5-3.1)	< 0.001	1.82 (1.4-2.5)	< 0.001
Diabetes Mellitus	0.52 (0.2-1.2)	0.112		
Final Cr	2.51			
≤ 0.8 mg/dL (ref.)	1.00	-		
0.8-.5 mg/dL	1.08 (0.7-1.6)	0.697		
> 1.5 mg/dL	1.28 (0.8-2.0)	0.280		
Active infection	0.91 (0.7-1.3)	0.564		
Use of VAD	0.93 (0.5-1.6)	0.785		
Cardiac arrest	1.08 (0.7-1.7)	0.746		
Days in the ICU	1.02 (1.0-1.0)	0.270		
Sodium	0.99 (1.0-1.0)	0.132		
TGO	1.00 (1.0-1.0)	0.954		
TGP	1.02 (1.0-1.0)	0.811		
CPK	1.00 (1.0-1.0)	0.436		
≤ 250 (ref.)	1.00	-		
251-1000	0.91 (0.6-1.3)	0.620		
> 1000	0.89 (0.6-1.3)	0.548		
TIF				
≤ 12h (ref.)	1.00	-	1.00	-
13-18h	1.13 (0.4-3.0)	0.801	1.00	ns
19-24h	1.10 (0.4-2.9)	0.849	1.00	ns
25-30h	1.27 (0.5-3.3)	0.629	1.00	ns
31-36h	1.21 (0.4-3.3)	0.713	1.00	ns
> 37h	4.03 (1.1-14.3)	0.032	1.99 (1.0-3.9)	0.047

1.5 mg/dl were associated with increased risk of DGF; and only over the age of 40 years, cold ischemic time greater than 36 hours and hypertension were associated with increased risk of PKF. These variables have been classically described as risk factors for the incidence of DGF and PKF.[12,18,19]

Age, serum creatinine and hypertension in deceased donors are characteristics that make up the definition of expanded criteria donor.[12] When donor age is greater than 50 years and combined with other risk factors such as hypertension, serum creatinine higher than 1.5 mg/dl and vascular etiology for brain death, or when over 60 years alone, ranks the deceased donor as expanded.[12] To receive a kidney from a deceased donor with expanded criteria is associated with a 70% increase in the risk of graft loss,[12] and the higher incidence of DGF, compared to deceased donor transplants that do not meet this classification.[18,19]

Prolonged cold ischemia time has also been associated with a worse kidney graft function and a higher incidence of DGF.[11,13,20-23] Furthermore, the transplants with longer cold ischemia time are those using kidneys from expanded criteria donors[24] - organs already associated with a higher incidence of DGF and PKF, regardless of the waiting time until transplantation. Since they are less accepted by transplant centers, kidneys from expanded donors have longer allocation times.

Interestingly, the cause of brain death did not appear as a risk factor associated with any of the outcomes assessed in this study. The cause of brain death is also a variable that plays a role in the main DGF and graft function risk assessment scores including DDS, DCE and KDRI,[12,20,25,26] besides, even alone, it is associated with DGF.[27] In this study, the high incidence of stroke as a cause of death (40%) may have prevented the appearance of the effects of this risk factor in the outcomes assessed.

Although the characteristics that confer increased risk for DGF and PKF already have a clear association with outcomes in the literature, one particular factor of this study was the observation that donors under the age of 50, who are not classified as expanded criteria donors, also had a greater risk of conferring DGF and PKF. It is possible that in Brazil, where approaches concerning the management of deceased potential donors are not standardized nor prioritized in emergency care or intensive care units, only very young donors can withstand major failures in the process of hemodynamic and electrolytic management before organ extraction, thus reducing the risk of age. Perhaps the inadequate management of deceased donors interfere negatively in organ quality, yielding a greater risk of the recipient developing DGF and PKF, even when younger donors are included.

The discussion on better hemodynamic management of deceased donors and strategies for reducing the incidence of DGF and PKF is pressing and becomes more important in the current context, in which the profile of deceased donors is changing, and the contribution of expanded criteria donors, and even donors whose hearts stopped have been increasing in some countries.[1,2] As previously discussed, this group of donors is associated with increased risk of DGF and PKF and graft loss. Thus, strategies to improve the quality of donors and minimize further injury to these organs should be thoroughly pursued. Therefore, interventions aimed at improving the quality of donor management before the extraction of multiple organs have been studied.

Recently, Malinoski *et al.*[28] studied the impact of completing a set of goals in the management of the deceased donor vis-à-vis the incidence of DGF. To have mean arterial pressure readings between 60 and 100 mmHg, central venous pressure between 4 and 10 mmHg, ejection fraction greater than 50% in lowest possible dose of vasopressors, blood pH between 7.30 and 7.45, PaO_2/FiO_2 over 300, serum sodium between 135 and 155 mEq/l, blood glucose less than 150 and urine output between 0.5 and 3 ml/kg/h, together, at the time of family consent, were associated with a lower incidence of DGF (17.3% *vs.* 30.1%, p 0.007). It is noteworthy that only 14% of donors studied met all the criteria at this time.

As in the present study, the study from Malinoski *et al.*[28] showed that only age, serum creatinine and TIF were associated with higher risk of DGF. The authors did not analyze the risk factors for PKF, as in the present study.

Among the variables that were significantly associated with worse transplantation outcome, only two are modifiable and, therefore, liable to intervention. They are: donor creatinine level and cold ischemia time. Therefore, based on this study, we need to install measures to reduce cold ischemia time up to 24 hours and decrease levels of serum creatinine to normal limits. The reduction in donor serum

creatinine implies the need for a joint action between the Organs and Tissues Search Service and intensive care physicians to optimize hydration, minimizing the need for vasoactive drugs, and improve water balance, i.e. improving the management quality of the potential organ donor. To reduce the average time of cold ischemia, agility is needed in the process of locating and calling the recipient as well as minimizing clinical and laboratory evaluation times. The investigation regarding HLA compatibility, even before crossmatch results - strategy already adopted by some transplant centers, can help reduce this time.

This study has limitations because it is a retrospective study with a long evaluation period. Between 1998 and 2008, there were changes in the approach used to manage deceased donor. In addition, the follow-up time of recipients is of only six months. This alleviates the effects of other complications occurring after transplantation, such as acute rejection or infection; however, these events may have influenced the outcomes, particularly the PKF outcome.

Conclusion

The incidence of DGF and PKF was high in this population, possibly due to inadequate management of the deceased donor. Protocols for managing these donors should be adopted by the hospital critical care units, to improve the quality of organs offered for transplantation. A prospective study should be performed, evaluating the performance of these protocols and their impact on the function and survival of transplanted organs.

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References

1. Relatório anual, Ano XVI - no 4 - Janeiro/Dezembro 2010. Em: Registro Brasileiro de Transplantes [Acesso 15 de dezembro de 2012]. Disponível em: http://www.abto.org.br
2. Organ Procurement and Transplant Network. - 2011. In: OPTN/SRTR 2011 annual report: summary tables, transplant data 1998 - 2010 [Acesso 16 de agosto de 2012]. Disponível em: http://www.srtr.transplant.hrsa.gov/
3. Rabbat CG, Thorpe KE, Russell JD, Churchill DN. Comparison of mortality risk for dialysis patients and cadaveric first renal transplant recipients in Ontario, Canada. J Am Soc Nephrol 2000;11:917-22.
4. Ojo AO, Hanson JA, Meier-Kriesche H, Okechukwu CN, Wolfe RA, Leichtman AB, et al. Survival in recipients of marginal cadaveric donor kidneys compared with other recipients and wait-listed transplant candidates. J Am Soc Nephrol 2001;12:589-97.
5. Meier-Kriesche H, Port FK, Ojo AO, Leichtman AB, Rudich SM, Arndorfer JA, et al. Deleterious effect of waiting time on renal transplant outcome. Transplant Proc 2001;33:1204-6. PMID: 11267259 DOI: http://dx.doi.org/10.1016/S0041-1345(00)02387-3
6. Rosengard BR, Feng S, Alfrey EJ, Zaroff JG, Emond JC, Henry ML, et al. Report of the Crystal City meeting to maximize the use of organs recovered from the cadaver donor. Am J Transplant 2002;2:701-11. DOI: http://dx.doi.org/10.1034/j.1600-6143.2002.20804.x
7. McCullough KP, Keith DS, Meyer KH, Stock PG, Brayman KL, Leichtman AB. Kidney and pancreas transplantation in the United States, 1998-2007: access for patients with diabetes and end-stage renal disease. Am J Transplant 2009;9:894-906. DOI: http://dx.doi.org/10.1111/j.1600-6143.2009.02566.x
8. Jayaram D, Kommareddi M, Sung RS, Luan FL. Delayed graft function requiring more than one-time dialysis treatment is associated with inferior clinical outcomes. Clin Transplant 2012;26:E536-43.
9. Harada KM, Sampaio ELM, Freitas TVS, Felipe CR, Park SI, Machado PGP, et al. Fatores de risco associados à perda do enxerto e óbito após o transplante renal. J Bras Nefrol 2008;30:213-20.
10. Hariharan S, McBride MA, Cherikh WS, Tolleris CB, Bresnahan BA, Johnson CP. Post-transplant renal function in the first year predicts long-term kidney transplant survival. Kidney Int 2002;62:311-8. PMID: 12081593 DOI: http://dx.doi.org/10.1046/j.1523-1755.2002.00424.x
11. Doshi MD, Garg N, Reese PP, Parikh CR. Recipient risk factors associated with delayed graft function: a paired kidney analysis. Transplantation 2011;91:666-71. PMID: 21317839 DOI: http://dx.doi.org/10.1097/TP.0b013e318209f22b
12. Port FK, Bragg-Gresham JL, Metzger RA, Dykstra DM, Gillespie BW, Young EW, et al. Donor characteristics associated with reduced graft survival: an approach to expanding the pool of kidney donors. Transplantation 2002;74:1281-6. DOI: http://dx.doi.org/10.1097/00007890-200211150-00014
13. Nyberg SL, Matas AJ, Kremers WK, Thostenson JD, Larson TS, Prieto M, et al. Improved scoring system to assess adult donors for cadaver renal transplantation. Am J Transplant 2003;3:715-21. DOI: http://dx.doi.org/10.1034/j.1600-6143.2003.00111.x
14. Nyberg SL, Baskin-Bey ES, Kremers W, Prieto M, Henry ML, Stegall MD. Improving the prediction of donor kidney quality: deceased donor score and resistive indices. Transplantation 2005;80:925-9. PMID: 16249740 DOI: http://dx.doi.org/10.1097/01.TP.0000173798.04043.AF
15. Blasi-Ibanez A, Hirose R, Feiner J, Freise C, Stock PG, Roberts JP, et al. Predictors associated with terminal renal function in deceased organ donors in the intensive care unit. Anesthesiology 2009;110:333-41. PMID: 19194160
16. Klein R, Galante NZ, de Sandes-Freitas TV, de Franco MF, Tedesco-Silva H, Medina-Pestana JO. Transplantation with kidneys retrieved from deceased donors with acute renal failure. Transplantation 2013;95:611-6. DOI: http://dx.doi.org/10.1097/TP.0b013e318279153c
17. Cockcroft DW, Gault MH. Prediction of creatinine clearance from serum creatinine. Nephron 1976;16:31-41. PMID: 1244564 DOI: http://dx.doi.org/10.1159/000180580
18. Oppenheimer F, Aljama P, Asensio Peinado C, Bustamante Bustamante J, Crespo Albiach JF, Guirado Perich L. The impact of donor age on the results of renal transplantation. Nephrol Dial Transplant 2004;19:iii11-5.

19. Domagala P, Kwiatkowski A, Perkowska-Ptasinska A, Wszola M, Panufnik L, Paczek L, et al. Assessment of kidneys procured from expanded criteria donors before transplantation. Transplant Proc 2009;41:2966-9. PMID: 19857651 DOI: http://dx.doi.org/10.1016/j.transproceed.2009.08.004
20. Nyberg SL, Matas AJ, Rogers M, Harmsen WS, Velosa JA, Larson TS, et al. Donor scoring system for cadaveric renal transplantation. Am J Transplant 2001;1:162-70. DOI: http://dx.doi.org/10.1034/j.1600-6143.2001.10211.x
21. Kayler LK, Srinivas TR, Schold JD. Influence of CIT-induced DGF on kidney transplant outcomes. Am J Transplant 2011;11:2657-64. DOI: http://dx.doi.org/10.1111/j.1600-6143.2011.03817.x
22. Moore J, Tan K, Cockwell P, Krishnan H, McPake D, Ready A, et al. Predicting early renal allograft function using clinical variables. Nephrol Dial Transplant 2007;22:2669-77. DOI: http://dx.doi.org/10.1093/ndt/gfm249
23. van der Vliet JA, Warlé MC. The need to reduce cold ischemia time in kidney transplantation. Curr Opin Organ Transplant 2013;18:174-8. DOI: http://dx.doi.org/10.1097/MOT.0b013e32835e2a08
24. Chiurchiu C, Riva V, Bürgesser MV, de Arteaga J, Douthat W, de la Fuente J, et al. Expanded criteria donors, histological scoring, and prolonged cold ischemia: impact on renal graft survival. Transplant Proc 2011;43:3312-4. PMID: 22099786 DOI: http://dx.doi.org/10.1016/j.transproceed.2011.09.085
25. Rao PS, Schaubel DE, Guidinger MK, Andreoni KA, Wolfe RA, Merion RM, et al. A comprehensive risk quantification score for deceased donor kidneys: the kidney donor risk index. Transplantation 2009;88:231-6. PMID: 19623019 DOI: http://dx.doi.org/10.1097/TP.0b013e3181ac620b
26. Swanson SJ, Hypolite IO, Agodoa LY, Batty DS Jr, Hshieh PB, Cruess D, et al. Effect of donor factors on early graft survival in adult cadaveric renal transplantation. Am J Transplant 2002;2:68-75. DOI: http://dx.doi.org/10.1034/j.1600-6143.2002.020112.x
27. Shao MJ, Ye QF, Ming YZ, She XG, Liu H, Ye SJ, et al. Risk factors for delayed graft function in cardiac death donor renal transplants. Chin Med J (Engl) 2012;125:3782-5.
28. Malinoski DJ, Patel MS, Ahmed O, Daly MC, Mooney S, Graybill CO, et al.; United Network for Organ Sharing (UNOS) Region 5 Donor Management Goals (DMG) Workgroup. The impact of meeting donor management goals on the development of delayed graft function in kidney transplant recipients. Am J Transplant 2013;13:993-1000.