Comparative study between kidney transplantation with deceased donor expanded criteria and donor standard criteria in a single center in Brazil

Estudo comparativo entre transplantes renais com doador falecido critério expandido e critério padrão em um único centro no Brasil

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Abstract

Introduction: Kidney transplants with expanded criteria donor have been associated with improved patient survival compared to those who remain on dialysis. **Objective:** To compare renal function and survival of the kidney graft of deceased donor with expanded criteria and standard criteria over a year in a single transplant center. **Methods:** 255 kidney transplant recipients with deceased donor were included in the study between the years 2011 to 2013 and they were separated into two groups according to the type of donor (expanded criteria donor - ECD - and standard criteria donor - SCD). **Results:** 231 deceased donor transplants (90.6%) were performed with standard criteria donor (SCD) and 24 (9.4%) with expanded criteria donor (ECD). There was no difference in the prevalence of delayed graft function - DGF - (62.9% *vs*. 70.8%; p = 0.44). Expanded criteria donor group had lower glomerular filtration rate (GFR) at the end of the 1st year (56.8 ± 26.9 *vs*. 76.9 ± 23.7; p = 0.001). Patient survival was significantly lower in the ECD group, but the graft survival was not different after death-censored analysis. **Conclusion:** The ECD group was associated with significantly lower levels of GFR during the first year of transplant and a lower patient survival at the 1st year when compared to the SCD.

Keywords: delayed graft function; graft rate; kidney transplantation; survival rate.

Resumo

Introdução: A aceitação dos rins com critério expandido de doação tem sido associada com melhor sobrevida do paciente em comparação àqueles que permanecem em terapia dialítica. **Objetivo:** Comparar a função renal e a sobrevida do enxerto renal de doador falecido critério expandido com os de doador falecido critério padrão ao longo de um ano em um único centro de transplantes. **Métodos:** Foram incluídos 255 receptores de transplante renal com doador falecido, realizados entre os anos de 2011 a 2013, sendo divididos em dois grupos segundo o tipo de doador (critério expandido - DCE - ou padrão -DCP). **Resultados:** Foram avaliados 231 receptores com doador critério ideal (90,6%) e 24 com doador critério expandido (9,4%). Não houve diferença na prevalência de função retardada do enxerto - DGF - (62,9% no DCP *vs*. 70,8% no DCE; p = 0,44) nos dois grupos. Os transplantes com DCE apresentaram uma taxa de filtração glomerular (TFG) significativamente inferior aos 12 meses (56,8 ± 26,9 *vs*. 76,9 ± 23,7; p = 0,001). A sobrevida dos pacientes em 1 ano foi significativamente inferior no grupo de DCE, mas não houve diferença na sobrevida dos enxertos após exclusão de perdas por óbito com rim funcionante. **Conclusão:** O grupo com DCE associou-se com níveis significativamente mais baixos de TFG ao longo do primeiro ano de transplante, bem como uma menor sobrevida dos pacientes em 1 ano, quando comparado ao grupo com doador padrão.

Palavras-chave: função retardada do enxerto; sobrevivência de enxerto; taxa de sobrevida; transplante de rim.

Introduction

Kidney transplantation has been described as the most effective treatment for chronic kidney disease (CKD), with better long-term quality-of-life and patient survival.[1] The increases seen in the demand for kidney transplantation procedures and the consequent ever longer recipient waiting lists have led to a wider acceptance of organs from deceased borderline (expanded criteria) donors, which would have been otherwise discarded.[2-6]

The following factors contribute to the imbalance between the supply and demand for organs: families of potential deceased donors refusing to allow the donation; underreporting of patients diagnosed with brain death (BD) to donation centers (despite the legal obligation to do so in Brazil); lack of ongoing education to health care workers on the donation-transplant process; and the high rate of clinical contraindications to donation.[7]

Expanded criteria donor (ECD) grafts increased the number of transplants performed and the survival of organ recipients by three to nine years when compared to patients kept on dialysis.[8] In terms of function, expanded criteria donors are individuals aged 60 years or older or subjects aged 50-59 years with at least two of three additional risk factors: stroke, history of hypertension, or serum creatinine above 1.5 mg/dl before transplantation.[9]

Although these organs are eligible for transplantation, advanced age and other clinical characteristics may result in decreased post-transplant renal function. Additionally, the survival of recipients of ECD kidneys has been described as inferior when compared to recipients of standard criteria donor kidneys.[10]

The challenge lies in decreasing the prognostic difference observed between kidneys coming from expanded and standard criteria donors. This requires the adoption of appropriate strategies before, during, and after the transplantation procedure, which include the reduction of cold ischemia times; careful recipient selection; adequate immunosuppression therapy; improved graft selection based on histological criteria, vascular status and degree of glomerulosclerosis; and, in some cases, placing both donor kidneys in the same recipient.[8]

Although continuous perfusion reduces the incidence of delayed graft function (DGF) and improves the utilization of ECD kidneys, it does not modify the long-term survival of the graft when compared to conventional infusion. Kidneys from the same donor preserved by conventional methods or by continuous perfusion have survival rates of 88.4% and 89.8% in the first year and 62% and 64.4% six years after transplantation, respectively.[11]

This study aimed to compare the prevalence of DGF, graft and patient survival, and renal function one year after transplantation in patients given ECD kidneys versus patients given standard criteria donor (SCD) kidneys. There is limited data from Brazil on this topic.[12]

Methods

This retrospective cohort study was carried out in a single transplant center in Brazil. The study met the scientific and ethical requirements of Resolution 466/12.[13] The study design was reviewed by the Research Ethics Committee of the Walter Cantidio University Hospital at the Federal University of Ceará via *Plataforma Brasil*, and was granted license no. 839863.

The study population consisted of recipients of ECD kidneys with transplantation procedures carried out from January 2011 to December 2013 in the hospital mentioned above. In the period covered by the study, 323 kidney transplants were carried out, including procedures with living and deceased donors, and double-organ transplants (liver/kidney and pancreas/kidney).

The study population included 255 transplant recipients given ECD and SCD kidneys followed for at least 12 months. Recipients of double-organ transplant (n = 14) and living donor (n = 13) recipients and patients lost during the first 12 months of follow-up (n = 41) were excluded from the study. Data were collected from patient medical charts and files.

The protocol in effect at the hospital includes the prescription of induction therapy with thymoglobulin to high immune risk recipients and high-risk donors (function-based expanded criteria donor; cold ischemia time > 24 hours; donor age > 50 years; donors with acute tubular necrosis; donors on high-dose inotropic agents; delayed graft function in borderline or involved donors).

Induction therapy with thymoglobulin is administered with four doses (1.5 mg/kg) of the drug every other day. Induction with basiliximab is prescribed to live donor transplant patients and

subjects assigned low immune risk levels; the drug is given in two doses of 20 mg each, the first on day zero and the second on day 4. Steroid-free maintenance therapy is recommended for children and patients with diabetes, coronary artery disease, dyslipidemia, obesity and hepatitis B or C.

Patients requiring dialysis within the first week of transplantation were diagnosed with delayed graft function. Acute graft rejection cases were confirmed with renal biopsies. Creatinine levels and the glomerular filtration rate (GFR) estimated by the CKD-EPI formula were used to assess renal function six and 12 months after surgery.[14] The *Kidney Donor Profile Index (KDPI) and the Kidney Donor Risk Index* (KDRI) were calculated for expanded and standard criteria kidneys from deceased donors, and the impact on graft survival was assessed for patients in both groups.[15]

Statistical analysis

Mean values ± standard deviations were used to describe continuous variables; percentages or relative frequencies were used to describe categorical variables. Student's *t*-test, the Mann-Whitney U test, or Fisher's exact test were used to compare between continuous and categorical variables of recipients of ECD and SCD grafts. Descriptive values below 5% ($p < 0.05$) were considered statistically significant. The survival of grafts and patients 12 months after transplantation was assessed using the Kaplan Meyer curves. Statistical analysis was performed with SPSS 20.0 for Windows (SPSS Inc., Chicago, IL, USA).

Results

The study enrolled 255 renal transplant recipients; 231 (90.6%) were given deceased donor kidneys from standard criteria donors and 24 (9.4%) received deceased donor kidneys from expanded criteria donors; all were first-time recipients. Nine donors in the group given ECD kidneys were 60 years of age or older (37.5%) and 15 donors were aged 50-59 years (62.5%). More than a third (33.7%) of the patients had kidney disease for unknown causes; the other etiologies were hypertensive nephrosclerosis (21.5%), glomerular disease (15.4%), diabetic nephropathy (10.8%), and other conditions (18.6%). Table 1 describes the demographic characteristics of the study population.

There was no significant difference in the distribution of genders in the groups given SCD or ECD grafts, with males accounting for 53.7% and 58.2% in each of the groups, respectively ($p = 0.675$). However, 75% of the standard criteria donors and 50% of the expanded criteria donors were males ($p = 0.015$). Recipients in the ECD group were significantly older than the recipients in the SCD group. The main cause of death in the ECD group was hemorrhagic stroke (75% *vs*. 13.9% in the SCD group), while head trauma was the main cause of death in the SCD group (76.2% *vs*. 12.5% in the ECD group).

Only 37.5% of the individuals in the ECD group were older than 60 years. Donors aged 50-59 years had a mean terminal serum creatinine level of 1.38 ± 0.69 mg/dl; hypertension was observed ub 53.3% of them; hemorrhagic stroke was the cause of brain death in 86.6% of the cases. On the other hand, the mean terminal serum creatinine level of individuals aged 60 years or older in the ECD group was 1.34 ± 0.49 mg/dl; systemic hypertension was observed in 22.2% of them; and hemorrhagic stroke occurred in 55.5% of the cases.

Immediate post-transplant progress

The mean cold ischemia time was 21.17 ± 3.88 hours in the ECD group and 21.82 ± 4.97 hours in the SCD group ($p = 0.794$). Delayed graft function was observed in 70.8% of the subjects in the ECD group versus in 62.9% of the individuals in the SCD group ($p = 0.441$). There was no significant difference in the number of hemodialysis sessions held in the immediate postoperative care of the groups (5.04 *vs*. 3.66; $p = 0.58$) (Table 2).

Graft biopsies before renal transplantation were carried out in 37.5% of the individuals in the ECD group versus 10.8% of the subjects in the SCD group ($p = 0.001$). The perfusion machine was used in 16.7% of the recipients of ECD grafts versus 13.0% of the recipients of SCD kidneys ($p = 0.539$).

Thymoglobulin was administered to 73.8% of the recipients on induction immunosuppression, followed by basiliximab (23.4%), and basiliximab followed by thymoglobulin (2.8%). Tacrolimus, mycophenolate sodium, and prednisone ranked first among maintenance immunosuppression therapies, followed by tacrolimus and mycophenolate sodium (30.2%) and other therapies (3.7%). Induction with thymoglobulin was prescribed to 87% of the recipients in the ECD group versus 74.2% in the SCD group ($p = 0,177$).

Table 1 Demographic characteristics of th study population (n = 255)

Variables	Groups		*p*
	Case (Mean ± SD)	Control (Mean ± SD)	
Recipient age (years)	53.04 ± 11.30	43.46 ± 13.34	0.001*
Recipient gender	Male: 58.2%	Male: 53.7%	0.675
Primary renal disease	SH: 25.0% DM: 8.3% Glomerulopathy: 8.3% Undefined: 29.2% Other: 29.2%	SH: 16.5% DM: 5.6% Glomerulopathy: 22.1% Undefined: 33.8% Other: 22.1%	0.436
Donor age (years)	58.42 ± 5.29	29.48 ± 11.83	0.000*
Donor gender	Male: 50%	Male: 74.9%	0.015
Donor cause of death	Hemorrhagic stroke: 75% Ischemic stroke: 8.2% Head trauma: 12.5% Other: 4.2%	Hemorrhagic stroke: 13.9% Ischemic stroke: 2.6% Head trauma: 76.2% Other: 7.4%	0.000*
Initial donor creatinine level	0.97 ± 0.33 mg/dl	1.27 ± 0.64 mg/dl	0.061
Terminal donor creatinine level	1.37 ± 0.61 mg/dl	1.48 ± 0.85 mg/dl	0.749
Donor weight (kg)	68.96 ± 9.74	68.29 ± 13.85	0.882
Donor height (m)	1.64 ± 0.07	1.65 ± 0.11	0.129
PRA	< 20%: 73.9% 20-5-%: 17.4% > 50%: 8.7%	< 20%: 67.4% 20-5-%: 12.6% > 50%: 20.0%	0.386
Induction therapy	Thymoglobulin: 87% Basiliximab: 13 %	Thymoglobulin: 74.2% Basiliximab: 25.8%	0.177
Steroid-free maintenance therapy	41.6%	30.8%	0.28
Length of hospitalization (days)	30.24 ± 26.79	24.02 ± 17.09	0.382

*Statistically significant differences. SH: systemic hypertension; DM: *diabetes mellitus*; PRA: panel-reactive antibody.

Table 2 Immediate postoperative progress during hospitalization, according to donor type (expnded criteria donors *vs.* standard criteria donors)

	ECD n = 24 Mean ± SD	SCD n = 231 Mean ± SD	*p*
Time of cold ischemia (hours)	21.17 ± 3.88	21.82 ± 4.97	0.794
Duration of DGF (days)	11.67 ± 18.17	8.61 ± 13.53	0.565
Hemodialysis session (N)	5.04 ± 7.31	3.66 ± 5.11	0.580
Length of hospitalization (days)	30.24 ± 26.79	24.02 ± 17.09	0.382
Creatinine level at discharge (mg/dl)	2.24 ± 1.53	1.73 ± 0.75	0.089

DGF: Delayed graft function; ECD: Expanded criteria donors; SCD: Standard criteria donors.

The study population's mean hospitalization time was 24.6 ± 18.2 days (5-105 days); the individuals in the ECD group stayed in hospital for a mean of 30.2 days versus 24.1 days for the SCD group (p = 0.382). The mean serum creatinine level at discharge was 2.24 mg/dl in the ECD group and 1.73 mg/dl in the SCD group (p = 0.089). Acute graft rejection was seen in 9.9% of the recipients; when separated by group, 16.7% of the recipients in the ECD group and 9.2% of the recipients in the SCD group (p = 0.249) had episodes of acute graft rejection.

Patients on steroid-based or steroid-free immunosuppression therapy had no significant differences in serum creatinine levels six and 12

months after transplantation, in the GFR 12 months after the procedure, or on delayed graft function (64.3% *vs.* 62,5%; $p = 0.779$).

Kidney transplant patient 12-month follow-up

After 12 months of follow-up, the recipients of SCD grafts had significantly lower serum creatinine levels than patients given ECD kidneys (1.15 ± 0.45 mg/dl vs. 1.63 ± 1.00 g/dl; $p = 0.047$). The GFR estimated by the CKD-EPI formula was significantly lower six and 12 months into follow-up in the ECD group (Table 3).

More than a fifth (20.8%) of the recipients in the ECD group lost their grafts within a year of transplantation *vs.* 8.2% in the SCD group ($p = 0.044$). Graft losses in the ECD group were caused by infection in one case, death associated with infection in three cases, and a nonfunctioning kidney in one case; meanwhile, in the SCD group the causes were infection in three cases, venous thrombosis in three cases, arterial thrombosis in two cases, renal cortical necrosis in two cases, nonfunctioning kidneys in two cases, and death in seven cases.

One eighth (12.5%) of the patients in the ECD group and 3.0% of the individuals in the SCD group died of infection within a year of transplantation ($p = 0.023$). The causes of death were infection (n = 3) in the ECD group, and infection (n = 6) and bleeding (n = 1) in the SCD group.

The graft and patient survival curves are presented in Figures 1 and 2. A significant difference was seen in patient survival one year after transplantation (ECD: 87.5% *vs.* SCD: 97%; $p = 0.025$) and a trend toward statistical significance in graft survival one year after transplantation (SCD: 91.8% *vs.* ECD: 79.2%; $p = 0.057$), according to donor type. However, when the patients who died despite having a functioning kidney were excluded from the analysis, no significant difference was seen in graft survival (ECD: 90.5% *vs.* SCD: 94.6%; $p = 0.452$).

Additional analysis not considered in the main scope of this study looked into the KDPI of the deceased donors, and found that 6.7% of them had a KDPI ≥ 85%. In the ECD group, 62.5% of the patients had a KDPI ≥ 85% *vs.* 0.86% of the donors in the SCD group ($p < 0.001$). More than two thirds (70.5%) of the recipients of grafts taken from donors with a KDPI ≥ 85% had DGF *vs.* 63.0% of the group given kidneys from donors with a KDPI < 85% ($p = 0.529$).

A KDPI ≥ 85% was not associated with worse graft (88.2% *vs.* 90.8%; $p = 0.769$) or patient survival (93.8% *vs.* 96.1%; $p = 0.689$) one year after transplantation. However, it was associated with worse renal function six months after transplantation based on the GRF estimated by the CKD-EPI formula (GFR at six months: 57.5 ± 9.1 ml/min *vs.* 70.7 ± 24.4 ml/min; $p = 0.005$; and GFR at 12 months: 61.3 ± 29.2 ml/min *vs.* 73.8 ± 25.6 ml/min; $p = 0.071$).

No differences were seen in acute graft rejection rates (11.8% *vs.* 10.3%; $p = 0.691$), cold ischemia time (23.5 ± 3.6 hours *vs.* 23.3 ± 5.1 hours; $p = 0.587$), length of DGF (median: 11 *vs.* 9 days; $p = 0.783$), number of dialysis sessions (median: 5 *vs.* 4 days; $p = 0.522$), hospitalization time (29.6 ± 19.9 days *vs.* 30.0 ± 17.3 days; $p = 0.182$) when the group with a KDPI ≥ 85% was compared to the group with a KDPI < 85%.

Discussion

In 2013, transplants with three types of deceased donors were carried out in the United States: standard criteria donors, expanded criteria donors, and donors after circulatory death; 84.2% of the donors ere

Table 3 Postoperative renal function in expanded and standard criteria donor groups

	ECD n = 24 Mean ± SD	SCD n = 231 Mean ± SD	*p*
Creatinine (1 m)	2.41 ± 1.54	1.82 ± 1.34	0.005*
Creatinine (6 m)	1.58 ± 0.71	1.20 ± 0.50	0.012*
GFR (6 m)	49.99 ± 16.49	73.11 ± 23.28	< 0.001*
Creatinine (12 m)	1.63 ± 1.00	1.15 ± 0.45	0.047*
GFR (12 m)	56.78 ± 26.99	76.87 ± 23.67	0.001*

*$p < 0.05$; ECD: expanded criteria donor; SCD: standard criteria donor; GFR: glomerular filtration rate estimated by the CKD-EPI formula.

Figure 1. Causes of graft loss within the first year of transplantation in the expanded and standard criteria donor groups.

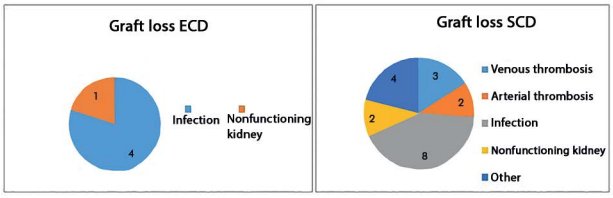
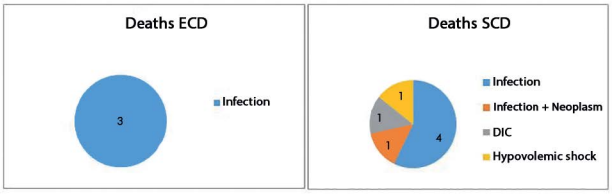


Figure 2. Causes of death within the first year of transplantation in the expanded and standard criteria donor groups.



diagnosed with brain death and 15.8% with circulatory death. Seventeen percent of the donors were expanded criteria donors. Nearly half (48.1%) of the patients in the transplant waiting list agreed to receive expended donor criteria kidneys.[16] At the time, the Brazilian Transplant Register did not contain information on the percentage of procedures carried out with expended criteria donor kidneys from deceased donors.[6]

In 2012, although Brazil ranked second in absolute number of kidney transplants in a list of 30 countries, falling behind the United States with 15,549 transplants, the 5,385 procedures carried out in the country were not enough to meet the need for 11,445 kidney transplants.[6] Between 2011 and 2013, 24,134 reports of potential donors were made in Brazil, but only 28.9% of these were eventually converted into actual organ donors.

Family refusal (40%) accounted for a significant portion of the reports not converted into organ donations, followed by cardiac arrest (21%), medical contraindication (16%), and other reasons (22%).[6] The use of expended donor criteria kidneys is an attempt to reduce the growing mismatch between the numbers of donors and recipients, and shorten the time for which patients stay in waiting lists.[11,16,17]

The low incidence of ECD transplants in this study (9.4%) may be explained by the increased supply of deceased donors in the State of Ceará, with a less significant trend of using expended criteria donors. During the study, transplants using deceased donor kidneys accounted for 95.9% of the procedures carried out in the renal care center where the study was carried out.

In a recent Brazilian study, 16.5% of 1,412 renal patients had ECD kidney transplants, 14.4% in the group without DGF and 18.5% in the group with DGF.[18] However, in another Brazilian cohort of 346 kidney transplant recipients, 30.6% were given expended criteria donor grafts.[19]

Head trauma was the cause of brain death in 70.2% of the donors included in the study, versus 38% according to Brazilian data and 56% as per data from the State of Ceará.[6] The analysis of donor demographic characteristics revealed a difference in gender distribution between SCD and ECD donors, with a predominance of male individuals in the SCD group. It is likely that this younger and more active group of individuals is at a higher risk of suffering accidents, and thus of having head trauma.

However, the recipients of expanded criteria donor grafts were older than the group given standard criteria donor kidneys, a finding consistent with the trend of offering renal grafts from expanded criteria donors to older recipients, and the wider acceptance and consent given for expanded criteria donor grafts by older recipients.

A high prevalence of delayed graft function, although consistent with previously published Brazilian data, was observed in this study (63.5%). A study carried out in two renal transplant reference centers in Ceará looking at induction therapy with thymoglobulin and basiliximab found prevalence rates of DGF of 56.5% and 63.0%, respectively.[20] de Sandes-Freitas *et al.*[18] and Helfer *et al.*[19] reported rates of DGF in their cohort of 54.2% and 70.8%, respectively.

The prevalence of DGF in Brazil has been significantly higher (60.6%) than in the USA (28%) and Europe (24.7%),[21-23] probably due to inadequate donor maintenance and prolonged ischemia times. In our study, the prevalence of DGF and the mean number of dialysis sessions after transplantation were similar in both donor groups (SCD and ECD), thus suggesting that other factors common to the two donor groups have greater impact on immediate postoperative graft function than the age of the donor or the presence of comorbidities, such as inadequate donor maintenance before transplantation.

The mean time of cold ischemia was not different between the SCD and ECD groups. The mean time of cold ischemia reported in Brazilian studies is 23.2 hours, a significantly longer time when compared to

the United States (14.2 h) and Europe (18.0 h).[21,24,25] On the other hand, terminal serum creatinine levels of the ECD group were not significantly higher than the levels seen in the SCD group, which revealed a tendency of the team of using expanded criteria donor grafts with better renal function, since not all kidneys were examined with frozen-section analysis.

Pre-transplant kidney biopsies in the ECD group play a fundamental role in the decisions around the use of the graft, implantation of one or two kidneys in the recipient, and in the comparisons against post-transplant biopsies.[12] However, in this study only 37.5% of the individuals in the ECD group underwent frozen-section analysis, a factor that might contribute to worse outcomes in this group of donors.

Lehtonen *et al*.[26] described a relationship between chronic disease scores in pre-transplant kidney biopsies, graft function, and the onset of chronic rejection within a year of transplantation. Snoeijs *et al*.[27] enrolled 199 donors aged 60+ years and described preexisting chronic injury as more important than other clinical parameters for the outcome of transplantation.

In the present study, biopsies were not performed in 62.5% of the accepted transplanted ECD kidneys. In order to improve expanded donor selection and post-transplantation outcomes, this is no longer done at the renal care center. According to the protocol in effect today, all ECD kidneys are biopsied and categorized based on the Maryland Aggregate Pathology Index (MAPI), a scoring system that uses glomerulosclerosis, donor vascular disease, periglomerular fibrosis, and renal cortical scarring.[28] ECD grafts are currently placed in a perfusion machine.

No difference was seen in immunosuppression in regards to the use of thymoglobulin in induction or in steroid-based or steroid-free maintenance therapies between donor types. The immunosuppression scheme used in induction and post-transplant graft maintenance therapy was similar to the protocol adopted in other Brazilian and international transplant centers.[16,29,30]

According to American registers, thymoglobulin was used in the induction therapy of more than 60% of the transplant patients in this time period; maintenance immunosuppression included a combination of tacrolimus and mycophenolate, while steroids were used in less than 40% of the patients.[16]

Induction with thymoglobulin may delay the introduction of calcineurin inhibitors, which possibly contributes to faster renal graft function recovery.[31] However, recent studies suggested that the administration of calcineurin inhibitors in the early graft recovery period does not perpetuate or impede the recovery from DGF.[32]

In short, this study did not find significant differences between times of cold ischemia, donor terminal serum creatinine levels, prevalence of DGF, presence of acute rejection, and type of immunosuppression according to donor type (SCD or ECD) in the variables possibly associated with worse ECD graft transplant outcome.

Among the variables significantly associated with worse transplant outcomes, Baptista *et al*.[21] categorized only two as modifiable variables or, in other words, variables upon which one could intervene: time of cold ischemia and donor terminal creatinine levels. The required measures identified were decrease the time of cold ischemia and bring down donor terminal serum creatinine levels to normal values.

Decreasing donor creatinine levels requires a combination of efforts involving the Organ and Tissue Procurement Organizations and intensive care physicians, in order to optimize hydration, minimize the need for vasoactive drugs, achieve proper fluid balance, and ultimately improve the quality of maintenance therapy provided to potential organ donors. Cold ischemia times can be reduced through quicker recipient location and invitation to come to a renal care center and faster recipient clinical and workup examination.

The lack of standardization of procedures and the low priority given to deceased potential donors in emergency and intensive care units in Brazil might produce an artificial effect upon the risks related to donor age, since only very young donors are able to withstand the impact of flawed hemodynamic and hydroelectrolytic maintenance processes put in place until the removal of their organs. It is also possible that inadequate management of deceased donors interferes with organ quality.[21]

The two donor groups were statistically different in terms of their serum creatinine levels and GFR as a marker of renal function within the first year of transplantation. Serum creatinine levels above 1.5 mg/dL six months after transplantation have been described in the literature as an important risk factor for graft survival.[21,33]

This study showed significantly greater graft loss rates and death within 12 months o transplantation in the expanded criteria donor group, but differences in graft survival were not significant after the exclusion of graft losses caused by death with a functioning kidney. These outcomes are consistent with recent studies.[34-36]

Other authors have shown that ECD kidneys had worse long-term graft function and survival outcomes.[3,37] However, they provide acceptable function and significantly better patient survival when compared to dialysis.[38,39] Once the present study did not follow the enrolled patients after the first year of transplantation, follow-up studies might find whether the differences in serum creatinine and GFR seen six and 12 months after the procedure in individuals given ECD kidneys will result in shorter survival three and five years after transplantation.

Although the utilization of kidneys from deceased donors with serum creatinine levels ≥ 1.5 mg/dL has been associated with a 10% risk of graft loss regardless of donor age, multivariate analysis of the data from the *Scientific Registry of Transplant Recipients (SRTR*) in the United States indicated that, including history of hypertension or brain death caused by stroke, serum creatinine levels ≥ 2mg/dL do not increase the risk of graft loss.[37] American data show that the survival of ECD grafts is 87.4% within the first year of transplantation and 66.4% five years after the procedure, while patients given SCD grafts had respective survival rates of 93.7% and 79.4%.[40]

The KDPI is a numerical variable that combines ten donor characteristics – including clinical and demographic parameters – devised to compare the quality of kidney donors. The inclusion of donor traits relevant for graft prognosis brings more specificity to the current categorization of donors into ECD or non-ECD, since it incorporates ten donor-related factors (instead of four used to define ECD), and provides for more accurate indication of donor quality.

Additional advantages of using the KDPI over the current ECD categorization include the following: it is a continuous scale, instead of a binary indicator (yes/no); it makes it clear that not all expanded criteria donors are alike, as some provide for relatively good grafts; and it shows that some SCD may provide for worse grafts than some ECD.

O KDPI was initially derived from the *kidney donor risk index* (KDRI) for deceased donors. The KDRI estimates the relative risk of failure of a graft from a deceased donor after transplantation versus a donor in the 50th percentile; lower KDRI values are assigned to better quality donors and greater values to lower quality donors. Physicians and patients may use the KDRI to decide whether to accept a donor graft.[15]

No associations were seen in this study with graft and patient survival, but impacts were observed in renal function 12 months after transplantation. A future study with a closer analysis of the quartiles or quintiles of the KDPI distribution might reveal such an association. The new policy for organ allocation adopted in the United States, now based on the KDPI instead of the principles of expanded criteria organ donation, aims to increase the utilization or borderline kidneys and reduce the number of discarded organs. However, caution and a better understanding of this index are required in order to avoid the discarding of organs that would have been deemed acceptable by other criteria.[41]

The retrospective nature of this study, its short follow-up period (one year), and the fact that kidney biopsies were not performed in every case – a standard procedure for expanded criteria donors – are the limitations of this study.

The question still persists as to whether using expanded criteria donor kidneys – an option deemed safe in the short term – to increase the supply of organs and reduce transplant waiting times is a valid option. In a scenario fraught with precarious donor maintenance, the growth in the number of donors has not been large enough to serve everyone in need of a kidney. And a significant number of families still refuse to allow the donation of organs from their deceased loved ones. It seems clear that other strategies may be implemented concurrently, such as providing the population with more clarification on the process of organ donation and investing more heavily in improving the maintenance therapy provided to potential donors.

Conclusion

No significant differences were found in terms of length of hospitalization, delayed graft function, serum creatinine levels a discharge, and acute rejection between recipients of ECD and SCD grafts. In the ECD group, statistically higher serum creatinine levels and GFR were observed in the first year after transplantation; graft losses and deaths had a higher relative frequency in the ECD than in the SCD group.

The KDPI used in a Brazilian cohort showed an association with worse renal function six months after transplantation, but no correlations were found with increased prevalence of DGF or worse renal function 12 months after transplantation, a finding not previously described in the local literature. Additional studies with greater patient populations and longer follow-up periods are required to assess the medium and long-term survival of ECD grafts and the applicability in Brazil of a donor risk index developed for the American population.

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