Expanding the limits with deceased donors: successful renal transplantations from a donor with serum creatinine of 13.1 mg/dL

Authors

Rodrigo Klein[1]
Nelson Zocoler Galante[1]
Marcello Franco[2]
Maurício Costa Manso de Almeida[3]
Mário Nogueira Júnior[3]
Hélio Tedesco Silva-Júnior[1]
José O. Medina Pestana[1]

[1]Department of Medicine, Discipline of Nephrology, Universidade Federal de São Paulo – UNIFESP
[2]Department of Pathology, UNIFESP
[3]Department of Surgery, Discipline of Urology, UNIFESP

Abstract

Non-expanded deceased donors with acute kidney failure can be a safe option to increase the number of kidneys for transplantation. Histological evaluation is fundamental to establish the functional prognosis of those grafts. Two kidney transplantations were performed from a young deceased donor with severe acute kidney failure and no structural change in the renal parenchyma. Both patients had postoperative delayed graft function, but one of them, who had good initial urinary volume, required no dialysis. Adequate renal function was present at day 30 after transplantation. Severe acute kidney failure in deceased donors is not an independent risk factor for short-term outcome of renal graft and should not be considered an absolute contraindication for transplantation.

Keywords: tissue donors, acute kidney failure, kidney transplantation, case reports.

[J Bras Nefrol 2010;32(1):131-135]

Submitted on: 08/04/2009
Accepted on: 10/28/2009

Corresponding author:
José O. Medina Pestana
Hospital do Rim e Hipertensão
Rua Borges Lagoa 960, 11º andar, Vila Clementino
São Paulo - SP, Brasil
CEP: 04038-002
Phone: (11) 5087-8056
Fax: (11) 5087-8008
E-mail: medina@hrim.com.br

We declare no conflict of interest.

Introduction

The increasing demand for renal transplants and the challenge represented by the insufficient number of donors have stimulated the development of new strategies to increase kidney offer for transplantation.[1] Following the tendency of using more frequently kidneys from living donors not related to recipients, kidneys from deceased donors meeting fewer restricted criteria of donation have been increasingly used in clinical practice.[2] In the United States, the number of patients on the waiting list increases 20% every year, while the number of transplantations in the past five years had a mean annual increase of only 3.1%.[3] Currently the estimated need for renal transplants in Brazil is 10,000 per year. In 2008, 3,780 renal transplantations were performed, slightly over one third of the need. Of those, 2,033 were from deceased donors.[4]

The use of kidneys from deceased donors with acute kidney failure (AKF) is controversial. However, the 2006 case series from Kumar *et al.*, involving 55 recipients, has demonstrated that the graft survival and function obtained with that type of donors may be comparable to those of kidneys from donors without AKF.[5] This study shows the results of two successful renal transplantations performed with grafts obtained from a deceased donor with severe AKF, and emphasizes the importance of the histological assessment during the selection of potential donors.

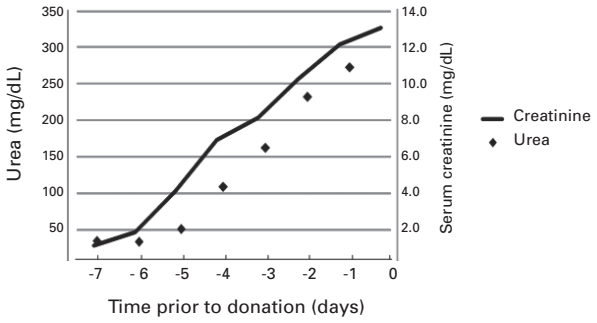
Case Report

Donor

The patient was a 37-year-old white man, who was admitted to the hospital after sudden malaise followed by loss of

consciousness. He was dehydrated. His peripheral blood pressure measured in both upper limbs was lower than 120/80 mm Hg. He had no spontaneous eye opening, no verbal response, and no motor response to verbal and pain stimuli (Glasgow Coma Scale equal to 3). No previous pathologies were reported. The cranial tomography evidenced subarachnoid hemorrhage on the cortical territory adjacent to the sylvian fissures, on the inter-hemispheric region, and also in the cerebral ventricles. Cerebral death was diagnosed seven days after hospital admission. During follow-up at the intensive care unit, he received empirical antibiotic therapy with ceftriaxone and clindamycin for lung infection. Daily clinical and laboratory monitoring showed progressive loss of renal function (Figure 1) with no reduction in the urinary volume. Neither significant hemodynamic instability, nor need for vasoactive drugs, nor cardiac arrest was observed until the removal of the donated organs (heart, liver, and kidneys). The renal biopsy showed severe acute tubular necrosis and no abnormalities in the glomeruli, vessels, and interstitium (Figure 2). Complementary laboratory assessment performed on the occasion of organ removal indicated rhabdomyolysis. Nephrotoxicity induced by myoglobinuria was considered to be a possible etiologic factor related to acute kidney failure (Table 1).

Figure 1. Measurements of serum urea and creatinine during the follow-up of the deceased donor.



Recipients

One of the kidneys was transplanted to a 50-year-old Caucasian male who had chronic kidney failure attributed to focal segmental glomerulosclerosis, and had been on hemodialysis for 2 years. The preoperative assessment showed type B blood, non reagent serologies for HIV, CMV, and hepatites B and C, negative crossmatch, zero reactivity against a panel of cells and HLA A 24,68, B 51,35 and DR 1,15. Cold ischemia time was 26 hours and 23 minutes. Immunosuppression consisted in induction with basiliximab (20 mg EV on the first and forth days after

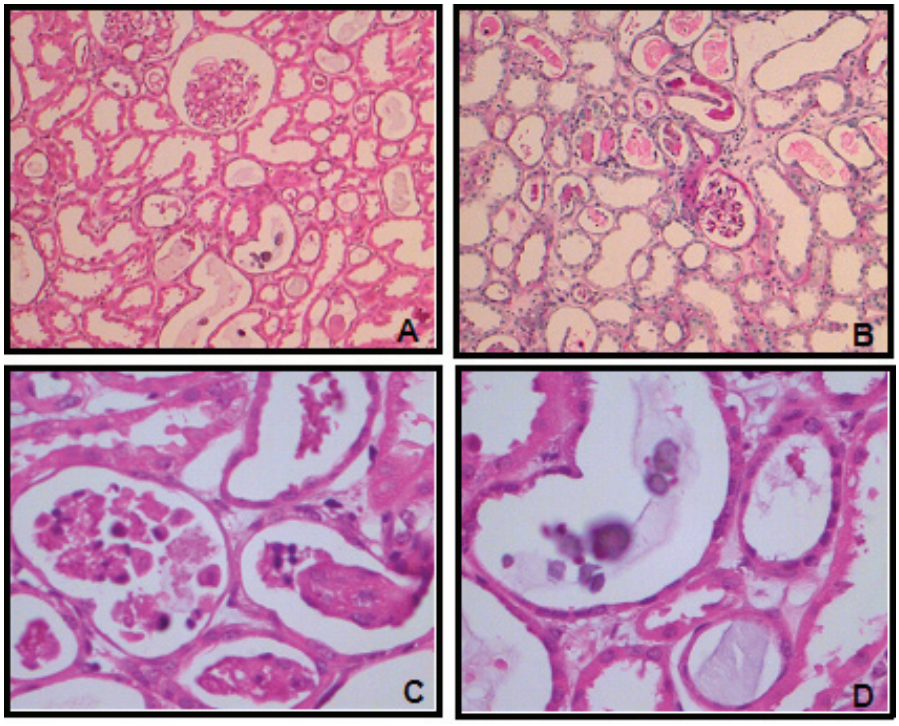


Figure 2. Renal biopsy from the donor. Severe acute tubular necrosis. A and B: dilated tubules, with flattened epithelial lining; note the granular casts and lack of inflammatory alterations or interstitial fibrosis (HE and PAS, respectively; 40x). C and D: Higher magnification of the tubules with cell necrosis, lack of epithelial lining, and presence of granular casts (HE; 200x and 400x, respectively).

Table 1 Complementary laboratory assessment of the donor

	Day 0 (donation)
Hematology	
Hb (g/dL)	12.9
Ht (%)	39.2
Leukocytes (n/mm^3)	18,000
Platelets (n/mm^3)	38,000
Blood type	B
Serum biochemistry	
Urea (mg/dL)	317
Creatinine (mg/dL)	13.1
Na (mEq/L)	156
K (mEq/L)	8.2
Glycemia (mg/dL)	240
Total CPK (U/L)	3,116
CPK-MB fraction (U/L)	33.2
Amylase (U/L)	231
Aspartate aminotransferase (U/L)	76
Alanine aminotransferase (U/L)	36
Alkaline phosphatase (U/L)	88
Gamma-glutamyl transpeptidase (U/L)	100
Total bilirubin (MG/dL)	0.7
Albumin (g/dL)	3.1
Immunogenetics	
HLA A	24.66
HLA B	15.35
HLA DR	1.8
Serologies	
Hepatitis B (Ag-HBs, anti-HBs, and total anti-HBc)	NR
HIV (anti-HIV1 and anti-HIV2)	NR
Hepatitis C (anti-HCV)	NR
Toxoplasmosis	
(anti-toxoplasm IgG)	R
(anti-toxoplasm IgM)	NR
Syphilis (VDRL)	NR
Cytomegalovirus	
(anti-CMV IgG)	R
(anti-CMV IgM)	NR

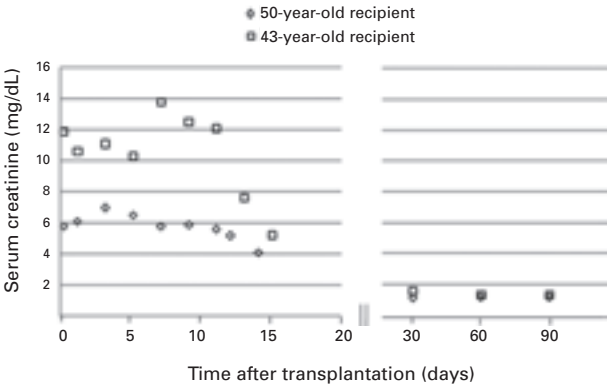
Hb = hemoglobin; Ht = hematocrit; Na = sodium; K = potassium; CPK = creatine phosphokinase; HLA = human leukocyte antigen; HIV = human immunodeficiency virus; VDRL = venereal disease research laboratories; CMV = cytomegalovirus; R = reactive; NR = non reactive.

transplantation), prednisone (0.3 mg/kg/day reduced to 0.25 mg/kg/day at the end of the first month and to 0.1 mg/kg/day at the end of the third month), sodium mycophenolate (2.16 g/day), and tacrolimus (0.12 mg/kg/day) initiated on the 11th day. It was diagnosed acute cell rejection Banff IA on the 9th day after transplantation, which was treated with five daily doses of methylprednisolone (500mg EV). The urinary volumes on the first, third, and fifth days after transplantation were 2L, 5.6L, and 4.8L, respectively. No hemodialysis was required after transplantation. The patient was discharged from hospital on the 14th day after transplantation.

The other kidney was transplanted to a 43-year-old Afro-descendent male, who had chronic kidney failure of undetermined etiology and had been on hemodialysis for two years. The preoperative assessment showed type B blood, non reagent serologies for HIV, CMV, and hepatites B and C, negative crossmatch, zero reactivity against a panel of cells and HLA A 1,24, B 35,0 and DR 8,14. The cold ischemia time was 27 hour and 55 minutes. Immunosuppression was similar to that used in the other recipient, except for the introduction of tacrolimus on the forth day after transplantation. It was not diagnosed acute rejection. The urinary volumes on the first, third, and fifth days after transplantation were 1.5L, 0.8L, and 0.5L, respectively. Hemodialysis was required up to the 11th day after transplantation. The patient was discharged from the hospital on the 15th day after transplantation.

Monitoring of the serum levels of creatinine of both recipients is shown in Figure 3.

Figure 3. Measurements of serum creatinine according to time elapsed after transplantation in recipients of renal grafts from a deceased donor with acute kidney failure.



Discussion

The decision to transplant kidneys of deceased donors involves the determination of their functional prognosis after transplantation. The use of kidneys from extended-criteria deceased donors is currently considered the most efficient way to increase the number of transplantations in the short term. Although there is no universally accepted definition of what conditions should be considered borderline for donation, donors with ages higher than or equal to 60 years or higher than 50 years and lower than 60 years associated to two or three of the additional risk factors (cerebrovascular accident as cause of death, history of systemic blood hypertension, and serum creatinine higher than 1.5mg/dL) have a 70% higher risk of kidney graft failure.6 Such conditions are currently considered as extended criteria for donation.1 The allocation of kidney grafts from extended criteria donors is always based on the clinical judgment and experience of the transplant team, since written informed consent has been provided by the recipient.

The AKF of a deceased donor aged less than 50 years is a relatively frequent condition associated with the reduced use of such donors. Although the refusal of kidneys from donors with AKF may be very intuitive, the outcome of kidney transplantation from that type of donors may be satisfactory. Two studies have assessed the effects of the allocation of kidneys from donors with serum creatinine ≥ 2 mg/dL at the time of donation. A multivariate analysis of the North-American Scientific Registry of Transplant Recipients (SRTR) has shown that, although the use of kidneys from deceased donors with serum creatinine ≥ 1.5mg/dL has been associated with a 10% greater risk for graft failure and independently from the donor's age and history of hypertension or cerebral death due to cerebrovascular accident, serum creatinine ≥ 2mg/dL did not further increase the risk for graft failure.6 In addition, Ugarte *et al.*, in a retrospective study of 262 kidney transplants with non-borderline deceased donors, have reported that AKF kidney failure did not modify the incidences of graft function delay and acute rejection, and did not even reduce the graft and patient's survivals assessed six years after transplantation.[7]

A borderline deceased donor is currently defined by using only clinical characteristics, with no histological assessment of renal structural integrity. Thus, the benefit of performing kidney biopsy before graft placement has been considered. Histological assessment has been initially suggested after the observation that kidneys from deceased donors aged between 60

and 75 years with sclerosis in less than 15% of the glomeruli provided one-year survival after transplantation similar to kidneys of donors aged less than 60 years, and even better than those of same age donors when chosen considering only clinical criteria.[8] More recently, the observations by Remuzzi *et al.* have also confirmed that histological assessment significantly predicts long-term survival of kidneys from borderline donors.[9]

Histological assessment has also been used for selecting kidneys from non-borderline deceased donors with AKF. In 2006, Kumar *et al.* have shown that grafts from deceased donors aged 50 years or less with AKF and histological confirmation of preservation of the renal structure have survival similar to those of non-borderline donors without AKF.[5] Those authors have reported that, in the group of donors with ARF, serum creatinine at the time of graft removal was 4.6 ± 4.2 mg/dL. In the present study, kidneys from donors with severe AKF (serum creatinine equal to 13.1 mg/dL) were accepted after histological confirmation that the glomerular, vascular, and interstitial compartments of renal tissue were anatomically preserved. Despite the graft function delay, both recipients achieved satisfactory renal function since from the first month of follow-up on. Those results suggest that the severity of AKF is not an independent risk factor for short-term graft outcome.

The results show that serum creatinine in isolation should not interfere with the acceptance of kidneys from non-borderline deceased donors with AKF. The histological analysis of renal tissue should always be performed aiming at eliminating possible thrombotic microangiopathy or cortical necrosis, conditions that absolutely contra-indicate donation. Another recommendation is that grafts should be destined to patients without high risks for cardiovascular or infectious complications, considering the expected prolonged evolution of AKF after transplantation.

References

1. Rosengard B, Feng S, Alfrey E *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.
2. Audard V, Matignon M, Dahan K *et al.* Renal transplantation from extended criteria cadaveric donors: problems and perspectives overview. Transpl Int 2008; 21:11-7.
3. Online National Data of Organ Procurement and Transplantation Network [Internet]. Rockville: Department of Health and Human Services, Health Resources and Services Administration, Healthcare Systems Bureau, Division of Transplantation. [cited 2009 August 3]. Available from: http://optn.transplant.hrsa.gov/.
4. ABTO. Associação Brasileira de Transplante de Órgãos. Análise Comparativa Anual. Registro Brasileiro de Transplantes 2008; 14:1-33.
5. Kumar M, Khan S, Jaglan S *et al.* Successful transplantation of kidneys from deceased donors with acute renal failure: Three-year results. Transplantation 2006; 82:1640-5.
6. Port F, Bragg-Gresham J, Metzger R *et al.* Donor characteristics associated with reduced graft survival: an approach to expanding the pool of kidney donors. Transplantation 2002; 74:1281-6.
7. Ugarte R, Kraus E, Montgomery R *et al.* Excellent outcomes after transplantation of deceased donor kidneys with high terminal creatinine and mild pathologic lesions. Transplantation 2005; 80:794-800.
8. Andrés A, Morales J, Herrero J *et al.* Double *versus* single renal allografts from aged donors. Transplantation 2000; 69:2060-6.
9. Remuzzi G, Cravedi P, Perna A *et al.* Long-term outcome of renal transplantation from older donors. N Engl J Med 2006; 354:343-52.