

Characterization of kidney transplant patients with expanded criteria donors

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Abstract

Introduction: Kidney transplantation is the treatment of choice for patients with chronic kidney disease; however, the number of donors is insufficient, and waiting lists grow exponentially each year. Transplantation from expanded criteria donors benefits a significant number of patients, improving their survival when compared to those who remain on dialysis. The objective of this study is to describe the characteristics of patients who have received transplants from expanded criteria donors and their renal function at the first and third years after transplantation.

Methods: A descriptive observational study was conducted. Patients older than 18 years who received transplants from an expanded criteria donor were chosen between 2007 and 2015.

Results: Of a total of 227 patients analyzed, 18 received transplants from an expanded criteria donor. The recipients were 59.5 years old (37-79) and had spent 22.4 months on the waiting list (2.6-77.8) and 4.5 years on dialysis (0.5-18.4). The donors' age was 61 years (50-73). Graft survival at one year was 88.9%; at three years, it was 80%. A total of 11.1% of the patients presented acute cellular rejection at one year, and the average glomerular filtration rate at the first and third years was 58.4 mL/min/1.73 m².

Conclusion: Patients who received transplants from expanded criteria donors have good kidney graft function at three years, with graft and patient survival, similar to that reported for patients who received transplants from standard criteria donors (*Acta Med Colomb* 2019; 44. DOI: <https://doi.org/10.36104/amc.2019.1185>).

Keywords: donor selection, graft survival, graft rejection, kidney transplant.

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Introduction

Chronic kidney disease (CKD) is a public health problem that affects all populations and has grown exponentially in recent years. Currently, more than 2,500,000 people worldwide depend on renal replacement therapy to manage their pathology. Renal replacement therapy decreases quality of life and survival and places a high economic burden on health systems; in 2014, it accounted for 2% of health spending in Colombia (1).

Kidney transplantation is the best treatment for stage 5 CKD; it allows full recovery of renal function and improves patients' quality of life and survival. However, the supply of organs is low, and there is a need for strategies that increase the donor pool, such as the use of expanded criteria donors (ECD) (2). ECDs are defined as those older than 50 or 60 years who meet two of the following three criteria:

hypertension, serum creatinine > 1.5 mg/dL or death due to cerebrovascular disease (CVD) (3, 4). In this scenario, some of the factors influencing the results of kidney transplantation, such as the age of the donor, the presence of comorbidities such as hypertension and diabetes mellitus (5) and ischemia-reperfusion phenomena (6) generates concern about short-, medium- and long-term repercussions for graft functionality and survival. Large-scale studies conducted in different geographical locations worldwide have shown comparable results for graft and patient survival between ECD and standard criteria donors (SCD), mainly in recipients older than 40 years (2, 3, 7).

In Colombia, there were 2607 patients on the waiting list for kidney transplant in December 2018, and the rate of donation was 8.3 per million population (8); thus, the use of these strategies in our country is essential.

Materials and methods

A descriptive observational study was conducted. Patients were selected according to the inclusion criteria: age over 18 years with an ECD kidney transplanted from 2007 to 2015. All donors had a kidney biopsy with a Remuzzi score ≤ 3 (9). Patients for whom follow-up was not possible were excluded. Descriptive analyses of the sociodemographic and clinical characteristics of the study population were performed. Summary measures for qualitative variables are presented as proportions and those for quantitative variables are presented as medians and ranges, considering the small convenience sample size.

Results

A total of 227 kidney transplant patients were analyzed; 18 were transplanted with ECD kidneys (7.9%).

The recipients had a median age of 59.5 years (37-79). One of the transplant patients was under 40 years of age but had been on dialysis for 12 years and had decided to opt for a ECD. Among the causes of CKD, in six patients, the etiology was unknown; of the other patients, three were diabetic, four had polycystic kidney disease, two had glomerular disease, two had hypertension, and another had tubulointerstitial disease. The median time spent on the waiting list was 22.4 months (2.6-77.8); the median time spent in dialysis was 4.5 years (0.5-18.4). A total of 38.8% of the sample had a panel-reactive antibodies (PRA) greater than 20%. The donor age was 61 years (50-73), and the mean cold ischemia time was 14.5 hours (Table 1). Sixty-seven percent of patients underwent induction with thymoglobulin, and the rest received basiliximab. The main cause of death was stroke in 15 of the 18 donors.

Clinical results show graft and patient survival rates of 88.9 and 80% at one year and three years, respectively. The causes of mortality were infectious, due to cytomegalovirus, histoplasmosis and bacterial sepsis; additionally, there was one case of mortality of cardiovascular origin five years after transplantation.

A total of 11.1% of the patients had acute cellular rejection to one year, and the average glomerular filtration rate by MDRD4 after the first and third years was 58.4 mL/min/1.73 m² (Table 2).

Discussion

Despite recent efforts and changes in Colombian legislation, the donation rate has decreased during the past year (8), and the number of patients with CKD who are on dialysis and on the transplant waiting list continue to increase (10). The mortality of patients on dialysis is high, with figures reaching 50% at five years (11); thus, the search for strategies that increase the donor population is a necessity.

We present a series of patients who received ECD grafts and had optimal graft function at one and three years and a low rate of complications.

The use of ECDs generates controversies due to the higher rates of delayed graft function and primary failure

Table 1. Demographic data of patients who received transplants from ECDs.

Variable	n = 18
Male	11 (61.1%)
Recipient age in years	59.5 (37-79)
Etiology of CKD	
• Idiopathic	6 (33.3%)
• Polycystic disease	4 (22.2%)
• Diabetes mellitus	3 (16.7%)
• Hypertension	2 (11.1%)
• Glomerulonephritis	2 (11.1%)
• Other	1 (5.6%)
Time on list (months)	22.4 (2.6 - 77.8)
Time on dialysis (years)	4.5 (0.5 - 18.4)
PRA greater than 20%	7 (38.8%)
Cold ischemia time (hours)	14.5 (8 - 19)
Induction	
• Thyroglobulin	12 (66.7%)
• Basiliximab	6 (33.3%)
Donor data	
Age in years	61 (50 - 73)
Creatinine (mg/dL)	0.75 (0.6 - 2.1)
<i>PRA: Panel-reactive antibody</i>	

Table 2. Clinical results of recipients of kidneys from ECDs.

Variable	n = 18 (%)
Delayed graft function	4 (22.2%)
Primary failure	1 (5.6%)
MDRD4 TFG (mL/min/1.73 m ²)	
• 6 months	51.6
• 1 year	58.4
• 3 years	58.4
Cell rejection in the first year	2 (11.1%)
Patient survival	
• 1 year	88.9%
• 3 years	80%
Graft survival	
• 1 year	88.9%
• 3 years	80%

that have been reported when compared to the use of SCD organs. Bokzurt B et al. found graft loss in 26% of ECD cases, compared to 10% of SCD transplant recipient (12). Additionally, ECD transplants can be associated with higher costs and increase the probability of requiring dialysis, being admitted for emergencies and having higher intraoperative mortality; however, ECD recipients have 72% less mortality compared to patients on the waiting list (13).

A French multicenter observational study included 2763 kidney transplant patients, of whom 33.2% had ECD transplants, with an average follow-up of 5.54 years. A higher rate of graft loss (HR 1.87) was documented in ECD compared to SCD. Among the independent risk factors for graft loss, the following were identified: positive donor-specific antibody (DSA) (HR 4.59), ischemia time of 12-24 hours (HR 2.49) and ischemia time greater than 24 hours (HR 3.77) (2). In our study, the cold ischemia time averaged 14.5 hours, which could favorably impact the results.

A Greek retrospective study with 310 patients, 86 who received ECD transplants and 114 who received SCD transplants, evaluated graft survival at one, three and five years. Comparing the standard donors with the ECD showed that survival in the latter was significantly lower after the third year. In this study, ECDs were categorized as follows to establish survival up to five years in *type I*: donors older than 60 years without risk factors; *Type II*: donors aged between 50 and 59 years with two or three risk factors; and *type III*: donors older than 60 years with at least one risk factor. The survival of patients who had received a kidney from a type I was 95% at one, three and five years; the survival of those who had received a kidney from a type II donor was 92-80% in the first and fifth years; and the survival of those who had received a kidney from a type III donor was 78, 73 and 59% in the first, third and fifth years, respectively (14). Taking into account the above classification, our study showed that 38.8% of donors were type II and III, and only 16% were type I. The patients in our study who died were over 65 years old, and their donors were older than 60 years.

Several studies have reported very good results for patient and graft survival rates in those who received an ECD transplant compared with similar patients who remained on the waiting list (6, 15, 16). Savoye shows in his study that patients on the waiting list who do not have a transplant have a 2.3 times higher risk of dying than those transplanted with ECD (17). Countries such as Spain have shown that the average age of their donors is increasingly higher, given the decrease in violent deaths and the increase in older donors with cerebrovascular disease. Batista recently published the experience in his center and did not find differences in dysfunction or rejection in transplant patients with grafts who fulfilled the expanded criteria vs. standard criteria (15). Similar results had already been described by Di Cocco in 2011 (18) as well as by other groups, such as Remuzzi, who found equal survival at three and four years (19). The study by Tennankore compared the survival of patients who were

undergoing intensive hemodialysis at home, had received transplants from living donors, those with SCD and those with ECD. The results showed that survival was better among the ECD transplant group compared to the intensive hemodialysis group (20).

Watson et al. found that the main predictors of poor graft function were donor age, history of hypertension, obesity, adrenaline use in the donor and prolonged hospital stay, findings that support the recommendation of using ECD for older recipient and applying the “*old for old*” strategy, which in the long term has shown to improve quality of life and patient survival compared to patients who remain on the waiting list (21-24).

The Spanish guidelines state that ECD kidneys should preferably be used in patients over 60 years of age or in recipients between 55 and 60 years of age with risk factors such as prolonged waitlist time and that it should be considered for patients under 55 years who are hyperimmunized (25). Although there are systematic reviews that find that patients under 40 years do not benefit from receiving ECD, an individualized approach should be used (3). Another group of patients for which the use of ECD can be considered is those with vascular access problems (26, 27).

Regarding immediate complications, a Spanish single-center observational study compared 60 patients who had received an ECD transplant between January 2010 and December 2012, with 14 patients with SCD and found no differences in graft survival at two years (95 vs 100%), nor in complications such as delayed graft function, thrombosis, urinary fistula and lymphocele. However, there was a higher incidence of acute tubular necrosis in 84.5% vs. 57.1% ($p=0.025$) of ECD recipients (28). Another study conducted by Valjalo in Chile showed that 34 of 213 kidney transplant patients had transplants from ECD and presented more surgical and vascular complications, more acute rejection and more hospitalizations; furthermore, 5-year survival was lower in the ECD group, 61 vs. 89% (29). In our study, there were no urological or vascular complications. The incidence of delayed graft function was 22%, and the incidence of cellular rejection at one year was 11.1%, similar to that described in the literature for SCD.

With regard to immunosuppressive therapy, thymoglobulin is recommended for use during induction, and tacrolimus, mycophenolate, and steroids are recommended as the first line treatment in the maintenance phase (30). A total of 67% of our patients followed this schedule. Schedules free of calcineurin inhibitors are not recommended in cases of ECD, and some authors recommend using levels 25-50% lower to minimize toxicity (13).

In our population, patients with transplants from ECDs had good renal graft function at three years with adequate survival of the graft and the patient, similar to values reported for patients with a transplant from an SCD. In our population's age group, infectious comorbidities should be taken into account because they are the main cause of

mortality and clear parameters for their management should be established.

In Colombia, there are no published studies of kidney transplantation using organs from ECDs; therefore, determining the outcomes of these patients can help to incentivize the use of these donors.

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