Retrospective Analysis of the Kidney Donor Profile Index to Predict Patient and Graft Survival at 5 Years Posttransplantation in a Colombian Cohort

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ABSTRACT

Background. The Kidney Donor Profile Index (KDPI) has been used to predict patient and graft outcomes in deceased donor kidney transplantation. We aimed to evaluate the impact of KDPI on transplantation major outcomes applied to a Colombian cohort.

Methods. We retrospectively assessed 260 adult patients who underwent kidney transplantation (KT) from January 2011 to June 2014 at our center and compared their KDPIs with graft and patient outcomes at 5 years posttransplantation. Kaplan-Meier survival method and Cox analysis were fitted to analyze the impact of the 3 KDPI categories on graft and patient outcomes.

Results. A total of 18.4% of transplants were from donors with a KDPI ≥75%. There was a significant decrement in renal function with increasing KDPI at 5 years posttransplantation ($P < .05$). The final model indicates that donor diabetes was associated with elevated risk for graft loss (hazard ratio [HR], 6.5; 95% confidence interval [CI] 1.35-31.8; $P = .019$) at 5 years posttransplantation. Recipient age (HR, 2.3; 95% CI, 1.1-4.5; $P = .001$), diabetes status (HR, 2.17; CI, 1.04-5.5; $P = .003$), dialysis duration (HR, 1.08; 95% CI, 1.00-1.16; $P = .003$), and operating room time (HR, 1.47; 95% CI, 1.02-2.12; $P = .003$) were associated with elevated risk for death at 5 years posttransplantation. KDPI categories were not significantly associated with graft loss or death.

Conclusions. We found limited KDPI power to predict graft and patient survival when applied to a Latin American population in Colombia. Our findings highlight the importance of analyzing the application of KDPI in different populations. Therefore, our findings may not be generalizable to other regions outside of Colombia.

CHRONIC kidney disease (CKD) has increased worldwide, having been responsible for 1.2 million deaths in 2015, a 31.7% increase since 2005 [1,2]. CKD shows a high prevalence in Latin American countries such as Colombia, which has 2.7 CKD cases per 100 inhabitants [2]; unfortunately, only 1.7 out of 1000 Colombian patients receive a kidney transplant (KT) [2]. The number of patients on the KT waitlists exceeds the number of donors, a situation also reported in other countries [2]. Efforts to increase the donor pool (live and deceased donors) are the current focus of transplant programs worldwide [3]. However, 30% of available kidneys are from donors older than 50 years or with a history of diabetes mellitus, resulting in a high discard rate [4,5]. There is an ongoing controversy about whether to accept or reject expanded-criteria donors (ECDs) [5].

The United Network of Organ Sharing created the Kidney Profile Donor Index (KDPI) in 2014 as a tool to optimize organ use and minimize organ shortage [5]. The KDPI score is defined as a numerical measure that combines 10 clinical and demographic factors to determine the quality of deceased donor

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kidneys relative to other recovered kidneys [6]. This score proposes "longevity matching" to allocate kidneys according to the longest estimated posttransplant survival [7]. Preliminary analysis published by United Network of Organ Sharing found an increase in the number of KTs for patients with high panel reactive antibody calculator; Hispanic and African American patients; younger patients; and fewer kidney accepted offers for older, diabetic, pediatric and polycystic kidney recipients compared to the past [8].

Organ distribution in Colombia is determined by the government through the National Health Institute. Geographic criteria are applied for local, regional, and national distribution, with local distribution being prioritized within a region. An available organ is offered nationally if a match cannot be found regionally. In deceased donor organ transplantation, priority is assigned based on the existence of compatibility between donor and recipient in blood group, HLA, age, and factors related to the recipient, such as years on the waiting list and background of having been a kidney donor [9]. Nevertheless, there is no valid stratification score tool to assist physicians in their decision to accept or decline a kidney offer. However, as the data required to calculate the KDPI are available, we aimed to evaluate the impact of the KDPI on KT outcomes in a transplant program.

MATERIALS AND METHODS

Study Population

We conducted a retrospective cohort study. Inclusion criteria encompassed all adult (aged ≥18 years) recipients of deceased donor kidney transplants from January 2011 to June 2014 by Colombiana de Trasplantes in Bogota, Colombia. All pediatric patients receiving kidney transplantation were excluded. Recipients were observed up to 5 years posttransplantation by a single institution, Colombiana de Trasplantes. Ethical committee approval was obtained at the institution. Data collection was conducted by reviewing hospital records and by contact follow-up.

Component variables of the KDPI score included age, height, weight, ethnicity/race, history of hypertension, history of diabetes, cause of donor death, serum creatinine, hepatitis C virus status, and whether the donor met criteria for circulatory death. The study population was categorized into 3 groups according to KDPI score [10]. ECDs were defined as those aged 60 years or older or aged over 50 years with at least 2 of the following conditions: hypertension history, serum creatinine >1.5 mg/dL, or death from cerebrovascular accident. These ECDs are subjected to a biopsy before implantation, with results within 3 to 4 hours; Remuzzi scores [11] up to 3 were allocated as single transplants.

Recipient variables included age, sex, race, type and time on dialysis, presence of comorbidities such as hypertension and diabetes, previous transplants, and HLA mismatch with donor. Operative variables comprised preservation solution, cold and warm ischemia times, and anatomic variations of the kidney.

All patients received standard induction therapy with alemtuzumab, basiliximab, or antihuman thymocyte immunoglobulin according to immunologic risk and depending on availability of pharmaceuticals. All patients received a fixed dose of methylprednisolone perioperatively for 3 days with a transition to fixed-dose oral prednisone by postoperative day 4 up to day 9 posttransplant, when steroids were withdrawn. Maintenance immunosuppression protocol includes tacrolimus and mycophenolate.

Outcomes

Study outcomes of interest were patient and graft survival. Graft loss was defined as retransplantation, need for permanent return to dialysis, or death. The death-censored allograft survival rate was defined as the time from KT to the commencement of an alternative renal replacement therapy, censored for death. Patient survival was defined as the time from KT until death from any cause. All missing data were managed by censoring since the last follow-up date. Patients were contacted by phone when they did not attend clinic visits for more than 3 months at our institution.

Statistical Analysis

Descriptive statistics were used to report population characteristics, using mean and standard deviation for normally distributed variables and median and interquartile range for non-normally distributed variables.

The KDPI score was calculated with a "KDPI calculator" on the Organ Procurement and Transplantation Network website [12,13]. Three groups of KDPI were defined as low (≤20%), moderate (21% to 74%), and high (≥75%) risk of poor graft survival according to the distribution of KDPI scores presented in Fig 1. Baseline characteristics were compared among the 3 groups using χ^2 or analysis of variance, as appropriate. Time to posttransplantation death and graft loss were assessed using the Kaplan-Meier method and the log-rank test to compare the equality of survivor functions. Patient follow-ups were censored if the patient was transferred to another dialysis unit or lost to follow-up. Cox proportional hazard models were fitted to examine the multivariable-adjusted relationship between KDPI and graft loss and KDPI and death, respectively. The proportional hazard assumption was evaluated using Schoenfeld residuals for each predictor. In nonsignificant values with a P value > .05, we considered that there was no violation of the proportional hazard assumption. For model building, we evaluated any prior knowledge of specific interactions and multicollinearity that were not present and were not included in the model. The backward stepwise regression method was applied to have a more parsimonious model. The cutoff probability was .15 for removing variables. All reported P values were 2-tailed, and $P < .05$ was considered significant. Analyses were conducted using Stata statistical software, version 14.2 (StataCorp LLC, College Station, Tex, United States).

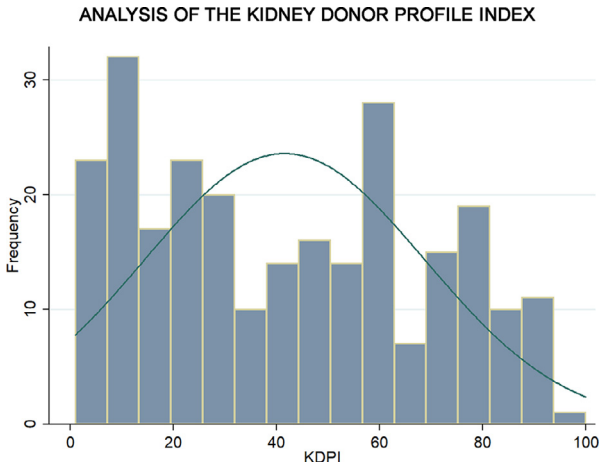


Fig 1. Distribution of deceased donors by Kidney Donor Profile Index (KDPI) score.

RESULTS

Characteristics of the Kidney Transplant Population

Recipient characteristics. A total of 304 patients underwent deceased donor KT between January 2011 and June 2014. Of those, 260 patients met the inclusion criteria and 44 were excluded (15 pediatric transplants, 3 from a different center, and 26 with incomplete or no available information). There were more male than female recipients. A total of 74 patients received a deceased donor kidney with a KDPI of 0 to 20; 138 with a KDPI of 21 to 74; and 48 with a KDPI of 75 to 100. Compared with patients receiving a transplant with low KDPI, patients receiving a higher KDPI kidney were on average older and more likely to have a history of diabetes. Table 1 depicts baseline characteristics.

Donor characteristics. Among the study population, 210 (80.5%) KTs were from standard-criteria donors (SCD) and 51 from ECDs (19.5%). Table 2 depicts donor characteristics. Donors with lower KDPI were younger (mean age of 24, 41, and 56, respectively; $P \leq .001$), had no comorbidities (hypertension or diabetes), had lower baseline serum creatinine ($P = .011$), and died of cause other than cerebrovascular accident ($P \leq .001$). Biopsies were performed in 53 donors (20%, 51 ECDs and 2 SCDs), with histologic Remuzzi classifications of 0 (32%), 1 (43.3%), 2 (11.3%), and 3 (13.2%). Data of baseline characteristics of population are shown in Table 1.

Kidney Allograft Function

We evaluated kidney allograft function at 3, 6, 12, 36, and 60 months. There was a decrease in kidney function with increasing KDPI. Figure 2 shows estimated glomerular filtration rate by CKD-Epidemiology Collaboration (CKD-EPI) at each time point in grafts surviving beyond 3 months posttransplantation comparing KDPI groups.

Table 1. Baseline Characteristics of Transplant Recipients by KDPI Category

Variable	KDPI ≤20%(n = 74)	KDPI 21%-75%(n = 138)	KDPI ≥75%(n = 48)	*P* value
Recipient				
Age at KT, y, mean (SD)	41 (11.6)	45 (11.9)	56 (8.8)	≤ .001
Sex (female:male)	21:53	53:85	13:35	.197
Race/ethnicity, n (%)				.281
Hispanic	67 (90.5)	120 (86.9)	41 (85.4)	
Black	7 (9.46)	18 (13.0)	6 (12.5)	
Asian	0	0	1 (2.0)	
Dialysis duration, y, mean (SD)	5.6 (4.4)	5.6 (3.6)	5.3 (4.1)	.895
Diabetes	5 (6.7)	18 (13.0)	12 (25)	.015
Previous transplant, n (%)	6 (8.1)	4 (2.9)	4 (8.3)	.168
Cold ischemia time, h, mean (SD)	18 (7)	17 (6.4)	15 (4.7)	.014
Induction, n (%)				.393
Alemtuzumab	27 (36.4)	41 (29.7)	14 (29.1)	
Basiliximab	14 (18.9)	28 (20.29)	15 (31.2)	
ATG	33 (44.5)	69 (50)	19 (39.5)	
Preservation solution, n (%)				≤ .001
HTK	71 (95.9)	128 (92.7)	37 (77.0)	
UW	3 (4)	10 (7.2)	11 (22.9)	
Donors				
Age, y, mean (SD)	24.1 (5.4)	41.3 (11.8)	56.9 (6.2)	≤ .001
Sex (female:male)	13:61	49:89	29:19	≤ .001
BMI (kg/m^2), mean (SD)	25.1 (4.4)	25.4 (4.3)	26.1 (4.5)	.422
Hypertension, n (%)	0	35 (20.4)	11 (84.6)	≤ .001
Diabetes mellitus, n (%)	0	0	4 (8.3)	≤ .001
Cause of donor death: CVA, n (%)	4 (5.4)	60 (43.4)	33 (68.7)	≤ .001
Serum creatinine	0.7 (0.27)	1.1 (0.69)	0.96 (0.29)	≤ .001
Type of donor, n (%)				≤ .001
Expanded criteria	0	12 (8.7)	39 (81.25)	
Standard criteria	74 (100)	126 (91.3)	9 (18.7)	
Remuzzi score, n (%)				≤ .001
0	0	1 (0.7)	16 (33.3)	
1	0	6 (4.3)	17 (35.4)	
2	0	0	6 (12.5)	
3	0	5 (3.6)	2 (4.7)	

ATG, antithymocyte globulin; CVA, cerebrovascular accident; BMI, body mass index; HTK, histidine tryptophan ketoglutarate solution; KDPI, Kidney Donor Profile Index; KT, kidney transplantation; SD, standard deviation; UW, University of Wisconsin solution.

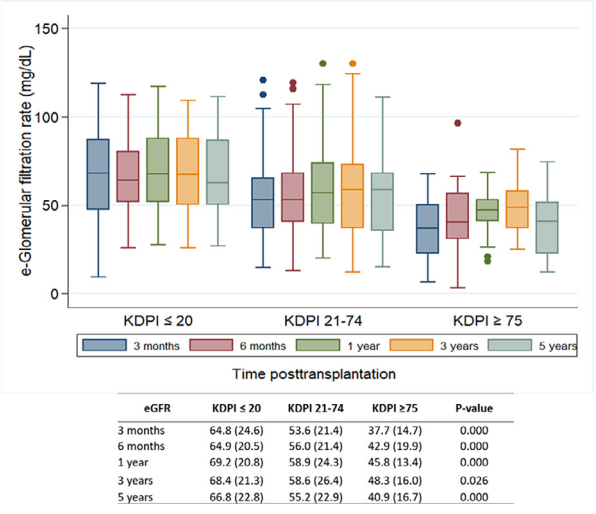
Table 2. Proportional Hazard Model for Time to Transplantation Graft Loss

	Model Building			Final Model		
Variable	HR	95% CI	*P*	HR	95% CI	*P*
Recipient sex	1.03	.49-2.14	.926			
Recipient age >55	0.91	.34-2.40	.856			
Dialysis duration, y	1.03	0.95-1.13	.361			
Recipient diabetes	0.80	0.27-2.4	.698			
Donor sex	1.57	0.75-3.31	.228			
Donor age	1.00	0.96-1.04	.971			
Donor hypertension	1.27	0.89-1.80	.182	1.35	1.03-1.78	.030
Donor diabetes	3.65	0.33-40.5	.291	6.57	1.35-31.8	.019
Donor type	3.99	0.46-3.4	.206			
Remuzzi score	1.39	0.74-2.62	1.03			
Donor creatinine	0.82	0.39-1.73	.612			
Operating room time	1.04	0.58-1.73	.881			
Preservation solution	0.47	0.12-1.86	.287			
Cold ischemia time, h	0.98	0.93-1.04	.664			
Warm ischemia time, min	0.97	0.91-1.04	.520			
Induction	2.03	1.2-3.27	.003	1.87	1.21-2.8	.004
Alentuzumab (reference)						
Basiliximab				1.7	0.5-5.29	.315
ATG				3.3	1.4-8.1	.007
BMI (kg/m^2)	0.92	0.82-1.02	.136	0.91	0.84-1.004	.051
Previous transplant	0.92	0.15-6.16	.976			
KDPI score	1.6	0.99-2.6	.053			
KDPI ≤20 (reference)						
KDPI 21-74	1.7	0.76-3.8	.189			
KDPI ≥75	2.6	1.02-7.03	.043			

ATG, antithymocyte globulin; BMI, body mass index; CI, confidence interval; HR, hazard ratio; KDPI, Kidney Donor Profile Index.

KDPI and Graft Survival

We examined the impact of the KDPI score on graft survival. After a median follow-up of 4.9 years (interquartile range, 1.0-5.0 years), 31 patients (out of 41) died with a functioning graft and 57 returned to dialysis. The rate of graft loss censored for death was 25%. We disregarded surgical complications (patients with arterial or venous renal thrombosis) of graft loss for the survival analysis owing to such complications' immediate nature (n = 15; 5.7%). Uncensored graft survival at 5 years was 77% for recipients of KDPI score ≤20% (95% confidence interval [CI], 65-85), 66% for those with KDPI score 21% to 74% (95% CI, 56-74), and 49% for those with KDPI score ≥75% (95% CI, 32-64). Death-censored graft survival at 5 years was 87% for recipients of KDPI score ≤20%, 79% for those with KDPI score 21% to 74%, and 66% for those with KDPI score ≥75%. Figure 3 shows the comparison of graft survival among recipients stratified by KDPI categories.



eGFR	KDPI ≤ 20	KDPI 21-74	KDPI ≥75	P-value
3 months	64.8 (24.6)	53.6 (21.4)	37.7 (14.7)	0.000
6 months	64.9 (20.5)	56.0 (21.4)	42.9 (19.9)	0.000
1 year	69.2 (20.8)	58.9 (24.3)	45.8 (13.4)	0.000
3 years	68.4 (21.3)	58.6 (26.4)	48.3 (16.0)	0.026
5 years	66.8 (22.8)	55.2 (22.9)	40.9 (16.7)	0.000

Fig 2. Graft function posttransplantation comparing KDPI groups. eGFR, estimated glomerular filtration rate; KDPI, Kidney Donor Profile Index.

Results of multivariable Cox proportional hazard model on time to posttransplantation graft loss are shown in Table 2. The final model indicates that after adjusting for confounding factors, only donor diabetes was associated with elevated risk for graft loss. KDPI scores were not significantly associated with graft loss. The proportional hazards assumption was tested using plots of Schoenfeld residuals over time and revealed no significant violations of the proportional hazard assumption.

Patient Survival

The crude mortality rate was 15.7% (n = 41). Patient survival at 5 years was 86.9% for recipients of KDPI score ≤20%, 79% for those with KDPI score 21% to 74%, and 68.8% for those with KDPI score ≥75%. Causes of death were sepsis/infection (n = 14; 34.1%), cardiovascular disease (n = 8;19.5%), and

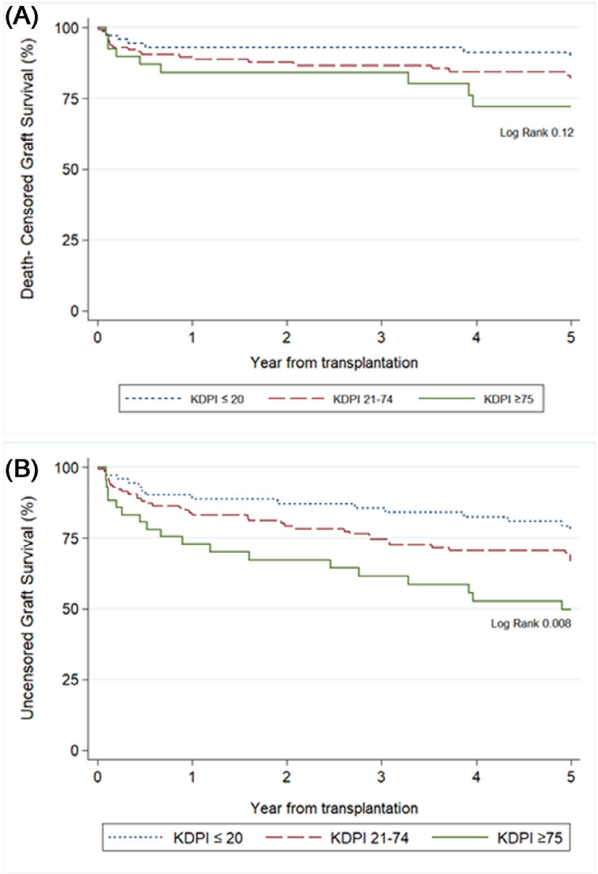


Fig 3. Graft survival stratified by Kidney Donor Profile Index (KDPI) score. **(A)** Death-censored graft survival. **(B)** Uncensored graft survival.

hypovolemic shock (n =3; 7.3%) caused by postoperative bleeding (n = 1), massive hemoptysis (n = 1), and anticoagulant therapy (n = 1); the remaining causes were unknown (n = 16; 39%). Among deaths, 8 occurred in KDPI ≤20%, 22 in KDPI 21% to 74%, and 11 in KDPI ≥75%. There was no significant association between death and KDPI category ($P = .2$). Figure 4 depicts the comparison of patient survival among recipients stratified by KDPI category.

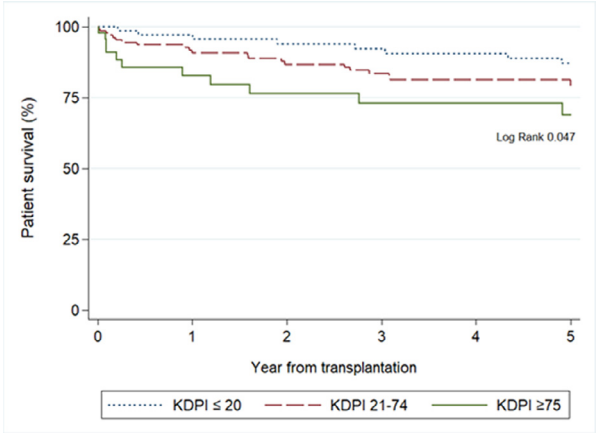


Fig 4. Patient survival and survival curves according to the Kidney Donor Profile Index (KDPI) categories.

Results of the multivariable Cox proportional hazard model on time to posttransplantation death are shown in Table 3. The final model indicates that after adjusting for confounding factors, recipient age, history of diabetes, and anastomosis time were associated with increased risk of death. KDPI categories were not significantly associated with mortality. The proportional hazards assumption was tested using plots of Schoenfeld residuals over time and revealed no significant violations of the proportional hazard assumption.

DISCUSSION

The use of the KDPI could contribute to a significant improvement in the acceptance of kidneys for transplantation. However, its discriminatory power in terms of graft survival is limited in a Latin American population in Colombia.

A higher KDPI score was not significantly associated with graft loss or survival rates at 5 years posttransplantation. Our results are supported by those of other studies suggesting that a lower KDPI score is not associated with better transplantation outcomes. In a Canadian cohort, Rose et al reported that KDPI score did not improve the prediction of allograft failure in comparison with the simple criterion of donor age [14]. In an Irish study, Sexton et al reported similar findings [15]. Parker et al noted that the KDPI predicted poor allograft survival in pediatric KT [16]. It should be taken into account that this study did not include KT involving African American donors, donors with the hepatitis C virus, or donors having undergone cardiocirculatory arrest. Under these circumstances, KDPI can be underestimated. On the other hand, recent studies have reported that KDPI is a significant predictor of graft survival [17,18].

Our study showed that diabetic donors are associated with a high risk of graft loss compared with nondiabetic donors. Cohen et al evaluated transplants from 9074 diabetic donors and 152,555 nondiabetic donors and noted a modest difference in the overall graft survival (37% vs 50% at 10 years) [19]. In contrast, Luan et al suggest that diabetic donor kidneys with or without diabetic nephropathy may not have a negative effect on graft survival [20]. The patient-survival model identified recipient age >55 years, recipient diabetes, donor diabetes, dialysis duration, and operating room time of as risk factors of patient mortality. Age, diabetes, and dialysis duration are pretransplant variables previously identified as a risks factors for patient mortality [21,22]. A prolonged operative duration has been associated with an increase in the risk of complications [23]. When analyzing the operative times, we found that prolonged operative time was associated with morbid obesity (body mass index >35kg/m2), and this could explain our findings.

Kidney graft function was significantly decreased up to 5 years posttransplantation in the high-KDPI group compared with the low-KDPI group. We hypothesize that the capacity for recovery in kidneys from high-KDPI donors is lower than those from low-

Table 3. Proportional Hazard Model for Time to Transplantation Death

Variable	Model Building			Final Model		
	HR	95% CI	*P*	HR	95% CI	*P*
Recipient sex	2.32	0.88-6.06	.086	2.15	0.90-5.14	.084
Recipient age >55	2.6	1.11-8.18	.028	2.3	1.18-4.50	.014
Dialysis duration, y	1.09	1.33-7.17	.027	1.08	1.007-1.16	.030
Recipient diabetes	1.65	1.33-4.14	.204	2.17	1.04-4.54	.038
Donor sex	0.61	0.27-1.36	.229			
Donor age	0.97	0.93-1.018	.255			
Donor hypertension	0.93	0.64-1.37	.743			
Donor diabetes	2.30	1.11-4.14	.024	1.38	1.68-1.14	.014
Donor type	2.65	0.39-1.78	.316			
Remuzzi score	1.59	0.82-3.06	.164			
Donor creatinine	0.28	0.084-0.97	.045			
Operating room time	1.36	1.33-0.10	.200	1.47	1.02-2.12	.036
Preservation solution	0.55	0.16-1.83	.337			
Cold ischemia time, h	1.01	0.95-1.07	.640			
Warm ischemia time, min	1.00	0.94-1.06	.909			
Induction	1.04	0.69-1.56	.837			
Alentuzumab (reference)						
Basiliximab						
ATG						
BMI (kg/m^2)	1.09	1.01-1.18	.025			
Previous transplant	0.22	0.019-1.57	.229			
KDPI score	2.96	1.079-8.12	.035			
KDPI ≤20 (reference)						
KDPI 21-74	3.6	.947-14.15	.060			
KDPI ≥75	9.3	.981-88.42	.052			

ATG, antithymocyte globulin; BMI, body mass index; CI, confidence interval; HR, hazard ratio; KDPI, Kidney Donor Profile Index.

KDPI donors. Indeed, baseline serum creatinine was reported to be higher in high-KDPI donors than in low-KDPI donors [24].

This study had some limitations. First, we retrospectively calculated KDPI scores, which may interfere with confounding factors. Second, this study included a small sample population from one center in Colombia. However, Colombiana de Trasplantes performed about 21% of all kidney transplants in Colombia [25], which could constitute a representative sample. Allograft biopsies were not performed in all kidneys; it is unclear whether chronic changes can predict long-term allograft outcomes. Third, because the calculation of mortality rate relied largely on family reports, the underlying cause of death is sometimes unknown, creating uncertainty in our estimates. Finally, our findings may not be generalizable to other regions outside of Colombia.

In conclusion, we found that use of the KDPI could increase the acceptance rate of kidneys for transplantation. However, it did not predict graft survival when applied to a Latin American population in Colombia. Our findings highlight the importance of analyzing the application of KDPI in different populations, particularly in regions where alternate mechanisms exist to facilitate longevity matching in allocation [9].

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