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Characteristics associated with the type of donor in kidney transplant; an experience in a high-altitude city

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ABSTRACT

Introduction: Renal transplantation has been mainly studied in coastal cities or low-altitude areas, which is a significant limitation of the field.

Objectives: The objective of this study was to determine the survival rates, and characteristics associated with the type of donor, in patients with renal transplantation at a high-altitude Peruvian hospital.

Patients and Methods: We performed a retrospective cohort study of 63 transplanted patients in Cusco, Peru. Depending on the type of donor (living or cadaveric), associations were found according to sociocultural characteristics of the donor and recipient, and according to physio-anthropometry and characteristics of the disease. It was used analytical statistics.

Results: Fifty-one percent (32) of kidney transplants came from a cadaveric donor. Statistically significant differences were found according to the kinship of the donor ($P<0.001$), recipient age ($P=0.042$), cold ischemia time ($P<0.001$), and blood urea value ($P=0.008$). A year after the transplant, there was a 98% patient survival rate (CI: 89-100%) and a 97% graft survival rate (CI: 87-99%). Ten years later, the survival rate was 92% for patients (CI: 75-98%) and 53% for grafts (CI: 33-70%); there were no differences in patient survival ($P=0.654$) or graft survival ($P=0.851$) between donor types.

Conclusion: The results indicate that in a high-altitude population study, survival rate is slightly higher than in studies performed at sea level, and this does not depend on donor type (living or cadaveric). In addition, statistically significant differences in survival rates were found depending on the kinship of the donor, recipient age, and cold ischemia time.

Implication for health policy/practice/research/medical education:
Kidney transplantation results in higher survival rates and lower costs than in peritoneal dialysis and hemodialysis, making it the most effective therapy in patients with chronic kidney disease. Our study found that the survival rate of patients with kidney transplants at a high-altitude Peruvian hospital was slightly higher than that of those at sea level, and did not depend on the type of donor (living or cadaveric). The findings showed statistically significant differences in survival rate depending on the relationship with the donor, recipient age group, time of cold ischemia, and blood urea value.

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Original Article

Introduction

Recent years have witnessed global demographic, social, and epidemiological changes. The decrease in infectious diseases and a longer life expectancy have led to an increase in non-communicable diseases that include chronic kidney disease (CKD), which is considered an increasing public health problem (1). Currently, the number of deaths has doubled due to an increase in diseases such as diabetes (2) and hypertension (3), which are two of the main causes of CKD. Peru is no exception to this reality, and despite exhibiting an increasing prevalence of CKD and higher mortality rates (4), there is a deficit of specialist clinicians (nephrologists) and dialysis centers.

Renal transplantation is the treatment of choice and

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the most effective treatment for CKD (5), improving the survival rate (6), and decreasing costs than with peritoneal dialysis and hemodialysis (7). Globally, there has been an increase in renal transplant registries, especially in developed countries (8). Peru has a long waiting list for renal transplantation, with 6.1 renal transplants being performed per million inhabitants, and was one of the last countries in Latin America to carry out this practice (9). In addition, renal transplantation has not been evaluated in a high-altitude area, such as Cusco, a city located in the Peruvian mountains, where a 1.8-fold higher prevalence of end-stage renal disease has been reported (10). Being affected by sustained hypoxia (11), which stimulates erythropoiesis by the kidneys, may play a role in the recovery or survival of high-altitude transplanted patients.

Objectives

The objective of this study was to determine the survival rate, as well as characteristics associated with the type of donor, in patients with a renal transplantation at a high-altitude Peruvian hospital.

Patients and Methods

Study patients

A retrospective cohort study was carried out between January and March of 2019 in the transplant center of Adolfo Guevara Velasco hospital in the city of Cusco, located in the Andean mountains of Peru, at 3400 m above sea level.

The study included all patients who underwent renal transplantation performed by the hospital transplant center. Patients whose medical record data were incomplete or those who migrated and/or carried out their medical controls in other cities were excluded. The population comprised 100% of patients who underwent renal transplantation between 1986 and 2018 and who met the selection criteria.

For data collection, a revised datasheet was used, which was subsequently submitted to an evaluation process supervised by specialists in renal transplantation. The datasheet included general information about the donor such as age, gender, kinship, and general information about the recipient, such as age (according to age group: adolescent, young, adult, and elderly), marital status, level of instruction, body mass index (BMI), cause of CKD, type of dialysis therapy, previous kidney transplant, dialysis time (years), cold ischemia time (hours), hemoglobin, blood urea, and blood creatinine values measured at hospital discharge.

Ethical issues

The research project was approved by the ethics committee of "Madre-Niño San Bartolome" hospital (RCEI-40), located in the city of Lima, Peru. Data was collected with the authorization of the hospital's director from the medical records of each transplanted patient, ensuring anonymity and confidentiality of the participants.

Statistical analysis

A database was generated using the Microsoft Excel® program (Windows 2013 version), which was reviewed by the authors; a descriptive analysis of the categorical variables was then performed using relative and absolute frequencies. According to the type of donor (living or cadaveric), associations were evaluated with sociocultural characteristics, physio-anthropometry, and characteristics of the recipient disease. For the analysis, the chi-square test or Fisher's exact test was used, depending on the type of distribution. Graft and patient survival analysis were performed using the Kaplan-Meier method and the log rank test. Patients were censored at the time of last contact (if lost during follow-up) or death; in the case of grafts, patients whose graft stopped functioning or who died were censored. The Stata version 11.1 statistical program (StataCorp LP, College Station, TX, USA) was used to analyze the data.

Results

During the study period, there were a total of 76 kidney transplants, of which 63 met the selection criteria, with 50.8% (32) from a cadaveric donor. Most of the living donors were siblings and mothers. The recipients were mostly adults between 30 and 59 years of age. Statistically significant differences were found according to kinship ($P<0.001$) and age of the recipients ($P=0.042$), however were not found between age groups ($P=0.248$) or gender ($P=0.244$) of the recipients (Table 1).

No associations were found between the type of donor and the recipient's weight ($P=0.588$), the cause of CKD ($P=0.166$), the type of dialysis therapy ($P=0.086$), any previous kidney transplant ($P=0.613$), the time of dialysis ($P=0.141$), the value of hemoglobin ($P=0.223$), or blood creatinine levels ($P=0.373$). On the other hand, there were statistical differences corresponding to the time of cold ischemia ($P<0.001$) and the blood urea value ($P=0.008$; Table 2).

According to the type of donor, recipients from living donors had a 97% patient survival rate (CI: 79-100%) and a 97% graft survival rate (CI: 79-100%), a year after the transplant. The survival rate after five years was 97% for patients (CI: 79-100%) and 90% for grafts (CI: 71-97%), and ten years later, the survival rate was 91% for patients (CI: 67-98%) and 46% for grafts (CI: 21- 67%). On the other hand, recipients from cadaveric donors had a 100% patient survival rate and a 96% graft survival rate (CI: 76-99%), a year after the transplant. The survival

Table 1. Sociocultural characteristics of donor and recipient according to the type of donor in a high-altitude city

Variable	Living Donor	Cadaveric Donor	*P* value
Amount of each donor	31 (49.2%)	32 (50.8%)	
Donor age (y)*	41 (29-46)	43 (42-49)	0.248[a]
Donor gender			
Male	15 (62.5%)	9 (37.5%)	0.244[b]
Female	15 (79.0%)	4 (21.0%)	
Kinship with the donor			
Unrelated	2 (5.9%)	32 (94.1%)	<0.001[c]
Mother	10 (100.0%)	0 (0.0%)	
Father	3 (100.0%)	0 (0.0%)	
Sibling	11 (100.0%)	0 (0.0%)	
Child	5 (100.0%)	0 (0.0%)	
Recipient age group			
Adolescent	3 (100.0%)	0 (0.0%)	0.042[c]
Young	9 (75.0%)	3 (25.0%)	
Adult	17 (39.5%)	26 (60.5%)	
Elderly	2 (40.0%)	3 (60.0%)	
Recipient marital status			
Single	15 (57.7%)	11 (42.3%)	0.414[c]
Married	13 (43.3%)	17 (56.7%)	
Divorced	0 (0.0%)	2 (100.0%)	
Partner	3 (60.0%)	2 (40.0%)	
Recipient level of instruction			
Secondary education	10 (43.5%)	13 (56.5%)	0.490[b]
College degree	21 (52.5%)	19 (47.5%)	

[a] Sum of ranks; [b] Chi-square test; [c] Fisher exact test.

Table 2. Physio-anthropometry and disease characteristics according to donor type in a high-altitude city

Variable	Living Donor	Cadaveric Donor	*P* value
Weight			
Low weight	3 (60.0%)	2 (40.0%)	0.588[c]
Normal	21 (53.9%)	18 (46.2%)	
Overweight	7 (38.9%)	11 (61.1%)	
Type I Obesity	0 (0.0%)	1 (100.0%)	
Cause of CKD			
Unknown	2 (66.7%)	1 (33.3%)	0.146[c]
Primary glomerulonephritis	17 (58.6%)	12 (41.4%)	
Hypertension	6 (37.5%)	10 (62.5%)	
Diabetes mellitus	0 (0.0%)	5 (100.0%)	
Uropathy	2 (66.7%)	1 (33.3%)	
Polycystic renal disease	1 (33.3%)	3 (66.7%)	
Others	3 (75.0%)	1 (25.0%)	
Type of dialysis therapy			
Peritoneal dialysis	8 (72.7%)	3 (27.3%)	0.086[b]
Hemodialysis	23 (44.2%)	29 (55.8%)	
Previous renal transplant			
Yes	30 (50.9%)	29 (49.1%)	0.613[c]
No	1 (25.0%)	3 (75.0%)	
Time on dialysis (y)	2.1 (0.9-5.0)	4.0 (2.0-6.9)	0.141[a]
Cold ischemia time (h)	1.5 (1.0-1.6)	13.2 (9.1-16.5)	<0.001[a]
Hemoglobin (g/dL)	10.0 (9.0-11.4)	9.8 (8.6-10.6)	0.223[a]
Blood urea (mg/dL)	50.0 (42.1-62)	60.5 (50.9-78.6)	0.008[a]
Blood creatinine (mg/dL)	1.3 (1.1-2.2)	1.5 (1.2-2.1)	0.373[a]

[a] Sum of ranks; [b] Chi-square test; [c] Fisher exact test.

rate after five years was 95% for patients (CI: 71-99%) and 78% for grafts (CI: 55-90%), and ten years later, the survival rate was 95% for patients (CI: 91-99%) and 73% for grafts (CI: 49- 87%). There were no differences in patient survival ($P=0.654$) or graft survival ($P=0.851$) between donor types (Table 3).

Figures 1 and 2 show the rates of overall survival and of survival according to the type of donor, respectively. In the graphic depicting the survival of the donor type according to patient mortality and renal graft failure, the intersection of the curves at several points is shown confirming that there is no statistically significant difference.

Discussion

Our study showed that the survival rate of kidney transplant recipients at the end of the first, fifth, and tenth year was 98%, 96%, and 73%, respectively; for the graft, the survival rate was 97%, 84%, and 43%, respectively. In Colombia, patient survival was shown to be 97.2% and 90.8% after the first and fifth year, respectively (12), and in Cuba it was 82.7%, 78.3% and 73.4% after the first, third and fifth year, respectively (13). In Johannesburg, south Africa, graft survival was 81%, 66%, and 50% at the end of the first, fifth, and tenth year, respectively (14). Therefore, our results show a slightly better survival rate than those in other studies. In addition, we found that the relationship between survival (of the patient or graft) and the type of donor (living or cadaveric) was not significant, which could indicate that in our study population, the survival of renal transplantation does not depend on the type of donor. This observation is consistent with other studies such as those carried out in Chile (15) and Italy (13). This is despite the fact that a meta-analysis indicated better survival rates for kidney transplants from living donors (related or unrelated) compared to cadaveric transplants (16), which is probably due to the optimal conditions with which the kidneys are obtained from living donors (13) or due to the establishment of better immunosuppressive schemes and better management of complications during postoperative care (17).

In our study, the cause of CKD in patients was most often caused by primary glomerulonephritis, as these usually occur in young people who are given a preference in the waiting list because of their higher life expectancy. This is in contrast to observations in the United States

Table 3. Graft characteristics and patient survival in a high-altitude city

Survival Time	Patient	Graft
All donors		
At 1 year	98% (89-100%)	97% (87-99%)
At 5 years	96% (85-99%)	84% (71-92%)
At 10 years	92% (75-98%)	53% (33-70%)
At 15 years	73% (41-90%)	43% (19-65%)
Living donor		
At 1 year	97% (79-100%)	97% (79-100%)
At 5 years	97% (79-100%)	90% (71-97%)
At 10 years	91% (67-98%)	46% (21-67%)
At 15 years	71% (36-89%)	34% (11-59%)
Cadaveric donor		
At 1 year	100%	96% (76-99%)
At 5 years	95% (71-99%)	78% (55-90%)
At 10 years	95% (71-99%)	73% (49-87%)
At 15 years	95% (71-99%)	73% (49-87%)
Failure Events		
Living donor	5 deaths	13 rejections
Cadaveric donor	1 death	6 rejections
P value	0.654	0.851

The *P* values of failure events were obtained using the Wilcoxon test.

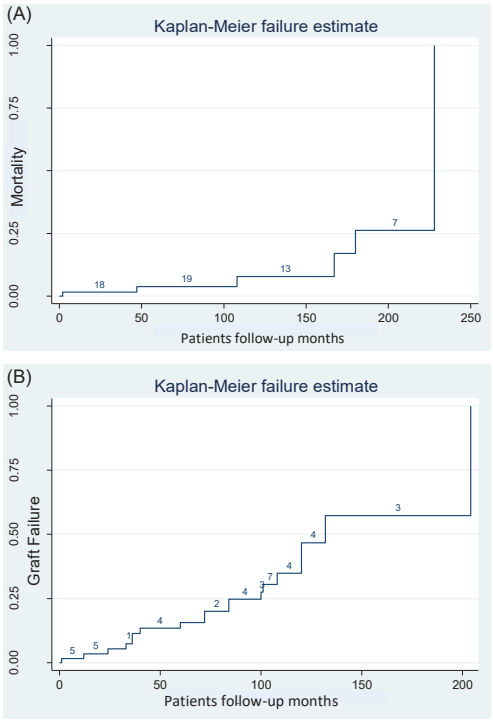

Figure 1. Survival curves for patient mortality (A) and renal graft failure (B) at a high altitude.

where diabetes is the most common cause of CKD, followed by hypertension and glomerulonephritis, and where older populations are more likely to require kidney transplantations (8). The number of kidney transplants in our study was similar for living and cadaveric donors as that observed in Thailand (8), but different from those in the United States (13), where the majority were from cadaveric donors. A special case is Iran (12), where approximately 90% of kidney transplants were from unrelated living donors, since their policy encourages this type of practice. In Peru, the kidney transplant law is based on a presumed relative consent, where the decision to donate depends on immediate family members who, due to unawareness, are resistant to organ donation. In addition, the time of dialysis for patients who received a renal transplant from a cadaveric or living donor, was four and two years on average, respectively. In India, the permanence on dialysis was shown to be less than one year (18), which means that there is a shortage of donors, which translates into longer waiting times and lower quality of life for patients who need a transplant.

Our study found a significant relationship with the kinship of the recipient, with siblings and mothers comprising more than half of all living donors, the same as that previously observed in India and China, where donors were immediate relatives (19), However unlike the United States, where living donors were mostly spouses and friends of the recipient (5). Renal transplantation is not commonly performed in Peru; strategies should therefore be developed to increase the supply of organs, such as the use of kidneys from selected donors with expanded criteria (20), or older donors, which has proven to be an alternative for transplants (5), thereby reducing the gap between supply and demand in transplants.

Our findings also demonstrated that the relationship to the recipient age group was significant, with more frequent transplants to adult recipients aged between 30 and 59 years being carried out. A significant relationship was found with the time of cold ischemia of the transplanted kidney, where a kidney of cadaveric and living donors remained on average for 13 and 1.5 hours, respectively, in cold ischemia, indicating that the kidneys in a cadaveric donor are exposed to a longer ischemia time than in a living donor. Although our study could not determine whether cold ischemia had survival implications, some studies have shown that prolonged cold ischemia time is associated with an increased risk of graft dysfunction (20).

Our study is one of the earliest to address the problem of kidney transplants in a high-altitude population. We found that survival results in our study were slightly higher than those observed in other studies carried out at sea level. In addition, Peru remains a developing country with multiple health problems, where monetary poverty affects 21.7% of the population. Renal transplantation should therefore be the main therapy used for CKD since it is a practice that is being increasingly employed in Latin America,

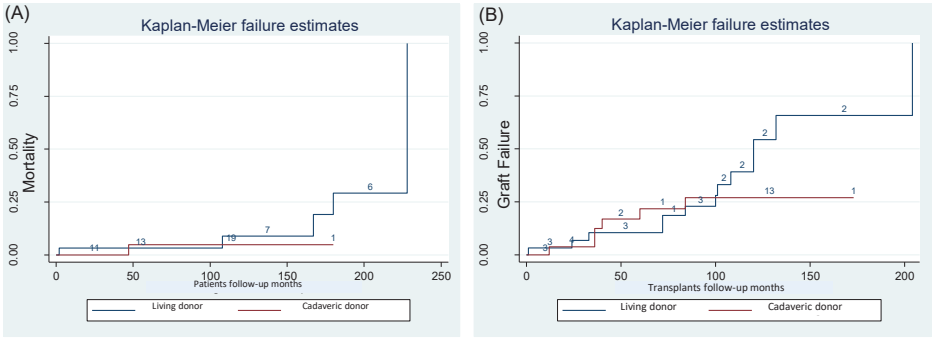

Figure 2. Survival curves of the donor type (living or cadaveric) according to patient mortality (A) and renal graft failure (B) at a high altitude.

and because it has been shown to increase survival and improve quality of life more than with peritoneal dialysis and hemodialysis, and be more economical. However, this would require state institutions to generate an entire new system of support and incentives.

Conclusion

Together, the findings of this study indicate that the survival of kidney transplants in a high-altitude population is slightly higher than those in other studies, and that the survival rate does not depend on the type of donor (living or cadaveric). In addition, statistically significant differences were found according to the kinship of the donor, recipient age group, time of cold ischemia, and the blood urea value.

Limitations of the study

The study had the main limitation of selection bias since there was a reduced sample of cases, all of which have been registered so far in our hospital. Therefore, the results obtained must be considered as primary results, which must be generated in a larger population, and even in different high-altitude populations, in order to have a greater diversity of events and circumstances.

Authors' contribution

GMC, RRC, and CM designed the study. CLM and RRC collected the data. CM and GMC completed the data analysis. GMC, CM, and JRE supervised the study. GMC, CM, and JRE wrote the document. All authors approved the final version of the manuscript.

Conflicts of interest

The authors declare no conflicts of interest.

Ethical considerations

This study complies with all ethical considerations, and ethical issues (including plagiarism, data fabrication and double publication) were overseen by the authors.

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