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Original (translation)

Survival and Mortality of Kidney Transplant Patients in Costa Rica 2019-2023

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Abstract

Aim: To determine the survival of patients receiving kidney transplants in Costa Rica, the factors associated with it, and differences between hospitals.

Methods: Time-survival data from 292 KTs performed in five hospitals in Costa Rica from 2019 to 2023. Mortality rates (hazards) per transplanted person-year. Kaplan-Meier survival curves. Relative risks of death by characteristics, estimated with Cox multiple regression.

Results: The 5-year post-transplant survival rate was 78%; the average of 91% for living donor transplants and 69% for cadaveric donor. The risk of death for the latter is critically high in the first six months post-transplant with a annualized death rate of 26%, which is almost six times higher than in the following 4.5 years and that of the living donor transplants. Patients who survived the first six months post-transplant had a mortality rate eight times higher than the general population. The small number of observations in the database did not allow for the identification of significant mortality differences between hospitals. Mortality among patients transplanted during the COVID-19 pandemic was not higher than in other years.

Conclusions: Compared to successful countries, the survival rate of kidney transplant patients in Costa Rica is high and similar to those countries for living donors, but lower for deceased donors, indicating room for improvement. Kidney transplant patients are at high risk of dying, especially in the first months after transplantation. The existence of a national transplant registry has made it possible to estimate the survival and mortality rates of recipients nationwide for the first time. It is important that this registry be kept up-to-date and expanded with information that will help optimize the kidney transplant program.

Keywords: Kidney transplant. Survival. Mortality. Living donor. Cadaveric donor. Kidney Transplantation

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Abbreviations:
CI; Confidence Interval
RR; Relative Risk
KT; Kidney Transplant
TSE; Supreme Electoral Tribunal.

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Organ transplantation is a well-established form of treatment, recognized as the best and often the only way to save lives in the case of various diseases. In patients with end-stage chronic kidney disease, kidney transplantation (KT) is the treatment of choice for improving both these patients' survival and their quality of life. For healthcare systems, KT is also a more cost-effective measure than renal replacement therapy (dialysis). It has been stated that KT is "the greatest advance in modern medicine in providing years of survival with a high quality of life for patients with irreversible kidney failure."[1]

According to the World Observatory on Organ Donation and Transplantation, although more than 100,000 KTs are performed worldwide each year, there are more than 5 million

people undergoing dialysis (World Health Organization. *Transplantation of Human Organs and Tissues: Report of the Director-General. 2022. 75th World Health Assembly.* April 12, 2022. nA75/41. A75_41-sp.pdf). In other words, these transplants meet only a small percentage of global needs.

The first successful KT was performed in the United States in 1954.[2] KTs have been performed in Latin America since 1957. Argentina was a pioneer, and Mexico followed six years later. Costa Rica performed its first kidney transplant at a private clinic in 1969. The Calderón Guardia Hospital of the Costa Rican Social Security Fund (CCSS) has been performing kidney transplants since 1982.[3]

Law 9222 on the donation and transplantation of human organs and tissues has regulated this procedure since 2014. The Ministry of Health has maintained a single waiting list for transplant candidates since 2018. The allocation of organs from deceased donors is centralized at the Ministry of Health through the Technical Executive Secretariat for Donation and Transplantation (SETDT). This allocation is carried out in accordance with the current candidate list and in accordance with the "National Standard for the Distribution and Allocation of Kidneys from Deceased Donors" (Executive Decree 41461-S of October 23, 2018, https://acortar.link/7qOiJh). Transplants from living donors are performed at health facilities authorized by the SETDT and must be reported to the Costa Rican National Donation and Transplant System (SINADOC). The Ministry of Health maintains a national database, which was used as a reference for this study.

It has been established that survival rates for people who receive a liver transplant are higher when the organ comes from a living donor.[4] A comparative study of KT programs in 15 countries, almost all of them developed, shows that five-year survival rates with living donors range from 93% to 98% (India is the exception at 80%), while with deceased donors, the rates range from 84% to 93%.[5]

The United States and Spain are the two countries that perform the most KTs per million inhabitants, with 79 and 71 transplants annually, respectively. The vast majority of these KTs come from deceased donors (77% and 90%, respectively) and have a five-year survival rate of 86% in both countries.[5]

Data on KT survival rates in Latin America are scarce. In Cuba, the five-year survival rate for KTs from deceased donors between 2015 and 2019 has been estimated at 82%.[6] In Brazil, this rate is 84%.[5] A study of patients at the National Children's Hospital of Costa Rica estimates a 5-year survival rate of 99% for kidney transplants in the children and adolescents treated at this hospital (64% of the transplants came from living donors).[7] No national studies were found that estimate KT survival rates in Costa Rica.

This study was conducted with three objectives: to determine mortality and survival rates among KT patients in Costa Rica; to identify factors associated with survival and mortality rates; and to determine potential differences in mortality rates among the hospitals where the transplants were performed.

Methods

Data from the registry of KTs performed in Costa Rica during the period from 2019 through 2023 were reviewed. This national registry, managed by the Technical Executive Secretariat for Donation and Transplantation of the Ministry of Health, is populated with information provided by the nephrology departments of the five public hospitals that perform transplants in the country.

The information was supplemented and validated using the birth and death records from the Supreme Electoral Tribunal (TSE) to verify deaths and their dates, as well as to identify possible omissions of deaths. The TSE provided the patients' sex, date of birth, and age. For 31 patients, the identification number did not correspond to a valid ID number in the TSE registry (these were likely foreign residents), so it was not possible to validate or track them in the TSE databases. In these cases, the CCSS provided the date of birth for these patients, and gender was imputed based on their names.

The follow-up cutoff date for the survival registry was February 29, 2024. The death count includes one death from December 2023 that was identified using TSE data. In addition, an error in the date of death (day and month reversed) was detected in five records in the TSE data.

Mortality rates were calculated as the ratio of the number of deaths to person-years of exposure. For example, the exposure—the denominator of the rate—for a transplant recipient in January 2019 who had not died as of August 2024 is 5.7 person-years of exposure. It should be noted that these are annualized rates, even if the observation period differs from one year.

To account for confounding effects when comparing rates, relative risks of death were estimated using a nonparametric Cox multiple regression model, and survival analysis over time following transplantation was performed by estimating Kaplan-Meier curves.[8] In observational epidemiological studies, it is common to use a multiple regression model, such as the aforementioned nonparametric Cox model, to control for mutual confounding effects among the explanatory variables of KT mortality. The relative risk (RR) of death was calculated for one group compared to a reference group; for comparisons between hospitals, Hospital México was chosen as the reference because it performs the highest number of transplants.

For comparative purposes, the number of expected deaths was estimated assuming that the group's mortality rate was typical of the Costa Rican population. To do this, mortality rates by sex and age from the general population for 2019–2023 were used, including mortality due to COVID-19.

Data analysis was performed using the *st ("survival time")* module of the Stata-17 statistical software package (Statacorp. *Stata Statistical Software: release 17.* Stata Corporation; 2020).

Results

A total of 292 transplants were recorded over a 5-year period, including one individual who received two transplants; that is, 291 people received a kidney transplant. The highest number of KTs occurred in 2019, with 85 cases (Table 1). In the following two years, this number fell to less than half, likely due to the pandemic. In subsequent years, there was a recovery, but the 2019 peak was not reached. In the year with the highest number of transplants, the national rate was 17 KTs per million inhabitants.

Nearly half of the KTs (45%) were performed using organs from living donors. KTs were performed primarily on men (70%). The ages of transplant recipients ranged from 6 to 73 years, with an average age of 42 years. Only two patients were over 70 years old.

Hospital México performed the most transplants (39%), followed at a distance by Hospital Dr. Calderón Guardia (23%). Hospital San Juan de Dios, Hospital Dr. Max Peralta, and the National Children's Hospital each performed approximately 10% of the transplants (Table 1).

Table 1. Profile of the characteristics of kidney transplant recipients, broken down by hospital, with post-transplant follow-up and mortality estimates, Costa Rica, 2019–2023

			Mortality			
Characteristic	Number of transplants	Distribution %	Number of deaths	Years of exposure	**Rate %**	(C.I. at 95%))
Total	292	100	40	707	**5.7**	(4.2 – 7.7)
Year of KT						
2019	85	29	16	353	**4.5**	(2.8 – 7.4)
2020	41	14	7	137	**5.1**	(2.4 – 10.7)
2021	32	11	3	75	**4.0**	(1.3 – 12.4)
2022	65	22	6	99	**6.0**	(2.7 – 13.4)
2023	69	24	8	43	**18.8**	(9.4 – 37.5)
Donor						
Deceased	160	55	33	378	**8.7**	(6.2 – 12.3)
Living	132	45	7	328	**2.1**	(1.0 – 4.5)
Sex						
Male	204	70	30	484	**6.2**	(4.3 – 8.9)
Female	88	30	10	223	**4.5**	(2.4 – 8.3)
Age						
6 – 29 years	82	28	7	217	**3.2**	(1.5 – 6.8)
30 – 49	110	38	10	267	**3.7**	(2.0 – 7.0)
50 – 75	100	34	23	223	**10.3**	(6.9 – 15.5)
Average age		42				
Hospital						
México	115	39	11	291	**3.8**	(2.1 – 6.8)
Calderón G.	68	23	11	171	**6.4**	(3.6 – 11.6)
S Juan de Dios	39	13	7	101	**7.0**	(3.3 – 14.6)
Max Peralta	44	15	8	76	**10.5**	(5.3 – 21.0)
Children's	26	9	3	67	**4.5**	(1.4 – 13.8)
Nationality						
Costa Rican	261	89	36	628	**5.7**	(4.1 – 7.9)
Foreigner	31	11	4	78	**5.1**	(1.9 – 13.6)
Months since transplant						
<6 months	292	...	22	134	**16.4**	(10.8 – 24.9)
6 to 60	251	...	18	572	**3.1**	(2.0 – 5.0)

C.I.: Confidence interval

There were 40 deaths among recipients of KT; this represents a crude annual mortality rate of 6%; that is, six out of every 100 transplant recipients died each year during the study period (Table 1, right panel). The confidence interval (CI) for this estimate ranges from 4.2 to 7.7, a wide range due to the small number of observations available for the study. In other words, a few deaths occurring for random reasons could alter the estimated rate by up to nearly 2 percentage points.

The risk of death is five times higher in the first six months after transplantation than in the following 4.5 years (16% vs. 3%). The highest rate was 18.8% for transplants performed in 2023, compared with, for example, the 4.0% mortality rate for transplants in 2021, which is the cohort with the lowest mortality rate. Furthermore, the mortality rate is much higher among recipients of deceased donors than among those of living donors: 8.7% vs. 2.1% of patients who die annually. Table 1 illustrates this critically high risk of death in the first few months after transplantation and among patients who received transplants from deceased donors. Figure 1 combines these two characteristics and shows the extraordinarily high mortality rate among patients who received transplants from deceased donors in the first six months after transplantation; here, the annualized mortality rate is 26.5%, nearly six times higher than that of patients who received transplants from living donors during the same period (4.8%) and than that of those who received transplants from deceased donors after six months post-transplant (4.6%), which subsequently decreases to an annual mortality rate of 1.5%.

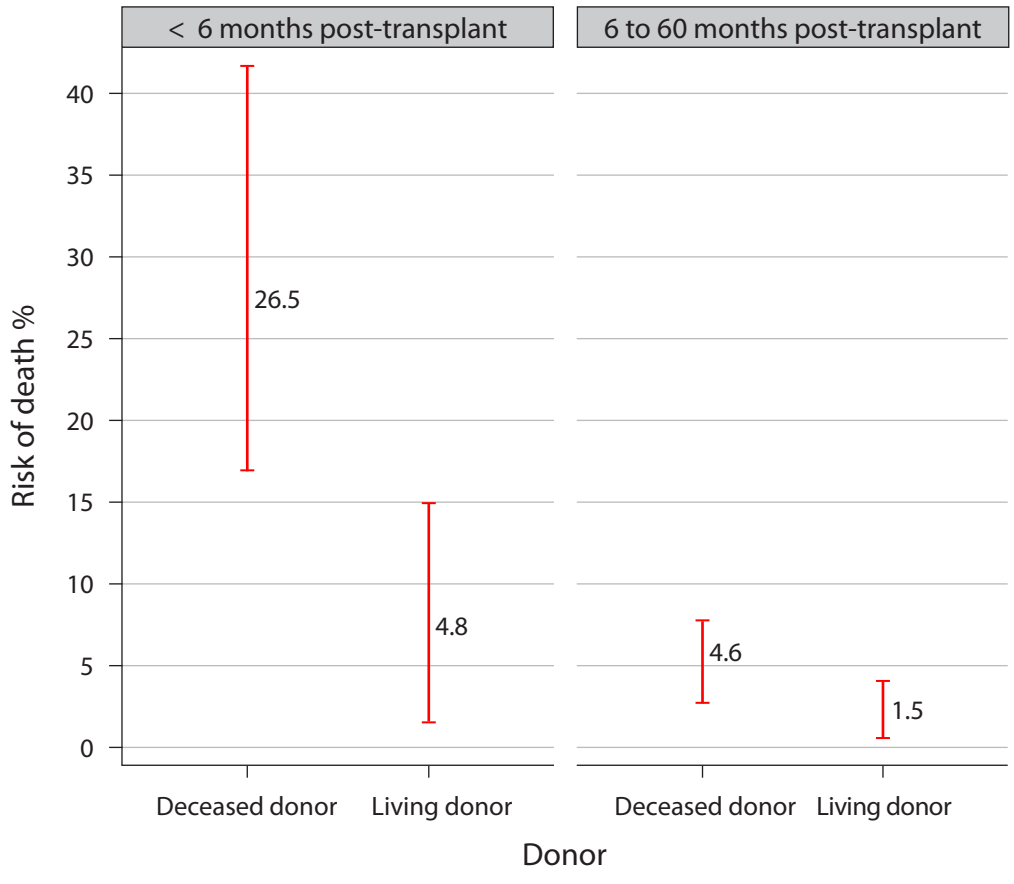

Figure 1. Risk of death by time since kidney transplantation and donor type (N=292). Costa Rica, 2019–2023.

Mortality among male transplant recipients (6%) is higher than among female recipients (4.5%), but this difference was small and not statistically significant, as the confidence intervals overlap.

When considering age, the risk of death increased with the age of transplant recipients: 3.2 vs. 10.3 deaths per 100 people in the two extreme age groups shown in Table 1.

Variations in the mortality rate were observed among hospitals. The National Children's and México hospitals have the lowest rates, with 4% of patients dying annually. In contrast, the Dr. Max Peralta Hospital had the highest rate, with a mortality rate of 10.5%.

Table 2 shows that the percentage of transplants from living donors, who have lower mortality rates, is significantly higher at the Mexico Hospital (67%), San Juan de Dios Hospital (54%), and Dr. Max Peralta Hospital (50%) than at Dr. Calderón Guardia Hospital (16%) and the National Children's Hospital (4%). Meanwhile, the age of transplant recipients is, for obvious reasons, much lower at the National Children's Hospital (13 years on average). Conversely, San Juan de Dios Hospital had the highest average age at 49 years.

The trend in the survival rate over time following transplantation is shown for all transplants and broken down by whether the donor was living or deceased, given the significant difference in mortality between these two groups (Figure 2).

Table 2. Distribution of kidney transplant recipients by hospital, by donor type and mean age at the time of transplantation, Costa Rica, 2019–2023

Hospital	Total	Deceased dono	%	Living donor	%	Average age (years)
Total	292	160	54,7	132	45,2	41
México	115	38	33,0	77	66,9	43
Calderón G.	68	57	83,8	11	16,2	45
S Juan de Dios	39	18	46,1	21	53,8	49
Max Peralta	44	22	50,0	22	50,0	42
Niños	26	25	96,0	1	4,0%	13

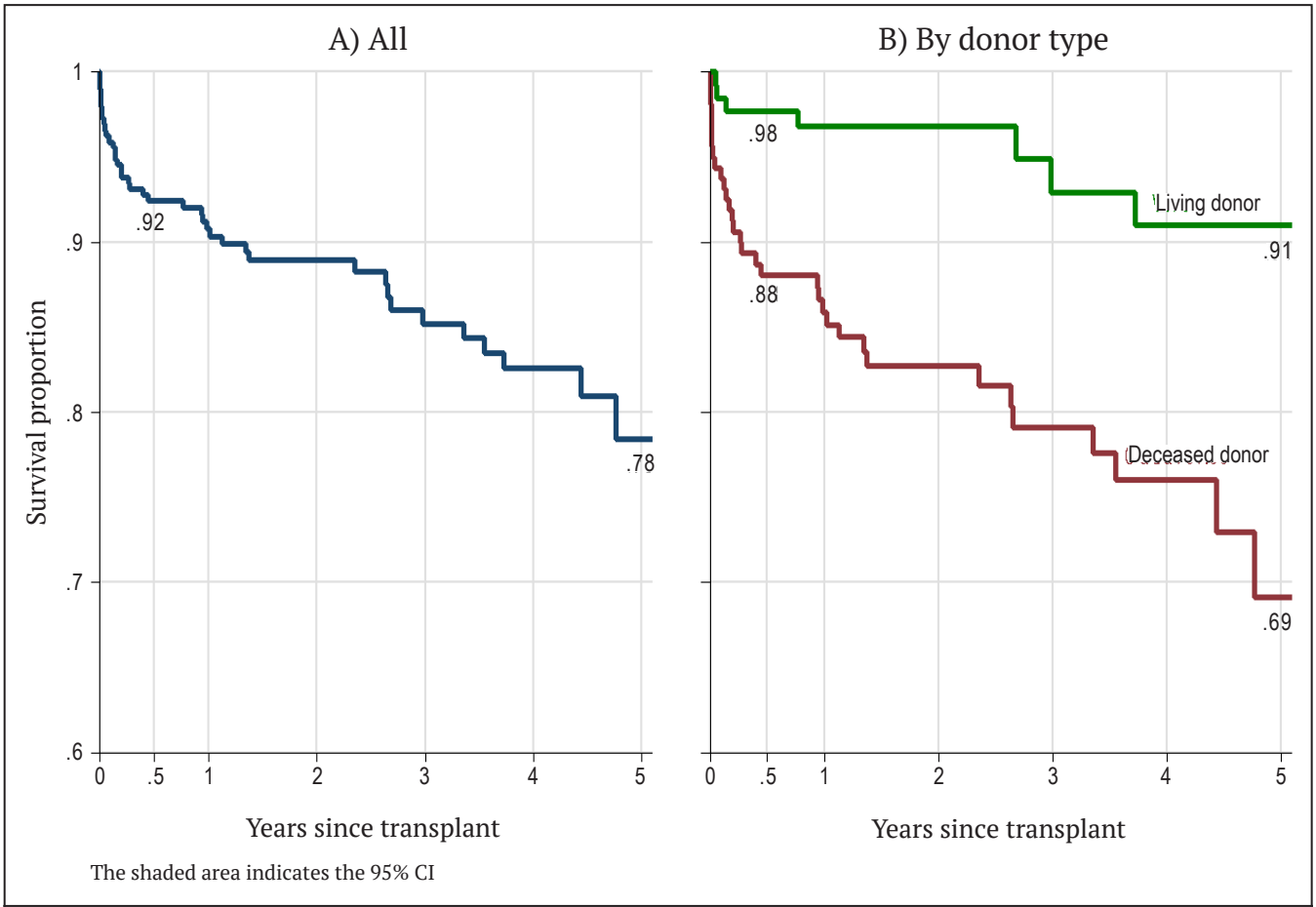

Figure 2. Kaplan-Meier estimate of the proportion of survivors by donor type for kidney transplantation (N=292). Costa Rica, 2019–2023.

After the critical period of the first six months post-transplant, 92% (CI 87%–94%) of patients are still alive. In the long term—that is, five years after transplant—survival is 78% (CI 70%–85%). Furthermore, survival among recipients of kidneys from living donors is clearly higher than among those from deceased donors: 91% at five years, compared with 69%, respectively.

Table 3 shows the results of applying the nonparametric Cox model, which provide the most robust and least biased estimate of mortality differences among hospitals. Patients at Dr. Calderón Guardia Hospital and the National Children's Hospital had essentially the same risk of death (RR close to 1.0) as those at Hospital México. Patients at San Juan de Dios Hospital had an RR of 1.39, that is, a 39% higher risk of death, and those at Dr. Max Peralta Hospital had an RR of 1.54, or a 54% higher risk than those at Hospital México. If the analysis is restricted to cadaveric donor transplants, excess mortality relative to Hospital México increases at San Juan de Dios Hospital and Max Peralta Hospital (right panel of Table 3). It is not possible to replicate this estimate for living donors because the number of observations is insufficient: only 7 deaths (5 at Hospital México and 2 at Dr. Calderón Guardia) out of 132 transplants.

Table 3. Estimated relative risk of death using Cox regression for kidney transplant recipients, comparing all kidney transplants with those from deceased donors only. Costa Rica, 2019–2023

Characteristic	All KTs , N=292		Deceased donor, N=160	
	RR death	(C.I. at 95%)	RR death	(C.I. at 95%)
Hospital del TR				
México	1.00	Reference	1.00	Reference
Calderón G.	0.97	(0.40- 2.35)	1.30	(0.47 - 3.61)
S Juan de Dios	1.39	(0.52- 3.70)	1.67	(0.49 - 5.74)
Max Peralta	1.54	(0.61- 3.92)	2.31	(0.79 - 6.74)
Children's	1.02	(0.20- 5.13)	0.91	(0.17 - 4.81)
Donor				
Living	1.00	Reference		
Deceased	4.22	(1.80 - 9.93)		
Age at KT				
6–29 years	1.00	Reference	1.00	Reference
30–49	1.22	(0.38 - 3.93)	0.88	(0.26 - 2.94)
50–73	2.74	(1.05 - 7.13)	1.67	(0.55 - 5.08)
Sex				
Male	1.00	Reference	1.00	Reference
Female	0.77	(0.37 - 1.61)	0.74	(0.32 - 1.70)
Nationality				
Costa Rican	1.00	Reference	1.00	Reference
Foreigner	0.71	(0.25 - 2.05)	0.84	(0.29 - 2.44)
Year of KT				
2019	1.00	Reference	1.00	Reference
2020-22	0.74	(0.35 - 1.57)	0.92	(0.39 - 2.17)
2023	1.42	(0.54 - 3.75)	1.99	(0.66 - 5.99)

KT = kidney transplant. RR = relative risk. CI = confidence interval. Highlighted in bold: $p < 0.05$.

The only two statistically significant effects in Table 3 are the higher mortality among patients with cadaveric donors, RR = 4.2 (CI 1.8–9.9) and the higher mortality among patients aged 50 or older, RR = 2.7 (CI 1.1–7.1), compared with those under 30 years of age.

It is worth noting that KTs performed during the three years of the COVID-19 pandemic (2020–2022) do not show higher mortality. On the contrary, compared with transplants in 2019, the RR = 0.74 indicates a 26% lower mortality rate; and compared with transplants in 2023, the mortality rate is approximately half (differences not statistically significant) (Table 3).

Discussion

The 292 transplants performed in Costa Rica during the 2019–2023 five-year period show a five-year post-transplant survival rate of 78%. This represents an average survival rate of 91% for patients who received an organ from a living donor and 69% for those who received an organ from a deceased donor. The risk of death among the latter group is critically high (26.5% annual mortality) during the first six months after transplantation; it is nearly six times higher than in subsequent months and than among patients who received organs from living donors.

Other studies have documented that survival rates in successful transplant programs such as those in South Korea, Japan, Italy, or Finland range from 93% to 95% for living donors and from 86% to 93% for deceased donors.[5] The Costa Rican program approaches these high survival rates for living donors, but its results are not as good for deceased donors. In other words, the mortality gap between living-donor and deceased-donor transplants is wider in Costa Rica than in the most successful countries. There appears to be room to improve survival rates for deceased-donor kidney transplants in the country.

On the other hand, the possibility that the COVID-19 pandemic may have increased mortality among transplant patients during this period was ruled out upon finding that, in fact, the lowest mortality rates correspond to kidney transplants performed during the 2020–2022 period.

The kidney transplant rate in 2019 was 17 per million inhabitants. Countries with high rates, such as the United States and Spain, exceed 70 transplants per million inhabitants annually. Meanwhile, the proportion of living-donor transplants was 45%, significantly higher than the 10% to 15% seen in Brazil, Spain, France, or Italy, but lower than the 93% in Japan or the 63% in South Korea.[5]

A comparison among hospitals shows a higher risk of death among patients at the San Juan de Dios Hospital (39% higher) and the Max Peralta Hospital in Cartago (54%) compared to the México Hospital, but this excess mortality is not statistically significant due to the small number of observations in the study and, consequently, the wide confidence intervals for the survival estimates in Figure 1-A, especially as time passes and the number of observed individuals decreases; that is, it may be due to chance and would likely change with a larger number of observations. However, it can be taken as an indication of the need for further analysis to investigate the possibility that patients face a higher risk of death in certain hospitals.

In addition to the above, it should be noted that because the proportions of living donors and minors vary substantially among hospitals, the comparison of crude mortality rates is heavily distorted by confounding effects generated by these two variables. Furthermore, hospitals with a higher proportion of living donors and younger patients tend to have lower mortality rates. Nevertheless, in light of the analysis of risks affecting survival, it is important to emphasize that none of the differences in mortality between hospitals are statistically significant (all CIs in Table 3 cross the value of one). This study, based on the observation of 292 transplants, lacks sufficient statistical power to detect significant differences between hospitals; and it has even less power to stratify the analysis according to whether the donor was living or deceased.

On the other hand, hypothetically, if the 292 patients studied had had mortality rates typical of the general population living in Costa Rica, there would have been only three deaths, instead of the 40 observed. Patients with KT are definitely a high-risk group. If we exclude the period of very high risk of death during the first six months post-transplant, the annual mortality rate of 3.1 per 100 transplant recipients is eight times higher than the 0.4% rate observed in the general population of similar age and sex.

The other side of the coin regarding the previous analysis is the estimation of the expected number of deaths if the patients studied had not received a transplant. Preliminary results from an ongoing study of the registry of patients on renal replacement therapy (dialysis) suggest an annual mortality rate of 14.5%; that is, a rate nearly three times higher than the 5.7% rate among transplant recipients. Given the mortality rate among dialysis patients, without transplantation, 102 patients would have died instead of the 40 deaths observed: transplants saved 62 lives during the study period.

Another important factor affecting transplant mortality is the selection of patients who receive transplants. Hospitals or programs that perform transplants on high-risk patients (those who are elderly or have conditions with high mortality rates) would have higher mortality rates. In contrast, programs that do not take risks and perform transplants only on very healthy patients would show lower mortality rates. This selection bias requires that mortality results be interpreted with caution. To get a complete picture, it is important to also analyze the mortality of patients with chronic kidney disease who did not receive a transplant, that is, patients on dialysis. It is important to note that low mortality among transplant recipients would not be a desirable outcome if access to transplantation is low, waiting lists are long, and dialysis patients have very high mortality rates.

A strength of this study is that the data were validated against the TSE's population and death records. This ensures that there is no bias due to underreporting of deaths; in fact, the TSE data identified a death that had been omitted from the transplant database. However, this validation could not be performed for the 31 patients without a valid Costa Rican national ID number (presumably foreign residents). This variable is relevant because available information suggests that the risk of death is slightly lower among foreign nationals. It would be important for the kidney transplant registry to include the date of the most recent contact with the patient (date of the last follow-up appointment) to identify cases of foreign patients who have been lost to follow-up and who may well have died.

In conclusion, in Costa Rica, the survival rate of patients who have received a KT reaches 78% five years post-transplant. Access to this treatment option for people with severe kidney dysfunction is essential, and the benefit is clearly greater when the organ comes from a living donor; this also supports the country's healthcare efforts through the Social Security system. In this country, the existence of a national transplant registry has made it possible, for the first time, to estimate the survival and mortality rates of kidney transplant recipients nationwide. It is important that this registry be kept up to date and expanded with relevant information to generate data that will help improve the program.

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