

Review and analysis of the results of kidney transplantation programs in Mexico

Revisión y análisis de los resultados de los programas de trasplante renal en México

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Abstract

Objective: To know, analyze and compare kidney transplant programs; considering the survival of recipients at 1 and 5 years, from hospitals in Mexico. **Method:** A systematic review was carried out whose search focused on the survival of kidney transplant recipients. All publications found in PubMed and Google from 1963 to 2021 were included. The expectation-maximization algorithm was applied, proposing a mixture of normals, and hierarchical grouping to establish if there is any type of pattern and determine if there is a difference between the percentages of survival at 1 and 5 years between the groups formed. **Results:** Eight hospitals that published the survival of kidney transplant recipients were found. Survival rates ranged, at 1 year, from 94.7% to 100%, and at 5 years, from 85% to 96.2%. The methods used for their comparison indicated that there is a difference between survival at 1 and 5 years. **Conclusions:** In Mexico there is little information on the results of kidney transplant programs, and the information found shows great heterogeneity in said programs. Some strategies and actions are proposed to improve survival underreporting.

Keywords: Kidney transplant. Survival. Mexico.

Resumen

Objetivo: Conocer, analizar y comparar los programas de trasplante renal, considerando la supervivencia de los receptores a 1 y 5 años, en los hospitales en México. **Método:** Se realizó una revisión sistemática cuya búsqueda se centró en la supervivencia de los receptores de trasplante renal. Se incluyeron todas las publicaciones encontradas en PubMed y Google de 1963 a 2021. Se aplicó el algoritmo de expectation-maximization, proponiendo una mezcla de normales, y agrupamiento jerárquico para establecer si hay algún tipo de patrón y determinar si hay diferencia entre los porcentajes de supervivencia a 1 y 5 años entre los grupos formados. **Resultados:** Se encontraron ocho hospitales que publicaron la supervivencia de los receptores de trasplante renal. Los rangos de las tasas de supervivencia fueron, a 1 año, del 94.7% al 100%, y a los 5 años, del 85% al 96.2%. Los métodos empleados para su comparación indican que hay diferencia entre la supervivencia a 1 y 5 años. **Conclusiones:** En México se tiene poca información sobre los resultados de los programas de trasplante renal, y la información encontrada muestra gran heterogeneidad en dichos programas. Se proponen algunas estrategias y acciones para mejorar el subregistro de supervivencia.

Palabras clave: Trasplante Renal. Supervivencia. México.

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Date of reception: 17-03-2023

Date of acceptance: 13-05-2023

DOI: 10.24875/CIRUE.M23000597

Cir Cir (Eng). 2024;92(1):96-102

Contents available at PubMed

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Introduction

In Mexico, the first kidney transplant was performed in 1963 at the Mexican Social Security Institute (IMSS)¹. Since then, a total of 273 kidney transplant centers have been established, although only 122 of them are currently active. Currently, Mexico has a kidney transplant rate of 15.2 per million population (PMP), with a total of 58 668 kidney transplants performed from 1963 through 2021². As of October 7th, 2022, there is a waiting list for kidney transplants of 15 411 individuals³. The National Transplant Registry was established back in 1984, and since 2000, a decentralized body under the Federal Public Administration, the CENATRA (National Transplant Center), has been responsible for regulating, coordinating, supporting, and promoting actions related to organ and tissue transplantation in Mexico⁴. Although CENATRA designed a form back in 2015 for tracking transplant patients, only the 1-year follow-up data of 953 kidney transplant recipients has been reported until 2016, with a survival rate of only 33%⁵ of these patients. Subsequently, the National Transplant Registry Information System (SIRNT) was created, and from the second half of 2019, modules for reporting recipient and post-transplant graft survival were implemented in the SIRNT, which allowed for establishing information reporting obtained from monitoring their transplant recipient patients. However, as of February 3rd, 2022, only 1402 kidney transplant recipients had, at least, 1 survival report out of a total of 15 218 patients operated on from 2016 through 2021, representing information available for only 9.2% of patients transplanted during that time².

In general, all centers performing transplants consider the number of transplants performed as the main indicator of success. However, we should not dismiss that the only way to objectively know clinical success, and what kind of thing will eventually have an impact on the patients and their family, is the survival of the transplant recipient and the survival of the kidney graft; unfortunately, this information is not available from official sources, which is why we conducted this study to understand, analyze, and compare kidney transplant programs in hospitals in Mexico, considering the survival of kidney transplant recipients at 1 and 5 years.

Method

We conducted a systematic review on the survival of kidney transplant recipients in hospitals located in

Mexico. All publications found in PubMed and Google up to December 2021 were included. Studies that did not report the 1 and 5-year survival of kidney transplant recipients or did not use the Kaplan-Meier estimator of the survival function as a non-parametric analysis technique were excluded.

Data analysis was performed using R statistical software⁶. The analysis conducted was exploratory due to the lack of necessary individual data for estimating survival functions, as well as the variance of these estimates via the Kaplan-Meier estimator. Two clustering techniques were used to analyze reported estimate values. The first technique was used to analyze the change between the reported values for year 1 and 5. This involved considering a mix of normal distributions for these differences. The second technique was hierarchical clustering⁷.

Results

We found a total of 8 (6.5%) out of 122 hospitals active in kidney transplantation in Mexico that reported on the survival of kidney transplant recipients within their programs, with an overall 6545 kidney transplant recipients across these 8 hospitals. The mean number of transplants performed per hospital included in this study was 818, with a standard deviation (SD) of ± 677 and a range of 83 up to 1940 transplants performed. The mean period reported by these 8 hospitals was 17 years (SD, ± 13), ranging from 7 up to 24 years. The 1- and 5-year survival of patients reported in each of the 8 hospitals is shown in table 1.

The data analyzed are estimate values, according to the Kaplan-Meier method, of the survival function for 2 different time periods (1 and 5 years) reported in the publications included in this study⁸⁻¹⁵. We should mention that supplementary data was not found in the articles from which specific data for estimating the Kaplan-Meier survival function, such as patients at risk in each timeframe and censored patients, could be extracted. Therefore, the log-rank test—the most common technique for comparing survival curves—cannot be used. The log-rank test is, in fact, a chi-square technique that compares an observed parameter (sample survival curves) and an expected one (bringing all values into a single sample). The goal is to verify that each of these samples allows us to deduce that the differences between them are statistically significant or, on the contrary, can be attributed to chance.

Table 1. Survival of kidney transplant recipients per hospital

Hospital	No. of patients analyzed	Cumulative rate of patients currently alive		Period considered (years of follow-up)
		1 year	5 years	
UMA134 Unidad Médica de Alta Especialidad No. 134 del IMSS ₈	1940	100%	87%	1987-2011 (24 years)
CMN Centro Médico Nacional Siglo XXI ₉	1544	95%	91.8%	1991-2010 (19 years)
INCMNSZ Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán ₁₀	1000	94.9%	86.8%	1967-2011 (45 years)
HRAEB Hospital Regional de Alta Especialidad del Bajío ₁₁	837	95.4%	88.1%	2008-2016 (8 years)
IMT Instituto Mexicano de Trasplantes ₁₂	754	98.8%	96.2%	1999-2012 (13 years)
INCICH Instituto Nacional de Cardiología Ignacio Chávez ₁₃	292	95%	85%	2000-2007 (7 years)
HRAEV Hospital Regional de Alta Especialidad de Veracruz ₁₄	95	94.7%	85.2%	2006-2016 (10 years)
HUNL Hospital Universitario José E. González, Nuevo León ₁₅	83	98.8%	85.9%	2003-2011 (8 years)
Total	6545			

Therefore, as an alternative, we used an exploratory analysis of the reported estimate values for 1 and 5 years, as illustrated in figure 1. We should mention that these 2 values can be considered a rough approximation to the estimate survival function.

Based on the slope, we can see there are hospitals for which the values reported have similar variations; for example, the case of UMA134 and HUANL, or INCICH and HRAEB. To study the aforementioned, the slope of the line connecting the estimates is calculated. Considering that the point estimators of the survival function are asymptotically normal¹⁶, and that the slope is a linear transformation of 2 of these, a mixed model of Gaussian distributions⁷ is suggested to group hospitals based on their slope.

Figure 2 illustrates the density function adjusted using the expectation-maximization algorithm employing the library¹⁷. As we can see, in the case of the middle group, the estimate variance is large. With this, no pattern related to the number of participants in the study or the years in which it was conducted can be seen.

Therefore, hierarchical clustering was performed⁷, which consists of forming groups among data based on the distance between them. Figure 3 illustrates the

values of these data. This image can be considered an estimate of the position of hospitals based on their estimate survival function.

The size of the name in figure 3 is given by the following formula:

$$\frac{ns}{1000} + 0.05$$

where ns is the number of participants involved in the study. As we can see, although the number of study participants is similar across different hospitals, the value of estimates differs significantly. At least 3 types of records can be distinguished: those with high estimate values for both 1 and 5 years, those with high values for 1 year and low values for 5 years, and those with low values for both 1 and 5 years.

To study the existence of the mentioned groups, the hierarchical data clustering technique was used. This technique involves considering the progressive formation of groups, taking the distance between them as the criterion for union. The result obtained when using this technique is shown in figure 4. Since HRAEV and INCICH are the closest, these hospitals are grouped first. Subsequently, the HRAEB-INCMNSZ group is formed. The last group of 2 elements to form is HUANL-UMA134. Since the closest groups

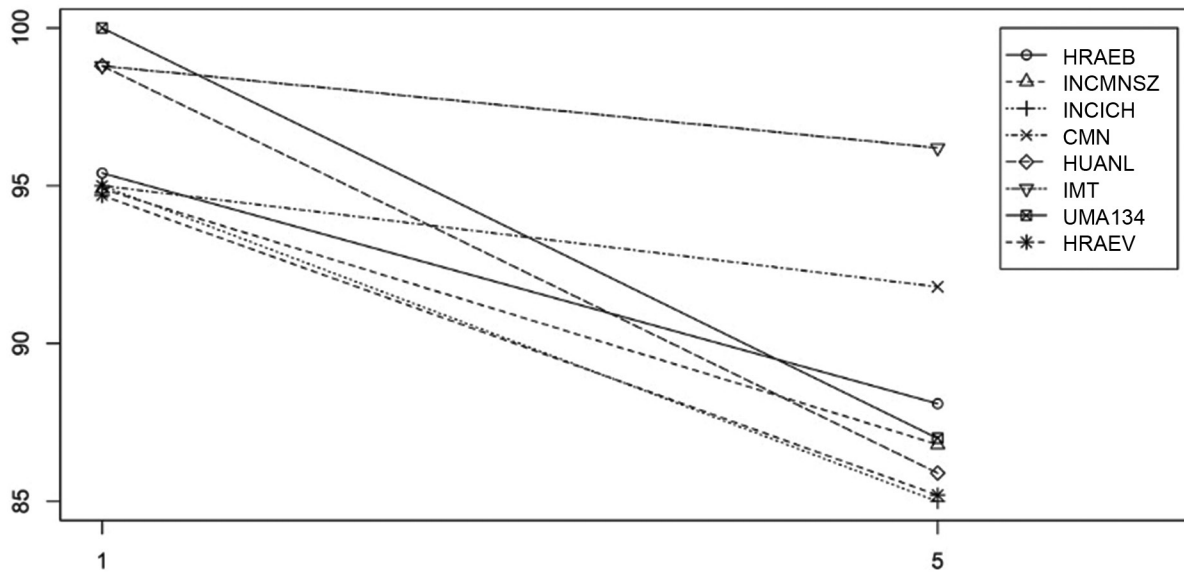


Figure 1. Estimated values reported for 1 and 5 years.

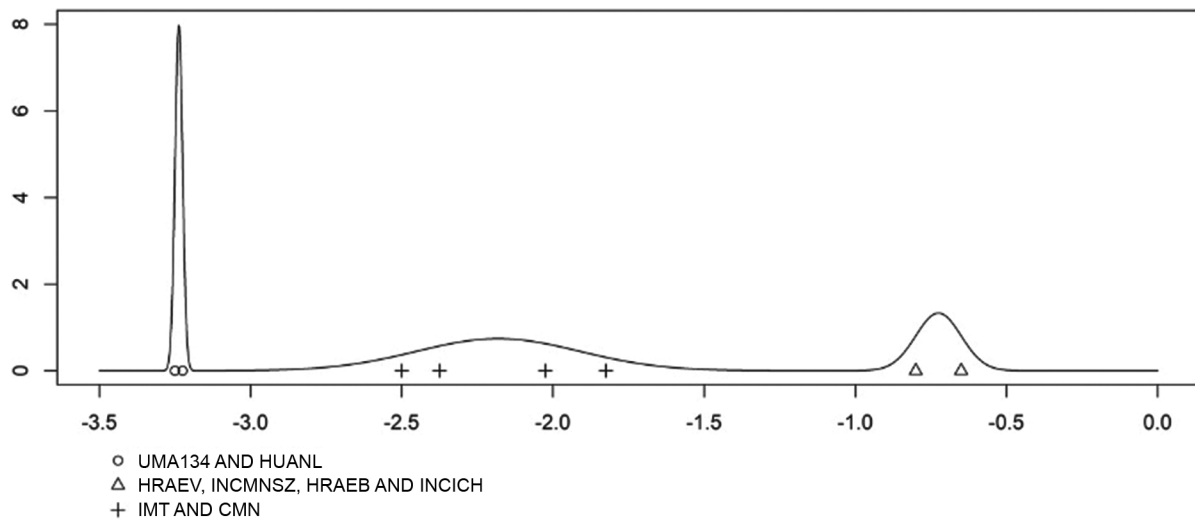


Figure 2. Density adjusted using the expectation-maximization algorithm.

are HRAEB-INCMNSZ and HRAEV-INCICH, the HRAEB-INCMNSZ-HRAEV-INCICH group is formed. Similarly, the other groups are formed by joining the closest ones.

Again, we should mention that the values of the variables associated with conducting the study do not seem to reveal any kind of pattern. This could be an indicator that there is, indeed, a real difference between the survival rates at 1 and 5 years among the formed groups. However, in the absence of complete data for the patients considered, a standard hypothesis test to

study the difference between the reported values could not be performed.

Discussion

The results found in the 8 articles published on survival in kidney transplant recipients in hospitals located in Mexico included in this study⁸⁻¹⁵ show a great heterogeneity in the activity of kidney transplant programs, with a mean number of transplants per hospital of 818, a standard deviation of ± 677 , and a range of

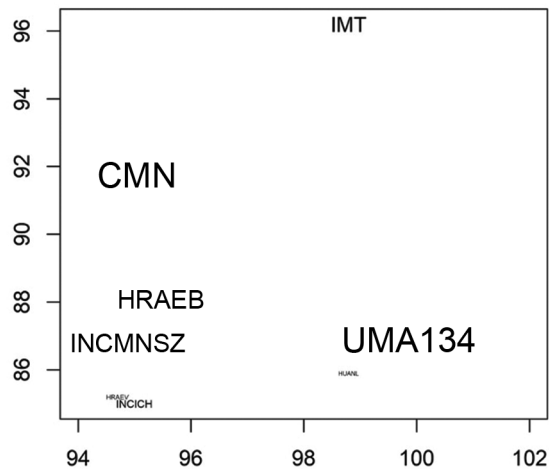


Figure 3. Position of hospitals based on their estimated survival function.

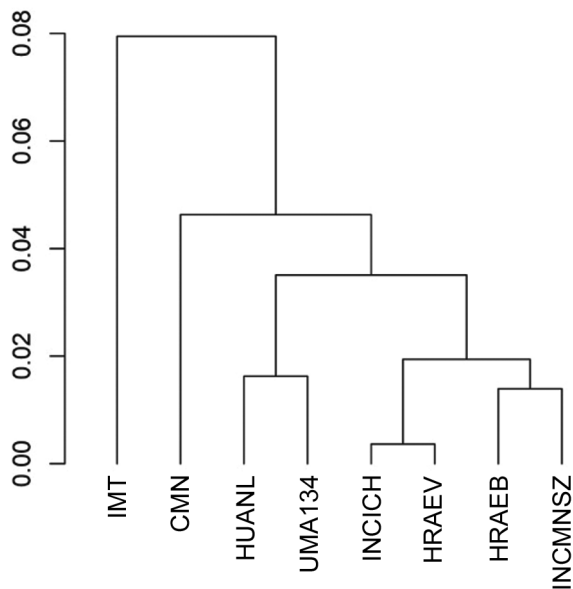


Figure 4. Hierarchical clustering.

83 to 1940, as well as in the periods considered in each publication, with a mean 17 years, a standard deviation of ± 13 , and a range of 7 to 24 years. All hospitals included in this study reported the survival of kidney transplant recipients from 1967 through 2016, when the cumulative number of transplant recipients in Mexico was 46 495. Therefore, this study only shows the survival of 14.07% (6545 recipients out of 46 495), and if we added the number of kidney transplant recipients reported by the SIRNT from 2016 through 2021 (1402 recipients), we would unfortunately

have follow-up data for only 13.54% (7947 recipients out of 58 668).

The ranges of survival rates for kidney transplant recipients in the hospitals included in this study went from 94.7% to 100% (at 1 year), and from 85% to 96.2% (at 5 years), which at first glance shows differences. However, it is necessary to conduct a survival analysis and use a statistical comparison technique.

Survival analysis is an inferential technique whose essential aim is to model the time elapsed until a certain event occurs¹⁸. In the case of kidney transplants, this event, when talking about the survival of recipients, is death.

In survival analysis, the sample consists of following a series of individuals from the beginning of the study until the end of it, and in a situation like this, it is common for some of these individuals who enter the study to disappear. It is also possible that, when an individual enters the study, it ends before the event we are trying to detect even occurs. Although these are 2 isolated events, in practice, they are the same. In statistics, these individuals are referred to as "censored"¹⁸.

A censored data point represents an individual who disappears. We had this patient but he/she has been lost before the event we are analyzing even occurs, either because the patient has been lost from the study or because the study has ended, and the event never occurred. A censored data point is not a data point that does not provide information. In fact, it does, but partially. Disregarding it outright would be wasting information, and that, in statistics, is not good¹⁸.

Since the Kaplan-Meier estimator of the survival function is based on the times at which patients' deaths occurred and all those patients who were in the study at that time, this involves the number of censored patients (those who are lost to follow-up). Therefore, this type of data certainly needs to be reported, as with them it is possible to calculate the standard errors in the estimates, which in turn allows for a deeper statistical analysis; it is even advisable to construct confidence intervals for the estimate survival function¹⁹.

The most common technique for comparing survival curves is the log-rank test. This is, in fact, a chi-square technique where a comparison is drawn between an observed parameter (the sample survival curves) and an expected one (bringing together all the values into a single sample)¹⁹. Since the publications found in this study on the survival of kidney transplant recipients do not provide the number of censored

patients, or have complete databases, this comparison with the log-rank test cannot be drawn. Therefore, we used 2 clustering techniques to analyze the reported estimated values, finding differences in survival across different hospitals. However, we should mention that no standard tests have become available to measure the statistical significance of these differences when applying clustering techniques, as it is currently a topic of research in statistics²⁰.

Finding differences in the survival of kidney transplant recipients in the hospitals included in this study has important implications: 1) the possibility of knowing the effectiveness of kidney transplantation in each of the hospitals to improve their results, and 2) the possibility of knowing the evolution of kidney transplant programs to support their development and strengthen them.

The inefficiency and ineffectiveness of the SIRNT are exposed since after 2 and a half years, there were only 1402 kidney transplant recipients available, with, at least, 1 survival report, out of a total of 15 218 transplanted patients from 2016 through 2021, that is, we had post-kidney transplant information from only 9.2% of the patients from that period², with the limitation of not being able to construct survival curves with that information. This should encourage government and institutional authorities to keep a record not only from the traditional perspective of the number of transplants performed but also from the responsibility of keeping a follow-up of kidney transplant recipients to estimate their survival and evaluate the results of kidney transplant programs.

Underregistration of survival among renal transplant recipients can be attributed to several factors, among which the following are the primary ones:

- Lack of a legal framework mandating the reporting of kidney transplant recipient survival.
- A fragmented health care system (including the Ministry of Health, IMSS, ISSSTE, PEMEX, SEDENA, and state health services) lacking intercommunication.
- Health care service collapse, leading to patients being transplanted in tertiary care centers and then being transferred to second-level hospitals for follow-up 1 year after transplantation.
- This overload also makes patients in need for a renal transplant have to migrate between sectors, seeking faster transplantation and returning to their original health insurance provider for immunosuppressant drugs.

Knowing these factors, we can propose the following strategies and actions to improve the registration of renal transplant recipient survival:

- Establishing a legal framework mandating the registration and reporting of renal transplant recipient survival:
 - Adding to the General Health Act, “Article 338.- The National Transplant Center shall be responsible for the National Transplant Registry, which shall integrate and keep updated the following information,” an additional section that could state “VI. The survival of organ transplant recipients”.
 - Amending the Regulations of the General Health Act on Transplants, “Article 33.- The Internal Transplant Committees, in addition to those provided for by the Law, shall have the following functions:.. XI Evaluate the results of the Transplant Programs available at the Health Establishment,” it would need to be more specific too: “XI Evaluate the results of the Transplant Programs available at the Health Establishment, through the number of transplants performed, morbidity, mortality, and the survival of transplant recipients”.
 - Adding to the Regulations of the General Health Act on Transplants, “Article 62. The integration, management, and updating of information from the National Transplant Registry, in addition to complying with the provisions established by the Federal Law on Transparency and Access to Government Public Information, shall be subject to the following:”, an additional section that could state: “The health authority of the Health Establishment where a transplant will be performed must record the survival of organ transplant recipients”.
- To improve communication between different health services, and taking advantage of the infrastructure of CENATRA, namely the SIRNT, both transplanting centers and hospitals providing follow-up care should have access to the database of all kidney transplant recipients in Mexico. This way, the patient, even if changing sectors or hospitals, would have their follow-up and specifically their survival recorded.

Conclusions

The information gathered on renal transplant programs in hospitals located in Mexico demonstrates

significant heterogeneity, both in the number of transplants performed per hospital and in recipient survival. To comprehensively assess the results of renal transplant programs in Mexico, it is important to include not only the number of transplants performed per hospital but also recipient and graft survival. However, in Mexico, there is limited information on the follow-up of renal transplant recipients: only 13.54% of the total accumulated. This needs strategies and actions to understand the survival of a greater number of recipients, as it is a useful tool for evaluating the effectiveness of various renal transplant programs. Such strategies and actions would include: 1) establishing a legal framework mandating the reporting of transplant recipient survival, and 2) improving intercommunication among centers using the SIRNT.

When analyzing the data, this study identified differences in reported survivals, but due to incomplete databases and the number of censored patients, the differences found may not be as reliable as if the log-rank test had been applied.

Funding

None declared.

Conflicts of interest

None declared.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained approval from the Ethics Committee for analysis and publication of routinely acquired

clinical data and informed consent was not required for this retrospective observational study.

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