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Analysis of post-transplant renal graft survival

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Abstract

Introduction: Post renal transplant patients have a survival mean lower than the general population. This survival decreases more when it is related to graft failure. This paper aims to identify the contribution of risk factors to graft loss.

Materials and methods: Retrospective Cohort Study of post renal transplantation; the general characteristics of the patients were described; the RR (Risk ratio) was calculated for the risk of graft lost ($p < 0.05$) and survival differences were explored through Kapplan Meier diagrams.

Results: 164 cases were analyzed; the median age was 48 years; weight was 68 kg, creatinine clearance a year from transplant was 57.17 mg/dl; overall graft survival at 5 years was 88.4%, and 92.1% for patients. Risk ratio (RR) of graft loss in those who experienced rejection in the first year was 3.86; ($p = 0.002$). Significant differences in graft survival at five years in patients older than fifty years vs patients younger than fifty years (96.8 vs 83.2%, respectively) were found. The extent of these differences was the same after 70 months (5.8 years).

Conclusions: The contribution of pre-transplant risk factors to graft loss were identified, having age as the single associated factor, as this is lower in patients older than 50 years. Given these results, a closer monitoring of patients younger than 50 years is recommended until the fifth year after transplantation.

Key words: Disease-free survival, Graft rejection/Epidemiology, Graft rejection, Medical Care Statistics (MeSHsource).

Análisis de supervivencia del injerto post-trasplante renal

Resumen

Introducción: Los pacientes post trasplante renal presentan una Supervivencia media inferior a la de población general, esta supervivencia se disminuye más cuando está relacionada con pérdida del injerto; se pretende identificar la contribución de los factores de riesgo con la pérdida del injerto.

Materiales y métodos: Estudio de Cohorte retrospectiva post-trasplante renal; se describieron las características generales de los pacientes; se calculó el RR (Riesgo relativo) para el riesgo de pérdida del injerto ($p<0,05$) y se exploraron diferencias de supervivencia en diagramas de Kapplan Meier.

Resultados: Se analizaron 164 casos; la mediana de edad fue de 48 años; de peso fue 68 kg, de depuración

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de creatinina al año del trasplante de 57,17 mg/dl; la supervivencia global del injerto a 5 años fue del 88,4% y la de los pacientes del 92,1%.

El Riesgo relativo (RR) de pérdida del injerto en quienes presentaron rechazo en el primer año fue de 3,86; (p = 0,002).

Se encontraron diferencias significativas en la supervivencia del injerto a cinco años en pacientes mayores vs menores de cincuenta años de edad (96,8 vs 83,2 % respectivamente), la amplitud de estas diferencias se igualó posterior a los 70 meses (5,8 años).

Conclusiones: Se identificó la contribución de los factores de riesgo pretrasplante con la pérdida del injerto; encontrando a la edad como el único factor relacionado; siendo esta menor en mayores de 50 años.

Según los resultados, se sugiererealizar seguimientos más estrechosa los menores de 50 años hasta el quinto año del trasplante.

Palabras clave: Supervivencia libre de enfermedad, Rechazo del injerto / epidemiología, Rechazo de Injerto, Estadísticas de Atención Médica (fuente DeCS).

Introduction

Chronic kidney disease is a public health problem worldwide, and is associated with increased risk of cardiovascular, bone, disease; metabolic, nutritional and infectious disorders; and increased mortality. More than 40% of dialysis patients die as a result of cardiovascular disease[1-3]. Kidney transplantation is the treatment of choice in these patients, as it offers improved survival and quality of life, compared to dialysis[4,5].

This study aims to describe the relationship between risk factors and graft loss in the last 5 years in patients with renal transplantation (2009-2014 period) from Shaio Clinic Foundation.

Materials and methods

A retrospective cohort was analyzed. Data were extracted from the admission and monitoring database of the cohort of renal transplant and exported to SPSS V.22.0 statistical software. The general characteristics of the patients were described. Qualitative variables were presented as absolute and relative frequencies, and quantitative ones were presented with medium and interquartile ranges. Risk ratio for graft loss of qualitative variables was explored through crosstabs and chi square analysis, and the difference in means of quantitative variables was analyzed through Student's t test for independent samples; all of them at a confidence level of 95%.

With the data obtained, differences in graft survival were explored with Kapplan Meier diagrams, and contrast of values through the use of the Log-Rank test (Mantel Cox) for the difference in survival by subgroups, for a value of $p < 0.05$ for the presence of differences (two-tailed).

Results

164 cases of renal transplantation were reviewed. Median age was 48 years (interquartile range (IQR): 35-55 years); median weight was 68 kg (IQR: 60-73 kg); creatinine clearance a year after transplant, determined through Cockroft Gault method, was 57.17 mg/dl (IQR: 44.53 to 68.79); median monitoring time for graft survival was of 42.29 months (IQR: 17.78 to 61.65 months), with an overall graft survival of 88.4% at 5 years; median monitoring time for patient survival was 46.68 months (IQR: 23.47 to 64.75 months) with a 92.1% overall survival at 5 years (Table 1).

In patients who experienced rejection in the first year, the relative risk (RR) of graft loss was 3.86; (P = 0.002); no significant differences for other risks in connection with graft loss were found (Table 2).

Graft survival at five years in Kapplan Meier curves showed significant differences (p= 0.014) compared by age (Mantel-Cox Log Rank) in older vs younger than fifty years (96.8 vs 83.2%, respectively), the extent of these differences was equalized after 70 months (5.8 years) (Figure 1).

Table 1.

General characteristics (quantitative variables)		
Variable	**Count**	**Median (p25-p75)**
Age	164	48 (35 ; 55,75)
Weight	94	68 (60 ; 73)0
Monitoring time, graft survival (months)	164	42,29 (17,78 ; 61,65)
Monitoring time, patient survival (months)	164	46,68 (23,47 ; 64,75)
Cockroft Gault	53	57,170 (44,503 ; 68,795)
Graft survival at 5 years = 88.4%		
Patient survival at 5 years = 92.1%		

Table 2.

General characteristics of patients (qualitative variables)

Risk factor	Graft loss	Total	RR	P value
	Yes (%)	No (%)		
Rejection in the first year	9(5,5)	22(13,4)	31(18,9)	3,86 (8,7 ; 1,72)	0,002
Opportunistic infection in the first year	3(1,8)	26(15,9)	29(17,7)	0,87 (2,8 ; 0,27)	0,557
Postoperative complications in the first year	2(1,2)	11(6,7)	13(7,9)	1,37 (5,29 ; 0,35)	0,46
Immunological complications in the first year	3(1,8)	10(6,1)	13(7,9)	2,18 (6,49 ; 0,73)	0,178
Sex Male	13(7,9)	97(59,1)	110(67,1)	0,94 (2,34 ; 0,38)	0,559
Donor Deceased	16(9,8)	123(75)	139(84,8)	0,96 (3,05 ; 0,3)	0,582
Cytotoxic antibodies	1(1,7)	1(1,7)	2(3,3)	5,81 (29,41 ; 1,15)	0,192
HBcAG IgG	1(1,7)	5(8,3)	6(10)	1,8 (12,99 ; 0,25)	0,484
CMV IgG	6(10)	50(83,3)	56(93,3)	*	*

N= 164 patients; *not calculated data (subgroups with under 5 members); CMV IgG: cytomegalovirus immunoglobulin G; HBcAG IgG: Immunoglobulin G for Core antigens for hepatitis B virus

Discussion

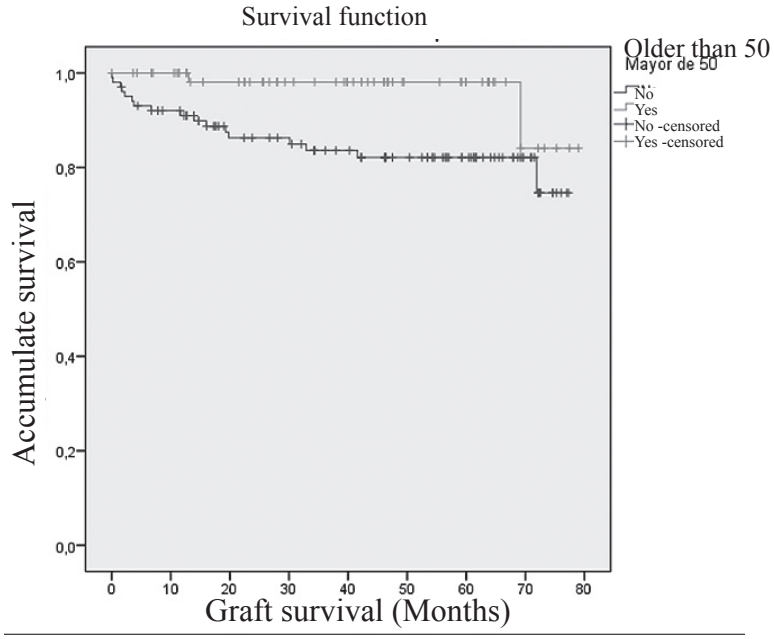
A descriptive study was conducted to a cohort of renal transplant patients, risk factors for graft loss were explored and survival rates among risk factors which implied significant differences were compared.

None of the patients in the cohort proved positive for HIV, VDRL, HBsAg, HBcAg IgM, HCV or CMV IgM as an antecedent to transplant.

The incidence of rejection during the first year reported in this cohort was lower than that reported by other studies (18.9%), which explains the high rate of graft survival in our patients to 5 years (88.4%)[6-8].

Figure 1.

Graft survival in patients older and younger than 50 years.



Older than 50	Total N	Events N	Censored N	Log Rank (Mantel-Cox)
No	101	17	84 (0,832)	0,0143
Yes	63	2	61 (0,968)	
Global	164	19	145 (0,884)	

Test of equality of survival distributions for different levels of Older than 50.

Table 3.

Characteristics of patients who experienced graft loss (quantitative variables)

Variable (CI 95%)	Difference in means P Value	
Monitoring time, Draft surviaval (Months)	-24,62 (-35,34 ; -13,9)	0,000
Monitoring time, Patient survival (Months)	5,51 (-8,57 ; 19,59)	0,213
Class I antibodies reactivity percentage	26% (-17% ; 69%)	0,092
Class II antibodies reactivity percentage	25% (-23% ; 72%)	0,122
Age	-7,72 (-14,18 ; -1,26)	0,010

The overall rate of graft loss was similar to that reported by other cohorts[9].

In the study by Campbell SB in 2013, higher patient survival times and graft survival in the case of living donor were found[10,11]. In this study, graft loss among living-donor and deceased-donor groups showed no significant difference (p <0.582).

Acute cytomegalovirus (CMV) in post-renal transplant patients has been linked with a cytopathic effect on glomerular and tubular epithelial cells, with impaired adhesion and inflammation molecules, resulting in interstitial nephritis, which explains the lower graft survival on the long term[12]. An anti-viral prophylaxis program in seronegative patients reduces the incidence of this infection after transplantation and the risk of graft loss[13]. In this study, there were limitations in the sample size to explore associations by subgroup, presenting a concluding association of CMV and graft loss.

The median glomerular filtration rate (Crockoft-Gault) one year after transplantation was similar to that reported in other studies[14].

No neoplasia was observed during the monitoring time of this cohort.

The limitations of this study correspond with cohort studies, exposure was not assigned randomly. Therefore, it does not necessarily prove causality. One strength is that we count on data from the close monitoring of patients, and for this reason, losses were not a drawback. Moreover, given the size of the series, comparisons among subgroups were able to be conducted.

Conclusions

The contribution of pre-transplant risk factors to graft loss was identified; finding age as the only associated factor; as this is lower in patients older than 50 years.

The results recommend a closer monitoring to under 50 years until the fifth year after transplantation (after this time the risk was shown to be similar for the entire population).

Interest Conflict

The authors declare no conflict of interest.

Bibliographical references

1. Jha V, Wang AYM, Wang H. The impact of CKD identification in large countries: The burden of illness. Nephrology Dialysis Transplantation. 2012.
2. Jha V, Modi GK. Cardiovascular disease: The price of a QALY-cost-effectiveness of statins in CKD. Nat Rev Nephrol. 2013;1–2.
3. Jha V, García-García G, Iseki K, Li Z, Naicker S, Plattner B, et al. Chronic kidney disease: global dimension and perspectives. Lancet. 2013;382(1474-547X (Electronic)):260–72.
4. Wolfe RA, Ashby VB, Milford EL, Ojo AO, Ettenger RE, Agodoa LY, et al. Comparison of mortality in all patients on dialysis, patients on dialysis awaiting transplantation, and recipients of a first cadaveric transplant. N Engl J Med. 1999;341(23):1725–30.
5. Laupacis A, Keown P, Pus N, Krueger H, Ferguson B, Wong C, et al. A study of the quality of life and cost-utility of renal transplantation. Kidney Int. 1996;50(1):235–42.
6. Hamida F Ben, Barbouch S, Bardi R, Helal I, Kaaroud H, Fatma L Ben, et al. Acute rejection episodes after kidney transplantation. Saudi J Kidney Dis Transpl. 2009;20(3):370–4.
7. de Fijter JW, Mallat MJ, Doxiadis II, Ringers J, Rosendaal FR, Claas FH, et al. Increased immunogenicity and cause of

graft loss of old donor kidneys. J Am Soc Nephrol. 2001;12(7):1538–46.

8. Shin M, Park JB, Kwon CHD, Joh JW, Lee SK, Kim SJ. Enhanced significance of donor-recipient age gradient as a prognostic factor of graft outcome in living donor kidney transplantation. World J Surg. 2013;37(7):1718–26.

9. Morales JM, Marcén R, del Castillo D, Andrés A, González-Molina M, Oppenheimer F, et al. Risk factors for graft loss and mortality after renal transplantation according to recipient age: a prospective multicentre study. Nephrol Dial Transplant [Internet]. 2012;27(suppl_4):39–46. Available from: http://ndtoxfordjournalsorg/content/27/suppl_4/iv39.full

10. Campbell SB, Hothersall E, Preston J, Brown AM, Hawley CM, Wall D, et al. Frequency and severity of acute rejection in live- versus cadaveric-donor renal transplants. Transplantation. 2003;76(10):1452–7.

11. Eghlim N, Behzad E, Lesan PM, Vahid P, Reza FM. Does Kidney Transplantation with deceased or living donor affect graft survival? Nephro Urol Mon. 2014;6(4): e12182.

12. Cainelli F, Vento S. Infections and solid organ transplant rejection: A cause-and-effect relationship? Lancet Infectious Diseases. 2002. p. 539–49.

13. Fernández-Ruiz M, Arias M, Campistol JM, Navarro D, Gómez-Huertas E, Gómez-Márquez G, et al. CMV prevention strategies in seropositive kidney transplant recipients: an insight into current clinical practice. Transpl Int. 2015;28(9):1042–54.

14. Ayub S, Zafar MN, Aziz T, Iqbal T, Khan S, Rizvi SAH. Evaluation of renal function by cystatin C in renal transplant recipients. Exp Clin Transplant. 2014 Feb;12(1):37–40.