

Study of graft survival rates of renal transplants in Cairo University Hospitals

Mohamed G. Saadi, Sahier O. El-Khashab, Rabab M.A. Mahmoud

Department of Internal Medicine and Nephrology, Kasr Al-Aini School of Medicine, Cairo University, Cairo, Egypt

Correspondence to Rabab M.A. Mahmoud, MD, Department of Internal Medicine and Nephrology, Kasr Al-Aini School of Medicine, Cairo University, Cairo, Egypt;
Tel: +20 106 013 9196;
e-mail: ruby_mahmoud_555@yahoo.com

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Background

Many factors and events can complicate the outcome of renal transplantation and can eventually lead to progressive renal dysfunction and graft failure. We aimed in this study to identify the risk factors for the entire course after transplantation, and then to analyze the relative impact of these risk factors on short-term and long-term graft survival in our patients.

Patients and methods

This analytical retrospective study was conducted at the King Fahd Unit, the Faculty of Medicine, Cairo University, on 104 patients for the study of 1-year graft survival, though 43 patients were followed-up for 3 years for the study of 3-year graft survival. Serum creatinine was used to evaluate the renal function; graft dysfunction was defined as serum creatinine more than 2.5 mg/dl. Survival analysis was carried out by using the Kaplan–Meier survival curve estimation. To predict the value of graft survival after 5 years, regression analysis was used.

Results

In our study, the overall graft survival rates were 88.6 and 76.7% at 1 and 3 years, respectively. The corresponding overall patient survival rates were 89.4 and 79.1% at the first and third years after transplant. Our study showed that among the long list of predictors for graft outcome variables, factors that had a significant impact on outcome by Kaplan–Meier analysis included donor's age, primary immunosuppression, and serum creatinine 1 month after transplant. There was a greater rate of graft dysfunction with the presence of hypertension and hepatitis C virus but these results did not reach statistically significant values.

Conclusion

Old donor's age, primary immunosuppression, and serum creatinine 1 month after transplant are the most effective factors on graft survival in kidney transplantation. Whatever the cause, graft dysfunction should be treated early and aggressively.

Keywords:

Cairo University Hospitals, graft survival, kidney transplantation

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Introduction

Kidney transplantation is the most desired and cost-effective modality of renal replacement therapy for patients with irreversible chronic kidney failure [1].

The quality of life of transplant patients with good biochemical control was clearly better than that of chronic dialysis patients [2].

Epidemiologic studies have shown that renal allograft survival is associated with a large number of risk factors, such as donor or recipient age, sex, and race, or comorbid conditions, type of donor (living vs. cadaver), and the presence of delayed graft function or acute rejection. Moreover, renal function is also a major determinant of patient survival. Thus, it has been suggested that strategies to improve renal function after transplantation may contribute to increased patient and allograft survival [3].

We aimed to identify the risk factors for the entire course of renal transplantation, and then analyzed the

relative impact of these risk factors on the probability of graft loss.

Patients and methods

This retrospective study was conducted at the King Fahd Unit, Faculty of Medicine, Cairo University. This protocol was approved by local ethical committee.

For evaluating 1-year graft survival rates we studied 104 patients and for evaluating 3-year graft survival rates we studied 43 patients.

In our study, serum creatinine was used to evaluate the renal function; graft dysfunction was defined as serum creatinine more than 2.5 mg/dl.

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The following variables were recorded for each patient.

- (1) Demographic data.
- (2) History taking and clinical examination.
- (3) Immunosuppressive medications.
- (4) Assessment of renal graft functions by serial measurement of serum creatinine during the follow-up period.

Statistical analysis

Statistical package for social science, version 9.0 was used for data analysis. Data were summarized as mean, SD, and percentage. Nonparametric test (Mann–Whitney *U*) was used for the analysis of two independent variables as data was not symmetrically distributed. The χ^2 -test was used for the analysis of qualitative data. Survival analysis was carried out by using the Kaplan–Meier survival curve estimation. Statistical significance was judged at the two-sided 0.05 levels. To predict the value of graft survival after 5 years, the regression analysis was used.

All the parameters are significant at 5% significance level. R^2 is an indicator of the goodness of fit for the line.

Results

The 1-year graft survival rate was 88.6% in 104 patients and the 3-year graft survival rate was 76.7% in 43 patients (Table 1).

To predict the value of projected graft survival after 5 years in those patients, the regression analysis was used; this means that the graft survival after 5 years will be 60.5% (Fig. 1).

The corresponding overall patient survival rates were 89.4 and 79.1% at the first and third post-transplant years (Table 2).

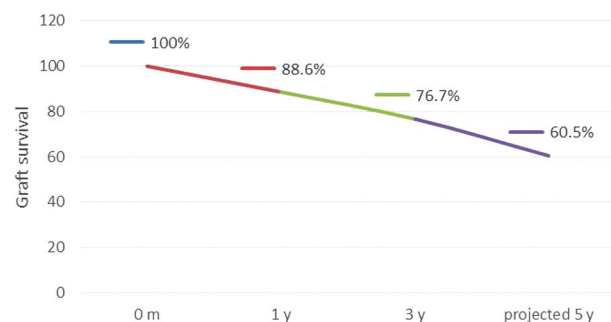
The Kaplan–Meier analysis identified several factors that may affect graft survival. As regards recipient's age, there was no statistically significant difference as

the 1-year graft survival rates for various age groups (<10, 10–18, 19–30, 31–40, and 41–50 years) were 100, 77.3, 80, 73.4, and 85.7%, respectively ($P=0.9$).

Three-year graft survival rates for various age groups (<10, 10–18, 19–30, 31–40, and 41–50 years) were 100, 82.4, 70, 55.6, and 100%, respectively ($P=0.4$).

As shown in Tables 3 and 4 and Fig. 2, graft survival showed a tendency to be lower in the older donor age groups, as the 1-year graft survival rates for various age groups (21–30, 31–40, 41–50, and 51–60 years) were 81.5, 79.6, 76, and 75%, respectively. Yet, this result did not reach statistical significance. For 3-year graft survival, there was a statistically significant difference regarding donor age: it was 0% in the donor age group older than 50 years ($P=0.01$).

Figure 1



Graft survival in King Fahd Unit at 1, 3, and 5 years.

Table 1 Overall graft survival rates after 1 and 3 years in King Fahd Unit

Variables	1 year (N=104) [n (%)]	3 years (N=43) [n (%)]
Functioning graft	92 (88.6)	33 (76.7)
Graft dysfunction	12 (11.4)	10 (23.3)

Table 2 Overall patient's survival rates after 1 and 3 years in King Fahd Unit

Variables	1 year (N=104) [n (%)]	3 years (N=43) [n (%)]
Alive patients	93 (89.4)	34 (79.1)
Dead patients	11 (10.5)	9 (20.9)

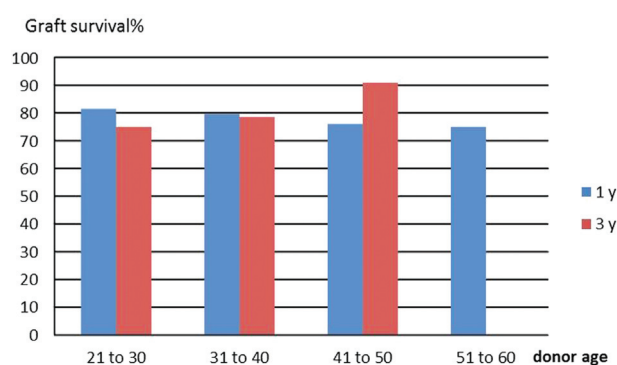
Table 3 Survival analysis (1 year) by the Kaplan–Meier test in relation to donor's age group

Variables	21–30 years	31–40 years	41–50 years	51–60 years
Total number	27	44	25	8
Number of dysfunctioning grafts	5	9	6	2
Number of functioning	22	35	19	6
Percentage of functioning	81.48	79.55	76	75
Survival time				
Mean	0.97	0.90	0.89	0.89
SE	0.04	0.05	0.07	0.15
95% confidence interval	0.89–1.04	0.81–0.99	0.76–1.02	0.60–1.18

Log rank=0.71. $P=0.9$.

Table 4 Survival analysis (3 years) by the Kaplan–Meier test in relation to donor's age group

Variables	21–30 years	31–40 years	41–50 years	51–60 years
Total number	16	14	11	2
Number of dysfunctional grafts	4	3	1	2
Number of functioning	12	11	10	0
Percentage of functioning	75	78.57	90.91	0
Survival time				
Mean	2.88	2.64	2.82	1.55
SE	0.14	0.29	0.17	1.45
95% confidence interval	0.15–2.60	2.06–3.21	2.48–3.16	0–4.39

Log rank=11.38. $P=0.01$.**Figure 2**

Graft survival in relation to donor's age.

Table 5 Survival analysis (1 year) by Kaplan–Meier test in relation to recipient's sex

Variables	Males	Females
Total number	77	27
Number of dysfunctional grafts	17	5
Number of functioning	60	22
Percentage of functioning	77.92	81.48
Survival time		
Mean	0.91	0.93
SE	0.03	0.05
95% confidence interval	0.84–0.97	0.83–1.03

Log rank=0.18. $P=0.7$.

As shown in Tables 5 and 6, male recipients had an inferior 1-year graft survival rates compared with female recipients. Whereas female recipients had an inferior 3-year graft survival rates compared with male recipients. Yet, these results did not reach statistical significance.

As regards donor's sex, male donors had an inferior 1- and 3-year graft survival rates compared with female donors. Yet, this result did not reach statistical significance (Tables 7 and 8).

As shown in Tables 9 and 10, an increasing number of HLA and DR loci mismatches did not significantly lower graft survival rates in kidney transplantation. Yet, these results did not reach statistical significance.

Table 6 Survival analysis (3 years) by the Kaplan–Meier test in relation to recipient's sex

Variables	Males	Females
Total number	29	14
Number of dysfunctional grafts	5	5
Number of functioning	24	9
Percentage of functioning	82.76	64.29
Survival time		
Mean	2.79	2.59
SE	0.13	0.30
95% confidence interval	2.53–3.04	1.99–3.18

Log rank=1.67. $P=0.2$.**Table 7 Survival analysis (1 year) by the Kaplan–Meier test in relation to donor's sex**

Variables	Males	Females
Total number	45	59
Number of dysfunctional grafts	10	12
Number of functioning	35	47
Percentage of functioning	77.78	79.66
Survival time		
Mean	0.92	0.91
SE	0.04	0.04
95% confidence interval	0.84–1.0	0.84–0.98

Log rank=0.03. $P=0.9$.**Table 8 Survival analysis (3 years) by the Kaplan–Meier test in relation to donor's sex**

Variables	Males	Females
Total number	19	24
Number of dysfunctional grafts	6	4
Number of functioning	13	20
Percentage of functioning	68.42	83.33
Survival time		
Mean	2.79	2.67
SE	0.15	0.21
95% confidence interval	2.49–3.09	2.26–3.08

Log rank=0.85. $P=0.4$.

There was no statistically significant difference regarding consanguinity, as unrelated donor transplants exhibited a high graft survival rate similar to the outcome of related donor transplants (Fig. 3).

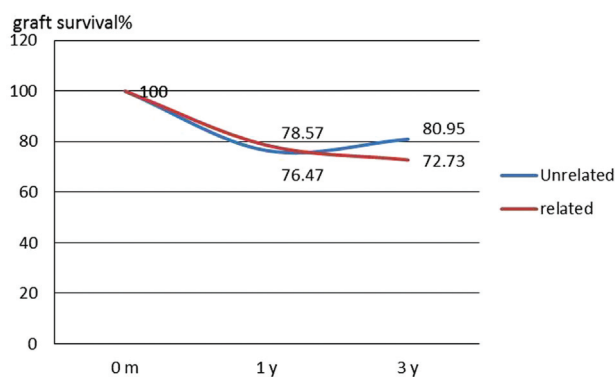
Figures 4 and 5 shows that, there was a greater rate of graft dysfunction with the presence of hypertension

Table 9 Survival analysis (1 year) by the Kaplan–Meier test in relation to HLA and DR mismatching between recipients and donors

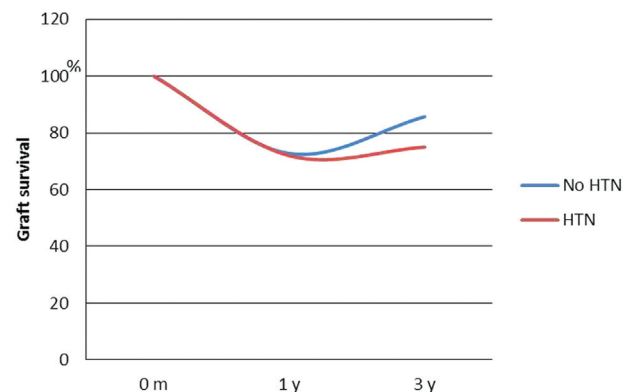
Variables	Zero mismatch	One mismatch	Two mismatch	Three mismatch	Four mismatch
Total number	17	40	37	8	2
Number of dysfunctioning grafts	4	9	6	3	0
Number of functioning	13	31	31	5	2
Percentage of functioning	76.47	77.50	83.78	62.50	100
Survival time					
Mean	0.95	0.87	0.98	0.78	–
SE	0.06	0.05	0.03	0.17	–
95% confidence interval	0.83–1.06	0.76–0.97	0.92–1.03	0.44–1.11	–

Log rank=2.84. $P=0.4$.**Table 10 Survival analysis (3 years) by the Kaplan–Meier test in relation to mismatch of HLA and DR between recipients and donors**

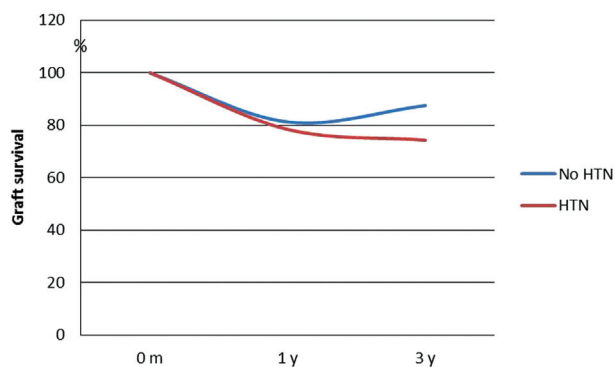
Variables	Zero mismatch	One mismatch	Two mismatch	Three mismatch	Four mismatch
Total number	5	19	17	1	1
Number of dysfunctioning grafts	1	6	3	0	0
Number of functioning	4	13	14	1	1
Percentage of functioning	80	68.42	82.35	100	100
Survival time					
Mean	3	2.5	2.83	–	–
SE	0	0.24	0.20	–	–
95% confidence interval	3.0–3.0	2.04–2.98	2.43–3.23	–	–

Log rank=1.99. $P=0.7$.**Figure 3**

Graft survival in relation to consanguinity.

Figure 4

Graft survival in relation to HTN before transplantation. HTN, hypertension.

Figure 5

Graft survival in relation to HTN after transplantation. HTN, hypertension.

(HTN). However, this result did not reach statistical significance.

One-year graft survival rate for HTN patients before transplantation was 71.95% compared with 72.73% for non-HTN patients. Whereas 1-year graft survival rate for HTN patients after transplantation was 78.41% compared with 81.25% for non-HTN patients.

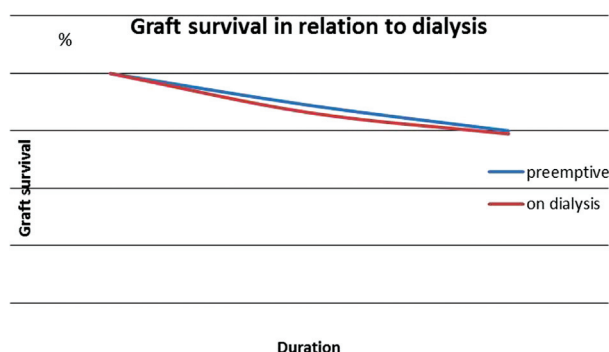
The 3-year graft survival rate for HTN patients before transplantation was 75% compared with 85.7% for non-HTN patients. Whereas the 3-year graft survival rate for HTN patients after transplantation was 74.29% compared with 87.5% for non-HTN patients.

The results show that hepatitis C virus (HCV)-positive patients can be transplanted with the success close to that of HCV-negative patients, although there is a tendency to better outcome in HCV-negative patients. Yet, this result did not reach statistical significance. Graft survival rates in HCV-positive and HCV-negative patients of living kidney were 66.7 and 80% at 1-year after transplant, respectively (Table 11).

As shown in Fig. 6, preemptive patients had a tendency to have better outcome. Yet, this result did not reach statistical significance. Graft survival rates in preemptive transplants and transplants performed after initiation of dialysis of living kidney donors were 88.9 and 86.3% at 1 year, and 80 and 78.9% at 3 years after transplant, respectively.

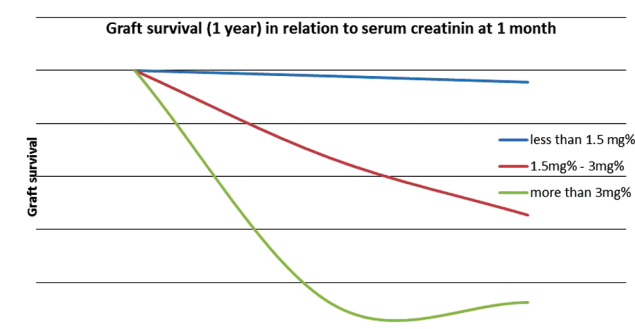
There was a statistically significant relation ($P=0.0001$) between graft survival and serum creatinine 1 month after transplant. Graft survival rate when serum creatinine is less than 1.5 mg was 95.9%, 45.5% when serum creatinine ranged between 1.5 and 3 mg, and 12.5% when serum creatinine was more than 3 mg (Fig. 7).

Figure 6



Graft survival in relation to dialysis.

Figure 7



Graft survival in relation to serum creatinine at 1 month after transplant.

As shown in Tables 12 and 13, there was a statistically significant relation ($P=0.0003$) between graft survival and maintenance immunosuppressive treatment protocol. The 1-year graft survival rate was 92.2% when cyclosporine, prednisolone, and mycophenolate mofetil (MMF) were used, and 78.6% when azathioprine was used instead of MMF. The 3-year graft survival rate was 93.1% for cyclosporine, prednisolone, and MMF and 78.6% when azathioprine was used instead of MMF.

Discussion

Renal transplantation has been the main treatment option for end-stage renal disease patients. Life satisfaction, physical, emotional wellbeing, and the

Table 11 Survival analysis (1 year) by the Kaplan–Meier test in relation to hepatitis C virus of recipient

Variables	Negative	Positive
Total number	95	9
Number of dysfunctioning grafts	19	3
Number of censored	76	6
Percentage of censored	80	66.67
Survival time		
Mean	0.91	0.90
SE	0.03	0.12
95% confidence interval	0.86–0.97	0.67–1.13

Log rank=0.78. $P=0.38$.

Table 12 Graft survival (1 year) by the Kaplan–Meier test in relation to the immunosuppressive treatment protocol

Variables	Protocol 1	Protocol 2
Total number	14	90
Number of dysfunctioning grafts	3	7
Number of functioning grafts	11	83
Percentage of functioning grafts	78.57	92.2
Survival time		
Mean	0.87	0.96
SE	0.10	0.02
95% confidence interval	0.67–1.07	0.92–1.01

Log rank=18.90. Protocol 1: steroid and azathioprine and cyclosporine. Protocol 2: steroid and mycophenolate mofetil and cyclosporine. $P=0.0003$.

Table 13 Graft survival (3 years) by the Kaplan–Meier test in relation to the immunosuppressive treatment protocol

Variables	Protocol 1	Protocol 2
Total number	14	29
Number of dysfunctioning grafts	3	2
Number of functioning	11	27
Percentage of functioning	78.57	93.12
Survival time		
Mean	2.64	3
SE	0.29	0
95% confidence interval	2.06–3.21	3–3

Log rank=18.90. Protocol 1: steroid and azathioprine and cyclosporine. Protocol 2: steroid and mycophenolate mofetil and cyclosporine. $P=0.0003$.

ability to return to work are all significantly better among transplant recipients than among dialysis patients. Yet, despite the continuous progress in immuno-suppressive and supportive therapy, a number of factors still interfere with the complete success of renal transplantation.

Some factors present at the time of transplantation, which concern the donor as well as the recipient, whereas other complications originate after transplantation. In our study, particular attention was paid to the main factors and events that impair graft function in the short-term and long-term. Although the quality of life and survival rates following organ transplantation have greatly improved due to advances in surgical technique, immunosuppressive therapy, and medical management, allograft rejection and infection remain the major causes of morbidity and mortality [4].

In our study, we retrospectively analyzed renal transplants in King Fahd Unit: we aimed to identify the risk factors for the entire course, and then to analyze the relative impact of these risk factors on short-term and long-term graft survival in the patients.

The gold standard to measure renal function is the glomerular filtration rate, evaluated according to the insulin clearance or an isotopic method. Because these procedures cannot be applied in the clinical setting because of their cost and complexity, serum creatinine was used to evaluate the renal function; graft dysfunction was defined as serum creatinine more than 2.5 mg/dl.

In our study, the overall graft survival rates were 88.6 and 76.7% at 1 and 3 years, respectively. The corresponding overall patient survival rates were 89.4 and 79.1% at the first and third post-transplant years. The projected graft survival rate after 5 years in those patients at King Fahd Unit was predicted to be 60.5%.

This comes with the fact that we accept some marginal living donors. Another explanation might be the fact that we do not use induction therapy routinely in all cases; only anti-Thymocyte Globulins (ATG) was used in few cases before transplantation. Furthermore, 43.3% of our patients received azathioprine-based de-novo immunosuppression.

In the Mansoura experience, the overall graft survival rate was 76.1 and 49.5% at 5 and 10 years, respectively. The corresponding patient survival rate was 87.1 and 71.5%, respectively.

In our study, as regards the relation between graft survival rate and age of both recipients and donors, the 1-year graft survival rates for various age groups (<10, 10–18, 19–30, 31–40, and 41–50 years) were 100, 77.3, 80, 73.4, and 85.7%, respectively, whereas the 3-year graft survival rates for various age groups (<10, 10–18, 19–30, 31–40, and 41–50 years) were 100, 82.4, 70, 55.6, and 100%, respectively. However, this difference did not reach statistical significance. Graft survival rates were especially low in the second decade of life. This may be attributed to the fact that in this age group patients are less compliant to treatment. In addition, low graft survival rates in the fourth decade can be explained by the fact that patients in this age group are not compliant to treatment because of financial reasons.

Regarding donor age we found that graft survival rate had a tendency to be lower in older age groups and there was a statistically significant difference regarding donor age at the 3-year graft survival; the grafts did not survive in the old donor group (>50 years old).

The UNOS registry documented that the higher the age of the donor, the worse the long-term outcome of the graft [5].

Some investigators feel that the poorer results of grafts of elderly donors are mainly caused by the age-dependent progressive reduction of glomerular filtration rate and renal reserve [6].

Regarding the relation to the sex of recipients, male recipients had an inferior 1-year graft survival rate compared with female recipients, whereas female recipients had an inferior 3-year graft survival rate compared with male recipients. Regarding the relation to the sex of donors, male donors had an inferior 1- and 3-year graft survival rates compared with female donors; however, these findings did not reach statistical significance.

In a study that included 85 135 patients from the Organ Procurement and Transplantation Network/United Network for Organ Sharing, it was found that older donor age, younger recipient age, male recipient sex, and the presence of acute rejection were associated with elevated serum creatinine at 1-year, graft survival, and death-censored graft survival [7].

McGee *et al.* [8] reported that, 146 female recipients of male kidneys had an inferior graft survival rates (86, 79, and 78% at 1, 2, and 3 years, respectively; log-rank $P=0.01$).

As regarding HLA and DR matching between recipients and donors and their relation to graft survival in our study, increasing number of HLA and DR loci mismatches did not significantly lower the graft survival rates in kidney transplantation. This might be attributed to the fact that these mismatches were in class I and not in class II.

Our results were in agreement with a study by Gjertson and Cecka [9] that reported that increasing numbers of HLA-A, HLA-B, and HLA-DR loci mismatches did not significantly ($P=0.50$) lower graft survival rates among living unrelated donor kidney transplant recipients.

Regarding the relation between graft survival and HTN in our study, there was a greater rate of graft dysfunction with the presence of HTN but this result does not reach statistical significance.

In a study on 196 patients by Raiss Jalali and colleagues, a slow but significant increase in mean creatinine levels was observed in the HTN group during 3 years of follow-up, whereas in the non-HTN group, graft function remained stable. Cardiovascular events were observed only in HTN patients. They concluded that HTN accelerates the deterioration of transplanted kidney function [10].

As regards HCV infection of our patients and its relation to graft survival, the results indicated that HCV-positive patients can be transplanted with the success close to that of HCV-negative patients, although there was a tendency to get better outcomes in HCV-negative patients. The follow-up of these HCV-positive patients revealed no elevation in their liver enzymes with acceptable serum creatinine.

These results are in agreement with Arango *et al.* [11] who found that patient survival was not significantly different in 39 HCV-positive and 96 HCV-negative patients transplanted with living-related donors (71 and 77% at 5 years, respectively).

Regarding relation of graft survival to serum creatinine of the recipients at 1 month after transplant, there was a statistically significant relation ($P=0.0001$) between graft survival and serum creatinine 1 month after transplant. Graft survival rate when serum creatinine was less than 1.5 mg was 95.9%, 45.5% when serum creatinine ranged between 1.5 and 3 mg, and 12.5% when serum creatinine was more than 3 mg; and regarding the relation of graft survival to maintenance

immunosuppression post-transplant, there was a statistically significant relation ($P=0.0003$) between graft survival and maintenance immunosuppressive treatment protocol.

One-year graft survival rates was 92.2% for cyclosporine, prednisolone, and MMF and 78.6% when azathioprine was used instead of MMF. On the other hand, 3-year graft survival rates was 93.1% for cyclosporine, prednisolone, and MMF and 78.6% when azathioprine was used instead of MMF.

The introduction of calcineurin inhibitors – cyclosporine and tacrolimus – in the last two decades has resulted in a significant decrease in acute rejection and an improvement in short-term graft survival [12].

Conclusion

Despite the continuous advancement in immunosuppressive and supportive therapy, a number of factors still interfere with the complete success of renal transplantation.

Among the long list of predictors for graft outcome variables, factors that had a significant impact on outcome by the Kaplan–Meier analysis included donor's age, serum creatinine at 1 month after transplant, and primary immunosuppression.

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Conflicts of interest

There are no conflicts of interest.

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