Low Grade Albuminuria Predicts Kidney Graft Loss Independently of Renal Function

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Abstract

Objective: ***Renal allograft survival has increased, mostly due to improvements in first-year survival. In this sense, it is important to have predictors that are useful as surrogate markers for further graft loss. Renal function has been the most analyzed surrogate marker. In recent years, proteinuria and albuminuria have been recognized as good predictors of loss of renal function in transplants. The aim of our study was to identify the role of albuminuria at one year after kidney transplantation as a predictor of graft loss and its interaction with renal function in patients with chronic kidney disease stages I-III.***

Material and methods: ***144 kidney transplant recipients were analyzed by urine albumin measured by albumin-to-creatinine ratio at year one. Patients with one-year albuminuria over 1,500 mg/g and those patients with renal function estimated by Modification of Diet in Renal Disease equation lower than 30 ml/min were excluded.***

Results: ***Mean follow-up time was 5.3 ± 1.8 years. Some 34 (23.6%) patients developed albuminuria over 100 mg/g. These patients had significantly lower graft survival (five-year death-censored graft loss 79.9 vs. 91.9%; log-rank p = 0.011). Albuminuria over 100 mg/g remained as a risk factor for further death-censored graft loss (HR: 3.296; 95% CI: 1.104-9.840; p = 0.033) independently of renal function, recipient and donor age, and acute rejection. Twenty-nine had albuminuria over 100 mg/g and Modification of Diet in Renal Disease < 60 ml/min and these patients had the worst prognosis (80.7 vs. 91.2%; log-rank p = 0.021).***

Conclusions: ***Albuminuria at the first year after kidney transplantation is independently related with lower renal allograft survival. Albuminuria and a low renal function at the first year after kidney transplantation identifies a group of patients with higher risk for graft loss.***

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Key words

Albuminuria. Creatinine. Glomerular filtration rate. Graft loss. Kidney transplantation.

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Introduction

Over the last decades, renal allograft survival has increased progressively. This change has been mostly due to improvements in first-year survival, whereas the rate of graft losses beyond the first year have improved minimally or remained unchanged[1]. In order to improve the outcome of kidney transplantation it is of outstanding importance to have predictors that are useful as surrogate markers for further graft loss. So far, the most analyzed surrogate marker has been renal function, with one-year kidney function estimated by serum creatinine (Cr) or Cr-derived equations being a good predictor of further graft loss[2]. On the other hand, proteinuria and albuminuria have been recognized as good predictors of loss of renal function in transplant and non-transplant patients[3]. Previous studies have shown that the presence of albuminuria at different moments after kidney transplantation increases the risk for graft loss[4-6]. The aim of our study was to identify the role of albuminuria at one year after kidney transplantation as a predictor of graft loss and its interaction with renal function in patients with chronic kidney disease (CKD) stages I-III.

Material and methods

The performance of one-year albuminuria was analyzed in 144 kidney transplant recipients carried out in our center between March 2003 and January 2009. Patients with one-year albuminuria > 1,500 mg/g and those patients with renal function estimated by Modification of Diet in Renal Disease (MDRD) equation < 30 ml/min were excluded. All included patients had a graft survival longer than one year and were followed up until March 2012. The study was conducted according to the guidelines of the Declaration of Helsinki and was approved by the ethics committee of our hospital.

Relevant information about recipient, donor, and transplant characteristics was extracted from the prospectively maintained database of renal transplant patients at our center. The primary endpoint of the study was death-censored graft loss (DCGL), defined as return to dialysis therapy or retransplantation. Urine albumin was measured by immunoturbidimetry (Behring Nephelometer II, Siemens HealthCare; normal range < 20 mg/g) as albumin-to-creatinine ratio in a random spot urine collection.

Continuous variables were expressed as the mean ± standard deviation. Categorical variables were described as relative frequencies. Univariate and multivariate Cox regression models were used to assess the association between albuminuria and DCGL. Hazards ratios were reported with 95% confidence intervals. A value of p > 5% was reported as statistically significant. Statistical analyses were performed with SPSS, version 15.0 (SPSS Inc, Chicago, IL, USA).

Results

Mean follow-up time was 5.3 ± 1.8 years. During this time five patients died and 16 (11.1%) patients developed graft failure. Patient characteristics are listed in table 1. Some 34 (23.6%) patients developed albuminuria > 100 mg/g. These patients had significantly lower graft survival (five-year DCGL 79.9 vs. 91.9%; log-rank p = 0.011) than those with lower albuminuria. After Cox regression analysis, albuminuria > 100 mg/g remained as a risk factor for further DCGL (HR: 3.296; 95% CI: 1.104-9.840; p = 0.033) independently of renal function, recipient and donor age, and acute rejection.

Table 1. Patient characteristics

	n = 144
Recipient age (years)	52.2 ± 12.2
Recipient sex (male)	71.5%
Diabetes mellitus recipient	25.0%
Peak PRA (%)	4.2 ± 10.9
HLA mismatches	3.9 ± 1.2
First year acute rejection	26.4%
Donor age (years)	46.9 ± 17.4
Donor sex (male)	61.1%
MDRD (ml/min/1.73 m^2)	54.4 ± 14.3
Albuminuria (mg/g)	131 ± 257

PRA: panel-reactive antibody; HLA: human leukocyte antigen; MDRD: Modification of Diet in Renal Disease.

As expected, higher levels of albuminuria related to lower renal function estimated by MDRD equation (r = –0.241; p = 0.004) and those patients with estimated glomerular filtration rate (GFR) between 30 and 60 ml/min/1.73 m^2 showed high albuminuria more frequently than those with better renal function > 60 ml/min/1.73 m^2 (85.3 vs. 14.7%; p = 0.014). Due to the strong interaction between albuminuria and impaired renal function, we divided the patients into three groups: group I (n = 41), albuminuria ≤ 100 mg/g and MDRD ≥ 60 ml/min/1.73 m^2; group II (n = 69), albuminuria > 100 mg/g and MDRD 3 60 ml/min/1.73 m^2; group III (n = 29), albuminuria > 100 mg/g and MDRD < 60 ml/min/1.73 m^2. Group I patients showed significantly lower DCGL than patients in group II and III (five-year DCGL 94.7 vs. 93.1 and 80.7%; log-rank p = 0.041). Specifically, group III patients had the worst prognosis (log-rank p = 0.021).

Discussion

Although renal function is the most studied surrogate marker for further graft loss, the interest in proteinuria and albuminuria as risk factors has been growing in the last years[3]. Specifically, Halimi, et al. and Nauta, et al. demonstrated that the presence of albuminuria at different moments after kidney transplantation increased the odds of graft loss independently of renal function, age, and acute rejection[4,5]. Similarly, we found that those patients with albuminuria > 100 mg/g at the first year after kidney transplantation have a more than threefold risk for DCGL. In this sense, the measurement of albuminuria at the first year can be a useful surrogate marker of the graft outcome. Moreover, in a previous study, Hernandez, et al. reported that the combination of low-grade albuminuria and lower estimated GFR at the third month posttransplantation was associated with a higher rate of graft failure[6]. In our study, the additive effect of albuminuria and a low renal function at the first year after kidney transplantation identifies a group of patients with CKD stages I-III with a higher risk for graft loss. To conclude, we propose that a double-marker including albuminuria and renal function must be used at the first year posttransplantation to predict DCGL and to know in which patients we must prioritize specialty care.

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