

## Original article

# Progression of urinary protein excretion after kidney transplantation: A marker for poor long-term prognosis

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## ABSTRACT

**Introduction:** Post-transplantation proteinuria is a risk factor for graft failure. A progressive decline in renal graft function is a predictor for mortality in kidney transplant patients.

**Objectives:** To assess the development and the progression of urinary protein excretion (UPE) in the first year post-transplant in recipients of kidney transplants and its effect on patient and graft outcomes.

**Materials and methods:** We analysed 1815 patients with 24-h UPE measurements available at 3 and 12 months post-transplant. Patients were divided based on their UPE level: below 300 mg, 300–1000 mg and over 1000 mg (at 3 and 12 months), and changes over time were analysed.

**Results:** At 3 months, 65.7% had UPE below 300 mg/24 h, 29.6% 300–1000 mg/24 h and 4.7% over 1000 mg/24 h. At one year, 71.6% had UPE below 300 mg/24 h, 24.1% 300–1000 mg/24 h and 4.4% over 1000 mg/24 h.

In 208 patients (12%), the UPE progressed, in 1233 (70.5%) it remained stable and in 306 (17.5%) an improvement was observed.

We found that the level of UPE influenced graft survival, particularly if a progression occurred.

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Recipient's age and renal function at one year were found to be predictive factors for mortality, while proteinuria and renal function were predictive factors for graft survival.

**Conclusions:** Proteinuria after transplantation, essentially when it progresses, is a marker of a poor prognosis and a predictor for graft survival. Progression of proteinuria is associated with poorer renal function and lower graft survival rates.

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## Progresión de la excreción urinaria de proteínas después del trasplante renal: un marcador de mal pronóstico a largo plazo

### R E S U M E N

#### Palabras clave:

Proteinuria

Supervivencia del injerto

Trasplante renal

**Introducción:** La proteinuria después de un trasplante renal constituye un factor de riesgo para el fallo del injerto. Una disminución progresiva de la función del injerto renal es un predictor de la mortalidad en los pacientes trasplantados renales.

**Objetivos:** Analizar la aparición y la progresión de una excreción urinaria de proteínas (EUP) en el primer año siguiente al trasplante en pacientes trasplantados renales, y su efecto sobre la evolución del paciente y del injerto.

**Material y métodos:** Analizamos un total de 1815 pacientes en los que se dispuso de determinaciones de la EUP de 24 horas a los 3 y a los 12 meses del trasplante. Dividimos a los pacientes según el nivel de EUP, de la siguiente forma: inferior a 300 mg, 300-1000 mg y más de 1000 mg (a los 3 y 12 meses), y analizamos los cambios a lo largo del tiempo.

**Resultados:** A los 3 meses, el 65,7% presentaban una EUP inferior a 300 mg/24 h, el 29,6% 300-1000 mg/24 h y el 4,7% más de 1000 mg/24 h. A un año, el 71,6% tenían una EUP inferior a 300 mg/24 h, el 24,1% 300-1000 mg/24 h y el 4,4% más de 1000 mg/24 h.

En 208 pacientes (12%), la EUP mostró una progresión, en 1233 (70,5%) se mantuvo estable y en 306 (17,5%) se observó una mejoría.

Observamos que el nivel de EUP influía en la supervivencia del injerto, en especial si se producía una progresión.

La edad y la función renal del receptor al año del trasplante fueron factores predictivos de la mortalidad, mientras que la proteinuria y la función renal lo fueron de la supervivencia del injerto.

**Conclusiones:** La proteinuria después del trasplante, fundamentalmente cuando muestra una progresión, es un marcador de mal pronóstico y un factor predictivo de la supervivencia del injerto. La progresión de la proteinuria se asocia a una peor función renal y a una tasa de supervivencia del injerto inferior.

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## Introduction

In the world of transplants, the introduction of new immunosuppressants has led to an improvement in short- and medium-term graft survival<sup>1-3</sup>; nevertheless, long-term graft loss remains a problem.<sup>4</sup> The many factors associated with these long-term losses have been analysed by a large number of studies.<sup>5</sup> Among them, recent studies<sup>6</sup> show that proteinuria is an independent risk factor predictive of graft failure for recipients of all ages.<sup>7</sup> At the same time, continued renal graft function decline is a strong predictor of mortality in renal transplant patients.<sup>6</sup>

The prevalence of proteinuria one year after transplantation ranges from 11% to 45%,<sup>8</sup> or even higher in patients treated with proliferation signal inhibitors (PSI). Two mechanisms for the development of proteinuria after

transplantation are described: tubular origin, due to inadequate protein reabsorption in the proximal tubule cells damaged by ischaemia/reperfusion phenomena, rejection or tubular toxicity, or glomerular origin due to increased passage of higher molecular weight proteins such as albumin through the glomerular barrier due to de novo or transplant glomerular disease, chronic rejection or drug toxicity.

Proteinuria in transplantation is usually indicative of some type of graft disease and generally tends to occur in relation to chronic graft nephropathy (histological substrate with interstitial fibrosis and tubular atrophy), acute rejection, transplant glomerular disease or recurrence of primary kidney disease.<sup>8-10</sup> It can be associated with immunological or non-immunological factors<sup>11</sup> and factors related to both the donor and the recipient. Degree of HLA sensitisation, age, obesity, hypertension and other cardiovascular risk factors can all

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