PROGNOSTIC SIGNIFICANCE OF CHANGES IN PROTEINURIA IN EARLY STAGES OF KIDNEY TRANSPLANTATION

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INTRODUCTION

Proteinuria is considered the main independent risk factor of end stage renal disease[1], and some authors consider that changes in proteinuria could be as a surrogate of kidney disease progression. [2]

Proteinuria is highly prevalent in renal transplantation and it has been asociated to a lower graft and patient survival[3,4], but there is no information about the relation between the absolute or relative changes in proteinuria in early stages of transplantation and long term graft and patient survival.

AIMS

To analize the effect of the magnitud of proteinuria and its relative changes, betwen the 3rd and the 12th month after transplantation, on long term graft and patient survival.

MATERIAL AND METHODS

Retrospective analisys of 701kidney transplant recipients in our Unit. Minimum follow-up: 12 months.

• Basal proteinuria (3rd month) was measured in 24h urine sample and categorized **depending on its magnitude** as follows:

-(0): 0-149 mg/d (no proteinuria),

-(1): 150-299 mg/d,

-(2): 300-999 mg/d,

-(3): ≥1000 mg/d.

• **Relative changes of proteinuria between 3rd and 12th months** were analized and categorized as follows:

- (0): Reduction of proteinuria ≥ 50% (lower risk)
- (1): Δ proteinuria < 50%
-(2): Δ proteinuria ≥ 50% (higher risk)

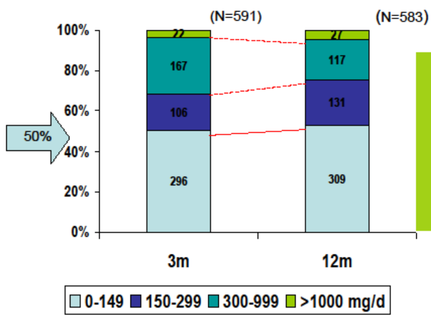
Statistical analysis:

Kaplan-Meier method was used to analyze graft (censoring for death with functioning graft) and patient survival. Log-rank test was used to compare survival curves. Cox models were used to asses the relative risk on graft and patient survival, with increasing proteinuria. $\chi 2$ (or Fisher test) and t-Student test (or Anova) in univariant analisys, and Logistic regression ("step by step") to identify variables related to progression of proteinuria ≥ 50% . P values < 0.05 were considered statistical significant. SPSS 15.0 for Windows.

RESULTS

Mean follow-up: 84.5 ± 48.6 months (range: 12.1-191.6)

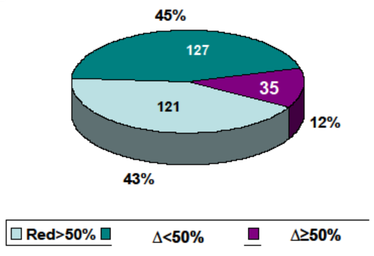
Distribution of population depending on proteinuria magnitude



PROTEINURIA APPEARS IN NEARLY 50% OF OUR POPULATION SINCE 3rd MONTH AFTER TRANSPLANTATION.

Distribution of population depending on changes (Δ) in proteinuria between 3rd and 12th month

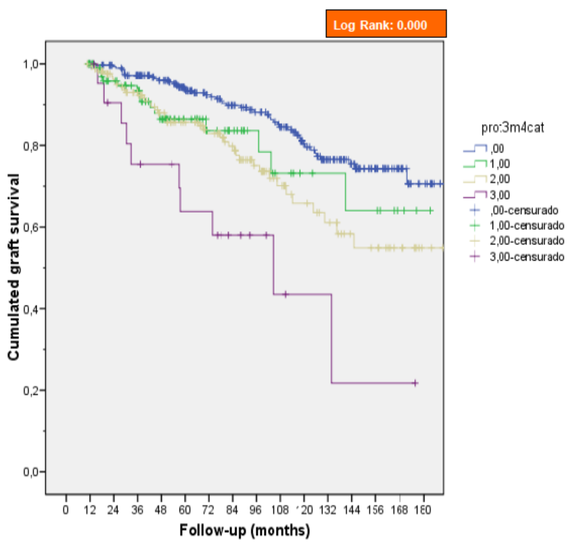
N= 283



AMONG PATIENTS WITH PROTEINURIA AT 3rd MONTH, 57% OF THEM MAINTAINED OR INCREASED PROTEINURIA AT 12th MONTH.

MAGNITUDE OF PROTEINURIA AND GRAFT AND PATIENT SURVIVAL

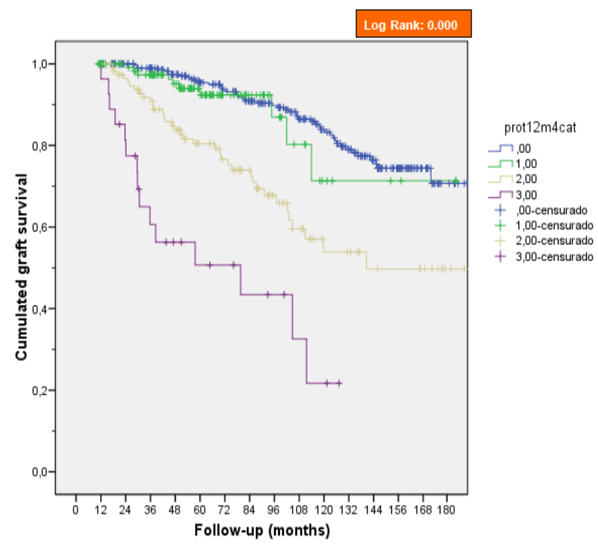
Prot 3rd m & graft survival



Cox analysis

Prot 3rd month & graft survival	B	Sig	Exp(B)	CI 95% Exp(B)
150-299 mg/d	0,587	0,051	1,799	0,999 - 3,242
300-999 mg/d	0,734	0,001	2,083	1,362 - 3,187
> 1000 mg/d	1,591	0,000	4,907	2,465 - 9,767

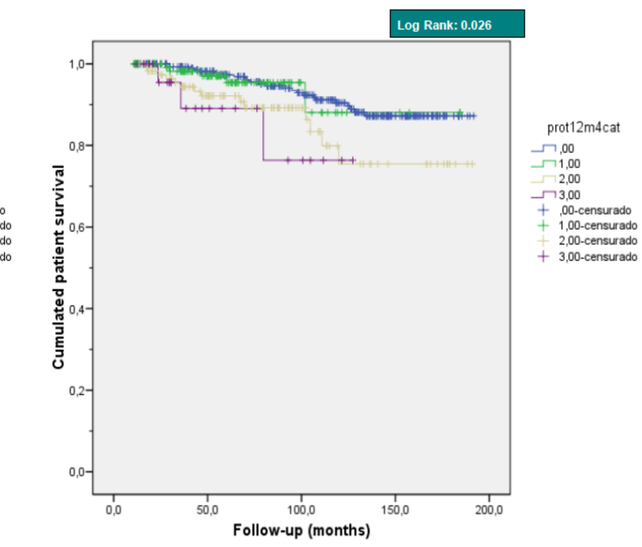
Prot 12th m & graft survival



Cox analysis

Prot 3rd month & patient survival	B	Sig	Exp(B)	CI 95% Exp(B)
150-299 mg/d	0,134	0,706	1,144	0,569 - 2,296
300-999 mg/d	1,115	0,000	3,051	1,966 - 4,733
> 1000 mg/d	2,244	0,000	9,434	5,200 - 17,118

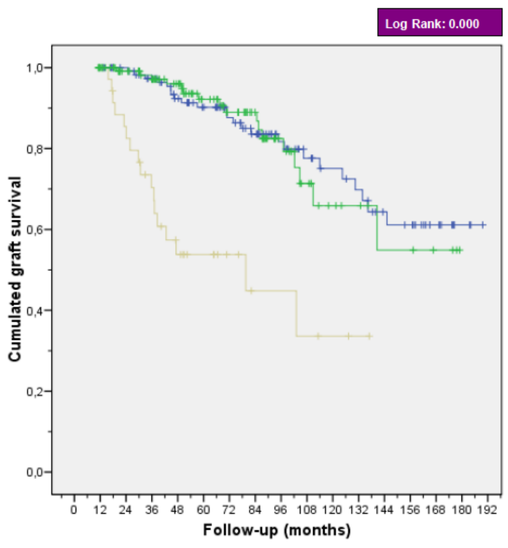
Prot 12th m & patient survival



Cox analysis

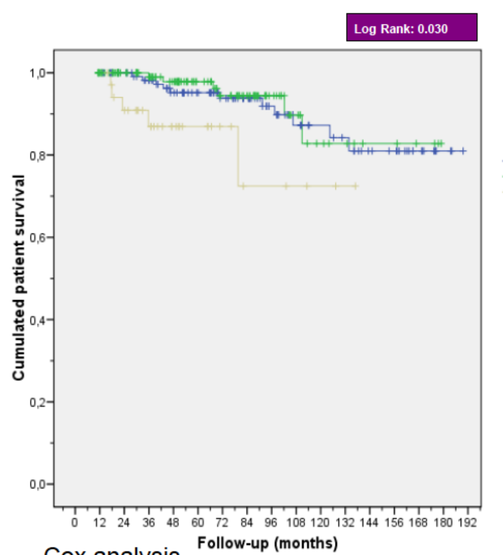
Prot 12th month & patient survival	B	Sig	Exp(B)	CI 95%Exp(B)
150-299 mg/d	0,068	0,893	1,070	0,399 - 2,866
300-999 mg/d	0,820	0,016	2,271	1,167 - 4,419
> 1000 mg/d	1,234	0,046	3,435	1,022 – 11,540

CHANGES OF PROTEINURIA BETWEEN 3-12th month AND GRAFT AND PATIENT SURVIVAL



Cox analysis

Δ Prot 3-12th month & graft survival	B	Sig	Exp (B)	CI 95% Exp(B)
Δ <50%	0,023	0,944	1,023	0,544 – 1,923
Δ ≥ 50%	1,684	0,000	5,385	2,829 – 10,248

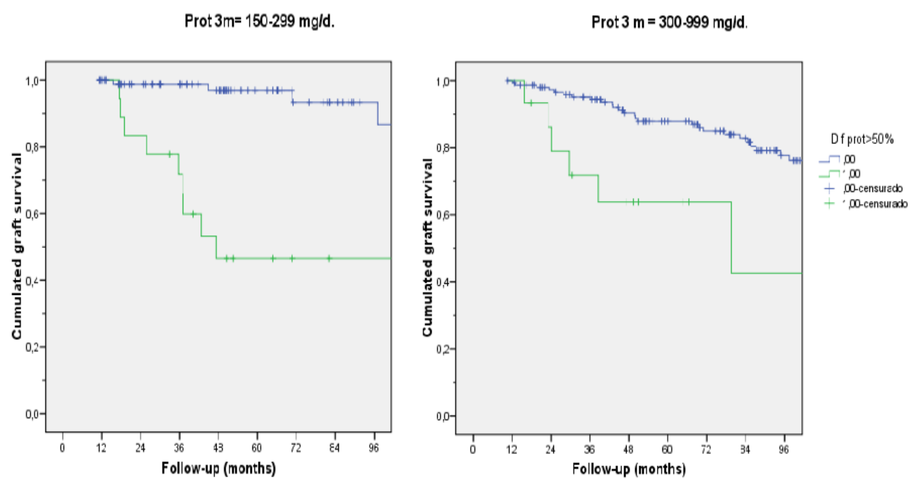


Cox analysis

Δ Prot 3-12th month & patient survival	B	Sig	Exp (B)	CI 95% Exp(B)
Δ <50%	-0,250	0,627	0,779	0,285 – 2,133
Δ ≥ 50%	1,160	0,035	3,191	1,085 – 9,384

EFFECT OF Δ PROTEINURIA ≥ 50% ON GRAFT AND PATIENT SURVIVAL IN LOWER CATHEGORIES OF BASAL PROTEINURIA

Graft survival (P= 0.000)



Patient survival (P=0.000)

RISK FACTORS OF Δ PROTEINURIA ≥ 50%

Multivariant analysis (*)

	B	Sig	HR	95%CI
Post- transplant HLA sensitization	1,002	0,038	2,723	1,057-7,019
Creatinine 12thmonth(mg/dl)	0,416	0,159	1,516	0,850-2,702

(*) We included variables that resulted statistically significant in univariante analysis: age and gender, cardiovascular death, high blood pressure, and renal function of the donor, cold ischemia time, recipient age and gender, pretransplant sensitization, blood transfusions, previos transplants, chronic renal disease, delayed graft function, acute rejection, 3 rd month creatinine (mg/dl), induction therapy, main mmunosuppressant drug, ECAI and/or RAS blockade use.

CONCLUSIONS

1.- Proteinuria magnitude in early stages of kidney transplantation was related to an increasing risk of graft loss and mortality in long term follow-up.

2.- Progresion of proteinuria ≥ 50% between 3rd and 12th months is also related to a lower graft and patient survival. It could be considered as an early marker of graft loss and mortality in long term follow-up, regardless of the magnitude of basal proteinuria, as well as an expression of the existence of immunological graft damage.

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1.- Taal MW. Kidney Int 2006; 70: 1694-1705.
2.- Levey AS. AJKD 2009, 54: 205-226.
3.- Knoll GA. AJKD 54 2009: 1131-1144.
4.- Amer H. Am J Transplant 2007; 7: 2748-2756.

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