

Treatment of Early Subclinical Rejection is associated to Graft Survival Improvement: 10 years Single Center Experience

Gigliotti P¹, Lofaro D¹, Leone F¹, Perri A¹, Vizza D¹, Toteda G¹, Lupinacci S¹, La Russa A¹, De Stefano R², Greco R¹, Papalia T¹, Romeo F², Bonofiglio R¹

¹"Kidney and Transplantation" Research Center, Dep. Nephrology, Dialysis and Transplantation;

² Department of Anatomic Pathology;
Annunziata Hospital, Cosenza, Italy



INTRODUCTION and OBJECTIVES

Subclinical rejection (SCR) has been variably associated with reduced graft survival, development and progression of interstitial fibrosis/tubular atrophy and chronic allograft nephropathy, but controversial data exist about early SCR treatment in terms of long-term graft survival improvement.

In this single-center retrospective study we enrolled 174 adult kidney transplant recipients (between July 1998 and December 2013) with a protocol biopsy performed at 30 days after transplantation.

WE EVALUATE THE INCIDENCE RATE AND RISK FACTORS FOR EARLY SCR AND THE IMPACT OF TREATING SCR WITH LOW DOSE I.V. STEROIDS (METHYLPREDNISOLONE (SOLU-MEDROL, PHARMACIA, THE NETHERLANDS) 250 MG/D FOR THREE CONSECUTIVE DAYS) ON 1,5 AND 10 YEARS DEATH-CENSORED GRAFT SURVIVAL.

METHODS

All participants received an induction treatment based on basiliximab, steroids, mycophenolate mofetil followed by a maintenance with calcineurin inhibitors (after the second day post transplantation), steroids and mycophenolate mofetil. Tacrolimus was used in 113 patients and Cyclosporine in 61.

Renal biopsies slides were scored by two independent figures (a pathologist and a nephrologist) according to the Banff '97 working classification. For minimization of the inter observer variability, every tenth biopsy was scored by both doctors, and the findings were discussed. All biopsy specimens included five or more glomeruli.

Presence of SCR was based on the absence of functional deterioration and histologic findings indicative of rejection on the basis of the tubulitis ("t") and mononuclear cell infiltration ("i") scores. All findings including "t" score ≥ 1 and "i" score >0 in absence of functional deterioration were classified as SCR.

Our 174 patients were divided into normal, SCR and Acute rejection groups according to the Banff classification.

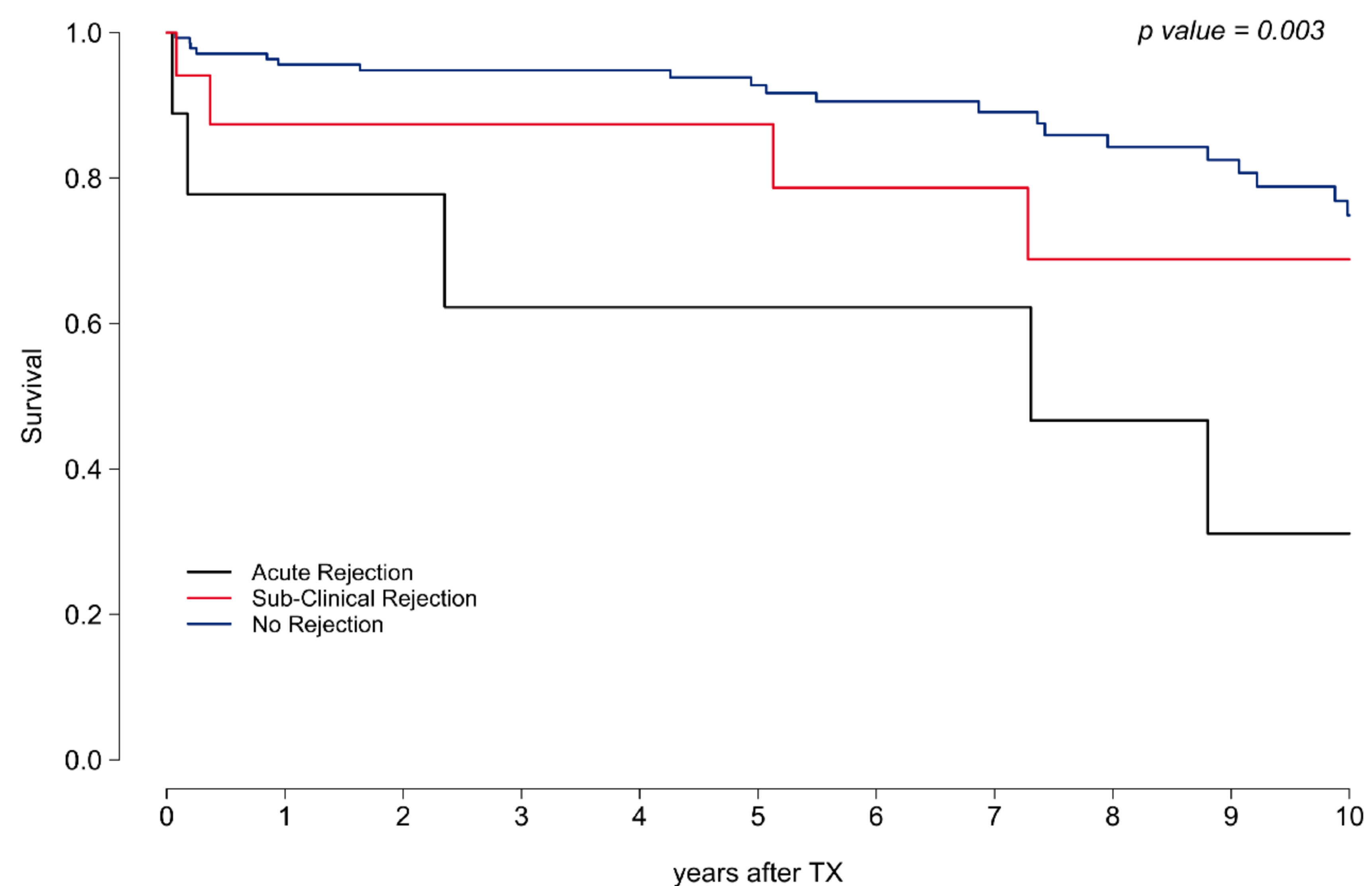
RESULTS

Among 159 patients (94.08%) who showed stable graft function, protocol biopsy revealed normal findings in 142 patients (89.30%) while 17 (10.7%) showed SCR. 5 patients showed a primary non function and among 10 patients with functional impairment, 8 (4.73%) showed acute rejection.

At multivariate regression analysis donor age (OR 1.04, 95% CI, 1.01 - 1.09), and delayed graft function (OR 1.08, 95% CI, 1.03 - 1.12), were significantly associated with SCR.

The 10-year graft survival rate in the subclinical rejection group was similar to the normal finding group (76.5% vs. 74.9% respectively; $p=0.61$). Despite a lower 10-year graft survival in acute rejection group respect to other groups, this difference did not reach significant difference ($p=0.215$) (Figure 1).

Figure 1. Graft survival rate in patients with normal histological findings, subclinical rejection and acute rejection at 30 days protocol biopsy.



CONCLUSIONS

IN CONCLUSION, EARLY PROTOCOL BIOPSY IS A USEFUL TOOL TO DETECT SCR AND LOW DOSE I.V. STEROIDS COULD BE AN APPROPRIATE STRATEGY TO IMPROVE KIDNEY TRANSPLANT LONG-TERM GRAFT SURVIVAL.

REFERENCES

- Nankivell BJ, Borrows RJ, Fung CL, O'Connell PJ, Allen RD, Chapman JR (2004) Natural history, risk factors, and impact of subclinical rejection in kidney transplantation. *Transplantation* 78 (2):242-249.
- Rush D, Nickerson P, Gough J, et al. (1998) Beneficial effects of treatment of early subclinical rejection: a randomized study. *J Am Soc Nephrol* 9 (11):2129-2134.
- Nankivell BJ, Chapman JR (2006) The significance of subclinical rejection and the value of protocol biopsies. *Am J Transplant* 6 (9):2006-2012.
- Shapiro R, Randhawa P, Jordan ML, et al. (2001) An analysis of early renal transplant protocol biopsies--the high incidence of subclinical tubulitis. *Am J Transplant* 1 (1):47-50.

