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## **Reduction in proteinuria after immunosuppressive therapy and long-term kidney outcome in patients with IgA nephropathy**

**Shin Chan Kang**<sup>1</sup>, Hyung Woo Kim<sup>1</sup>, Tae Ik Chang<sup>2</sup>, Ea Wha Kang<sup>2</sup>, Jung Tak Park<sup>1</sup>, Tae-Hyun Yoo<sup>1</sup>, Shin-Wook Kang<sup>1</sup>, Seung Hyeok Han<sup>1</sup>

<sup>1</sup>Department of Internal Medicine-Nephrology, Yonsei University College of Medicine, Korea, Republic of

<sup>2</sup>Department of Internal Medicine-Nephrology, National Health Insurance Service Ilsan Hospital, Korea, Republic of

**Objectives:** Despite controversy on the benefits of immunosuppressive therapy in IgA nephropathy (IgAN), the use of immunosuppression is still a therapeutic option and clinical outcome may vary depending on its responsiveness. This study evaluated long-term kidney outcome according to the extent of proteinuria reduction after immunosuppressive therapy in IgAN patients.

**Methods:** We analyzed 174 patients with biopsy-proven IgAN who undertook immunosuppressive therapy at Severance Hospital between 2005 and 2017. The time-averaged urine protein-creatinine ratio before and within 1 year after start of immunosuppressive therapy were calculated and responsiveness to immunosuppression was assessed as the reduction of proteinuria between the two periods. Patients were classified into tertiles of the extent of proteinuria reduction. We compared the slopes of eGFR decline using linear mixed model and hazard ratios (HRs) for disease progression (defined as development of a  $\geq 30\%$  decline in eGFR or end stage renal disease) using Cox proportional hazard model.

**Results:** The mean extents of proteinuria reduction were -2.8, -0.9, and 0.0 g/g in 1st, 2nd, and 3rd tertile groups, respectively. There were concomitant changes in the slopes of annual eGFR decline among tertile groups. Piecewise linear mixed model showed that the slower rate of eGFR decline in patients with higher proteinuria reduction persisted over time. During a mean follow-up of 5.1 years, incidence rates of disease progression in 1st, 2nd, and 3rd tertile groups were 81.2, 93.1 and 145.5 per 1000 person-years, respectively. In multivariable Cox model, the HRs (95% CI) for disease progression were 0.40 (0.17-0.92) in 1st tertile and 0.81 (0.39-1.68) in 2nd tertile compared with 3rd tertile.

**Conclusions:** This study showed that greater proteinuria reduction after immunosuppression was associated with lower risk of disease progression in IgAN, suggesting that responsiveness to immunosuppression may be an important determinant of adverse kidney outcome.

Figure 1. Change of annualized eGFR decline rate using a piecewise linear mixed model

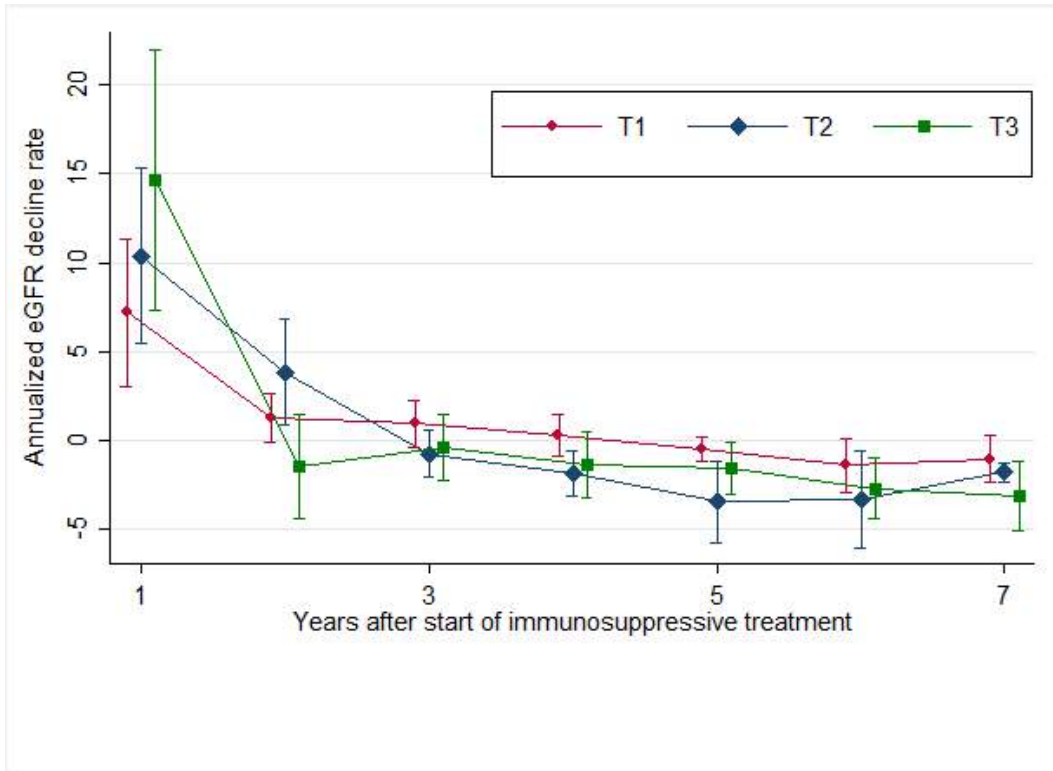


Figure 2. Adjusted survival curves of incidence of 30% decline in eGFR or ESRD according to decrement of proteinuria after immunosuppressive therapy

