

**Abstract Type : Poster**

**Presentation No. : PGN 006**

### **Prognostic value of mesangial C3 and C4d deposition in IgA nephropathy**

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**Objectives:** Activation of complement system can play an important role in the pathogenesis of IgA nephropathy (IgAN). C3 and C4d can be representative markers of alternative and lectin pathway, respectively. We studied whether mesangial C3 or C4d deposits can predict adverse renal outcome better than conventional risk factors and determined relative contribution of each pathway to disease progression.

**Methods:** A total of 265 patients with biopsy-proven IgAN between 2000 and 2013 were enrolled. The degree of C3 was evaluated by immunofluorescence staining and graded as 0, 1+, 2+, and 3+. We also determined C4d deposition by immunohistochemistry. The study endpoint was a composite of a  $\geq 30\%$  decline in estimated glomerular filtration rate or the onset of end-stage renal disease.

**Results:** During a mean follow-up of 6.8 years, 82 (30.9%) patients reached the composite end point. In the fully adjusted multivariable model, risk of reaching renal outcome was significantly higher in patients with mesangial C3 deposition of 2+ to 3+ (HR, 1.89; 95% CI, 1.11-3.20; P = 0.019) than in those with the deposition of 0 to 1+. In addition, patients with positive C4d deposition had a 1.9-fold increased risk of adverse outcome compared with those without deposition (HR, 1.90; 95% CI, 1.07-3.40; P = 0.03). The risk was highest in patients with both C3 and C4d deposition (HR, 2.61; 95% CI, 1.08-6.27; P = 0.03). Adding mesangial C3 deposition to risk prediction model significantly increased the integrated discrimination improvement and the net reclassification improvement, whereas C4d-added model did not. However, adding both mesangial C3 and C4d deposition together significantly improved risk prediction over C3-added model.

**Conclusions:** This study showed that mesangial C3 and C4d deposition were independent risk factors for renal progression. In addition, predictability of C3 was superior to that of C4d. C4d may play an additive role in increasing predictive power.