

C3 POSITIVE STAINING IN GLOMERULI AND SMALL BLOOD VESSELS IS POTENTIAL PROGNOSTIC FACTOR IN ANCA ASSOCIATED VASCULITIS

Crnogorac M*, Horvatic I*, Kacinari P*, Bacalja J[±], Galesic Ljubanovic D[±], Galesic K*

* Department of nephrology, Dubrava university hospital, Zagreb, Croatia

[±] Department of pathology and clinical cytology, Dubrava university hospital, Zagreb, Croatia

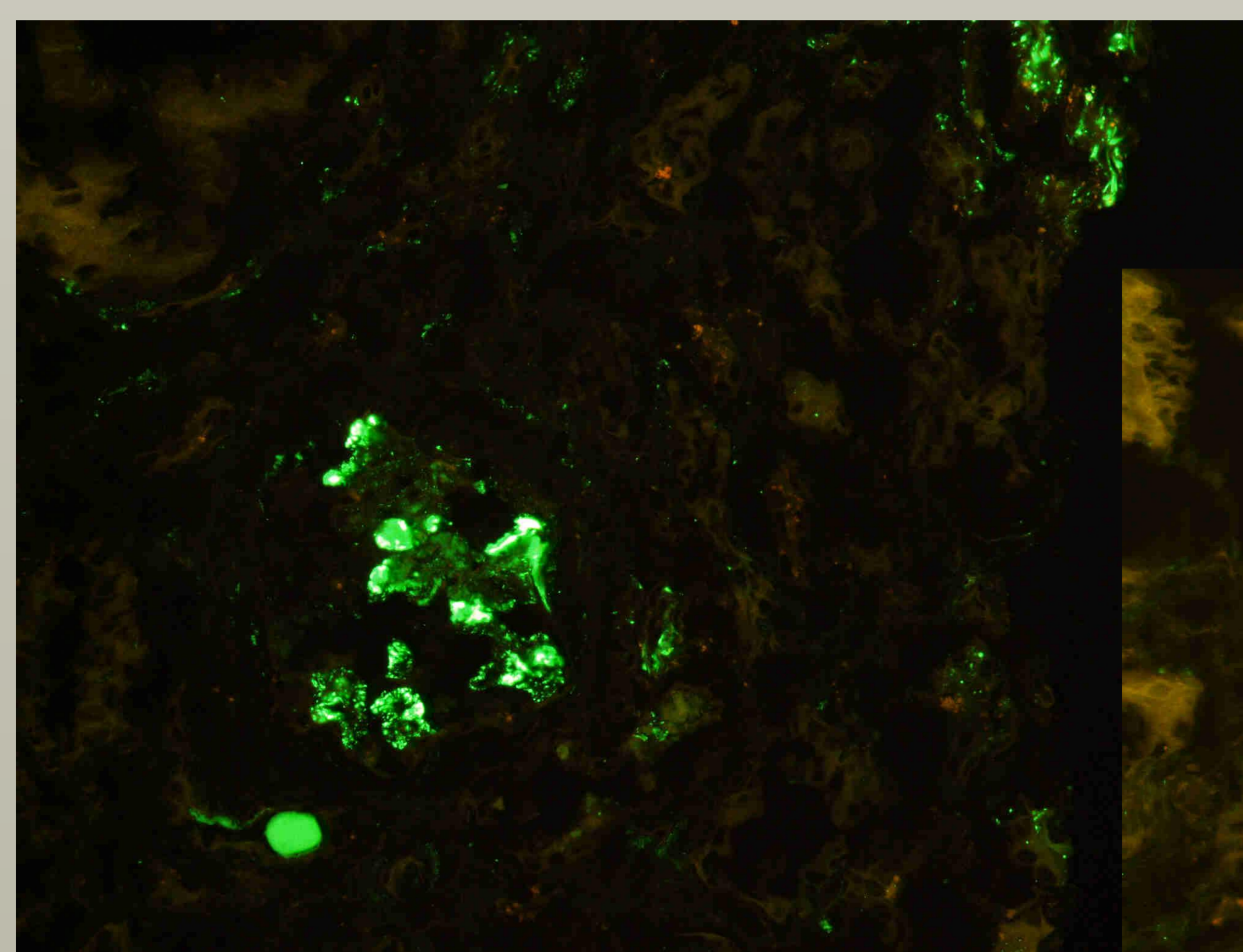
Introduction: In recent years there have been many research attempts to explain the etiopathogenesis of the ANCA associated vasculitis (AAV) and predict the patient outcomes. There are papers showing the important role of alternative complement pathway in AAV. Prognostic factors have been based on the clinical and serological data as well as histological classification by Berden et al. We hypothesized the importance of the C3 positive staining in glomeruli and blood vessels of kidney tissue as signes of alternative complement pathway activity and the use of aforementioned as possible prognostic factors.

Patients and methods: Retrospective study included 73 consecutive patients diagnosed with pauci-immune crescentic glomerulonephritis from January 2005. to December 2015. We performed renal biopsy on patients using automatic 16 Gauge needle. Light, immunofluorescent and electronic microscopy were performed. Even weak granular C3 staining in glomeruli or in the walls of the arteriolas was deemed positive. Primary definition was combined end-point patient death or progression to end-stage renal disease (ESRD). Secondary outcomes were patient survival and progression to ESRD (renal survival) singularly and disease relapse. Mann U Whitney test was used to compare differences in continuous variables and Chi-square and Fisher exact test for categoric variables. Kaplan Meyer with log-rank test were used to analyse the effect of C3 staining regarding these outcomes.

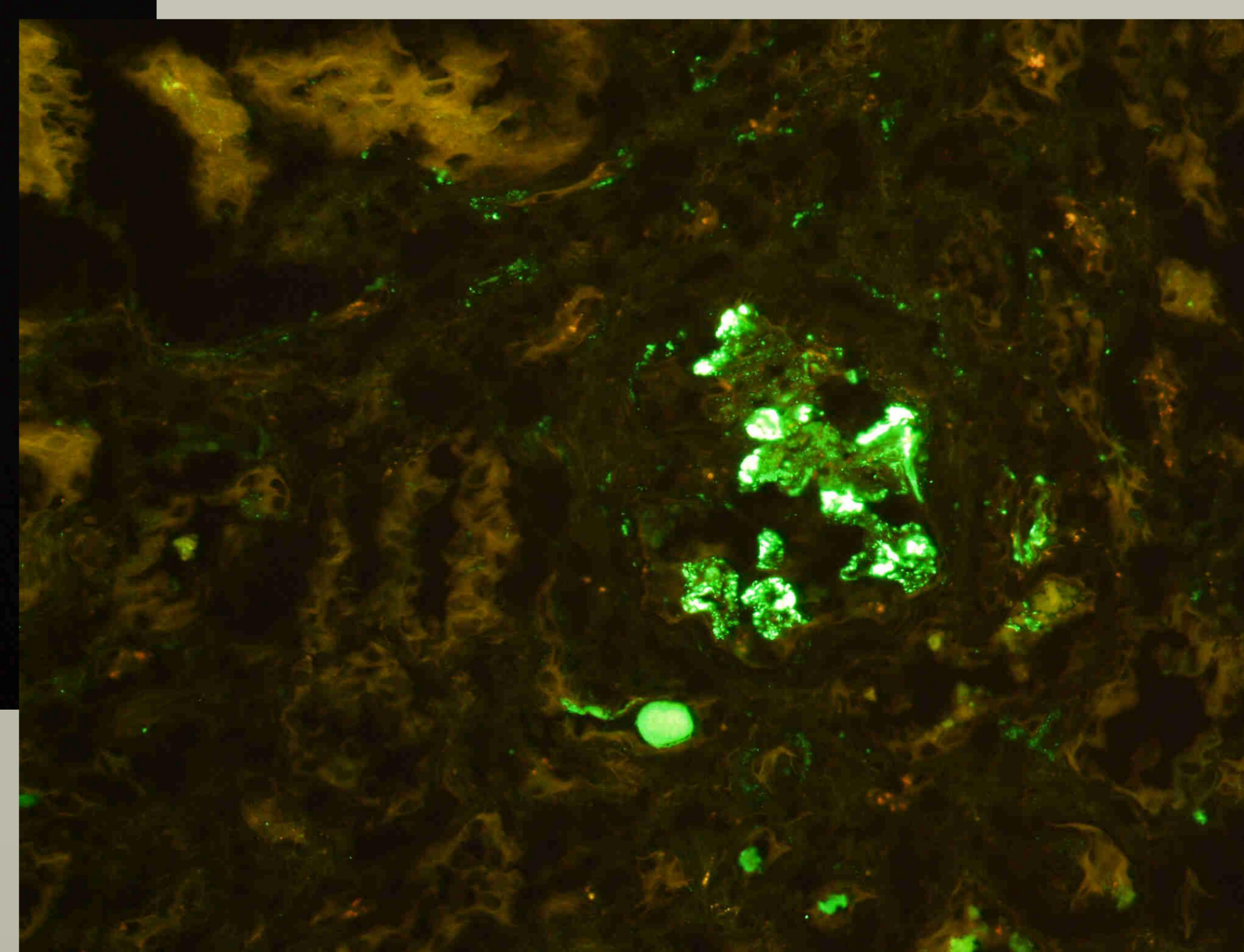
Results: Out of 73 patients 38,3% reached primary outcome, 24,6% reached ESRD, 21,9% died and 8% relapsed. Mann-U-Whitney analysis showed that patients with positive C3 glomerular staining had significantly higher proteinuria rates (p=0.042), higher CRP (p=0.025) as well as lower percentage of normal glomeruli (p=0.025) and higher percentage of crescentic glomeruli (p=0.025).

In contrast patients with positive C3 staining in blood vessels had lower proteinuria rates (p=0.024), better EGFR (p=0.05) and tendency to significantly lower percentage of interstitial fibrosis and tubular atrophy (IFTA; p=0.051). There was no significant correlation between positive C3 staining in either glomeruli or blood vessels with any of the clinical phenotypes (MPA, GPA, RLV).

Kaplan-Meier survival analysis found C3 positive staining in glomeruli wasn't associated with any of the outcomes while patients with positive C3 staining in blood vessels had significantly better combined patient and renal survival (p=0.028) and also better renal survival singularly (p=0.049), while there was no significant effect on either patient survival or relapse rate.



Granular C3 staining - glomeruls



Conclusion: Better understanding of etiopathogenesis of AAV and alternative complement pathway involvement in it is essential to understanding AAV. C3 staining in kidney tissue samples could prove to be a useful tool for perhaps predicting the severity and the course of the disease. Better outcomes for positive C3 staining in blood vessels could be perhaps explained by the fact that such positivity represents earlier lesion meaning patient was diagnosed earlier in the course of disease thus making treatment timely and more effective in terms of all end-points. These data need further confirmation from future studies.

