

Glomerular C1q positivity is associated with the presence of IgG3 subclass in non-lupus immune-complex mediated glomerulonephritis

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BACKGROUND

Glomerular C1q positivity by immunofluorescence is typically a specific marker of lupus nephritis, but in recent years C1q-positivity has been observed, for example, in some forms of monoclonal gammopathy of renal significance (MGRS). Among IgG subclasses, C1q affinity is higher for IgG3 and IgG1 compared to IgG2 and IgG4¹. The aim of this study was to assess the relationship between C1q positivity and IgG subclasses in non-lupus immune-complex (IC) mediated glomerular diseases.

METHODS

We retrospectively studied a cohort of 24 patients who underwent kidney biopsy between 2018 and 2022 and had IgG subclasses and C1q immunofluorescence (IF) available for review. The diagnostic conclusions and clinical data were retrieved from medical records. The correlation between C1q IF and the positivity of other reactants on immunofluorescence was assessed with Spearman rho coefficient.

RESULTS

There was a spectrum of glomerular diagnoses among the 24 patients (10 with membranous glomerulopathy, 3 with proliferative glomerulonephritis with monoclonal IgG deposits, 2 with membranoproliferative glomerulonephritis, 2 with IgA-dominant glomerulonephritis, 2 with IC-mediated glomerulonephritis (not otherwise specified), 4 with assorted diagnoses including: fibrillary glomerulonephritis, post-infectious glomerulonephritis, light chain deposition disease and membranous glomerulonephritis associated with IgA glomerulonephritis). Overall, C1q IF was positive (any intensity) in 10 (42%) of the cases. C1q on IF directly correlates with the presence of IgG3 subclass (rho 0.644, p=0.001), while showing inverse correlation with IgG1 and IgG4 subclasses (rho -0.426 and -0.543, p=0.043 and 0.007 respectively) (Figure 1). Principal component analysis suggests that the existence C1q/IgG3/IgM co-deposition constitutes a distinct entity from IgG1/IgG4/IgG2 deposition (Figure 2).

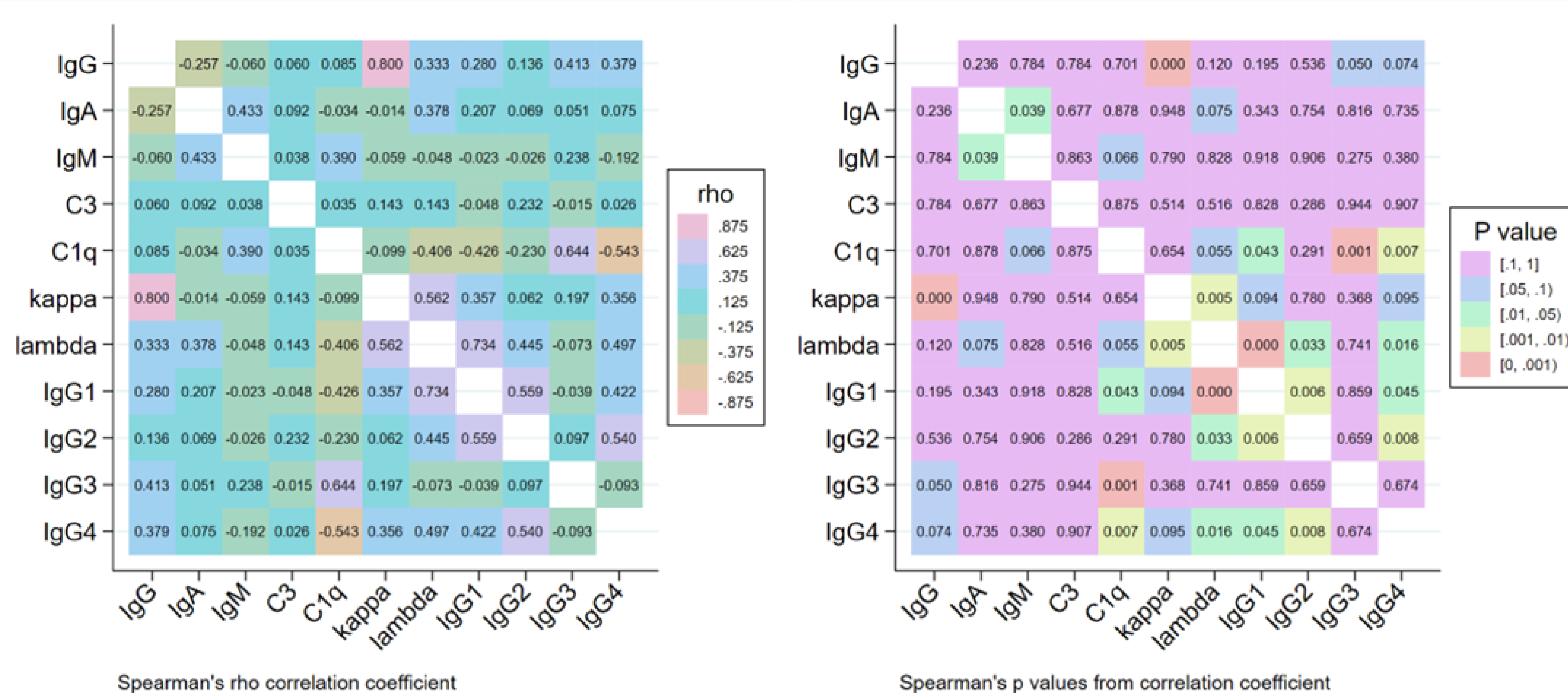


Figure 1. Spearman's rho correlation coefficient between different IF antisera positivity.

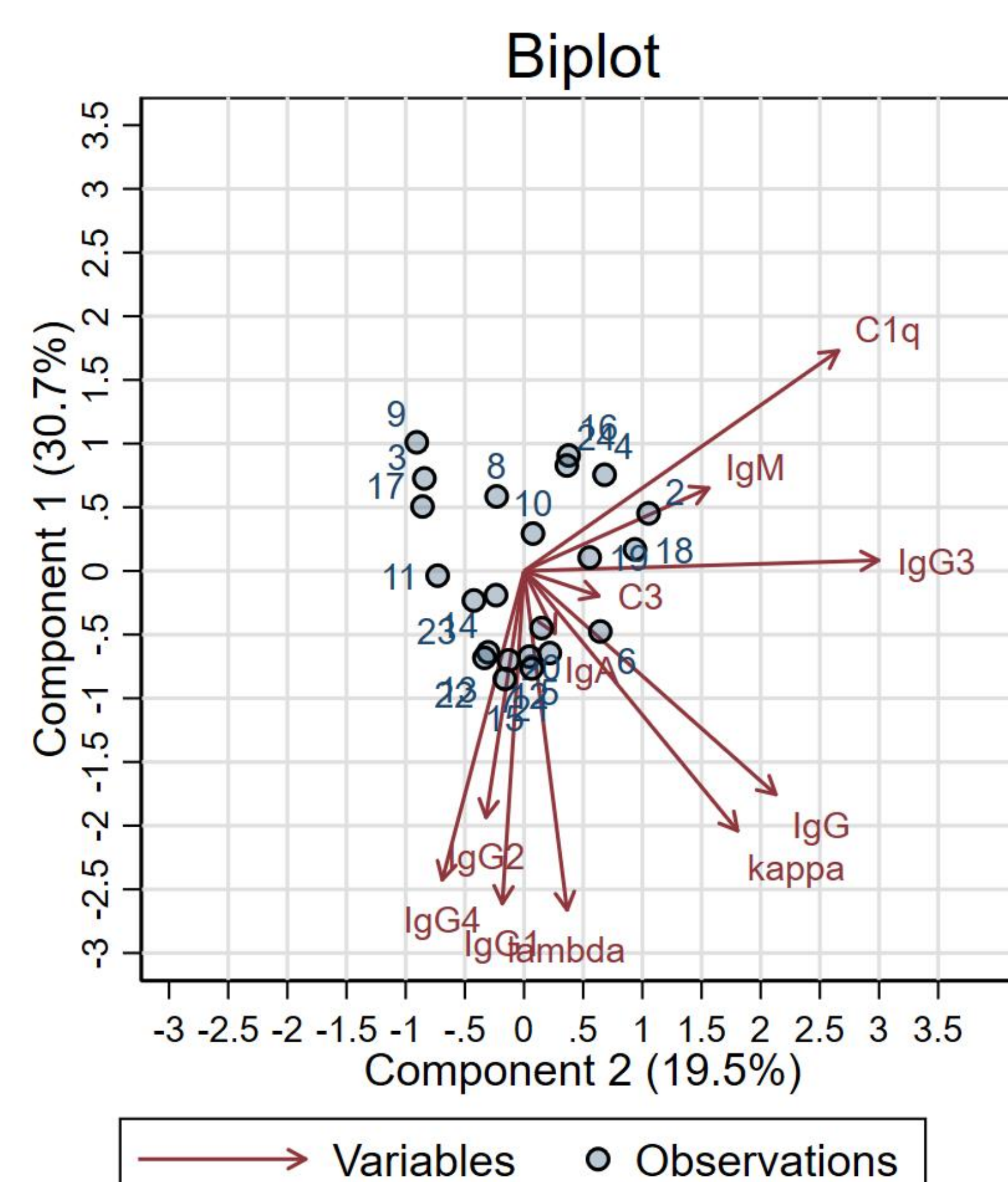


Figure 2. Principal component analysis. Dots represent each patients, arrows show different variables.

CONCLUSIONS

- Outside of lupus nephritis, C1q positivity should raise the possibility of IgG3 subclass presence.
- The clinical significance of IgG3 deposition in different kidney diseases is variable and not completely understood.

REFERENCES

1. Vidarsson G, Dekkers G, Rispens T. IgG subclasses and allotypes: from structure to effector functions. *Front Immunol.* 2014;5:520. doi:10.3389/fimmu.2014.00520