MO136 **RELATIONSHIP BETWEEN UPCR AND EGFR IN C3 GLOMERULOPATHY**

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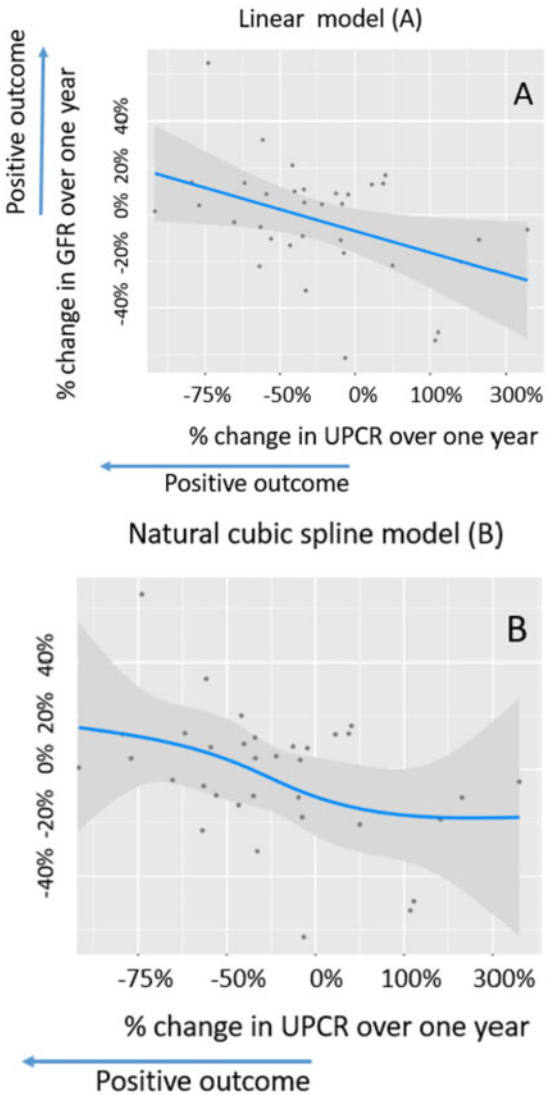
BACKGROUND AND AIMS: Considerable knowledge gaps exist in our understanding of the natural history of C3 glomerulopathy (C3G). Disease rarity, multiple nomenclature changes, and the inclusion of dissimilar cases in historical cohorts have precluded retrospective studies to define the natural course of C3G and identify risks for progression to kidney failure (end stage renal disease/ESRD). In the present analysis, we focus on C3G patients with native kidneys and examine the relationship between reductions in UPCR and disease progression as indicated by changes in eGFR.

METHOD: Patients included in this study were consented and enrolled in the University of Iowa C3G ReCom Registry, which was created in 2013. Beginning in 2017, complement activity and renal function data were collected prospectively at approximately 6-month intervals to define the natural history of C3G. Analyses were performed across 1-year periods of time ("spans"). To be included in a span, a patient had to meet the following criteria at the start of the 1-year period: native C3G, eGFR $\geq$30 mL/min/1.73 m^2, UPCR $\geq$1 g/g and $\geq$12 years of age. An individual patient could be included in more than one span.



MO136 Figure: Linear regression and natural cubic spline models for the relationship of change in UPCR to change in eGFR for all 1-year spans (N=34) included in the analysis ($p<0.05$).

RESULTS: Analyses were performed using 34 one-year spans for 24 patients who met inclusion criteria at the beginning of the 1-year span. Baseline characteristics for the 34 spans were: male, 59%; mean age, 22.7 years; mean eGFR, 83.1 ml/min/1.73m2; mean UPCR, 2.86 g/g; mean plasma C3, 75.1 mg/dL.

eGFR / UPCR correlation analyses: Linear regression and natural cubic spline models that included explanatory variables of log2 change from baseline UPCR, baseline C3, baseline UPCR and baseline eGFR, were consistent in demonstrating the relationship between reductions in UPCR and preservation of eGFR (see Figure 1). The linear regression model based on 34 spans indicated that a 50% reduction in UPCR over 1 year is associated with a predicted 9% relative improvement in percent change from baseline in eGFR ($p=0.03$), whereas a 30% reduction in UPCR is associated with a predicted 4.6% relative improvement in eGFR.

Stratified analyses based on UPCR: Further analyses were performed in two subgroups: (i) those with a reduction in UPCR $<$ 50% over 1 year (N=23), and (ii) those with a reduction in UPCR $\geq$ 50% over 1 year (N=11). eGFR decreased by a mean value of 10.5% during 1-year spans in which there was a $<$ 50% reduction in UPCR; however, for 1-year spans with a $\geq$ 50% decrease in UPCR, eGFR increased by 8.1%. Furthermore, a categorical variable was defined such that renal progression was categorized as at least a 30% or at least a 10% decline in eGFR over 1 year. For the 23 spans with a $<$ 50% reduction in UPCR, eGFR decreased by $\geq$ 10% and $\geq$ 30% in 10 (44%) and 5 (22%) of the spans, respectively. In contrast, for spans with a $\geq$ 50% reduction in UPCR, eGFR decreased by $\geq$ 10% in 2 (18%) spans but was not reduced by $\geq$ 30% in any spans.

Similar analyses using only the first 1-year span for each of the 24 patients produced results that were consistent with those generated using all 1-year spans. Limitations of this study include its small sample size and data variability due to its observational nature.

CONCLUSION: The findings of this observational study support the premise that reductions in proteinuria are associated with a more stable eGFR in native kidney C3G. Regression analyses using UPCR as a continuous variable demonstrate the relationship between reduction in UPCR and preservation of eGFR. This association was also observed using both change in eGFR by UPCR reduction subgroup and UPCR-eGFR categorical analyses.