Poster# FR-PO858

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Concordance of proteinuria thresholds between Chinese and UK cohorts with IgA nephropathy

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KEY FINDINGS AND CONCLUSIONS

- Despite differences in baseline characteristics between the UK and Chinese cohorts, higher time-varying proteinuria and low baseline eGFR consistently correlated with poorer kidney outcomes in patients with IgAN
- In both cohorts, the risk of kidney failure persisted even in patients below the recommended proteinuria threshold of <1 g/day
- Reducing proteinuria as much as possible should be a key consideration when setting treatment goals for IgAN

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INTRODUCTION

- IgA nephropathy (IgAN) is the leading cause of primary glomerulonephritis globally[1–3]
- Proteinuria is an established biomarker for clinical outcomes in IgAN and a strong predictor of progression to kidney failure[2,4–6]
  - At the time of this study, KDIGO guidelines recommend a treatment goal of proteinuria <1 g/day;[4] However, a recent Chinese study suggested that even patients with proteinuria as low as 0.3–<0.5 g/day could be at risk of progression to kidney failure[7]
  - Additionally, updates to KDIGO guidelines are expected to propose a therapeutic target of <0.3–0.5 g/day[8]
- To determine the applicability of the conclusion of the Chinese study to other patient cohorts, we compared the baseline characteristics and kidney outcomes of UK patients with IgAN,[9] with patients from this Chinese cohort[7]

METHODS

- This retrospective cohort study analyzed data from 950 adult patients with biopsy-proven IgAN enrolled in the UK RaDaR* registry, which is one of the largest and most comprehensive population-based datasets of rare kidney diseases[9]
- Baseline characteristics, proteinuria findings, and kidney survival analysis were conducted on the UK patient dataset and compared with a Chinese cohort of 1530 adult patients with IgAN[7]
- Kidney survival was calculated from baseline to first composite kidney failure (CKF) event; CKF1 was defined as kidney replacement therapy (KRT; dialysis or transplant) or a 50% reduction in the estimated glomerular filtration rate (eGFR); CKF2 was defined as KRT only

RESULTS

Baseline characteristics

- A higher number of UK patients were male (68.1% vs 51.4%) and older (43.0 ± 15.1 years vs 36.5 ± 12.0 years) compared with Chinese patients (**Table 1**)
- UK patients had higher proteinuria (48.0% vs 32.5% ≥2 g/day) and more advanced chronic kidney disease (CKD) (68.0% stage 3+ vs 31.0%) at baseline compared with Chinese patients (**Table 1**)

Table 1. Baseline characteristics of UK and Chinese cohorts

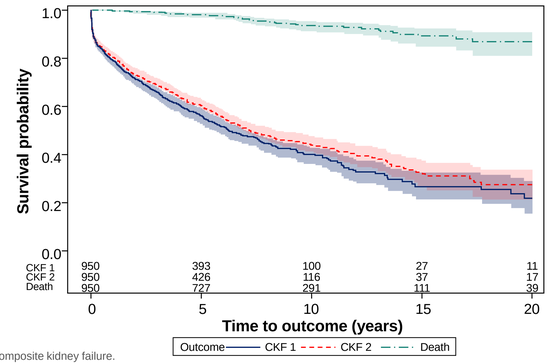
	UK cohort (N=950)	Chinese cohort[7] (N=1530)
Age, years, mean (SD)	43.0 (15.1)	36.5 (12.0)
Male, %	68.1	51.4
Female, %	31.9	48.6
CKD stage 3+, %	68.0	31.0
Baseline proteinuria, %		
<0.3 g/day	10.3	8.3
0.3–<0.5 g/day	5.1	9.1
0.5–<1 g/day	13.4	22.9
1–<2 g/day	23.1	27.1
≥2 g/day	48.0	32.5
Baseline eGFR, mean (SD), mL/min/1.73 m^2	49.1 (31.1)	78.4 (30.4)

eGFR, estimated glomerular filtration rate; SD, standard deviation.

Kidney survival time varied between the UK and Chinese cohorts

- In the UK cohort, the mean (standard error) kidney survival† was 8.69 (0.32) years and 8.89 (0.27) years for CKF1 and CKF2, respectively (**Figure 1**)
- At 5 years, CKF1 was reached by 42.1% of patients from the UK cohort equating to a 5-year survival rate (95% confidence interval [CI]) of 0.56 (0.53–0.59)
  - In the same time period, death was recorded for 1.8% of patients from the UK cohort equating to a 5-year survival rate (95% CI) of 0.98 (0.97–0.99)
  - In the Chinese cohort, 16.1% and 0.2% of patients reached CKF1 and death over 5 years, respectively[7]

Figure 1. Kaplan-Meier analysis of CKF1 and CKF2‡ in UK patients



CKF, composite kidney failure.

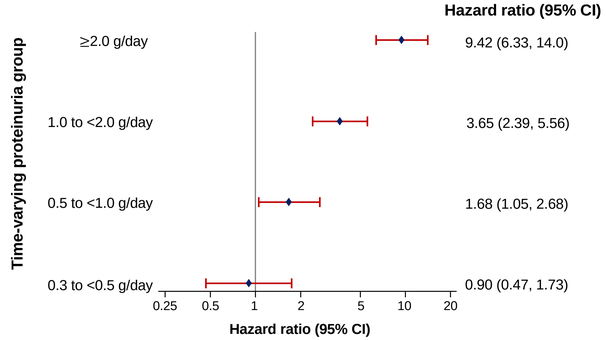
Time-varying proteinuria was associated with prognosis

- Consistent with findings from the Chinese cohort,[7] time-varying proteinuria was associated with prognosis in the UK cohort
  - Similar to the Chinese cohort,[7] the risk of kidney failure (CKF1) in the UK cohort increased with higher levels of time-varying proteinuria (**Figure 2**)
  - Patients with time-varying proteinuria levels ≥2 g/day had the highest hazard ratios for kidney failure (CKF1), but even those with levels ≥0.5 g/day were at an elevated risk
  - Patients with time-varying proteinuria between 0.3 to <0.5g/day did not have an increased hazard ratio for kidney failure (CKF1)

Low baseline eGFR correlated with reduced kidney survival

- In both the UK and Chinese cohort, patients with low baseline eGFR had a higher probability of experiencing a CKF event
  - Over the median follow-up time of 7.3 years, UK patients with a baseline eGFR of <60 mL/min/1.73 m^2 had a significantly increased risk of reaching CKF1 (65.3%) or CKF 2 (63.6%) compared with patients with a baseline eGFR of ≥60 mL/min/1.73 m^2 (26.6% and 19.7%, respectively)
- The risk of death was elevated in patients with lower eGFR, with 7.1% in the lower eGFR subgroup at risk compared with 1.3% in the higher eGFR subgroup

Figure 2. Hazard ratios for CKF1 based on time-varying proteinuria¶



CI, confidence interval; CKF, composite kidney failure.

Limitations of the analysis

- Statistical methods varied between studies; the Chinese study used marginal structural models,[7] whereas this study used Cox regression analysis, which limits adjustment for time-dependent confounders but considers the effect of time-varying proteinuria on event hazard
- Only patients in the UK cohort with baseline eGFR measurements were included in this analysis, which could potentially introduce bias into the results; however, a sensitivity analysis confirmed that similar trends were observed within the total UK RaDaR population
- For the UK cohort, proteinuria levels were converted from mg/mmol to g/day to allow a direct comparison with the proteinuria levels published for the Chinese cohort[7]

*National Registry of Rare Kidney Diseases; †The mean survival time and its standard error were underestimated due to censoring of the largest observation and estimation restriction to the largest event time;
‡Both CKF1 and CKF2 were censored at death; §Based on urine protein–creatinine ratios;
¶Reference group is time-varying proteinuria of <0.3 g/day, data were adjusted for age, sex, CKD stage, ethnicity, and deprivation status.

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Disclosures

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