PO1529

Natural History of FSGS: The UK National RaDaR Idiopathic Nephrotic Syndrome Cohort

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Introduction

Background

- Focal segmental glomerulosclerosis (FSGS) is a common glomerular lesion in nephrotic syndrome (NS)[1] that often leads to kidney failure[2]
- Published studies to date are small with short follow-up periods, limiting understanding of the natural history of FSGS

Objective

- To describe the natural history of primary/idiopathic and genetic FSGS in adult and paediatric patients in the United Kingdom (UK)

Methods

Data Source

- The National Registry of Rare Kidney Diseases (RaDaR) is a UK Kidney Association (UKKA) initiative that collects retrospective and prospective data from patients with rare kidney diseases in the UK
- The Idiopathic Nephrotic Syndrome Rare Disease Group (RaDaR-INS) includes 3,907 patients with NS not attributable to glomerulonephritis or systemic disorders
- Recruitment began in 2010 to RaDaR-INS and is ongoing in 107 adult and paediatric kidney units across the UK

Definitions and Clinical Measures

- Disease onset defined as the first occurrence of positive diagnostic renal biopsy, primary renal diagnosis, symptom presentation, initiation of immunosuppression, or first recorded proteinuria >1 g/g
- Estimated glomerular filtration rate (eGFR) calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula (adults) and the modified Schwartz formula (paediatric)
- End-stage kidney disease (ESKD) defined as CKD stage 5 (confirmed eGFR <15 mL/min/1.73m^2 or CKD stage 5 recorded in RaDaR) or receiving chronic dialysis or kidney transplant

Eligibility Criteria

- Patients with biopsy-proven or monogenic FSGS and ≥12 months observation from disease onset were included
- Patients with ESK at or prior to disease onset as defined were excluded

Statistical Analyses

- Comparisons across groups evaluated via Chi-square test, a two-sample t-test, or Wilcoxon-Mann-Whitney test, as appropriate
- eGFR slope calculated as an annualised value from disease onset to ESKD onset date/death date or last follow up date. Linear mixed model used to estimate each patient's intercept and slope of (eGFR).
- Renal survival defined as absence of ESKD or death with survival time calculated from disease onset to ESKD onset date/death date or last follow-up

RaDaR, the UK Rare Renal Disease Registry (www.rarerenal.org), was established by the UK Kidney Association (https://ukkidney.org) in 2010 and now includes more than 26,000 patients at over 100 UK hospitals who have been diagnosed with one of 30 categories of rare kidney disease and who have provided written informed consent to participate. It is hosted by the UK Renal Registry (https://ukkidney.org/about-us/who-we-are/uk-renal-registry) and incorporates links to other national databases and, for the majority of participants, automated upload of biochemical and other hospital medical record data.

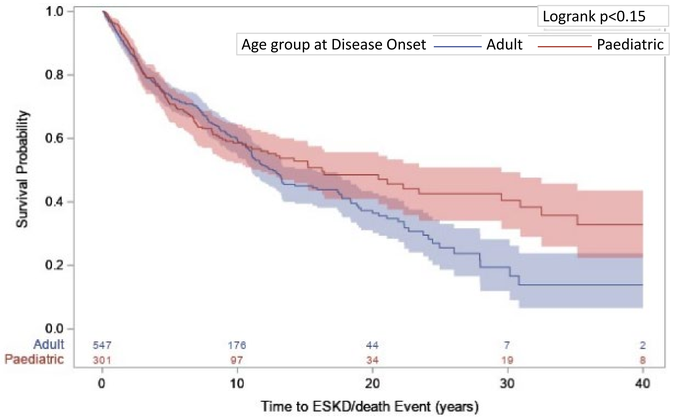
Results

Table 1. Disease onset characteristics and outcomes of paediatric and adult patients with FSGS

		Overall (N=848)	Paediatrics (<18 years) (n=301)	Adults (≥18 years) (n=547)	P-Value*
Age, Median (IQR)		29.5 (10.7-49.7)	5.4 (2.7-12.1)	42.2 (30.6-55.9)	
Sex (F), %		44.0	50.2	40.6	<0.01**
Race/Ethnicity, %					<0.01**
White		70.4	67.4	72.0	
Asian		11.4	16.3	8.8	
Black		6.8	4.0	8.4	
Multiple Races		1.4	3.0	0.6	
Other		1.3	1.3	1.3	
Not stated / Missing		8.6	8.0	9.0	
PCR (g/g)	n (%)	157 (18.5)	49 (16.3)	108 (19.7)	0.2**
	Median (IQR)	5.8 (3.1-10.7)	11.1 (5.7-18.6)	4.7 (2.0-7.9)	<0.01‡
	≥3.0 g/g, %	75.2	93.9	66.7	<0.01**
eGFR (mL/min/1.73m^2)	n (%)	200 (23.6)	67 (22.3)	133 (24.3)	0.58**
	Median (IQR)	75.1 (43.6-106.0)	101.9 (73.8-133.9)	59.6 (35.1-90.2)	<0.01‡
Duration of Follow-up (years), Median (IQR)		10.0 (5.9-16.3)	10.9 (6.9-18.0)	9.7 (5.4-15.7)	<0.01‡
ESKD or Death Events, n (%)		381 (44.9)	131 (43.5)	250 (45.7)	
First ESKD or Death Event, %					0.07**
CKD Stage 5		63.5	63.4	63.6	
Chronic Dialysis		25.2	23.7	26.0	
Kidney Transplant		7.4	9.9	6.0	
Death		3.9	3.1	4.4	
Time to First ESKD Event (years), Median (IQR)		4.2 (1.9-8.9)	4.0 (2.0-7.0)	4.2 (1.9-10.0)	0.28‡
Median (95% CI) Renal Survival (years)#		13.2 (11.6-17.4)	16.2 (11.7-29.5)	12.6 (11.0-15.6)	
Age at First ESKD Event (years), Median (IQR)		37.9 (17.3-54.4)	12.7 (6.6-17.4)	48.2 (37.9-61.3)	
Rate of Loss of eGFR (mL/min/1.73m^2/year)	n (%)	619 (73.0)	212 (70.4)	407 (74.4)	
	Median (IQR)	-3.2 (-8.9,-0.6)	-6.0 (-24.8, -0.6)	-2.6 (-6.1, -0.5)	<0.01‡

Abbreviations: CI, confidence interval; **CKD**, chronic kidney disease; **eGFR**, estimated glomerular filtration rate; **ESKD**, end-stage kidney disease; **IQR**, interquartile range; **PCR**, urine protein to creatinine ratio. *Paediatric vs. adult comparison; **Chi-square; Albumin to creatinine ratio values converted to PCR by applying a factor of 1.43;[3] ‡Mann-Whitney; #See Figure 1.

Figure 1. Kaplan-Meier survival curves (95% CI) for time to first ESKD/death event among paediatric and adult patients with FSGS



Conclusion

Summary and Discussion

- Of 848 FSGS patients meeting eligibility, children represent 35% of the study population
- While eGFR at onset was higher in children, proteinuria was greater and rate of loss of eGFR more rapid than in adults, indicative of a more aggressive course of progression to ESKD
- Kaplan Meier survival curves of children and adults show 50% renal survival probability of 16 years & 13 years, respectively
- These data confirm a poor outcome of FSGS in the largest cohort of its kind to date, and detail the renal survival probabilities in children and adults
- Other associations with outcome, such as response to immunotherapy, will be examined in ongoing analyses

Strengths and Limitations

- Large patient sample with high level of completeness for renal events derived from a nationwide database involving a large proportion of UK kidney units
- Data were presented from both paediatric and adult FSGS populations with lengthy follow-up
- Reporting of proteinuria and eGFR data at disease onset is incomplete and may not be representative of the full cohort, however data are likely to be missing at random with limited bias

Conclusions

- The data demonstrate the power of studying a large national cohort of patients with FSGS over a >10-year time period. These analyses indicate progression and poor outcomes, particularly in children, highlighting a need for early diagnosis and effective treatments for patients with FSGS

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