FR-PO662

Predictors of Progression to Kidney Failure in Patients with Focal Segmental Glomerulosclerosis

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[1]Providence Health Washington; [2]University of Washington School of Medicine; [3]Travere Therapeutics Inc.; [4]Genesis Research LLC.; [5]University of California, Los Angeles, David Geffen School of Medicine

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Presented at the American Society of Nephrology's Kidney Week 2022, November 3-6, 2022, Orlando, FL

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DISCLOSURES

- **KRT, RA:** Providence Health Washington, University of Washington School of Medicine
- **KD, CJ, LK:** Providence Health Washington
- **MB, KMT, LP, KW:** Travere Therapeutics Inc
- **DA:** Genesis Research LLC
- **KN, SN:** University of California, Los Angeles, David Geffen School of Medicine

- FSGS is a glomerular disease phenotype that often progresses to kidney failure
- However, to risk stratify patients treated in usual clinical practice, predictors of progression are not well-delineated
- The study aim was to use real-world data to identify patients with FSGS and determine predictors of substantial eGFR decline, which is associated with a high risk of reaching kidney failure

eGFR, estimated glomerular filtration rate; FSGS, focal segmental glomerulosclerosis.

METHODS

Study Time Periods

- Entry: Date of FSGS identification between 2016-2020
- Baseline period: Date of FSGS identification through the next 180 days
- Follow-up period: After baseline period until study outcome or censorship for last eGFR measure calculated by CKD-EPI 2021

Inclusion Criteria

- Data source is the CURE-CKD Registry based on electronic health records from Providence and UCLA Health[1,2]
- Adults, ≥18 years
- FSGS identified by ICD-10 diagnosis codes

Exclusion Criteria

- Kidney failure before or during baseline period:
  - Baseline eGFR <15 mL/min/1.73 m^2
  - Diagnosis code for kidney failure (ICD-10)
  - Procedure (ICD-9/10) or diagnosis (ICD-10) codes for dialysis
  - Procedure code for kidney transplant (ICD-9/10)
- No eGFR measurements during baseline or follow-up

1. Tuttle KR, et al. *JAMA Netw Open*. 2019;2(12):e1918169; 2.Norris KC, et al. *BMC Nephrol*. 2019;20(1):416.

CKD-EPI, chronic kidney disease epidemiology collaboration; eGFR, estimated glomerular filtration rate; FSGS, focal segmental glomerulosclerosis.

METHODS

Outcomes

- Primary: Composite of ≥40% eGFR decline or kidney failure
- Secondary:
  - ≥40% eGFR decline: Indicator of high risk for kidney failure
  - Kidney failure:
    - eGFR <15 mL/min/1.73 m^2
    - Diagnosis code for kidney failure (ICD-10)
    - Procedure (ICD-9/10) or diagnosis code (ICD-10) for dialysis
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Statistical Analyses

- Kaplan-Meier survival estimates of time to first event for primary composite outcome and secondary outcomes
- Cox Proportional Hazard modeling to identify baseline predictors of primary composite outcome (N=325)
- Sensitivity: Macroalbuminuria (UACR >300 mg/g)/overt proteinuria (UPCR >0.5 g/g) status was added to the model for the subset of patients with available baseline measures (N=195)

eGFR, estimated glomerular filtration rate; UACR, urine albumin-creatinine ratio; UPCR, urine protein creatinine ratio.

RESULTS

Table 1. Characteristics of Patients with FSGS, 2016-2020 (N=325)

Demographics	
Sex, n (%)	
Men	175 (53.8)
Women	150 (46.2)
Race and ethnicity, n (%)	
American Indian or Alaska Native	5 (1.5)
Asian	49 (15.1)
Black	33 (10.2)
Hispanic or Latino(a)	12 (3.7)
Native Hawaiian or Pacific Islander	4 (1.2)
White	168 (51.7)
Other[a]	46 (14.2)
Missing	8 (2.5)
Age, y, mean, SD	51, 17
Primary health insurance, n (%)	
Medicare	81 (24.9)
Medicaid	26 (8.0)
Commercial	177 (54.5)
Uninsured	5 (1.5)
Missing	36 (11.1)

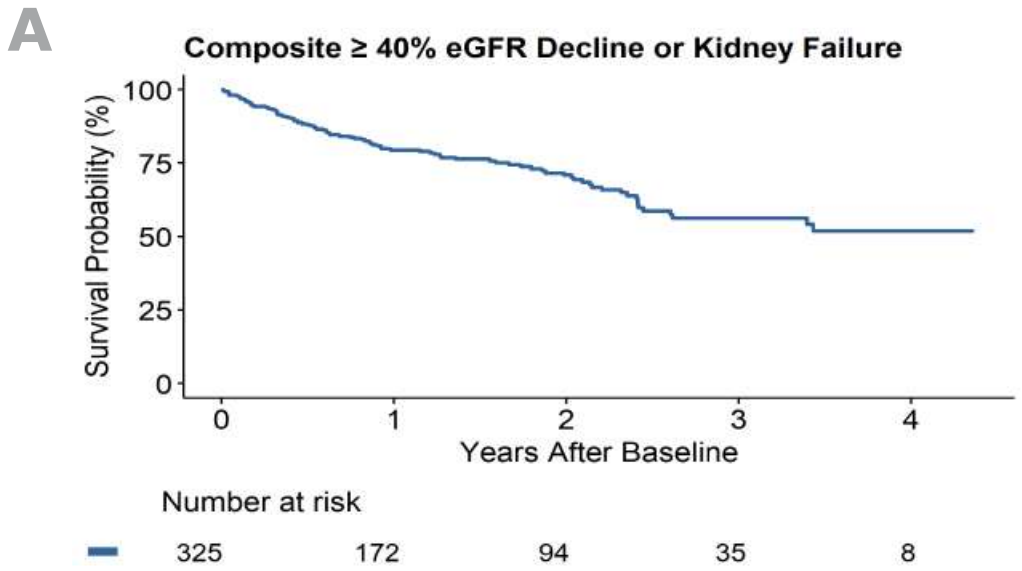
[a] Includes patients that did not identify with main census categories.

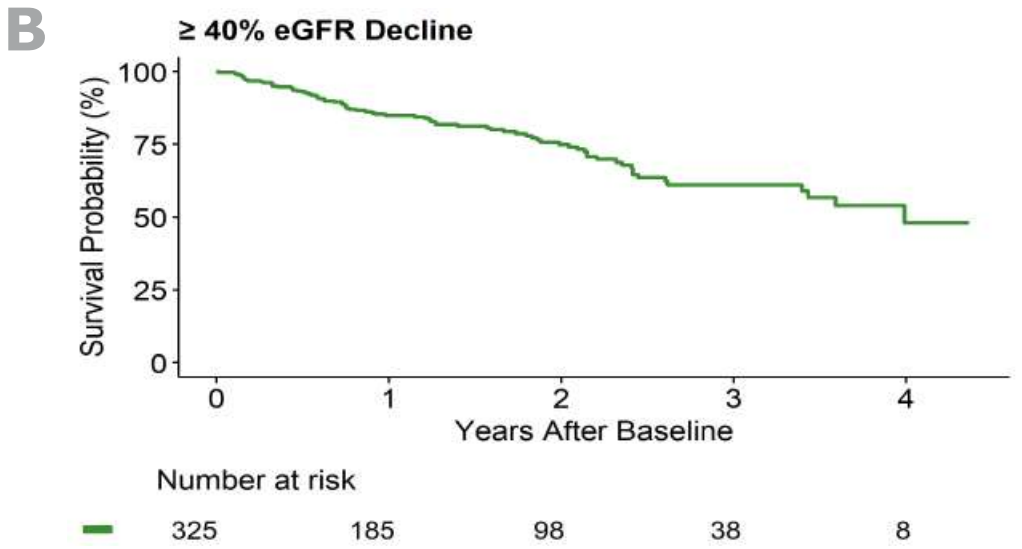
Baseline Medications, n (%)	
ACE inhibitor/ARB	216 (66.5)
Calcineurin inhibitor	52 (16.0)
Glucocorticoid	115 (35.4)
Baseline Clinical Characteristics	
Hypertension, n (%)	276 (84.9)
Diabetes, n (%)	112 (34.5)
eGFR, mL/min/1.73 m²	
n (%)	325 (100.0)
mean, SD	58.4, 29.1
CKD Stage 1-2: ≥60, n (%)	139 (42.8)
CKD Stage 3a: 45-59, n (%)	57 (17.5)
CKD Stage 3b: 30-44, n (%	61 (18.8)
CKD Stage 4: 15-29, n (%)	68 (20.9)
HbA1c, %	
n (diabetes) (%)	68 (60.7)
mean, SD	7.0, 1.2
UACR, mg/g	
n (%)	109 (33.5)
median (IQR)	939 (156-2134)
UPCR, g/g	
n (%)	106 (32.6)

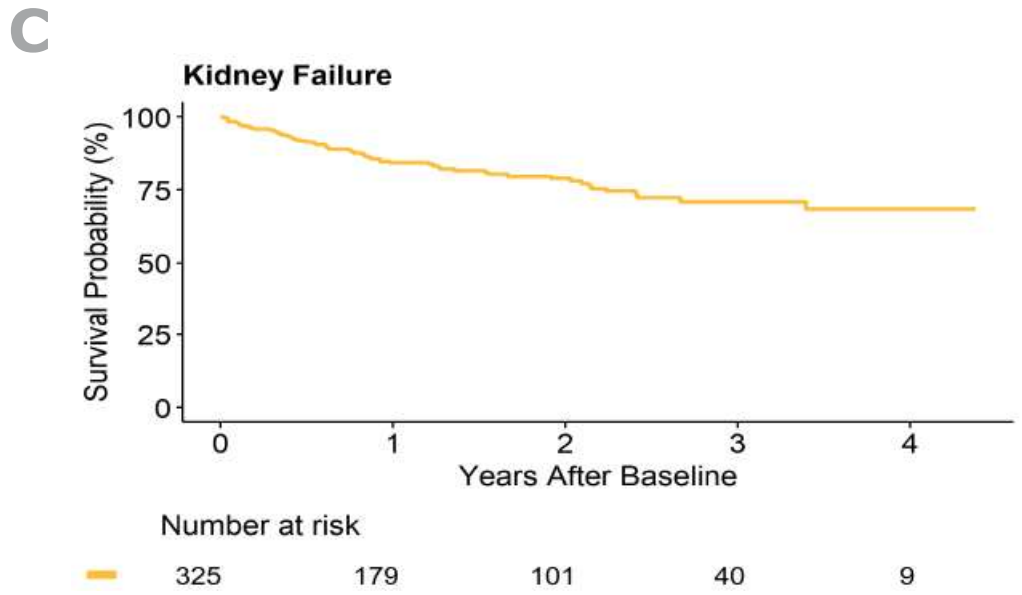
ACE, angiotensin converting enzyme; ARB, angiotensin receptor blocker; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; FSGS, focal segmental glomerulosclerosis; HbA1c, hemoglobin A1c; UACR, urine albumin-creatinine ratio; UPCR, urine protein creatinine ratio.

RESULTS

Figure 1. Kaplan-Meier Survival Analysis for (a) Composite ≥40% eGFR Decline or Kidney Failure (b) ≥40% eGFR Decline (c) Kidney Failure







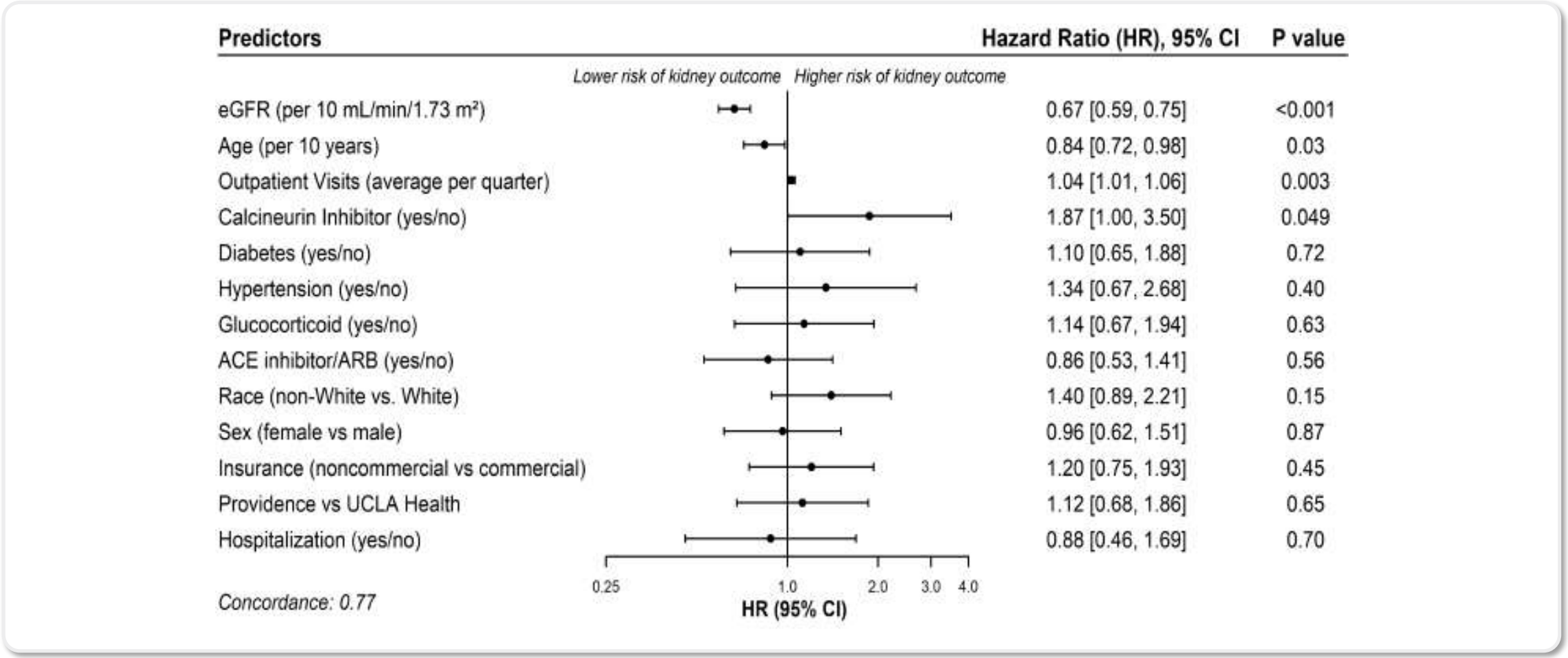
eGFR, estimated glomerular filtration rate.

Outcomes Frequency

- Primary composite outcome ≥40% eGFR decline or kidney failure
  - 88/325 (27.1%) reached a first event at a median of 1.2 years
- ≥40% eGFR Decline
  - 75/325 (23.1%) total events
- Kidney Failure
  - 61/325 (18.8%) total events
- In the presence of unmeasured competing risks (eg, death) predictors are limited to the cause-specific hazard function

eGFR, estimated glomerular filtration rate.

Figure 2. Predictors of Primary Composite Outcome of ≥40% eGFR Decline or Kidney Failure in Patients with FSGS (N=325)



ACE, angiotensin converting enzyme; ARB, angiotensin receptor blocker; eGFR, estimated glomerular filtration rate, FSGS, focal segmental glomerulosclerosis.

CONCLUSIONS

- Risks of progression to kidney failure are high in real world patients with FSGS treated in usual clinical practice.
- Earlier detection, with particular attention to younger patients, is needed to detect FSGS when therapeutic strategies may be most beneficial.

FSGS, focal segmental glomerulosclerosis.

Predictors of Progression to Kidney Failure in Patients with Focal Segmental Glomerulosclerosis

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Background and Study Aim

Focal segmental glomerulosclerosis (FSGS) is a glomerular disease phenotype that often progresses to kidney failure. However, to risk stratify patients treated in usual clinical practice, predictors of progression are not well-delineated.

The study aim was to use real-world data to identify patients with FSGS and determine predictors of substantial estimated glomerular filtration rate (eGFR) decline, which is associated with a high risk of reaching kidney failure, or kidney failure.

Methods

Study Time Periods

- Entry: Date of FSGS identification between 2016-2020
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- **Primary: Composite of ≥40% eGFR decline or kidney failure**
- **Secondary:**
  - **≥40% eGFR decline:** Indicator of high risk for kidney failure
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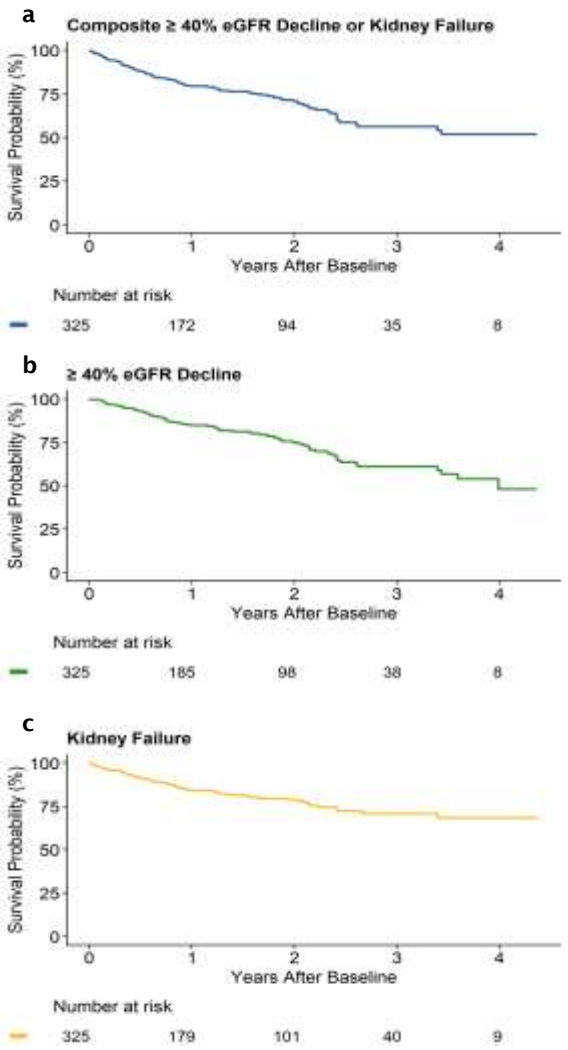

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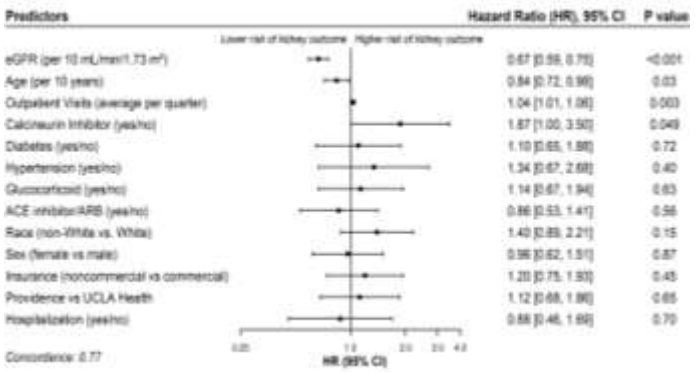

Sensitivity Analysis

- Macroalbuminuria/overt proteinuria (HR: 4.06, 95% CI: 1.34-12.34, p=0.01) was an independent predictor for the composite outcome
- Overall model stability persisted for other predictors

Summary

- Real world patients with FSGS have high rates of ≥40% eGFR decline or kidney failure within a relatively short timeframe
- Younger patients and those with lower kidney function were at greater risk.
- More frequent outpatient visits and calcineurin inhibitor use may reflect bias by indication in higher risk patients

Conclusions

Risks of progression to kidney failure are high in real world patients with FSGS treated in usual clinical practice.

Earlier detection, with particular attention to younger patients, is needed to detect FSGS when therapeutic strategies may be most beneficial.

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References
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