Predictors of Major Adverse Kidney Disease Events in a Real-World Population With IgA Nephropathy

Katherine R. Tuttle,[1,2] Lindsey M. Kornowske,[1] Cami R. Jones,[1] Kenn B. Daratha,[1] Radica Z. Alicic,[1,2] Christina L. Reynolds,[1] Joshua J. Neumiller,[1,3] Mark E. Bensink,[4] Wu Gong,[4] Keith C. Norris,[5] Susanne B. Nicholas,[5] on behalf of CURE-CKD Investigators

[1]Providence Health & Services, Spokane, WA; [2]University of Washington School of Medicine, Seattle, WA; [3]Washington State University, Spokane, WA; [4]Travere Therapeutics, Inc, San Diego, CA; [5]University of California, Los Angeles, David Geffen School of Medicine, Los Angeles, CA

Background and Aims

IgA nephropathy (IgAN) is a glomerular disease that may progress to kidney failure.[1] While albuminuria or proteinuria and reduced kidney function are associated with greater risk, other predictors are less clear.[2,3] This study used a real-world population to assess clinical predictors of major adverse kidney disease events (MAKDE) in IgAN.

Study Population and Methods

Data Source

Approximately 4 million electronic health records from the Center for Kidney Disease Research, Education, and Hope (CURE-CKD) Registry were used to derive the study population from Providence and UCLA Health systems.[4,5]

Cohort Selection

- Adults (≥18 years) identified with IgAN from 2016 to 2020 (*ICD-10* code N02.0, N02.8, or N02.9); N=1105
  - No history of kidney failure (baseline estimated glomerular filtration rate (eGFR) <15 mL/min/1.73 m^2, codes for kidney failure, dialysis, transplant)
  - Measured for eGFR at baseline and during follow-up
- Diabetes and hypertension were identified by established CURE-CKD criteria (clinical data, medications, diagnostic codes)[4]

Study Outcome

Patients were followed for a MAKDE composite outcome beginning 6 months after IgAN identification through the last eGFR measurement:

- 40% eGFR decline from baseline
- eGFR <15 mL/min/1.73 m^2
- *ICD-10* diagnosis or procedure code for kidney failure, dialysis, or transplant

Analysis

- Kaplan-Meier estimates for MAKDE survival were computed
- Cox proportional hazards modeling evaluated possible clinical predictors of MAKDE hazard
- Additional descriptive and modeling analysis was conducted for patients with urine albumin-to-creatinine ratio (UACR)/urine protein-to-creatinine ratio (UPCR) measurements

Table 1. Characteristics of Patients With IgAN, 2016-2020

		UACR/UPCR measures	
	Total	**Yes**	**No**
Patients, n (% of total)	1105 (100.0)	339 (30.7)	766 (69.3)
Demographics			
Age, mean (SD), years	55 (18)	49 (16)	58 (18)
Sex, n (%)			
Men	549 (49.7)	174 (51.3)	375 (49.0)
Women	556 (50.3)	165 (48.7)	391 (51.0)
Race and ethnicity, n (%)			
American Indian or Alaska Native	11 (1.0)	3 (0.9)	8 (1.0)
Asian	159 (14.4)	72 (21.2)	87 (11.4)
Black	36 (3.3)	7 (2.1)	29 (3.8)
Hispanic or Latino(a)	39 (3.5)	11 (3.2)	28 (3.7)
Native Hawaiian or Pacific Islander	10 (0.9)	2 (0.6)	8 (1.0)
White	683 (61.8)	182 (53.7)	501 (65.4)
Other or missing	167 (15.1)	62 (18.3)	105 (13.7)
Primary health insurance, n (%)			
Commercial	621 (56.2)	229 (67.6)	392 (51.2)
Medicaid	98 (8.9)	33 (9.7)	65 (8.5)
Medicare	350 (31.7)	69 (20.4)	281 (36.7)
Uninsured	20 (1.8)	3 (0.9)	17 (2.2)
Missing/unknown	16 (1.4)	5 (1.5)	11 (1.4)
Health system and care utilization, n (%)			
System			
Providence	392 (35.5)	118 (34.8)	274 (35.8)
UCLA Health	713 (64.5)	221 (65.2)	492 (64.2)
Hospitalization	214 (19.4)	50 (14.7)	164 (21.4)
Medications (prescribed ≥45 d), n (%)			
ACE inhibitor/ARB	539 (48.8)	221 (65.2)	318 (41.5)
Corticosteroids	283 (25.6)	103 (30.4)	180 (23.5)
Other immunomodulators*	70 (6.3)	29 (8.6)	41 (5.4)
SGLT2 inhibitor	2 (0.2)	2 (0.6)	–
Clinical characteristics			
Hypertension, n (%)	868 (78.6)	276 (81.4)	592 (77.3)
Diabetes, n (%)	260 (23.5)	94 (27.7)	166 (21.7)
eGFR, mL/min/1.73 m^2, n (%)	1105 (100.0)	339 (100.0)	766 (100.0)
mean (SD)	77 (28)	71 (32)	79 (25)
UACR, mg/g, n (%)	196 (17.7)	196 (57.8)	–
median (IQR)	120 (30-518)	120 (30-518)	–
UPCR, g/g, n (%)	166 (15.0)	166 (49.0)	–
median (IQR)	0.7 (0.3-1.9)	0.7 (0.3-1.9)	–

*Biologics, calcineurin inhibitors, cytotoxic agents, mammalian target of rapamycin inhibitors, hormonal agents, and pyrimidine synthesis inhibitors.

ACE, angiotensin converting enzyme; ARB, angiotensin receptor blocker; eGFR, estimated glomerular filtration rate; IgAN, immunoglobulin A nephropathy; SLGT2, sodium-glucose cotransporter-2; UACR, urine albumin-to-creatinine ratio; UPCR, urine protein-to-creatinine ratio.

Contact
Katherine R. Tuttle, MD, FASN, FACP, FNKF
katherine.tuttle@providence.org

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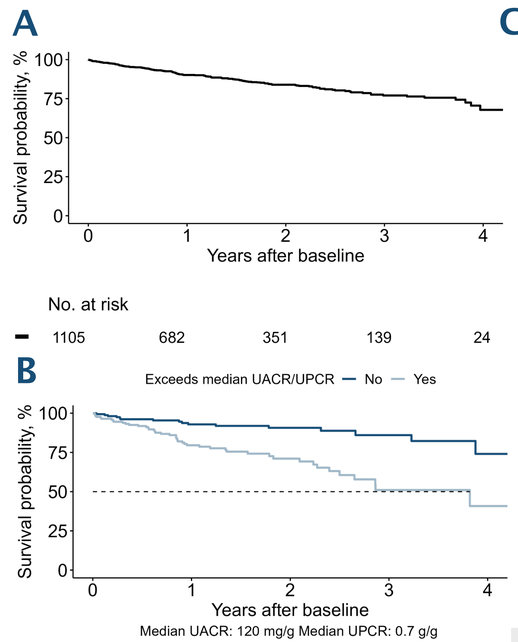
References
1. Rauen T, et al. *Kidney Int.* 2020;98(4)1044-52.
2. Rovin BH, et al. *Kidney Int.* 2021;100(4)753-79.
3. Floege J, et al. *Kidney Int.* 2022;102(1)22-4.
4. Tuttle KR, et al. *JAMA Netw Open.* 2019;2(12):e1918169.
5. Norris KC, et al. *BMC Nephrol.* 2019;20(1):416.

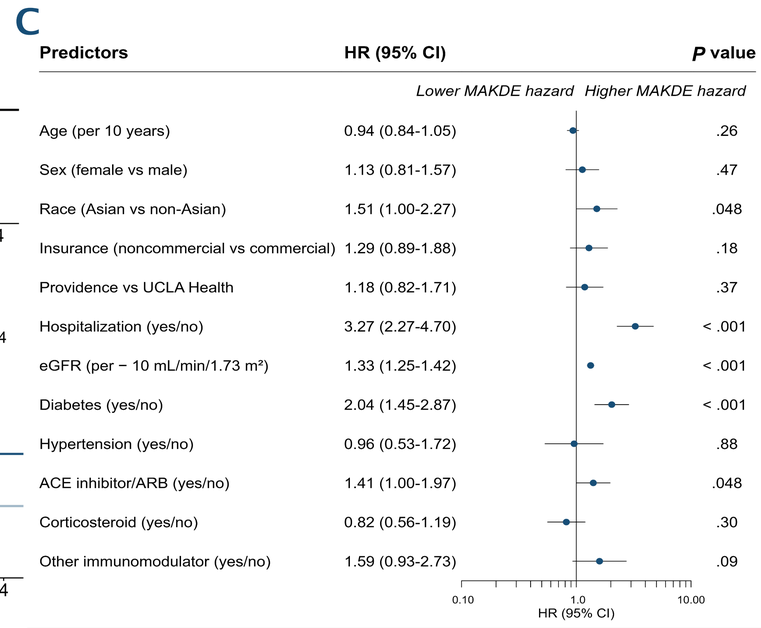
Results

- Median (IQR) follow-up was 1.6 (0.8-2.5) years
- MAKDE occurred in 13% of the total IgAN population by 3 years (**Figure 1A**)
- In a sensitivity analysis that included baseline UACR or UPCR measurements (**Figure 1B**), levels above vs below the median predicted higher MAKDE hazard (hazard ratio, 2.23; 95% CI, 1.15-4.30; *P*=.02)
- Predictors of MAKDE were Asian race, hospitalization, diabetes, renin-angiotensin system inhibitor use, and lower baseline eGFR (**Figure 1C**)

Figure 1. Summary of MAKDE Survival

A) Kaplan-Meier survival estimates of MAKDE in patients with IgAN. (N=1105)
B) Kaplan-Meier survival estimates of MAKDE by UACR/UPCR measure above vs below the median, 120 mg/g/0.7 g/g (N=339)
C) Forest plot with predictors of MAKDE in patients with IgAN (N=1105)





ACE, angiotensin-converting enzyme; ARB-angiotensin receptor blocker; CI, confidence interval; eGFR, estimated glomerular filtration rate; HR, hazard ratio; IgAN, immunoglobulin A nephropathy; MAKDE, major adverse kidney disease event; UACR, urine albumin-to-creatinine ratio; UPCR, urine protein-to-creatinine ratio.

Conclusions

- MAKDE were common in patients with IgAN treated in contemporary clinical practice at 2 large US health systems
- Asian race and illness severity reflected by hospitalizations, diabetes, and angiotensin-converting enzyme inhibitor/angiotensin receptor blocker use, as well as reduced kidney function and the presence of albuminuria or proteinuria, predicted MAKDE events
- To improve access to care and reduce disparities, identifying high-risk patients within health systems can enable better detection of those who may benefit from monitoring and intervention