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Age-adjusted global glomerulosclerosis is important prognostic factor in IgA nephropathy

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Objectives: The Oxford classification using histopathological finding was developed and reported to predict outcome of IgA nephropathy (IgAN). The upper reference limit (95th percentile) for the number of globally sclerotic glomeruli (GSG) expected on biopsy according to age was determined. And based on the age-adjusted reference of upper limits for GSG, the prognosis of chronic kidney disease is best predicted independently. We aimed to determine whether the prognosis of IgAN is affected by the age-adjusted number of GSG independently of T score of the Oxford classification.

Methods: Patients with a biopsy-proven IgAN were enrolled in a single center. Patients with a follow-up of less than one year were excluded. A total of 217 patients were studied retrospectively. The renal biopsy pathologic examination was reviewed by two pathological experts using Oxford classification; METS-C score. When there are more GSG than the upper reference limit (95th percentile) for the number of GSG expected on biopsy according to age, it is defined as GSG abnormal for age. The primary outcomes were annual eGFR decline and eGFR level 40% lower than baseline eGFR lasting at least one month.

Results: Patients with GSG abnormal for age was 111. They were associated with higher serum creatinine, more 24hr urine protein, higher blood pressure, lower eGFR, and higher MEST-C scores (Table1). In multivariable Cox model, patients of GSG abnormal for age had more rapid eGFR decline (Δ eGFR -2.382, P = 0.019, Table 2A) and poor renal outcome (HR 27.675 [2.307 – 331.997], Table 2B). Kaplan-Meier curve showed that patients in GSG abnormal for age developed more renal outcome, especially in patients with T score of 0 (Figure, p-value < 0.001, by log-rank test).

Conclusions: Our results suggest that the number of age-adjusted GSG might be an independent prognostic factor of IgAN in addition to Oxford classification

Table1. Clinical characteristics Table2. eGFR decline and renal outcome

Table 1. Clinical characteristics between GSG normal for age and GSG abnormal for age

	GSG normal for age (n = 106)	GSG abnormal for age (n = 111)	p-value
Age, year	40.5 (24.5 – 51.0)	40.0 (33.0 – 50.0)	0.434
BMI,	24.4 ± 4.3	24.0 ± 3.4	0.484
Total glomeruli, count	22 (13 – 35)	23 (15 – 33)	0.900
GSG, count	1 (0 – 1)	5 (3 – 10)	< 0.001
Creatinine, mg/dL	0.8 (0.6 – 1.0)	1.0 (0.8 – 1.3)	< 0.001
eGFR, ml/min/1.73 m ²	108.2 (88.8 – 124.3)	80.7 (63.6 – 108.0)	< 0.001
24hr urine protein, g/day	0.491 (0.262 – 1.463)	0.763 (0.425 – 1.681)	0.012
Rates of eGFR decline, ml/min/1.73 m ² per year	-2.61 (-7.56 – -0.53)	-4.37 (-8.45 – -1.67)	0.024
Male, n%	59 (55.7%)	67 (60.4%)	0.483
The Oxford classification			
M1, n(%)	37 (34.9%)	76 (68.5%)	< 0.001
E1, n(%)	48 (45.3%)	60 (54.1%)	0.196
S1, n(%)	76 (71.7%)	102 (91.9%)	< 0.001
T1, n(%)	7 (6.6%)	42 (37.8%)	< 0.001
T2, n(%)	1 (0.9%)	2 (1.8%)	
C1, n(%)	24 (22.6%)	42 (37.8%)	0.029
C2, n(%)	0 (0.0%)	1 (0.9%)	
Current smoker, n(%)	16 (15.1%)	19 (17.1%)	0.685
Diabetes, n(%)	6 (5.7%)	5 (4.5%)	0.698
Hypertension, n(%)	25 (23.6%)	46 (41.4)	0.005
Median follow-up duration, year	3.71 (2.08 – 5.89)	3.56 (2.25 – 5.57)	0.996

Abbreviations: BMI, body mass index; eGFR, estimated glomerular filtration rate; M, mesangial proliferation; S, segmental sclerosis; E, endocapillary proliferation; T, interstitial fibrosis/tubular atrophy; C, crescents.

Table 2. Multivariable cox model for (A) annual eGFR decline and (B) renal outcome of patients of GSG abnormal for age group

2A	Model 1 ^a	Model 2 ^b	Model 3 ^c
GSG			
Normal for age	Reference	Reference	Reference
Abnormal for age	-1.56 (-3.11 – 0.01) ^d	-2.41 (-4.04 – -0.79) ^e	-2.06 (-3.90 – -0.22) ^d
2B	Model 1 ^a	Model 2 ^b	Model 3 ^c
GSG			
Normal for age	Reference	Reference	Reference
Abnormal for age	30.02 (4.05 – 222.50) ^d	41.18 (4.44 – 381.92) ^e	19.18 (1.88 – 195.25) ^f

^a Model 1: not adjusted

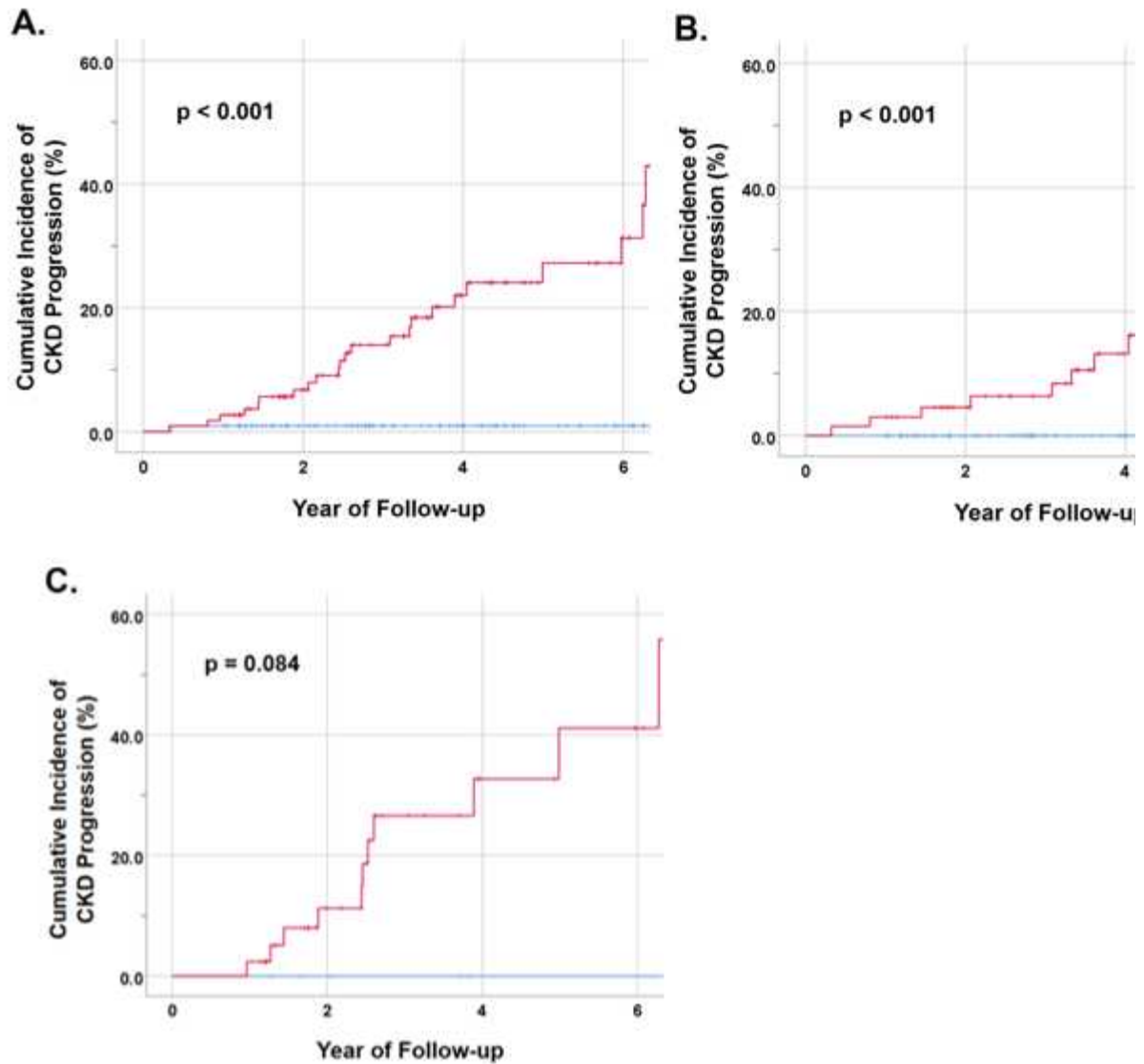
^b Model 2: adjusted for sex, smoking, HTN, DM, age, BMI, baseline eGFR, baseline 24hr urine protein

^c Model 3: adjusted for Model 2 variables plus Oxford classification (M, E, S, T, and C).

^d p < 0.05; ^e p < 0.010; ^f p < 0.001.

Figure. Cumulative incidence of CKD progression

Figure. Cumulative incidence of CKD progression among (A) total patients, (B) patients with T-score of 0, and (C) patients with T-score



Red line, GSG abnormal for age; Blue line, GSG normal for age