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Promoting Sustainable Kidney Health: The Asia-Pacific and Beyond

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Clinicopathological predictors of rapid kidney function decliners with biopsy-proven diabetic kidney disease in type 2 diabetes

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Objectives : Kidney function rapid decliners in diabetic kidney disease (DKD) perform a high annual rate of estimated glomerular filtration rate (eGFR) decline and usually have poor prognoses. It is of interest to identify more proper clinicopathological predictors of rapid eGFR decliners in type 2 diabetes (T2D) patients since the performance of proteinuria alone as a predictor is far from perfect.
Methods : The current study was longitudinal and retrospective, with 181 biopsy-proven DKD patients with T2D. Rapid eGFR decline was defined as the eGFR decline slope ≤ -5 ml/min/1.73 m^2/year. Multivariate logistic analysis, propensity score method (PSM), net reclassification index (NRI), and integrated discrimination improvement (IDI) were used to determine clinicopathological predictors of rapid kidney function decline.
Results : Among these 181 patients, 108 and 73 were classified as rapid and non-rapid decliners, respectively. In the multivariate logistic model, higher baseline eGFR, mesangiolysis/microaneurysm, and interstitial fibrosis and tubular atrophy (IFTA) were independent predictors of rapid eGFR decline [odds ratio (OR) and 95% confidence interval (CI): 1.40 (1.12-1.76), P = 0.004; 5.40 (2.37-12.29), P < 0.001; 2.92 (1.46-5.86), P = 0.002, respectively]. These variables significantly improved model fit and calibration (P < 0.001), discrimination [area under the curve 0.80 (0.73-0.86), P < 0.001], and reclassification [NRI and 95% CI: 0.83 (0.57-1.18); IDI and 95% CI: 19% (13.1%-24.8%)]. The multivariable linear regression analysis revealed that the correlation between eGFR decline slope and the variables including baseline eGFR, mesangiolysis/microaneurysm, and IFTA remained significant.
Conclusions : Higher baseline eGFR, mesangiolysis/microaneurysm, and IFTA were independent predictors of rapid eGFR decline in DKD patients with T2D.

Figure1.jpg

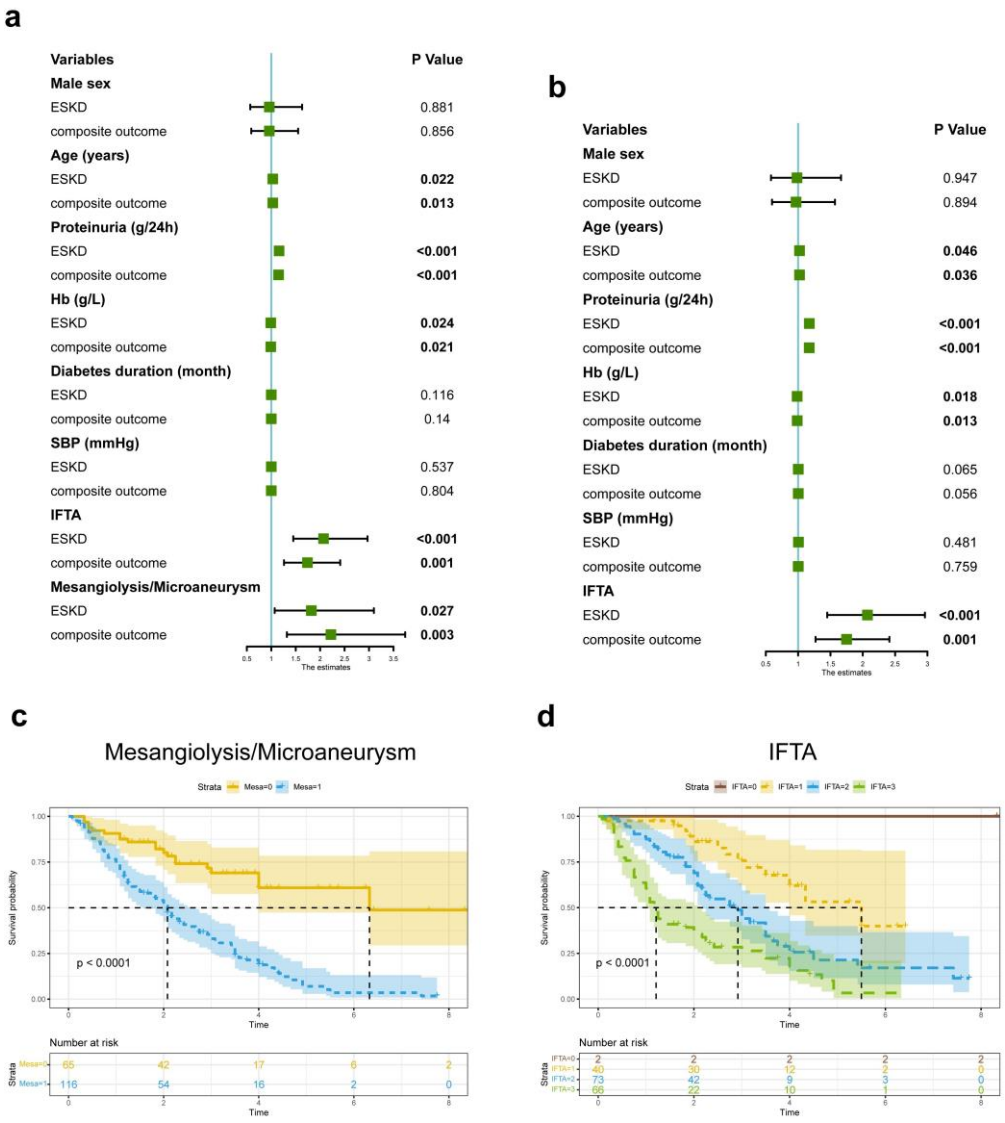
a
Variables
P Value
Male sex
ESKD
0.881
composite outcome
0.856
Age (years)
ESKD
0.022
composite outcome
0.013
Proteinuria (g/24h)
ESKD
<0.001
composite outcome
<0.001
Hb (g/L)
ESKD
0.024
composite outcome
0.021
Diabetes duration (month)
ESKD
0.116
composite outcome
0.14
SBP (mmHg)
ESKD
0.537
composite outcome
0.804
IFTA
ESKD
<0.001
composite outcome
0.001
Mesangiolysis/Microaneurysm
ESKD
0.027
composite outcome
0.003
The estimates
b
Variables
P Value
Male sex
ESKD
0.947
composite outcome
0.894
Age (years)
ESKD
0.046
composite outcome
0.036
Proteinuria (g/24h)
ESKD
<0.001
composite outcome
<0.001
Hb (g/L)
ESKD
0.018
composite outcome
0.013
Diabetes duration (month)
ESKD
0.065
composite outcome
0.056
SBP (mmHg)
ESKD
0.481
composite outcome
0.759
IFTA
ESKD
<0.001
composite outcome
0.001
The estimates
c
Mesangiolysis/Microaneurysm
Strata Mesa=0 Mesa=1
Survival probability
p < 0.0001
Time
Number at risk
Mesa=0 65 42 17 6 2
Mesa=1 116 54 16 2 0
Time
d
IFTA
Strata IFTA=0 IFTA=1 IFTA=2 IFTA=3
Survival probability
p < 0.0001
Time
Number at risk
IFTA=0 2 2 2 2 2
IFTA=1 40 30 12 2 0
IFTA=2 73 42 9 3 0
IFTA=3 66 22 10 1 0
Time

Figure1.jpg

Variables	Clinical model 1 (N = 177)	Clinical model 2 (model 1 + proteinuria) (N = 177)	Clinical and histopathological model 3 (model 2 + histopathological variables) (N = 177)
Male sex	1.15 (0.53, 2.47), 0.73	1.01 (0.46, 2.20), 0.99	0.85 (0.36, 2.01), 0.71
Age (years)	0.98 (0.95, 1.01), 0.15	1.00 (0.96, 1.03), 0.65	1.02 (0.98, 1.06), 0.31
Higher baseline eGFR (per 10ml/min/1.73 m^2)	1.02 (1.01, 1.06), 0.78	1.11 (0.95, 1.30), 0.21	**1.40 (1.12, 1.76), 0.004**
SB*P* (mmHg)	**1.02 (1.00, 1.04), 0.04**	1.01 (0.99, 1.03), 0.21	1.02 (0.99, 1.04), 0.20
Duration of diabetes (mo)	1.00 (1.00, 1.01), 0.07	1.00 (1.00, 1.01), 0.09	1.00 (1.00, 1.01), 0.27
Hb (g/l)	**0.98 (0.97, 1.00), 0.05**	0.98 (0.97, 1.00), 0.06	0.99 (0.97, 1.01), 0.48
Proteinuria (g/24h)	-	**1.17 (1.05, 1.29), 0.003**	1.09 (0.97, 1.21), 0.14
IFTA	-	-	**2.92 (1.46, 5.86), 0.002**
Mesangiolysis/Microaneurysm	-	-	**5.40 (2.37, 12.29), 0.00006**
Performance measure			
LRT x^2test, P	13.54, $P < 0.01$	23.57, $P < 0.001$	50.62, $P < 0.001$
δLRT x^2test, P	-	10.03, $P < 0.001$	37.09, $P < 0.001$
H-L test x2, P	17.52, 0.03	16.63, 0.03	4.75, 0.78
Sensitivity (%)	0.90	0.93	0.42
Specificity (%)	0.39	0.33	0.63
Positive predictive value (%)	0.68	0.67	0.63
Negative predictive value (%)	0.74	0.77	0.43
AUC	0.65 (0.56, 0.73)	0.71 (0.63, 0.80)	0.80 (0.73, 0.86)
δAUC, P	-	0.06, 0.03	0.15, $P < 0.001$
NRI> 0	-	0.59 (0.24, 0.89)	0.83 (0.57, 1.18)
NRI_R	-	0.08 (-0.08, 0.31)	0.47 (0.28, 0.67)
NRI_{nR}	-	0.50 (0.24, 0.63)	0.36 (0.20, 0.60)
IDI (%)	-	6.20 (3.00, 9.40)	19.00 (13.10, 24.80)