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The association of transferrin saturation (TSAT) with renal progression in non-dialysis chronic kidney disease (NDCKD): Results from KNOW-CKD study

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Objectives: Higher TSAT is prone to produce non-transferrin bound iron which can cause oxidative stress via Fenton reaction. Oxidative stress is an important mechanism for renal progression. Hence, we evaluated the relationship between TSAT and renal outcomes among patients with NDCKD.

Methods: We analyzed the data from 2,168 subjects from KNOW-CKD study which is an ongoing prospective cohort study for Korean patients with NDCKD. The main outcome was the renal events, defined by the composite of doubling of serum creatinine or 50% decrease in CKD-EPI eGFR from the baseline, or the occurrence of end stage renal disease. Multivariable cause-specific hazards model was used to assess the association between TSAT and renal progression.

Results: Among 2,168 participants, a total of 654 (30.2%) renal events occurred during the follow-up period of 1502.8 ± 765.0 days. The patients with higher TAST had baseline characteristics favorable for the delay in renal progression such as higher eGFR, lower albuminuria, lower frequency of diabetes mellitus and lower blood pressure, etc. However, TSAT was associated with the increased risk of renal events in multivariable Cox regression adjusted by variables related to renal progression (HR=1.014, 95% CI; 1.003-1.024, p=0.010). Highest TSAT quartile group had a 1.46-fold higher risk of CKD progression than the lowest group in the same model (95% CI, 1.07 to 2.00; P = 0.009). Erythropoiesis stimulating agents (ESA) had significant interaction with TSAT (p interaction= 0.001) in which TSAT was associated with lower risk of renal events in participants using ESA (HR=0.949, 95% CI; 0.913-0.986, p=0.008), and vice versa in those without ESA (HR=1.019, 95% CI; 1.008-1.030, p=0.000).

Conclusions: High TSAT was significantly associated with renal progression in patients with NDCKD especially those without ESA.

Table 1. Assoications of transferrin saturation with CKD progression among 2168 participatns in the Korean Cohort Study for Outcome in Paintets with CKD

Table 1. Associations of transferrin saturation with CKD progression among 2168 participatns in the Korean Cohort Study for Outcome in Paintets with CKD

Transferrin satruation, %	No. of Events (%)	Unadjusted		Model 1		Model 2		Model 3		Model 4		Model 5		Model 6	
		HR (95% CI)	*P* Value for Trend*	HR (95% CI)	*P* Value for Trend*	HR (95% CI)	*P* Value for Trend*	HR (95% CI)	*P* Value for Trend*	HR (95% CI)	*P* Value for Trend*	HR (95% CI)	*P* Value for Trend*	HR (95% CI)	*P* Value for Trend*
Q1=2.3-23.3	174 (26.6)	1	0.132	1	0.18	1	0.094	1	0.024	1	0.004	1	0.018	1	0.009
Q2=23.4-30.3	172 (26.3)	0.95 (0.77 to 1.17)		0.92 (0.75 to 1.14)		0.91 (0.73 to 1.13)		0.85 (0.68 to 1.07)		0.87 (0.66 to 1.14)		0.88 (0.66 to 1.16)		0.88 (0.66 to 1.17)	
Q3=30.4-37.9	162 (24.8)	0.94 (0.76 to 1.17)		0.94 (0.76 to 1.16)		0.93 (0.74 to 1.15)		0.86 (0.68 tp 1.08)		1.00 (0.76 to 1.31)		1.01 (0.75 to 1.35)		1.02 (0.76 to 1.38)	
Q4=38.0-99.6	146 (22.3)	0.78 (0.62 to 0.97)		0.78 (0.63 to 0.98)		1.19 (0.94 to 1.49)		1.18 (0.93 to 1.49)		1.45 (1.09 to 1.93)		1.41 (1.03 to 1.92)		1.46 (1.07 to 2.00)	

Model 1: adjusted for age, sex. Model 2 : model 1 plus eGFR-EPI, random urinary albumin-to-creatinine ratio, and baseline kidney disease. Model 3: model 2 plus comorbid diseases (diabets, coronary artery disease, hypertension), smoking status, alcohol status, systolic blood pressure, BMI (Body mass index), and charlson cormobidity index. Model 4: model 3 plus phosphous level, albumin level, C-reactive protein level, total CO2 level and cholesterol level (LDL, HDL, Triglyceride). Model 5: model 4 plus ferritin level, hemoglobin level, and hepcidin level. Model 6: renin-angiotensin system blocker, statin, diuretics, iron supplement (intravenous and oral), and erythropoiesis-stimulating agent. HR, hazard ratio; 95% CI, 95% confidence interval; Q, quartile. *P values for trend across quartiles of transferrin saturation. *P* values for trend were calculated by treating quartiles as a continous variable in each model.

Figures 1. Cubic spline analysis of the association between transferrin saturation and adverse renal outcomes. Hazard ratios (HRs) were full adjusted sex, age, eGFR-EPI, random urinary albumin-to-creatinine ratio, baseline kidney disease, comorbid diseases (diabets, coronary artery disease, hypertension), smoking status, alcohol status, systolic blood pressure, BMI (Body mass index), charlson corm

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