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### **Elevated Insulin Resistance Predicts Renal Hyperfiltration in Young Adults.**

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**Objectives:** Insulin resistance(IR) increases the risk for renal hyperfiltration(RHF), a mechanism for kidney injury in diabetes. However, the association between triglyceride-glucose(TyG)index, a novel marker for IR, and RHF is not well established. This study aimed to investigate the association between TyG index and RHF in Korean young adults.

**Methods:** Data were retrieved from the Korean National Health and Nutrition Examination Surveys (2010-2019). Total of 15,764 participants aged 19~39 years with normal kidney function were enrolled. Participants were divided into tertile based on TyG index [ $\ln(\text{fasting triglyceride}[\text{mg/dL}] \times \text{fasting glucose} [\text{mg/dL}]/2)$ ]. RHF was defined as eGFR with residuals  $>90^{\text{th}}$  percentile adjusted for sex, age, weight, and height.

**Results:** The mean age of the participants was  $30.4 \pm 6.1$  years, and 43.8% were male. The mean levels of TyG index were  $7.70 \pm 0.25$ ,  $8.28 \pm 0.15$  and  $9.07 \pm 0.45$  in tertile 1, 2, and 3 respectively. The prevalence of RHF was significantly higher tertile (9.1%, 10.0%, and 10.9%, respectively,  $P$  for trend= 0.03). When the association between TyG index and risk for RHF was evaluated by multivariable logistic regression analysis, the higher tertiles showed increased risks for RHF compared to lowest tertile. (OR, 1.24; 95% CI, 1.08-1.41,  $P=0.002$  in tertile 2 and OR, 1.64; 95% CI, 1.41-1.90,  $P<0.001$  in tertile 3). This association was consistent when TyG index was treated as continuous variable (OR, 1.53; 95% CI, 1.39-1.38;  $P<0.001$ ). TyG index increased risks for metabolic syndrome (MetS) (OR, 3.04; 95% CI, 1.86-4.97;  $P<0.001$  in tertile 2 and OR, 46.36; 95% CI, 29.36-73.21;  $P<0.001$  in tertile 3). Fasting glucose, low HDL and obesity of MetS criterion showed higher risk of RHF (OR 1.19; 95% CI 1.01-1.40;  $P=0.035$ , OR 1.17; 95% CI 1.03-1.32;  $P=0.014$ , OR 1.74; 95% CI 1.47-2.06;  $P<0.001$ , respectively).

**Conclusions:** Higher TyG index is associated with increased risk of RHF and MetS in Korean young adults with normal kidney function. Longitudinal studies are need to investigate whether TyG index and MetS associated RHF is a risk factor for kidney injury in young adults.

Table1. Baseline characteristics

**Table 1.** Baseline characteristics

Characteristics	TyG index tertile group			P
	T1 (n=5244)	T2 (n=5278)	T3 (n=5242)	
<b>Demographic data</b>				
Age, years	29.21±6.14	30.17±6.12	31.95±5.60	<0.001
BMI, kg/m <sup>2</sup>	21.40±2.92	22.63±3.46	25.50±4.12	<0.001
Smoking status, n (%)	1241(23.7%)	2033(38.5%)	2923(55.8%)	<0.001
Alcohol status, n (%)	2421(46.2%)	2731(51.7%)	3244(61.9%)	<0.001
SBP, mmHg	105.82±10.02	108.93±11.01	115.49±12.88	<0.001
DBP, mmHg	69.92±8.18	72.39±8.86	77.90±10.71	<0.001
Education, n (%)				<0.001
Low	1030(19.6%)	1263(23.9%)	1462(27.9%)	
High	4214(80.4%)	4015(76.1%)	3780(72.1%)	
Income, n (%)				<0.001
Low	2454(46.8%)	2629(49.8%)	2728(52.0%)	
High	2790(53.2%)	2649(50.2%)	2514(48.0%)	
<b>Comorbidities, n (%)</b>				
Hypertension	95(1.8%)	227(4.3%)	788(15.0%)	<0.001
Diabetes	7(0.1%)	24(0.5%)	284(5.4%)	<0.001
Dyslipidemia	16(0.3%)	61(1.2%)	217(4.1%)	<0.001
Metabolic SD	22(0.4%)	115(2.2%)	1723(32.9%)	<0.001
<b>Laboratory data</b>				
Renal hyperfiltration(%)	478(9.1%)	528(10.0%)	570(10.9%)	0.011
eGFR(MDRD), mL/min/1.73 m <sup>2</sup>	100.30±15.66	99.41±16.47	97.52±17.38	<0.001
Proteinuria (%)	665(14.1%)	628(13.0%)	670(13.6%)	0.485
Hemoglobin, g/dL	13.51±1.49	14.10±1.64	14.92±1.58	<0.001
Fasting plasma glucose, g/dL	86.68±6.82	90.18±7.77	97.67±22.81	<0.001
HbA1c, %	5.29±0.29	5.35±0.36	5.57±0.78	<0.001
Total cholesterol, mg/dL	169.88±27.68	180.07±29.53	199.99±35.95	<0.001
LDL-C, mg/dL	95.64±23.47	106.05±27.16	122.17±32.54	<0.001
Cal HDL-C, mg/dL	59.01±11.48	54.00±11.32	46.65±11.20	<0.001
Triglyceride, mg/dL	52.31±11.57	88.92±14.85	202.57±133.34	<0.001
TyG index	7.70±0.25	8.28±0.15	9.07±0.45	<0.001

*Note:* Data are presented as mean (SD), median [IQR], or number (%).

*Abbreviations:* BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; LDL-C, low density lipoprotein-cholesterol; HDL-C, high density lipoprotein-cholesterol; SD, standard deviation.

**Table 2.** Risk of RHF according to TyG index group

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Group	Model 1		Model 2		Model 3	
	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P
TyG index*	1.20[1.11-1.30]	<0.001	1.43[1.31-1.55]	<0.001	1.53[1.39-1.68]	<0.001
T1	(Reference)					
T2	1.11[0.97-1.26]	0.120	1.22[1.07-1.39]	0.003	1.24[1.08-1.41]	0.002
T3	1.22[1.07-1.38]	0.003	1.55[1.35-1.77]	<0.001	1.64[1.41-1.90]	<0.001

*Note:* Model 1: Unadjusted model

Model 2: Adjusted for age, sex

Model 3: Adjusted for age, sex, hemoglobin, BMI, HTN, alcohol, education, income, smoking

*Abbreviations:* BMI, body mass index; HTN, hypertension; OR, odds ratio; CI, confidence interval

\*TyG index as continuous variable.