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Original Article

ORIGINAL ARTICLE

Cardiovascular risk prediction in hemodialysis patients using the triglyceride-glucose index: a multicenter prospective cohort study

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ABSTRACT

Background. Triglyceride-glucose (TyG) index has recently been established as an indicator of insulin resistance and has predictive value for cardiovascular (CV) disease. However, the clinical significance of the TyG index in patients undergoing hemodialysis remains unknown.

Methods. We prospectively enrolled 759 patients undergoing maintenance hemodialysis. The participants were divided into tertiles based on their baseline TyG index. Echocardiographic parameters, vascular calcification scores, and several plasma biomarkers were obtained and compared using the TyG index.

Results. The TyG index was positively correlated with levels of circulating vascular pathologic markers, endostatin ($\rho = 0.134$, $P = .025$) and vascular adhesion protein-1 ($\rho = 0.130$, $P = .012$), but not with vascular calcification score. The TyG index was not correlated with any echocardiographic parameters. Patients in tertile 3 showed the highest cumulative event rates of CV and cardiac events ($P < .001$ and $P = .001$, respectively). In the multivariable Cox regression analysis, patients in the TyG index tertile 3 had a significantly increased risk of CV and cardiac events compared to those in the TyG index tertile 1 [adjusted hazard ratio (HR): 1.89, 95% confidence interval (CI): 1.08–3.30, and adjusted HR: 2.01, 95% CI: 1.05–3.82, respectively]. A 1 standard deviation increase in the TyG index was also associated with significantly higher risks of CV and cardiac events.

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Conclusions. The TyG index was associated with vascular pathology markers and an increased risk of adverse CV outcomes in patients undergoing hemodialysis. Our study suggests that the TyG index has the potential to assist clinicians in identifying a high CV risk in hemodialysis patients.

Keywords: biomarker, cardiac disease, cardiovascular disease, hemodialysis, triglyceride-glucose index

KEY LEARNING POINTS

What was known:

- Patients undergoing maintenance hemodialysis are at high risk for cardiovascular disease and death.
- The triglyceride-glucose (TyG) index is a marker of insulin resistance.
- The clinical significance of the TyG index in hemodialysis patients remains unclear.

This study adds:

- The TyG index is positively correlated with vascular markers in hemodialysis patients.
- No significant association was found between TyG index and echocardiographic parameters.
- Higher TyG index levels are associated to increased cardiovascular risks in hemodialysis patients.

Potential impact:

- The TyG index could help clinicians identify hemodialysis patients with high cardiovascular risk.
- Targeting the TyG index could help pinpoint patients who may benefit from intervention.

INTRODUCTION

The cardiovascular (CV) risk and mortality rate of patients with end-stage kidney disease (ESKD) is extremely high [1, 2]. Diabetes and hypertension substantially increase the risk of CV events in patients with ESKD receiving hemodialysis (HD) treatment. Furthermore, these patients are continuously exposed to other risk factors specifically associated with impaired renal function [3–5]. Vascular endothelial cell dysfunction is widespread in this population, leading to pathological vascular calcification [6, 7]. HD-associated factors, such as chronic volume overload, left ventricular (LV) remodeling, and low-grade inflammation, contribute to cardiac ischemia and deformation [3, 8]. These conditions synergistically increase the risk of CV events, which is a leading cause of mortality in patients undergoing HD [9]. Therefore, the identification of patients at high risk of CV events is important for the adequate care of patients on HD.

Insulin resistance (IR) refers to the reduced responsiveness of insulin-target tissues to high physiological insulin levels [10]. Among the various markers of IR, the triglyceride-glucose (TyG) index, calculated from fasting plasma triglyceride and glucose levels, is easily accessible and correlates well with IR severity [11]. Previous studies have consistently demonstrated that a high TyG index is associated with increased risks of major adverse CV events and mortality in the general population [12, 13]. The TyG index is also correlated with the presence and severity of major CV risk factors, such as vascular calcification and LV dysfunction [14–16]. Therefore, the TyG index may serve as a crucial marker of CV risk and mortality.

IR is commonly observed in patients with impaired renal function [17]. The TyG index was found to be significantly higher in patients with renal impairment than in individuals with normal kidney function and was negatively correlated with renal function [18, 19]. However, data on the clinical significance of the TyG index in patients undergoing HD are currently lacking and no studies have evaluated its relationship with established CV risk factors. Therefore, this study aimed to investigate the association between the TyG index and the risk of CV events and to examine its relationship with LV dysfunction, vascular calcification, and circulating vascular markers.

MATERIALS AND METHODS

Study participants and data collection

This multicenter prospective cohort study used data from the K-cohort registry. Patients from eight general hospitals were enrolled in the registry if they were aged >18 years and had received maintenance HD for at least 3 months. The exclusion criteria included pregnancy, presence of hematological or solid malignancy, and life expectancy <6 months [20]. Among the 776 patients recruited between June 2016 and September 2023, 18 were excluded because of a lack of clinical information ($n = 17$). Finally, 759 participants were included in this study. Patient follow-up was censored at the time of transfer to peritoneal dialysis or kidney transplantation and loss to follow-up. The study protocol was approved by the local ethics committee (KHNMC 2016–04-039) and was conducted in accordance with the principles of the Declaration of Helsinki. All participants provided written informed consent before enrollment.

Data collection

Baseline characteristics, dialysis information, and laboratory data of all patients were recorded at the time of inclusion. Information on patient comorbidities was obtained to calculate the Charlson Comorbidity Index score [21]. Vascular calcification was assessed by calculating abdominal aortic calcification scores using lateral lumbar radiography, as previously described [22, 23]. Predialysis plasma samples were obtained at the time of study enrollment, and circulating markers were measured in 368 (48.5%) patients. Enzyme-linked immunosorbent assays were performed using Magnetic Luminex® Screening Assay multiplex kits (R&D Systems, Inc., Minneapolis, MN, USA) to

measure the following circulating markers: endostatin, vascular adhesion protein-1 (VAP-1), osteoprotegerin (OPG), receptor activator of nuclear factor κB ligand (RANKL), monocyte chemoattractant protein-1 (MCP-1), and tumor necrosis factor-α (TNF-α).

Echocardiography was performed by experienced cardiologists at the time of enrollment and evaluated based on the recommendations of the American Society of Echocardiography [24]. M-mode and 2D measurements included LV mass indexed to the body surface area, LV end-diastolic diameter (LVDd), LV end-systolic diameter (LVDs), LV posterior wall thickness, interventricular septal thickness (IVST), LV end-diastolic volume (LVEDV), LV end-systolic volume (LVESV), and LV ejection fraction (LVEF). Early diastolic flow velocity (*E*) and peak late diastolic flow velocity (*A*) were determined from the mitral valve inflow velocity curve using pulsed-wave Doppler ultrasonography. The early diastolic tissue velocity (*E′*) was measured at the septal aspect of the mitral annulus using tissue Doppler imaging.

TyG index

Plasma fasting glucose and triglyceride levels were measured at the time of study enrollment. The TyG index was calculated using the following formula [25]: Ln [triglyceride (mg/dl) × fasting blood glucose (mg/dl)/2]. Participants were classified into tertiles based on their TyG index levels. The cut-off values for each tertile were as follows: tertile 1, <8.49; tertile 2, 8.49–<9.07; and tertile 3, ≥9.07.

Outcomes measures

The study outcomes included all-cause mortality and a composite of CV events, including both cardiac and non-cardiac events. Cardiac events included acute coronary syndrome, coronary artery disease requiring percutaneous coronary intervention, coronary artery bypass surgery, congestive heart failure, ventricular arrhythmia, cardiac arrest, and sudden death. Non-cardiac events included cerebral infarction and peripheral vascular occlusive diseases requiring revascularization or surgical intervention.

Statistical analysis

Data are expressed as means ± standard deviation (SD) or as the number of patients and percentages. The analysis of variance with Tukey's multiple comparison and chi-square tests were used to compare variables between groups. Circulating markers are expressed as medians and interquartile ranges (IQRs) and were analyzed using the Kruskal–Wallis test because these data were non-normally distributed. Correlations between the TyG index, circulating markers, and echocardiographic parameters were analyzed using Spearman's analyses. The cumulative event rates of the participants were estimated using Kaplan–Meier curves and compared using the log-rank test. A Cox proportional hazard model was constructed to identify independent variables associated with predefined outcomes. In the multivariate Cox model, the following parameters were included for adjustment: age, sex, body mass index (BMI), dialysis duration, Charlson Comorbidity Index, anti-diabetic drugs, statins, hemoglobin, and serum albumin levels. Statistical analyses were performed using the SPSS software (version 22.0; IBM Corp., Armonk, NY, USA). *P* values <.05 were considered statistically significant.

RESULTS

Baseline demographics and laboratory data

The baseline demographics and clinical parameters of patients on HD according to TyG tertiles are shown in Table 1. The median TyG indices were 8.1, 8.8, and 9.6 in tertiles 1, 2, and 3, respectively. The patients in tertile 3 were more obese, had a shorter dialysis duration, worse Charlson Comorbidity scores, and had a higher prevalence of diabetes than those in tertile 1. Single pool Kt/V was lower in patients in tertile 3 compared to those in tertile 2. Plasma VAP-1 levels were marginally higher in patients in tertile 3 than in those in tertiles 1 and 2 ($P = .051$), whereas the remaining circulating markers, high-sensitivity C-reactive protein (hs-CRP), and vascular calcification scores showed no significant differences between the groups. Echocardiographic findings did not show significant differences across the TyG tertiles (Supplementary Table 1).

Correlations of the TyG index with circulating biomarkers, vascular calcification score, and echocardiographic parameters

We evaluated the relationship between baseline values of the TyG index, circulating biomarkers, vascular calcification score, and echocardiographic parameters. The TyG index significantly correlated with circulating vascular markers (Table 2). Plasma endostatin ($\rho = 0.134$, $P = .025$) and VAP-1 levels ($\rho = 0.130$, $P = .012$) were positively correlated. CKD-mineral bone disorder (CKD-MBD) markers, including the OPG/RANKL ratio and vascular calcification scores, were not correlated with the TyG index. Additionally, plasma MCP-1, TNF-α, and hs-CRP levels, as markers of inflammation, did not show significant correlations with the TyG index. There was no significant correlation between the TyG index and any of the echocardiographic parameters (Supplementary Table 2).

Risks of CV events, cardiac events, and all-cause mortality based on TyG index tertiles

During a median follow-up duration of 30.0 months (IQR, 17–54), CV events, cardiac events, and patient death occurred in 104, 82, and 132 patients (incidence rates of 50.8, 39.7, and 52.2 per 1000 person-years), respectively. The cumulative event rates for CV and cardiac events were significantly different among patients on HD with different TyG index tertiles ($P < .001$ and $P = .001$, respectively; Fig. 1). Patients in tertile 3 had the highest event rates for both CV and cardiac events compared to those in tertiles 1 and 2. However, all-cause mortality did not differ between the groups.

The univariable Cox regression analysis demonstrated that patients on HD in tertile 3 had a significantly higher risk of CV events than those in the tertile 1 [unadjusted hazard ratio (HR): 2.24, 95% confidence interval (CI): 1.38–3.63, $P = .001$; Table 3]. This association remained significant after multivariable adjustments for possible confounders (adjusted HR: 1.89, 95% CI: 1.08–3.30, $P = .025$). The risk of cardiac events was also greater in patients on HD in tertile 3 compared to those in tertile 1 (adjusted HR: 2.01, 95% CI: 1.05–3.82, $P = .034$). Consistently, an increase in the TyG index per SD was associated with significantly higher risks of CV and cardiac events (adjusted HR: 1.55, 95% CI: 1.24–1.94, $P < .001$, and adjusted HR: 1.45, 95% CI: 1.12–1.87, $P = .004$ per 1 SD increase, respectively). The TyG index tertiles were not associated with a higher risk of all-cause mortality.

Table 1: Baseline demographic and laboratory data of the study population.

	Tertiles of TyG index			
	Tertile 1 ($n = 253$)	Tertile 2 ($n = 253$)	Tertile 3 ($n = 253$)	*P* value
TyG index	8.1 ± 0.4	8.8 ± 0.2[a]	9.6 ± 0.5[a,b]	<.001
Age (years)	60.4 ± 12.9	59.3 ± 13.2	59.8 ± 12.7	.618
Male (%)	168 (66.4)	145 (57.3)[a]	146 (57.7)	.061
BMI (kg/m^2)	21.8 ± 2.9	22.9 ± 3.6[a]	24.9 ± 4.5[a,b]	<.001
HD duration (month)	121.5 ± 20.5	99.1 ± 66.2[a]	84.6 ± 63.5[a]	<.001
History of CV event (%)	85 (33.6)	80 (31.6)	90 (35.6)	.642
Charlson Comorbidity Index	3.7 ± 1.6	3.9 ± 1.7	4.4 ± 1.5[a,b]	<.001
Diabetes (%)	84 (33.2)	133 (52.6)[a]	193 (76.3)[a,b]	<.001
Predialysis SBP (mmHg)	145.0 ± 20.5	144.9 ± 21.9	146.2 ± 21.1	.759
Hemoglobin (g/dl)	10.6 ± 1.3	10.7 ± 1.2	10.7 ± 1.1	.917
Fasting blood glucose (mg/dl)	109.2 ± 28.5	135.7 ± 44.3[a]	190.3 ± 88.0[a,b]	<.001
Triglyceride (mg/dl)	65.3 ± 21.7	107.4 ± 35.2[a]	186.9 ± 95.7[a,b]	<.001
Albumin (g/dl)	3.9 ± 0.3	3.9 ± 0.3	3.9 ± 0.3	.737
Vascular calcification score	8.8 ± 0.8	7.2 ± 5.9	8.1 ± 6.2	.273
Anti-diabetic drugs (%)	64 (25.4)	94 (37.6)[a]	165 (66.0)[a,b]	<.001
Statin (%)	108 (43.4)	127 (50.6)	136 (54.4)[b]	.044
Single pool Kt/V	1.59 ± 0.29	1.60 ± 0.26	1.53 ± 0.30[b]	.017
Endostatin (ng/ml)	203.6 (152.5, 316.4)	226.4 (171.9, 351.3)	234.5 (174.6, 449.2)	.188
VAP-1 (ng/ml)	364.1 (303.4, 364.1)	391.5 (331.5, 485.8)	398.0 (331.1, 506.5)	.051
OPG/RANKL	248.5 (118.5, 2004.6)	259.2 (117.1, 1252.4)	228.7 (105.4, 1118.2)	.371
MCP-1 (pg/ml)	161.7 (134.3, 207.4)	169.4 (122.2, 216.0)	160.3 (131.1, 213.9)	.978
TNF-α (pg/ml)	9.5 (6.8, 13.2)	1.9 (7.7, 13.2)	10.9 (7.1, 14.0)	.504
hs-CRP (mg/ml)	1.0 (0.3, 3.5)	0.8 (0.2, 3.0)	1.3 (0.4, 3.9)	.090

Data are expressed as (mean ± SD or median IQR).
SBP, systolic blood pressure.
[a]$P < .05$ vs tertile 1.
[b]$P < .05$ vs tertile 2.

Table 2: Correlation between TyG index and circulating markers.

	Correlation coefficient	*P* value
Vascular markers		
Endostatin (ng/ml)	0.134	.025
VAP-1 (ng/ml)	0.130	.012
CKD-MBD marker		
OPG/RANKL	−0.112	.061
Vascular calcification score	−0.041	.542
Inflammatory markers		
MCP-1 (pg/ml)	0.017	.783
TNF-α (pg/ml)	0.069	.253
hs-CRP (mg/ml)	0.063	.106

Circulating marker were measured in 368 (48.5%) patients.

A sensitivity analysis of patients with diabetes consistently demonstrated that an elevated TyG index was an independent risk factors of CV and cardiac events, even after adjusting for relevant confounders including HbA1c (adjusted HR: 2.28, 95% CI: 1.05–4.91, $P = .036$ and adjusted HR: 2.44, 95% CI: 1.01–5.90, $P = .048$, tertile 1 vs. tertile 3, respectively; Supplementary Table 3).

Subgroup analysis on the association between TyG levels and CV events

Table 4 shows the subgroup analysis of the TyG index per SD increase for CV events based on age, sex, BMI, and the presence of diabetes. There was a generally consistent increase in the HRs with an increasing TyG index across the predefined subgroups. Patients aged <65 years and those with diabetes exhibited a significantly more pronounced increase in the adjusted HRs with an increasing TyG index than older patients and those without diabetes. There was a significant interaction between age and diabetes in the association between the TyG index and the risk of CV events (*P* for interaction = 0.018 and 0.049, respectively).

DISCUSSION

We divided the 759 patients on HD into tertiles based on the TyG index. We evaluated various biomarkers, echocardiographic parameters, CV events, cardiac events, and all-cause mortality. Our results showed a positive association between the TyG index and two vascular biomarkers (endostatin and VAP-1), CV, or cardiac events. Furthermore, we performed subgroup analyses based on age, sex, BMI, and the presence of diabetes. The positive association between the TyG index and CV events was more prominent in patients with diabetes or at a young age.

Our study demonstrates that a higher TyG index tertile is associated with an increased risk of incident CV and cardiac events. In addition, the risk of CV events increased as the TyG index increased. These findings suggest that the TyG index is a reliable marker for predicting future adverse CV events in patients on HD and that its clinical significance extends to the HD population. This is particularly important because the prediction of CV events in patients on HD is challenging despite their higher CV risk. Patients on HD with CV disease often do not present with typical symptoms or signs, and several nonconventional risk factors for CV diseases, unseen in individuals with normal renal function, contribute to the difficulty in preventing CV events [3, 26]. Therefore, our results are valuable for

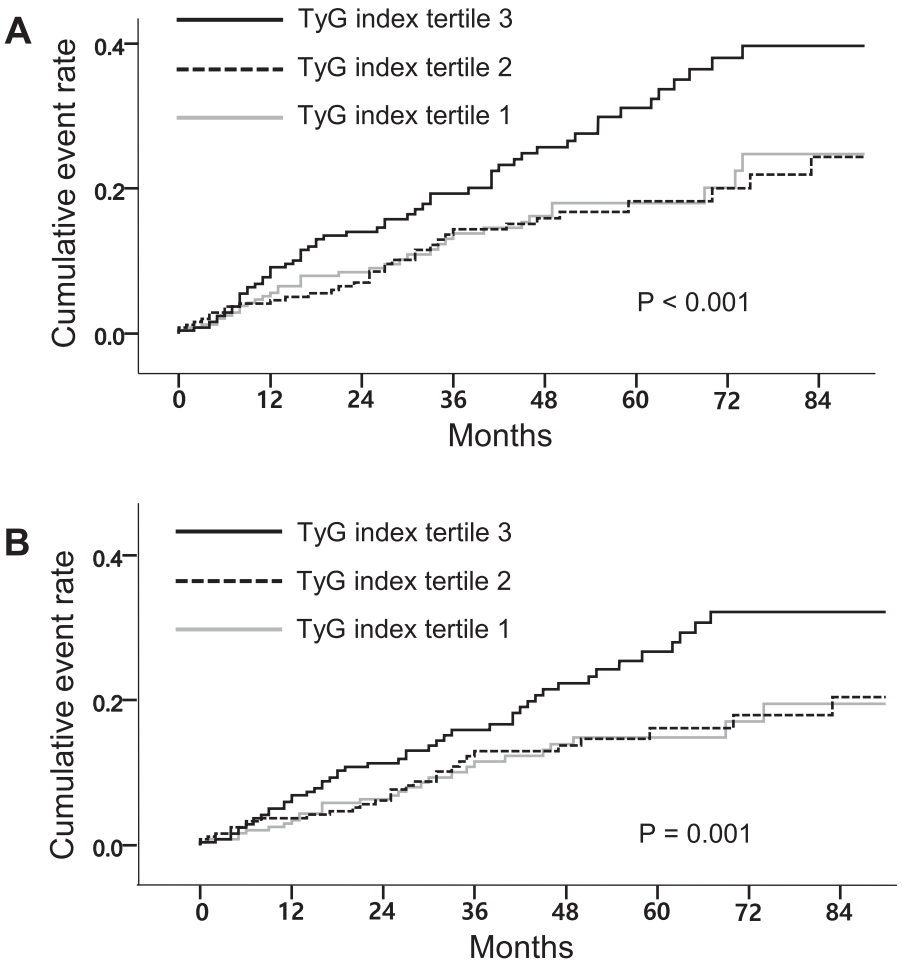

Figure 1: Cumulative event rates of cardiovascular (**a**) and cardiac (**b**) events according to TyG index quartiles. Between-group comparisons are calculated by log-rank test.

identifying patients on HD at a higher risk of CV events and for developing appropriate preventive strategies.

One of the strengths of our study is that it elucidated the differences in the clinical significance of the TyG index according to different subgroups. Notably, more pronounced results were observed in younger patients. Most studies included populations with a single disease without age restrictions; therefore, a clear interpretation of our results may be limited. Nevertheless, we can still discuss several issues that remain unaddressed. Young patients have a higher likelihood of having fewer comorbidities than older patients. Young patients with fewer underlying comorbidities may be less affected by classical CV risk factors, thereby highlighting the pronounced effect of the TyG on CV diseases. Conversely, in older patients, the presence of multiple morbidities could make the classical CV risk factors dominant, potentially diminishing the relative effect of the TyG.

Our study also demonstrated that the association between the TyG index and CV outcomes was more pronounced in HD patients with diabetes, and the TyG index remained a significant factor in multivariate analysis for diabetic patients, even after adjusting for HbA1c. This finding underscores the role of IR in CV outcomes. In patients with diabetes, there is often more intensive management of dyslipidemia and blood glucose control, leading to the increased use of dyslipidemia and anti-diabetic medications. Our study enrolled patients from specialized dialysis centers, suggesting that these patients are likely to receive a certain level of adequate management. Despite this, high TyG levels may indicate severe IR that does not respond well to medication or a lack of adherence to dietary and lifestyle modifications. This may explain the close association between the TyG levels and CV outcomes in patients with diabetes. Another possibility is that patients whose TyG levels are reduced through appropriate medication may also experience a reduction in CV events due to the independent effects of the medications themselves. While the evidence is limited in patients on dialysis, some medications, such as statins, GLP-1 receptor agonists, and pioglitazone, are known to be effective in preventing CV disease [27–29]. However, future research that includes medication use, type, diet, and lifestyle factors is necessary to better understand the underlying reasons.

Increased circulating levels of endostatin and VAP-1 are reliable markers of atherosclerotic vascular changes and are well-known risk factors for CV morbidity and mortality in the general population [30, 31]. Our previous studies also demonstrated their clinical significance in incident CV disease among patients on HD [20, 23]. Additionally, endostatin levels are elevated in the obese population and are positively correlated with increasing BMI [32]. Another study reported a decline in VAP-1 levels after gastroplasty in obese patients [33]. These findings suggest that endostatin and VAP-1 are relevant to IR status, and our results

Table 3: Hazard ratios of TyG index tertiles for cardiovascular event, cardiac events, and all-cause death.

				Univariable analysis		Multivariable analysis	
	No. of event (%)	Person-year	Incidence rate	HR (95% CI)	P	HR (95% CI)	P
Cardiovascular events							
TyG tertile 1	35 (13.8)	819	42.8	Reference		Reference	
TyG tertile 2	35 (13.8)	827	42.3	1.12 (0.65–1.93)	.687	1.03 (0.58–1.85)	.918
TyG tertile 3	58 (22.9)	873	66.4	2.24 (1.38–3.63)	.001	1.89 (1.08–3.30)	.025
TyG per SD				1.60 (1.32–1.93)	<.001	1.55 (1.24–1.94)	<.001
Cardiac event							
TyG tertile 1	28 (11.1)	865	32.4	Reference		Reference	
TyG tertile 2	30 (11.9)	876	34.2	1.30 (0.69–2.43)	.412	1.09 (0.56–2.14)	.801
TyG tertile 3	48 (19.0)	927	51.8	2.54 (1.45–4.46)	.001	2.01 (1.05–3.82)	.034
TyG per SD				1.56 (1.26–1.92)	<.001	1.45 (1.12–1.87)	.004
All-cause mortality							
TyG tertile 1	46 (18.2)	800	57.5	Reference		Reference	
TyG tertile 2	38 (15.0)	821	46.3	0.75 (0.49–1.15)	.762	0.79 (0.50–1.23)	.292
TyG tertile 3	48 (19.0)	908	52.9	0.98 (0.66–1.46)	.900	0.87 (0.55–1.40)	.575
TyG per SD				1.01 (0.85–1.20)	.880	0.95 (0.78–1.16)	.590

The incidence rate is expressed as event number per 1000 person-years.
All analyses are adjusted for the following covariates: age, sex, BMI, dialysis duration, Charlson Comorbidity Index, anti-diabetic drugs, statin, hemoglobin, albumin, and single pool Kt/V.

Table 4: Hazard ratios of TyG index for cardiovascular events based on predefined subgroups.

	No. of event (%)	Univariable analysis HR (95% CI)	Multivariable analysis HR (95% CI)	P for interaction
Age				.018
<65 years	66 (13.9)	1.91 (1.48–2.46)	1.88 (1.38–2.55)	
≥65 years	62 (21.9)	1.28 (0.96–1.70)	1.27 (0.88–1.83)	
Sex				.333
Male	72 (15.7)	1.47 (1.14–1.91)	1.49 (1.08–2.04)	
Female	56 (18.7)	1.74 (1.32–2.28)	1.70 (1.21–2.38)	
BMI				.592
<25 kg/m^2	87 (16.7)	1.67 (1.28–2.18)	1.41 (1.05–1.90)	
≥25 kg/m^2	51 (21.0)	1.73 (1.23–2.44)	1.63 (1.11–2.40)	
Diabetes				.049
No	37 (10.6)	0.88 (0.57–1.36)	0.89 (0.53–1.48)	
Yes	91 (22.2)	1.53 (1.23–1.92)	1.65 (1.30–2.11)	

All analyses are adjusted for the following covariates: age, sex, BMI, dialysis duration, Charlson Comorbidity Index, anti-diabetic drugs, statin, hemoglobin, albumin, and single pool Kt/V.

show a positive correlation between the TyG index and these two biomarkers, further supporting this relationship in patients on HD. We suggest that patients on HD with a higher TyG index are predisposed to atherosclerotic changes and that these relationships are ultimately thought to be associated with an increased risk of atherosclerotic CV events.

Previous studies have demonstrated a positive association between TyG levels and echocardiographic findings, circulating CKD-MBD markers, and vascular calcification. Research evaluating patients with heart failure or the asymptomatic general population has shown that high TyG levels are associated with a low LVEF, elevated levels of natriuretic peptide, and LV dysfunction [34, 35]. Several studies on vascular calcification have also reported a positive association between the TyG index and the severity and progression of coronary artery calcification [16, 36]. However, in our study, the TyG index was not significantly correlated with vascular calcification or echocardiographic parameters.

There are several possible explanations for the discrepancy between our study and previous findings, which did not demonstrate a significant association between TyG and vascular calcification, CKD-MBD indicators, or echocardiographic findings. First, it is likely that we cannot fully eliminate the effects of other confounding factors that might have influenced these indices independently of the TyG. Specifically, in cases of vascular disease and CKD-MBD, factors, such as phosphate control, the type of phosphate binder, and the administration of vitamin D or cinacalcet, can have a considerable impact. The influence of these factors may not have been adequately controlled for in the present study. Additionally, dialysis-specific factors, such as volume control and repeated cardiac remodeling due to intradialytic hypotension, may have had a greater impact on the echocardiographic findings. Proper control of these factors in future analyses could help clarify the independent associations between IR, vascular calcification, CKD-MBD, and echocardiographic findings. Moreover, heterogeneity in baseline

characteristics based on TyG levels, which may not have been sufficiently balanced, could also be a contributing factor.

Our study had some limitations. First, our study lacked sufficient data to confirm a cause-and-effect relationship. Circulatory markers and echocardiographic findings were mostly measured at baseline. There were no data on changes during follow-up, which limited our ability to observe temporal changes in the indicators associated with the TyG index. Additionally, we did not measure other indicators of IR. We did not include well-known indicators of insulin, such as the homeostasis model assessment of insulin resistance-IR or direct measurements of fat mass, preventing comparisons with these indicators. This ultimately limits the accuracy of TyG as an indicator of IR.

In conclusion, The TyG index is positively correlated with circulating levels of VAP-1 and endostatin and an increased risk of adverse CV outcomes in patients on HD. Our study suggests that the TyG index has the potential to assist clinicians in identifying patients on HD with a high CV risk and potential target patients that require intervention.

SUPPLEMENTARY DATA

Supplementary data are available at *Clinical Kidney Journal* online.

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DATA AVAILABILITY STATEMENT

The data underlying this article will be shared on reasonable request to the corresponding author.

CONFLICT OF INTEREST STATEMENT

None declared.

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