Original Article

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Triglyceride-glucose index and risk of renal function decline and death-censored renal allograft loss in kidney transplant recipients

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Background: Although insulin resistance is common, its significance in kidney transplant recipients remains unclear. We explored clinical implications of the triglyceride-glucose (TyG) index as a marker for unfavorable allograft outcomes in kidney transplant recipients.

Methods: A total of 6,354 kidney transplant recipients were enrolled in a multicenter prospective cohort study between May 2014 and December 2022. The TyG index was assessed between 6 and 12 months after transplantation. We evaluated the association between the TyG index and the risk of adverse kidney outcomes.

Results: The cumulative rates of ≥50% decline in estimated glomerular filtration rate (eGFR), death-censored graft survival, and major adverse kidney events differed across TyG index quartiles, with the highest rate observed in quartile 4 ($p < 0.001$). TyG index quartile 4 was associated with the highest risk of death-censored graft loss after multivariable adjustment (adjusted hazard ratio, 2.13; 95% confidence interval [CI], 1.28–3.55). The risk of ≥30% decline in eGFR was 1.46 times higher (95% CI, 1.17–1.82) in quartile 4 compared with quartile 1, and the risk of ≥50% decline was 1.78 times higher (95% CI, 1.30–2.44). Quartile 4 also showed a significantly steeper decline in renal function, with an adjusted mean difference in eGFR slope of −4.72 mL/min/1.73 m^2 (95% CI, −7.39 to −2.04).

Conclusion: Kidney transplant recipients with high TyG index were at increased risk of eGFR decline and graft loss, and also exhibited a more rapid deterioration in renal function. The TyG index is a useful marker for identifying individuals at high risk for adverse graft outcomes.

Keywords: Kidney transplantation, Insulin resistance, Graft survival, Delayed graft function

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Introduction

Insulin resistance is a prevalent disorder among kidney transplant recipients [1]. Immunosuppressants such as tacrolimus, decreased renal function, and low-grade inflammation undoubtedly contribute to insulin resistance in kidney transplant recipients. The significance of insulin resistance is emphasized through its associations with hyperglycemia, dyslipidemia, and increased blood pressure [2,3]. When insulin resistance progresses, it contributes to the development of metabolic syndrome—a cluster of metabolic abnormalities. This condition increases the risk of new-onset diabetes mellitus after transplantation and cardiovascular complications, both of which significantly threaten patient survival [4]. In addition, the presence of metabolic syndrome is associated with unfavorable kidney outcomes, a concern heightened because of the high prevalence of metabolic syndrome among transplant recipients [5].

The homeostasis model assessment is currently used to assess insulin resistance [6,7]. However, assessing insulin levels in a homeostatic model is complex and may limit its utility in patients undergoing insulin therapy [8]. To overcome these limitations, the triglyceride-glucose (TyG) index was developed as a simple and reliable marker of insulin resistance, demonstrating high sensitivity and specificity [9]. Calculated from fasting plasma triglyceride and glucose levels, the TyG index is easily accessible and has shown strong correlation with the severity of insulin resistance and with several other commonly used markers. Recent studies demonstrate that the TyG index is strongly linked to metabolic syndrome and consistently predicts adverse cardiovascular events across diverse clinical settings [10–12]. Moreover, in kidney transplant recipients, the TyG index has also been significantly associated with an increased risk of cardiovascular events and the development of new-onset diabetes mellitus after transplantation [13,14].

However, studies investigating the association between the TyG index and allograft outcomes, such as renal function decline and graft survival, remain limited in kidney transplant recipients. This gap underscores the need to clarify the prognostic significance of the TyG index in this population. Therefore, we aimed to evaluate its association with adverse kidney outcomes in a prospective, multicenter, nationwide cohort. We hypothesized that a higher TyG index would be associated with increased risk of moderate-to-severe renal function decline and death-censored allograft loss.

Methods

Study population

This study utilized data from a registry derived from the Korean Organ Transplantation Registry (KOTRY), a national, prospective, multicenter observational cohort of kidney transplants established in 2012 [15]. Patients who underwent kidney transplantation were subsequently registered in the database at the initiation of transplant surgery and were followed up during the posttransplantation period. We screened 8,539 kidney transplant recipients from the KOTRY database between May 2014 and December 2022, all of whom had documented TyG index data during the posttransplantation period. Among them, we excluded recipients lost to follow-up before 6 months after transplantation (n = 1,214), those with a posttransplant vintage of less than 6 months (n = 792), and individuals with a history of end-stage kidney disease or death before 6 months after transplantation (n = 179). Therefore, 6,354 recipients were included in the analysis.

Data collection and definitions

Baseline demographic data, comorbidities, and clinical and laboratory parameters of the kidney transplant recipients were collected. Furthermore, information on human leukocyte antigen (HLA) typing, desensitization procedures, and the induction and maintenance of immunosuppressant regimens was also collected. We set the index date at the time of the TyG index assessment. The evaluation of the TyG index between 6 and 12 months after transplantation was based on the protocol used in previous studies because of high fluctuations in serum glucose levels and high doses of immunosuppressants at the early stage of transplantation [16–18]. The TyG index was calculated using the following formula: ln [fasting triglyceride (mg/dL) × fasting blood glucose (mg/dL)/2] [19]. The patients were classified into four groups based on the level of TyG index as follows: quartile 1, <8.46; quartile 2, 8.46 to <8.80; quartile 3, 8.80 to <9.18; and quartile 4, ≥9.18. Renal allograft

function was evaluated using the estimated glomerular filtration rate (eGFR) calculated using the 2009 CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration) formula [20]. Body mass index (BMI) was calculated as body weight divided by height squared. The definition of metabolic syndrome followed the criteria as defined in the International Diabetes Federation guideline [21]. A BMI ≥25.0 kg/m^2 was used as an indicator of abdominal obesity, because this threshold corresponds to waist circumference cut-offs recommended for Asian populations [22,23].

Outcome measures

Study endpoints included eGFR decline ≥30%, eGFR decline ≥50%, death-censored graft loss, and patient death. eGFR decline was calculated relative to baseline eGFR at study enrollment. Renal allograft loss was defined as the onset of end-stage kidney disease requiring renal replacement therapy or retransplantation, with death treated as a censoring event. Major adverse kidney event (MAKE) was defined as a composite of eGFR decline ≥50%, death-censored graft loss, and patient death.

Statistical analysis

Baseline characteristics and parameters are presented as mean ± standard deviation or as counts and percentages. Differences between groups were assessed using analysis of variance and chi-square tests, as appropriate. The incidence rate was calculated as the number of events per 1,000 person-years, with events defined relative to the cumulative individual time each patient was exposed to the risk. Cumulative event rates were estimated using the Kaplan-Meier method and compared using the log-rank test. Cox proportional hazard models were used to identify the independent variables associated with clinical outcomes. The variables included in the multivariable Cox regression model were age, sex, BMI at enrollment, previous history of cardiovascular disease, donor type (living vs. deceased), underlying etiology of end-stage kidney disease, time on dialysis, desensitization, HLA mismatching number, maintenance immunosuppressant, and eGFR at enrollment. The patients in the lowest TyG index quartile were designated as references. A multivariate-adjusted restricted cubic spline model was employed in the analysis, treating exposure as a continuous variable. These curves were constructed with three knots, with a TyG index level of 8.2 as the reference point.

To compare the slopes of eGFR after the index date across different TyG index quartiles, a linear mixed-effects model with an unstructured covariance matrix was utilized. This model included age, sex, BMI, history of cardiovascular disease, donor type, underlying etiology of end-stage kidney disease, duration of dialysis, desensitization, HLA mismatch number, maintenance immunosuppressants, eGFR at enrollment, time (linear), and TyG index quartiles. Differences in the eGFR slope were examined using the interaction between the TyG index quartiles and time. Individual-level random intercepts were included, and TyG index quartiles, time, and their interactions were incorporated as fixed factors. All statistical analyses were performed using IBM SPSS for Windows (version 26.0; IBM Corp.) and R software (version 4.2.0). A p-value <0.05 indicated statistical significance.

Statement of ethics

This study protocol was reviewed and approved by the Institutional Review Board of Kyung Hee University Hospital (2020-01-045) and CHA Bundang Medical Center (2024-04-034). Written informed consent was obtained from all patients before enrollment.

Results

Baseline characteristics and laboratory data

Table 1 shows the baseline characteristics and clinical parameters of kidney transplant recipients in each TyG index quartile. The mean level of TyG index was 8.2 ± 0.2 in quartile 1 (n = 1,588), 8.6 ± 0.1 in quartile 2 (n = 1,589), 9.0 ± 0.1 in quartile 3 (n = 1,589), and 9.6 ± 0.4 in quartile 4 (n = 1,588). Recipients in TyG index quartile 4 were older, had a low proportion of males, as well as a high BMI. The prevalence of previous cardiovascular events was higher in patients with high TyG index quartiles. Higher levels of fasting plasma glucose, low-density lipid cholesterol, and triglycerides were observed in recipients in quartile 4 than in those in the other quartiles, while eGFR was the lowest in recipients in quartile 4. The characteristics related to

Table 1. Basic characteristics of the study population according to the triglyceride-glucose index

Characteristic	Triglyceride-glucose index				p-value
	Quartile 1 (n = 1,588)	Quartile 2 (n = 1,589)	Quartile 3 (n = 1,589)	Quartile 4 (n = 1,588)	
Triglyceride-glucose index	8.2 ± 0.2	8.6 ± 0.1	9.0 ± 0.1	9.6 ± 0.4	<0.001
Age (yr)	48.3 ± 12.4	49.2 ± 11.8	50.0 ± 11.1	51.4 ± 10.3	<0.001
Male sex	874 (55.0)	694 (43.7)	631 (39.7)	524 (33.0)	<0.001
BMI (kg/m^2)	22.1 ± 3.2	22.4 ± 3.2	22.9 ± 3.5	24.1 ± 3.6	<0.001
Causes of ESKD					<0.001
Diabetes mellitus	335 (21.1)	270 (17.0)	364 (22.9)	620 (39.0)	
Hypertension	242 (15.2)	290 (18.3)	251 (15.8)	232 (14.6)	
Glomerulonephritis	557 (35.1)	540 (34.0)	508 (32.0)	334 (21.0)	
Polycystic kidney	74 (4.7)	85 (25.4)	65 (4.1)	75 (4.7)	
Others	380 (23.9)	404 (25.4)	401 (25.2)	327 (20.6)	
Time on dialysis (yr)	3.5 ± 4.9	3.6 ± 5.1	3.5 ± 6.3	3.1 ± 4.3	0.02
History of CV events	160 (10.1)	173 (10.9)	168 (10.6)	214 (13.5)	0.01
Living donor	1,085 (68.3)	1,082 (68.1)	1,088 (68.5)	1,106 (69.6)	0.79
Desensitization	412 (25.9)	381 (24.0)	388 (24.4)	432 (27.2)	0.14
HLA mismatching number	3.2 ± 1.8	3.3 ± 1.8	3.3 ± 1.8	3.4 ± 1.8	0.09
eGFR (mL/min/1.73 m^2)	68.5 ± 19.1	67.6 ± 18.6	67.3 ± 19.1	65.2 ± 19.7	<0.001
Fasting plasma glucose (mg/dL)	97 ± 18	104 ± 51	113 ± 29	148 ± 62	<0.001
Triglyceride (mg/dL)	77 ± 18	112 ± 20	147 ± 30	224 ± 96	<0.001
LDL-cholesterol (mg/dL)	87 ± 32	97 ± 32	99 ± 33	106 ± 37	<0.001
Induction immunosuppressant					
Basiliximab	1,201 (75.6)	1,199 (75.5)	1,203 (75.7)	1,217 (76.6)	0.87
Anti-thymocyte globulin	412 (25.9)	419 (26.4)	422 (26.6)	401 (25.3)	0.84
Maintenance immunosuppressant					
Calcineurin inhibitor	1,584 (99.7)	1,587 (99.9)	1,587 (99.9)	1,587 (99.9)	0.55
Mycophenolate mofetil	1,490 (93.8)	1,484 (93.4)	1,516 (95.4)	1,499 (94.4)	0.08
Glucocorticoid	1,558 (98.1)	1,557 (98.0)	1,565 (98.5)	1,560 (98.2)	0.74

Data are expressed as mean ± standard deviation or number (%).
BMI, body mass index; ESKD, end-stage kidney disease; CV, cardiovascular; HLA, human leukocyte antigen; eGFR, estimated glomerular filtration rate; LDL, low-density lipoprotein.

transplantation and types of immunosuppressants did not differ across the quartiles.

Triglyceride-glucose index and the risk of adverse kidney outcomes

During the mean follow-up period of 39.2 ± 26.1 months, 327 events of ≥50% decline in eGFR, 153 cases of renal allograft loss, and 114 patient deaths were observed. The cumulative rates of ≥50% decline in eGFR, death-censored graft survival, and MAKE differed significantly among recipients with different TyG index quartiles (all p < 0.001) (Fig. 1). The highest cumulative event rate for all clinical outcomes was observed in recipients in the TyG index quartile 4.

Table 2 shows the number of events, incidence rates, and observed hazard ratios (HRs) of adverse kidney outcomes based on the TyG index quartiles. Univariable Cox regression analysis revealed that the TyG index quartile 3 or 4 was significantly associated with an increased risk for kidney outcomes. The risks of the death-censored graft loss, eGFR decline ≥30%, eGFR decline ≥50%, patient death, and MAKE in recipients in the TyG index quartile 4 were 2.31 (95% confidence interval [CI], 1.80–2.95), 1.39 (95% CI, 1.13–1.72), 1.70 (95% CI, 1.25–2.30), 1.64 (95% CI, 0.98–2.76), and 1.55 (95% CI, 1.22–1.96), respectively.

Compared with recipients in TyG index quartile 1, the adjusted HRs for death-censored graft loss were 1.24 (95%

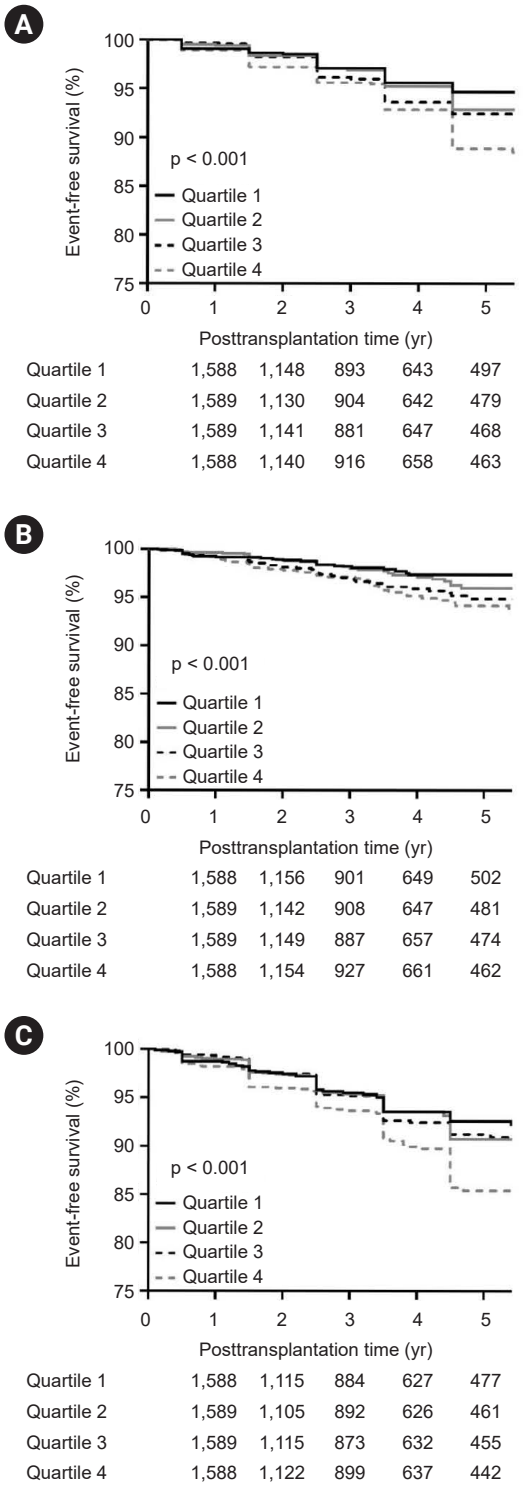

Figure 1. Cumulative rate for each outcome in different triglyceride-glucose index quartiles. (A) Estimated glomerular filtration rate decline ≥50%, (B) death-censored graft survival, and (C) major adverse kidney events among recipients. The p-values are calculated by log-rank tests.

CI, 0.75–2.06), 1.52 (95% CI, 0.93–2.48), and 2.13 (95% CI, 1.28–3.55) for quartiles 2, 3, and 4, respectively, indicating a progressive increase in risk. Recipients in the highest TyG index quartile showed a significantly increased risk of ≥30% and ≥50% decline in eGFR, with adjusted HRs of 1.46 (95% CI, 1.17–1.82) and 1.78 (95% CI, 1.30–2.44), respectively, compared with those in Q1. The composite outcome of MAKE showed a similar trend, with adjusted HRs of 1.00 (95% CI, 0.77–1.29), 1.12 (95% CI, 0.87–1.45), and 1.56 (95% CI, 1.22–1.99) for quartiles 2, 3, and 4. However, the risk of patient death did not differ significantly across TyG quartiles (HR for Q4 vs. Q1, 1.57; 95% CI, 0.91–2.65). Variables that were significantly associated with patient death included age (adjusted HR, 1.08; 95% CI, 1.06–1.11), deceased donor (adjusted HR, 1.73; 95% CI, 1.11–2.70), and time on dialysis (adjusted HR, 1.04 per year; 95% CI, 1.03–1.06).

Restricted cubic spline curves were generated to assess the continuous relationship between the TyG index and the HRs of the death-censored graft loss (Fig. 2). A gradual increase in the risk of composite events and graft loss was observed with an incremental increase in the TyG index.

Triglyceride-glucose level and the estimated glomerular filtration rate slopes of renal allograft

The annual eGFR slopes were –1.15 mL/min/1.73 m^2 (95% CI, –1.33 to –0.96), –1.14 mL/min/1.73 m^2 (95% CI, –1.32 to –0.96), –1.24 mL/min/1.73 m^2 (95% CI, –1.44 to –1.04), and –1.06 mL/min/1.73 m^2 (95% CI, –1.18 to –0.94) for recipients in the TyG index quartile 1, 2, 3, and 4, respectively. Linear mixed models were constructed to characterize the eGFR slopes based on the TyG index (Table 3). A significant unadjusted interaction was observed for eGFR between the TyG index quartile and time (p = 0.005). Adjusted analyses of change in eGFR indicated that, compared to recipients in the TyG index quartile 1, those in the TyG index quartile 3 and 4 were significantly associated with the excess eGFR decline of –3.00 mL/min/1.73 m^2 (95% CI, –5.63 to –0.36) per year and –4.72 mL/min/1.73 m^2 (95% CI, –7.39 to –2.04) per year, respectively.

Subgroup analysis

We evaluated the association between a one-quartile in-

Table 2. Incidence rate and HRs of predefined kidney outcomes based on the triglyceride-glucose index quartiles

Triglyceride-glucose index	No. of events	Person-years	Incidence rate	Univariable analysis		Multivariable analysis	
				HR (95% CI)	p-value	HR (95% CI)	p-value
Death-censored graft loss							
Quartile 1	24	4,389	5.5	Reference	-	Reference	-
Quartile 2	31	4,343	7.1	1.32 (0.77–2.36)	0.31	1.25 (0.73–2.16)	0.42
Quartile 3	44	4,297	10.2	1.86 (1.12–3.07)	0.02	1.76 (1.05–2.95)	0.03
Quartile 4	54	4,276	12.6	2.31 (1.80–2.95)	0.001	2.13 (1.28–3.55)	0.004
eGFR decline ≥30%							
Quartile 1	151	4,438	34.0	Reference	-	Reference	-
Quartile 2	136	4,384	31.0	0.92 (0.73–1.16)	0.48	0.92 (0.73–1.16)	0.49
Quartile 3	167	4,336	38.5	1.15 (0.43–0.92)	0.23	1.18 (0.94–1.47)	0.16
Quartile 4	197	4,320	45.6	1.39 (1.13–1.72)	0.002	1.46 (1.17–1.82)	0.001
eGFR decline ≥50%							
Quartile 1	67	4,438	15.1	Reference	-	Reference	-
Quartile 2	68	4,385	15.5	1.03 (0.74–1.45)	0.85	1.03 (0.74–1.45)	0.85
Quartile 3	84	4,337	19.4	1.29 (0.93–1.77)	0.13	1.31 (0.95–1.82)	0.10
Quartile 4	108	4,324	25.0	1.70 (1.25–2.30)	0.001	1.78 (1.30–2.44)	<0.001
Patient death							
Quartile 1	23	4,539	5.1	Reference	-	Reference	-
Quartile 2	31	4,470	6.9	1.36 (0.79–2.34)	0.26	1.37 (0.80–2.36)	0.26
Quartile 3	23	4,443	5.2	0.97 (0.54–1.75)	0.93	1.01 (0.56–1.81)	0.98
Quartile 4	37	4,405	8.4	1.64 (0.98–2.76)	0.06	1.57 (0.91–2.65)	0.10
MAKE							
Quartile 1	88	4,404	20.0	Reference	-	Reference	-
Quartile 2	89	4,359	20.4	1.01 (0.78–1.31)	0.95	1.00 (0.77–1.29)	0.98
Quartile 3	100	4,317	23.2	1.11 (0.86–1.43)	0.44	1.12 (0.87–1.45)	0.39
Quartile 4	139	4,298	32.3	1.55 (1.22–1.96)	<0.001	1.56 (1.22–1.99)	<0.001

CI, confidence interval; eGFR, estimated glomerular filtration rate; HR, hazard ratio; MAKE, major adverse kidney events.
Incidence rate was represented as 1,000 person-years. Multivariable analyses were adjusted for the following covariates: age, sex, body mass index at enrollment, previous history of cardiovascular disease, donor type (living vs. deceased), underlying etiology of end-stage kidney disease, time on dialysis, desensitization, human leukocyte antigen mismatching number, maintenance immunosuppressant, and eGFR at enrollment.

crease in the TyG index and the risk of ≥50% decline in eGFR and death-censored graft loss across clinically relevant subgroups, including age, sex, diabetes mellitus, hypertension, BMI, and metabolic syndrome (Supplementary Table 1, available online). In most subgroups, a higher TyG index was consistently associated with increased risks of both eGFR decline and graft loss. No statistically significant interaction was observed for any subgroup, suggesting that the association was consistent across diverse clinical subgroups.

Discussion

We hypothesized that kidney transplant recipients with a high TyG index would have an elevated risk of major adverse kidney outcomes, including a composite of moderate-to-severe renal function decline and death-censored renal allograft loss. In this nationwide, prospective, observational cohort study, a higher TyG index was significantly associated with increased susceptibility to these outcomes. Furthermore, recipients with a higher TyG index showed a steeper slope of eGFR decline over time in linear mixed-effects models. These findings highlight the clinical significance of the TyG index in kidney transplant recipients, suggesting its potency as a risk factor for unfavorable renal allograft outcomes.

While renal transplantation resolves several complications related to impaired kidney function, recipients con-

tinue to encounter new metabolic challenges driven by factors such as obesity, immunosuppressive therapy, dyslipidemia, hypertension, and imbalanced glucose metabolism [24,25]. These metabolic disorders have been recognized as significant alloantigen-independent contributors to adverse kidney outcomes [26,27]. In our study, recipients with a high TyG index showed a higher cumulative incidence of adverse kidney outcomes and a significantly increased risk of MAKE compared to those with a lower TyG index. These findings highlight the TyG index as a useful marker of metabolic disturbances in predicting adverse renal graft outcomes. Notably, insulin resistance is a primary manifestation of these metabolic disorders and represents a central pathophysiologic feature of this syndrome [28,29]. Therefore, the TyG index could be a clinically meaningful marker of posttransplant metabolic stress, allowing identification of individuals at higher risk for adverse kidney outcomes.

Although several reports have indicated that metabolic syndrome and obesity contribute to poor kidney outcomes in the general population [30,31], few studies have evaluated the role of insulin resistance in renal allograft outcomes. Our study demonstrates a clear association between TyG index quartiles 3 and 4 and an increased risk of graft loss, which increased gradually in proportion to the TyG index level. These findings extend the clinical relevance of insulin resistance to the field of renal allograft outcomes. In our subgroup analysis, the association between a high TyG index and the risk of both ≥50% eGFR decline and graft loss was consistently observed without significant interaction across subgroups. This suggests that the predictive value of the TyG index for graft loss may be generalizable regardless of baseline characteristics, and highlights its potential utility in diverse transplant populations.

To explore the association between the TyG index and renal injury prior to the occurrence of graft loss, we analyzed outcomes related to renal function decline and the magnitude of eGFR change. We found that a high TyG index was associated with a greater risk of ≥50% decline in eGFR from baseline, and that recipients in TyG index quartiles 3 and 4 exhibited a significantly steeper eGFR decline slope compared to those in quartile 1. These findings suggest that the TyG index may facilitate the early identification of transplant recipients at increased risk for renal allograft deterioration and provide an opportunity for proactive management to prevent further injury. In sensitivity analyses, recipients in TyG index quartile 4 showed a significantly increased risk of experiencing ≥30% decline in renal function and exhibited a more rapid decline in eGFR slope. These findings further support the utility of the TyG index in detecting recipients with initial-stage graft dysfunction. Therefore, we suggest that the TyG index is a valuable

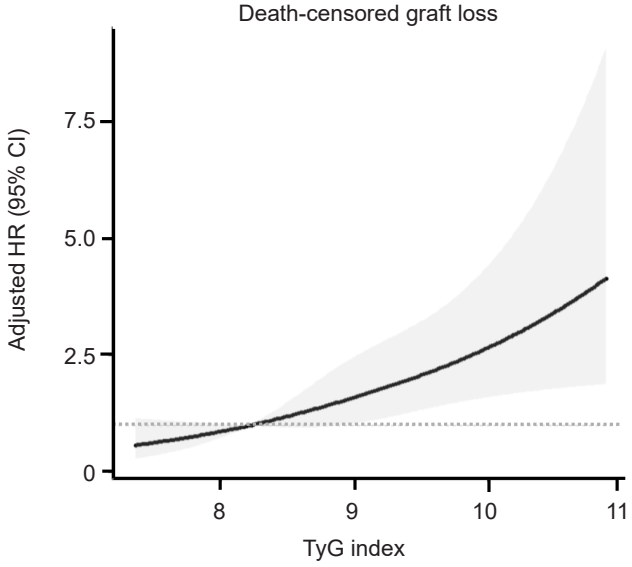

Figure 2. Restricted cubic spline curves demonstrate a continuous relationship between TyG index and HRs of death-censored graft loss.
CI, confidence interval; HR, hazard ratio; TyG, triglyceride-glucose.

Table 3. Association between triglyceride-glucose index quartiles and changes in eGFR of renal allograft

Triglyceride-glucose index	Univariable analysis		Multivariable analysis	
	Differences in eGFR (95% CI)	p-value	Differences in eGFR (95% CI)	p-value
Quartile 1	Reference	-	Reference	-
Quartile 2	0.00 (−2.25 to 2.26)	0.997	−1.24 (−3.88 to 1.39)	0.36
Quartile 3	−2.41 (−4.68 to −0.38)	0.04	−3.00 (−5.63 to −0.36)	0.03
Quartile 4	−3.09 (−5.36 to −0.81)	0.008	−4.72 (−7.39 to −2.04)	0.001

marker for ongoing surveillance of metabolic risk, which is closely associated with graft dysfunction from the early posttransplant period.

Insulin resistance affects kidney function and the development of chronic kidney disease through multiple pathways [32]. Mechanistically, insulin resistance leads to glomerular hyperfiltration, increased sodium retention, tubular dysfunction, and renal tissue inflammation and fibrosis [1,33,34]. Single renal allografts in recipients are more susceptible to renal hyperfiltration compared to two native kidneys due to a reduced number of glomeruli. Additionally, the adverse effects of immunosuppressants and immunological injury induce renal interstitial inflammation and fibrosis [35,36]. Therefore, increased insulin resistance can substantially exacerbate the underlying damage in renal allografts, and our results provide further support for the biological pathway through which insulin resistance deteriorates the kidneys.

Several previous studies have evaluated the association between the TyG index and all-cause mortality in patients with diabetes mellitus or those requiring intensive care, and found that a higher TyG index was associated with increased mortality risk [37]. However, the strength of this association has been inconsistent. Some studies found no significant relationship between the TyG index and all-cause mortality, or observed significance only within specific subpopulations [38,39]. We also assessed the clinical relevance of the TyG index for all-cause mortality in kidney transplant recipients, but the association was not significant among those in the higher TyG index quartiles. These findings suggest that the relationship between the TyG index and mortality risk may differ across clinical populations, and that the TyG index may have a limited prognostic value for mortality in kidney transplant recipients.

This study has several limitations. First, the KOTRY database does not include detailed information on important lifestyle and clinical variables such as dietary habits, physical activity, alcohol consumption, or family history of disease. These unmeasured factors are known to influence metabolic status and kidney outcomes, and their absence may have introduced residual confounding in our analysis. In addition, although information on the types of immunosuppressive agents was available and adjusted for in the multivariable models, data on immunosuppressive drug levels and adherence were not accounted for. These unmeasured treatment-related factors may have influenced both metabolic parameters and graft outcomes, and should be considered in future studies. Second, the present study was limited to the assessment of the TyG index, which was based on a single value obtained on the index date. Transient fluctuations may affect the diagnostic or predictive value of the TyG index. Future studies incorporating serial TyG index measurements or cumulative exposure over time, or latent class mixture modeling, may better reflect long-term metabolic burden and improve the prediction of graft outcomes. Third, observational study designs inherently involve residual or unmeasured confounding factors that could influence the results. Moreover, such designs have limited capacity to establish a causal relationship between the TyG index and adverse kidney outcomes. Further studies would be valuable in confirming the predictive utility of the TyG index for long-term kidney outcomes.

In conclusion, this study demonstrated that kidney transplant recipients with a high TyG index had an elevated risk of ≥30% and ≥50% declines in eGFR, along with graft loss. In addition, a high TyG index was associated with a steeper decline in eGFR over time. Monitoring the TyG index is useful to identify recipients at increased risk of adverse kidney outcomes and support risk-based management strategies to optimize care in kidney transplant recipients.

Conflicts of interest

All authors have no conflicts of interest to declare.

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Data sharing statement

The datasets supporting the conclusions of this article are available in the KOTRY upon reasonable request.

Authors' contributions

Conceptualization: JSK, KHJ, HSH
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References

1. Porrini E, Delgado P, Torres A. Metabolic syndrome, insulin resistance, and chronic allograft dysfunction. *Kidney Int Suppl* 2010;(119):S42–S46.
2. Lann D, LeRoith D. Insulin resistance as the underlying cause for the metabolic syndrome. *Med Clin North Am* 2007 91:1063–1077. viii.
3. Ling Q, Huang H, Han Y, et al. The tacrolimus-induced glucose homeostasis imbalance in terms of the liver: from bench to bedside. *Am J Transplant* 2020;20:701–713.
4. Prasad GV, Huang M, Silver SA, et al. Metabolic syndrome definitions and components in predicting major adverse cardiovascular events after kidney transplantation. *Transpl Int* 2015;28:79–88.
5. de Vries AP, Bakker SJ, van Son WJ, et al. Metabolic syndrome is associated with impaired long-term renal allograft function; not all component criteria contribute equally. *Am J Transplant* 2004;4:1675–1683.
6. Bonora E, Targher G, Alberiche M, et al. Homeostasis model assessment closely mirrors the glucose clamp technique in the assessment of insulin sensitivity: studies in subjects with various degrees of glucose tolerance and insulin sensitivity. *Diabetes Care* 2000;23:57–63.
7. Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC. Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. *Diabetologia* 1985;28:412–419.
8. Kang ES, Yun YS, Park SW, et al. Limitation of the validity of the homeostasis model assessment as an index of insulin resistance in Korea. *Metabolism* 2005;54:206–211.
9. Simental-Mendía LE, Rodríguez-Morán M, Guerrero-Romero F. The product of fasting glucose and triglycerides as surrogate for identifying insulin resistance in apparently healthy subjects. *Metab Syndr Relat Disord* 2008;6:299–304.
10. Tao LC, Xu JN, Wang TT, Hua F, Li JJ. Triglyceride-glucose index as a marker in cardiovascular diseases: landscape and limitations. *Cardiovasc Diabetol* 2022;21:68.
11. Lee YH, Han K, Yoon HE, Chung S, Sitapati AM, Hwang HS. Triglyceride-glucose index and risks of all-cause and cause-specific mortality in young adults. *J Clin Endocrinol Metab* 2025;110:e3607-e3616.
12. Lee YH, Kang SH, Kim DK, et al. Cardiovascular risk prediction in hemodialysis patients using the triglyceride-glucose index: a multicenter prospective cohort study. *Clin Kidney J* 2025;18:sfaf016.
13. Colladant M, Chabannes M, Crepin T, Bamoulid J, Courivaud C, Ducloux D. Triglyceride-glucose index and cardiovascular events in kidney transplant recipients. *Kidney Int Rep* 2023;8:2307–2314.
14. Sokooti S, Szili-Török T, Heerspink HJ, Dullaart RP, Bakker SJ. Indirect insulin resistance indices and their cut-off values for the prediction of post-transplantation diabetes mellitus in kidney transplant recipients. *J Clin Med* 2023;12:7296.
15. Yang J, Jeong JC, Lee J, et al. Design and methods of the Korean Organ Transplantation Registry. *Transplant Direct* 2017;3:e191.
16. LaGuardia H, Zhang R. Obesity and metabolic syndrome in kidney transplantation. *Curr Hypertens Rep* 2013;15:215–223.
17. Hjelmesaeth J, Midtvedt K, Jenssen T, Hartmann A. Insulin resis-

tance after renal transplantation: impact of immunosuppressive and antihypertensive therapy. *Diabetes Care* 2001;24:2121–2126.
18. Courivaud C, Kazory A, Simula-Faivre D, Chalopin JM, Ducloux D. Metabolic syndrome and atherosclerotic events in renal transplant recipients. *Transplantation* 2007;83:1577–1581.
19. Guerrero-Romero F, Simental-Mendía LE, González-Ortiz M, et al. The product of triglycerides and glucose, a simple measure of insulin sensitivity: comparison with the euglycemic-hyperinsulinemic clamp. *J Clin Endocrinol Metab* 2010;95:3347–3351.
20. Levey AS, Stevens LA, Schmid CH, et al. A new equation to estimate glomerular filtration rate. *Ann Intern Med* 2009;150:604–612.
21. Grundy SM, Cleeman JI, Daniels SR, et al. Diagnosis and management of the metabolic syndrome: an American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement. *Circulation* 2005;112:2735–2752.
22. Kim MK, Lee WY, Kang JH, et al. 2014 Clinical practice guidelines for overweight and obesity in Korea. *Endocrinol Metab (Seoul)* 2014;29:405–409.
23. Kim JH, Lee YH, Kim DK, et al. Comparisons of clinical outcomes between hypertensive and normotensive living kidney donors: a prospective, multicenter nationwide cohort study. *Kidney Res Clin Pract* 2025;44:602–611.
24. Leyking S, Fliser D. Insulin resistance in CKD. *Clin J Am Soc Nephrol* 2014;9:638–640.
25. Lee YH, Song SH, Song SH, et al. Clinical implications of changes in metabolic syndrome status after kidney transplantation: a nationwide prospective cohort study. *Nephrol Dial Transplant* 2023;38:2743–2753.
26. Piotti G, Gandolfini I, Palmisano A, Maggiore U. Metabolic risk profile in kidney transplant candidates and recipients. *Nephrol Dial Transplant* 2019;34:388–400.
27. de Vries AP, Bakker SJ, van Son WJ, et al. Insulin resistance as putative cause of chronic renal transplant dysfunction. *Am J Kidney Dis* 2003;41:859–867.
28. Eckel RH, Grundy SM, Zimmet PZ. The metabolic syndrome. *Lancet* 2005;365:1415–1428.
29. Davidson MB. Metabolic syndrome/insulin resistance syndrome/pre-diabetes: new section in diabetes care. *Diabetes Care* 2003;26:3179.
30. Zhang X, Lerman LO. The metabolic syndrome and chronic kidney disease. *Transl Res* 2017;183:14–25.
31. Kurella M, Lo JC, Chertow GM. Metabolic syndrome and the risk for chronic kidney disease among nondiabetic adults. *J Am Soc Nephrol* 2005;16:2134–2140.
32. Okamura T, Hashimoto Y, Hamaguchi M, Obora A, Kojima T, Fukui M. Triglyceride-glucose index is a predictor of incident chronic kidney disease: a population-based longitudinal study. *Clin Exp Nephrol* 2019;23:948–955.
33. Artunc F, Schleicher E, Weigert C, Fritsche A, Stefan N, Häring HU. The impact of insulin resistance on the kidney and vasculature. *Nat Rev Nephrol* 2016;12:721–737.
34. Whaley-Connell A, Sowers JR. Insulin resistance in kidney disease: is there a distinct role separate from that of diabetes or obesity? *Cardiorenal Med* 2017;8:41–49.
35. Bia MJ. Nonimmunologic causes of late renal graft loss. *Kidney Int* 1995;47:1470–1480.
36. Bosma RJ, Kwakernaak AJ, van der Heide JJ, de Jong PE, Navis GJ. Body mass index and glomerular hyperfiltration in renal transplant recipients: cross-sectional analysis and long-term impact. *Am J Transplant* 2007;7:645–652.
37. Zhang Q, Xiao S, Jiao X, Shen Y. The triglyceride-glucose index is a predictor for cardiovascular and all-cause mortality in CVD patients with diabetes or pre-diabetes: evidence from NHANES 2001-2018. *Cardiovasc Diabetol* 2023;22:279.
38. Zhang P, Mo D, Zeng W, Dai H. Association between triglyceride-glucose related indices and all-cause and cardiovascular mortality among the population with cardiovascular-kidney-metabolic syndrome stage 0-3: a cohort study. *Cardiovasc Diabetol* 2025;24:92.
39. Chen J, Wu K, Lin Y, Huang M, Xie S. Association of triglyceride glucose index with all-cause and cardiovascular mortality in the general population. *Cardiovasc Diabetol* 2023;22:320.