Cardiovascular Diabetology

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Association between triglyceride–glucose index and mortality in critically ill patients with atrial fibrillation: a retrospective cohort study

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Abstract

Background The triglyceride–glucose (TyG) index, an emerging surrogate marker of insulin resistance, has been implicated in adverse cardiovascular outcomes. However, its prognostic value in critically ill patients with atrial fibrillation (AF) remains unclear. This study aimed to investigate the association between the TyG index and all-cause mortality in this high-risk population.

Methods We identified critically ill patients with AF from the Medical Information Mart for Intensive Care IV (MIMIC-IV) database and categorized them into tertiles based on their TyG index levels. The primary outcome was 30-day mortality, with 90-day and 365-day all-cause mortality as secondary outcomes. Cox proportional hazards regression analysis and restricted cubic splines were used to elucidate the relationship between the TyG index and all-cause mortality. Kaplan–Meier survival analysis was performed to visualize survival differences among the tertiles.

Results A total of 1473 patients were included; the 30-day, 90-day, and 365-day all-cause mortality rates were 26.8%, 33.3%, and 41.1%, respectively. Multivariate Cox proportional hazards analysis revealed that the TyG index was independently associated with mortality at 30 days [hazard ratio (HR) (95% confidence interval (CI)) 1.26 (1.09–1.45), $P=0.002$], 90 days [HR (95% CI) 1.27 (1.11–1.45), $P<0.001$], and 365 days [HR (95% CI) 1.24 (1.10–1.40), $P<0.001$]. Restricted cubic splines regression showed a positive linear association between the TyG index and mortality risk. Kaplan–Meier survival curves further confirmed the significant survival disparities across TyG index tertiles.

Conclusions A significant linear association was observed between higher TyG index and increased all-cause mortality at 30, 90, and 365 days in critically ill patients with AF. This underscores the role of the TyG index as a key prognostic indicator for risk stratification and management in intensive care.

Keywords Triglyceride–glucose index, Atrial fibrillation, Insulin resistance, All-cause mortality, MIMIC- IV database

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Background

Cardiovascular diseases continue to be the leading cause of disease burden worldwide [1]. Atrial fibrillation (AF) is a major cardiovascular health problem characterized by a profound disorder in atrial electrical activity, leading to the impairment of effective atrial contractions [2]. AF is closely associated with severe complications, including stroke, sudden cardiac death, and heart failure, and has a substantial and growing impact on public health worldwide [1, 3]. The prevalence of AF rises with age, from 0.1% in individuals under 55 to 9.0% in those aged 80 and older [4]. In intensive care units (ICUs), the incidence of AF can be 15.6% or even higher [5, 6]. Patients in the ICU with AF often experience multiple complications, complex health issues, and a high risk of mortality [7]. Existing evidence has established a strong correlation between hyperglycemia, dyslipidemia, and AF development [8, 9], with insulin resistance (IR) playing a crucial role in these pathological processes [10, 11]. Several studies have reported correlations among IR and AF prognosis, its recurrence after ablation, and its occurrence in the general population [12–15].

IR, defined by the diminished ability of insulin to facilitate glucose transport into cells, is a key feature of metabolic syndromes that disrupt metabolic pathways across multiple organs [16, 17]. The TyG index, initially proposed as a marker for identifying IR in healthy individuals [18], has recently gained attention as a cost-effective alternative. The integration of fasting triglyceride and glucose levels provides a simple surrogate for IR. The TyG index is linked to a range of health outcomes, encompassing cardiovascular disease, arterial stiffness, and cancer [19–21]. Furthermore, it contributes to the risk assessment of conditions such as diabetes, stroke, renal conditions, and coronary artery disease [22–26]. The TyG index has been associated with all-cause mortality in patients with diverse underlying conditions in intensive care units [27–29], underscoring its potential as a mortality risk marker. However, the relationship between the TyG index and mortality in ICU patients with AF remains unclear.

This study aimed to explore the association between the TyG index and all-cause mortality in critically ill patients with AF using data from the Medical Information Market for Intensive Care IV (MIMIC-IV) database.

Materials and methods

Data source

This retrospective analysis used the Medical Information Mart for Intensive Care IV (MIMIC-IV, Version 3.1) database, which is a comprehensive and publicly accessible resource that includes records of ICU admissions at the Beth Israel Deaconess Medical Center in Boston, MA, USA, from 2008 to 2019. All personal identifiers were removed to protect patient privacy. Ethical approval, including a consent waiver, was obtained from the MIT and Beth Israel Deaconess Medical Center Review Boards. The author, Rong Ding, completed an online course on human research participant protection offered by the US National Institutes of Health, securing access to the dataset. The certificate number was 64,760,223. This study adhered to the strengthening the reporting of observational studies in epidemiology (STROBE) guidelines and complied with the principles of the Declaration of Helsinki [30].

Study population

This study included patients with AF who were hospitalized and admitted to the ICU for the first time. The diagnosis of AF was confirmed using the International Classification of Diseases (ICD)-9/10 codes (Supplementary Table 1). The exclusion criteria were as follows: (1) multiple hospital admissions, (2) lack of serum fasting blood glucose and triglyceride data on the first day of ICU admission, and (3) death or discharge within 24 h of ICU admission.

Demographical and laboratory variables

Structured query language was used to gather data on patient demographics (age, sex, height, weight, and race); medical history (hypertension, diabetes, myocardial infarction, congestive heart failure, chronic pulmonary disease, cerebrovascular disease, paraplegia, renal disease, malignant cancer, sepsis, and acute kidney injury); initial laboratory parameters (white blood cell count, platelet count, hemoglobin, sodium, potassium, calcium, blood glucose, anion gap, international normalized ratio, triglycerides, bicarbonate, and creatinine); medications (aspirin, clopidogrel, beta-blockers, angiotensin-converting enzyme inhibitors/angiotensin receptor blockers, calcium channel blocker, digitalis, diuretics, amiodarone, insulin, statins, dabigatran, rivaroxaban, heparin, and warfarin); special treatments (continuous renal replacement therapy and vasoactive drug and mechanical ventilation); important scoring systems (SAPS II score, OASIS score); vital sign (heart rate, mean arterial pressure, respiratory rate, and pulse oximetry-derived oxygen saturation); and survival time. All laboratory parameters were recorded on the first day of the initial ICU admission.

The primary exposure in this study was the TyG index, a composite measure of fasting triglycerides and fasting blood glucose, calculated using the formula: TyG index = ln [fasting TG (mg/dL) × FBG (mg/dL)] / 2 [20].

The primary endpoint was 30-day all-cause mortality, and the secondary endpoints were 90-day and 365-day all-cause mortality. Deaths were recorded as events that occurred within a specific time frame of ICU admission.

Statistical analysis

In this study, critically ill patients diagnosed with AF were grouped into three categories based on TyG index tertiles and additionally divided into two groups according to their 30-day survival status. The baseline characteristics are described for each group. Continuous variables are presented as mean ± standard deviation or median (interquartile range), whereas categorical variables are shown as numbers and frequency percentiles (%). Fisher's exact test or Pearson's chi-square test was used to compare categorical variables across groups.

Kaplan–Meier survival analysis was used to evaluate the incidence of endpoint events across varying TyG index levels, and differences were assessed using the log-rank test. The relationship between the TyG index and the study endpoints was determined using Cox proportional hazards models, providing hazard ratios (HRs) and 95% confidence intervals (CIs). Covariates were selected if their addition to the model changed the matched HR by at least 10% or based on previous findings and clinical considerations. The variance inflation factor method was used to test for multicollinearity, with a variance inflation factor of five or higher indicating multicollinearity. None of the variables showed multicollinearity (Supplementary Table 2). Three models were used to adjust for confounders: Model 1 (baseline model, not adjusted), Model 2 (adjusted for age, sex, weight, race, hypertension, diabetes, myocardial infarction, congestive heart failure, cerebrovascular disease, malignant cancer, chronic pulmonary disease, and renal disease), and Model 3 (adjusted covariates in Model 2 and heart rate, mean arterial pressure, white blood cell count, hemoglobin, international normalized ratio, creatinine, potassium, sodium, insulin, beta-blockers, statins, amiodarone, and digitalis). Both continuous and tertile-based TyG indices were examined, and the *P*-value for the trend was calculated across the TyG tertiles.

Restricted cubic spline models were applied to explore the potential linear relationships between TyG levels and all-cause mortality rates at 30, 90, and 365 days. Subgroup analyses were conducted for age (< 65 or > = 65 years), sex, race, hypertension, diabetes, congestive heart failure, cerebrovascular disease, and malignant cancer, with interaction effects evaluated via *P*-values. These findings are presented as forest plots.

All analyses were conducted using R version 4.2.2 (http://www.R-project.org, R Foundation) and Free Sta tistics software (version 2.0). A statistical *P*-value below 0.05 was considered statistically significant.

Results

Baseline characteristics of study subjects

The final study cohort included 1,473 individuals, as shown in Fig. 1. The median hospital stay was 13.9 days for survivors and 8.9 days for non-survivors. Participants were stratified into tertiles according to the TyG index: T1 (≤ 8.54, $n = 491$), T2 (8.54–9.09, $n = 491$), and T3 (> 9.09, $n = 491$). The baseline characteristics are summarized in Table 1 and Supplementary Tables 3 and 4.

Patients in T3 were younger but had higher body weights and a greater proportion of males compared with T1. From T1 to T3, an upward trend was observed in heart rate, respiratory rate, potassium, anion gap, creatinine, white blood cells, triglycerides, glucose, and TyG index, whereas the mean arterial pressure, sodium, calcium, bicarbonate, and hemoglobin showed a decline. Clinical severity, as indicated by the SAPS II and OASIS scores, progressively increased with increasing TyG tertiles. Additionally, the prevalence of type 2 diabetes, myocardial infarction, renal disease, sepsis, and acute kidney injury increased from T1 to T3, whereas cerebrovascular disease and paraplegia showed decreasing trends.

TyG and mortality

Of the 1,473 patients, 395 (26.8%), 491 (33.3%), and 605 (41.1%) died within 30, 90, and 365 days of follow-up, respectively. Kaplan–Meier survival analysis was performed to compare mortality rates among patients categorized into tertiles based on the TyG index. Patients with higher TyG indices exhibited significantly higher all-cause mortality rates at 30, 90, and 365 days than those with lower TyG indices. Moreover, there were notable differences in mortality rates among the three groups, with log-rank *P*-values of 0.0022, 0.0050, and 0.0017, respectively. Figure 2 illustrates the detailed results of the analysis.

Using Cox proportional hazards analysis, we evaluated the relationship between the TyG index and 30-day mortality. When considered a continuous variable, the TyG index was identified as a significant risk factor across all models: unadjusted [HR (95% CI) 1.31 (1.16–1.48), $P < 0.001$] and fully adjusted [HR (95% CI) 1.23 (1.06–1.43), $P = 0.005$]. Similarly, when the TyG index was categorized, the highest tertile group showed a notably increased risk of 30-day mortality in both the initial Model 1 [HR (95% CI) 1.54 (1.20–1.97), $P = 0.001$] and fully adjusted Model 3 [HR (95% CI) 1.39 (1.05–1.83), $P = 0.021$] compared with the lowest tertile. This indicates an increasing trend in mortality risk associated with higher TyG index levels. Cox regression analysis for 90-day and 365-day mortality rates mirrored this trend (Table 2).

Furthermore, restricted cubic spline regression modeling demonstrated a linear relationship between TyG index levels and the risk of mortality at 30, 90, and 365 days (P for nonlinearity = 0.818, 0.911, and 0.909, respectively), as shown in Fig. 3.

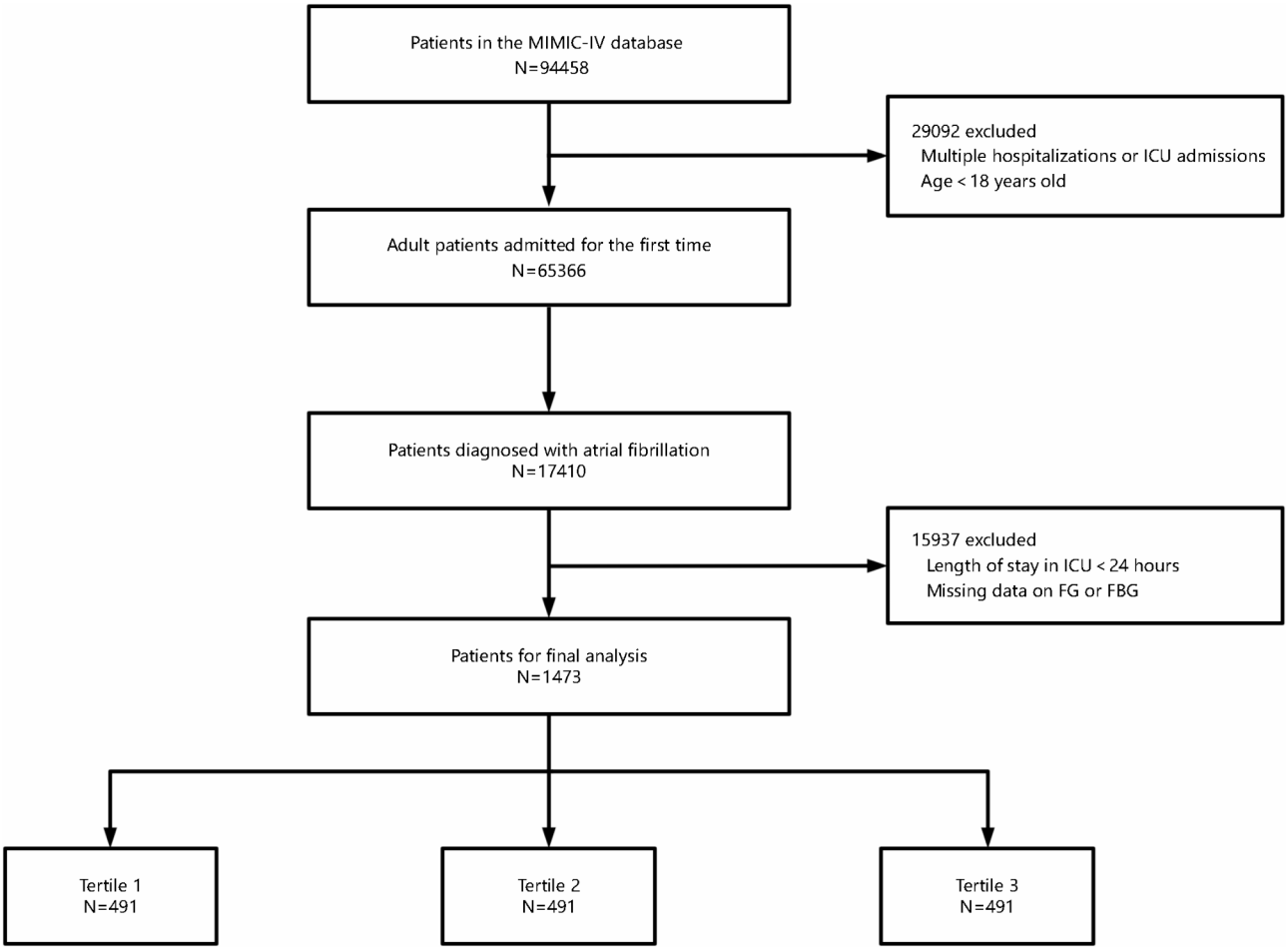

Fig. 1 Flowchart of the study cohort. *MIMIC-IV,* Medical Information Mart for Intensive Care IV; *ICU,* Intensive Care Unit

Subgroup analysis

Subgroup analyses were conducted to evaluate the effectiveness of the TyG index in stratifying the mortality risk across various factors, including age, sex, race, hypertension, diabetes, heart failure, cerebrovascular disease, and malignant cancer (Fig. 4). A consistent positive association between the TyG index and mortality was found in most subgroups, particularly among patients aged ≥ 65 years. The TyG index showed a stronger prognostic value in non-diabetic individuals, with HRs (95% CIs) for 30, 90, and 365 days of 1.43 (1.17–1.74), 1.44 (1.21–1.73), and 1.40 (1.18–1.65), respectively, compared with 0.93 (0.74–1.17), 0.95 (0.77–1.17), and 0.98 (0.82–1.18) in patients with diabetes. The interaction *P*-values (0.046, 0.051, and 0.056) suggested a potential interaction that requires further investigation.

Discussion

Our study comprehensively evaluated the relationship between the TyG index and all-cause mortality in critically ill patients with AF using the MIMIC database. We found that higher TyG index values were consistently linked to increased 30-, 90-, and 365-day mortality, even after adjusting for potential confounding factors. We identified a linear dose-response relationship, suggesting the clinical utility of early risk stratification in ICU settings, where patients with AF face heightened mortality rates.

AF is the most prevalent cardiac arrhythmia, and its incidence escalates with advancing age [31]. AF is not solely an atrial issue; it is linked to systemic inflammation, endothelial dysfunction, metabolic disturbances, and changes in myocardial structure and function [32]. Metabolic stress and remodeling further increase AF susceptibility, influencing atrial function through alterations in glucose, lipid, and ketone metabolism, mitochondrial function, and myofibrillar energetics [33]. Research has shown that metabolic disorders increase the risk of death in patients with AF [34]. Identifying biomarkers for evaluating disease severity in individuals affected by AF is a pivotal field of research.

IR is not only the main component of diabetes mellitus but also a modulator of AF substrate development [34]. The potential mechanisms underlying IR-induced

Table 1 Baseline characteristics and outcomes of participants classified by TyG index tertiles

Characteristics	Total ($n=1473$)	T1 ($n=491$)	T2 ($n=491$)	T3 ($n=491$)	*P*-value
Age, years	75.1 ± 12.4	78.5 ± 11.7	75.5 ± 12.2	71.1 ± 12.1	< 0.001
Sex, n (%)					0.006
Male	777 (52.7)	234 (47.7)	259 (52.7)	284 (57.8)	
Female	696 (47.3)	257 (52.3)	232 (47.3)	207 (42.2)	
Race, n (%)					0.079
White	831 (56.4)	295 (60.1)	276 (56.2)	260 (53)	
Others	642 (43.6)	196 (39.9)	215 (43.8)	231 (47)	
Weight, kg	84.1 ± 27.3	78.0 ± 23.2	81.7 ± 24.5	92.5 ± 31.3	< 0.001
BMI, kg/m^2	30.5 ± 9.5	27.9 ± 8.5	29.4 ± 8.2	32.9 ± 10.4	< 0.001
Hypertension, n (%)	1177 (79.9)	394 (80.2)	395 (80.4)	388 (79)	0.834
Diabetes, n(%)	477 (32.4)	82 (16.7)	137 (27.9)	258 (52.5)	< 0.001
MI, n (%)	385 (26.1)	91 (18.5)	137 (27.9)	157 (32)	< 0.001
CHF, n(%)	623 (42.3)	206 (42)	206 (42)	211 (43)	0.933
CPD, n(%)	311 (21.1)	100 (20.4)	100 (20.4)	111 (22.6)	0.611
CVD, n(%)	876 (59.5)	341 (69.5)	309 (62.9)	226 (46)	< 0.001
Paraplegia, n(%)	531 (36.0)	213 (43.4)	182 (37.1)	136 (27.7)	< 0.001
Renal disease, n(%)	330 (22.4)	96 (19.6)	97 (19.8)	137 (27.9)	0.002
Malignant cancer, n(%)	133 (9.0)	34 (6.9)	53 (10.8)	46 (9.4)	0.101
Sepsis, n(%)	714 (48.5)	182 (37.1)	227 (46.2)	305 (62.1)	< 0.001
AKI 2 day, n(%)	1031 (70.0)	315 (64.2)	331 (67.4)	385 (78.4)	< 0.001
RRT use, n(%)	82 (5.6)	11 (2.2)	24 (4.9)	47 (9.6)	< 0.001
Vasoactive drug, n(%)	327 (22.2)	66 (13.4)	101 (20.6)	160 (32.6)	< 0.001
Ventilator use, n(%)	470 (31.9)	96 (19.6)	144 (29.3)	230 (46.8)	< 0.001
Insulin, n(%)	1033 (70.1)	315 (64.2)	333 (67.8)	385 (78.4)	< 0.001
Beta blockers, n(%)	996 (67.6)	359 (73.1)	344 (70.1)	293 (59.7)	0.003
Statins, n(%)	109 (7.4)	40 (8.1)	29 (5.9)	40 (8.1)	0.302
Amiodarone, n(%)	214 (14.5)	54 (11.0)	77 (15.7)	83 (16.9)	0.021
Digitalis, n(%)	96 (6.5)	22 (4.5)	44 (9.0)	30 (6.1)	0.016
OASIS	36.6 ± 9.5	34.4 ± 8.5	35.8 ± 9.3	39.4 ± 9.9	< 0.001
SAPS II	40.0 ± 13.9	37.1 ± 11.7	38.7 ± 12.8	44.3 ± 15.8	< 0.001
HR, bpm	84.2 ± 17.7	82.2 ± 16.9	84.5 ± 18.4	85.8 ± 17.6	0.004
MAP, mmHg	84.4 ± 12.0	85.7 ± 12.2	84.8 ± 11.7	82.9 ± 12.0	0.001
RR, bpm	20.1 ± 3.7	19.4 ± 3.1	20.1 ± 3.6	21.0 ± 4.3	< 0.001
SpO2, %	96.6 ± 2.1	96.5 ± 1.7	96.7 ± 2.1	96.6 ± 2.5	0.562
INR	1.3 (1.1, 1.6)	1.3 (1.1, 1.5)	1.3 (1.1, 1.6)	1.3 (1.1, 1.5)	0.693
Sodium, mmol/L	137.4 ± 5.1	137.7 ± 5.0	137.9 ± 4.7	136.7 ± 5.4	0.001
Potassium, mmol/L	4.6 ± 0.9	4.4 ± 0.8	4.5 ± 0.9	4.7 ± 0.9	< 0.001
Calcium, mmol/L	8.4 ± 0.9	8.5 ± 0.7	8.4 ± 0.8	8.1 ± 1.0	< 0.001
Chloride, mmol/L	101.6 ± 5.7	102.0 ± 5.4	102.0 ± 5.4	100.8 ± 6.2	< 0.001
Bicarbonate, mmol/L	21.4 ± 4.6	22.3 ± 4.1	21.5 ± 4.4	20.4 ± 5.1	< 0.001
Anion gap, mmol/L	16.4 ± 4.6	15.3 ± 3.9	16.3 ± 4.3	17.6 ± 5.3	< 0.001
Creatinine, mg/dL	1.1 (0.9, 1.6)	1.0 (0.8, 1.3)	1.1 (0.8, 1.5)	1.3 (0.9, 2.3)	< 0.001
WBC, 10^9/L	11.5 (8.6, 15.5)	9.8 (7.7, 12.9)	11.6 (8.8, 15.1)	13.6 (10.0, 18.4)	< 0.001
Platelets, 10^9/L	186.0 (145.0, 241.0)	183.0 (144.0, 236.0)	195.0 (152.0, 250.0)	184.5 (138.0, 239.0)	0.038
Hemoglobin, g/L	11.2 ± 2.3	11.3 ± 2.1	11.3 ± 2.3	10.9 ± 2.4	0.016
TG, mg/dL	98.0 (73.0, 143.0)	70.0 (58.0, 83.0)	101.0 (83.0, 120.0)	172.0 (127.0, 242.0)	< 0.001
Glucose, mg/dL	131.0 (106.0, 170.0)	107.0 (94.0, 125.5)	131.0 (110.0, 156.5)	179.0 (136.0, 241.0)	< 0.001
TyG index	8.9 ± 0.7	8.2 ± 0.2	8.8 ± 0.2	9.7 ± 0.6	< 0.001
30-day mortality, n (%)	395 (26.8)	109 (22.2)	130 (26.5)	156 (31.8)	0.003
90-day mortality, n (%)	491 (33.3)	141 (28.7)	164 (33.4)	186 (37.9)	0.010
365-day mortality, n (%)	605 (41.1)	174 (35.4)	205 (41.8)	226 (46)	0.003
Length of ICU stay, day	3.6 (2.0, 7.0)	3.1 (1.9, 5.4)	3.6 (1.9, 7.0)	4.5 (2.3, 9.5)	< 0.001
Length of hospital stay, day	8.6 (4.8, 15.9)	7.6 (4.7, 13.0)	8.1 (4.6, 15.1)	10.5 (5.3, 19.8)	< 0.001

Table 1 (continued)

Characteristics	Total ($n=1473$)	T1 ($n=491$)	T2 ($n=491$)	T3 ($n=491$)	*P*-value
Ventilation-free days at 28 days, day	27.6 (0.0, 28.0)	28.0 (23.4, 28.0)	27.8 (0.0, 28.0)	25.1 (0.0, 28.0)	< 0.001
Vasopressor-free days at 28 days, day	28.0 (0.0, 28.0)	28.0 (25.5, 28.0)	28.0 (0.0, 28.0)	27.7 (0.0, 28.0)	< 0.001
ICU-free days at 28 days, day	22.6 (0.0, 25.7)	24.1 (9.7, 26.0)	22.5 (0.0, 25.9)	18.8 (0.0, 25.0)	< 0.001

BMI, Body mass index; *MI,* Myocardial infarction; *CHF,* Congestive Heart failure; *CPD,* Chronic pulmonary disease; *CVD*, Cerebrovascular disease; *AKI*, Acute kidney injury; *RRT*, Renal replacement therapy; *OASIS*, Oxford acute severity of illness score; *APSII*, Acute physiology score II; *SOFA*, Sequential Organ Failure Assessment; *HR*, Heart rate; *MAP,* Mean arterial pressure; *RR,* Respiratory rate; *SpO2,* Pulse oximetry-derived oxygen saturation; *INR,* International normalized ratio; *WBC,* White blood cell; *TG,* Triglycerides; *TyG index,* Triglyceride-glucose index; *ICU,* Intensive care unit

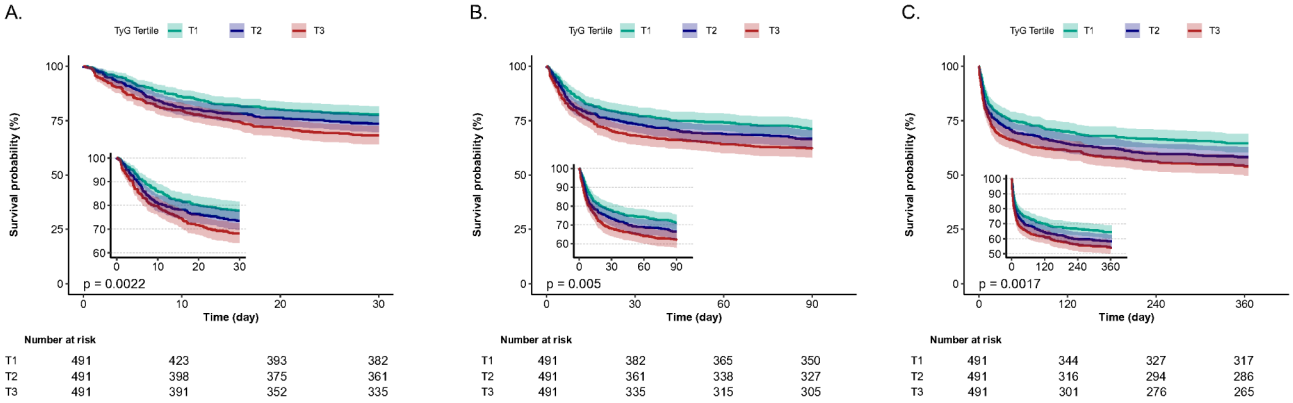

Fig. 2 Kaplan–Meier survival analysis curve for all-cause mortality in the overall study population. **A** 28-day mortality; **B** 90-day mortality; **C** 365-day mortality. TyG index: T1 (TyG index ≤ 8.54), T2 (8.54 < TyG index ≤ 9.09, T3 (TyG index>9.09)

Table 2 Multivariate Cox regression analyses for 30-day, 90-day, and 365-day mortality

Variable	Model 1		Model 2		Model 3	
	HR (95%CI)	*P*-value	HR (95%CI)	*P*-value	HR (95%CI)	*P*-value
30-day mortality						
TyG continuous	1.31 (1.16–1.48)	< 0.001	1.42 (1.24–1.64)	< 0.001	1.23 (1.06–1.43)	0.005
TyG tertiles						
T1	1(Ref)		1(Ref)		1(Ref)	
T2	1.24 (0.96–1.59)	0.102	1.28 (0.99–1.66)	0.064	1.21 (0.93–1.57)	0.155
T3	1.54 (1.20–1.97)	0.001	1.73 (1.31–2.27)	< 0.001	1.39 (1.05–1.83)	0.021
Trend test		0.001		< 0.001		0.021
90-day mortality						
TyG continuous	1.27 (1.13–1.42)	< 0.001	1.41 (1.24–1.61)	< 0.001	1.25 (1.09–1.43)	0.001
TyG tertiles						
T1	1(Ref)		1(Ref)		1(Ref)	
T2	1.21 (0.97–1.52)	0.093	1.27 (1.01–−1.60)	0.040	1.21 (0.96–1.53)	0.106
T3	1.44 (1.15–1.79)	0.001	1.67 (1.30–2.13)	< 0.001	1.40 (1.09–1.79)	0.009
Trend test		0.001		< 0.001		0.009
365-day mortality						
TyG continuous	1.24 (1.12–1.38)	< 0.001	1.38 (1.22–1.55)	< 0.001	1.23 (1.09–1.39)	0.001
TyG tertiles						
T1	1(Ref)		1(Ref)		1(Ref)	
T2	1.24 (1.01–1.52)	0.037	1.28 (1.04–1.58)	0.018	1.24 (1.01–1.53)	0.043
T3	1.43 (1.17–1.74)	< 0.001	1.64 (1.31–2.04)	< 0.001	1.41 (1.12–1.76)	0.003
Trend test		< 0.001		< 0.001		0.003

TyG index: T1 (TyG index ≤ 8.54), T2 (8.54 < TyG index ≤ 9.09, T3 (TyG index>9.09). HR: hazard ratio; CI: confidential interval

Model 1: No adjusted

Model 2: adjusted for age, sex, weight, race, hypertension, diabetes, myocardial infarction, congestive heart failure, cerebrovascular disease, malignant cancer, chronic pulmonary disease and renal disease

Model 3: adjusted for age, sex, weight, race, hypertension, diabetes, myocardial infarction, congestive heart failure, cerebrovascular disease, malignant cancer, chronic pulmonary disease, renal disease, heart rate, mean arterial pressure, white blood cell, hemoglobin, international normalized ratio, creatinine, potassium, sodium, insulin, beta-blockers, statins, amiodarone and digitalis

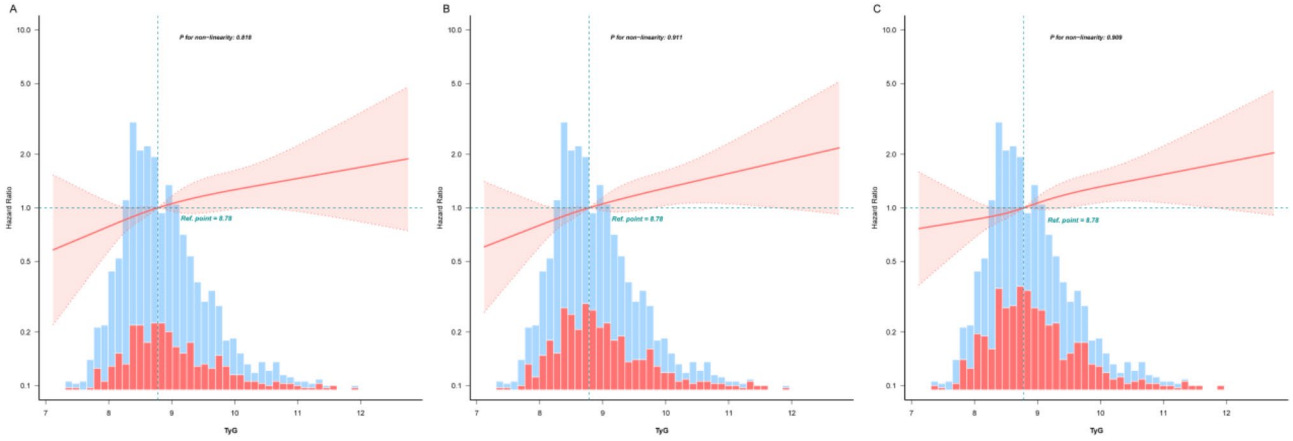

Fig. 3 Association between TyG index and all-cause mortality in critically ill patients with atrial fibrillation. **A** 28-day mortality; **B** 90-day mortality; **C** 365-day mortality. Solid and dashed lines represent the predicted values and 95% confidence intervals, respectively. Adjusted for age, sex, weight, race, hypertension, diabetes, myocardial infarction, congestive heart failure, cerebrovascular disease, malignant cancer, chronic pulmonary disease, renal disease, heart rate, mean arterial pressure, white blood cell count, hemoglobin, international normalized ratio, creatinine, potassium, sodium, insulin, beta-blockers, statins, amiodarone, and digitalis. TyG index, triglyceride-glucose index

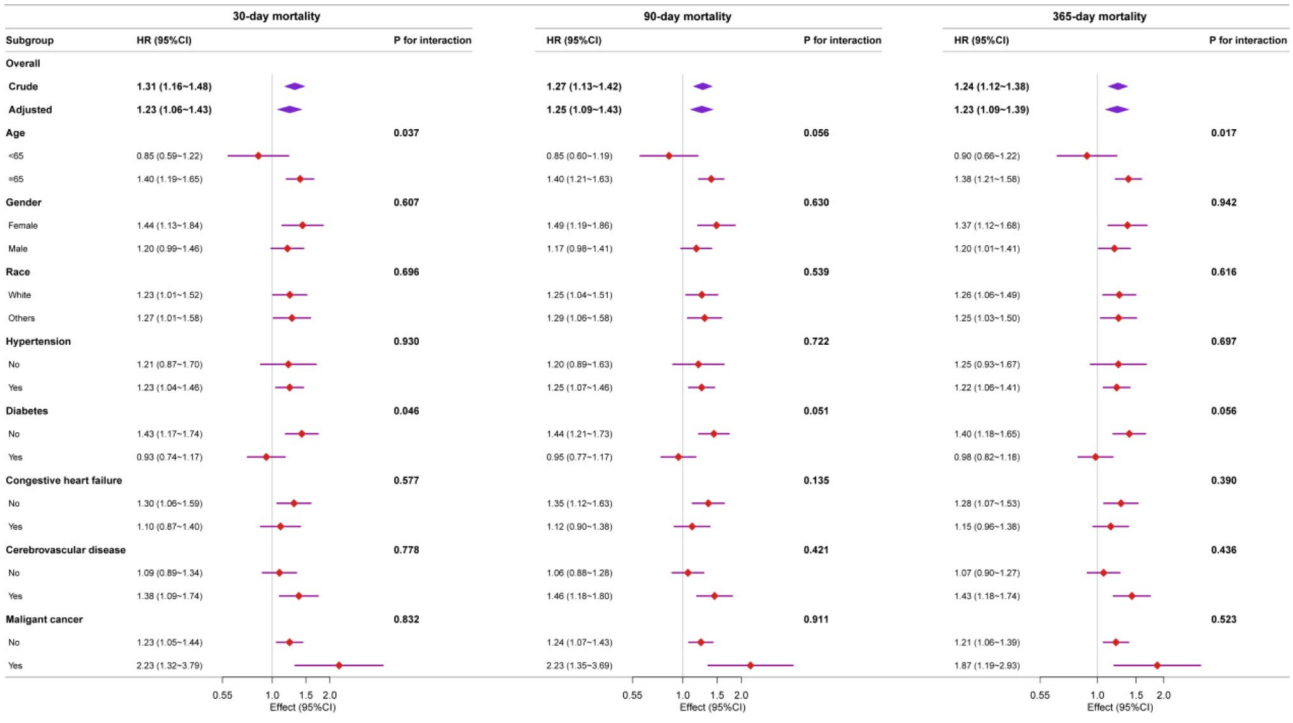

Fig. 4 Subgroup analyses of the association between TyG index and all-cause mortality in critically ill patients with atrial fibrillation. **A** 28-day mortality; **B** 90-day mortality; **C** 365-day mortality. Adjusted for age, sex, weight, race, hypertension, diabetes, myocardial infarction, congestive heart failure, cerebrovascular disease, malignant cancer, chronic pulmonary disease, renal disease, heart rate, mean arterial pressure, white blood cell count, hemoglobin, international normalized ratio, creatinine, potassium, sodium, insulin, beta-blockers, statins, amiodarone, and digitalis. TyG index, triglyceride-glucose index

mortality in patients with AF are multifaceted. IR-induced activation of the mitogen-activated protein kinase pathway and upregulation of transforming growth factor-beta 1 promote atrial fibrosis and electrical remodeling [35, 36]. Second, metabolic dysregulation associated with IR leads to chronic inflammation and oxidative stress, which exacerbate endothelial dysfunction [37–39]. Third, excessive fatty acid oxidation in cardiomyocytes exceeds their mitochondrial oxidative capacity, leading to mitochondrial overload and cardiomyocyte injury [40]. As a validated surrogate for IR [41–43], the TyG index effectively captures these pathological cascades and serves as a comprehensive marker of underlying metabolic and inflammatory disturbances in patients with AF.

Some studies have shown that it is superior to the traditional assessment method homeostatic model assessment of IR [44, 45]. In critically ill patients, an elevated TyG index reflects worsening metabolic disorders and IR, which further exacerbates systemic inflammation and organ dysfunction, significantly increasing the mortality risk in those with AF [46, 47].

Growing evidence supports TyG's prognostic value across cardiovascular domains [28, 48–50]. For instance, a high TyG index has been shown to be independently associated with poor outcomes in acute heart failure as well as with the risk of developing hypertension and myocardial infarction. Previous studies have primarily investigated the link between the TyG index and the incidence or recurrence of AF across different populations [14, 51, 52], as well as its connection to adverse complications in patients with AF [53]. A study on patients undergoing interventions for AF elimination found that the TyG index was an independent risk factor positively correlated with AF recurrence [13]. Surveys based on populations with AF have shown a significant correlation between the TyG index and major adverse cardiovascular and cerebrovascular events [53, 54]. Liu et al. observed a U-shaped relationship between the TyG index and the incidence rate of AF among participants in the Atherosclerosis Risk in Communities (ARIC) study who were free of known cardiovascular diseases at the outset [15].

In this study, we observed a significant positive correlation between the TyG index and all-cause mortality among non-diabetic individuals, which was not evident in patients with diabetes, a finding consistent with previous studies [41, 46, 55, 56]. This discrepancy can be attributed to several factors. First, IR and glucose metabolism inherent to diabetes could result in less marked TyG index changes in patients with diabetes [51]. Second, insulin and oral hypoglycemic medications commonly used by patients with diabetes may mask the impact of the TyG index on mortality risk [41, 56]. For example, sodium-glucose co-transporter 2 the cardioprotective effects in patients with AF, such as easing the cardiac load and curbing inflammation, along with Van den Berghe et al.'s report of intensive insulin therapy cutting ICU mortality rates by half, indicated that glycemic management could be a key factor [57, 58]. Furthermore, patients with diabetes often have more severe comorbidities, such as cardiovascular events and infections, which may have a more immediate and significant effect on mortality risk [55]. However, research into these mechanisms is limited, indicating the need for further studies to better understand these interactions.

Our study highlights the TyG index as an independent correlate of mortality and a pragmatic biomarker for risk stratification in critically ill patients with AF. As an easily calculable parameter derived from routine glucose and lipid measurements upon ICU admission, the TyG index provides immediate insights into metabolic dysregulation. Consistent with prior findings by Yang et al. [28], it may complement traditional severity scores (e.g., SOFA) that rely on complex dynamic parameters, thereby enhancing the early identification of high-risk individuals. Given the global burden of AF, integrating the TyG into clinical workflows could facilitate timely resource allocation, which is critical for mitigating adverse outcomes through prioritized management. Furthermore, since elevated TyG levels may partially stem from chronic metabolic abnormalities or lifestyle factors, we cautiously speculated that dietary and lifestyle modifications to lower TyG levels could attenuate the susceptibility to major adverse events during future episodes of critical illness. Such interventions may mitigate baseline metabolic dysregulation, thereby enhancing physiological resilience to acute stressors and improving clinical outcomes. However, the translational validity of these strategies for improving prognosis under acute critical conditions requires rigorous validation through prospective high-quality studies.

The advantage of our study is that it is the largest retrospective cohort study to investigate the association between the TyG index and all-cause mortality in patients with AF. However, this study has certain limitations. First, it focused on patients with AF in the ICUs, limiting its generalizability to other populations. Second, as a single-center retrospective cohort derived from the MIMIC-IV database, our study was inevitably subject to selection bias. Third, the analysis was limited to the baseline TyG index, which overlooked dynamic variations in the TyG index across different stages of the disease. Finally, we did not conduct a hyperinsulinemic-euglycemic clamp test, preventing us from assessing the correlation between the TyG index and the gold standard of IR.

Conclusions

Our study confirmed a significant linear association between a higher TyG index and elevated all-cause mortality rates at 30, 90, and 365 days in critically ill patients with AF. These findings suggest that the TyG index is a valuable prognostic indicator capable of enhancing risk stratification and clinical management in intensive care settings. Further research is needed to explore whether interventions targeting the TyG index can improve the clinical outcomes in this patient population.

Abbreviations

IR	Insulin resistance
TyG	Triglyceride-glucose
MIMIC-IV	Medical Information Mart for Intensive Care IV
ICU	Intensive care unit
STROBE	Strengthening the reporting of observational studies in epidemiology
SAPS II	Simplified Acute Physiology Score II

OASIS	Oxford acute severity of illness score
TG	Triglyceride
FBG	Fasting blood glucose
HR	Hazard ratio
CI	Confidence interval
SD	Standard deviation
IQR	Interquartile range
AKI	Acute kidney injury

Supplementary Information

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Supplementary Material 1.

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Data sharing statement
The corresponding author will provide the datasets used and analyzed during the current work upon reasonable request.

Author contributions
RD designed the study, conducted data collection and analysis, drafted the manuscript, and reviewed the manuscript. EC, MW, LP, LY, YH, XZ, CX, and JL performed data analysis and reviewed the manuscript. JG and HZ designed the study and reviewed the manuscript. All authors contributed to the article and approved the submitted version.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
This research was conducted in compliance with the Helsinki Declaration's guidelines. Approval for using the MIMIC-IV database was obtained from the IRBs of both MIT and BIDMC. The ethical approval previously granted for the MIMIC database covers the data used in this study, obviating the need for further ethical approval or informed consent.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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