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The association between triglyceride glucose-body mass index and mortality in critically ill patients with respiratory failure: insights from ICU data

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Respiratory failure (RF) lead to high mortality rates and extended hospital stays in intensive care unit (ICU). The Triglyceride-Glucose (TyG) index, a reliable surrogate marker for insulin resistance (IR), predicted adverse outcomes in various diseases. Combining weight-related indices like body mass index (BMI) with TyG to form the TyG-BMI enhanced the assessment of IR and its impact on patient outcomes. However, the association between TyG-BMI and outcomes in patients with RF remained underexplored. This study retrospectively analyzed data from the MIMIC-IV database, focusing on critically ill patients with RF. From an initial cohort of 19,429 patients, 2177 met the inclusion criteria and were divided into quartiles based on TyG-BMI values. Key clinical information was collected within the first 24 h of ICU admission, including demographics, lab results, vital signs, and scoring systems such as SAPS II and SOFA. Primary outcome was 28-day, secondary outcomes were 180-day and 1-year mortality. Data were analyzed using multivariable Cox regression models, Kaplan–Meier survival curves, and restricted cubic splines to assess the nonlinear relationship between TyG-BMI and mortality. The study found significant differences in baseline characteristics across TyG-BMI quartiles. Kaplan–Meier survival curves indicated a higher survival probability for patients in the lowest TyG-BMI quartile (Q1) compared to higher quartiles (Q2–Q4). Adjusted hazard ratios demonstrated a nonlinear association between higher TyG-BMI values and increased mortality risk at all three time points. The RCS-derived cut-off value of 269 for TyG-BMI was identified as a significant threshold, with higher TyG-BMI values correlating with lower mortality risks. Subgroup analyses reinforced these findings across different patient demographics and clinical profiles. Higher TyG-BMI was associated to lower short-term and long-term mortality, suggesting a potential protective effect. These findings highlighted the importance of the TyG-BMI as a robust prognostic marker, providing valuable insights for improving treatment strategies for patients with RF.

Keywords Triglyceride glucose-body mass index (TyG-BMI), Respiratory failure, Insulin resistance, Mortality

Abbreviations

RF	Respiratory failure
TyG	Triglyceride-Glucose
BMI	Body mass index
IR	Insulin resistance
ICU	Intensive care unit
COPD	Chronic obstructive pulmonary disease
MIMIC-IV	Medical Information Mart for Intensive Care IV
BIDMC	Beth Israel Deaconess Medical Center

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CITI	Collaborative Institutional Training Initiative
ICD	International Classification of Diseases
SAPS II	Simplified Acute Physiology Score II
SOFA	Sequential Organ Failure Assessment
SQL	Structured query language
ARDS	Acute respiratory distress syndrome
CAD	Coronary artery disease
HF	Heart failure
T2DM	Type 2 diabetes mellitus
MAP	Mean arterial pressure
WBC	White blood cell
PO2	Arterial oxygen pressures
PCO2	Arterial carbon dioxide pressures
RCS	Restricted cubic splines
SD	Standard deviation
HR	Hazard ratio
CI	Confidence interval

Background

Respiratory failure (RF) is a common organ failure in intensive care unit (ICU)[1,2], contributing to increased mortality rates and prolonged ICU stays[3]. This syndrome is characterized primarily by impairments in oxygenation or ventilation, stemming from both pulmonary and extrapulmonary diseases[4]. Critically ill patients, including those with RF, exhibit significant metabolic disturbances, with insulin resistance (IR) being a important factor[5,6].

IR, defined as a reduced biological response to insulin, is commonly observed among critically ill patients and is a key contributor to metabolic dysregulation in this population[7]. IR can precipitate hyperglycemia, which exacerbates systemic inflammation and oxidative stress, thereby worsening the prognosis of these patients[5,8]. Notably, IR frequently occurs in primary diseases causing RF, such as chronic obstructive pulmonary disease (COPD)[9], asthma[10], pulmonary infections[11], and extrapulmonary diseases[12,13], resulting in decreased pulmonary function and poorer outcomes.

The Triglyceride-Glucose (TyG) index, calculated from fasting triglyceride and glucose levels, has emerged as a reliable surrogate marker for insulin resistance[14]. It demonstrates predictive value for outcomes in cardiovascular diseases, including coronary artery disease[15], acute myocardial infarction[16], and heart failure[17], as well as in sepsis[18] and critically ill patients[19]. An elevated TyG index is strongly associated with adverse outcomes in these conditions, underscoring the harmful effects of insulin resistance. Similarly, the TyG index effectively predicts poor outcomes in patients with COPD[20] and asthma[21], proving particularly useful for assessing IR regardless of concurrent diabetes.

Recent studies suggested that combining weight-related indices, such as body mass index (BMI) and waist circumference, enhanced the assessment of insulin resistance[22]. The TyG-BMI, which integrates these parameters, has been shown to be effective in assessing IR and predicting outcomes[23–25]. The innovation of TyG-BMI in respiratory failure contexts lies in its synergistic capture of dual metabolic risks: lipid-glucose axis dysregulation (reflected by TyG) and chronic adipose tissue burden (quantified by BMI)[26]. This integration proves particularly relevant for RF populations where both components exhibit unique pathophysiological interactions. Adiposity-related cytokines (e.g., leptin, adiponectin) modulate pulmonary inflammation and ventilator weaning outcomes, while acute hypoxia in RF directly impairs insulin signaling through HIF-1α pathways[27]. Traditional single-dimension indices like TyG or BMI alone cannot address this multidimensional interplay. TyG-BMI's combined metric may therefore provide superior risk stratification by concurrently evaluating metabolic derangements and their adipose amplification effects. However, despite TyG-BMI's emerging utility in metabolic-cardiovascular contexts, its prognostic value remains unexplored in RF populations where hypoxia-induced insulin resistance and obesity-related inflammation create distinct pathophysiological dynamics.

Despite these advances, two critical knowledge gaps persist: (1) Existing mortality prediction models for respiratory failure predominantly rely on pulmonary function parameters (e.g., PaO_2/FiO_2) and generic severity scores (APACHE II), neglecting the prognostic weight of metabolic-adipose axis dysregulation; (2) No study has evaluated whether TyG-BMI's predictive power extends beyond cardiovascular outcomes to respiratory mortality contexts where hypoxia-hypercapnia may fundamentally alter insulin signaling pathways[28]. Therefore, this study aimed to elucidate the association of the TyG-BMI with mortality in patients with RF and investigate whether it could serve as a robust prognostic marker in this critically ill population.

Methods

Data source

The study was a retrospective analysis, utilizing data extracted from the Medical Information Mart for Intensive Care IV (MIMIC-IV) database, version 2.0[29,30]. The MIMIC-IV database comprised detailed demographics, laboratory test results, administration of medication, vital signs, complication, and both in-hospital and post-discharge survival status records from 2008 to 2019, which were collected with MetaVision system at the Beth Israel Deaconess Medical Center (BIDMC) in Boston, Massachusetts, United States. One of our team members has successfully completed the Data or Specimens Only Research course, which is organized by the Collaborative Institutional Training Initiative (CITI) Program. Consequently, our team has been officially granted access to

the MIMIC-IV database (Record ID 6775305). The Institutional Review Board (IRB #2001P001699) of the Beth Israel Deaconess Medical Center approved a waiver of informed consent, as all patient information within the database had been de-identified to protect patient privacy. All methods and procedures in this study were performed in accordance with the principles of the Declaration of Helsinki. Additionally, this study adheres to the guidelines outlined in the RECORD (Reporting of Studies Conducted using Observational Routinely-collected health Data) Statement for the reporting of observational studies.

Study population and data collection procedures

The current study focused on the association of the TyG-BMI and the prognosis of adult patients with RF. To identify eligible patients, we first extracted all ICU admissions with a primary or secondary diagnosis of RF using the codes of International Classification of Diseases, Ninth (ICD-9) and Tenth (ICD-10) Editions. Patient demographics, clinical measurements, and laboratory test results were retrieved from the electronic ICU database. Specifically, we collected information on blood glucose, triglycerides (TG), height, and weight recorded on the first day of ICU admission. These variables were necessary for calculating the TyG-BMI index. Data extraction was performed by trained researchers using a standardized protocol to ensure accuracy and consistency.

Exclusion criteria were established as follows: (1) patients under the age of 18, and (2) patients lacking data on fasting blood glucose, triglycerides (TG), height, or weight on the first day of ICU admission (necessary for BMI calculation). Based on these criteria, we selected 2177 patients and subsequently divided them into four groups according to the TyG-BMI quartiles (Q1, Q2, Q3 and Q4) for further analysis (Fig. 1).

Data extractioneading

We collected all relevant clinical information within the first 24 h of ICU admission, which included demographic details, study outcomes, laboratory results, vital signs, and widely recognized scoring systems such as the Simplified Acute Physiology Score II (SAPS II) and Sequential Organ Failure Assessment (SOFA) score. These data provide valuable insights into the severity of illness and organ dysfunction, allowing for a more comprehensive and reliable assessment of patient condition.

To efficiently extract the necessary data from the MIMIC-IV database, we developed and rigorously tested structured query language (SQL) codes using DBeaver Community version 23.0.0, a powerful database management software. The DBI package, a database interface for R, was then employed to execute these SQL codes seamlessly. This process facilitated the creation of relevant tables within the MIMIC-IV database and the generation of associated variables in the R global environment, streamlining the data collection process and ensuring data integrity.

The combination of DBeaver and the DBI package provided a robust and reliable workflow for data extraction, enabling us to efficiently handle the complex structure of the MIMIC-IV database and extract the specific patient information required for our study.

Outcomes

The primary outcome of our study was 28-day mortality. Secondary outcomes were 180-day and 1-year mortality.

Calculation of TyG-BMI

The TyG-BMI, a novel indicator combining the TyG index and BMI, was calculated using a multi-step process. First, the TyG index was determined using the formula: ln[fasting glucose (mg/dl) × fasting triglycerides (mg/dl)] / 2, as described by Simental-Mendía et al.[14]. This index provides an estimate of IR based on fasting glucose

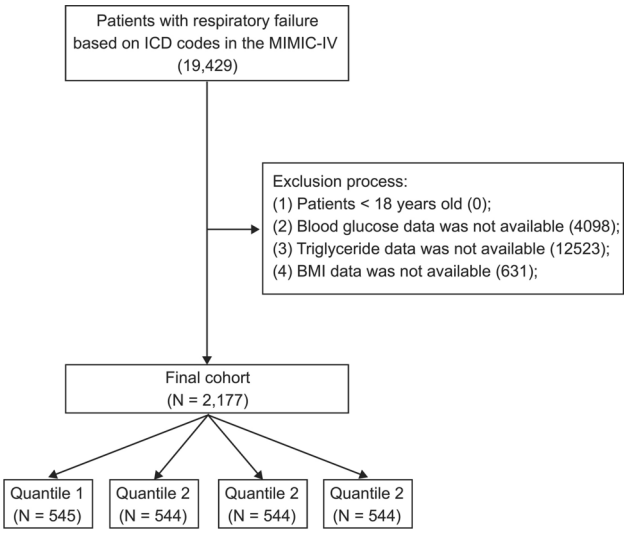

Fig. 1. Study flowchart.

and triglyceride levels. Next, BMI was calculated using the standard formula: body weight (kg)/height^2 (m). BMI is a widely used measure of body fat based on an individual's weight and height. Finally, the TyG-BMI was computed by multiplying the TyG index and BMI, as represented by the equation: TyG-BMI = TyG index × BMI.

Variables selection

In this retrospective study, we identified a comprehensive set of potential confounders and categorized them into five distinct clusters. The first cluster encompassed demographic and admission profiles, including age, gender, race, weight, SAPS II, SOFA score, and the Charlson comorbidity index. The second cluster consisted of various therapeutic interventions, such as mechanical ventilation, renal replacement therapy, sedative therapy, albumin infusion, and vasopressor therapy. The third cluster comprised a wide range of pre-existing comorbidities, including pneumonia, asthma, acute respiratory distress syndrome (ARDS), COPD, coronary artery disease (CAD), heart failure (HF), hypertension, atrial fibrillation (AFIB), type 2 diabetes mellitus (T2DM), chronic renal disease, liver disease, stroke, and malignancy. The fourth cluster included crucial physiological parameters, such as respiratory rate, heart rate, mean arterial pressure (MAP), and temperature. Finally, the fifth cluster encompassed a comprehensive array of hematological and biochemical assays, including white blood cell (WBC) count, hemoglobin, platelet count, potential of hydrogen (pH), arterial oxygen and carbon dioxide pressures (PO2 and PCO2), lactate levels, and creatinine.

To determine the importance of these variables, we employed two distinct approaches. First, we utilized the Boruta package, which implements a feature selection method based on the random forest algorithm. This technique assesses the significance of each variable by comparing its relevance to randomly generated shadow features using the Z-score as a criterion. Variables that consistently demonstrate higher Z-scores than their shadow counterparts are considered essential and retained, while those with lower scores are deemed redundant and removed from the model. This statistical process ensures that only the most influential variables are included, resulting in a more robust and predictive model.

In addition to the Boruta package, we also applied univariate Cox regression to select variables. Variables that achieved $P < 0.1$ in the univariable analysis were subsequently incorporated into multivariable models. This approach complements the feature selection performed by the Boruta package, providing a more comprehensive assessment of variable importance[31].

Sensitivity and subgroup analyses

By employing these two complementary methods for variables selection, we aimed to identify the most significant confounders and risk factors associated with the outcomes of interest in our study. The sensitivity analyses were performed with the random forest-based and univariate Cox regression for variables selection, allows for a thorough evaluation of the complex relationships between the variables and the studied outcomes, ultimately enhancing the validity and reliability of our findings. In addition, we also used restricted cubic splines (RCS) analyses based on Cox regression model to explore the nonlinear relationship between TyG-BMI and mortality, and then set the corresponding effect threshold, and generated a new cohort divided by this threshold as an effective measure of sensitivity analysis, in order to prove the robustness of our study and confirm the threshold effect. Meanwhile, the Cox regression was also applied to subgroup analyses according to different stratified factors to explore the influence of TyG-BMI on the prognosis of patients with RF in different subgroups.

Statistical analysis

We assessed the data normal distribution with the Shapiro–Wilk normality test and evaluated the homogeneity of variances with the Levene test. For continuous covariates, we applied the one-way ANOVA when the data followed a normal distribution and exhibited variance homogeneity. In cases where these conditions were not met, we employed the Wilcoxon rank-sum test as a non-parametric alternative. Categorical covariates were analyzed using the Chi-square test. Continuous variables were presented as mean with standard deviation (SD), while categorical variables were expressed as count and percentage.

To handle missing data in the original cohort, we performed multiple imputations using the mice package. Variables with more than 40 percent missing values were excluded from the analysis[32]. Survival estimates for the original cohort were obtained using the unadjusted log-rank test within the survival package[33].

To ensure the robustness of our findings, we conducted sensitivity analyses using three different models for 28-day, 180-day, and 1-year mortality. The first model employed multivariable Cox regression, adjusting for all covariates. The second model included covariates identified through univariable analyses, while the third model incorporated covariates selected by the random forest algorithm. We assessed the proportional hazards assumption by examining Schoenfeld residuals. In cases of statistical significance, we integrated time-varying covariates into the Cox model using the "tt" function to account for time-dependent effects. Subgroup analysis was performed using the Cox regression model.

All statistical analyses were conducted using R version 4.3.1, with two-sided $P < 0.05$ was considered statistically significant. By employing a combination of parametric and non-parametric tests, handling missing data through multiple imputations, and validating our findings through sensitivity analyses and subgroup analysis, we aimed to provide a comprehensive and reliable assessment of the associations between the variables of interest and the studied outcomes.

Results

Baseline characteristics of included patients

Figure 1 illustrated the process of patient inclusion and exclusion for the study. Initially, 19,429 patients with RF were identified based on ICD codes in the MIMIC-IV database. The exclusion criteria were then applied to this cohort. First, patients under 18 years old were excluded, but none met this criterion. Next, 4098 patients were

excluded due to the unavailability of blood glucose data. Subsequently, 12,523 patients were excluded because triglyceride data was not available. Finally, 631 patients were excluded due to the absence of BMI data. After applying the exclusion criteria, the final cohort consisted of 2177 patients. The final cohort of 2177 patients was divided into four quantiles based on the values of the TyG-BMI. The cutoff points for these quantiles were 221.90, 269.42, and 331.56. Quantile 1 (Q1) included patients with TyG-BMI values less than or equal to 221.90, Quantile 2 (Q2) consisted of patients with TyG-BMI values between 221.90 and 269.42, Quantile 3 (Q3) comprised patients with TyG-BMI values between 269.42 and 331.56, and Quantile 4 (Q4) included patients with TyG-BMI values greater than 331.56. Each quantile contained either 544 or 545 patients.

Table 1 presented the baseline characteristics of the study cohort (N = 2177), stratified by quartiles, which was divided into 4 quartile groups (Q1–Q4) based on the TyG-BMI. Comparative analysis revealed significant differences ($P < 0.05$) in several variables across these groups. The mean age of the overall cohort was 61.41 (SD 15.96) years, and 38.22% were female. The majority of patients were White (59.49%), followed by Other (28.43%), Black (9.60%), and Asian (2.48%). The mean SAPS II score was 44.23 (SD 15.59), SOFA score was 7.81 (SD 4.25). Demographic characteristics exhibited variations, with age and race distribution differing significantly among the quartile groups. Notably, the Q4 group had the lowest mean age (58.87 years) compared to the other groups, suggesting a potential age-related effect on the exposure variable or outcomes. Clinical parameters, including disease severity scores (SAPS II and SOFA), and requirements for critical care interventions like mechanical ventilation, sedation, and vasopressors within the first 24 h, also varied significantly across the quartile groups. Comorbidity profiles differed among the groups, with varying prevalence rates of conditions such as ARDS, COPD, CAD, hypertension, T2DM, chronic renal disease, liver disease, and malignancy. Vital signs and laboratory parameters measured within the first 24 h, including mean arterial pressure, temperature, white blood cell count, hemoglobin, platelet count, pH, partial pressures of oxygen and carbon dioxide, lactate levels, and creatinine levels, also exhibited significant differences across the quartile groups. These observed differences across the quartile groups highlight the importance of accounting for potential confounders in the subsequent analyses to accurately evaluate the association between the exposure variable and outcomes of interest. We employed multivariable regression models or sensitivity analyses to adjust for these confounding factors and obtain unbiased effect estimates in the further data analysis. The percentage of missing data was generally low, with the highest being 18.19% for PCO2.

Survival analyses

Figure 2 presented the Kaplan–Meier survival curves for patients stratified by quartiles over 28 days (A), 180 days (B), and 1 year (C). Panel A shows the 28-day survival probability. The survival probability was highest in the Q1 group, followed by Q2, Q3, and Q4 groups. The difference in survival probability among the four groups was statistically significant ($P = 0.007$). Panel B illustrated the 180-day survival probability. The survival probability remained highest in the Q1 group, followed by Q2, Q3, and Q4 groups. The difference in survival probability among the four groups was statistically significant ($P < 0.001$). Panel C depicted the 1-year survival probability. Similar to the 28-day and 180-day results, the survival probability was highest in the Q1 group, followed by Q2, Q3, and Q4 groups. The difference in survival probability among the four groups was statistically significant ($P < 0.001$).

As the follow-up time increased, the difference in survival probability among the four groups gradually widened, suggesting that the impact of grouping on prognosis may be time-dependent. Overall, the Q1 group had the best long-term survival, while the Q4 group had the worst survival outcome. The results indicated that the variable used for stratification was a significant associated with patient survival over time.

Nonlinear relationship between TyG-BMI and mortality

Figure 3 presented the adjusted hazard ratios for mortality at 28-day (A), 180-day (B), and 1-year (C) across the range of TyG-BMI values using RCS with the Cox regression model. The results demonstrated a significant nonlinear association between higher TyG-BMI values and increased mortality risk at all three time points (overall $P < 0.01$ and nonlinear $P < 0.05$ for 28-day mortality; overall and nonlinear $P < 0.001$ for both 180-day and 1-year mortality). The cut-off value for the TyG-BMI is set at 269 for all three time points. The adjusted hazard ratio increased more rapidly when the TyG-BMI exceeds approximately 300, suggesting a potential threshold effect.

Primary and secondary outcomes for the cohort

The Boruta random forest algorithm was employed to identify the most relevant variables associated with the outcome of interest. The algorithm created shadow features, which were shuffled copies of the actual features, to provide a benchmark for feature importance. Figure S1 were presented in the feature importance plot, where features are ranked based on their relative importance scores. The plot categorizes the features into four groups: Confirmed, Tentative, Rejected, and Shadow. The Confirmed features, shown in green, were the most important variables that have been conclusively deemed relevant by the algorithm. These include Charlson comorbidity index, SAPS II score, age, SOFA score, lactate levels, presence of liver disease, platelet count, temperature, hemoglobin levels, and creatinine levels. This feature selection was processed as well as univariate Cox regression model highlighted the most influential variables that should be considered in subsequent analyses, such as multivariable regression models as sensitivity analyses, to accurately assess the association between the exposure variable and the outcome while adjusting for relevant confounders.

The study analyzed the association between different quartile groups (Q1–Q4) and mortality outcomes (28-day, 180-day, and 1-year mortality) using three Cox proportional hazards models with different covariate adjustment approaches (Table 2). For 28-day mortality, all three models consistently showed a significant reduction in mortality risk for quartile groups Q2, Q3, and Q4 compared to the reference group Q1. The hazard

	Overall (N = 2177)	Q1 (N = 545)	Q2 (N = 544)	Q3 (N = 544)	Q4 (N = 544)	*P*-value	Missing data (%)
Age	**61.41 (15.96)**	**62.79 (17.66)**	**63.08 (16.48)**	**60.92 (14.99)**	**58.87 (14.15)**	**< 0.001**	**0.00**
Gender (Female)	832 (38.22%)	216 (39.63%)	206 (37.87%)	190 (34.93%)	220 (40.44%)	0.248	0.00
Race							
Asian	**54 (2.48%)**	**28 (5.14%)**	**15 (2.76%)**	**10 (1.84%)**	**1 (0.18%)**	**< 0.001**	**0.00**
Black	**209 (9.60%)**	**53 (9.72%)**	**49 (9.01%)**	**48 (8.82%)**	**59 (10.85%)**		
White	**1295 (59.49%)**	**312 (57.25%)**	**345 (63.42%)**	**325 (59.74%)**	**313 (57.54%)**		
Other	**619 (28.43%)**	**152 (27.89%)**	**135 (24.82%)**	**161 (29.60%)**	**171 (31.43%)**		
Weight	**88.54 (28.69)**	**62.91 (11.31)**	**78.06 (11.45)**	**91.61 (13.82)**	**121.61 (31.20)**	**< 0.001**	**0.00**
SAPS II	**44.23 (15.59)**	**42.79 (14.66)**	**44.01 (16.36)**	**45.50 (15.94)**	**44.61 (15.27)**	**< 0.05**	**0.00**
SOFA score	**7.81 (4.25)**	**7.02 (4.06)**	**7.67 (4.32)**	**8.06 (4.29)**	**8.48 (4.21)**	**< 0.001**	**0.00**
Charlson comorbidity index	5.17 (2.98)	5.40 (3.05)	5.24 (3.05)	5.09 (2.98)	4.96 (2.81)	0.079	0.00
Interventions (boolean for 1st 24 h)							
Mechanical ventilation (Yes)	**1775 (81.53%)**	**431 (79.08%)**	**436 (80.15%)**	**444 (81.62%)**	**464 (85.29%)**	**< 0.05**	**0.00**
RRT (Yes)	165 (7.58%)	33 (6.06%)	37 (6.80%)	42 (7.72%)	53 (9.74%)	0.115	0.00
Sedative therapy (Yes)	**1802 (82.77%)**	**434 (79.63%)**	**449 (82.54%)**	**451 (82.90%)**	**468 (86.03%)**	**< 0.05**	**0.00**
Albumin therapy (Yes)	350 (16.08%)	72 (13.21%)	94 (17.28%)	93 (17.10%)	91 (16.73%)	0.213	0.00
Vasopressor therapy (Yes)	1215 (55.81%)	289 (53.03%)	293 (53.86%)	310 (56.99%)	323 (59.38%)	0.13	0.00
Comorbidities (Boolean)							
Pneumonia (Yes)	1177 (54.07%)	296 (54.31%)	288 (52.94%)	287 (52.76%)	306 (56.25%)	0.635	0.00
Asthma (Yes)	**187 (8.59%)**	**44 (8.07%)**	**26 (4.78%)**	**37 (6.80%)**	**80 (14.71%)**	**< 0.001**	**0.00**
ARDS (Yes)	70 (3.22%)	14 (2.57%)	16 (2.94%)	20 (3.68%)	20 (3.68%)	0.658	0.00
COPD (Yes)	383 (17.59%)	100 (18.35%)	91 (16.73%)	93 (17.10%)	99 (18.20%)	0.867	0.00
CAD (Yes)	**515 (23.66%)**	**116 (21.28%)**	**128 (23.53%)**	**162 (29.78%)**	**109 (20.04%)**	**< 0.001**	**0.00**
HF (Yes)	739 (33.95%)	173 (31.74%)	168 (30.88%)	194 (35.66%)	204 (37.50%)	0.065	0.00
Hypertension (Yes)	**1362 (62.56%)**	**303 (55.60%)**	**324 (59.56%)**	**367 (67.46%)**	**368 (67.65%)**	**< 0.001**	**0.00**
AFIB (Yes)	270 (12.40%)	67 (12.29%)	68 (12.50%)	71 (13.05%)	64 (11.76%)	0.935	0.00
T2DM (Yes)	**663 (30.45%)**	**108 (19.82%)**	**110 (20.22%)**	**191 (35.11%)**	**254 (46.69%)**	**< 0.001**	**0.00**
Renal (Yes)	491 (22.55%)	114 (20.92%)	118 (21.69%)	119 (21.88%)	140 (25.74%)	0.225	0.00
Liver (Yes)	250 (11.48%)	67 (12.29%)	64 (11.76%)	54 (9.93%)	65 (11.95%)	0.613	0.00
Stroke (Yes)	**420 (19.29%)**	**115 (21.10%)**	**120 (22.06%)**	**99 (18.20%)**	**86 (15.81%)**	**< 0.05**	**0.00**
Malignancy (yes)	**394 (18.10%)**	**114 (20.92%)**	**108 (19.85%)**	**83 (15.26%)**	**89 (16.36%)**	**< 0.05**	**0.00**
Vital signs (1st 24 h)							
Respiratory rate	21.51 (6.61)	21.18 (6.59)	21.54 (6.35)	21.58 (6.60)	21.74 (6.91)	0.378	0.23
Heart rate	94.88 (22.16)	93.87 (22.19)	94.19 (21.97)	95.01 (22.37)	96.47 (22.06)	0.207	0.23
MAP	**84.01 (19.73)**	**84.40 (19.19)**	**83.72 (18.44)**	**85.57 (21.16)**	**82.34 (19.94)**	**< 0.05**	**0.23**
Temperature	**36.84 (1.01)**	**36.74 (0.99)**	**36.86 (1.02)**	**36.81 (0.93)**	**36.94 (1.07)**	**< 0.001**	**3.81**
Laboratory tests (1st 24 h)							
WBC count	**14.30 (11.42)**	**13.37 (10.68)**	**14.21 (9.47)**	**14.14 (7.71)**	**15.47 (16.03)**	**< 0.01**	**0.05**
Hemoglobin	**10.79 (2.49)**	**10.56 (2.45)**	**10.62 (2.41)**	**10.96 (2.59)**	**11.03 (2.47)**	**< 0.01**	**0.05**
Platelet	**204.47 (116.88)**	**212.76 (129.91)**	**193.83 (117.39)**	**203.43 (106.22)**	**207.84 (112.16)**	**< 0.05**	**0.05**
pH	**7.33 (0.12)**	**7.35 (0.11)**	**7.34 (0.12)**	**7.32 (0.11)**	**7.31 (0.11)**	**< 0.001**	**5.37**
PO2	**137.29 (97.25)**	**148.25 (105.19)**	**142.44 (103.17)**	**139.80 (96.17)**	**120.17 (81.98)**	**< 0.01**	**17.13**
PCO2	**44.67 (15.81)**	**42.54 (14.30)**	**42.88 (14.95)**	**43.89 (15.17)**	**48.95 (17.57)**	**< 0.001**	**18.19**
Lactate	**2.74 (2.59)**	**2.43 (2.29)**	**2.82 (2.77)**	**2.95 (2.85)**	**2.74 (2.39)**	**< 0.05**	**6.71**
Creatinine	**1.75 (1.70)**	**1.54 (1.63)**	**1.59 (1.51)**	**1.89 (1.81)**	**1.98 (1.80)**	**< 0.001**	**0.00**
Outcomes (Boolean)							
28-day mortality (Death)	**660 (30.32%)**	**195 (35.78%)**	**164 (30.15%)**	**160 (29.41%)**	**141 (25.92%)**	**< 0.01**	**0.00**
180-day mortality (Death)	**935 (42.95%)**	**281 (51.56%)**	**232 (42.65%)**	**221 (40.62%)**	**201 (36.95%)**	**< 0.001**	**0.00**
1-year mortality (Death)	**1018 (46.76%)**	**304 (55.78%)**	**252 (46.32%)**	**243 (44.67%)**	**219 (40.26%)**	**< 0.001**	**0.00**

Table 1. Basic demographic characteristics of the original cohort. Values are presented as mean (standard deviation) for continuous variables and number (percentage) for categorical variables. Variables in bold have p-value < 0.05

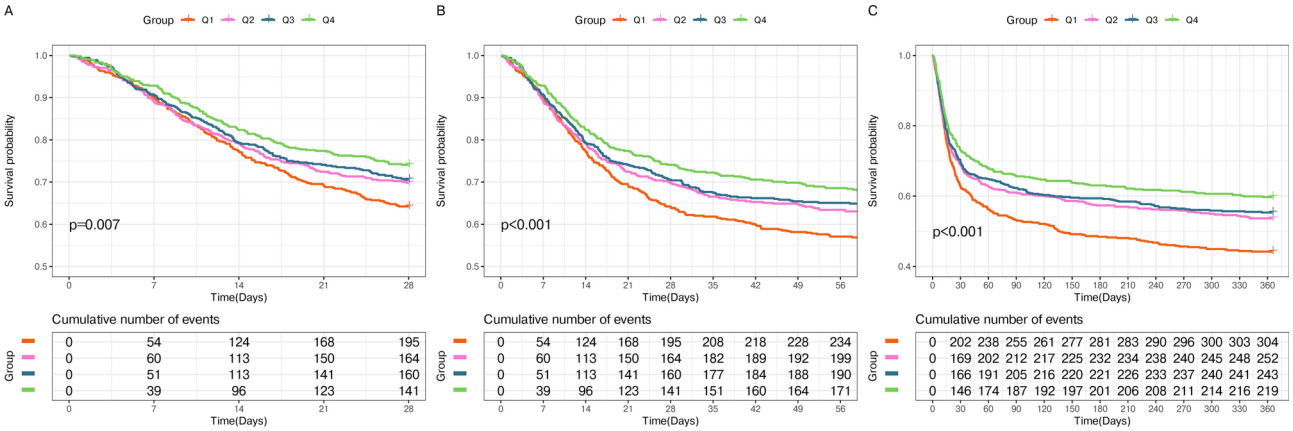

Fig. 2. Unadjusted Kaplan–Meier survival curve for 28-day mortality (**A**), 180-day mortality (**B**) and 1-year mortality (**C**) of original cohort. The y-axis represents survival probability, and the x-axis represents time (days). The *P*-values ($P = 0.007$ for 28-day, $P < 0.001$ for 180-day and 1-year mortality) were calculated using the log-rank test, indicating significant differences between groups. The numbers below each panel indicate the cumulative number of patients at risk at different time points.

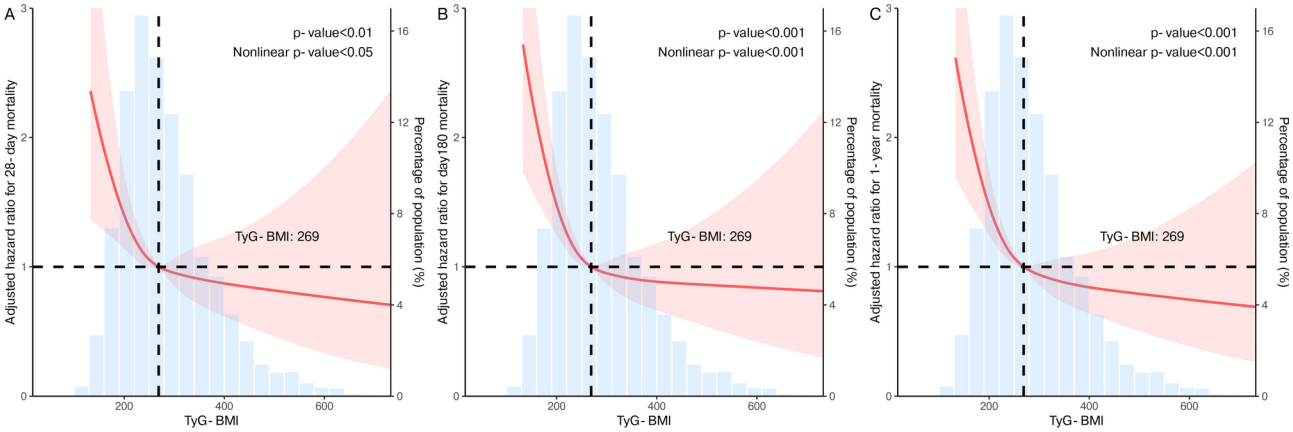

Fig. 3. The nonlinear relationship of TyG-BMI and the risk of mortality fit by multivariable Cox regression with RCS analyses. (**A**) the nonlinear relationship of TyG-BMI and the risk of 28-day mortality. (**B**) the nonlinear relationship of TyG-BMI and the risk of 180-day mortality. (**C**) the nonlinear relationship of TyG-BMI and the risk of 1-year mortality. The cut-off value for the TyG-BMI is set at 269 for all three time points.

ratios (HRs) ranged from 0.54 to 0.72, with $P < 0.01$ across all models and quartile groups. Similarly, for 180-day mortality, the quartile groups Q2, Q3, and Q4 had significantly lower mortality risk compared to Q1, with HRs ranging from 0.53 to 0.70 ($P < 0.01$) across all models. The results for 1-year mortality followed a similar pattern, with quartile groups Q2, Q3, and Q4 showing significantly reduced mortality risk compared to the reference group Q1. The HRs ranged from 0.58 to 0.72, with $P < 0.01$ for all models and quartile groups. These findings consistently demonstrate a significant inverse association between the quartile groups and mortality outcomes at different time points (28-day, 180-day, and 1-year), suggesting a potential protective effect of higher quartile levels on mortality risk in the studied cohort. The results were robust across different covariate adjustment approaches used in the different models (Table S1–S9).

Primary and secondary outcomes for the cut-off cohort

The cohort was stratified into two groups based on the RCS-derived cut-off value of 269 for the TyG-BMI (Table S10). As shown in Table 3, in terms of 28-day mortality, the HRs for patients with TyG-BMI ≥ 269 ranged from 0.76 (95% CI 0.62–0.94, $P < 0.05$) to 0.81 (95% CI 0.67–0.99, $P < 0.05$), indicating a 19–24% lower risk of 28-day mortality compared to the reference group (TyG-BMI < 269). For 180-day mortality, the HRs for the TyG-BMI ≥ 269 group ranged from 0.78 (95% CI 0.65–0.92, $P < 0.01$) to 0.80 (95% CI 0.67–0.94, $P < 0.01$), suggesting a 20–22% lower risk of 180-day mortality compared to the reference group. Similarly, for 1-year mortality, patients with TyG-BMI ≥ 269 had HRs ranging from 0.80 (95% CI 0.67–0.94, $P < 0.01$) to 0.82 (95% CI 0.70–0.97, $P < 0.05$), indicating an 18–20% lower risk of 1-year mortality compared to the TyG-BMI < 269 group (Table S1–S19). These consistent findings across different mortality outcomes and covariate adjustment approaches suggest

Model	Group	28-day mortality		180-day mortality		1-year mortality	
		p-Value	Result	*P*-value	Result	*P*-value	Result
Model 1[a]	Q1		1 (Reference)		1 (Reference)		1 (Reference)
	Q2	**< 0.01**	**0.72 (0.58, 0.90)**	**< 0.001**	**0.68 (0.57, 0.82)**	**< 0.001**	**0.69 (0.57, 0.82)**
	Q3	**< 0.01**	**0.67 (0.52, 0.86)**	**< 0.001**	**0.65 (0.52, 0.80)**	**< 0.001**	**0.66 (0.54, 0.81)**
	Q4	**< 0.01**	**0.56 (0.40, 0.80)**	**< 0.001**	**0.54 (0.40, 0.73)**	**< 0.001**	**0.55 (0.41, 0.73)**
Model 2[a]	Q1		1 (Reference)		1 (Reference)		1 (Reference)
	Q2	**< 0.01**	**0.70 (0.56, 0.87)**	**< 0.001**	**0.68 (0.57, 0.82)**	**< 0.001**	**0.68 (0.57, 0.82)**
	Q3	**< 0.001**	**0.63 (0.49, 0.81)**	**< 0.001**	**0.63 (0.51, 0.78)**	**< 0.001**	**0.64 (0.53, 0.79)**
	Q4	**< 0.001**	**0.53 (0.38, 0.75)**	**< 0.001**	**0.54 (0.40, 0.72)**	**< 0.001**	**0.54 (0.41, 0.72)**
Model 3[a]	Q1		1 (Reference)		1 (Reference)		1 (Reference)
	Q2	**< 0.01**	**0.72 (0.58, 0.90)**	**< 0.001**	**0.70 (0.59, 0.85)**	**< 0.001**	**0.71 (0.59, 0.85)**
	Q3	**< 0.01**	**0.69 (0.54, 0.88)**	**< 0.001**	**0.66 (0.54, 0.82)**	**< 0.001**	**0.68 (0.56, 0.83)**
	Q4	**< 0.01**	**0.59 (0.42, 0.83)**	**< 0.001**	**0.58 (0.44, 0.77)**	**< 0.001**	**0.60 (0.46, 0.78)**

Table 2. Primary and secondary outcome analyses with different models for cohort. Statistical analyses of different models with *p*-value < 0.05 were displayed in bold. [a]*HR* Hazard ratio, *CI* Confidence interval. [a]Model 1: Cox model adjusted with all covariates [HR (95% CI)] Model 2: Cox model adjusted with covariates selected by uni-variable analyses [HR (95% CI)] Model 3: Cox model adjusted with covariates selected by selected by random forest algorithm [HR (95% CI)].

Model	Group	28-day mortality		180-day mortality		1-year mortality	
		P-value	Result	*P*-value	Result	*P*-value	Result
Model 1[a]	TyG-BMI < 269		1 (Reference)		1 (Reference)		1 (Reference)
	TyG-BMI > = 269	**< 0.05**	**0.79 (0.65, 0.98)**	**< 0.05**	**0.79 (0.66, 0.94)**	**< 0.05**	**0.81 (0.69, 0.96)**
Model 2[a]	TyG-BMI < 269		1 (Reference)		1 (Reference)		1 (Reference)
	TyG-BMI > = 269	**< 0.05**	**0.76 (0.62, 0.94)**	**< 0.01**	**0.78 (0.65, 0.92)**	**< 0.01**	**0.8 (0.67, 0.94)**
Model 3[a]	TyG-BMI < 269		1 (Reference)		1 (Reference)		1 (Reference)
	TyG-BMI > = 269	**< 0.05**	**0.81 (0.67, 0.99)**	**< 0.01**	**0.8 (0.67, 0.94)**	**< 0.05**	**0.82 (0.70, 0.97)**

Table 3. Primary and secondary outcome analyses with different models for cut-off cohort. Statistical analyses of different models with *p*-value < 0.05 were displayed in bold. [a]*HR* Hazard ratio, *CI* Confidence interval. [a]Model 1: Cox model adjusted with all covariates [HR (95% CI)] Model 2: Cox model adjusted with covariates selected by uni-variable analyses [HR (95% CI)] Model 3: Cox model adjusted with covariates selected by selected by random forest algorithm [HR (95% CI)].

that a higher TyG-BMI was associated with a lower risk of mortality in this cohort. The RCS-derived cut-off value of 269 for TyG-BMI appeared to be a clinically threshold for stratifying patients into distinct risk groups.

Subgroup analyses

As shown in Fig. 4, the subgroup analysis revealed a consistent pattern of lower risk associated with TyG-BMI ≥ 269 compared to TyG-BMI < 269 for 28-day mortality, although the associations were not statistically significant in all subgroups. The significant associations were observed in subgroups defined by age ≥ 65 years (HR 0.74, 95% CI 0.60–0.91, $p = 0.004$), SOFA score < 5 (HR 0.54, 95% CI 0.36–0.79, $p = 0.002$), non-HF (HR 0.81, 95% CI 0.67–0.99, $p = 0.035$), non-CAD (HR 0.81, 95% CI 0.67–0.97, $p = 0.02$), and non-T2DM (HR 0.67, 95% CI 0.50–0.90, $p = 0.007$).

For 180-day mortality (Fig. S2A), patients with TyG-BMI ≥ 269 exhibited a significantly lower risk compared to those with TyG-BMI < 269 in several subgroups, including age (≥ 65 years: HR 0.77, 95% CI 0.65–0.92, $P = 0.002$), SOFA score (< 5: HR 0.57, 95% CI 0.42–0.78, $P < 0.001$; ≥ 5: HR 0.80, 95% CI 0.69–0.93, $P = 0.003$), HF (HR 0.76, 95% CI 0.62–0.94, $P = 0.01$), non-HF (HR 0.77, 95% CI 0.66–0.91, $P = 0.02$), non-CAD (HR 0.92, 95% CI 0.88–0.95, $P < 0.001$), T2DM (HR 0.69, 95% CI 0.55–0.88, $P = 0.002$), and non-T2DM (HR 0.80, 95% CI 0.69–0.94, $P = 0.007$).

Similarly, for 1-year mortality (Fig. S2B), patients with TyG-BMI ≥ 269 consistently exhibited a significantly lower risk compared to those with TyG-BMI < 269 across most subgroups, including age (≥ 65 years: HR 0.77, 95% CI 0.66–0.91, $P = 0.002$), SOFA score (< 5: HR 0.59, 95% CI 0.44–0.79, $P < 0.001$; ≥ 5: HR 0.81, 95% CI 0.70–0.92, $P = 0.002$), HF (HR 0.78, 95% CI 0.64–0.95, $P = 0.012$), non-HF (HR 0.77, 95% CI 0.66–0.90, $P = 0.001$), and non-CAD (HR 0.73, 95% CI 0.63–0.84, $P < 0.001$), T2DM (HR 0.67, 95% CI 0.54–0.84, $P < 0.001$), and non-T2DM (HR 0.81, 95% CI 0.70–0.95, $P = 0.007$).

In summary, the subgroup analyses consistently demonstrated a lower risk of mortality associated with TyG-BMI ≥ 269 compared to TyG-BMI < 269 across various subgroups and mortality outcomes, although the

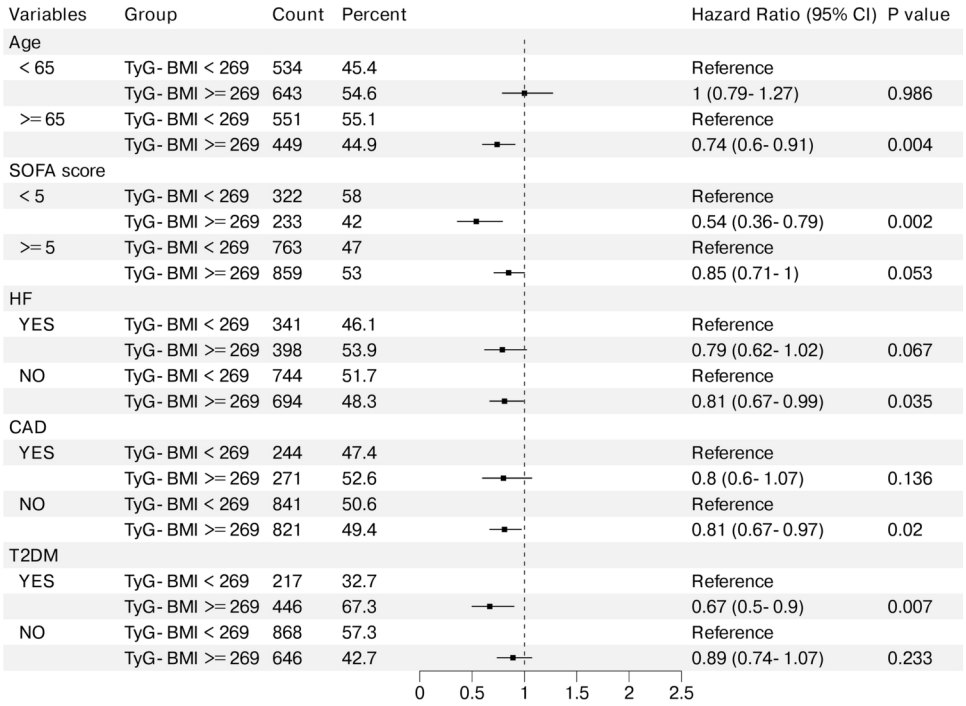

Fig. 4. Forest plot of subgroup analysis for 28-day mortality. *P*-values are reported for each subgroup, with significant results highlighted. The vertical dashed line at HR = 1 indicates the reference point (no effect).

strength of the association varied across different subgroups. These findings suggested that the protective effect of higher TyG-BMI was robust and consistent across different patient populations, reinforcing the potential clinical relevance of this risk stratification approach.

Discussion

To our knowledge, this study was the first to investigate the relationship between the TyG-BMI and all-cause mortality in critically ill patients with RF. We discovered that the TyG-BMI is significantly associated with mortality at 28 days, 180 days, and 1 year. A lower TyG-BMI correlates with a higher risk of mortality in these patients. These findings may contribute to enhancing treatment protocols for patients suffering from RF.

IR describes a condition where the body's response to insulin is impaired, commonly seen as a metabolic disorder among critically ill and obese populations[34,35]. The pathophysiological mechanisms linking IR and RF may vary based on different primary diseases. Generally, there is a bidirectional influence between IR and RF. Primary diseases of RF often exhibit an overactive inflammatory response, such as in asthma[21,36], infections[37], heart failure[38], or chronic inflammatory conditions like COPD[39]. These heightened inflammatory responses can lead to abnormal inflammatory factor expression and mitochondrial dysfunction, precipitating a state of IR[40–42]. Conversely, the presence of IR might promote the onset of RF. The mechanisms are multifaceted; for example, IR can reduce skeletal muscle glucose utilization, leading to respiratory muscle dysfunction and exacerbating RF[43,44]. Additionally, IR contributes to stress-induced hyperglycemia, weakening host immunity and enhancing microbial virulence, thereby increasing the risk of pulmonary infections and worsening RF[45,46]. Moreover, IR can induce systemic inflammation and oxidative stress, leading to lung and bronchial damage from inflammatory infiltration, thus promoting RF[47,48].

Several clinical studies have investigated these phenomena. For instance, a prospective cohort study in Korea involving 4827 patients found that for every unit increase in log-transformed HOMA-IR, there was a 0.23% decrease in FEV1 and a 0.20% decrease in FVC, highlighting the detrimental effects of IR on lung function[49]. Another study indicated that in patients with COPD, HOMA-IR significantly increased with higher GOLD stages and was inversely related to patients whose FEV1 was below 60% prediction, underscoring that IR is a risk factor for worsening lung function and RF[50]. Another cross-sectional study showed that the proportion of abnormal lung function was significantly higher in patients with comorbid IR than in those without IR (30.2% vs. 16.6%, $p = 0.039$), suggesting that lower lung function is associated with IR status[51].

The TyG index, an effective alternative marker for assessing IR, has been reported to be closely associated with various respiratory diseases. For example, research by Tianshi David Wu and others found that a higher TyG index correlates with a higher likelihood of respiratory symptoms (such as cough, phlegm production, wheeze, exertional dyspnea) and lower lung function (such as FEV1, FVC), even after adjusting for HOMA-IR[52]. Zhou and colleagues, through a retrospective cohort study involving 684 patients, discovered that a high TyG index correlates with higher 90-day and 180-day mortality rates among COPD and asthma patients in critical condition[20]. During the COVID-19 pandemic, several studies also indicated that an elevated TyG index

significantly correlates with increased mortality risk among COVID-19 and ARDS patients[53,54]. These findings underscore the prognostic importance of the TyG index in respiratory-related diseases.

However, there is currently a lack of research on the correlation between TyG-BMI and RF, particularly in critically ill patients with RF. Our research demonstrates that the TyG-BMI can predict both short-term and long-term all-cause mortality in patients with severe RF. Specifically, the relationship between the TyG-BMI and mortality in patients with severe RF is L-shaped. A higher TyG-BMI correlates with lower 28-day, 180-day, and one-year mortality rates, especially in patients over 60 years old. This finding can help identify patients at higher risk of mortality from RF. Additionally, the protective effect of a higher TyG-BMI is independent of the SOFA score and diabetes status. This discovery might be linked to the widely discussed "obesity paradox" observed among critically ill and respiratory disease patients in clinical settings[55,56].

Previous research has revealed that among critically ill patients, a higher BMI correlates with a lower mortality[57,58]. However, the relationship between obesity and the incidence and prognosis of respiratory diseases remains controversial. Many studies have identified obesity as a risk factor for various conditions, including ARDS[59], COPD[60], and asthma[61]. Patients with obesity are at an increased risk of RF compared to those with normal weight. However, some studies offer contrary viewpoints. For instance, a meta-analysis involving 6,268 patients demonstrated that in severe cases of ARDS, obesity was associated with a lower mortality rate (OR 0.68, 95% CI 0.57–0.80, $P < 0.00001$)[62]. Similar findings have been observed in patients with COPD, as noted in the SUMMIT study, where overweight (HR 0.62, 95% CI 0.52–0.73) and class I obese (HR 0.75, 95% CI 0.62–0.90) patients exhibited lower mortality[63]. Clinical studies have also highlighted a significant inverse trend between BMI and mortality from pneumonia[64,65]. This inverse correlation between the TyG-BMI and mortality has been observed in studies on heart failure[66] and atrial fibrillation[67]. These phenomena are consistent with our observations and might provide a reasonable explanation for our study results.

The obesity paradox in RF could be attributed to several potential mechanisms. Firstly, obesity may induce a state of chronic low-level inflammation, providing a pre-conditioning effect that protects the lungs from further damage during subsequent high-level inflammatory states[68]. Additionally, the fat and muscle reserves in obese patients might offer an energy source during the catabolic process of RF, potentially reducing the risk of mortality[69,70]. Another perspective is that clinicians' awareness of obesity might lead to early preventative measures, such as stricter fluid and glucose control, more precise adjustments of mechanical ventilation parameters, and other care practices, possibly improving the prognosis for patients with obesity and RF[55,71].

The relationship and underlying mechanisms between obesity and RF are complex and require further validation through extensive clinical and basic research. TyG and BMI are clinically accessible parameters and effective substitutes for identifying metabolic abnormalities. Our study provides a simple clinical parameter that can help swiftly identify high-risk patients, facilitating more efficient stratification and management.

Limitations

Our study has several limitations. Firstly, research based on databases often encounters issues such as missing values and potential confounders that are not identified but could influence outcomes. Secondly, the values we used for calculations were the initial measurements of patients' blood sugar and lipids, and it is unclear whether these were measured in a fasting state. Thirdly, as the database did not record the time of diagnosis, we could not determine the exact timing of RF occurrence in relation to the TyG-BMI. Lastly, our study did not provide a biological explanation for the link between the TyG-BMI and mortality in critically ill patients with RF. These issues should be carefully considered in future prospective clinical trials. Further investigations are warranted to understand the complex interplay between insulin resistance, adiposity, and clinical outcomes in this patient population.

Conclusion

Higher TyG-BMI was closed to lower short-term and long-term mortality, suggesting a potential protective effect for critically ill patients with RF. These findings highlighted the importance of the TyG-BMI as a robust prognostic marker, providing valuable insights for improving treatment strategies for patients with RF.

Data availability

The MIMIC-IV database is publicly available on PhysioNet (https://www.physionet.org/content/mimiciv/2.0/). Concepts codes are available in the MIMIC Code Repository (https://github.com/MIT-LCP/mimic-code/).

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References

1. López, E. B., Díaz, J. S., López, S. A., Flórez, J. V. & Olivares, P. G. Epidemiology and outcome in acute respiratory failure. *Crit. Care* **12**(2), P493 (2008).
2. Adhikari, N. K. J., Fowler, R. A., Bhagwanjee, S. & Rubenfeld, G. D. Critical care and the global burden of critical illness in adults. *The Lancet* **376**(9749), 1339–1346 (2010).
3. Kempker, J. A. et al. The epidemiology of respiratory failure in the United States 2002–2017: A serial cross-sectional study. *Crit. Care Explorat.* **2**(6), e0128 (2020).
4. Chen, L. & Rackley, C. R. Diagnosis and epidemiology of acute respiratory failure. *Crit. Care Clin.* **40**(2), 221–233 (2024).
5. Zauner, A. et al. Severity of insulin resistance in critically ill medical patients. *Metabol. – Clin. Exper.* **56**(1), 1–5 (2007).
6. Gunst, J. & Verbruggen, S. C. Insulin resistance in critical illness: Consequences for nutrition therapy and glucose management. *Curr. Opin. Crit. Care* **29**(4), 286–292 (2023).
7. Carlson, G. L. Insulin resistance and glucose-induced thermogenesis in critical illness. *Proceed. Nutrit. Soci.* **60**(3), 381–388 (2001).
8. Dungan, K. M., Braithwaite, S. S. & Preiser, J.-C. Stress hyperglycaemia. *The Lancet* **373**(9677), 1798–1807 (2009).

9. Machado, F. V. C., Pitta, F., Hernandes, N. A. & Bertolini, G. L. Physiopathological relationship between chronic obstructive pulmonary disease and insulin resistance. *Endocrine* **61**(1), 17–22 (2018).
10. Cardet, J. C., Ash, S., Kusa, T., Camargo, C. A. & Israel, E. Insulin resistance modifies the association between obesity and current asthma in adults. *Eur. Respir. J.* **48**(2), 403–410 (2016).
11. Baker, E. H. et al. Hyperglycaemia and pulmonary infection. *Proceed. Nutrit. Soci.* **65**(3), 227–235 (2006).
12. Ingelsson, E., Sundström, J., Ärnlöv, J., Zethelius, B. & Lind, L. Insulin resistance and risk of congestive heart failure. *JAMA* **294**(3), 334–341 (2005).
13. Mowery, N. T. et al. Stress insulin resistance is a marker for mortality in traumatic brain injury. *J. Trauma Acute Care Surg.* **66**(1), 145–153 (2009).
14. Simental-Mendía, L. E., 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.* **6**(4), 299–304 (2008).
15. Piironen, M. et al. Trends in long-term prognosis after acute coronary syndrome. *Eur. J. Prev. Cardiol.* **24**(3), 274–280 (2020).
16. Luo, E. et al. High triglyceride–glucose index is associated with poor prognosis in patients with acute ST-elevation myocardial infarction after percutaneous coronary intervention. *Cardiovasc. Diabetol.* **18**(1), 150 (2019).
17. Zhou, Q. et al. High triglyceride-glucose (TyG) index is associated with poor prognosis of heart failure with preserved ejection fraction. *Cardiovasc. Diabetol.* **22**(1), 263 (2023).
18. Zheng, R. et al. Association between triglyceride-glucose index and in-hospital mortality in critically ill patients with sepsis: Analysis of the MIMIC-IV database. *Cardiovasc. Diabetol.* **22**(1), 307 (2023).
19. Liao, Y. et al. Triglyceride-glucose index linked to all-cause mortality in critically ill patients: A cohort of 3026 patients. *Cardiovasc. Diabetol.* **21**(1), 128 (2022).
20. Zhou, W.-Q., Song, X., Dong, W.-H. & Chen, Z. Independent effect of the triglyceride-glucose index on all-cause mortality in critically ill patients with chronic obstructive pulmonary disease and asthma: A retrospective cohort study. *Chron. Respir. Dis.* **21**, 14799731241245424 (2024).
21. Staggers, K. A., Minard, C., Byers, M., Helmer, D. A. & Wu, T. D. Metabolic dysfunction, triglyceride-glucose index, and risk of severe asthma exacerbation. *J. Allergy Clin. Immunol.: In Pract.* **11**(12), 3700-3705.e3702 (2023).
22. Bala, C. et al. The Association between six surrogate insulin resistance indexes and hypertension: A population-based study. *Metab. Syndr. Relat. Disord.* **17**(6), 328–333 (2019).
23. Hu, H., Han, Y., Cao, C. & He, Y. The triglyceride glucose-body mass index: A non-invasive index that identifies non-alcoholic fatty liver disease in the general Japanese population. *J. Transl. Med.* **20**(1), 398 (2022).
24. Yang, S. et al. Association between triglyceride glucose-body mass index and heart failure in subjects with diabetes mellitus or prediabetes mellitus: a cross-sectional study. *Front. Endocrinol.* https://doi.org/10.3389/fendo.2023.1294909 (2023).
25. Cheng, Y. et al. Association between triglyceride glucose-body mass index and cardiovascular outcomes in patients undergoing percutaneous coronary intervention: A retrospective study. *Cardiovasc. Diabetol.* **22**(1), 75 (2023).
26. Er, L.-K. et al. Triglyceride glucose-body mass index is a simple and clinically useful surrogate marker for insulin resistance in nondiabetic individuals. *PLoS ONE* **11**(3), e0149731 (2016).
27. Kuiper-Makris, C., Selle, J., Nüsken, E., Dötsch, J. & Alejandre Alcazar, M. A. Perinatal nutritional and metabolic pathways: Early origins of chronic lung diseases. *Front. Med.* **8**, 667315 (2021).
28. Wang, Y. et al. Chronic intermittent hypoxia disturbs insulin secretion and causes pancreatic injury via the MAPK signaling pathway. *Biochem. Cell Biol.* **95**(3), 415–420 (2017).
29. Johnson, A. E. W. et al. MIMIC-IV, a freely accessible electronic health record dataset. *Sci. Data* **10**(1), 1 (2023).
30. Goldberger, A. L. et al. PhysioBank, PhysioToolkit, and PhysioNet. *Circulation* **101**(23), e215–e220 (2000).
31. Kursa, M. B. & Rudnicki, W. R. Feature selection with the Boruta package. *J. Stat. Softw.* **36**(11), 1–13 (2010).
32. Jakobsen, J. C., Gluud, C., Wetterslev, J. & Winkel, P. When and how should multiple imputation be used for handling missing data in randomised clinical trials – A practical guide with flowcharts. *BMC Med. Res. Methodol.* **17**(1), 162 (2017).
33. Therneau, T. M. & Grambsch, P. M. The Cox Model. In *Modeling Survival data: Extending the cox model* (eds Therneau, T. M. & Grambsch, P. M.) 39–77 (New Springer, 2000).
34. Knopp, J. L., Chase, J. G. & Shaw, G. M. Increased insulin resistance in intensive care: Longitudinal retrospective analysis of glycaemic control patients in a New Zealand ICU. *Therap. Adv. Endocrinol. Metabol.* **12**, 20420188211012144 (2021).
35. Wu, H. & Ballantyne, C. M. Metabolic inflammation and insulin resistance in obesity. *Circ. Res.* **126**(11), 1549–1564 (2020).
36. Peters, M. C. et al. The impact of insulin resistance on loss of lung function and response to treatment in asthma. *Am. J. Respir. Crit. Care Med.* **206**(9), 1096–1106 (2022).
37. Rivas, A. M. & Nugent, K. Hyperglycemia, insulin, and insulin resistance in sepsis. *Am. J. Med. Sci.* **361**(3), 297–302 (2021).
38. Huang, R. et al. Prognostic value of triglyceride glucose (TyG) index in patients with acute decompensated heart failure. *Cardiovasc. Diabetol.* **21**(1), 88 (2022).
39. Dogra, M. et al. Role of interleukin-6 and insulin resistance as screening markers for metabolic syndrome in patients of chronic obstructive pulmonary disease. A hospital-based cross-sectional study. *Monaldi Arch. Chest Dis.* https://doi.org/10.4081/monaldi.2021.2024 (2021).
40. Shoelson, S. E., Lee, J. & Goldfine, A. B. Inflammation and insulin resistance. *J. Clin. Investig.* **116**(7), 1793–1801 (2006).
41. Cyphert, T. J. et al. NF-κB-dependent airway inflammation triggers systemic insulin resistance. *Am. J. Physiol. –Regulat., Integr. Compar. Physiol.* **309**(9), R1144–R1152 (2015).
42. Kim, J. A., Wei, Y. & Sowers, J. R. Role of mitochondrial dysfunction in insulin resistance. *Circul. Res.* **102**(4), 401–414 (2008).
43. St-Pierre, P., Genders, A. J., Keske, M. A., Richards, S. M. & Rattigan, S. Loss of insulin-mediated microvascular perfusion in skeletal muscle is associated with the development of insulin resistance. *Diabetes Obes. Metab.* **12**(9), 798–805 (2010).
44. Wells, C. E., Polkey, M. I. & Baker, E. H. Insulin resistance is associated with skeletal muscle weakness in COPD. *Respirology* **21**(4), 689–696 (2016).
45. Fernández-Real, J.-M. et al. Burden of infection and insulin resistance in healthy middle-aged men. *Diabetes Care* **29**(5), 1058–1064 (2006).
46. Jafar, N., Edriss, H. & Nugent, K. The effect of short-term hyperglycemia on the innate immune system. *Am. J. Med. Sci.* **351**(2), 201–211 (2016).
47. Singh, S. et al. Hyperinsulinemia adversely affects lung structure and function. *Am. J. Physiol. -Lung Cell. Mol. Physiol.* **310**(9), L837–L845 (2016).
48. Park, Y. H. et al. Insulin resistance mediates high-fat diet-induced pulmonary fibrosis and airway hyperresponsiveness through the TGF-β1 pathway. *Exp. Mol. Med.* **51**(5), 1–12 (2019).
49. Kim, S. H., Kim, H. S., Min, H. K. & Lee, S. W. Association between insulin resistance and lung function trajectory over 4 years in South Korea: Community-based prospective cohort. *BMC Pulm. Med.* **21**(1), 110 (2021).
50. Zuberi, F. F., Bader, N., Rasheed, T. & Zuberi, B. F. Association between insulin resistance and BMI with FEV1 in non-hypoxemic COPD out-patients. *Clin. Respir. J.* **15**(5), 513–521 (2021).
51. Sagun, G. et al. The relation between insulin resistance and lung function: A cross sectional study. *BMC Pulm. Med.* **15**(1), 139 (2015).
52. Wu, T. D. et al. Association of triglyceride-glucose index and lung health: A population-based study. *Chest* **160**(3), 1026–1034 (2021).

53. Ren, H. et al. Association of the insulin resistance marker TyG index with the severity and mortality of COVID-19. *Cardiovasc. Diabetol.* **19**(1), 58 (2020).
54. Chang, Y., Jeon, J., Song, T.-J. & Kim, J. Association of triglyceride-glucose index with prognosis of COVID-19: A population-based study. *J. Infect. Public Health* **15**(8), 837–844 (2022).
55. Ball, L., Serpa Neto, A. & Pelosi, P. Obesity and survival in critically ill patients with acute respiratory distress syndrome: A paradox within the paradox. *Crit. Care* **21**(1), 114 (2017).
56. Yao, S., Zeng, L., Wang, F. & Chen, K. Obesity paradox in lung diseases: What explains it?. *Obes. Facts* **16**(5), 411–426 (2023).
57. Karampela, I., Chrysanthopoulou, E., Christodoulatos, G. S. & Dalamaga, M. Is there an obesity paradox in critical illness? Epidemiologic and metabolic considerations. *Curr. Obes. Rep.* **9**(3), 231–244 (2020).
58. Arabi, Y. M. et al. Clinical characteristics, sepsis interventions and outcomes in the obese patients with septic shock: an international multicenter cohort study. *Crit. Care* **17**(2), R72 (2013).
59. Hibbert, K., Rice, M. & Malhotra, A. Obesity and ARDS. *Chest* **142**(3), 785–790 (2012).
60. Lambert, A. A. et al. Obesity is associated with increased morbidity in moderate to severe COPD. *Chest* **151**(1), 68–77 (2017).
61. Peters, U., Dixon, A. E. & Forno, E. Obesity and asthma. *J. Allergy Clin. Immunol.* **141**(4), 1169–1179 (2018).
62. Ni, Y.-N. et al. Can body mass index predict clinical outcomes for patients with acute lung injury/acute respiratory distress syndrome? A meta-analysis. *Crit. Care* **21**(1), 36 (2017).
63. Brigham, E. P. et al. Challenging the obesity paradox: Extreme obesity and COPD mortality in the SUMMIT trial. *ERJ Open Res.* **7**(3), 00902–02020 (2021).
64. Inoue, Y. et al. Risk and protective factors related to mortality from pneumonia among middleaged and elderly community residents: The JACC study. *J. Epidemiol.* **17**(6), 194–202 (2007).
65. Hespanhol, V. & Bárbara, C. Pneumonia mortality, comorbidities matter?. *Pulmonology* **26**(3), 123–129 (2020).
66. Dou, J. et al. Association between triglyceride glucose-body mass and one-year all-cause mortality of patients with heart failure: A retrospective study utilizing the MIMIC-IV database. *Cardiovasc. Diabetol.* **22**(1), 309 (2023).
67. Hu, Y., Zhao, Y., Zhang, J. & Li, C. The association between triglyceride glucose-body mass index and all-cause mortality in critically ill patients with atrial fibrillation: A retrospective study from MIMIC-IV database. *Cardiovasc. Diabetol.* **23**(1), 64 (2024).
68. Halasz, G., Leoni, M. L. G., Villani, G. Q., Nolli, M. & Villani, M. Obesity, overweight and survival in critically ill patients with SARS-CoV-2 pneumonia: Is there an obesity paradox? Preliminary results from Italy. *Eur. J. Prev. Cardiol.* **28**(9), e15–e17 (2020).
69. Poulain, M. et al. Metabolic and inflammatory profile in obese patients with chronic obstructive pulmonary disease. *Chron. Respir. Dis.* **5**(1), 35–41 (2008).
70. DeLapp, D. A., Glick, C., Furmanek, S., Ramirez, J. A. & Cavallazzi, R. Patients with Obesity Have Better Long-Term Outcomes after Hospitalization for COPD Exacerbation. *COPD: J. Chronic Obstr. Pulm. Dis* **17**(4), 373–377 (2020).
71. Pompilio, C. E., Pelosi, P. & Castro, M. G. The bariatric patient in the intensive care unit: Pitfalls and management. *Curr. Atheroscler. Rep.* **18**(9), 55 (2016).

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Author contributions
S.C. and Z.L.X. conceived and designed the study. S.C. developed SQL, R codes for data analysis. N.X.L. and S.C. drafted the initial manuscript. N.X.L. verified the data and contributed to the data interpretation. S.C., N.X.L. and Z.L.X. revised the manuscript and provided methodological guidance. All authors reviewed and approved the ultimate version of the submitted manuscript.

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Declarations

Competing interests
The authors declare no competing interests.

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Not applicable. The Beth Israel Deaconess Medical Center's Institutional Review Board waived informed written consent because all patient data was deidentified (IRB #2001P001699). Because the study in the MIMIC-IV database was retrospective and observational, there was no requirement to acquire consent to participate. Our team can now access the MIMIC-IV database (Record ID 6775305).

Consent for publication
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