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The impact of the triglyceride-glucose index on the risk of respiratory failure in patients with COPD: a study from the MIMIC database and Chinese cohorts

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Abstract

Background The Triglyceride-Glucose (TyG) index, a reliable marker for insulin resistance, is now employed to assess the onset and prognosis of various conditions like acute coronary syndrome, chronic kidney disease, and ischemic stroke. However, whether the TyG index can be used to assess respiratory failure (RF) risk among Chronic obstructive pulmonary disease (COPD) patients remains uncertain. The present study aims to delve into the link between the TyG index and the risk of RF in COPD patients.

Methods Individuals with COPD were retrospectively acquired from the MIMIC-IV 2.2 (The Medical Information Mart for Intensive Care IV, version 2.2) database. The association between the TyG index and the probability of RF among COPD patients was evaluated using Cox proportional hazards models and restricted cubic spline (RCS) curves. Cumulative incidence curves were generated to appraise the RF risk across the quartile groups. Finally, 1188 patients were recruited from the First Hospital of Jiaxing City to externally validate the Cox modeling results for the primary outcome.

Results This study incorporated a total of 1,232 participants from MIMIC database. Among these individuals, 134 cases (10.9%) experienced RF. According to Cox regression analysis, a one-unit increment in the TyG index was linked to a 1.821-fold elevated risk of RF in the COPD population (HR, 1.821[95% CI 1.349–2.459], $P < 0.001$). High TyG index levels were significantly linked to a higher RF risk (HR, 3.510 [95% CI 1.885–6.535], $P < 0.001$). RCS curve analysis also signaled a linear correlation between the TyG index and RF risk (P-Nonlinear = 0.074).

Conclusion There exists a certain correlation between high-level TyG index and the risk of RF occurrence in COPD patients, indicating promising prospects for utilizing the TyG index to assess the severity of COPD patients.

Keywords Chronic obstructive pulmonary disorder, Respiratory insufficiency, TyG index, Medical Information Mart for Intensive Care IV (MIMIC-IV) dataset, Externally validate

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Introduction

Chronic obstructive pulmonary disease (COPD) represents a notable category of enduring and progressive respiratory disorders, characterized by high rates of disability and mortality. As per the data provided by the World Health Organization (WHO), COPD ranks as the third leading cause of death globally, following ischemic heart disease and stroke. It places a growing economic strain on low- and middle-income nations, with high prevalence and mortality [1, 2]. As COPD advances, patients often develop serious complications such as pulmonary hypertension, cor pulmonale, respiratory failure (RF), and pneumothorax. Among these, RF stands out as the most prevalent risk factor leading to recurrent hospitalization, poor prognosis, and mortality [3–6]. Consequently, clinicians have turned their attention to predicting the RF risk in COPD patients. Early identification of RF risk is critical for preventive and early-stage treatment, as it can significantly mitigate the risk of worsening COPD, improve patient prognosis, and enhance their quality of life.

Insulin resistance (IR) signifies a decline in the responsiveness of peripheral tissues to insulin [7], and it has been correlated with reduced lung function [8]. The conventional method for diagnosing IR is the hyperinsulinemic euglycemic glucose clamp (HEGC) [9], an invasive and time-intensive procedure [10]. Laboratory-based alternatives to this test, including the Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) and the Quantitative Insulin Sensitivity Test Index (QUICKI), necessitate the direct measurement of insulin and have limited applicability in clinical practice [11].

The TyG index, a dependable biomarker and surrogate for IR [10, 12], is calculated utilizing the formula Ln (fasting triglyceride (mg/dl) × fasting blood glucose (mg/dl)/2) [13]. The data required for computing this index are derived from routine biochemistry tests, making it a convenient and easily accessible alternative to traditional detection methods that demand specialized equipment and technology. Over the years, numerous investigations have explored the link between the TyG index and disease prognosis. TyG index has been demonstrated significantly correlated with the onset and prognosis of circulatory system diseases [14], chronic kidney disease [15], stroke [16], fatty liver [17], and other conditions, showcasing its strong potential for application. Furthermore, the TyG index has also been associated with the occurrence and prognosis of certain respiratory diseases. A prior study [18] has revealed that an elevated TyG index may serve as a risk factor for declining lung function, which is a key determinant in the development of RF in COPD patients. The occurrence of RF is closely tied to the prognosis of COPD. Therefore, the present study seeks to explore the correlation between the TyG index and the risk of RF in COPD patients, offering valuable insights for predicting RF in this patient population.

Materials and methods

Data source

This retrospective investigation utilized data extracted from the Medical Information Mart for Intensive Care (MIMIC-IV version 2.2) (https://physionet.org/content/mimiciv/2.2/). It is an expansive, publicly accessible, and freely available database. It was meticulously curated and developed by the Laboratory of Computational Physiology at the Massachusetts Institute of Technology, Beth Israel Deaconess Medical Center (BIDMC) at Harvard Medical School, and Philips Healthcare. MIMIC-IV 2.2 includes clinical records (including data from both general ward and ICU admissions) from over 450,000 hospital admissions involving 299,712 patients treated at BIDMC between 2008 and 2019. [19]. We have successfully completed the requisite training and examination process for database access, we received approval from the Institutional Review Boards of both the Massachusetts Institute of Technology and BIDMC (Certificate Number: 52663507). The detailed certificate information is in Supplementary Material 1. It's essential to note that all sensitive patient information within the MIMIC project has been de-identified, ensuring that the research remains ethically compliant.

Additionally, to verify the generalizability of the results, we conducted a retrospective study of COPD patients hospitalized at the First Hospital of Jiaxing City from January 2021 to December 2023. The study was conducted from February to June 2024. Ethical approval for the external validation participants was obtained from our institution (Ethical Approval No. 2023-KY-607).

Study population

All data pertaining to the study population is sourced from the MIMIC-IV database. Inclusion criteria comprised: (1) Patients diagnosed with COPD based on the ICD codes (ICD-10: J44, J440, J441, J449; ICD-9: 49,120, 49,121, 4912, 496); and (2) Adult patients aged 18 years and older. Exclusion criteria encompassed: (1) Patients without follow-up time; (2)Patients who were not hospitalized; (3) Patients with pre-existing RF prior to admission; and (4) Patients lacking glucose and triglyceride data within 48 h following patient admission. Furthermore, we focused our analysis on the initial admission for patients with multiple admissions. The ultimate study cohort included 1,232 patients, who were split into four groups according to quartiles of the TyG index.

Data collection

Clinical data on eligible participants were acquired from the MIMIC-IV database employing Navicat Premium software (version 16.0, https://navicat.com.cn). Essential patient demographics were obtained, including age, gender, BMI, and ethnicity. Additionally, we systematically compiled the blood test parameters at initial admission, comprising (i) blood indicators: white blood cell count (WBC), neutrophil count (Ncell), lymphocyte count (Lcell), platelet count (PLT), and red blood cell count (RBC)); (ii) biochemical indexes: sodium (Na^+), potassium (K^+), glucose, triglyceride, serum creatinine (Scr), blood urea nitrogen (BUN), alanine aminotransferase (ALT), aspartate aminotransferase (AST), albumin, total bilirubin (TBil), indirect bilirubin (IBil), total cholesterol (TC), low-density lipoprotein (LDL), high-density lipoprotein (HDL), and hemoglobin A1c (HbA1c); (iii) coagulation parameters: prothrombin time (PT), activated partial thromboplastin time (APTT), and D-dimer; (iv) arterial blood gas analysis: partial pressure of oxygen (PO_2) and partial pressure of carbon dioxide (PCO_2). We also extracted data on complications, such as asthma, respiratory tract infection (RTI), hypertension, heart failure (HF), coronary heart disease (CHD), diabetes, cerebrovascular disease (CVD), Interstitial lung disease (ILD), and sepsis. Furthermore, we cataloged the administration of pharmaceuticals, including corticosteroids, antibiotics, bronchodilators, and albumin. Various clinical assessment scores were also acquired, namely the Sequential Organ Failure Assessment (SOFA) score, Acute Physiology Score III (APS III), and Simplified Acute Physiology Score II (SAPS II) on Day 1. For all laboratory indicators, we analyzed the data from the initial measurements taken within 48 h after patient admission. It is important to note that data collected subsequent to the occurrence of RF was deemed unsuitable for analysis to mitigate any potential for reverse causality. In this study, the TyG index was calculated as ln(fasting blood glucose (mg/dL) × fasting triglycerides (mg/dL)) / 2.

Primary and secondary outcomes

The follow-up for both study cohorts commenced at the time of admission, with the endpoint being either the occurrence of RF or discharge. The principal endpoint was the likelihood of RF in patients diagnosed with COPD. RF is defined as arterial oxygen pressure (PaO_2) < 60 mmHg or the oxygenation index (PaO_2/FiO_2) ≤ 300 mmHg under oxygen supplementation, with or without hypercapnia. Secondary endpoints encompassed the hospitalization stay and the utilization of invasive mechanical ventilation. Invasive mechanical ventilation encompasses the rates of endotracheal intubation and tracheostomy.

Statistical analysis

Normally distributed continuous variables were depicted as the mean and standard deviation (SD). Meanwhile, if continuous variables were abnormally distributed, they were presented by the median and interquartile range (IQR). Categorical variables were delineated by both quantity and frequency (%).

Comparisons of continuous variables were executed utilizing either Student's t-test or nonparametric testing methods according to their respective distributions. On the other hand, comparative analyses of categorical variables were carried out employing either Pearson's chi-square test or Fisher's exact test. Data with missing values of less than 20% were handled with multiple imputation techniques using the random forest method from the "missForest" package. However, when data displayed missing values exceeding 20%, we utilized dummy variables for data processing.

To investigate the correlation between the risk of RF and various TyG index levels, cumulative incidence curves were utilized to assess the RF risk in each group based on TyG index quartiles. The differences between groups were analyzed using log-rank tests.

The modeling analysis was then performed using both the continuous variable form and the quartile-based categorical form of the TyG index. Following an evaluation of the TyG index's normality, a Cox proportional hazards model was employed to examine the link between the TyG index and the likelihood of experiencing RF among individuals diagnosed with COPD. The outcomes were presented utilizing hazard ratio (HR) accompanied by a 95% confidence interval (CI). Three distinct models were formulated for analysis. No covariates were adjusted in Model 1, while Model 2 adjusted for three key variables: age, gender, and BMI. Building upon Model 2, Model 3 additionally adjusted for covariates that could potentially influence the incidence of RF, encompassing comorbidities (e.g., asthma, hypertension, HF, CHD, diabetes mellitus, and CVD), laboratory parameters (including albumin, potassium, HbA1c, TC, APTT, PT, HDL, LDL, Na+), and medication use (specifically, glucocorticoids antibiotics and bronchodilators). Furthermore, logistic regression was employed to delve into the correlation between the TyG index and the utilization of invasive mechanical ventilation. Multivariate linear regression was utilized to assess the connection between the TyG index and the duration of hospitalization stay.

To explore any potential nonlinear relationships, we harnessed restricted cubic splines (RCSs) to delve into the link between RF risk and TyG index as a continuous variable.

Moreover, we conducted additional subgroup analysis based on gender, age (categorized as < 60 years

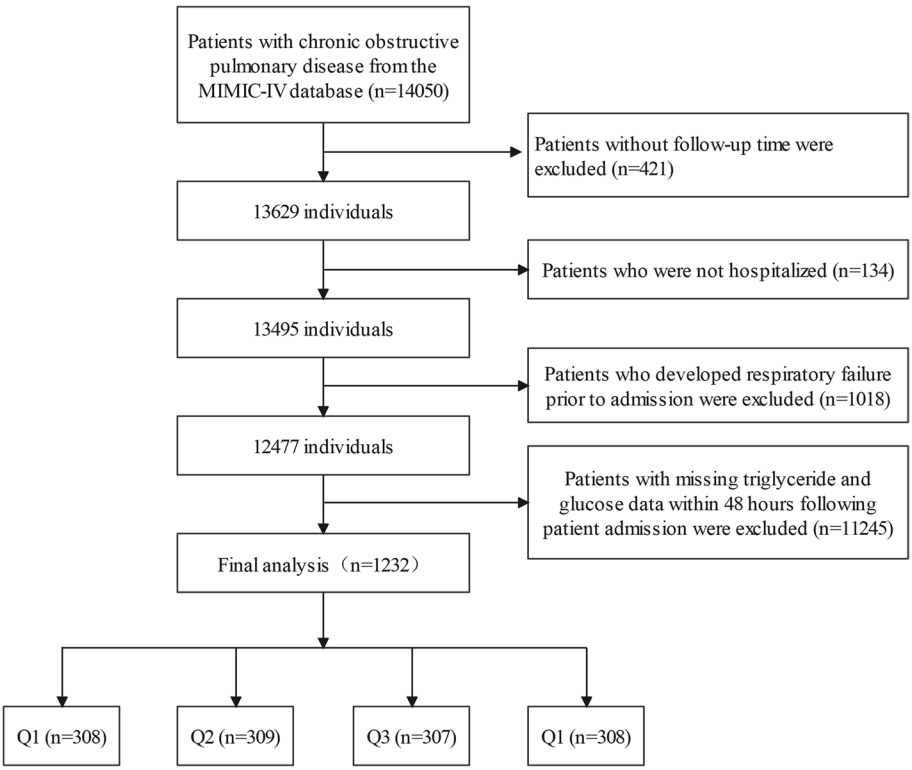

Fig. 1 Flowchart of patient screening. MIMIC-IV: Medical Information Mart for Intensive Care-IV; n: Number; COPD: chronic obstructive pulmonary disease

and ≥ 60 years), and the presence of various comorbidities including diabetes, hypertension, HF, liver cirrhosis, sepsis, and respiratory tract infection. The primary aim was to appraise the uniformity of the TyG index's impact on outcomes across these groups and to delve into potential interactions between the TyG index and the stratification variables.

Data analysis was conducted utilizing R software (available at www.R-project.org; version 4.2.3). All statistical tests were conducted with a two-tailed approach, and $P < 0.05$ was utilized to define statistical significance.

Chinese cohort

We conducted a retrospective study of COPD patients hospitalized at the First Hospital of Jiaxing City from January 2021 to December 2023. The inclusion and exclusion criteria, data collection, processing, and analysis methods, as well as the definitions of outcomes for the Chinese cohort, were consistent with those in the MIMIC database.

Results

A total of 14,050 individuals diagnosed with COPD were retrospectively acquired from the MIMIC-IV 2.2 database. Ultimately 1,232 patients were eligible for this investigation (Fig. 1). The median age within this cohort stood at 72.0 years [63.0; 80.0], with 640 (51.9%) males and 592 (48.1%) females. The majority of patients belonged to the Caucasian ethnic group. The median TyG index for all enrolled patients equated to 8.76 [8.4, 9.2]. Among these individuals, 134 patients (10.9%) developed RF, while 1098 patients (89.1%) did not suffer from RF.

A retrospective review was conducted at the First Hospital of Jiaxing City, including 1,188 patients. The median age was 75.0 years [65.0, 82.0], with 911 (76.7%) being male. For external validation patients, the median TyG index was 8.37 [8.0, 8.7], with a total of 455 (38.3%) cases experiencing RF.

Baseline characteristics

Table 1 delineates patient baseline features in the MIMIC database. Patients with the higher TyG index quartile (Q4) were generally younger ($P < 0.001$) and exhibited elevated BMI in comparison to those with lower TyG index quartile (Q1). Moreover, the prevalence of diabetes mellitus, RTI, and CHD upon admission was higher in patients with a higher TyG index. They also presented with heightened levels of WBC, liver transaminases, BUN, LDL and TC, while HDL levels were lower. Furthermore, APTT and PT were shorter ($P < 0.05$).

Table 1 The baseline clinical characteristics of the study population

Categories	Overall (*n* = 1232)	Q1 (*n* = 308)	Q2 (*n* = 309)	Q3 (*n* = 307)	Q4 (*n* = 308)	*P*-value	Text
Demographic							
Age, years	72.0 [63.0, 80.0]	75.0 [64.0, 83.0]	73.0 [65.0, 81.0]	71.0 [63.0, 79.0]	68.0 [59.0, 76.0]	< 0.001	nonnorm
Male, n (%)	640 (51.9)	157 (51.0)	173 (56.0)	155 (50.5)	155 (50.3)	0.436	
Ethnicity, n (%)						0.535	
Asian	13 (1.1)	2 (0.6)	2 (0.6)	4 (1.3)	5 (1.6)		
Black	109 (8.8)	29 (9.4)	33 (10.7)	25 (8.1)	22 (7.1)		
White	954 (77.4)	245 (79.5)	234 (75.7)	241 (78.5)	234 (76.0)		
Other	156 (12.7)	32 (10.4)	40 (12.9)	37 (12.1)	47 (15.3)		
BMI,kg/m^2	27.60 [23.60, 33.15]	25.90 [22.50, 29.95]	27.10 [22.10, 33.15]	28.20 [23.80, 33.40]	29.30 [26.22, 35.80]	< 0.001	nonnorm
Comorbidities							
Asthma, n (%)	86 (7.0)	19 (6.2)	23 (7.4)	24 (7.8)	20 (6.5)	0.835	
RTI, n (%)	24 (1.9)	2 (0.6)	4 (1.3)	7 (2.3)	11 (3.6)	0.049	
CVD, n (%)	422 (34.3)	101 (32.8)	109 (35.3)	112 (36.5)	100 (32.5)	0.671	
CHD, n (%)	510 (41.4)	105 (34.1)	128 (41.4)	127 (41.4)	150 (48.7)	0.004	
Hypertension, n (%)	641 (52.0)	150 (48.7)	164 (53.1)	155 (50.5)	172 (55.8)	0.309	
HF, n (%)	411 (33.4)	96 (31.2)	100 (32.4)	113 (36.8)	102 (33.1)	0.484	
DM, n (%)	419 (34.0)	47 (15.3)	83 (26.9)	99 (32.2)	190 (61.7)	< 0.001	
Liver cirrhosis, n (%)	35 (2.8)	7 (2.3)	11 (3.6)	10 (3.3)	7 (2.3)	0.684	
Viral hepatitis, n (%)	35 (2.8)	7 (2.3)	11 (3.6)	10 (3.3)	7 (2.3)	0.684	
Sepsis, n (%)	37 (3.0)	4 (1.3)	9 (2.9)	12 (3.9)	12 (3.9)	0.188	
Laboratory tests							
WBC, K/μL	8.6 [6.6, 11.1]	7.8 [5.9, 10.3]	8.2 [6.6, 11.0]	8.7 [6.9, 11.4]	9.4 [7.2, 11.9]	< 0.001	nonnorm
Lcell, K/μL	1.3 [0.8, 1.9]	1.2 [0.8, 1.6]	1.1 [0.7, 1.8]	1.3 [0.9, 2.0]	1.4 [0.9, 2.3]	0.230	nonnorm
Ncell, K/μL	7.3 [4.7, 9.9]	7.4 [3.5, 9.5]	8.1 [5.8, 9.2]	7.1 [5.1, 9.6]	7.3 [3.9, 12.5]	0.729	nonnorm
RBC, K/μL	4.0 [3.6, 4.5]	3.9 [3.5, 4.4]	4.1 [3.6, 4.4]	4.0 [3.6, 4.5]	4.0 [3.6, 4.6]	0.030	nonnorm
PLT, K/μL	224.0 [175.0, 282.3]	225.0[182.0, 276.0]	226.0 [176.0, 279.3]	217.5 [171.0, 278.8]	228.0 [175.5, 297.0]	0.532	nonnorm
CRP, mg/L	32.2 [6.3, 87.9]	31.0 [11.6, 56.0]	15.4 [4.5, 78.6]	35.6 [6.5, 87.0]	44.7 [9.4, 107.8]	0.421	nonnorm
HbA1c, g/dL	12.0 [10.6, 13.4]	11.9 [10.6, 13.0]	12.2 [10.7, 13.4]	12.0 [10.5, 13.5]	12.0 [10.6, 13.5]	0.420	nonnorm
TBil, mg/dL	0.5 [0.4, 0.8]	0.5 [0.4, 0.9]	0.5 [0.4, 0.7]	0.6 [0.3, 0.9]	0.5 [0.3, 0.8]	0.341	nonnorm
IBil, mg/dL	0.6 [0.4, 1.6]	0.6 [0.4, 0.8]	0.8 [0.4, 1.8]	0.8 [0.5, 1.6]	0.7 [0.2, 1.6]	0.792	nonnorm
ALT, IU/L	21.0 [14.0, 36.0]	19.0 [13.0, 32.0]	19.0 [14.0, 33.0]	19.0 [14.0, 32.0]	27.0 [16.0, 48.0]	< 0.001	nonnorm
AST, IU/L	25.0 [17.0, 41.0]	24.0 [18.0, 40.0]	22.5 [17.0, 35.3]	23.0 [16.0, 41.0]	27.0 [20.0, 47.5]	0.040	nonnorm
Scr, mg/dL	4.0 [3.6, 4.5]	3.9 [3.5, 4.4]	4.1 [3.6, 4.4]	4.0 [3.6, 4.5]	4.0 [3.6, 4.6]	0.030	nonnorm
K^+, mEq/L	4.1 [3.8, 4.4]	4.0 [3.8, 4.4]	4.1 [3.8, 4.4]	4.0 [3.7, 4.4]	4.2 [3.8, 4.5]	0.007	nonnorm
Na^+, mEq/L	139.0 [137.0, 141.0]	140.0[137.0, 141.0]	139.0 [137.0, 142.0]	140.0 [138.0, 142.0]	139.0 [136.0, 141.0]	0.013	nonnorm
Albumin, g/dL	3.5 [3.0, 3.9]	3.5 [3.1, 3.9]	3.5 [3.0, 3.9]	3.4 [3.0, 3.8]	3.5 [3.0, 3.9]	0.338	nonnorm
BUN, mg/Dl	18.0 [14.0, 27.0]	17.0 [13.0, 25.0]	18.0 [13.0, 27.0]	19.0 [14.0, 27.0]	20.5 [15.0, 31.3]	< 0.001	nonnorm
Glucose, mg/dl	111.0 [94.0, 143.0]	93.0 [84.0, 108.0]	103.0 [94.0, 121.0]	118.0 [102.0, 146.0]	154.5 [118.8, 215.3]	< 0.001	nonnorm
Triglycerides, mg/dl	112.0 [83.0, 154.0]	71.0 [58.0, 84.0]	101.0 [88.0, 115.0]	133.0 [106.5, 157.0]	198.5 [150.0, 252.0]	< 0.001	nonnorm
TC, mg/dL	150.0 [126.0, 180.0]	142.0[118.0, 171.5]	146.0 [123.0, 170.0]	151.5 [126.8, 182.3]	165.0 [139.5, 202.5]	< 0.001	nonnorm
LDL, mg/dL	79.0 [57.0, 102.0]	75.0 [55.8, 95.5]	77.0 [56.5, 99.0]	82.0 [60.0, 104.0]	83.0 [59.0, 112.0]	0.015	nonnorm
HDL, mg/dL	44.0 [35.0, 56.0]	51.0 [41.0, 64.3]	46.0 [36.5, 57.5]	41.0 [34.0, 52.0]	39.0 [31.0, 47.0]	< 0.001	nonnorm
APTT, sec	30.6 [27.4, 38.1]	31.2 [228.0, 39.7]	30.6 [27.6, 37.7]	30.7 [27.2, 38.6]	29.7 [26.7, 37.0]	0.041	nonnorm
PT, sec	13.2 [12.0, 14.7]	13.4 [12.4, 15.6]	13.2 [11.9, 14.6]	13.1 [11.9, 14.6]	12.9 [11.8, 14.2]	0.005	nonnorm
D-Dimer, ng/ml	1177.5 [598.0, 2429.0]	577.0[382.0, 598.0]	1652.0 [797.8, 1915.0]	3437.0[1465.0,5013.88]	878.0 [253.0, 1144.0]	0.013	nonnorm
TyG index	8.8 [8.4, 9.2]	8.1 [88.0, 8.3]	8.6 [8.5, 8.7]	99.0 [8.99, 9.1]	9.66 [9.44, 9.9]	< 0.001	nonnorm

Table 1 (continued)

Categories	Overall (*n* = 1232)	Q1 (*n* = 308)	Q2 (*n* = 309)	Q3 (*n* = 307)	Q4 (*n* = 308)	*P*-value	Text
PO_2, mmHg	112.0 [74.0, 223.0]	122.0 [74.88, 245.5]	117.5 [80.0, 226.33]	105.0 [73.0, 213.0]	112.0 [72.88, 221.5]	0.704	nonnorm
PCO_2, mmHg	42.0 [36.0, 49.0]	41.0 [35.0, 46.33]	40.0 [35.33, 47.88]	42.0 [37.0, 50.0]	44.0 [38.88, 50.0]	0.172	nonnorm
OI, mmHg	231.0 [137.0, 320.0]	218.0 [123.0, 355.0]	240.0 [138.0, 326.0]	225.0 [127.0, 280.0]	236.0 [160.0, 328.0]	0.900	nonnorm
ICU admission							
APSIII	38.5 [28.0, 49.0]	39.5 [27.5, 47.88]	38.0 [27.0, 48.5]	37.0 [28.5, 45.0]	40.5 [30.88, 53.33]	0.114	nonnorm
SAPSII	33.0 [28.0, 41.0]	32.0 [29.0, 39.88]	34.0 [28.0, 41.0]	32.0 [27.0, 38.0]	33.0 [26.0, 42.0]	0.864	nonnorm
SOFA	3.0 [2.0, 5.0]	3.0 [1.0, 4.0]	3.0 [2.0, 4.5]	3.0 [2.0, 4.0]	3.0 [2.0, 6.0]	0.281	nonnorm
Medicine							
Glucocorticoid, n(%)	379 (30.8)	97(31.5)	97 (31.4)	85 (27.7)	100(32.5)	0.590	
Bronchodilators, n(%)	405 (32.9)	84 (27.3)	98 (31.7)	107 (34.9)	116 (37.7)	0.040	
Antibiotic, n(%)	514 (41.7)	117 (38.0)	138 (44.7)	131 (42.7)	128 (41.6)	0.395	
Usealbumin, n (%)	70 (5.7)	24 (7.8)	16 (5.2)	16 (5.2)	14 (4.5)	0.311	
Events							
LOS hospital, days	5.0 [3.0, 11.0]	4.0 [3.0, 9.0]	5.0 [3.0, 12.0]	6.0 [3.0, 12.0]	6.0 [3.0, 12.0]	0.006	
RF, n (%)	134 (10.9)	19 (6.2)	34 (11.0)	32 (10.4)	49 (15.9)	0.002	
Mechanical ventilation,n(%)	88(7.1)	14(4.5)	16(5.2)	19(6.2)	39(12.7)	< 0.001	

TyG index: Q1 (≤ 8.408048, Q2 (8.408048 < TyG ≤ 8.759355), Q3 (8.759355 < TyG ≤ 9.205240), Q4 (> 9.205240)

Abbreviations: *BMI* Body Mass Index, *RTI* Respiratory tract infection, *CVD* Cerebrovascular disease, *CHD* Coronary heart disease, *HF* Heart failure, *DM* Diabetes mellitus, *WBC* White blood cell, *Lcell* Lymphocyte, *Ncell* Neutrophile granulocyte, *RBC* Red blood cell, *PLT* Platelet, *CRP* C-reactive protein, *HbA1c* Glycosylated hemoglobin, *Tbil* Total bilirubin, *Ibil* Indirect bilirubin, *ALT* Glutamic-pyruvic transaminase, *AST* Glutamic oxalacetic transaminase, *Scr* Serum creatinine, K^+ Potassium, *Na* + Sodium, *BUN* Blood urea nitrogen, *TC* Total cholesterol, *LDL* Low Density Lipoprotein, *HDL* High density lipoprotein, *APTT* Activated partial thromboplastin time, *PT* Prothrombin time, *TyG index* Triglyceride glucose index, PO_2 pressure of oxygen, PCO_2 Pressure of Carbon Dioxide, *OI* Oxygenation Index, *APSIII* Acute physiology score III, *SAPSII* Simplified acute physiological score II, *SOFA* Sequential organ failure assessment, *LOS* length of stay, *ICU* Intensive care unit, *RF* Respiratory failure, *n* Number

In the Chinese cohort, baseline characteristics stratified by quartiles of the TyG index are shown in Table 2. Compared to the low TyG index level group (Q1), patients with high TyG index levels (Q4) had higher levels of BUN, D-Dimer, HbA1c, LDL, and Ncell, while APTT and PT levels were lower.

The baseline comparison between the two cohorts is presented in Table S1.

Risk of RF by quartiles

We utilized cumulative incidence curves to assess the RF risk across four TyG groups (Fig. 2). It is noteworthy that a significant difference in RF risk was observed among these groups ($P = 0.005$).

Correlation between TyG index and outcomes

We subsequently incorporated both forms of the TyG index, continuous and quartile-based variables, for distinct modeling analyses. In the MMIC database, the Cox proportional hazards analysis (Table 3) unveiled that, in the unadjusted model (Model 1), the risk of RF exhibited a substantial association with the TyG index (HR, 1.561[95% CI 1.219–2.000], $P < 0.001$). Furthermore, this association was notably maintained in Model 3 (HR: 1.821 [95% CI 1.349–2.459], $P < 0.001$); for each one-unit increase in the TyG index, the risk of developing RF increases by a factor of 1.821. Moreover, in comparison to the Q1 group, the Q4 group demonstrated a significant increase in the risk of RF; the likelihood of RF occurrence in the Q4 group is 3.51 times greater than that in the Q1 group. (Model 1: HR:2.400 [95% CI 1.413–4.078], $P = 0.001$; Model 2: HR: 2.551 [95% CI 1.485–4.381], $P < 0.001$; Model 3: HR: 3.510 [95% CI 1.885–6.535], $P < 0.001$).

In the Chinese cohort, Cox proportional hazards analysis yielded similar results (Table 4). Both in the unadjusted model (Model 1: HR, 1.568 [95% CI 1.350–1.822], $P < 0.001$) and the fully adjusted model (Model 3: HR, 1.786 [95% CI 1.513–2.108], $P < 0.001$), there was a significant association between the risk of RF occurrence and the TyG index; the risk of developing RF increases by 1.786 times for each one-unit increase in the TyG index. Additionally, compared to the low level of TyG index (Q1), the high level of TyG index (Q4) was also associated with a higher risk of RF occurrence; the risk of RF in the Q4 group is 1.911 times higher compared to the

Table 2 The baseline clinical characteristics of the study population in Chinese cohort

Categories	Overall (*N* = 1188)	Q1 (*N* = 297)	Q2 (*N* = 297)	Q3 (*N* = 297)	Q4 (*N* = 297)	*P*-value	Text
Demographic							
Age, years	75.0 [69.0, 82.0]	76.0 [69.0, 82.0]	74.0 [69.0, 81.0]	75.0 [70.0, 82.0]	75.0 [69.0, 81.0]	0.628	nonnorm
Male, n (%)	911(76.7)	250(84.2)	238(80.1)	211(71.0)	212(71.4)	< 0.001	
Ethnicity, n (%)							
Asian	1188(100%)	297 (100)	297 (100)	297 (100)	297 (100)		
BMI, kg/m^2	21.4 [19.5, 23.6]	19.8 [18.1, 22.6]	21.3 [20.2, 23.5]	20.9 [19.3, 23.8]	22.9 [21.0, 24.4]	0.012	nonnorm
Comorbidities							
Asthma, n (%)	92 (7.7)	24 (8.1)	20 (6.7)	28 (9.4)	20 (6.7)	0.557	
RTI, n (%)	702 (59.1)	164 (55.2)	179 (60.3)	177 (59.6)	182 (61.3)	0.452	
CHD, n (%)	88 (7.4)	27 (9.1)	19 (6.4)	25 (8.4)	17 (5.7)	0.342	
Hypertension, n (%)	561 (47.2)	123 (41.4)	132 (44.4)	143 (48.1)	163 (54.9)	0.007	
HF, n (%)	341 (28.7)	94 (31.6)	79 (26.6)	86 (29.0)	82 (27.6)	0.555	
DM, n (%)	122 (10.3)	16 (5.4)	21 (7.1)	22 (7.4)	63 (21.2)	< 0.001	
Liver cirrhosis, n (%)	60 (5.1)	18 (6.1)	15 (5.1)	15 (5.1)	12 (4.0)	0.738	
Viral hepatitis, n (%)	60 (5.1)	18 (6.1)	15 (5.1)	15 (5.1)	12 (4.0)	0.738	
Sepsis, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)		
Laboratory tests							
WBC, K/μL	7.1 [5.5, 9.5]	6.7 [5.2, 8.7]	7.1 [5.4, 9.8]	6.9 [5.4, 9.4]	7.6 [6.1, 10.4]	< 0.001	nonnorm
Lcell, K/μL	0.9 [0.6, 1.4]	0.9 [0.6, 1.4]	0.9 [0.6, 1.4]	1.0 [0.6, 1.4]	0.9 [0.6, 1.4]	0.829	nonnorm
Ncell, K/μL	5.5 [3.8, 7.6]	5.0 [3.6, 7.2]	5.2 [3.8, 7.5]	5.3 [3.8, 7.5]	6.0 [4.4, 8.5]	< 0.001	nonnorm
RBC, K/μL	4.3 [3.9, 4.7]	4.3 [3.8, 4.7]	4.3 [3.9, 4.7]	4.3 [4.0, 4.8]	4.4 [4.0, 4.8]	0.111	nonnorm
PLT, K/μL	177.0[131.6,232.0]	174.0 [127.8, 223.3]	176.0[123.0, 236.5]	187.0[136.0, 238.0]	175.0[134.5,233.0]	0.384	nonnorm
CRP, mg/L	14.8 [4.0, 61.0]	13.2 [3.4, 35.9]	17.1 [4.6, 62.9]	13.7 [3.9, 60.7]	15.3 [4.4, 87.2]	0.017	nonnorm
HbA1c, g/dL	6.1 [5.7, 6.5]	5.8 [5.6, 6.1]	6.0 [5.7, 6.3]	6.2 [5.8, 6.5]	6.4 [6.1, 7.5]	< 0.001	nonnorm
TBil, mg/dL	0.6 [0.4, 0.9]	0.6 [0.5, 0.9]	0.6 [0.4, 0.9]	0.6 [0.4, 0.9]	0.6 [0.5, 0.9]	0.161	nonnorm
IBil, mg/dL	0.4 [0.3, 0.5]	0.4[0.3,0.5]	0.4[0.3,0.5]	0.3[0.2,0.5]	0.3[0.2,0.5]	0.007	nonnorm
ALT, IU/L	17.0 [12.0, 27.0]	15.0 [11.0, 24.0]	18.0 [12.0, 28.0]	19.0 [13.0, 27.0]	17.0 [12.0, 28.0]	0.01	nonnorm
AST, IU/L	24.0 [18.0, 33.5]	23.0 [17.0, 32.0]	24.0 [19.0, 33.0]	24.0 [18.0, 35.0]	24.0 [18.0, 35.3]	0.27	nonnorm
Scr, mg/dL	0.8[0.7,1.0]	0.8[0.7,1.0]	0.8[0.7,1.0]	0.8[0.7,1.0]	0.9[0.7,1.1]	0.085	nonnorm
K^+, mEq/L	4.0 [3.7, 4.3]	4.0 [3.7, 4.3]	4.0 [3.8, 4.4]	4.0 [3.6, 4.3]	3.8 [3.6, 4.2]	< 0.001	nonnorm
Na^+, mEq/L	139.3[136.7,141.3]	139.4[136.3, 141.3]	138.8[136.4,141.0]	139.6[137.0,141.4]	139.4[137.3,141.4]	0.087	nonnorm
Albumin, g/dL	38.3 [35.1, 41.1]	37.7 [34.6, 40.6]	37.9 [35.2, 41.0]	38.5 [35.3, 41.7]	38.9 [35.2, 41.2]	0.051	nonnorm
BUN, mg/Dl	6.2 [4.8, 8.4]	5.9 [4.7, 7.5]	6.0 [4.7, 8.0]	6.3 [5.0, 8.5]	6.4 [4.7, 9.5]	0.037	nonnorm
Glucose, mg/dl	110.9 [90.2, 140.2]	88.9 [78.7, 104.4]	105.3 [89.5, 126.7]	118.3 [97.4, 139.5]	151.2[117.5,190.4]	< 0.001	nonnorm
Triglycerides, mg/dl	74.4 [58.5, 96.6]	54.9 [45.2, 63.8]	68.2 [56.7, 81.5]	85.0 [70.9, 104.5]	106.3 [85.0, 139.9]	< 0.001	nonnorm
TC, mg/dL	148.9 [125.3, 172.5]	143.5 [121.8, 163.2]	143.5 [120.3, 165.1]	155.8 [129.9, 175.6]	158.6 [133.8, 182.1]	< 0.001	nonnorm
LDL, mg/dL	84.0 [67.0, 101.6]	77.4[61.9,89.0]	81.3[65.8,96.8]	89.0[69.7,104.5]	92.9[73.5,112.2]	< 0.001	nonnorm
HDL, mg/dL	45.7 [37.5, 54.8]	46.4[38.7,58.1]	46.4[38.7,58.1]	42.6[38.7,54.2]	42.6[38.7,54.2]	0.007	nonnorm
APTT, sec	36.9 [34.3, 40.6]	38.2 [35.3, 42.0]	37.5 [34.6, 40.5]	36.3 [34.0, 40.4]	35.9 [33.5, 39.5]	< 0.001	nonnorm
PT, sec	13.5 [12.9, 14.2]	13.6 [13.0, 14.4]	13.5 [13.0, 14.3]	13.4 [12.8, 14.2]	13.3 [12.7, 14.1]	0.001	nonnorm
D-Dimer, ng/ml	700.0[380.0,1425.0]	625.0[310.0,1172.5]	720.0[400.0,1410.0]	760.0[422.5,1577.5]	785.0[387.5,1562.5]	0.004	nonnorm
TyG index	8.4 [8.0, 8.7]	7.8 [7.7, 8.0]	8.2 [8.1, 8.3]	8.5 [8.4, 8.6]	8.9 [8.8, 9.1]	< 0.001	nonnorm
PO_2, mmHg	80.0 [65.6, 106.1]	83.4 [68.0, 101.1]	84.7 [69.2, 112.6]	81.2 [64.5, 108.6]	74.5 [62.5, 95.4]	0.015	nonnorm
PCO_2, mmHg	51.1 [41.7, 66.8]	48.8 [41.8, 63.4]	50.9 [41.6, 66.0]	51.1 [42.1, 67.4]	54.7 [41.8, 69.7]	0.631	nonnorm
OI, mmHg	269.0 [211.0, 366.0]	277.0 [225.0, 372.0]	292.0 [229.0, 386.0]	250.0 [203.0, 350.0]	258.0 [202.0, 346.0]	0.071	nonnorm
Medicine							
Glucocorticoid, n(%)	742 (62.5)	171 (57.6)	173 (58.2)	193 (65.0)	205 (69.0)	0.009	
Bronchodilators,n(%)	976 (82.2)	250 (84.2)	240 (80.8)	247 (83.2)	239 (80.5)	0.578	
Antibiotic, n(%)	1137 (95.7)	287 (96.6)	284 (95.6)	280 (94.3)	286 (96.3)	0.502	

Table 2 (continued)

Categories	Overall (*N* = 1188)	Q1 (*N* = 297)	Q2 (*N* = 297)	Q3 (*N* = 297)	Q4 (*N* = 297)	*P*-value	Text
Usealbumin, n (%)	53 (4.5)	17 (5.7)	9 (3.0)	11 (3.7)	16 (5.4)	0.316	
Events							
LOS hospital, days	8.0 [6.0, 10.0]	8.0 [6.0, 10.0]	7.0 [6.0, 10.0]	8.0 [6.0, 10.0]	8.0 [6.0, 11.0]	0.236	
RF, n (%)	455 (38.3)	96 (32.3)	91 (30.6)	103 (34.7)	165 (55.6)	< 0.001	
Mechanicalventilation, n(%)	73 (6.1)	11 (3.7)	20 (6.7)	18 (6.1)	24 (8.1)	0.159	

TyG index: Q1 (≤ 8.038636, Q2 (8.038636 < TyG ≤ 8.371388), Q3 (8.371388 < TyG ≤ 8.702957), Q4 (> 8.702957)

Abbreviations: *BMI* Body Mass Index, *RTI* Respiratory tract infection, *CHD* Coronary heart disease, *HF* Heart failure, *DM* Diabetes mellitus, *WBC* White blood cell, *Lcell* Lymphocyte, *Ncell* Neutrophile granulocyte, *RBC* Red blood cell, *PLT* Platelet, *CRP* C-reactive protein, *HbA1c* Glycosylated hemoglobin, *Tbil* Total bilirubin, *Ibil* Indirect bilirubin, *ALT* Glutamic-pyruvic transaminase, *AST* Glutamic oxalacetic transaminase, *Scr* Serum creatinine, K^+ Potassium, *Na* + Sodium, *BUN* Blood urea nitrogen, *TC* Total cholesterol, *LDL* Low Density Lipoprotein, *HDL* High density lipoprotein, *APTT* Activated partial thromboplastin time, *PT* Prothrombin time, *TyG index* Triglyceride glucose index, PO_2 pressure of oxygen, PCO_2 Pressure of Carbon Dioxide, *OI* Oxygenation Index, *LOS* length of stay, *ICU* Intensive care unit, *RF* Respiratory failure, *HR* hazard ratio, *CI* confidence interval, *TyG index* Triglyceride glucose index

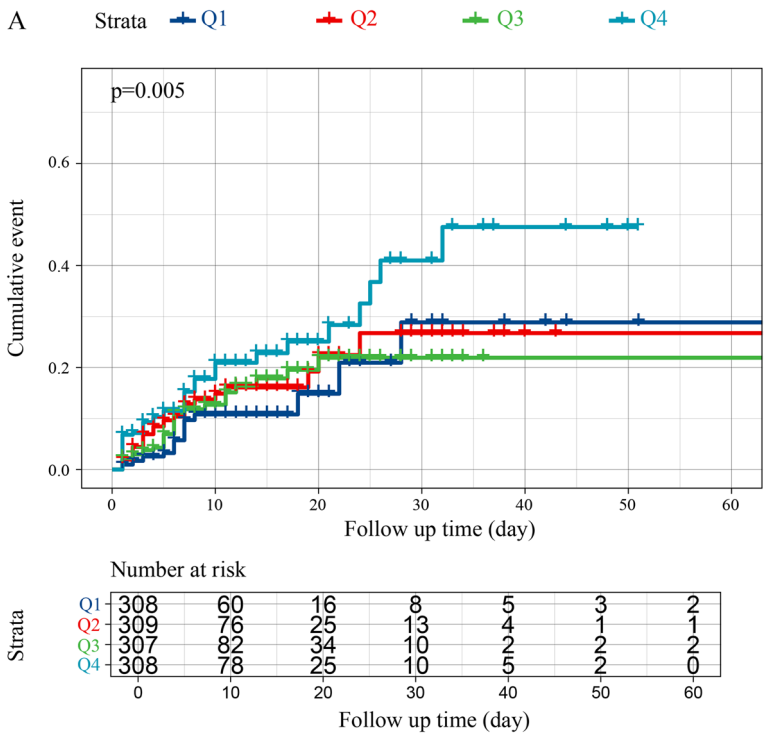

Fig. 2 Restricted cubic spline analysis of TyG index with respiratory failure incidence (Model 1, Model 2 and Model 3). HR: hazard ratio, CI: confidence interval, TyG index: Triglyceride-glucose index. Heavy central lines represent the estimated adjusted hazard ratios, with shaded ribbons denoting 95% confidence intervals. TyG index 8.765 was selected as the reference level represented by the vertical dotted lines in model 1and model 2, TyG index 8.580 was selected as the reference level represented by the vertical dotted lines in model 3. The horizontal dotted lines represent the hazard ratio of 1.0

Q1 group (Model 1: HR, 1.598 [95% CI 1.241–2.058], P < 0.001; Model 2: HR, 1.611 [95% CI 1.250–2.077], P < 0.001; Model 3: HR, 1.911 [95% CI 1.445–2.526], P < 0.001).

The RCS curves indicated a nearly linear relationship between the TyG index and the RF risk in COPD patients across all models (Fig. 3) (Model 1: P-non-linear = 0.209), Model 2: P-non-linear = 0.219, Model 3: P-non-linear = 0.074). Furthermore, heightened levels of the TyG index (TyG index > 8.765 in Model 1 and Model 2, TyG index > 8.580 in Model 3) were positively associated with the RF risk in COPD patients. It is noteworthy that the majority of RF patients had a TyG index of 8 to 10.

The logistic regression analysis unveiled a conspicuous link between the TyG index and the utilization of invasive

Table 3 Cox regression analysis for TyG index with respiratory failure in MIMIC database

Categories	Events (%)	Model 1		Model 2		Model 3	
		HR [95%CI]	*P*-value	HR [95%CI]	*P*-value	HR [95%CI]	*P*-value
Incidence of respiratory failure							
Continuous variable per 1 unit	134 (10.9)	1.561 [1.219–2.000]	< 0.001	1.632 [1.263–2.107]	< 0.001	1.821 [1.349–2.459]	< 0.001
Quartile[a]		*p*-value: 0.004		*p*-value: 0.001		*p*-value: < 0.001	
Q1 (*N* = 308)	19 (6.2)	Ref		Ref		Ref	
Q2 (*N* = 309)	34 (11.0)	1.638 [0.934–2.873]	0.085	1.674 [0.954–2.939]	0.073	2.372 [1.317–4.273]	0.004
Q3 (*N* = 307)	32 (10.4)	1.405 [0.795–2.480]	0.242	1.481 [0.836–2.625]	0.178	1.853 [1.017–3.376]	0.044
Q4 (*N* = 308)	49 (15.9)	2.400 [1.413–4.078]	0.001	2.551 [1.485–4.381]	< 0.001	3.510 [1.885–6.535]	< 0.001

Model 1: unadjusted

Model 2: adjusted for Age, Gender, BMI

Model 3: adjusted for Age, Gender, BMI, Cerebrovascular disease, Coronary heart disease, Heart failure, Diabetes mellitus, Hypertension, Asthma, use Bronchodilators, use Glucocorticoid, use Antibiotic, Albumin, High Density Lipoprotein, Low Density Lipoprotein, Total cholesterol, Activated partial thromboplastin time, Blood urea nitrogen, Potassium, Sodium, Glycosylated Hemoglobin, Type A1C

HR hazard ratio, *CI* confidence interval, *TyG index* Triglyceride glucose index

[a] TyG index: Q1 (≤ 8.408048, Q2 (8.408048 < TyG ≤ 8.759355), Q3 (8.759355 < TyG ≤ 9.205240), Q4 (> 9.205240)

Table 4 Cox regression analysis for TyG index with respiratory failure in Chinese cohort

Categories	Events (%)	Model 1		Model 2		Model 3	
		HR [95%CI]	*P*-value	HR [95%CI]	*P*-value	HR [95%CI]	*P*-value
Incidence of respiratory failure							
Continuous variable per 1 unit	341 (28.7)	1.568 [1.350–1.822]	< 0.001	1.581 [1.362–1.836]	< 0.001	1.786 [1.513–2.108]	< 0.001
Quartile[a]		*p*-value: < 0.001		*p*-value: < 0.001		*p*-value: < 0.001	
Q1 (*N* = 297)	94 (31.6)	Ref		Ref		Ref	
Q2 (*N* = 297)	79 (26.6)	0.797 [0.596–1.065]	0.125	0.796 [0.594–1.066]	0.125	0.833 [0.620–1.120]	0.226
Q3 (*N* = 297)	86 (29.0)	1.064 [0.805–1.406]	0.663	1.026 [0.775–1.358]	0.857	1.102 [0.822–1.478]	0.514
Q4 (*N* = 297)	82 (27.6)	1.598 [1.241–2.058]	< 0.001	1.611 [1.250–2.077]	< 0.001	1.911 [1.445–2.526]	< 0.001

Model 1: unadjusted

Model 2: adjusted for Age, Gender, BMI

Model 3: adjusted for Age, Gender, BMI, Coronary heart disease, Heart failure, Diabetes mellitus, Hypertension, Asthma, use Bronchodilators, use Glucocorticoid, use Antibiotic, Albumin, High Density Lipoprotein, Low Density Lipoprotein, Total cholesterol, Activated partial thromboplastin time, Blood urea nitrogen, Potassium, Sodium, Glycosylated Hemoglobin, Type A1C

HR hazard ratio, *CI* confidence interval, *TyG index* Triglyceride glucose index, *Ref.* reference

[a] TyG index: Q1 (≤ 8.038636, Q2 (8.038636 < TyG ≤ 8.371388), Q3 (8.371388 < TyG ≤ 8.702957), Q4 (> 8.702957)

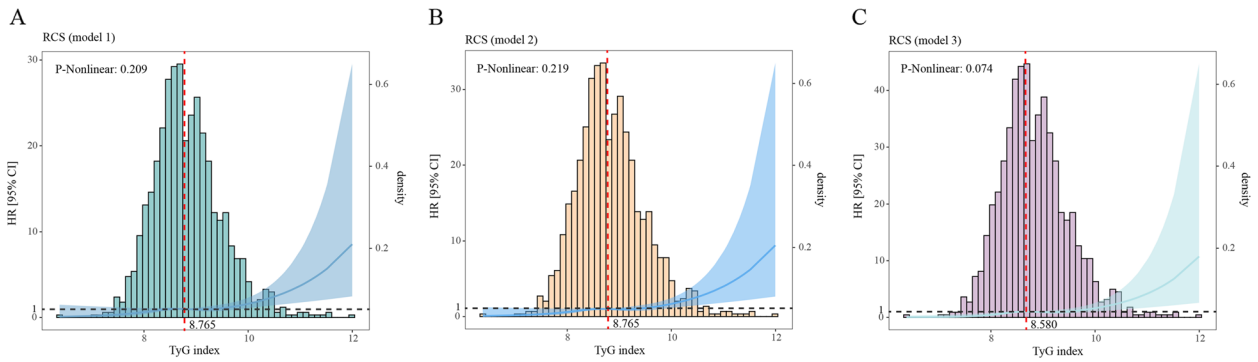

Fig. 3 Cumulative event rate analysis curves for respiratory failure. TyG index: Q1 (≤ 8.408048, Q2 (8.408048 < TyG ≤ 8.759355), Q3 (8.759355 < TyG ≤ 9.205240), Q4 (> 9.205240)

Table 5 Logistics regression analysis for TyG index with invasive mechanical ventilation

Categories	Events (%)	Model 1		Model 2		Model 3	
		OR [95%CI]	*P*-value	OR [95%CI]	*P*-value	OR [95%CI]	*P*-value
Whether using mechanical ventilate							
Continuous variable per 1 unit	88(7.1)	1.665[1.227, 2.243]	< 0.001	1.629[1.177, 2.244]	0.003	1.611[1.086, 2.392]	0.018
Quartile[a]							
Q1 (*N* = 308)	14(4.5)	Ref		Ref		Ref	
Q2 (*N* = 309)	16(5.2)	1.147[0.549, 2.423]	0.715	1.121[0.534, 2.379]	0.762	1.183[0.546, 2.592]	0.670
Q3 (*N* = 307)	19(6.2)	1.385[0.685, 2.867]	0.368	1.35[0.663, 2.812]	0.411	1.266[0.593, 2.758]	0.544
Q4 (*N* = 308)	39(12.7)	3.045[1.655, 5.921]	< 0.001	2.802[1.494, 5.539]	0.002	2.887[1.38, 6.315]	0.006

Model 1: unadjusted

Model 2: adjusted for Age, Gender, BMI

Model 3: adjusted for Age, Gender, BMI, Cerebrovascular disease, Coronary heart disease, Heart failure, Diabetes mellitus, Hypertension, Asthma, use Bronchodilators, use Glucocorticoid, use Antibiotic, Albumin, High Density Lipoprotein, Low Density Lipoprotein, Total cholesterol, Activated partial thromboplastin time, Blood urea nitrogen, Potassium, Sodium, Glycosylated Hemoglobin, Type A1C

HR hazard ratio, *CI* confidence interval, *TyG index* Triglyceride glucose index

[a] TyG index: Q1 (≤ 8.408048, Q2 (8.408048 < TyG ≤ 8.759355), Q3 (8.759355 < TyG ≤ 9.205240), Q4 (> 9.205240)

Table 6 Linear regression analysis for TyG index with Days in hospital

Categories	Model 1		Model 2		Model 3	
	Beta [95% CI]	*P*-value	Beta [95% CI]	*P*-value	Beta [95% CI]	*P*-value
Days in hospital						
Continuous variable per 1 unit	0.922[0.066, 1.777]	0.035	0.962[0.081, 1.842]	0.033	0.972[0.104, 1.840]	0.028
Quartile[a]						
Q1 (*N* = 308)	Ref		Ref		Ref	
Q2 (*N* = 309)	1.146[−0.452, 2.745]	0.200	1.007[−0.577, 2.591]	0.200	0.727[0.646, 2.099]	0.300
Q3 (*N* = 307)	1.830[0.229, 3.431]	0.025	1.872[0.280, 3.463]	0.021	1.477[0.070, 2.884]	0.040
Q4 (*N* = 308)	1.779[0.179, 3.379]	0.029	1.777[0.154, 3.400]	0.032	1.642 [0.073, 3.212]	0.041

Model 1: unadjusted

Model 2: adjusted for Age, Gender, BMI

Model 3: adjusted for Age, Gender, BMI, Cerebrovascular disease, Coronary heart disease, Heart failure, Diabetes mellitus, Hypertension, Asthma, use Bronchodilators, use Glucocorticoid, use Antibiotic, Albumin, High Density Lipoprotein, Low Density Lipoprotein, Total cholesterol, Activated partial thromboplastin time, Blood urea nitrogen, Potassium, Sodium, Glycosylated Hemoglobin, Type A1C

HR hazard ratio, *CI* confidence interval, *TyG index* Triglyceride glucose index

[a] TyG index: Q1 (≤ 8.408048, Q2 (8.408048 < TyG ≤ 8.759355), Q3 (8.759355 < TyG ≤ 9.205240), Q4 (> 9.205240)

mechanical ventilation (Table 5) (Model 1: OR, 1.665[95% CI 1.227, 2.243], P < 0.001; Model 3: OR, 1.611[95% CI 1.086, 2.392], P = 0.018). Moreover, elevated levels of the TyG index were linked to a heightened frequency of invasive mechanical ventilation use (Model 1: OR, 3.045[95% CI 1.655, 5.921], P < 0.001; Model 2: OR, 2.802[95% CI 1.494, 5.539], P = 0.002; Model 3: OR, 2.887[95% CI 1.38, 6.315], P = 0.006). It is notable that each incremental unit in the TyG index was linked to a 1.611-fold elevated risk of invasive mechanical ventilation use (OR,1.611[95% CI 1.086, 2.392], P = 0.018)]).

The multiple linear regression implied a positive relationship between the TyG index and the duration of hospitalization (Table 6) (Model 1: Beta, 0.922[95% CI 0.066, 1.777], P = 0.035; Model 3: Beta, 0.972[95% CI 0.104, 1.840], P = 0.028). Furthermore, in Models 1, 2, and 3, heightened TyG index levels were also markedly linked to prolonged hospital stay (Model 1: Beta, 1.779[95% CI 0.179, 3.379], P = 0.029; Model 2: Beta, 1.777[95% CI 0.154, 3.400], P = 0.032; Model 3: Beta, 1.642 [95% CI 0.073, 3.212], P = 0.041).

Subgroup analysis

Subgroup analysis was executed by gender, age (< 60 years and ≥ 60 years), and the presence or absence of diabetes, hypertension, heart failure, cirrhosis, sepsis,

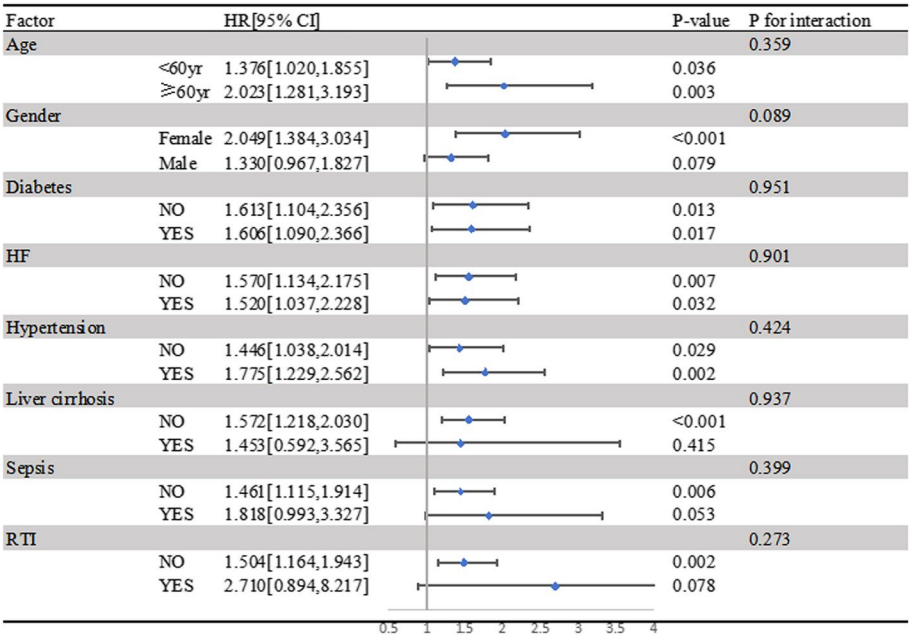

Fig. 4 Subgroup analysis of the relationship between TyG index and respiratory failure. *HR* hazard ratio, *CI* confidence interval, *TyG index* Triglyceride-glucose index, *HF* Heart Failure, *RTI* Respiratory tract infection

and respiratory tract infection Fig. 4). The results indicated that an elevated continuous TyG index was markedly linked to an increased RF risk in most subgroups, we also calculated the hazard ratio (HR) and confidence intervals (per one unit of TyG index), such as patients under the age of 60 years [HR(95% CI) 1.376(1.020–1.855)], patients aged 60 years and above [HR(95% CI) 2.023(1.281–3.193)], females [HR (95% CI) 2.049(1.384–3.034)], patients with diabetes [HR(95% CI) 1.606(1.090–2.366), patients without diabetes [HR (95% CI) 1.613(1.104–2.356)], patients without HF [HR(95% CI) 1.570(1.134–2.175)], patients with HF [HR(95% CI) 1.520(1.037–2.228)], patients without hypertension [HR(95% CI) 1.446(1.038–2.014)], patients with hypertension [HR(95% CI) 1.775(1.229–2.562)], patients without liver cirrhosis [HR (95% CI) 1.572(1.218–2.030)], patients without sepsis [HR(95% CI) 1.461(1.115–1.914)], patients without RTI [HR (95% CI)1.504(1.164–1.943)] ($P < 0.05$). Interaction analysis revealed that except for gender, which suggested an interaction (P for interaction = 0.089), the differences in effects among the various subgroups were not statistically significant (P for interaction > 0.1).

Discussion

The present study firstly probes into the link between the TyG index and the risk of RF in patients with COPD. The data on patients were acquired from the MIMIC-IV 2.2 database, and 1232 COPD patients were eligible and included. The substantial sample size has the potential to enhance the generalizability of these findings. Our analysis results unequivocally indicate that elevated TyG index levels serve as independent risk factors for RF in COPD patients. Besides, a direct association is noted between higher TyG index levels and an augmented risk of RF, as well as increased utilization of invasive mechanical ventilation, prolonged hospitalization. The cumulative incidence curves further corroborate that individuals with heightened TyG index values face a heightened risk of RF, thereby underscoring the clinical significance of a high TyG index in predicting the likelihood of RF occurrence in COPD patients. Furthermore,we performed external validation of the primary outcome Cox model, which yielded similar results.

In previous research, Wang et al. noted that the TyG index is associated with poor prognostic outcomes, such as hospital and ICU mortality, in patients with acute exacerbations of COPD [20]. Similarly, Zhou et al. reached a similar conclusion, showing a significant association between the TyG index and all-cause mortality in patients with asthma and COPD [21]. In our study, Cox proportional hazard model analysis clearly demonstrates that a high TyG index is an independent risk factor for respiratory failure in COPD patients, even after adjusting for confounding factors. This finding is consistent with and reinforces the results from earlier studies.

The relationship between the TyG index and the risk of RF in COPD patients is still not fully understood.

The TyG index is a reliable biomarker for insulin resistance (IR), which may be its primary mechanism. Previous studies have shown a high prevalence of IR in individuals with chronic obstructive pulmonary disease (COPD) [22], with more severe breathlessness [23] and a higher incidence of poor prognostic outcomes [24] in those who have IR. Elevated insulin levels induced by IR have been implicated in triggering laminin expression in airway smooth muscle through phosphatidylinositol 3 kinase (PI3K) and Rho-kinase dependent pathways. This, in turn, leads to heightened contraction of airway smooth muscle [25]. Moreover, increased insulin levels can provoke vagus nerve-mediated bronchoconstriction and the impairment of parasympathetic inhibitory muscarinic receptor 2 function [26, 27]. These effects lead to diminished lung function, which worsens the condition of COPD patients and ultimately results in respiratory failure. Furthermore, oxidative stress and inflammation are considered key factors in the progression of COPD. Studies have shown a persistent inflammatory response in the airways and lungs of COPD patients, which is closely linked to oxidative stress [28]. The increased levels of reactive oxygen species exceed the body's antioxidant defenses, causing cellular damage and dysfunction [29]. In the context of COPD pathophysiology, oxidative stress not only intensifies the inflammatory response but may also contribute to airway remodeling and a decline in lung function, thus highlighting its critical role in the disease's progression [30]. Prior research has also indicated that elevated blood glucose levels result in elevated glucose content and advanced glycation end products (AGEs) in airway secretions, thereby fostering local inflammation, respiratory tract infections, and consequent impairment of lung function [31, 32]. Elevated triglyceride levels can incite inflammatory responses in macrophages and various immune cells [33]. The TyG index, serving as a dependable biomarker for IR, integrates both glucose, reflecting hepatic IR, and triglyceride, indicating adipocyte IR. Consequently, it provides a more comprehensive representation of the interplay between IR and COPD patients.

An extended hospital stay may elevate the risk of complications like nosocomial infections, deep vein thrombosis, and pressure sores, potentially impacting a patient's rehabilitation progress [34]. Additionally, the duration of hospitalization can serve as an indirect indicator of disease severity. Hence, we examined the link between TyG index and hospital stay. Our findings indicated that the hospital stay were prolonged in tandem with higher TyG index levels. As a result, we surmised that the TyG index level might be employed to forecast the duration of hospitalization in COPD patients. This finding assists in early detection of COPD patients, and individuals with a high TyG index should be given additional care upon admission, in order to enhance disease management, reduce hospital stay, and prevent complications associated with prolonged hospitalization. Drawing from previous studies, the use of invasive mechanical ventilation has been associated with increased exacerbations in COPD patients [35], while noninvasive assisted ventilation has significantly reduced mortality in acute exacerbation of COPD (AECOPD) [36]. Therefore, pinpointing the indications for invasive mechanical ventilation and minimizing unnecessary usage can potentially enhance the prognosis for COPD patients. Our study discovered a significant increase in invasive mechanical ventilation usage in individuals with high TyG index levels. Consequently, for patients with elevated TyG index, optimizing the respiratory support treatment strategy and using non-invasive ventilation, instead of invasive treatment, can effectively reduce exacerbations and enhance the prognosis for COPD patients.

According to the baseline characteristics of COPD patients enrolled in the present study, younger patients tend to have higher TyG index levels, aligning with prior research findings [37]. This underscores the importance of focusing on the younger COPD population, as they might be at a heightened risk for developing RF. Additionally, we uncovered that patients with RF exhibited elevated levels of white blood cells (WBC), neutrophils, and C-reactive protein (CRP), further underscoring the role of the inflammatory response in the progression of COPD. We also observed that the BMI of the study population in the MIMIC database was notably higher than that in the Chinese cohort, which can be ascribed to several factors. Research has indicated that the American diet is characterized by a higher proportion of high-fat, high-sugar, and high-calorie foods, largely due to the widespread fast food culture, resulting in excessive calorie intake and an elevated risk of obesity [38]. In contrast, the traditional Chinese diet primarily consists of rice, vegetables, and legumes, with relatively lower meat consumption [39]. Furthermore, a sedentary lifestyle and insufficient physical activity are common in the United States [40]. Although China is experiencing lifestyle changes due to urbanization, the overall level of physical activity remains higher in comparison [41]. Additionally, there may be variations in the carrier frequency of obesity-related genes between the two populations [42], which could further contribute to the significant BMI difference.

Nonetheless, this study has several limitations. Firstly, our research did not encompass data related to lifestyle, nutritional status, and the use of antidiabetic or lipid-lowering medications. These factors could potentially influence the baseline TyG levels. Secondly,

it's important to acknowledge that this is a retrospective study, retrospective data may be subject to selection bias, and the quality and completeness of the data cannot be intervened or controlled, making it susceptible to statistical issues like selection bias and limited control of confounding variables. Third, there are variations in BMI and other characteristics between the study populations in the Chinese cohort and the MIMIC cohort. Consequently, the generalizability of the findings from this study may be limited when applied to different populations. In conclusion, the TyG index holds promise as an effective biomarker for predicting RF in COPD patients, with potential clinical utility. However, its validity still needs to be verified by prospective and multicenter investigations.

Conclusion

The TyG index can forecast the RF risk in COPD patients to some extent. Individuals with elevated TyG index levels tend to face a higher risk of RF. Additionally, it serves as an indicator for increased usage of invasive mechanical ventilation, and extended stays in the hospital. Our results unveil that TyG index is correlated with the risk of RF in COPD patients, and it is worthy of further exploration and practical application in clinical settings. Further studies are desired to investigate whether reducing TyG index levels can mitigate the risk of RF in COPD patients, and whether the TyG index can be integrated into the comprehensive evaluation of COPD.

Abbreviations

TyG	Triglyceride-Glucose
RF	Respiratory failure
COPD	Chronic obstructive pulmonary disease
RCS	Restricted cubic spline
QUICKI	Quantitative Insulin Sensitivity Test Index
BIDMC	Beth Israel Deaconess Medical Center

Supplementary Information

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Supplementary Material 1: Table S1. Baseline comparison between the database population and the Chinese cohort population.

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Authors' contributions

Conceptualization: SH, YZ(2), ZC. Data curation: SH, YZ(2), ZC. Formal analysis: SH, WC. Funding acquisition: SH. Investigation: XT, JW. Methodology: XT, WC. Project administration: XT. Resources: XT, WC. Software: YZ(1), JW. Supervision: YZ(1), ZC,YZ(2). Validation: YZ, WC.Visualization: YZ(1). Writing -original draft: SH, XT, YZ(1), YZ(2), JW, WC. Writing-review & editing: SH, XT, YZ(1), YZ(2), JW, WC.

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Data availability

This retrospective investigation utilized data extracted from the Medical Information Mart for Intensive Care (MIMIC-IV version 2.2) (https://physionet.org/content/mimiciv/2.2/).

Declarations

Ethics approval and consent to participate

Ethical approval for the external validation participants was obtained from our institution (Ethical Approval No. 2023-KY-607).

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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