Head-to-Head Comparison of the Ability of the Cardiometabolic Index and Triglyceride–Glucose Index to Predict 3-Year Major Adverse Cardiovascular Events in Patients with Atrial Fibrillation: Insights from a Community Cohort

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WORD COUNT 10526
TIME SUBMITTED 20-DEC-2025 05:51AM
PAPER ID 119579707

Title Page

Full Title:

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Total Word Count:

10327 words

Abstract

Background: Atrial fibrillation (AF) represents the most common sustained cardiac arrhythmia and confers an elevated risk of major adverse cardiovascular events (MACEs). Emerging evidence indicates that metabolic dysregulation substantially influences the AF prognosis. The cardiometabolic index (CMI) and triglyceride–glucose (TyG) index are non-insulin-dependent surrogate markers of metabolic dysfunction that are readily obtainable in clinical practice. However, their comparative prognostic value for predicting MACEs in patients with AF has not been previously evaluated within the same cohort.

Methods: This retrospective single-center cohort study enrolled 380 AF patients who received treatment at the Shanghai Jinyang Community Health Center between January 2022 and June 2025, with a maximum follow-up duration of 3 years. CMI and TyG were calculated from routinely collected baseline clinical and laboratory data. MACEs served as the primary endpoint. Predictive performance was examined using adjusted Cox regression with restricted cubic spline (RCS) to assess potential nonlinearity, along with Kaplan–Meier survival curves, discrimination analysis using receiver operating characteristic (ROC) curves-based discrimination, machine-learning approaches, and subgroup interaction testing. Incremental predictive benefit over the CHA2DS2-VASc score was further evaluated.

Results: A total of 53 patients (13.9%) experienced MACEs during follow-up. Baseline CMI and TyG values were statistically higher among patients with events

(both $P < 0.01$). In multivariable Cox regression analyses, elevated CMI (hazard ratio [HR], 3.25; 95% confidence interval [CI], 1.89–5.58) and elevated TyG index (HR, 4.52; 95% CI, 1.83–11.12) emerged as independent predictors of MACEs. RCS analyses revealed nonlinear associations, with threshold effects at a CMI ≈ 0.85 and TyG index ≈ 9.02. Its predictive ability was further supported by Kaplan–Meier and ROC curve analyses. Machine learning models, particularly extreme gradient boosting (XGBoost), demonstrated increased discrimination (area under the curve [AUC] reaching 0.93). Subgroup analyses revealed enhanced predictive performance in patients without heart failure, coronary artery disease, or diabetes, as well as in individuals aged ≥65 years. Incorporation of either CMI or TyG index into the CHA2DS2-VASc score yielded significant improvements in predictive accuracy, whereas adding both indices did not provide an additional benefit.

Conclusions: CMI and the TyG index function as robust, independent predictors of 3-year MACEs in patients with atrial fibrillation, and may help identify metabolically impaired individuals who are not adequately captured by conventional risk scores. The TyG index, in particular, offers strong predictive accuracy combined with ease of measurement from routine laboratory tests, making it widely accessible across diverse health care settings. These simple, cost-effective indices enable the prompt recognition of high-risk patients and facilitate timely initiation of preventive interventions to reduce cardiovascular morbidity and mortality, serving as practical adjuncts to the CHA2DS2-VASc score for more precise risk stratification and personalized management of AF.

Keywords: Atrial Fibrillation; Cardiovascular Diseases; Risk Assessment; Insulin Resistance; Triglycerides; Blood Glucose

Introduction

Worldwide, atrial fibrillation (AF) represents a major arrhythmic disorder, with a growing incidence attributable to demographic ageing and the expanding burden of cardiovascular risk factors [1,2]. AF is estimated to be present in roughly 2–4% of the adult population and is associated with elevated risks of stroke, heart failure, and all-cause mortality [3-5]. When metabolic disturbances coexist with other cardiovascular conditions, long-term outcomes tend to deteriorate, accompanied by an elevated incidence of major adverse cardiovascular events (MACEs) and a considerable impact on healthcare utilization and societal costs [6,7].

An increasing body of literature supports a close link between metabolic disturbances and the onset, progression, and complication risk of AF [8]. Central obesity, dyslipidaemia, and insulin resistance (IR) contribute to atrial structural and electrical remodelling, exacerbate cardiac dysfunction, and increase the thromboembolic risk through multiple pathophysiological mechanisms [9]. As a key feature of metabolic syndrome, IR serves as an established driver of cardiovascular disease and may contribute to cardiovascular impairment via reduced nitric oxide bioavailability with consequent endothelial dysfunction, aberrant activation of the renin–angiotensin system, and persistent low-grade inflammation [10,11]. Dysregulation of glucose and lipid handling may further intensify oxidative stress, compromise mitochondrial

integrity, and perturb calcium homeostasis, thereby impairing myocardial performance [12,13]. Notably, AF may also exacerbate IR, creating a bidirectional and self-reinforcing pathological cycle.

Although the hyperinsulinaemic–euglycaemic clamp method remains the reference standard for assessing IR, its technical demands, time-consuming nature, and substantial expense restrict its feasibility for routine clinical settings. Accordingly, non-insulin-based surrogate markers derived from glucose and lipid profiles have garnered increasing attention because of their simplicity, cost-effectiveness, and broad applicability. The cardiometabolic index (CMI), computed from the ratio of triglyceride to high-density lipoprotein cholesterol and waist circumference, offers an integrated evaluation of central adiposity and dyslipidaemia. The triglyceride–glucose (TyG) index, calculated from fasting glucose and triglyceride concentrations, demonstrate strong association with insulin resistance and reflects disturbances in both glucose and lipid metabolism. Both indices have been linked to elevated cardiovascular event risk in general populations and among individuals with established cardiovascular disease [14-16].

Although the CMI and TyG index share certain overlapping components, they differ in their underlying metabolic implications: the CMI primarily reflects disordered lipid metabolism and central adiposity, while the TyG index reflects broader disturbances spanning both glucose and lipid pathways [17,18]. These distinctions may lead to differential performance for predicting MACEs in patients with AF. However, direct

comparisons of these two indices in predicting medium- to long-term MACEs in AF patients—particularly within the same cohort—remain scarce. This evidence gap limits clinicians' ability to optimize risk assessment and deliver tailored preventive strategies for this vulnerable patient group.

This study evaluated and contrasted the predictive value of CMI and TyG index in forecasting 3-year MACEs among patients with AF using data from a real-world retrospective cohort. It further seeks to evaluate the potential utility of these indices for a midterm prognostic assessment. By systematically assessing their predictive performance, this study introduces a simple, cost-effective, and clinically applicable tool for cardiovascular risk stratification, thereby supporting individualized management and advancing precision prevention strategies in AF care.

Despite the accumulating evidence linking metabolic dysfunction to the cardiovascular risk, prior research has not undertaken a head-to-head comparison of CMI and TyG index prognostic capabilities within the same AF cohort, nor has their incremental value beyond established risk scores, such as CHA2DS2-VASc, been systematically evaluated. The study hypothesized that both CMI and TyG would independently predict 3-year MACEs in patients with AF, albeit with potentially differing predictive strengths reflecting their distinct metabolic constructs—CMI integrating central adiposity and dyslipidaemia, and TyG capturing glucose–lipid dysregulation.

Accordingly, the present study aims to (1) provide the first head-to-head comparison of the CMI and TyG index for predicting MACEs in patients with AF; (2) identify clinically relevant threshold values and dose–response relationships using restricted cubic spline modelling; (3) evaluate their performance across predefined, clinically relevant subgroups; and (4) determine their incremental predictive utility when added to the CHA2DS2-VASc score. To fill these gaps, the present study focuses on readily obtainable and inexpensive metabolic biomarkers, aiming to improve individualized cardiovascular risk assessment and facilitate precision-oriented preventive strategies for patients with AF.

Methods

Study population

A single-center retrospective cohort study was established at the Shanghai Jingyang Community Health Service Cente, including AF patients enrolled in a chronic disease monitoring program from January 2022 to June 2025. Eligibility screening was conducted consecutively for all AF referrals during this interval. Most participants originated from the Department of Cardiology at Shanghai Renji Hospital before being incorporated into a community-level high-risk population surveillance system operating within a regional medical consortium. All enrolled individuals received standardized clinical evaluation and routine laboratory testing.

Standardized clinical evaluation and laboratory testing were performed for all candidates. Inclusion required age ≥18 years, documented atrial fibrillation meeting European Society of Cardiology diagnostic criteria, and engagement in follow-up management [19]. Patients were excluded if AF criteria were not met; if follow-up was discontinued or no valid follow-up record was available; if moderate-to-severe valvular pathology existed, valve replacement surgery had occurred, or congenital heart disease surgery had been undertaken; if active malignancy existed; or if key lipid measurements needed to derive CMI or the TyG index were unavailable (baseline triglyceride [TG] and/or high-density lipoprotein cholesterol [HDL-C] levels). Overall, 475 patients were screened; 36 were removed because withdrawal or absence of a valid follow-up visit, yielding 439 patients with follow-up data. Subsequent exclusions comprised moderate-to-severe valvular disease (n=17), active malignancy (n=19), and missing baseline TG or HDL-C measurements (n=23). The remaining 380 patients with complete baseline data and confirmed 3-year MACE ascertainment constituted the analytic cohort (Figure 1). Comprehensive clinical, laboratory, and echocardiographic data were collected for these 380 participants. For excluded individuals, only minimal information (AF diagnosis and the specific reason for exclusion) was recorded, and a complete baseline dataset was not available in a consistent format.

Ethical approval for this human-participant study was granted by the Ethics Committee of Renji Hospital, Shanghai Jiao Tong University School of Medicine (Approval No. KY2022-105-B). The study was conducted in accordance with the

Helsinki Declaration and applicable institutional and national regulations. Owing to the retrospective design and utilization of existing medical records, written informed consent was not sought; individual consent requirements were waived by the Ethics Committee as the study posed minimal risk and was considered to have potential scientific and clinical value. Participant confidentiality was safeguarded through data anonymization and secure data management protocols.

Basic data collection

Electronic health records from Shanghai Jinyang Community Health Service Center were used to capture baseline characteristics. Demographic and anthropometric data (sex, age, body mass index (BMI), weight, height, waist circumference, and hip circumference) were collected, together with comorbidity history (prior stroke, hypertension, coronary artery disease (CAD), chronic kidney disease (CKD), heart failure, and diabetes mellitus). Information on treatment exposure included anticoagulation status. Laboratory indices were also retrieved. Collected laboratory data comprised high-density lipoprotein cholesterol (HDL-C) ,fasting plasma glucose (FPG), triglycerides (TG), glycated haemoglobin (HbA1c), serum creatinine, haematocrit, and platelet count. Creatinine level, haematocrit, and platelet count were retrieved as routine laboratory indices. Cardiac structure and function were assessed by echocardiography, including left ventricular ejection fraction (LVEF) alongside left atrial anteroposterior diameter (LAID). AF classification and CHA2DS2-VASc score were recorded. The endpoint of interest was the occurrence of MACEs,

operationalized as a composite outcome consisting of cardiovascular death, hospitalization for deteriorating heart failure, nonfatal stroke, nonfatal myocardial infarction, as well as coronary revascularization procedures for unstable angina and other ischaemic manifestations. The observation interval spanned from cohort entry to the earliest of a first MACE or completion of the observation period. Two cardiologists performed independent data abstraction, with a third reviewer resolving discrepant entries to maintain dataset quality.

Formulas used to calculate the CMI and TyG index

TyG = Ln [blood triglyceride (mg/ dL) × blood glucose (mg/dL)/2].

CMI = waist-to-height ratio (WHtR) × (TG [mmol/L]/HDL-C [mmol/L]), WHtR = waist circumference (cm)/height (cm).

Statistical analyses

All analyses were conducted using Python (version 3.11.8; Jupyter Notebook) and R (version 4.4.2), with commonly used data-analysis libraries (e.g., NumPy and pandas). Statistical tests were two-tailed. Statistical significance was defined as P <0.05, while P <0.01 was interpreted as strong evidence of significance. Before model construction, data quality control procedures were applied, including variable selection, imputation or exclusion of missing data, and an assessment of variable distributions. Variables with a missing rate exceeding 10% were excluded from subsequent analyses. Normality of continuous variables was evaluated with the Shapiro–Wilk test.

Variables approximating a normal distribution are summarized as mean ± standard deviation and analyzed between groups via one-way analysis of variance. Variables deviating from normality are expressed as median (interquartile range) and analyzed via the Kruskal–Wallis H test. Categorical data are presented as number (percentage), and between-group comparisons were performed using the χ^2 test or Fisher's exact test when appropriate, based on sample size and expected cell frequencies.

Baseline profiles were contrasted between patients with and without MACEs. The prognostic contributions of CMI and the TyG index were subsequently examined as continuous predictors using Cox proportional hazards regression, with hazard estimates derived for their independent relationships with 3-year MACE risk. CMI and TyG index served as the principal exposure variables in this investigation. A series of hierarchical Cox proportional hazards models were constructed to examine their relationships with 3-year MACEs while accounting for potential confounding factors. Associations were examined using sequentially adjusted Cox models. The initial model included only the index of interest (CMI or TyG) to provide crude hazard estimates for MACEs. A second model added age and sex to account for demographic differences. The fully adjusted model additionally included body mass index, major comorbid conditions (hypertension, diabetes mellitus, coronary artery disease, heart failure, prior stroke, and chronic kidney disease), haemoglobin A1c, platelet count, serum creatinine, left ventricular ejection fraction, left atrial internal diameter, and oral anticoagulants. Covariates were prespecified based on prior evidence, their established relevance to AF and cardiometabolic research, and

biological plausibility. The rationale for covariate selection is summarized in Supplementary Table S1. This hierarchical modelling strategy enabled an assessment of the crude association, adjustment for basic demographic confounding, and estimation of the association after controlling for a comprehensive set of potential confounders while avoiding data-driven overfitting. [23] The proportional hazards assumption for all Cox models was evaluated using tests of scaled Schoenfeld residuals for each covariate and for the global model ([33] cox.zph function in R), along with a visual inspection of log–log survival curves for quartiles of the TyG index and CMI (Supplementary Figure S1). Model [36] discrimination was quantified using Harrell's concordance index (C-index), and [46] overall model fit was further assessed using likelihood ratio chi-square statistics from the Cox models. As a sensitivity analysis assess the potential impact of unmeasured confounding, E values were computed for the fully adjusted associations between the CMI, the TyG index, and 3-year MACEs; detailed estimates are presented in Supplementary Table S2. Multicollinearity among covariates was assessed using variance inflation factors, and the results are provided in Supplementary Table S3. [3] Hazard ratios (HRs) with corresponding 95% confidence intervals (CIs) were used to express effect estimates, with detailed results provided in Supplementary Table S3. Potential nonlinear relationships between continuous CMI/TyG values and MACE risk were assessed using restricted cubic spline (RCS) modeling. Corresponding dose–response curves were derived, and tests for linear and non-linear trends were conducted.

To support categorical risk stratification, both CMI and the TyG index were divided into tertiles, with the lowest tertile used as the reference category. Cox proportional hazards regression was then applied to estimate associations across tertile strata, using the same three-stage covariate-adjustment scheme as in the analyses treating the indices as continuous variables. Effect estimates are presented as HRs with corresponding 95% CIs. For time-to-event visualization, Kaplan–Meier methods were used to display cumulative MACE incidence across tertiles of CMI and the TyG index, with between-group comparisons performed using the log-rank test. Receiver operating characteristic (ROC) analysis was conducted based on Cox regression models, and area under the curve (AUC) values with corresponding 95% CIs were calculated to further compare the discriminative ability of the CMI and TyG index in predicting MACEs. Four widely used machine learning algorithms were applied to increase the predictive performance: random forest, extreme gradient boosting (XGBoost), ridge regression, and least absolute shrinkage and selection operator (LASSO) regression. Data were randomly partitioned into training and test subsets using an 8:2 split ratio. Hyperparameter optimization was performed via fivefold cross-validation, and predictive accuracy was assessed by calculating the AUC for the test set.

To evaluate consistency across patient subsets, analyses were repeated within prespecified clinical subgroups for both CMI and TyG. Potential interaction effects were tested in Cox models by incorporating index-by-subgroup interaction terms. Incremental prognostic information beyond the CHA2DS2-VASc score was assessed

by comparing four nested prediction models: CHA2DS2-VASc alone, CHA2DS2-VASc with CMI, CHA2DS2-VASc with TyG, and a model including both indices in addition to CHA2DS2-VASc. Differences in predictive performance across the nested models were interpreted as evidence for (or against) added value of the indices.

Results

Baseline characteristics

This study enrolled 380 patients with AF. Throughout the observation period, 53 patients (13.9%) experienced MACEs, whereas 327 patients (86.1%) did not. Baseline characteristics stratified by MACE status are summarized in Table 1. Several metabolic and clinical variables differed between groups. Relative to patients without MACEs, patients who experienced MACEs had higher median body weight (69.00 vs. 67.00 kg), platelet count (196 vs. 178 × 10^9/L), HbA1c (6.60% vs. 5.80%), as well as fasting plasma glucose (6.50 vs. 5.70 mmol/L). Triglyceride levels were also significantly elevated (2.13 vs. 1.71 mmol/L), whereas HDL-C levels were markedly lower (0.84 vs. 1.03 mmol/L). Compared with participants without MACEs, the MACE group showed higher CMI (1.28 vs. 0.83) and TyG index values (9.36 vs. 9.00) (all $P < 0.01$). Higher prevalences of hypertension, heart failure, coronary artery disease, and diabetes mellitus were also observed among those with MACEs (all $P < 0.01$). By contrast, no significant between-group differences were detected for age,

sex, height, BMI, renal function, LAID, LVEF, prior stroke, anticoagulant therapy, or AF type (all $P > 0.05$).

Associations of the CMI and the TyG Index with the MACE Risk According to Cox Regression Analyses

CMI and TyG index were analyzed as continuous variables in Cox proportional hazards models with stepwise adjustment to assess their associations with MACE risk. The results are presented in Figure 2A and 2B. In Model 1 (unadjusted), both higher CMI (HR 2.93, 95% CI 2.04–4.21; $P < 0.01$) and a higher TyG index (HR 4.96, 95% CI 2.89–8.54; $P < 0.01$) were each statistically linked to increased risk of MACEs. These relationships persisted following adjustment for age and sex in Model 2, with CMI (HR 2.88, 95% CI 2.01–4.12; $P < 0.01$) and the TyG index (HR 4.82, 95% CI 2.82–8.25; $P < 0.01$) remaining statistically significant. After full covariate adjustment (Model 3), significant associations with MACEs persisted for both CMI (HR, 3.25; 95% CI, 1.89–5.58; $P < 0.01$) and the TyG index (HR, 4.52; 95% CI, 1.83–11.12; $P < 0.01$). Age and sex showed no statistical significance in the partially adjusted model (Model 2). Several clinical factors retained prognostic relevance in Model 3: heart failure was strongly associated with MACEs in both specifications (CMI model: HR, 5.78; 95% CI, 2.28–14.60; TyG model: HR, 6.60; 95% CI, 2.67–16.34; both $P < 0.01$), and CAD was also associated (HR, 4.14 and 4.54, respectively; both $P < 0.01$). Notably, CKD showed an inverse association with the outcome, with HR = 0.13 ($P < 0.01$) and HR = 0.12 ($P < 0.01$) in the respective models. Renal and

haematologic markers, including serum creatinine levels (HR: 1.03 in both models; $P < 0.01$) and haematocrit (HR: 0.92 in both models; $P < 0.05$), were also significantly associated with MACEs. Statistical significance was not observed for the other covariates (all $P > 0.05$).

Risk gradients for CMI and the TyG index were further examined by categorizing each index into tertiles, using tertile 1 as the reference; three sequential Cox models were applied, with results displayed in Figure 3A and Figure 3B. In the unadjusted analysis (Model 1), CMI tertile 3 (highest) demonstrated elevated MACE risk relative to tertile 1 (HR, 2.81; 95% CI, 1.45–5.46; $P < 0.01$), whereas tertile 2 showed no significance ($P = 0.65$). The TyG index exhibited a comparable pattern: tertile 3 demonstrated increased risk (HR, 4.54; 95% CI, 2.17–9.48; $P < 0.01$), while tertile 2 remained non-significant ($P = 0.53$). Following adjustment for age and sex (demographics-adjusted model), the highest tertile remained associated with MACEs for both indices: CMI tertile 3 (HR, 2.86; 95% CI, 1.47–5.60; $P < 0.01$) and TyG tertile 3 (HR, 4.51; 95% CI, 2.13–9.55; $P < 0.01$), whereas tertile 2 showed no significant association. In Model 3 (fully adjusted), these relationships persisted, with CMI tertile 3 (HR, 2.68; 95% CI, 1.12–6.40; $P < 0.05$) and TyG tertile 3 (HR, 4.34; 95% CI, 1.58–11.93; $P < 0.01$) remaining statistically significant. Tertile 2 remained nonsignificant, supporting a potential threshold effect for both indices. In Model 2, neither demographic variable (age or sex) reached statistical significance. In Model 3, several clinical covariates were independently associated with MACEs. Heart failure exhibited the most pronounced association with MACEs in both models

316 (CMI-adjusted: HR 5.78; TyG-adjusted: HR 7.83; both $P < 0.01$). Coronary artery
317 disease ranked next (CMI: HR 4.14; TyG: HR 5.20; both $P < 0.01$), followed by
318 HbA1c (CMI: HR 1.76; TyG: HR 1.70; both $P < 0.01$). Serum creatinine showed a
319 modest but significant effect, with an identical HR of 1.03 in each model ($P < 0.01$).
320 In contrast, chronic kidney disease (CMI: HR: 0.17; $P < 0.05$; TyG: HR: 0.10; $P <$
321 0.01) and haematocrit (CMI: HR: 0.91; TyG: HR: 0.93; both $P < 0.05$) were inversely
322 associated with MACEs. All other covariates were not statistically significant ($P >$
323 0.05). In the formal diagnostic test of the proportional hazards assumption for the
324 fully adjusted Cox models with the continuous CMI and TyG index as the main
325 exposures, the global tests based on scaled Schoenfeld residuals were statistically
326 significant, and several covariates, including the cardiometabolic indices, showed
327 evidence of time-dependent effects ($P < 0.05$). However, log–log survival curves for
328 quartiles of the TyG index and CMI (Supplementary Figure S1) demonstrated the
329 expected ordering of risk across quartiles and did not show gross crossing hazards,
330 suggesting that the estimated hazard ratios primarily reflect time-averaged
331 associations over the 3-year follow-up.

332 E-value analyses suggested that, to account for the continuous relationships between
333 CMI and TyG index with 3-year MACEs, any unmeasured confounder would require
334 associations with both exposure and outcome at approximately a threefold magnitude
335 (or greater) to fully explain the observed hazard ratios. By comparison, tertile-based
336 estimates appeared more susceptible to residual unmeasured confounding
337 (Supplementary Table S2). The fully adjusted Cox models incorporating the

continuous CMI and TyG index exhibited strong discrimination, with Harrell's C-indices of 0.859 (standard error [SE] 0.031) and 0.857 (SE 0.030), respectively. The corresponding likelihood ratio chi-square statistics were 131 and 123 for 17 degrees of freedom (both $P < 0.0001$), indicating an adequate overall model fit.

Nonlinear Associations and Survival Analysis of CMI and the TyG Index with the MACE Risk

RCS functions were incorporated into Cox proportional hazards models to explore potential nonlinear relationships of CMI and TyG index with MACE risk. A statistically significant, non-linear positive association was identified for CMI and MACE risk (P for non-linearity < 0.001), with the hazard rising steeply when CMI surpassed approximately 0.85 (Figure 4A). Similarly, the TyG index exhibited a nonlinear relationship with MACE risk (P for nonlinearity = 0.0175), with a pronounced increase in risk occurring beyond a TyG value of approximately 9.02 (Figure 4B). Kaplan–Meier survival analysis was performed to estimate cumulative MACE-free survival by tertiles, with between-group differences evaluated via the log-rank test to further validate the prognostic utility of CMI and TyG index stratification (Figure 5A and 5B). For the CMI, overall differences across tertiles were highly significant (log-rank $P < 0.001$). Kaplan–Meier analyses stratified by CMI tertiles demonstrated a clear gradient, with MACEs occurring most frequently in tertile 3. Comparisons across strata showed that T3 differed from both T1 and T2 (each $P < 0.01$), while T1 and T2 were not distinguishable ($P = 0.58$). The TyG index

exhibited the same pattern: overall log-rank test indicated a significant separation among tertiles ($P < 0.001$). This difference was primarily attributable to a higher event rate in T3 compared with both T1 and T2 (each $P < 0.01$), whereas no statistically significant difference was observed between T1 and T2 ($P = 0.63$).

Discriminative Power of the CMI and TyG Index for Predicting MACEs

To assess the discriminative capacity of CMI and TyG index for MACE risk, the study developed three stepwise (hierarchical) Cox regression models for each marker. Receiver operating characteristic (ROC) analysis was performed, and area under the curve (AUC) values with their respective 95% confidence intervals (CIs) were computed. As shown in Figure 6A, CMI-based models demonstrated progressive improvements in predictive performance. In the unadjusted analysis (Model 1), the AUC was 0.71 (95% CI 0.63–0.80). After controlling for age and sex (Model 2), AUC improved to 0.74 (95% CI 0.67–0.82), and it rose further to 0.90 (95% CI 0.84–0.96)with full covariate adjustment (Model 3). This comparable stepwise improvement in discrimination was observed for the TyG-based models (Figure 6B). Model 1 produced an AUC of 0.74 (95% CI: 0.65–0.82), Model 2 reached 0.75 (95% CI: 0.67–0.82), and Model 3 achieved 0.87 (95% CI: 0.80–0.94). Four commonly used machine learning algorithms were applied to further increase the predictive accuracy: random forest, XGBoost, ridge regression, and LASSO regression. As illustrated in Figure 7A and 7B, XGBoost consistently delivered the highest performance across both indices. Across the CMI-based models, XGBoost yielded the

largest AUC (0.92; 95% CI, 0.82–1.00), with slightly lower values for random forest (0.91; 95% CI, 0.82–1.00), LASSO regression (0.85; 95% CI, 0.69–1.00), and ridge regression (0.80; 95% CI, 0.66–0.93). For the TyG-based models, discrimination was highest for XGBoost (AUC, 0.93; 95% CI, 0.85–1.00), then random forest (0.92; 95% CI, 0.82–1.00), ridge regression (0.79; 95% CI, 0.65–0.93), and LASSO regression (0.77; 95% CI, 0.61–0.93).

Subgroup Analyses of the Performance of the CMI and TyG Index in Predicting the MACE Risk

In subgroup analyses, both the CMI and the TyG index remained significantly associated with MACEs across most clinical subgroups (all $P < 0.05$), although several subgroups exhibited significant interaction effects (Figure 8A and 8B). For the CMI, significant interactions were observed with diabetes, coronary artery disease (CAD), and heart failure status (for all interactions, $P < 0.05$). No significant interactions were detected with sex ($P = 0.78$), hypertension ($P = 0.34$), age ($P = 0.15$), chronic kidney disease (CKD) ($P = 0.16$), history of stroke ($P = 0.14$), or AF type ($P = 0.77$). In patients without heart failure, CMI demonstrated elevated MACE risk (HR 4.29, 95% CI 2.78–6.63; $P < 0.01$). Conversely, the association was not significant in those with heart failure (HR 1.10, 95% CI 0.40–3.03; $P = 0.85$). Consistent patterns were seen in participants without CAD (HR 4.41, 95% CI 2.42–8.06) and in those without diabetes (HR 4.58, 95% CI 2.50–8.38), with these associations being markedly stronger than those observed in the corresponding

comorbidity subgroups (both $P < 0.01$). For the TyG index, significant interactions were identified with age, sex, diabetes status, CKD status, and heart failure status (for all interactions, $P < 0.05$). In the ≥65-year stratum, the TyG index showed a significant effect estimate for MACEs (HR, 6.48; 95% CI, 3.53–11.90; $P < 0.01$). The corresponding estimate in participants <65 years was not statistically significant (HR, 1.31; 95% CI, 0.35–4.95; $P = 0.69$). In sex-stratified analyses, TyG index maintained its predictive significance for MACEs across both men (HR 3.59, 95% CI 1.94–6.65) and women (HR 1.32, 95% CI 1.02–2.32), with $P < 0.01$ for both. The strongest predictive effects of TyG were observed among patients lacking diabetes (HR: 7.70; 95% CI: 2.49–13.78), without heart failure (HR: 9.07; 95% CI: 4.74–17.37), and without CKD (HR: 4.26; 95% CI: 2.35–7.71), all $P < 0.01$. These findings suggest that the TyG index may provide increased prognostic utility in patients with fewer comorbid conditions or a lower baseline cardiovascular risk profile.

Added Prognostic Utility of CMI and TyG Beyond the CHA_2DS_2-VASc Score

Three extended models were developed based on the conventional CHA2DS2-VASc scoring system (Model 1) to assess the added prognostic utility of CMI and TyG index in predicting clinical risk. Model 2 incorporated the CMI (CHA2DS2-VASc + CMI), Model 3 included the TyG index (CHA2DS2-VASc + TyG), and Model 4 combined both indices (CHA2DS2-VASc + CMI + TyG). Model performance was evaluated using time-dependent AUC analyses (Figure 9A). At 365, 730, and 1000 days, Model 1 consistently yielded lower AUC values than the enhanced models. At

1000 days, the AUCs were Model 1 (0.735), Model 2 (0.844), Model 3 (0.873), and Model 4 (0.873), indicating improved discrimination with the inclusion of either the CMI or the TyG index. Further analysis of independent predictors of MACEs across the models (Figure 9B) showed that in Model 1, CHA2DS2-VASc score demonstrated significant predictive value (HR: 1.92; 95% CI: 1.60–2.31; $P < 0.01$). After adding the CMI (Model 2) or TyG index (Model 3), the CHA2DS2-VASc score remained statistically significant (HR for both models: 1.65; $P < 0.01$), whereas the CMI (HR: 2.10; 95% CI: 1.43–3.09; $P < 0.01$) and TyG index (HR: 2.96; 95% CI: 1.69–5.20; $P < 0.01$) independently predicted the MACE risk. However, in the fully adjusted model including both indices (Model 4), the CHA2DS2-VASc score remained significant (HR: 1.64; $P < 0.01$), whereas neither the CMI (HR: 1.19; $P = 0.70$) nor the TyG index (HR: 2.40; $P = 0.16$) remained statistically significant. This result suggests potential collinearity or overlapping predictive contributions when both indices are included simultaneously, supporting the use of either index, but not necessarily both, for enhancing risk stratification beyond the CHA2DS2-VASc score.

Discussion

To date, direct comparisons of CMI and the TyG index for 3-year MACE prediction in AF have been limited. The present retrospective cohort study addresses this gap by comparing their predictive performance and shows that each index contributes independent prognostic information. At baseline, patients who experienced MACEs had significantly higher levels of both indices compared with those without events

(CMI: 1.28 vs. 0.83; TyG: 9.36 vs. 9.00; both $P < 0.01$). Multivariate Cox regression demonstrated that after comprehensive adjustment for clinical confounders, both indices remained independently associated with the MACEs risk, yielding hazard ratios of 3.25 (95% CI: 1.89–5.58; $P < 0.01$) for the CMI and 4.52 (95% CI: 1.83–11.12; $P < 0.01$) for TyG. And RCS analyses additionally revealed significant non-linear associations of each index with MACE risk, with apparent inflection points at approximately 0.85 for CMI and 9.02 for the TyG index. Taken together, the results suggest that CMI and the TyG index may serve as practical, non–insulin-based measures for cardiovascular risk stratification in AF. The observed associations also motivate further mechanistic work and support consideration of their potential clinical use.

Prior research has demonstrated that CMI and TyG index correlate with cardiovascular events across general populations and among high-risk cardiovascular cohorts. Among patients with CAD, the TyG index has been validated as a prognostic biomarker for MACEs, displaying consistent predictive performance across large prospective studies [20]. Similarly, the CMI—capturing central adiposity and atherogenic dyslipidaemia—has been significantly linked to all-cause and cardiovascular mortality in diabetic or prediabetic populations [21]. However, these indices remain largely uninvestigated regarding their prognostic capacity in AF patients. In many of the non-AF cohorts reported to date, the effect sizes for the CMI or TyG index tend to be more modest than those observed in the present study, in which fully adjusted hazard ratios reached 3.25 for the CMI and 4.52 for the TyG

index. Although direct quantitative comparisons across studies are constrained by heterogeneity in study design, outcome definitions, follow-up duration, and covariate adjustment, the relatively larger effect estimates observed in the present AF cohort indicate that metabolic dysregulation may have a particularly pronounced impact on clinical outcomes in this arrhythmia-prone population. Several factors may account for these differences. First, AF itself confers a prothrombotic and haemodynamically unstable milieu, which may amplify the adverse consequences of insulin resistance, dyslipidaemia, and central adiposity. Second, the composite MACE endpoint used in this study included not only mortality and ischaemic events but also hospitalization for decompensated heart failure and coronary revascularization, thereby capturing a broader spectrum of the AF-related cardiovascular burden. Third, the population assessed in the present study was derived from a hospital-based cohort of symptomatic patients, who may have exhibited a higher baseline cardiovascular risk profile than community-based individuals. Taken together, these findings extend the literature by showing that, in patients with AF, both the CMI and TyG index remain independent predictors of MACEs following comprehensive adjustment for comorbidities and established risk factors. Moreover, the TyG index may provide slightly greater prognostic discrimination than the CMI, supporting its potential value in refining cardiovascular risk stratification among these vulnerable patients.

The contribution of metabolic abnormalities to cardiovascular events among AF patients is likely multifactorial. Insulin resistance, a central feature of metabolic syndrome, promotes endothelial dysfunction, low-grade inflammation, and activation

of the renin–angiotensin system, thereby accelerating atherosclerosis and myocardial remodelling [22-27]. The CMI, which integrates waist circumference and HDL-C levels, reflects central adiposity and atherogenic dyslipidaemia; higher CMI values therefore correspond to a proinflammatory, prothrombotic metabolic milieu that may exacerbate AF progression and downstream cardiovascular complications [28-30]. The TyG index represents a marker of concurrent glucose and triglyceride pathways dysregulation. Such metabolic disturbances have been linked to advanced glycation end product formation, oxidative stress, and a shift toward small, dense low-density lipoprotein cholesterol (LDL-C) particles, processes that can accelerate plaque vulnerability and vascular damage [31-33]. In the context of AF, these metabolic changes may synergize with pre-existing atrial and ventricular structural abnormalities, creating a "double hit" that may explain the relatively strong links of CMI and the TyG index with MACEs observed in the present study. Furthermore, AF itself may worsen insulin resistance and metabolic control through reduced cardiac output and neurohormonal activation, suggesting a bidirectional relationship in which arrhythmia and metabolic dysfunction mutually reinforce one another [34].

The nonlinear associations identified through the RCS analysis provide meaningful understanding of how CMI and TyG index may guide cardiovascular risk assessment. A pronounced elevation in MACE risk occurred when CMI exceeded approximately 0.85 and TyG values of approximately 9.02, indicating a threshold-like pattern whereby metabolic dysregulation may confer a disproportionately greater cardiovascular risk above these levels. Pathophysiologically, this pattern implies that

compensatory mechanisms may maintain cardiovascular homeostasis below these levels, whereas surpassing these thresholds may trigger a convergence of maladaptive processes, leading to a steep increase in risk. For the CMI, a value ≥0.85 likely represents the point at which the combined burden of central adiposity and atherogenic dyslipidaemia becomes clinically significant. Similarly, a TyG index >9.02 may indicate a transition at which of glucose and lipid metabolism achieve a severity of IR that meaningfully increases the cardiovascular risk. Although optimal cut-off values may differ across populations and study settings, the current data suggest that clinically meaningful metabolic risk thresholds in AF can emerge at comparatively modest increases in CMI and TyG index. From a practical standpoint, these thresholds provide actionable clinical benchmarks. In patients with a CMI ≥0.85 or a TyG index ≥9.02, clinicians may consider intensifying preventive strategies, including targeted lifestyle interventions, optimization of metabolic therapies, and more frequent cardiovascular monitoring. Incorporating these readily obtainable indices into the routine evaluation may be particularly valuable for individuals with borderline conventional risk markers or intermediate CHA2DS2-VASc scores, helping to refine decisions regarding the follow-up intensity and the initiation or escalation of preventive treatment.

The subgroup analysis revealed significant variability in prognostic capacity of the CMI and the TyG index across patients with differing clinical characteristics, underscoring their potential value in an individualized cardiovascular risk assessment. For the CMI, the most notable finding was its markedly stronger predictive value in

patients without heart failure than in those with heart failure (HR: 4.29 vs. 1.10). This disparity may reflect the complex pathophysiological profile of heart failure, which independently drives prognosis substantially. Among such patients, the incremental predictive utility of metabolic indices may be attenuated. Moreover, clinical manifestations common in heart failure, such as anorexia, cachexia, and fluid retention, may compromise the accuracy of CMI components, particularly waist circumference and lipid measures. Similarly, the CMI displayed greater predictive strength among patients without coronary artery disease (HR: 4.41) and without diabetes (HR: 4.58), suggesting that in AF patients who lack traditional cardiovascular comorbidities, metabolic dysfunction may emerge as a predominant driver of adverse outcomes. The TyG index displayed comparable trends. Among patients aged ≥65 years, the TyG index provided a substantially greater predictive value (HR: 6.48 vs. 1.31), likely reflecting the age-related metabolic decline and increase in vulnerability to glucose–lipid disturbances. A sex-based difference was also observed: the TyG index demonstrated greater predictive value among male patients (HR: 3.59 vs. 1.32), potentially because of the modulatory effects of sex hormones on metabolic pathways and cardiovascular risk profiles. These interaction effects have important clinical implications. In elderly patients, those without heart failure, and those without established cardiovascular comorbidities, both the CMI and TyG index appear to provide increased prognostic value and may serve as valuable adjuncts to conventional risk assessment tools. The TyG index, in particular, appears especially informative in older male patients. Taken together, these results support

considering the integration of metabolic indices into individualized risk stratification for patients with AF. Such an approach may support more nuanced, targeted interventions aimed at improving long-term cardiovascular outcomes.

In the present study, machine learning models showed superior predictive performance, offering a powerful complement to traditional statistical approaches. Among the algorithms evaluated, XGBoost achieved the highest accuracy for predicting outcomes using both the CMI and the TyG index, yielding AUCs of 0.92 for CMI and 0.93 for the TyG index—substantially outperforming the conventional Cox proportional hazards model. This advantage is largely attributable to the technical ability of machine learning algorithms to model complex, nonlinear data structures. Specifically, XGBoost can automatically identify nonlinear interactions among variables—a key strength given the restricted cubic spline analysis, which revealed nonlinearity in the associations between both indices and the MACE risk. Moreover, as an ensemble learning technique, XGBoost integrates multiple weak learners to reduce overfitting and improve model generalizability. The random forest algorithm also showed robust predictive performance (CMI: AUC 0.92; TyG: AUC 0.91). By incorporating random sampling of both features and observations, random forests effectively mitigate the challenges of multicollinearity and overfitting, key considerations when working with high-dimensional clinical datasets, particularly in cardiovascular risk modelling. Machine learning models offer a unique capacity to integrate diverse clinical variables, including demographic characteristics, comorbidities, laboratory biomarkers, and echocardiographic parameters, into a

unified predictive framework. This capability creates new opportunities for dynamic and individualized risk assessment among AF patients. The broader application of artificial intelligence in this context holds considerable potential for the development of intelligent clinical decision support systems capable of synthesizing multimodal data, including biochemical markers, imaging findings, and clinical indicators, to facilitate real-time, personalized management strategies. However, several challenges must be addressed before widespread clinical adoption can be achieved. Key barriers include limited model interpretability, variability in data quality and structure across clinical platforms, and unresolved regulatory and ethical considerations. Future research should focus on balancing technical innovation with clinical applicability to ensure that machine learning-based tools are not only accurate but also transparent, interpretable, and practical for frontline cardiovascular care.

This study extends existing risk stratification frameworks by demonstrating that incorporation of metabolic indices provides additional prognostic information beyond the conventional CHA_2DS_2-VASc score. Across time-dependent analyses, adding either CMI or the TyG index consistently enhanced model discrimination, indicating a sustained improvement in risk prediction throughout follow-up. These results align with prior evidence that adding metabolic or inflammatory biomarkers can improve risk prediction beyond clinical risk scores alone; however, the present study extends this finding by showing that simple, non-insulin-based indices such as the CMI and TyG index can meaningfully improve the performance of CHA2DS2-VASc specifically in patients with AF. Notably, the combined model incorporating both the

CMI and TyG index did not yield an additional improvement; the AUC remained at 0.873, and neither index retained statistical significance in the multivariable analysis. Several factors may account for this observation: (1) partial collinearity between the CMI and TyG index, as both reflect overlapping dimensions of metabolic dysfunction despite emphasizing distinct components; (2) an attenuation of individual predictor contributions in more complex multivariable models due to intervariable interactions; and (3) the relatively limited sample size, which may have compromised the precision and stability of effect estimates in the combined model. Based on these findings, clinicians may consider incorporating either the CMI or TyG index, but not both, along with the CHA2DS2-VASc score to improve risk stratification. From a predictive standpoint, the TyG index appears to provide marginally superior performance to the CMI and, given its simpler calculation, may be more practical for routine clinical application. Clinically, this approach may be particularly valuable for AF patients presenting with intermediate CHA2DS2-VASc scores, among whom decisions regarding treatment intensity, closer monitoring, or more aggressive risk factor modification often remain uncertain. In these cases, an elevated TyG index or CMI could help identify individuals who warrant intensified follow-up and earlier preventive interventions.

In summary, the findings indicate that both the CMI and the TyG index are valuable, easily accessible tools for cardiovascular risk stratification in AF patients. These simple, cost-effective indices derived from routine laboratory tests are applicable across diverse health care settings and can facilitate the early identification of

high-risk individuals who would benefit from targeted preventive strategies. The slightly superior performance of the TyG index, combined with its simplicity and widespread availability, supports its potential integration into routine clinical assessments to help reduce cardiovascular morbidity and mortality in AF patients. These metabolic indices complement traditional cardiovascular risk factors and may facilitate more personalized, proactive approaches to AF management.

32

Strengths and limitations

This study has several strengths. First, it provides a head-to-head comparison of two readily obtainable, non-insulin-based metabolic indices (the CMI and TyG index) for predicting 3-year MACEs in patients with atrial fibrillation within the same cohort. Second, the study adopted a comprehensive analytical strategy, including multivariable Cox modelling with clinically prespecified covariates, restricted cubic splines to explore nonlinearity and clinically meaningful thresholds, subgroup interaction analyses, and an assessment of incremental value beyond the CHA2DS2-VASc score, thereby enhancing interpretability and potential clinical translatability. Third, the study reflects a real-world community-based management setting, which supports the feasibility of applying these indices in routine practice where fasting glucose levels and lipid profiles are commonly available.

Several limitations should be acknowledged. First, the single-centre retrospective design may limit external generalizability to AF populations in other regions and health care systems. Second, the modest sample size (n = 380) and event count (n =

53) may reduce precision, particularly in subgroup and multivariable analyses. Third, although a 3-year follow-up captures the intermediate-term risk, longer follow-up is needed to clarify the long-term prognostic implications. Fourth, formal testing suggested potential nonproportional hazards for the CMI, TyG index, and some covariates; therefore, hazard ratios should be interpreted as time-averaged associations over the follow-up period. Finally, detailed baseline data were not available for excluded individuals, and selection bias cannot be fully excluded.

Conclusions

Both CMI and the TyG index independently predicted 3-year MACE risk in patients with atrial fibrillation, with the TyG index showing a modestly stronger discriminative ability. Collectively, these results support incorporating metabolic indices to refine risk stratification and guide clinical management in AF.

The clinical utility of these findings is multifaceted and addresses important health care challenges. First, both CMI and the TyG index are readily obtainable from routine measurements, including lipid parameters, glucose-related indices, and waist circumference without additional cost or specialized equipment, making them immediately applicable across diverse health care settings, from well-resourced academic centres to community hospitals and primary care facilities in resource-limited regions. This broad accessibility promotes health equity by enabling consistent risk stratification regardless of the socioeconomic status or geographic location. Second, identifying high-risk AF patients (CMI ≥0.85 or TyG index ≥9.02)

enables clinicians to implement timely, evidence-based preventive strategies, including (1) more intensive lipid-lowering therapy with higher-dose statins or combination therapy; (2) stricter glycaemic control with earlier initiation or intensification of antidiabetic medications; (3) enhanced lifestyle interventions targeting weight reduction, dietary modification, and physical activity; and (4) closer monitoring with more frequent follow-up visits and cardiovascular assessments. Third, these indices facilitate shared decision-making discussions with patients about their cardiovascular risk and the potential benefits of preventive interventions, enhancing patient engagement in their own care. Fourth, incorporating the CMI or TyG index into existing risk prediction models (such as CHA2DS2-VASc) may improve the risk stratification accuracy and enable more personalized treatment to be provided to AF patients. Ultimately, prompt recognition of high-risk patients and initiation of tailored preventive interventions may reduce major adverse cardiovascular event incidence, lower cardiovascular morbidity and mortality, improve life quality, and alleviate health care costs related to acute cardiovascular complications. By enabling proactive rather than reactive care, these simple, cost-effective tools support sustainable health care delivery and contribute to improved population health outcomes.

While this study provides valuable insights, several directions warrant further investigation. Larger prospective multicentre studies enrolling ethnically diverse populations are warranted to validate the cut-off values identified here and to establish the generalizability of these findings across different health care settings. Serial measurements of the CMI and TyG index during follow-up should be performed to

683 determine whether dynamic changes in these indices improve the risk prediction
684 beyond the baseline values. Further mechanistic investigations are required to clarify
685 the pathophysiological pathways through which cardiometabolic dysfunction
686 contributes to adverse outcomes in AF, potentially enabling the discovery of new
687 therapeutic targets. Clinical trials testing whether interventions guided by the levels of
688 the CMI or TyG index (compared with standard care) improve cardiovascular
689 outcomes would provide definitive evidence for their clinical implementation. Finally,
690 studies should explore whether integrating these indices with other biomarkers (such
691 as inflammatory markers, natriuretic peptides, or imaging parameters) further
692 increases the prediction of the risk in AF patients.

693 **List of abbreviations**

694 AF—atrial fibrillation

695 MACE—major adverse cardiovascular event

696 IR—insulin resistance

697 CMI—cardiometabolic index

698 TyG—triglyceride–glucose index

699 TG—triglyceride

700 BMI—body mass index

WHtR—waist-to-height ratio

CAD—coronary artery disease

CKD—chronic kidney disease

FPG—fasting plasma glucose

HbA1c—haemoglobin A1c (glycated haemoglobin)

LAID—left atrial anteroposterior diameter

HDL-C—high-density lipoprotein cholesterol

LDL-C—low-density lipoprotein cholesterol

LVEF—left ventricular ejection fraction

XGBoost—extreme gradient boosting

HR—hazard ratio

CI—confidence interval

RCS—restricted cubic spline

ROC—receiver operating characteristic

AUC—Area under the curve

LASSO—least absolute shrinkage and selection operator

Declarations

Ethics approval and consent to participate

Ethical approval for this retrospective investigation was obtained from the Ethics Committee of Shanghai Renji Hospital (KY2022-105-B). As the analysis utilized anonymized data, written informed consent was waived. The study was performed in compliance with the Declaration of Helsinki and applicable institutional and national regulations.

Consent for publication

Not applicable.

Data availability

Study population data were extracted from the hospital information system. To protect patient privacy, the dataset cannot be publicly shared. Nonetheless, pertinent data are available from the corresponding authors on reasonable request.

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Competing interests

The authors declare no competing interests.

Funding

This work was supported by the National Natural Science Foundation of China (Grant Nos. U21A20341 and 82470394) and the Healthcare Talents Youth Program of Shanghai Pudong New Area (Grant No. 2026PDWSYCQN-08).

Authors' contributions

Hao Huang, Meng Jiang, and Jun Pu conceived and designed the study. Xunhan Qiu and Jingjing Sha collected and curated the data and performed the formal analyses. Xunhan Qiu and Jingjing Sha drafted the original manuscript. Yan Li, Wei Song, and Long Shen critically reviewed and revised the manuscript. Tongjiu Ding, Jialiang Fang, Mangmang Pan, and Yu Zhao validated the data and performed the final proofreading. Xunhan Qiu and Jingjing Sha contributed equally as co-first authors. Hao Huang, Meng Jiang, and Jun Pu are the corresponding authors. All the authors read and approved the final manuscript.

Acknowledgements

The authors would like to thank all the participants of this study.

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867 **Tables**

868 Table 1 Baseline characteristics of patients grouped by major adverse cardiovascular
869 events

Variables	Total (n=380)	MACE group (n=53)	Non-MACE group (n=327)	*P* value
Sex, N (%)				0.36
Male	229 (60.3)	35 (66)	194 (59.3)	
Female	151 (39.7)	18 (34)	133 (40.7)	
Age (years)	73.00 (69.00–76.00)	70.00 (65.00–76.00)	73.00 (69.00–76.50)	0.06
Height (cm)	169.00 (160.00–172.00)	170.00 (162.00–172.00)	169.00 (160.00–172.00)	0.25
Weight (kg)	67.50 (62.00–70.00)	69.00 (64.00–73.00)	67.00 (62.00–70.00)	**<0.05***
Waist	84.00 (81.00–88.00)	84.00 (82.00–88.00)	84.00 (80.50–	0.30

circumference (cm)			88.00)	
Hip circumference (cm)	94.00 (92.00–96.00)	95.00 (92.00–96.00)	94.00 (92.00–96.00)	0.54
BMI	23.70 (22.98–25.35)	23.92 (22.99–25.51)	23.69 (22.98–25.24)	0.48
Haematocrit (%)	41.00 (37.50–43.55)	40.30 (36.90–43.20)	41.20 (37.60–43.60)	0.40
Platelets (×10⁹/L)	181.00 (149.00–212.00)	196.00 (157.00–227.00)	178.00 (147.50–208.00)	**<0.05***
Serum creatinine (μmol/L)	75.00 (66.00–88.00)	74.00 (66.00–88.00)	76.00 (66.50–88.00)	0.85
FPG (mmol/L)	5.70 (5.30–6.60)	6.50 (5.50–7.20)	5.70 (5.20–6.45)	**<0.01***
HbA1c (%)	5.90 (5.50–6.50)	6.60 (5.60–7.10)	5.80 (5.50–6.30)	**<0.01***
TG (mmol/L)	1.76 (1.20–2.12)	2.13 (1.59–3.25)	1.71 (1.17–2.02)	**<0.01***
HDL-C (mmol/L)	1.00 (0.86–1.16)	0.84 (0.77–0.98)	1.03 (0.90–1.17)	**<0.01***
LVEF (%)	61.00 (58.00–63.00)	60.00 (58.00–63.00)	61.00 (58.00–63.00)	0.37
LAID (mm)	43.00 (40.00–45.00)	43.00 (41.00–46.00)	42.00 (40.00–45.00)	0.07
Hypertension, N (%)				**<0.01***
Yes	185 (48.7)	37 (69.8)	148 (45.3)	

No	195 (51.3)	16 (30.2)	179 (54.7)	
Heart failure, N (%)				**<0.01***
Yes	37 (9.7)	16 (30.2)	21 (6.4)	
No	343 (90.3)	37 (69.8)	306 (93.6)	
CAD, N (%)				**<0.01***
Yes	106 (27.9)	34 (64.2)	72 (22.0)	
No	274 (72.1)	19 (35.8)	255 (78.0)	
CKD, N (%)				0.99
Yes	50 (13.2)	7 (13.2)	43 (13.1)	
No	330 (86.8)	46 (86.8)	284 (86.9)	
Diabetes mellitus, N (%)				**<0.01***
Yes	99 (26.1)	31 (58.5)	68 (20.8)	
No	281 (73.9)	22 (41.5)	259 (79.2)	
Prior stroke, N (%)				0.27
Yes	17 (4.5)	4 (7.5)	13 (4.0)	
No	363 (95.5)	49 (92.5)	314 (96.0)	
Anticoagulant use, N (%)				0.28
Yes	254 (66.8)	32 (60.4)	222 (67.9)	
No	126 (33.2)	21 (39.6)	105 (32.1)	
AF Type, N (%)				0.24

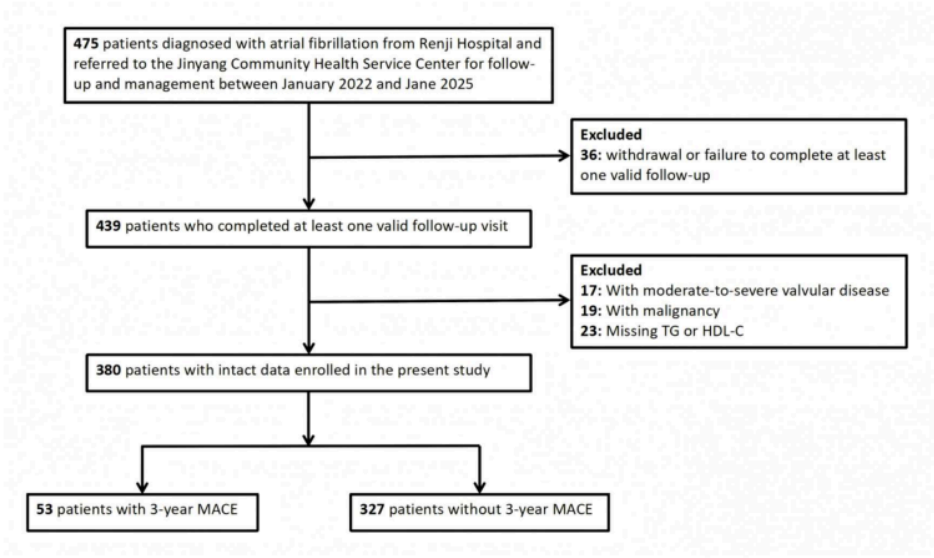
Persistent	191 (50.3)	31 (58.5)	160 (48.9)	
Paroxysmal	189 (49.7)	22 (41.5)	167 (51.1)	
CMI	0.85 (0.53–1.23)	1.28 (0.89–2.32)	0.83 (0.51–1.15)	**<0.01***
TyG index	9.02 (8.63–9.28)	9.36 (9.06–9.72)	9.00 (8.60–9.23)	**<0.01***

MACE, major adverse cardiovascular event; AF, atrial fibrillation; TG, triglyceride; BMI, body mass index; HbA1c, glycated haemoglobin; FPG, fasting plasma glucose; HDL-C, high-density lipoprotein cholesterol; LVEF, left ventricular ejection fraction; LAID, left atrial anteroposterior diameter; CAD, coronary artery disease; CKD, chronic kidney disease; CMI, cardiometabolic index; TyG index, triglyceride–glucose index. Continuous variables are presented as medians (interquartile ranges), and categorical variables are presented as n (%). *$P < 0.05$.

Figures with Legends

Figure 1 Study participant selection flow diagram

Among 475 screened patients with atrial fibrillation, 380 met the inclusion criteria and had complete data for analysis. During the 3-year follow-up, MACEs occurred in 53 patients; the remaining 327 patients did not experience events.



882

883 **Figure 2 Association of CMI and TyG index with incident MACEs in AF**

884 Figure 2 displays forest plots of hazard ratios (HRs) and 95% confidence intervals
885 (CIs) derived from Cox proportional hazards models for the CMI (panel A) and the
886 TyG index (panel B), treated as continuous measures. Three sequential models were
887 developed: an unadjusted baseline model (Model 1), an age- and sex-adjusted model
888 (Model 2), and a comprehensively adjusted model (Model 3) incorporating BMI,
889 anticoagulant therapy, haematocrit, platelet count, serum creatinine, HbA1c, LVEF,
890 LAID, hypertension, heart failure, CAD, CKD, diabetes, and stroke. Significant
891 associations were observed for the CMI and TyG index across all the models, as well
892 as for several clinical covariates in Model 3.

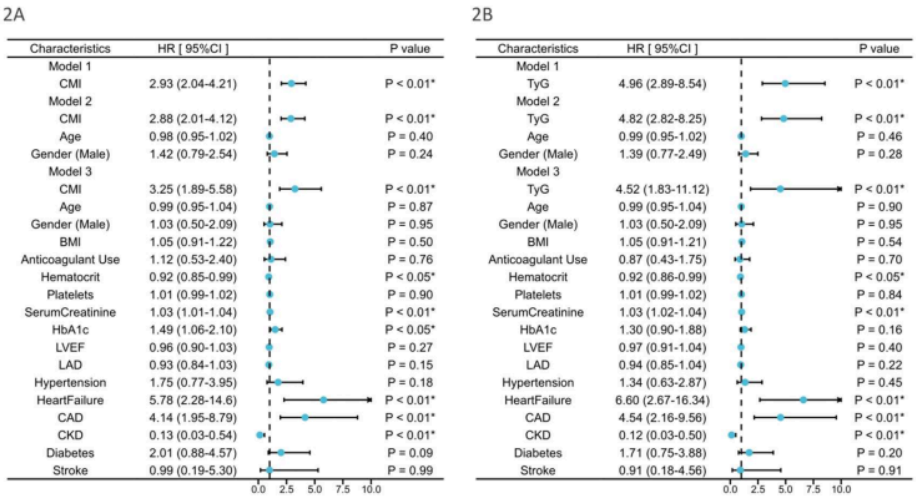


Figure 3 Associations of the tertiles of the CMI and the TyG index with MACEs risk

Forest plots summarise hazard ratios (HRs) with 95% confidence intervals (CIs) for 3-year MACEs across tertiles of the CMI (Figure 3A) and the TyG index (Figure 3B), based on Cox regression analysis. Model 1 presents crude estimates; Model 2 incorporates age and sex; while Model 3 additionally adjusts for BMI, anticoagulant use, haematocrit, platelet count, serum creatinine, HbA1c, LVEF, LAID, hypertension, heart failure, CAD, CKD, diabetes, and stroke. Statistically significant associations with MACEs were observed only in the highest tertile for both indices across all models.

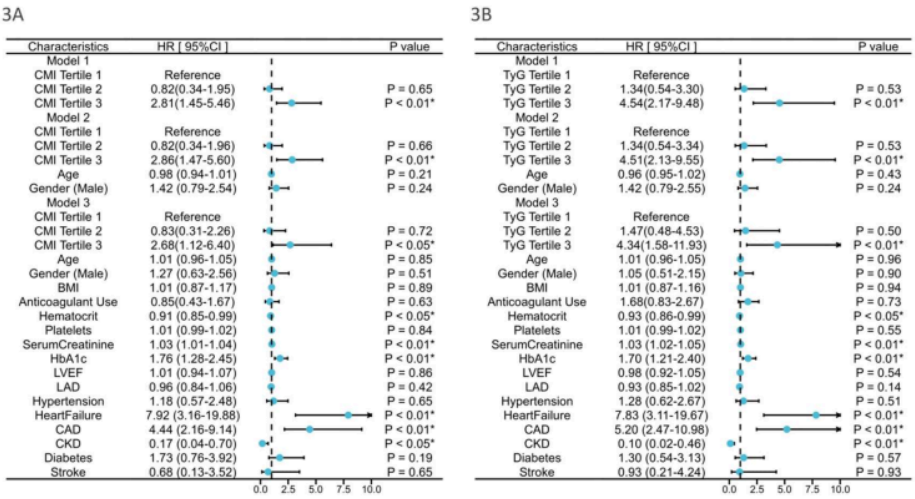


Figure 4 RCS analyses of the associations of the CMI and the TyG index with the risk of MACEs

Restricted cubic spline models illustrate nonlinear associations between the CMI (panel 4A) and the TyG index (panel 4B) and the risk of MACEs. The risk of MACEs increases sharply when the CMI exceeds approximately 0.85 and the TyG index exceeds approximately 9.02. *P* values for nonlinearity are indicated in each panel.

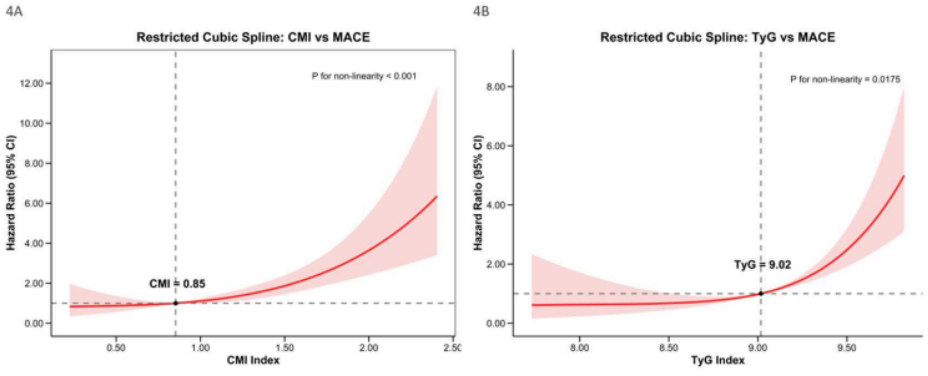


Figure 5 Kaplan–Meier curves for MACE-free survival stratified by the tertiles of the CMI and TyG index

Kaplan–Meier curves depict cumulative MACE-free survival across tertiles of the CMI (panel 5A) and the TyG index (panel 5B). In both analyses, participants in tertile 3 showed a significantly lower MACE-free survival probability than those in tertiles 1–2 (log-rank $P < 0.001$). Subsequent pairwise analyses revealed significant differences between tertile 3 versus each of the lower tertiles, whereas the contrast between tertiles 1 and 2 was not significant.

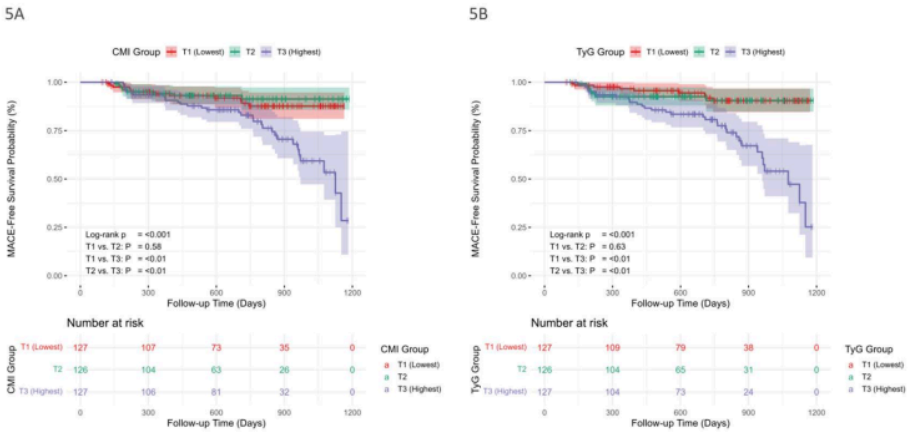


Figure 6 ROC curves for the prediction of MACEs using CMI- and TyG-based models

ROC curves for CMI-based (panel 6A) and TyG-based (panel 6B) models obtained using hierarchical Cox regression analyses. Model 1: unadjusted. Model 2: adjusted for age and sex. Model 3: fully adjusted for all covariates. The AUCs and 95% CIs for

each model are shown. The predictive performance improved with increasing model adjustment for both indices.

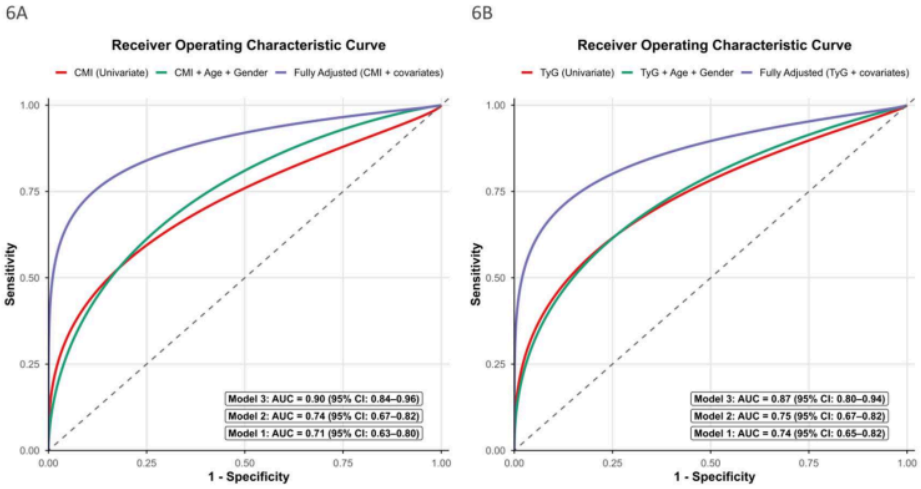


Figure 7 Performance of machine learning models in predicting MACEs

Panels A and B display ROC curves for CMI- and TyG-derived models, respectively, comparing four algorithms (random forest, XGBoost, ridge regression, and LASSO regression). XGBoost and random forest achieved the highest AUCs for both indices, indicating superior discriminative ability compared with penalized regression approaches. The AUC values and 95% CIs for each method are provided in the legend.

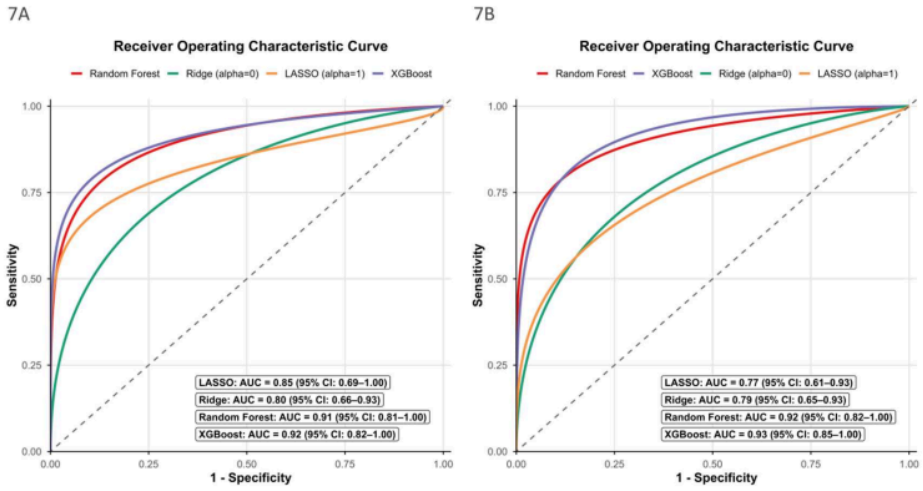


Figure 8 Subgroup-specific effects of CMI and the TyG index on MACE risk.

Forest plots display HRs and 95% CIs for CMI (panel 8A) and TyG (panel 8B) in relation to MACE risk across clinical subgroups. Significant associations were observed in most subgroups for both indices. Significant interaction effects were detected for diabetes, CAD, and heart failure for the CMI and for age, sex, diabetes, CKD, and heart failure for the TyG index (interaction $P < 0.05$ for each). HRs and P values for each subgroup are shown.

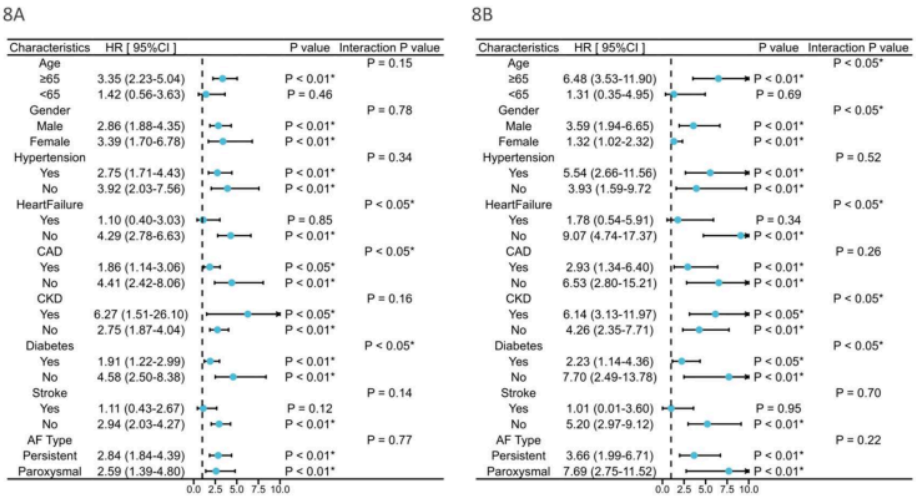
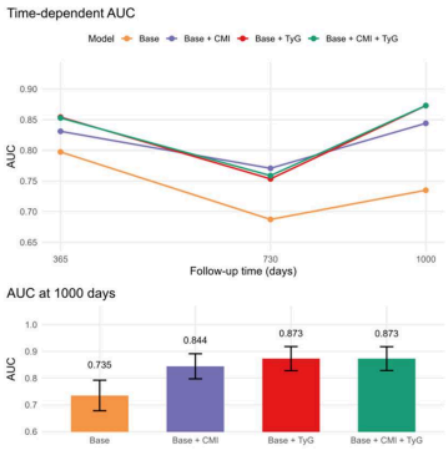


Figure 9 Added prognostic contribution of CMI and TyG index to the CHA2DS2-VASc score for predicting MACEs

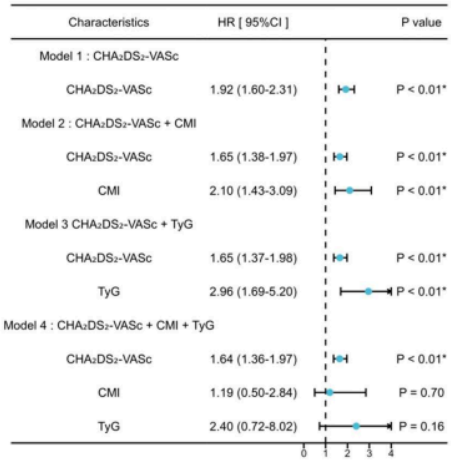
Time-dependent AUCs at 365, 730, and 1000 days for the CHA2DS2-VASc score alone (base model) and after the addition of the CMI, TyG index, or both indices. The inclusion of the CMI and/or TyG index enhanced MACE risk discrimination, with the highest AUC observed when either or both indices were added (panel 9A). Forest plot displaying HRs with 95% CIs for for independent predictors of MACEs in each model. The CMI and TyG index were independent predictors when added separately to the CHA2DS2-VASc score but not when included together, likely reflecting collinearity (panel 9B).

9A


Time-dependent AUC
Model Base Base + CMI Base + TyG Base + CMI + TyG
AUC
0.90
0.85
0.80
0.75
0.70
0.65
365
730
1000
Follow-up time (days)

AUC at 1000 days
AUC
1.0
0.9
0.8
0.7
0.6
0.735
0.844
0.873
0.873
Base
Base + CMI
Base + TyG
Base + CMI + TyG

9B


Characteristics
HR [95%CI]
P value
Model 1 : CHA2DS2-VASc
CHA2DS2-VASc 1.92 (1.60-2.31) P < 0.01*
Model 2 : CHA2DS2-VASc + CMI
CHA2DS2-VASc 1.65 (1.38-1.97) P < 0.01*
CMI 2.10 (1.43-3.09) P < 0.01*
Model 3 CHA2DS2-VASc + TyG
CHA2DS2-VASc 1.65 (1.37-1.98) P < 0.01*
TyG 2.96 (1.69-5.20) P < 0.01*
Model 4 : CHA2DS2-VASc + CMI + TyG
CHA2DS2-VASc 1.64 (1.36-1.97) P < 0.01*
CMI 1.19 (0.50-2.84) P = 0.70
TyG 2.40 (0.72-8.02) P = 0.16
0
1
2
3
4

955

Head-to-Head Comparison of the Ability of the Cardiometabolic Index and Triglyceride–Glucose Index to Predict 3-Year Major Adverse Cardiovascular Events in Patients with Atrial Fibrillation: Insights from a Community Cohort

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