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ORIGINAL RESEARCH

Predictive Effect of Alternative Insulin Resistance Indexes on Adverse Cardiovascular Events in Patients with Metabolic Syndrome with Heart Failure

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Purpose: Metabolic Syndrome (MS) greatly increases the risk of heart disease and Heart Failure(HF). Insulin Resistance (IR) is considered to be the key to the pathophysiology of MS. The purpose of this study was to evaluate the predictive effect of different alternative indicators of IR on adverse cardiovascular events in patients with MS complicated with HF.

Methods: Patients with HF who were diagnosed with MS in the heart center of the first affiliated Hospital of Xinjiang Medical University were selected continuously. The baseline data of the patients in the group were compared. The diagnostic value of alternative indexes of IR was evaluated by the working characteristic curve of subjects. The relationship between different alternative indicators of IR and survival rate was evaluated by survival curve. COX regression was used to analyze the effects of different alternative indicators of IR on the risk of end-point events.

Results: The levels of TyG, TyG-BMI, TyG-WC, TG/HDL-C and METS-IR were significantly increased in patients with Major Adverse Cardiovascular Events (MACEs). Among the five alternative indexes of IR, METS-IR had the highest AUC (0.691, 95% CI:0.657–0.752, $P < 0.001$) in predicting MACEs. No matter which alternative index of IR was used, the survival rate of MACEs in High group was significantly decreased. TyG, TyG-BMI, TyG-WC, TG/HDL-C and METS-IR can independently predict the occurrence of MACEs events, even if some confounding factors are adjusted.

Conclusion: Our study shows that alternative indicators of IR, especially METS-IR, are independently associated with adverse cardiovascular events in patients with MS and HF.

Keywords: insulin resistance indexes, metabolic syndrome, heart failure, predictive

Introduction

Heart failure (HF) is the end-stage manifestation of most heart diseases. HF has become the leading cause of death, hospitalization and medical expenses in people over the age of 65.[1] Traditional risk factors play an important role in HF, just as they do in many other manifestations of heart disease. It is increasingly obvious that some cardiovascular risk factors tend to gather or occur at the same time. The aggregation of some risk factors and their common responses to

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lifestyle changes show that they are not independent of each other, but share common root causes, mechanisms and characteristics.[2,3] It is increasingly recognized that these factors are associated with HF through various pathways.[4]

Patients with metabolic syndrome (MS) are characterized by a higher risk of cardiovascular disease because there are multiple risk factors in the same individual, such as obesity, hypertension, dyslipidemia and diabetes, any of which increases the risk of cardiovascular disease.[5] According to this view, it is considered convenient to combine several risk factors into a single entity, so that patients can easily be labeled as having a higher risk of CV. 22% to 68% of HF patients showed MS phenotype.[6–8] However, compared with the general population, the existence of MS is associated with twice the risk of HF.[9,10]

Insulin resistance (IR) is a key underlying mechanism in all components of MS. IR means that due to various reasons, the efficiency of insulin in promoting glucose uptake and utilization decreases, the body compensatively secretes too much insulin, and produces hyperinsulinemia to maintain the stability of blood sugar. It is well known that IR is a major risk factor for type 2 diabetes mellitus (T2DM) and cardiovascular disease, and is closely related to other metabolic abnormalities.[11,12] These metabolic abnormalities lead to the development of chronic non-communicable diseases around the world. Hyperinsulinemic euglycemic clamp is considered to be the gold standard for the determination of IR. Because of its complex clinical operation, expensive equipment and ethical problems, the homeostasis model assessment of IR (HOMA-IR) is used as an alternative tool for defining IR.[13] However, fasting blood glucose and fasting insulin are included in the calculation of HOMA-IR, while the measurement of insulin is limited because of its relatively high cost in clinical practice. Therefore, it is very important to actively look for a simple, robust and cost-effective alternative biomarker to predict IR before the emergence of clinical diseases.

In recent years, some new and easily available tools for predicting IR have been proposed. The Triglyceride/high density lipoprotein cholesterol ratio (TG/HDL-C), a simple marker derived from two routine blood lipid parameters, has been shown to have the ability to predict IR and cardiovascular disease risk.[14] In addition, compared with HOMA-IR index, triglyceride / glucose index (TyG index) derived from fasting triglyceride and glucose levels, TyG related indicators (TyG-BMI and TyG-WC) and insulin resistance metabolic score (METS-IR) have been reported as good alternative indicators of IR, which can reliably evaluate the IR of individuals with or without diabetes. A number of studies have shown that the degree of IR is associated with cardiovascular adverse events in patients with HF and can be used to independently predict mortality in patients with HF.[15–17]Insulin resistance is not only a characteristic of metabolic syndrome, but also related to heart disease caused by metabolic syndrome.Therefore, the purpose of this study is to evaluate the ability and accuracy of different insulin resistance alternative markers to predict clinical end-point events in patients with metabolic syndrome complicated with heart failure. Identify relatively good alternative markers for insulin resistance related to prognosis.

Materials and Methods

Study Population

Patients with MS and HF who attended the cardiac center of the First Affiliated Hospital of Xinjiang Medical University from January 2015 to December 2019 were enrolled in this study. MS was defined as waist circumference >102 cm in men and >88 cm in women; Blood pressure >130/85 mmHg or on medication; fasting plasma glucose (FPG) ≥110 mg/dL or on medication; triglycerides ≥150 mg/dL; and HDLC <40 mg/dL in men and <50 mg/dL in women.[18] Autoimmune diseases, acute or chronic infectious diseases were excluded, Severe hepatic or renal insufficiency, malignant tumors, hematologic disorders, familial hypertriglyceridemia, hormone shock therapy, patients with incomplete clinical data and lost to follow-up. The study complied with the Declaration of Helsinki. The study was approved by the Medical Ethics Committee of the First Affiliated Hospital of Xinjiang Medical University (20,141,201–03-1701A). All study participants provided written informed consent.

Collection and Definition of the Clinical Data

The gender, age, height, weight, waist circumference, smoking, alcohol consumption, and disease history of the enrolled patients were collected by the trained researchers. Fasting venous blood samples were collected by fasting for at least 12h

after admission. The clinical indexes such as fasting blood glucose, triglyceride, total cholesterol, low density lipoprotein cholesterol, high density lipoprotein cholesterol and serum creatinine were detected by the testing center of Xinjiang Medical University. Smoking is defined as smoking at least one cigarette a day for more than 6 months. Drinking is defined as at least 3 times a week for more than 6 months. All patients were examined by transthoracic echocardiography within 24 hours after admission. Body mass index (BMI) is calculated by dividing weight by height squared (kg/m^2). The glomerular filtration rate (eGFR) was estimated as [(140-age) × weight (kg)] × 0.85(if female) / [72 × serum creatinine (mg/dl)]. The alternative indicators of IR are calculated as follows: TyG=Ln[TG (mg/dL)×FPG (mg/dL)/2], TyG-BMI =TyG index×BMI, TyG-WC=TyG index ×WC,[19] TG/HDLc= TG (mg/dL)/ HDL-C(mg/dL), METS-IR was calculated as ln [(2 × FPG (mg/dL) + fasting TG (mg/dL)] × BMI (kg/m^2))/(ln[HDL-C (mg/dL]).[20]

Endpoints and Follow-Up

All patients were followed up for 36 months after discharge. The main adverse cardiovascular events (MACEs) were the combination of readmission of HF and cardiac death. Cardiac death is defined as death caused by acute myocardial infarction, HF, arrhythmia, cardiac surgery or other cardiovascular causes. Follow-up is mainly through phone calls and questionnaires, as well as collecting information about patients' treatment in our institution or other hospitals.

Statistical Analysis

The continuous variables with normal distribution are described by mean and standard deviation. The median and quartile spacing are used to describe the continuous variables that do not obey the normal distribution. *T*-test or rank sum test was used to compare the differences of continuity variables between the two groups. The classified variables were described by the number of cases and percentage, and compared by chi-square test. Receiver operating characteristic curve (ROC) was used to evaluate the diagnostic value of alternative indicators of IR in end events. The Yoden index is calculated according to the sensitivity and specificity of each index, and the best tangent point value is determined. Kaplan-Meier curve was used to evaluate the event-free survival rate of different levels of IR alternative indicators. Multivariate COX regression analysis was used to evaluate the relationship between different alternative indicators of IR and the risk of clinical end-point events. Calculate the risk ratio (HR) and its 95% confidence interval (CI). Statistical analysis was carried out using survival and survminer packages of SPSS 25.0 and R software (version 4.2.1).

Results

Baseline Characteristics of Patients

A total of 5087 patients with heart failure were enrolled in this study, and 1170 patients with heart failure and metabolic syndrome were finally included.1048 patients in the study completed 36 months of follow-up, with a loss of follow-up rate of 10.4%. Among the 1048 participants who completed a 36-month follow-up, the average age was 65 ±10 years old, including 768 males(73.3%) and 280 females(26.7%). During the follow-up period, there were 543 (51.8%) patients with cardiac death, 174 (16.6%) patients re-admitted for HF, and 717 (68.4%) patients with MACEs. The patients were divided into two groups according to the occurrence of MACEs, and the general characteristics and clinical data of the two groups were compared. There was no significant difference in sex, age, smoking, drinking and disease history between the two groups. Compared with non-MACEs group, the levels of BMI, WC, FPG, TyG, TyG-BMI, TyG-WC, TG/HDL-C and METS-IR in MACEs group were significantly increased. The levels of SBP and HDL-C in MACEs group were significantly lower than those in non-MACEs group (Table 1).

Five Alternative Indexes of Insulin Resistance Were Analyzed by ROC

In order to determine the predictive ability of five different IR alternative indicators for clinical end points, we performed ROC analysis. The results showed that the AUC (0.591, 95% CI:0.545–0.637, P < 0.001) of METS-IR was the highest in predicting re-admission of HF. The second is TyG-WC. In the prediction of cardiogenic death, METS-IR had the highest AUC (0.691, 95% CI:0.657–0.752, P < 0.001). The second is TyG-BMI. In terms of predicting MACEs, TyG-WC has a higher sensitivity, followed by METS-IR. METS-IR has a higher specificity, followed by TG/HDL-C (Tables 2 and 3). According to the cut-off

Table 1 Baseline Data of the Subjects Were Collected

	Non-MACEs	MACEs	P
Age, years	65±10	65±10	0.899
Male, n(%)	234(70.7)	534(74.5)	0.198
Smoking, n(%)	129(39.0)	295(41.1)	0.506
Drinking, n(%)	83(25.1)	201(28.1)	0.310
Previous stroke, n(%)	40(12.1)	87(12.1)	0.982
Previous MI, n(%)	106(32.0)	236(32.9)	0.775
BMI, kg/m^2	25.90±3.51	27.49±4.14	<0.001
WC, cm	96.5±10.9	100.5±12.0	<0.001
SBP, mmHg	129±21	126±20	0.014
DBP. mmHg	77±13	75±13	0.070
EGFR, mL/min/1.73 m^2	73.00(48.63,92.99)	71.09(49.27,95.77)	0.893
FPG, mg/dL	124.92(95.40,175.68)	153.00(110.07,226.71)	<0.001
TG, mg/dL	115.18(85.06,159.48)	119.61(88.60,170.99)	0.166
TC, mg/dL	129.26(105.65,160.99)	128.87(104.30,158.67)	0.499
HDL-C, mg/dL	35.60(29.41,41.02)	31.73(26.31,37.93)	<0.001
LDL-C, mg/dL	83.21(65.02,107.20)	82.82(61.92,105.07)	0.893
LVEF, %	43(37,49)	42(37,47)	0.121
BNP, pg/mL	3077.00(996.80,6816.00)	2603.21(922.38,6096.00)	0.439
NYHA			0.105
I	4(1.2)	2(0.3)	
II	66(19.9)	123(17.2)	
III	195(58.9)	419(58.4)	
IV	66(19.9)	173(24.1)	
TyG	8.89(8.45,9.51)	9.13(8.65,9.77)	<0.001
TyG-BMI	228.23(208.29,254.09)	251(223.64,279.47)	<0.001
TyG-WC	863.28(792.15,932.54)	918.80(832.01,1012.17)	<0.001
TG/HDL-C	3.43(2.36,4.82)	3.91(2.71,5.72)	<0.001
METS-IR	42.66(39.40,47.36)	48.13(43.20,54.31)	<0.001

Abbreviations: MI, myocardial infarction, WC, waist circumference, SBP, systolic pressure, DBP, diastolic blood pressure, eGFR, estimated glomerular filtration rate, FPG, fasting plasma glucose, TG, triglyceride, TC, total cholesterol, HDL-C, high density lipoprotein cholesterol, LDL-C, low density lipoprotein cholesterol, LVEF, left ventricular ejection fraction, BNP, brain natriuretic peptide, NYHA class, New York Heart function classification.

value of different insulin resistance indexes, they were divided into High group and Low group. Kaplan-Meier survival curve showed that no matter which IR replacement score was used, the survival rate of MACEs in High group decreased significantly ($p < 0.001$, Log rank test) (Figure 1).

COX Regression Model Was Used to Analyze the Relationship Between Different Alternative Indicators of Insulin Resistance and the Risk of Clinical End-Point Events

In order to clarify the relationship between different alternative indicators of Insulin Resistance and the risk of clinical end-point events, we further constructed a COX risk prediction model.Model 1 was adjusted for age and sex, model 2 was further adjusted for smoking, drinking previous stroke, previous MI and NYHA on the basis of model 1, and model 3 was further adjusted for eGFR, LDL-C, LVEF, and BNP on the basis of model 2. The results show that TyG, TyG-BMI, TyG-WC, TG/HDL-C, METS-IR were independently associated with the risk of HF readmission, TyG, TyG-BMI, TyG-WC, METS-IR were independently associated with the risk of cardiac death, and TyG, TyG-BMI, TyG-WC, TG/HDL-C, METS-IR were independently associated with the risk of MACEs, although some possible confounding factors were adjusted. Different insulin resistance substitution scores were still statistically significant for clinical end-point events. The HR and 95% CI of each variable are listed in Table 4.

Table 2 Predictive Value of Surrogate Indexes of Insulin Resistance for Endpoint Events

	AUC(95% CI)	P
Readmission for heart failure		
TyG	0.555(0.507–0.602)	0.022
TyG-BMI	0.570(0.522–0.619)	0.003
TyG-WC	0.575(0.527–0.623)	0.002
TG/HDL-c	0.563(0.515–0.612)	0.008
METS-IR	0.591(0.545–0.637)	<0.001
Cardiovascular death		
TyG	0.542(0.507–0.577)	0.020
TyG-BMI	0.585(0.550–0.619)	<0.001
TyG-WC	0.575(0.540–0.609)	<0.001
TG/HDL-c	0.533(0.498–0.568)	0.068
METS-IR	0.614(0.580–0.648)	<0.001
MACEs		
TyG	0.583(0.546–0.620)	<0.001
TyG-BMI	0.643(0.608–0.678)	<0.001
TyG-WC	0.634(0.600–0.669)	<0.001
TG/HDL-c	0.578(0.541–0.615)	<0.001
METS-IR	0.691(0.657–0.725)	<0.001

Table 3 Sensitivity, Specificity, and Cutoff Values of Surrogate Indexes of Insulin Resistance for Predicting MACEs

	Sensitivity	Specificity	Cut-Off
TyG	62.2	51.7	8.91
TyG-BMI	62.5	58.0	235.87
TyG-WC	65.0	56.8	873.44
TG/HDL-c	51.5	60.7	3.85
METS-IR	64.6	65.0	45.17

Discussion

In this study, we used several insulin resistance substitute scores to compare their predictive value for adverse cardiovascular events in patients with MS complicated with HF. To our knowledge, this is the first comparative study in patients with MS complicated with HF.

Based on our analysis, we found that different insulin resistance substitution scores were independently associated with MACEs in patients with MS complicated with HF. In contrast, the correlation between METS-IR and MS with HF was higher than other insulin resistance replacement scores. These results can help clinicians understand the relationship between IR, HF and poor prognosis according to the presence of MS.

Doctors and scientists have long known that certain conditions increase the risk of atherosclerotic cardiovascular disease. These risk factors include family history of premature coronary heart disease, hypertension, hyperlipidemia, diabetes and smoking. Age, male sex and postmenopausal hormonal status all increase the risk of cardiovascular disease. Patients with HF suffer from a variety of metabolic complications, which have a significant impact on prognosis.[21] In fact, MS is a series of cardiovascular risk factors that reflect the presence of IR, such as central obesity, impaired glucose homeostasis, dyslipidemia and systemic arterial hypertension. Epidemiological data show that the relationship between MS and HF is two-way.

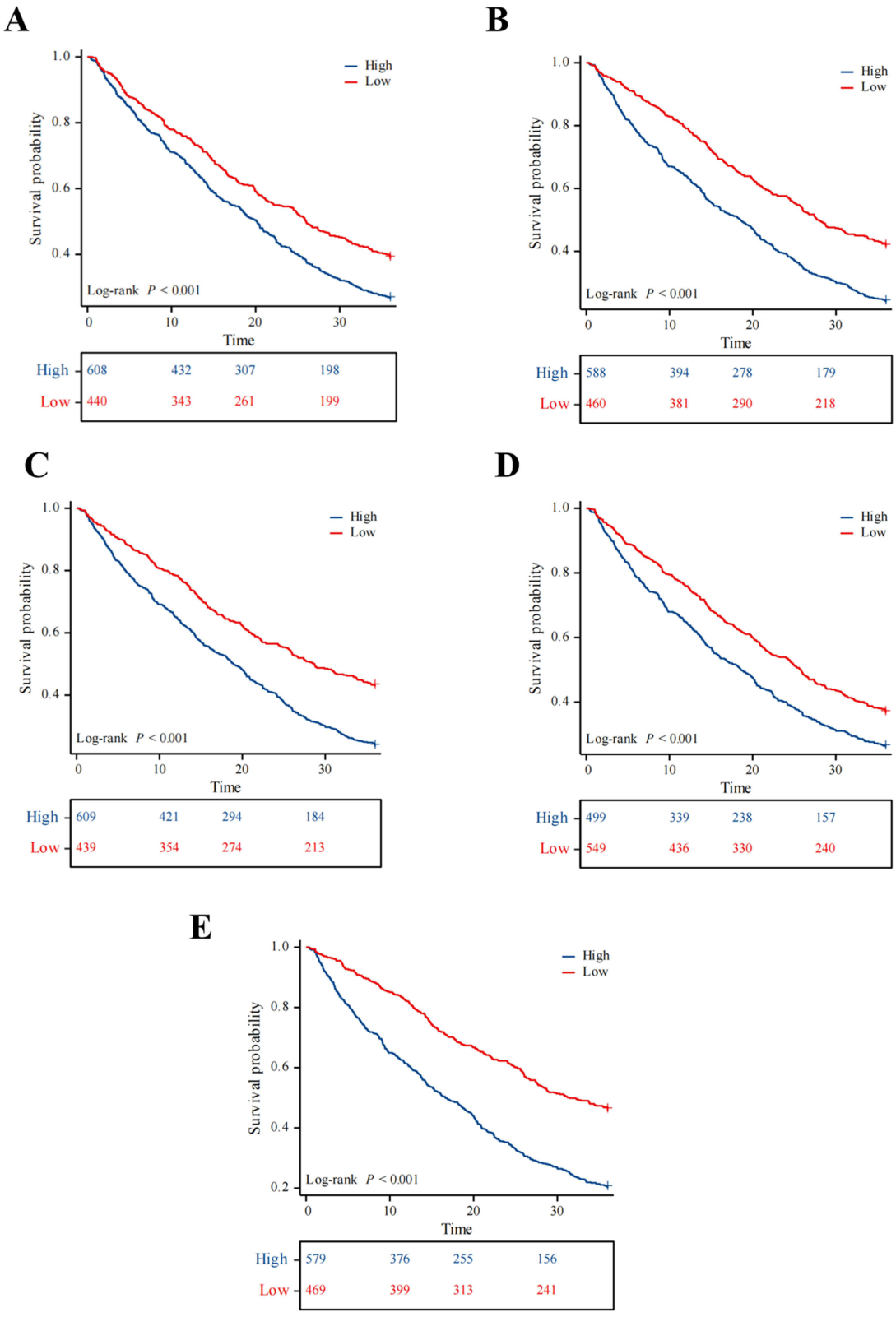

Figure 1 Kaplan–Meier analyses of adverse outcomes categorized by the cut-off values corresponding to different measures of Insulin Resistance. (A) TyG. (B) TyG-BMI. (C) TyG-WC. (D) TG / HDL-C. (E) METS-IR.

Table 4 Surrogate Indexes of Insulin Resistance Evaluated the Risk of Endpoint Events

	Readmission for Heart Failure		Cardiovascular Death		MACEs	
	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P
TyG						
Unadjusted	1.347(1.123–1.616)	0.001	1.141(1.031–1.264)	0.011	1.265(1.155–1.385)	<0.001
Model1	1.391(1.159–1.670)	<0.001	1.139(1.028–1.263)	0.013	1.281(1.168–1.404)	<0.001
Model2	1.381(1.151–1.657)	0.001	1.156(1.042–1.282)	0.006	1.289(1.175–1.413)	<0.001
Model3	1.419(1.169–1.723)	<0.001	1.185(1.061–1.324)	0.003	1.326(1.203–1.463)	<0.001
TyG-BMI						
Unadjusted	1.007(1.004–1.010)	<0.001	1.005(1.003–1.006)	<0.001	1.006(1.005–1.008)	<0.001
Model1	1.007(1.004–1.010)	<0.001	1.005(1.003–1.007)	<0.001	1.006(1.005–1.008)	<0.001
Model2	1.007(1.004–1.010)	<0.001	1.005(1.003–1.007)	<0.001	1.007(1.005–1.008)	<0.001
Model3	1.008(1.005–1.012)	<0.001	1.006(1.004–1.008)	<0.001	1.008(1.006–1.010)	<0.001
TyG-WC						
Unadjusted	1.002(1.001–1.003)	<0.001	1.001(1.001–1.002)	<0.001	1.002(1.001–1.002)	<0.001
Model1	1.002(1.001–1.003)	<0.001	1.001(1.001–1.002)	<0.001	1.002(1.001–1.002)	<0.001
Model2	1.002(1.001–1.003)	<0.001	1.001(1.001–1.002)	<0.001	1.002(1.001–1.003)	<0.001
Model3	1.002(1.001–1.003)	<0.001	1.002(1.001–1.002)	<0.001	1.002(1.002–1.003)	<0.001
TG/HDL-c						
Unadjusted	1.066(1.039–1.094)	<0.001	1.011(0.993–1.030)	0.230	1.045(1.028–1.062)	<0.001
Model1	1.071(1.043–1.099)	<0.001	1.011(0.992–1.030)	0.251	1.047(1.030–1.064)	<0.001
Model2	1.073(1.044–1.102)	<0.001	1.011(0.993–1.030)	0.219	1.048(1.031–1.065)	<0.001
Model3	1.078(1.047–1.109)	<0.001	1.013(0.994–1.032)	0.195	1.051(1.033–1.069)	<0.001
METS-IR						
Unadjusted	1.032(1.019–1.046)	<0.001	1.028(1.020–1.036)	<0.001	1.033(1.027–1.040)	<0.001
Model1	1.033(1.019–1.047)	<0.001	1.030(1.021–1.038)	<0.001	1.035(1.029–1.042)	<0.001
Model2	1.035(1.021–1.049)	<0.001	1.030(1.022–1.038)	<0.001	1.036(1.029–1.044)	<0.001
Model3	1.038(1.024–1.053)	<0.001	1.032(1.023–1.041)	<0.001	1.040(1.033–1.047)	<0.001

Notes: Model 1 was adjusted for age and sex, model 2 was further adjusted for smoking, drinking previous stroke, previous MI and NYHA class on the basis of model 1, and model 3 was further adjusted for eGFR, LDL-C, LVEF, and BNP on the basis of model 2.

MS is a collection of interrelated metabolic risk factors, including fat metabolic disorders, obesity, diabetes, insulin resistance and other risk factors, to help identify individuals with increased risk of type 2 diabetes and cardiovascular disease. According to previous research, MS has doubled the morbidity and mortality of CVD worldwide.[22,23] In other prospective European studies, the presence of this syndrome indicates an increase in mortality from cardiovascular disease and coronary heart disease. Again, this finding is not surprising because MS includes established risk factors for cardiovascular disease. With regard to the correlation between MS and CVD, an important question is whether the CVD risk of MS is greater than the sum of individual risk factors. This issue has been reviewed and debated elsewhere. Framingham's research has long shown that multiple risk factors increase the risk of CVD more than the sum of individual risk factors. The presence of MS is also associated with an increased risk of CVD events and mortality in patients with existing coronary heart disease. In fact, MS in patients with coronary heart disease was associated with a higher risk of CVD than patients with no known coronary heart disease. When MS exists, the risk of cardiovascular disease doubles in obese and diabetic patients. The greatest significance of MetS is the early identification of high-risk groups of CVD, so its ability to predict disease risk is the key to the definition.[24]

Individuals with insulin resistance showed impaired glucose metabolism or tolerance, characterized by abnormal responses to glucose challenges, increased fasting blood glucose levels and / or significantly hyperglycemia, or decreased insulin action after intravenous insulin injection. Reduced insulin-mediated glucose clearance and / or endogenous glucose production inhibition. Insulin resistance is very common in patients with HF (up to 60%), and there is a complex pathophysiological interaction between the two conditions, because IR may represent both the causes and consequences of HF.[25] As demonstrated by a landmark prospective cohort study conducted by Ingelsson et al, IR is a predictor of HF independent of diabetes and other known HF risk factors.[26] However, HF is also

considered to be a metabolic state of insulin resistance.[27] In addition, IR is significantly related to the survival time of patients with HF[28].

At present, the definition of MS can be summarized into four core characteristics: insulin resistance, visceral obesity, atherosclerotic dyslipidemia and endothelial dysfunction. Among them, the first two seem to be necessary for MS. There is no further simplification. Even if other related findings, such as systemic inflammation, hypercoagulable state, or microalbuminuria are important for pathophysiology, they are not necessary as part of the definition because these findings do not need to exist independently. Insulin resistance and visceral obesity are associated with atherosclerotic dyslipidemia.[29] The main characteristics of atherosclerotic dyslipidemia are high plasma TG level, low HDL cholesterol level and small and dense LDL increase. Insulin resistance leads to atherosclerotic dyslipidemia in many ways. In the case of insulin resistance, the flow of free fatty acids into the liver increased and the synthesis of triglycerides in the liver increased. Another major lipoprotein disorder of MS is the reduction of HDL cholesterol. This decrease is the result of changes in the composition and metabolism of HDL. In the case of hypertriglyceridemia, the decrease in the content of high-density lipoprotein cholesterol is due to a decrease in the cholesteryl ester content content of the lipoprotein core. Multiple effects of HDL have been described, which may explain its protective effects on the development of HF, including improving endothelial dysfunction, anti-inflammation, and antioxidant activity.[30,31] In atherosclerotic multi-ethnic studies, high triglyceride plasma levels were also independently associated with an increased risk of HF in patients with diabetes.

Although the gold standard method for evaluating insulin resistance is hyperinsulinemic euglycemic clamp, it is rarely used in clinical environment because of its high cost, low availability and low repeatability. Previous studies have shown that TG/HDL-C and TyG and their related indicators (TyG-BMI, TyG-WC) are often used as alternative markers for the assessment of insulin resistance. At the same time, it is clear that TyG index and related indexes are reliable predictors of risk stratification and poor prognosis in patients with heart failure.[32] However, these indices ignore the role of nutritional status in insulin sensitivity. Considering these limitations, the metabolic score of insulin resistance (METS-IR) index is considered to be another measure of IR, which represents the nutritional status of insulin resistance and is highly consistent with the gold standard in the evaluation of IR.This type of index has been widely used in all kinds of cardiovascular diseases, but for patients with MS complicated with HF, we found that TyG, TyG-BMI, TyG-WC, TG/HDL-C, METS-IR has varying degrees of correlation with clinical end-point events in patients with metabolic syndrome complicated with heart failure, among which METS-IR may be a relatively good usability index.At the same time, based on our team's previous study,[33] it was clear that there was a significant correlation between METS-IR and MACES in diabetic patients with ischemic cardiomyopathy, even after adjusting for other confounding factors. Adding METS-IR to the established risk prediction model has incremental value for the prediction of MACES, which further confirms the important role of Mets-IR in cardiovascular disease.Therefore, for our results, we further confirmed that there is an independent correlation between different insulin resistance substitution scores and adverse cardiovascular events in patients with metabolic syndrome complicated with heart failure in patients with MS with HF.

Study Limitations

In spite of this, this study has some limitations. First of all, the study is a retrospective design, and the results may be affected by selection bias or unobserved confounding factors. Secondly, due to the initial research design, we can not rule out the effects of drugs and related surgical history on clinical blood glucose and blood lipids.In addition, the final results presented by our data are only of moderate predictive value, but the summary analysis of a number of IR evaluation indicators provides a broader idea for the study of IR in patients with HF complicated with MS. Finally, we did not study the relationship between alternative indicators of insulin resistance and other end events. Despite some limitations in this study, we have identified the relationship between insulin replacement indicators and adverse cardiovascular events in patients with metabolic syndrome complicated with heart failure.

Conclusion

Our study shows that alternative indicators of insulin resistance, especially METS-IR, are independently associated with adverse cardiovascular events in patients with MS and HF.

Data Sharing Statement

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethical Approval

This study followed the Declaration of Helsinki. Approved by the Medical Ethics Committee of The First Affiliated Hospital of Xinjiang Medical University (20141201-03-1701A).

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Disclosure

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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