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The Impact of the Triglyceride-Glucose Index on the Development of Depression in Patients with Coronary Atherosclerotic Heart Disease

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Background: Depression is common among patients with coronary atherosclerotic heart disease and is a prevalent mental health issue, particularly among those with cardiovascular diseases. Depression is commonly associated with elevated blood glucose and lipid levels. The triglyceride-glucose index is a novel indicator reflecting insulin resistance, which has been proven in numerous studies to be associated with cardiovascular diseases.

Purpose: Study on the impact of the triglyceride-glucose index (TyG index) on the development of depression in patients with coronary atherosclerotic heart disease (CHD).

Patients and methods: Using the Patient Health Questionnaire-9 (PHQ-9), 197 CHD patients were classified into a non-depressed group (n = 44, PHQ-9 < 5) and a depressed group (n = 153, PHQ-9 ≥ 5). Fasting blood glucose (GLU), HDL, total cholesterol (TC), LDL, triglycerides (TG), and TyG index were compared between groups. Depression risk factors were identified via logistic regression, and the predictive value of TyG index was evaluated using ROC analysis.

Results: In depressed patients, TyG index, TG, TC, LDL, and GLU were significantly higher, while HDL was lower than in the non-depressed group ($p < 0.05$). Logistic regression identified TyG index, LDL, GLU, TG, TC, HDL, female sex, smoking, alcohol consumption, and older age as independent risk factors for depression in CHD patients ($p < 0.05$). ROC analysis showed the TyG index had an AUC of 0.76 (95% CI 0.687–0.829, $p < 0.001$) for predicting depression, with a cutoff of 1.613, sensitivity of 45.1%, and specificity of 97.7%. Endpoint events were more frequent in the depression group ($\chi^2 = 8.015$, $p = 0.005$).

Conclusion: The TyG index is an independent risk factor for depression in patients with CHD, indicating a significant predictive value. Depressed patients have a higher rate of readmission, and managing depression effectively contributes to better prognosis.

Keywords: depression, coronary atherosclerotic cardiopathy, triglyceride-glucose index

Introduction

Coronary heart disease (CHD) is one of the leading causes of old people's death in low and middle income countries. It is caused by a narrowing or occlusion of the coronary artery, resulting in a decrease in blood supply to the heart and a lack of oxygen in myocardium.[1] CHD is a chronic disease with a long course and high recurrence rate. The heavy economic burden often leads to psychological disorders such as depression in patients.[2] Studies have shown that the incidence of depression in CHD patients is three times higher than in healthy individuals, and the mortality rate of patients with comorbid depression is twice as high as that of healthy individuals within two years after the onset of CHD.[3] In recent years, an increasing number of studies have shown a close relationship between insulin resistance, cardiovascular diseases (CVD), and depression. Insulin resistance is not only a core feature of metabolic syndrome but is also considered an important risk factor for the development of cardiovascular diseases.[4]

The incidence of depression is significantly increased among patients with cardiovascular diseases, and this association may be related to inflammation and metabolic abnormalities caused by insulin resistance.[5] In recent years, the triglyceride-glucose

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index (TyG index) has been recognized as a simple measure of insulin resistance (IR). Insulin resistance refers to the reduced response of the body to insulin, while the TyG index is a measure of insulin resistance calculated using triglyceride and glucose levels. Research has shown that the TyG index has the potential to predict the risk of depression and may outperform traditional methods of assessing insulin resistance, such as HOMA-IR and QUICKI. For example, compared to HOMA-IR, the TyG index is easier to apply in clinical practice and demonstrates better correlation in patients with cardiovascular diseases.[6] By assessing the insulin resistance status of the body, it helps physicians accurately judge the patient's condition and is closely related to the degree of coronary artery disease and its prognosis.[7] Currently, the diagnosis of depression is based on symptoms and lacks objective, measurable biological markers.[8] Therefore, this study aims to analyze the correlation between the serum TyG index and CHD with comorbid depression, and analyzing its clinical significance and predictive value in the onset of CHD patients, is crucial. The findings of this study not only contribute to improving patient prognosis and reducing readmission rates but also provide clinicians with effective tools to identify and manage high-risk patients. Based on the assessment of the TyG index, physicians can develop more personalized treatment plans and conduct regular monitoring to enhance the overall health of patients.

Subjects and Methods

Subjects

From January 2023 to December 2023, 236 patients with CHD were hospitalized and treated in the Renhe Hospital, Cardiovascular Medicine, affiliated to China Three Gorges University. Finally, 197 patients were enrolled according to inclusion and exclusion criteria. Inclusion criteria: (1) The diagnosis of CHD was based on coronary angiography showing coronary stenosis greater than 50%, or a history of myocardial infarction; (2) Agreement to undergo the PHQ-9 depression scale assessment; (3) Complete demographic characteristics and clinical data. Exclusion criteria: (1) patients with malignant tumor or immune system disorders;[9] (2) Patients with mental disorders, especially patients with cognitive impairment, are unable to communicate with people normally; (3) History of trauma or surgical procedures and active infection history in the past six months;[9] (4) Incomplete clinical data (Figure 1). The study was approved by Renhe Hospital Ethics Committee. The ethical approval number is 2023–29.

Affiliated to China Three Gorges University, all the participants signed a written agreement and adhered to the Helsinki Declaration.

Methods

Data Collection

Our researchers collected demographic data (age, sex, marriage, education level, residence area), medical history (high blood pressure), personal history (smoking, drinking), and angiography results at admission. Educational level was measured based on the highest degree obtained. Marital status is categorized into married, unmarried, divorced, and widowed. Smoking is defined as having smoked at least one cigarette per day in the last six months. Drinking is defined as having consumed alcohol at least once a week in the last six months. Hypertension is defined as having a systolic BP of 140 mmHg or above and/or DBP of 90 mmHg on three separate occasions, or having a history of hypertension and being on antihypertensive medication. After admission, the severity of the coronary arteries is assessed by a certified cardiologist through coronary angiography. All patients meeting the inclusion criteria were followed up for 6 months to assess the impact on the composite endpoint of rehospitalization or all-cause mortality.

Laboratory Test and Blood Collection

On the day of admission or the following morning, blood samples were taken from the patient's elbow vein and collected in a 3 mL EDTA-K2 tube after fasting for at least 8 hours. The Sysmex XN-9000 (Sysmex, Kobe, Japan) Hematology Automated Analyzer, which was tested in our hospital's lab, was completely unknown to the examiner. The TyG index is calculated by another participating researcher using the formula: TyG index = ln[(fasting glucose (mg/dL) × fasting triglycerides (mg/dL))/2].

Psychological Assessment

All psychological evaluations were carried out independently by two psychiatrists. The PHQ-9 Depression Scale was used to measure the severity of depression in hospitalized patients by face-to-face interviews. A PHQ-9 score ≥ 5

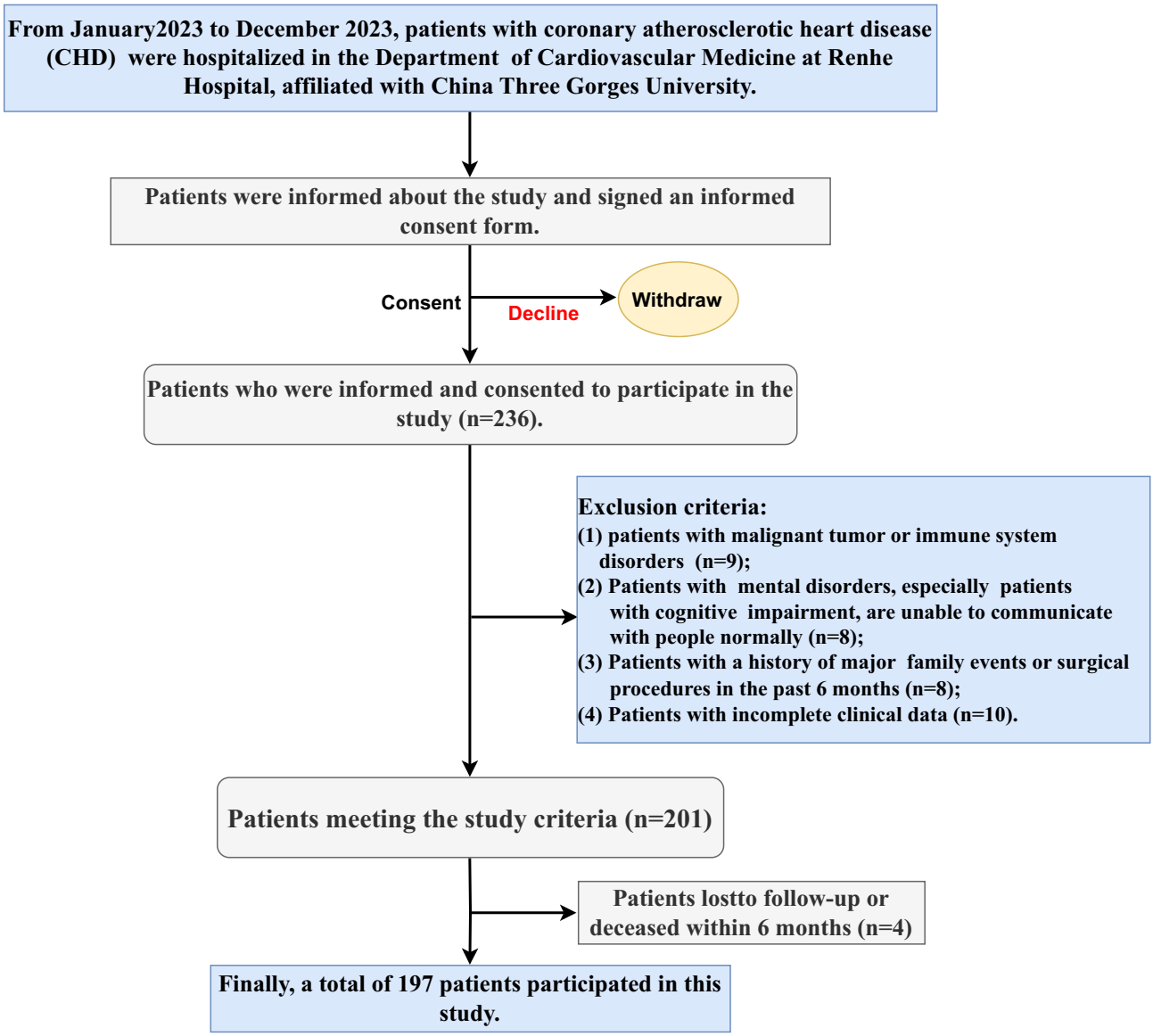

Figure 1 Recruitment Process Flowchart.

indicates a state of depression. Chinese Classification of Mental Disorders (Chinese Classification of Mental Disorders, Third Edition), Chinese Society of Psychiatry, which is based on the American psychiatric diagnostic standards and adapted to Chinese characteristics, a new and targeted method for diagnosing depressive states was proposed.

Statistical Analysis

The data were processed and analyzed with SPSS 26.0 software. The normal distribution of the measured data was expressed as the mean ± standard deviation, and the *T* test was used to compare the two groups. The abnormal distribution of measured data was expressed as median (P25, P75), and the Mann–Whitney *U*-test was used to compare the two groups. Categorical data were presented in terms of counts and percentages, with group comparisons using the $\chi 2$ test. Logistic regression analysis was used to assess the risk factors for depression in CHD patients, and the predictive value of the TyG index for depression in CHD patients was evaluated using the receiver operating characteristic (ROC) curve. Finally, the incidence of endpoint events was compared with the $\chi 2$ test, and the prognostic factors were explored. The p-value of < 0.05 was considered statistically significant.

Results

In this study, 236 patients with CHD were admitted to the Cardiovascular Medicine Division of China Three Gorges University, Renhe Hospital, from January 2023 to December 2023, and agreed to take part in the study. Among them, 12 patients were excluded due to hematologic, malignant tumors, cerebrovascular, or infectious diseases; 8 were excluded due to psychiatric disorders; 9 were excluded due to a history of major family events or surgical procedures in the past six months; and 10 were excluded due to incomplete clinical data. Additionally, 4 patients were lost to follow-up, resulting in a final study population of 197 patients.

A Comparative Study on the General Clinical Data Between Two Groups

The differences in age, gender, smoking history, alcohol consumption history, educational level, and serum levels of TG, LDL, HDL, TC, GLU, and TyG index between the depressed group and the non-depressed group were statistically significant ($P < 0.05$). Compared to CHD patients without depression, the depressed group had a higher proportion of females, higher educational levels, older age, and a higher proportion of patients with a smoking and drinking history. Serum levels of TyG index, TG, LDL, TC, and GLU were higher in CHD patients with depression compared to those without depression, while HDL levels were lower in the depressed group (Table 1).

Table 1 Comparison of General Conditions Between the Two Groups of Patients [M (P25, P75) / Number (%)]

Variables	Depressed Group (n=153)	Non-depressed Group (n=44)	Z/χ^2 value	p-value
Age (years)	67 (59,73)	60 (53.25,66.75)	−3.898	**<0.001**
Gender			13.417	**<0.001**
Male	60 (39.2)	31 (70.5)		
Female	93 (60.8)	13 (29.5)		
Marital Status			2.182	0.14
Married	135 (88.2)	35 (79.5)		
Divorced, Single, Widowed, Other	18 (11.8)	9 (20.5)		
Educational Level			25.421	**<0.001**
Below High School	49 (32.1)	32 (72.7)		
Technical Secondary School, High School	48 (31.3)	2 (4.6)		
College Diploma and Above	56 (36.6)	10 (22.7)		
Place of Residence			2.166	0.141
City	89 (58.2)	31 (70.5)		
Rural area	64 (41.8)	13 (29.5)		
Alcohol History			4.667	**0.031**
Yes	62 (40.5)	10 (22.7)		
No	91 (59.5)	34 (77.3)		
Smoking History			7.092	**0.008**
Yes	80 (52.3)	13 (29.5)		
No	73 (47.7)	31 (70.5)		
Hypertension History			0.846	0.358
Yes	115 (75.2)	36 (81.8)		
No	38 (24.8)	8 (18.2)		
TG	1.48 (1.05,2.08)	1.04 (0.73,1.45)	−4.175	**<0.001**
LDL	2.25 (1.63,2.86)	1.86 (1.53,2.36)	−2.249	**0.025**
HDL	1.17 (1.03,1.38)	1.39 (1.15,1.54)	−2.777	**0.005**
TC	4.32 (3.52,5.31)	3.78 (3.20,4.86)	−2.147	**0.032**
GLu	5.98 (5.43,7.11)	5.49 (5.06,5.96)	−4.085	**<0.001**
TyG Index	1.55 (1.13,1.89)	1.02 (0.75,1.39)	−5.216	**<0.001**

Note: The data in bold is significant ($P < 0.05$).

Table 2 Multivariate Logistic Regression Analysis of Factors Influencing Depression in CHD Patients

Factors	Standard Error	Wald Value	Odds Ratio (OR)	95% Confidence Interval	P-value
Age	0.022	14.445	1.085	1.04–1.132	**<0.001**
Gender	0.37	12.511	3.696	1.791–7.627	**<0.001**
Alcohol History	0.396	4.508	0.432	0.199–0.937	0.034
Smoking History	0.368	6.816	0.383	0.186–0.787	0.009
TG	0.369	14.731	4.125	2.001–8.505	**<0.001**
LDL	0.24	6.223	1.82	1.137–2.912	0.013
HDL	0.513	4.714	0.328	0.120–0.897	0.030
TC	0.163	5.033	1.440	1.047–1.981	0.025
GLu	0.238	12.433	2.317	1.452–3.695	**<0.001**
TyG Index	0.401	22.109	6.604	3.007–14.505	**<0.001**

Note: The data in bold is significant (P < 0.01).

Multivariate Logistic Regression Analysis of Factors Influencing Depression in CHD Patients

A multivariate logistic regression analysis was performed with the presence of depressive tendencies in CHD patients as the dependent variable. The independent variables included gender, LDL, GLU, TG, TC, HDL, and TyG index, which were compared between the two groups as described above. The results indicated that female gender, older age, smoking and drinking history, higher GLU, LDL, TG, TC, and TyG index, and lower HDL were independent risk factors for depression in CHD patients (P < 0.05). For each 1-unit increase in the TyG index, the risk of depression in CHD patients increased by approximately 6.6 times.(Table 2).

Predictive Value of TyG Index for Depression in CHD Patients

On the basis of ROC curves, the area under the ROC curve was 0.76 (95% CI 0.687–0.829, P < 0.001) for predicting CHD depression by TyG index. The optimal cutoff value for TyG index to predict depression occurrence in CHD patients was determined as 1.613 when the Youden index reached its maximum value of 0.428, corresponding to a sensitivity of 45.1% and specificity of 97.7%. Refer to Figure 2.

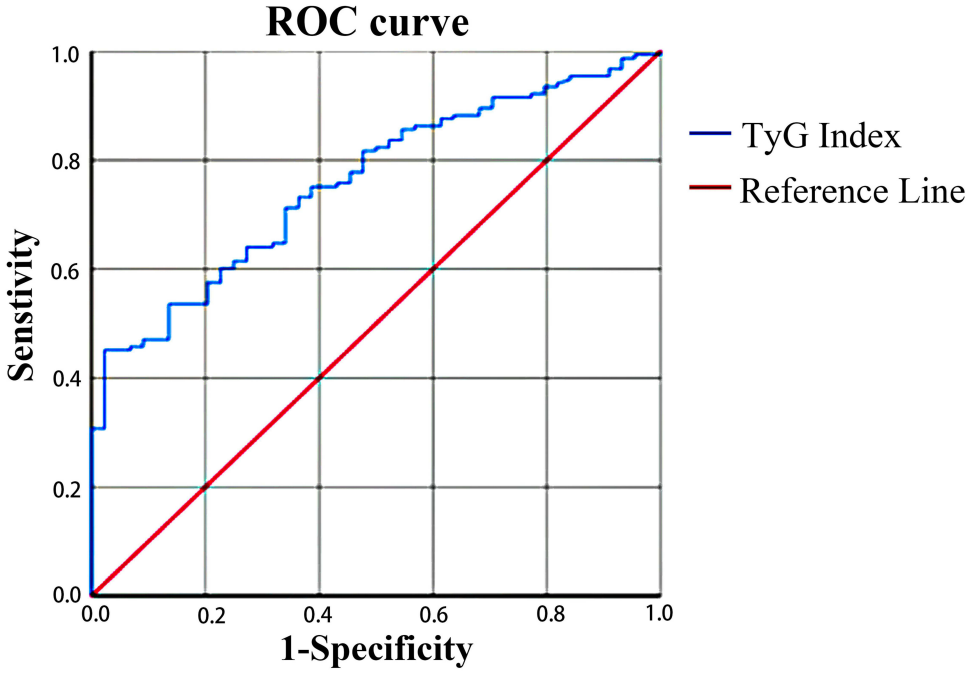

Figure 2 Illustrates the ROC curve depicting the predictive value of TyG index for depression in CHD patients.

Comparison of Endpoint Event Incidence Between the Two Groups

A total of 197 eligible patients were included in this study. After a six-month follow-up, 86 patients (43.7%) experienced endpoint events, defined as readmission due to CHD or myocardial infarction within six months. Among them, 75 cases (49%) were from the depression group and 11 cases (25%) were from the non-depression group. The incidence of endpoint events was significantly higher in the depression group compared to the non-depression group ($\chi 2=8.015$, $p=0.005$), indicating that patients without depressive symptoms had a better prognosis. See Table 3.

Analysis of Prognostic Factors in CHD Patients

An analysis of potential prognostic factors affecting CHD patients revealed significant impacts on prognosis (endpoint events) from factors such as female sex, advanced age, and depression ($p<0.05$). See Table 4 for details.

Discussion

Depression is a common mental disorder caused by the interaction of social, psychological, and biological factors. Thus, developing more potential treatments for depression has currently been an urgent challenge.[10] Major depressive disorder is a risk factor for the development of incident coronary heart disease events in healthy patients and for adverse cardiovascular outcomes in patients with established heart disease. Depression is present in 1 of 5 outpatients with coronary heart disease and in 1 of 3 outpatients with congestive heart failure, yet the majority of cases are not recognized or appropriately treated.[11] Research indicates that depression is an independent risk factor contributing to the heightened incidence and mortality of CHD.[12] Depression is a multi-factorial disorder affected by heredity and environment, and its incidence is rising year by year, with a highly complex pathogenesis. According to the report "Depression and Other Common Mental Disorders: WHO's 2017 Global Health Estimates, estimated at 322 million people around the world. Concurrently, the prevalence of depression among women aged 55–74 is estimated to exceed 7.5%.[12] Insulin resistance, a common feature of type 2 diabetes, hypertension, lipid metabolism disorders, and even cardiovascular diseases, signifies reduced responsiveness to insulin. Several large-scale observational studies have suggested a connection between depression and conditions such as diabetes, cardiovascular disease, and insulin resistance.[13] The TyG index has recently emerged as a novel marker of insulin resistance.[14] Currently, the diagnosis of depression primarily relies on clinical manifestations, with a notable lack of effective biomarkers. The TyG index can be easily derived from basic blood routine tests, providing advantages such as low cost and simplicity in calculation. It can be utilized for the early identification and screening of depression in CHD patients.

This study demonstrates that CHD patients with higher TyG indices are more susceptible to depression, aligning with survey findings. There is no significant difference in marital status, residence, and history of hypertension between the

Table 3 Comparison of Endpoint Event Incidence Between the Two Groups

	Example Number	The Group Diagnosed with Depression (n=153)	The Group without Depression (n=44)	χ^2	p-value
Endpoint Events n (%)				8.015	**0.005**
Yes	86	75 (49%)	11 (25%)		
No	111	78 (51%)	33 (75%)		

Note: The data in bold is significant ($P < 0.05$).

Table 4 Analysis of Prognostic Factors in CHD Patients

	Gender	Age	Smoking History	Alcohol History	Marital Status	Depressed
Z/χ^2	7.854	−7.854	0.559	3.681	0.557	8.015
p-value	**0.005**	**<0.001**	0.455	0.055	0.455	**0.005**

Note: The data in bold is significant ($P < 0.05$).

depressed group and the non-depressed group (P>0.05). However, some international studies indicate variations in the relationship between depression and marital status, as well as blood pressure levels.[15] Certain studies suggest a positive correlation between depression and the severity of hypertension. However, we did not obtain the above conclusion, which may be attributed to regional differences, experimental design, and blood pressure fluctuations. As we only selected a single blood pressure measurement during hospitalization, significant errors may exist.

Compared to specific lipids, glucose, or other biomarkers, the TyG index as a novel indicator signifies not only insulin resistance but also an overall poor health status. It is associated with cardiovascular diseases, obesity, diabetes, hypertension, metabolic syndrome, cerebrovascular diseases, and lipid metabolism disorders.[16] The results of this study suggest that individuals with elevated TyG index levels are more susceptible to complications. Furthermore, a high TyG index serves as an indirect marker of severe illness.[17] Under normal physiological conditions, a rise in blood and tissue glucose results in the secretion of insulin from the pancreas which increases the transport of glucose into tissues, including most importantly, the brain. Thus, it would be anticipated that if insulin-dependent glucose transport into the brain was reduced, this could have a detrimental effect on brain energy metabolism. Insulin resistance, resulting in impaired brain glucose metabolism, is associated with both major depression.[18] Although the mechanism of insulin resistance induced by glucocorticoids and pro-inflammatory cytokines is not fully understood, it has been shown that dysfunctional insulin receptors and receptor pathways influence glucose transport across the blood-brain barrier and subsequent uptake into neurons and neuroglia. In the brain, insulin stimulates glucose uptake and increases the mRNA of glucose transport in neurons and neuroglia. Therefore, a functional deficit in the brain due to insulin resistance can lead to emotional changes due to loss of glycaemic control. This may result in brain structure changes due to neuronal apoptosis, and in part due to the growth of neurofibrillary tangles.[18] This study found that the serum TyG index in the CHD depression group was significantly higher than in the CHD non-depression group, indicating poor health status and lipid metabolism disorders in depressed patients.[19] Logistic regression analysis results indicate that the TyG index is an independent risk factor for depression in CHD patients (OR=6.604, P<0.001). In this study, ROC curve analysis revealed that the area under the ROC curve for predicting depression in CHD patients using the TyG index was 0.76 (95% CI 0.687–0.829, P<0.001), indicating substantial diagnostic value. The diagnostic threshold was 1.613, suggesting that a TyG index greater than 1.613 in CHD patients may signify comorbid depression. Early assessment of the TyG index in CHD patients offers valuable predictive information regarding the onset of depression. A substantial body of research provides robust statistical evidence demonstrating that the TyG index is closely associated with the development and prognosis of cardiovascular diseases (CVD).[20] Therefore, for CHD patients with a high TyG index, early and effective intervention will help mitigate depressive symptoms, more effectively prevent and reduce adverse cardiovascular events, and decrease readmission rates.

Current research indicates that the TyG index level holds significant practical value in the clinical diagnosis, treatment, evaluation, and prognosis of depression. Although previous studies have focused on blood lipids and CHD, they have mostly been confined to CHD and have yielded inconsistent results. However, studies have shown that among American adults, an elevated TyG index is significantly correlated with an increase in depressive symptoms.[17] This study aims to investigate the correlation between the serum TyG index and depression in CHD patients, as well as its role in the pathogenesis of CHD. This investigation aids in enhancing our understanding of the impact of lipids and glucose on depression, offers a reference for the clinical prevention and treatment of CHD with comorbid depression, and establishes a theoretical basis for further research. Depression has a significant negative impact on development of cardiovascular disease and on cardiovascular disease outcomes. Further efforts to understand and mitigate these impacts are prudent.[21]

In conclusion, the TyG index is an independent risk factor for the development of depression in patients with CHD, offering substantial predictive value. Employing the TyG index as an evaluation metric is crucial for the early diagnosis of depression in CHD patients. Especially for female patients with elevated TyG index levels and older patients, more rigorous follow-up is necessary. For patients with elevated TyG index levels, lifestyle interventions—such as a low-salt, low-fat diet and moderate exercise—are recommended to enhance insulin sensitivity and potentially reduce depression risk. Additionally, regular mental health follow-ups, including depression screening and counseling, may be crucial for the comprehensive management of these individuals. So far, there have been no comparative studies examining the relationship between the TyG index and the severity of depression. Furthermore, no comparative studies have evaluated the effectiveness of drug treatments, as these studies rely on the subjective experiences of the participants. Thus, more research is necessary to accurately evaluate the impact of the TyG index on the severity of depression.

Conclusion

Our study indicates, the TyG index is an independent risk factor for depression in patients with CHD, indicating a significant predictive value. Depressed patients have a higher rate of readmission, and managing depression effectively contributes to better prognosis.

Ethics Statement

This study was approved by the Ethics Committee of the Renhe Hospital Affiliated to China Three Gorges University (2023-29), and complied with the Helsinki Declaration.

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Disclosure

The authors declare that they have no conflicts of interest in this study.

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