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ORIGINAL ARTICLE

Correlation of triglyceride glucose index as a marker of insulin resistance and heart failure with preserved ejection fraction in obese patients

Doaa Salah Elgendy*[1] and Mie Mohammed Abdalraouf[2]

[1]Internal Medicine Department, Endocrinology Unit, Faculty of Medicine Menofia University, Egypt

[2]Cardiology Department, Faculty of Medicine Menofia University, Egypt

***Corresponding author:** Doaa Salah Elgendy, **E-Mail:** doaa.algendy@med.menofia.edu.eg

Abstract

Background: Overweight people are more likely to have insulin resistance, which raises their risk of diabetes and cardiovascular diseases. Recently, it has been thought that the triglyceride glucose index (TyG) provides a straightforward substitute for the usual widely utilized measures of insulin resistance. Independent of other known risk factors, such as diabetes and hypertension, obesity is a recognised risk factor for preserved ejection fraction heart failure (HFpEF). TyG index has been linked to the development of cardiovascular disease and hypertension in the prvious studies. The association between the TyG index and the development of heart failure with preserved ejection fraction (HFpEF) in obese individuals has not yet been thoroughly researched.

Objectives: To assess the relation between the triglyceride glucose index (TyG) and the incidence of heart failure with preserved ejection fraction (HFpEF) among obese population.

Methods: 200 obese individuals were included in this cross-sectional research and divided into two groups: 100 obese individuals without HFpEF and 100 heart failure patients with preserved ejection fraction were admitted to the cardiology department at Menofia University Hospital. Data about patients' demographics, medical histories, current medications, and physical exams were obtained.

Results: In comparison with non-HFpEF patients, HFpEF patients had higher fasting blood glucose, fasting insulin, triglycerides, TyG index, left atrial diameter (LAD), left ventricular mass index (LVMI), the ratio of the peak E of the mitral orifice to the peak E of the early diastolic mitral annulus (E/e′), and SBP. Furthermore, there was a positive correlation between the TyG index and NT-proBNP, left atrial diltation(LAD), left ventricular mass index (LVMI), average e′ and E/e′.

Conclusion: a higher triglyceride glucose index was found in HFpEF patients which is closely associated to the cardiac diastolic function, both of which have a substantial correlation with the development of HFpEF in obese patients.

Keywords: Triglyceride glucose index, Insulin resistance, HFpEF, Obesity.

ISSN: 0975-3583,0976-2833 VOL12, ISSUE 01, 2021

Introduction

More than half of the heart failure (HF) diagnoses in the community are those with preserved ejection fraction (HFpEF) [1-3]. Even though, mortality rates have not altered over the previous two decades [4], its prevelance has been rising. Several pathophysiologic and phenotypic profiles within the spectrum of HFpEF are blamed for the lack of effective therapies and inability to improve clinical outcomes; each of which may need a different therapeutic strategy. Obesity, a condition with an alarming global rise in frequency, has been linked to HFpEF through clinical studies and experimental research using animal models [5-7]. Recent research has shown obesity-related HFpEF as a distinct and common HFpEF phenotype [8,9].

HFpEF is a term for a group of heterogeneous diseases. Trials have been made to classify HFpEF patients, based on their phenotypic characteristics. There have been hypothesised phenotypes based on predisposing variables, such as the hypertensive, metabolic/obese,coronary artery disease-related phenotypes and chronic renal disease-related, In addition, phenotypes based on clinical manifestation have been proposed [8], such as lung congestion, , pulmonary hypertension, atrial fibrillation and skeletal muscular weakness.

In order to further understand the relation between TyG index and cardiac function, this study concentrates on the observation of TyG index and HFpEF in obese individuals.

Patients and Methods

The medical history and lifestyle characteristics, such as physical activity, smoking, eating habits, and exercise, were collected using a standardised self-administered questionnaire. The participant data was gathered using predefined spreadsheets.

Obesity was divided into three categories: general obesity, visceral obesity, and ectopic obesity. A BMI of more than 30 kg/m2 was deemed obese [10]. Waist circumferences of more than 102 cm for males and 88 cm for women were used to determine visceral fat obesity. Ectopic fat obesity is characterised by abdominal ultrasound showing fatty liver.

Inclusion criteria: Heart failure symptoms or indicators, as well as high B-type natriuretic peptide (BNP) levels (BNP > 35 pg). Diastolic dysfunction functional characteristics. Left ventricular ejection fraction (LVEF) 50%, normal or slightly aberrant, and no enlargement of the left ventricle.

Exclusion criteria: White coat hypertension, which is characterised by high blood pressure at a clinic despite average ambulatory blood pressure monitoring or regular home blood pressure readings of 135/85 mmHg. Hypertension, both primary and secondary. Three. Diabetes. Valvular and congenital heart disease. Hypertrophic and restricted cardiomyopathy. Disorders of the pericardium, non-cardiogenic causes of heart failure (severe infection, anemia, and diseases of blood system). Any thyroid disorder, and Any hepatic or renal dysfunction.

The participants were categorized into the following two groups. **Group 1: (n = 100):** Obese patients with HFpEF and **Group 2: (n = 100):** Obese patient without HFpEF group.

The individuals who practised any kind of sport frequently (more than once per week) were referred to as regular exercisers. According to the results of abdominal ultrasonography, fatty liver was identified.

After admission, information on the patient's gender, age, vital signs (including systolic, diastolic, and heart rate), medical history, and fasting blood samples were taken to assess the following laboratory tests: B-type natriuretic peptide (BNP), kidney function tests, liver function tests ,total cholesterol (TC), triglycerides (TG), fasting blood glucose (FBG), and fasting insulin Body mass index (BMI) was computed by dividing weight (kg) by the square of height (m2) after height and weight were recorded.

- Calculation of HOMA-IR:

fasting plasma insulin (IU/L) x fasting glucose (mmol/L)/22.5.

ISSN: 0975-3583,0976-2833 VOL12, ISSUE 01, 2021

- Calculation of TyG index:

TyG index = Ln (serum TG [mg/dl] × FBG [mg/dl]/2).

Upon admission, regular echocardiography testing was performed on all patients. All patients' measurements of the following parameters were taken and recorded: left ventricular end-diastolic diameter (LVEDD), left ventricular ejection fraction (LVEF), interventricular septal thickness (IVST), left atrial diameter (LAD), septal peak early diastolic mitral annulus velocity (septal e′), lateral wall early diastolic mitral annulus velocity (lateral wall e′),

Statistical analysis:

Software SPSS 26.0 was used for statistical analysis (statistical package for social science for windows statistical package, IBM Corp., Armonk, NY, USA).. The measured data were checked for normality, and the data that passed muster was denoted as (X SD). Comparative analysis between groups was performed using the t-test. For comparisons between the two groups, the non-parametric test was used and count data were shown as an example (%). Depending on whether the data were regularly distributed, either the Pearson or Spearman correlation analysis was chosen. The receiver operating characteristic (ROC) curve was used to assess the diagnostic effectiveness of the TyG index for HFpEF in the patient population. All tests were run using a two-sided test with a p value of 0.05 as the test level.

Results

Age, gender, smoking, and diastolic blood pressure (SBP) were not statistically different between the HFpEF group and the non-HFpEF group, although BMI, smoking, andsystolic blood pressur SBP were significantly different between these two groups ($p < .05$). **(Table 1).**

Table (1): Demographic data of the two studied groups:

	HFpEF (n = 100)	**Non-HFpEF (n = 100)**	**Test of Sig.**	**p**
Gender				
Male	25(25%)	60(60%)	χ^2= 4.3	0.13
Female	75(75%)	40(40%)		
Age (years)				
Mean ± SD.	44.4 ± 5.3	43.28 ± 9.64	χ^2=1.69	0.191
Median (Min. – Max.)	36 (24 – 41)	34 (23 – 50)		
BMI				
Mean ± SD.	37.6 ±5.1	32.4 ±3.3	χ^2=0 .3	**0 .012**
Smoking	69(69%)	41(41%)	χ2=4.3	**0.057**
SBP, mmhg	143.79 ± 26.64	115.20± 19.19	___	**0 .04**
DBP, mmhg	81.51 ± 12.98	83.78 ± 15.73	____	0.176

ISSN: 0975-3583,0976-2833 VOL12, ISSUE 01, 2021

Moreover, there was no statistically significant difference in the function of the liver, kidneys, uric acid, or cholesterol between the HFpEF group and the non-HFpEF group. While there was a statistically significant difference between the two groups for fasting insulin, HOMA-IR, NT-proBNP, FBG, TG, HDL, LDL, and TyG index ($p < .05$.) **(Table 2).**

Table (2): Comparison between the two studied groups according to different parameters

	(HFpEF (n = 100)	**Non-HFpEF (n = 100)**	**P**
Cholesterol, mg/dl	253 ± 12	157.02±18	**<0.04***
Triglycerides, mg/dl	172.45 ± 35	186.72±23.98	**<0.001***
HDL-C	4747.56 ± 10.72	42.77 ± 8.74	**<0.01**
LDL-C	124.59 ±31.50	127.76 ±31.49	**<0.01**
CREAT (Mg/dl) Median (Min. – Max.)	89 (63 – 99)	85 (55 – 111)	0.314
FBG (mmol/L)	7.96± 2.98	6.37±2.74	**0.033**
Fasting Insulin (mIU/ml)			
Mean ± SD.	37.5 ± 13.3	35.4 ± 14	**<0.001***
Median (Min.-Max.)	38 (3 – 56)	35 (1 – 56)	
HOMA-IR			
≤1.4	10 (10%)	15 (15%)	
>1.4	90 (90%)	85 (85%)	**<0.001***
Mean ± SD.	7.1 ± 3.3	7.5 ± 2.6	**<0.001***
ALT			
Mean ± SD.	21.4 ± 10.5	22.6 ± 8.53	0.448
Median (Min. – Max.)	11.8 (8.6 – 13.3)	12 (9.3 – 13.7)	
AST			
Mean ± SD.	23.3 ± 10.8	24.35 ± 12.3	0.381
Median (Min. – Max.)	5.5 (1.8 – 7.9)	5.6 (2.2 – 10.8)	
NT-proBNP	588.16 (417.31– 99.62)	774.56 (87.70–221.68)	**<0.001***
URIC ACID			
Mean ± SD.	356.23 ± 89.2	348.9 ± 78.1	0.520
TYG index	9.18 ± 1.08	6.66±0.92	**<0.001***

ISSN: 0975-3583,0976-2833 VOL12, ISSUE 01, 2021

The results of the Spearman correlation analysis showed that the TyG index had positive correlations with NT-proBNP , BMI, HOMA-IR in the HFpEF group **(Table 3).**

Table (3): Correlation between TyG index (ug/ml) and different parameters in each group

	TyG index (ug/ml)			
	HFpEF group (n = 100)		Non HFpEFgroup (n = 100)	
	r_s	p	r_s	p
Age (years)	0.1	0.3	0.1	0.2
BMI	0.4	**0.007***	0.3	0.4
HOMA-IR	-0.4	**<0.003***	0.3	0.4
NT-proBNP	0.406	**<0.001***	0.3	0.2

r_s: Spearman coefficient

TyG index had positive correlations with LVEF, LVMI, LAD, and E/e′ and negative relationships with LVEF and average e′, according to the Spearman correlation analysis ($p < .05$) **(Table 4).**

Table (4): Correlation analysis of TyG index with echocardiographic indexes in HFpEF group:

Variable	TyG index (ug/ml)	
	r_s	p
LAD	0.312	**0.001***
IVS	-0.036	0.698
LVEDD	0.053	0.422
LVEF	-0.468	**0.001***
LVMI	0.253	**0.002**
E/A	-0.124	0.203
Average e′	-0.205	**0.114**
E/ e′	0.266	**0.002**

r_s: Spearman coefficient

ISSN: 0975-3583,0976-2833 VOL12, ISSUE 01, 2021

TyG index had the highest area under the ROC curve (95% CI: 0.951-0.994) for predicting the development of HFpEF in obese individuals **(Figure 1).**

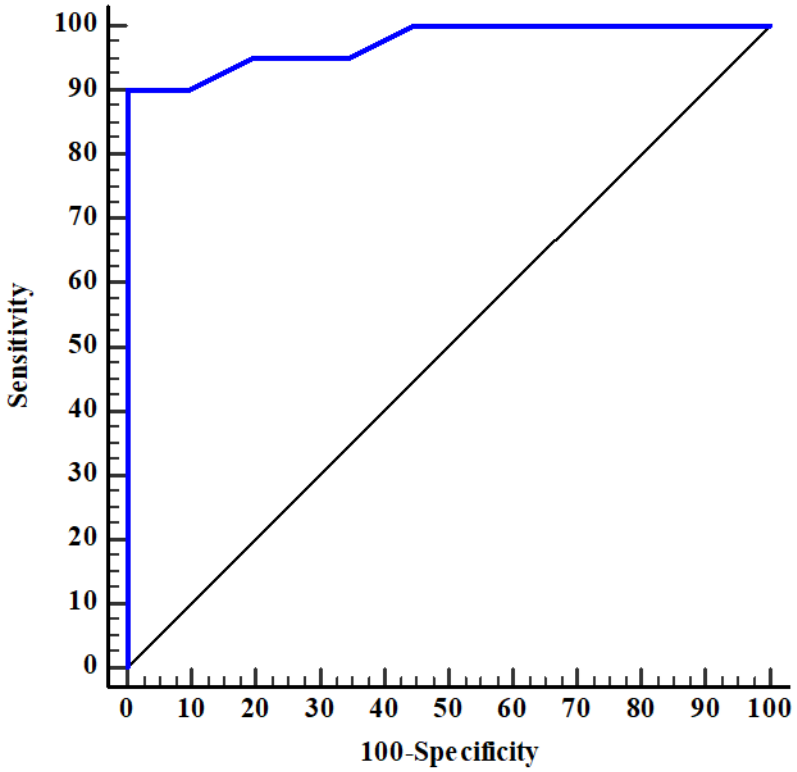

Figure (1): ROC curve for TyG index to predict HFpEF in obese patients.

Table (5): Prognostic performance for TyG index to discriminate obese patients with HFpEF (n = 100) from those without HFpEF (n = 100)

	AUC	p	95% C.I	Sensitivity	Specificity	PPV	NPV
ACE2 level	0.973	<0.001*	0.951 – 0.994	95.0	80.0	82.6	94.1

AUC: Area Under a Curve CI: Confidence Intervals

*: Statistically significant at $p \leq 0.05$

ISSN: 0975-3583,0976-2833 VOL12, ISSUE 01, 2021

Discussion

The association between the TyG index and the incidence of HFpEF in obese individuals was evaluated in this study. TyG index was seen to be considerably higher in HFpEF patients compared to non-HFpEF patients. Elevated TyG index may be directly associated to the prevalence of HFpEF in individuals who are obese. As comparison to the non-HFpEF group, the SBP in the HFpEF group was greater. An previous research also revealed that high blood pressure, particularly SBP, might easily result in heart failure by causing reduced myocardial compliance, enlarged left atrium, pulmonary vein congestion and increased left ventricular filling pressure [11].

Our findings supported the fact that stretch receptors have been activated since NTProBNP levels are greater in the HFpEF group. And it is well-known that NTProBNP ia a biomarker for evaluatingboth cardiac function and the severity of heart failure [12].

TyG index was validated to be related to NTproBNP in our correlation analysis. These findings supported the finding of a prior study by **Guo et al.** [13] which concluded that the higher TyG index, the higher the risk of chronic heart failure and the lower the cardiac function in patients with HFpEF.

Using the equation Ln (serum TG [mg/dl] FBG [mg/dl]/2) to calculate the TyG index. It was first put out as a stand-in indication of IR by **Guerrero-Romero et al. [14].**

TyG index was associated with carotid atherosclerosis in hypertensive individuals, according to **Alizargar et al.** [15]. Also, TyG index has been linked to stroke [16], hyperuricemia [17], and coronary artery calcification [18] in older individuals with hypertensionin previous studies. Whereas in our study, an increasing body of evidence has established a link between the TyG index and the development of cardiovascular disease in obese people.

Li et al. [20] showed that the index can predict negative outcomes in patients with acute coronary syndrome. While, **Wang et al.** [19] established a positive correlation between the TyG index and the risk of hypertension in the general adult population.

According to **Negi et al.** [21], NtproBNP, a precursor of BNP, has a significant diagnostic value for HFpEF and may reflect the function of left ventricular remodeling and contraction. In the HFpEF group of our study, TGY and NtproBNP had a positive correlation. This implies that we can use TGY as a marker to predict HFpEF in obese patients.

Also, the TyG index's area under the ROC curve was showing that the TGY had the ability to predict HFpEF in patients who were obese [22].

The mechanism of increased TyG index in heart failure is unclear. TyG index is thought to be related to insulin resistance. According to many current studies, ventricular fibrosis has been proven to be one of the most important links in the pathogenesis of heart failure [23].

IR contributes to the deposition of lipids inside and outside cardiomyocytes, accelerating the process of ventricular fibrosis. Second, it leads to activation of the renin angiotensin aldosterone system, thus promoting the reabsorption of sodium and water, which facilitates ventricular remodeling resulting in the development of heart failure **[24].**

Third, finally, the myocardium capacity to utilize free fatty acids and glucose is proportionally diminished during the process of insulin resistance, which results in a series of metabolic disorders in the body and decrease the myocardial tolerance to ischemia **[25].**

Not to mention, IR increases cardiac oxygen consumption, exacerbates myocardial damage, and stimulates the sympathetic nervous system [26].

TyG index is a simple, quick and affordable measure of insulin resistance that is useful to help clinicians to early screen individuals who are at high risk of developing HFpEF and insulin resistance especially among the obese population. As a result, it can be used for screening and

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routine monitoring during the management of these patients.

Clinical implications:

Although the TyG index is not directly implemented in clinical guidelines, certain guidelines consider the importance of glycemic and triglyceride management in the prevention of cardiovascular disease. According to recent information from the American Diabetes Association (ADA), those with increased TG (150 mg/dL [1.7 mmol/L]) should practice enhanced lifestyle interventions and maintain ideal glucose control. Consequently, Control of blood glucose and triglycerides is important in reducing the TyG index.

Our findings indicate that among obese individuals, an increased TyG index is strongly associated with a high risk of HFpEF, indicating that the incidence of CVD can be greatly decreased by reducing variables or triggers that increase the TyG index, such as blood glucose. The TyG index may be applied more frequently in clinical practise as a simple-measurement indicator. In terms of the effects on public health, determining the TyG index of the general population, particularly the obese population, can help with early detection of HFpEF and CVD.

Conclusion

A high TyG index may have a significant relationship with the incidence of CVD especially HFpEF in obese population. Furthermore, there is a potential positive correlations between the TyG index and NT-proBNP, HOMA-IR and other echocardiographic parameter diagnostic of HFpEF, suggesting that TGY can be used to predict insulin resistance and HFpEF in the obese population.

Therefore, TyG index might be added to health check-up programs for the purpose of screening of diabetes and cardiovascular disease. However, more research is required before application of the TyG index to evaluate the incidence of CVD in the clinic. Further studies are required to investigate dose–response relationships, establish cut of values, determine the predictive effect of the TyG index, and assess the TyG index's predictive impact and evaluate whether it may boost the predictive power of current cardiovascular risk scores.

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