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Article

The Triglycerides and Glucose (TyG) Index Is Associated with 1-Hour Glucose Levels during an OGTT

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Abstract: Background and Objectives: Among individuals with normal glucose tolerance (NGT), subjects with high levels of plasma glucose (≥155 mg/dL) at sixty minutes during an oral glucose tolerance test (1h-OGTT) are at an increased risk of developing type 2 diabetes. We investigated the association between the triglycerides and glucose (TyG) index, a novel marker of insulin resistance, with 1h-OGTT glucose plasma concentrations. Material and Methods: 1474 non-diabetic Caucasian subjects underwent a 75 g OGTT and were divided into two groups according to the cutoff 1h-OGTT plasma glucose < 155 mg/dL (NGT-1h-low) and ≥ 155 mg/dL (NGT-1h-high). The TyG index was calculated as ln [fasting triglycerides (milligrams per deciliter) × fasting blood glucose (milligrams per deciliter)/2]. Multivariable linear and logistic regression analyses were used to establish the contribution of the TyG index to the variability of 1h-OGTT glucose, and how the former affected the risk of being NGT-1h-high. Results: 1004 individuals were NGT-1h-low and 470 were NGT-1h-high. The TyG index was higher for NGT-1h-high ($p = 0.001$) individuals, and it was an independent factor influencing 1h-OGTT glycemia ($\beta = 0.191$, $p < 0.001$) after correcting for age, sex, and BMI. The TyG index was the strongest marker associated with the risk of being NGT-1h-high (OR = 1.703, CI 95% 1.34–2.17, $p < 0.001$) when compared with FPG (OR = 1.054, CI 95% 1.04–1.07, $p < 0.001$) and the HOMA-IR (OR = 1.156, CI 95% 1.08–1.23, $p < 0.001$). Conclusions: Our study demonstrated that the TyG index, an efficient and cost-effective marker of insulin resistance, is associated with the variability of early post-challenge glucose levels and is an independent marker of being NGT-1h-high.

Keywords: prediabetes; 1 h post-load glucose; triglyceride–glucose index; impaired glucose tolerance; insulin resistance

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1. Introduction

Type 2 diabetes mellitus (T2DM) is a chronic metabolic disorder characterized by persistent hyperglycemia due to impaired insulin secretion, peripheral tissue resistance to insulin action, or a combination of both [1]. Data from 2021 allows to estimate that 10.5% of 20–79 year-olds (536.6 million people) were affected by diabetes, expected to raise to 12.2% in 2045 (783.2 million people), with a large impact on health and social expenditures [2].

Currently, the adoption of pharmacological therapies alongside lifestyle interventions have proven to be capable of reducing the incidence and progression of macro- and microvascular-T2DM-linked complications [3,4]. In the field of prevention, a key aspect is the detection of high-risk subjects. Much evidence has already shown that the presence of high levels of plasma glucose at 1-hour post-load during an oral glucose tolerance test (OGTT) identifies a new category of individuals at an increased risk of developing T2DM among subjects with otherwise normal glucose tolerance (NGT) [5–7]. Indeed, the value of 1-hour post-load glucose levels during an OGTT (1h-OGTT) was revealed to be a better predictor of dysglycemia among individuals without T2DM than HbA1c 2 h post-load

plasma glucose during an OGTT and fasting plasma glucose (FPG) [8–14]. Moreover, it has now been established that normoglycemic subjects with a 1h-OGTT plasma glucose $\geq$ 155 mg/dL (NGT-1h-high) have higher incidence rates of diabetes complications, cardiovascular risks, and mortality [14–16]. This being the case, the detection of effective biomarkers (possibly non-invasive ones) able to refine the stratification of naive, prediabetic or 1-hour-high patients, could be useful for the design of tailored strategies for preventing and/or delaying macro- and microvascular complications that shorten life expectancy and reduce life quality in those patients [16].

Several studies have reported that non-insulin-based indices of insulin resistance could be useful tools for the early detection of insulin resistance [17,18]. Among the several indices available in the literature, our attention is focused on the "the TyG index" (triglycerides and glucose index), which takes into account fasting triglycerides and fasting plasma glucose levels [19–21]. Most intriguingly, the TyG index (a non-insulin-based index) has been demonstrated to have a good closeness of agreement to the gold standard, the hyperinsulinemic–euglycemic clamp, in estimating the severity of insulin-resistance and to be equal—or even superior—to the HOMA-IR index (homeostatic model assessment of insulin resistance) [17,22].

The aim of our cohort study was to investigate whether the TyG index was associated with 1h-OGTT glucose plasma concentrations in a large cohort of 1474 Caucasian non-diabetic adult individuals participating in the Catanzaro metabolic risk factors (CATAMERI) study.

2. Materials and Methods

2.1. Study Population

The study group consisted of 1474 self-reported non-diabetic Caucasian participants (661 men and 813 women, aged 18–83, mean age 46.01 $\pm$ 13.202), enrolled in the Catanzaro metabolic risk factors study (CATAMERIS), an observational study assessing cardiometabolic risk factors in individuals carrying at least one risk factor, including overweight/obesity, hypertension, dyslipidemia, dysglycemia, and a family history of type 2 diabetes [23,24].

The exclusion criteria were the presence of autoimmune diabetes, a diagnosis of T2DM, current or former therapy with hypoglycemic agents, chronic gastrointestinal diseases, chronic pancreatitis, a history of any malignant disease, a history of alcohol or drug abuse, liver or kidney failure, and treatments able to modulate glucose metabolism, including lipid-lowering and hypoglycemic agents. During the first visit in the morning after a 12 h fast, anthropometrical parameters, such as body mass index (BMI), systolic (SBP), and diastolic (DBP) blood pressure, were measured, and blood samples were collected for the assessment of biochemical parameters, including triglycerides levels. Height was measured to the nearest 0.1 cm, while body weight was measured with a calibrated electronic scale to the nearest 0.1 kg. BMI was calculated as body weight in kilograms divided by height in square meters (kg/m^2). A 75 g oral glucose tolerance test (OGTT) was performed with 0, 30, 60, 90, and 120 min samplings for circulating plasma glucose and insulin measurements. Glucose tolerance statuses were evaluated according to World Health Organization (WHO) criteria [25]. Individuals were thus classified as having:

- NGT when their fasting plasma glucose (FPG) was <110 mg/dL (6.1 mmol/L) and their 2 h post-load glucose was <140 mg/dL (7.77 mmol/L);
- IFG (impaired fasting glucose) when their FPG was 110–125 mg/dL (6.1–6.9 mmol/L) and their 2 h post-load glucose was <140 mg/dL (7.77 mmol/L);
- IGT (impaired glucose tolerance) when their FPG was <126 mg/dL (7 mmol/L) and their 2 h post-load glucose was 140–199 mg/dL (7.77–11.0 mmol/L).

Only individuals classified as having NGT were considered for the present report. The study was approved by the institutional ethics committee of the university "Magna Graecia" of Catanzaro (approval code: 2012.63). Written informed consent was obtained from each participant in accordance with the principles of the Declaration of Helsinki.

2.2. Laboratory Determinations

Glucose, triglycerides, and total and high-density lipoprotein (HDL) cholesterol concentrations were determined by enzymatic methods (Roche, Basel, Switzerland). The plasma insulin concentration was measured with a chemiluminescence-based assay (Immulite, Siemens Healthcare Diagnostics Inc., Marburg, Germany).

2.3. Calculations

Participants with normal glucose tolerance (NGT) were divided into two groups according to their 1 h plasma glucose concentrations during the OGTT. Those with a 1 h plasma glucose equal or above 155 mg/dL (8.6 mmol/L) were labeled NGT-1h-high; those with a 1 h plasma glucose below 155 mg/dL were defined as NGT-1h-low. The homeostasis model assessment (HOMA) index was calculated as fasting insulin × fasting glucose/22.5 [26]. The triglycerides–glucose (TyG) index was calculated as ln (fasting triglycerides [milligrams per deciliter] × fasting glucose [milligrams per deciliter]/2) [27].

2.4. Statistical Analysis

The results for the continuous variables are given as means ± SD. Anthropometric and metabolic differences between groups were tested after adjusting for age, gender, and BMI using a general linear model. The $\chi 2$ test was used for the comparisons of categorical variables. Variables with a skewed distribution (i.e., triglycerides, fasting, 30 min, 90 min, 1 h, and 2 h insulin, and the HOMA index) were log-transformed to meet the normality assumption for statistical purposes. A multivariable stepwise linear regression was used to examine the relation of 1h-OGTT glucose and the TyG index in a statistical model including several potential confounders: age, gender, BMI, fasting glucose levels, and the HOMA index. Similarly, a multivariable logistic regression model was computed in order to evaluate the risk of falling into the NGT-1h-low or NGT-1h-high groups. The Bonferroni post hoc correction for multiple comparisons was applied. The receiver–operating characteristic (ROC) analysis was used to assess the predictive value of the TyG index (area under the curve). Youden's J statistic was calculated to identify the optimal cutoff value of the TyG index for discriminating between the NGT-1h-low and NGT-1h-high groups (i.e., the value that maximizes the difference between the true positive and false positive rates of classification).

A p value < 0.05 was considered statistically significant. All analyses were performed using the statistical package SPSS 22.0 for Windows (SPSS, IBM, Chicago, IL, USA).

3. Results

The anthropometric and biochemical characteristics of the study cohort are summarized in Table 1. A total of 1474 non-diabetic participants with normal glucose tolerance (NGT) were evaluated and divided into two groups using a 1h-OGTT plasma glucose cutoff point of 155 mg/dL: 1004 (68%) participants with a 1h-OGTT plasma glucose < 155 mg/dL (NGT 1h -low) and 470 (32%) individuals with a 1h-OGTT plasma glucose ≥ 155 mg/dL (NGT-1h-high). Gender, age, and BMI distributions were unevenly scattered between the two groups. The NGT-1h-low group harbored more men than women, while the NGT-1h-high participants were older and exhibited higher glycemic values compared with the NGT-1h-low participants. Because these parameters were associated with glycemic control, all subsequent analyses were adjusted for age, gender, and BMI. After adjusting for age, gender, and BMI, the NGT-1h-high group exhibited significantly higher fasting, 2h-OGTT glucose, and insulin levels compared with the NGT-1h-low group. Additionally, the triglycerides levels and the TyG index were significantly higher in the NGT-1h-high group compared with the NGT-1h-low individuals, while no significant differences were observed between the groups for total cholesterol levels (Table 1).

Table 1. Anthropometric and metabolic characteristics of study subjects stratified according to one hour post load glycaemia.

Variables	Whole Study Group	NGT-1h-Low	NGT-1h-High	*p*
Gender (M/F)	813/661	623/381	190/280	<0.001 *
Age (years)	46 (±13)	43 (±13)	50 (±11)	<0.001 **
BMI (Kg/m^2)	29.7 (±6.4)	29.5 (±6.5)	30.3 (±6.0)	0.027 ***
SBP (mg/dL)	126.4 (±17.2)	125.1 (±17.4)	129.1 (±16.3)	<0.001
DBP (mg/dL)	79.2 (±11.3)	78.5 (±11.6)	80.7 (±10.5)	0.001
Tot-COL (mg/dL)	198.4 (±38.7)	197.1 (±39.4)	201.3 (±37.0)	0.052
HDL-Col (mg/dL)	52.2 (±13.4)	53.4 (±14.1)	49.7 (±13.3)	<0.001
LDL-Col (mg/dL)	127.2 (±34.2)	125.7 (±34.6)	130.3 (±33.2)	0.017
Triglycerides (mg/dL)	120.2 (±70.2)	113.4 (±68.4)	134.7 (±71.9)	<0.001
AST (UI/dL)	21.4 (±10.2)	20.9 (±10.2)	22.4 (±10.0)	0.008
ALT (UI/dL)	24.3 (±16.3)	23.1 (±14.2)	26.7 (±20.0)	<0.001
gamma-GT (ng/L)	25.0 (±22.9)	23.4 (±22.3)	28.5 (±23.6)	<0.001
Fasting glucose (mg/dL)	90.9 (±9.7)	88.8 (±8.8)	95.2 (±10.3)	<0.001
1-h glucose (mg/dL)	139.0 (±37.2)	118.9 (±23.1)	181.8 (±22.6)	<0.001
2-h glucose (mg/dL)	106.8 (±20.3)	102.6 (±19.5)	115.8 (±18.5)	<0.001
Fasting insulin (mU/mL)	12.9 (±8.6)	12.4 (±8.6)	14.1 (±8.4)	<0.001
HOMA-IR	2.9 (±2.0)	2.7 (±1.9)	3.3 (±2.0)	<0.001
TyG index	8.46 (±0.53)	8.39 (±0.52)	8.64 (±0.51)	<0.001
Smoking habits (Yes/No)	344/1130	224/780	120/350	0.173
Lipid-lowering therapy (Yes/No)	185/1289	86/918	99/371	0.004
Hypertension (Yes/No)	874/600	543/461	331/139	<0.001
Antihypertensive therapy (Yes/No)	667/807	403/601	264/206	<0.001

The data are presented as means ± SD for continuous variables and number for dichotomous variables. Comparisons were performed using a general linear model with post hoc Bonferroni correction for multiple comparisons and with the g^2 test for categorical variables. *p* values refer to results after analyses with adjustment for age, gender, and BMI. * *p* values refer to results after analyses with adjustment for age and BMI. ** *p* values refer to results after analyses with adjustment for gender and BMI. *** *p* values refer to results after analyses with adjustment for age and gender. BMI = body mass index; SBP = systolic blood pressure; DBP = diastolic blood pressure; Tot-COL = total cholesterol; HDL-Col = high-density lipoprotein; LDL-Col = low-density lipoprotein; AST = aspartate aminotransferase; ALT = alanine transaminase; gamma-GT = gamma-glutamyl transpeptidase; HOMA-IR = homeostasis-model-assessment-estimated insulin resistance; the TyG index = triglycerides and glucose index.

To evaluate the independent factors influencing the variability of 1h-OGTT plasma glucose, a multivariate linear stepwise regression analysis was run in four models including gender, age, and BMI as covariates (Table 2). Model 1 additionally included the TyG index, resulting in a significant association with 1h-OGTT (β = 0.191; $p < 0.001$; model-adjusted R^2 = 21.6%). In Model 2, FPG was inserted instead of the TyG index, and this resulted in a consistent association with 1h-OGTT glucose levels (β = 0.284; $p < 0.001$; model-adjusted R^2 = 25.3%). Model 3 evaluated the association of 1h-OGTT glucose levels with the HOMA-IR, the result of which was weaker than that with the TyG index (β = 0.159; $p < 0.001$; model-adjusted R^2 = 20.5%). Because the TyG index was calculated from fasting glucose measurements, we wondered whether the effects exerted by TyG on the early post-challenge glucose levels were merely a consequence of the FPG component of the formula. To assess this issue, we performed a sensitivity analysis in Model 4 by including the TyG index and FPG together as co-factors. The two variables remained significantly associated with 1h-OGTT; in particular, FPG showed a stronger association (β = 0.249; $p < 0.001$) compared with the TyG index (β = 0.115; $p = 0.032$; model-adjusted R^2 = 26.3%). Altogether, our models suggested that the TyG index was an independent marker of the variability of 1h-OGTT glucose levels, even if the association was partially attributable to FPG.

Table 2. Stepwise multivariable regression analysis of 1 h-OGTT as dependent variable and different covariates in the whole population.

Dependent Variable 1h-OGTT	Independent Contributors	Standardized Coefficient	*p*
Model 1	**Gender**	0.155	<0.001
	Age	0.300	<0.001
	BMI	0.109	<0.001
	TyG Index	0.191	<0.001
Model 2	**Gender**	0.157	<0.001
	Age	0.246	<0.001
	BMI	0.125	0.005
	FPG	0.284	<0.001
Model 3	**Gender**	0.189	<0.001
	Age	0.351	<0.001
	BMI	0.076	0.004
	HOMA-IR	0.159	<0.001
Model 4	**Gender**	0.133	<0.001
	Age	0.231	<0.001
	BMI	0.103	0.017
	TyG Index	0.115	0.032
	FPG	0.249	<0.001

OGTT = oral glucose tolerance test; BMI = body mass index; the TyG index = triglyceride glucose index; HOMA-IR = homeostatic model assessment for insulin resistance; FPG = fasting plasma glucose.

To estimate the independent contribution of the TyG index to the risk of falling in the NGT-1h-high group, we performed a multiple logistic regression analysis, summarized in Table 3. Models 1 to 4 included age, gender, and BMI as covariates. In the first model (Model 1), the TyG index was additionally included as an independent variable, resulting in a significant association with increased odds of being NGT-1h-high (OR = 1.703, CI 95% 1.34–2.17, $p < 0.001$). In Model 2, the independent contribution of FPG was evaluated; as expected, it was significantly associated with being NGT-1h-high (OR = 1.054, CI 95% 1.04–1.07, $p < 0.001$). Model 3 evaluated the contribution of th HOMA-IR, resulting in a significant association with a higher risk of being NGT-1h-high (OR = 1.156, CI 95% 1.08–1.23, $p < 0.001$). The final model (Model 4) included both the TyG index and FPG. Although the TyG index showed a reduction in effect size and statistical significance, it was still the major determinant of being NGT-1h-high compared with FPG (the TyG index: OR = 1.327, CI 95% 1.03–1.72, $p = 0.032$; FPG: OR = 1.049, CI 95% 1.03–1.06, $p < 0.001$). Notably, the TyG index remained significantly associated with the NGT-1h-high risk even after adding the presence of hypertension, dyslipidemia, and relative therapies to the statistical models.

Table 3. Multiple logistic regression analysis for the NGT 1 h-high risk.

NGT-1h-High Risk	Variable	OR	95% CI	*p*
Model 1	**Gender**	2.071	1.63–2.64	<0.001
	Age	1.042	1.03–1.05	0.045
	BMI	1.026	1.01–1.05	0.010
	TyG Index	1.703	1.34–2.17	<0.001
Model 2	**Gender**	2.055	1.62–2.61	<0.001
	Age	1.034	1.02–1.04	<0.001
	BMI	1.028	1.00–1.05	0.005
	FPG	1.054	1.04–1.07	<0.001

Table 3. *Cont.*

NGT-1h-High Risk	Variable	OR	95% CI	*p*
Model 3	Gender	2.232	1.76–2.82	<0.001
	Age	1.047	1.04–1.06	<0.001
	BMI	1.011	0.99–1.03	0.318
	HOMA-IR	1.156	1.08–1.23	<0.001
Model 4	Gender	1.942	1.52–2.48	<0.001
	Age	1.033	1.02–1.04	<0.001
	BMI	1.024	1.01–1.04	0.017
	TyG Index	1.327	1.03–1.72	0.032
	FPG	1.049	1.03–1.06	<0.001

NGT = normal glucose tolerance; BMI = body mass index; the TyG index = triglyceride glucose index; HOMA-IR = homeostatic model assessment for insulin resistance; FPG = fasting plasma glucose.

The ROC analysis demonstrated that the accuracy of the TyG index for identifying NGT-1h-high patients was 61.5% (AUC = 0.615, CI 95% 0.588–0.643, $p < 0.001$, Figure 1) and that the optimal TyG index cutoff value for discriminating patients with this alteration from those without it was 8.546, a threshold providing 60% sensitivity, 62.4% specificity, a positive predictive value of 42%, and a negative predictive value of 76%.

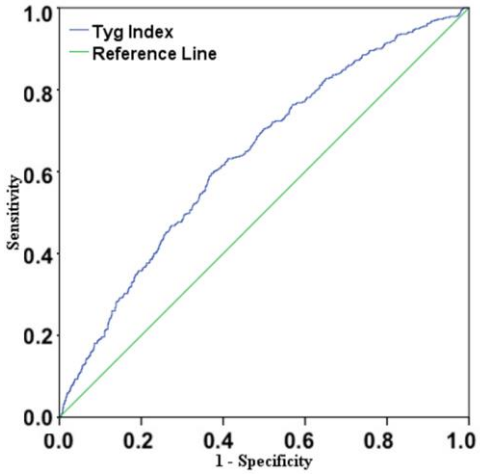

Figure 1. Receiver–operating characteristic (ROC) curve for the accuracy of the TyG index at discriminating NGT-1h-high individuals from NGT-1h-low ones. The accuracy of the TyG index was 61.5% (AUC = 0.615, $p < 0.001$).

To promote the use of the TyG index, we generated a simple spreadsheet calculator for the present manuscript (Supplementary File) in which we also embedded a visual indicator that shows if the TyG index values fell above or below our suggested cutoff.

4. Discussion

Increasing evidence has suggested that a 1h-OGTT plasma glucose value ≥ 155 mg/dL (8.6 mmol/L) in individuals with NGT is correlated with a higher risk of progression to diabetes. It is also now known that these individuals are more at risk to develop micro- and macrovascular complications or subclinical organ damage, such as common carotid artery thickness [28], left ventricular hypertrophy [7], vascular stiffness [12], and left ventricular diastolic dysfunction [6]; all these factors are independent predictors of cardiovascular events. Consistent with this, two longitudinal studies have shown that 1h-OGTT glucose levels ≥ 161 mg/dL and ≥155 mg/dL predict cardiovascular mortality and all-cause mortality, respectively [15,29].

This increased cardiovascular risk among individuals with dysglycemic conditions is aggravated by the presence of dyslipidemia, a common finding in this kind of patient.

In the literature, there is new evidence suggesting that individuals with 1h-OGTT plasma glucose values ≥ 155 mg/dL have a highly atherogenic lipid profile, very similar to that of patients with prediabetes or T2DM [30].

Indeed, it has been demonstrated that NGT-1h-high individuals are characterized by skeletal muscle insulin resistance, as confirmed by euglycemic hyperinsulinemic clamp studies and OGTT-derived indexes of insulin sensitivity and reduced insulin clearance; all these elements lead to sustained hyperinsulinemia after an oral glucose load [26,28,31,32]. Impaired insulin sensitivity in the skeletal muscle may divert ingested carbohydrates to the liver instead of muscle glycogen storage. This shift, associated with elevated plasma insulin levels, may lead to increased hepatic de novo lipogenesis. Additionally, hepatic insulin resistance reduces VLDL synthesis and apoB lipoprotein catabolism, resulting in an atherogenic lipid pattern characterized by increased triglyceride concentrations, as observed in NGT-1h-high individuals [33].

Several studies have shown that non-insulin-based indices of insulin resistance are a valid surrogate for the early identification of insulin resistance [17,18]. We focused our investigational work on the TyG index, as many others have evaluated the ability of the TyG index to predict the development of diabetes and prediabetes in patients without dysglycemic conditions [20,21] and with different ethnic backgrounds [20,34–36]. The TyG index was shown to possess high accuracy compared with the gold standard hyperinsulinemic–euglycemic clamp; furthermore, evidence has accumulated suggesting that the TyG index may be equal or even superior to the HOMA index in estimating the insulin resistance condition [17,22].

These observations, paired with the accessibility of an accurately characterized cohort of non-diabetic patients involved in the CATAMERI study, prompted us to assess the relationship between 1h-OGTT plasma glucose ≥ 155 mg/dL and the TyG index. Our hypothesis, in the present cross-sectional study, is that the TyG index could be an important instrument to identify patients with high 1h-OGTT plasma glucose levels, even before conducting an OGTT.

Our results showed that higher values in the TyG index were significantly associated with the risk of having 1h-OGTT plasma glucose levels ≥ 155 mg/dL (OR = 1.703, CI 95% 1.34–2.17). When comparing the standardized β coefficients estimated by linear regression, the TyG index was less precise at predicting 1h-OGTT glycemic values than FPG. On the other hand, the TyG index behaved better when used to predict which participants fell in the NGT-1h-high group. These observations point to the importance of the "other" component of the TyG index: triglycerides levels. It is widely recognized that FPG is the major predictor of the postprandial glycemic curve shape [37]; participants with similar FPG and higher triglycerides levels have a worse cardiometabolic risk profile, which may manifest also in increased 1h-OGTT levels.

Overall, the peculiarity of the TyG index is that it supplies information about the glycemic and lipid profiles joined as one single value. Several studies have shown evidence of the pancreatic β-cell's weak antioxidant defense, and oxidative stress has been proved to be an important factor for the pathogenesis of T2DM [38–40]. Both glucotoxicity and lipotoxicity can lead to an increased production of reactive oxygen species, causing oxidative stress and β-cell dysfunction, and eventually leading to IR and T2DM [38–40]. The long-term exposure to elevated concentrations of free fatty acids is related to the prolonged exposure to TG, resulting in impaired β-cell function [40–43] and reduced glucose-induced insulin secretion [44,45]. By synthetically representing both aspects, the TyG index may actually have an advantage in predicting a worse cardio-metabolic risk profile than the isolated reading of fasting glucose and triglyceride values. In addition to this, we should remark on the extreme usability of the TyG index, which is simple for calculations and linear interpretations; therefore, it can be easily employed to identify those individuals to be monitored for the development of diabetes.

We estimated that the TyG index had 61.5% accuracy for detecting those individuals whose 1h-OGTT glucose levels were above the risk threshold of 155 mg/dL in a population

that would otherwise be considered healthy according to the standard procedures. The negative predictive value of 76% indicated that 76% of individuals whose score was below the cutoff were actually true negatives and did not have 1h-OGTT values $\geq$ 155 mg/dL. In a real-world clinical context, this information would increase the confidence of the physician that the care supplied is accurate, at the price of a few seconds spent on a dedicated calculator (i.e., the one supplied as Supplementary Material). In difficult or under-resourced areas, this advantage has the potential to save money and improve the quality of life of the referred population. In contexts where gold standard investigative screenings are not accessible (i.e., the office of a general practitioner), consulting the TyG index may help with decision-making processes with the final goal of achieving precision medicine. The TyG index has also the merit of being calculated with variables commonly evaluated in clinical practice that are cheap and readily accessible. Moreover, all the components of the TyG index are modifiable risk factors that respond well to lifestyle modifications such as nutrition and exercise [46]. This means that the TyG index can be efficiently used to monitor throughout time the effectiveness of the strategies employed.

Notably, even if in the literature several studies consider values between four and eight as the normal range of the TyG index [20,47], currently, a cutoff value and stratification of risk linked to dysglycemic conditions are still missing, and the performance that we reported cannot be compared with other studies. Several studies adopting our same formula [48] have indicated similar cutoff values for discriminating the presence of metabolic syndrome [49], metabolic-dysfunction-associated fatty liver disease [50], a risk of cerebrovascular disease [51], and a risk of cardiovascular disease and mortality in the general population [52].

Nonetheless, we advise caution in drawing conclusions; a larger body of confirmatory and exploratory studies either in healthy subjects or in patients with prediabetes is necessary to confirm and elaborate on our hypothesis.

Among the strengths of our study, there was a large sample size encompassing both men and women from a real-world outpatient setting. We collected detailed anthropometric and metabolic variables according to a standardized protocol; biochemical analyses were performed in a single center and the assay of metabolites was realized in fresh blood samples instead of stored samples that may lead to their degradation. Furthermore, we also excluded participants with pharmacological treatments affecting glucose metabolism.

Caution is advised in the interpretation of our results. The population that we considered was poorly diversified; it was composed of Caucasian individuals residing in the south of Italy, and the generalizability of our results may be hindered in other ethnic groups. Another limitation of our study was that the participants underwent a single 75 g OGTT to evaluate glucose tolerance. Even if this approach is common in both clinical practice and epidemiological studies, the intra-individual variability of 1 h and 2 h post-challenge glucose could not be assessed, possibly leading to some inaccuracies in the classification of the recruited participants into glucose tolerance groups. Moreover, we recruited participants in a referral university hospital, and our findings may not be extendible to the general population.

Finally, the cross-sectional design of the study reflected only an association of the TyG index with 1h-OGTT plasma glucose and precludes us to draw any conclusion about the causal relationships between this dysglycemic condition and the development of metabolic diseases such as T2DM. This first report on the matter should be considered hypothesis-generating and requiring confirmation by additional prospective studies assessing the impact of the TyG index in predicting the variability of 1h-OGTT plasma glucose values.

5. Conclusions

In conclusion, our findings suggest that the TyG index could be a useful tool to screen, evaluate, and, where appropriate, beforehand treat individuals with high 1h-OGTT glucose levels.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/ijerph20010787/s1.

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