# Triglyceride glucose index for the detection of asymptomatic coronary artery stenosis in patients with type 2 diabetes

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# Abstract

Background Triglyceride Glucose index (TyG) was associated with an increased risk of cardiovascular events. Silent coronary disease is common in patients with type 2 diabetes. In Vietnam, a low-middle income country, the burden of cardiovascular disease is growing in parallel to the epidemiologic transition. The aim was in patients with type 2 diabetes and no history or symptom of cardiovascular disease, to assess the prevalence of coronary stenoses (CS) and investigate the association between TyG and cardiovascular risk factors and the presence and severity of CS.

Methods We recruited 166 patients at Ninh Thuan General Hospital, Vietnam. TyG and HOMA-IR were calculated, and a coronary computed tomography angiography (CCTA) was performed.

Results The population was separated according to tertiles of TyG. Patients with highest TyG had higher BMI, waist circumference, total cholesterol, LDL-cholesterol, triglycerides, plasma glucose and HbA1c levels, lower HDL-cholesterol; more of them had a metabolic syndrome and less practiced physical activity ($p<0.05$ to $<0.001$). TyG correlated with HOMA-IR ($p<0.001$). CS ≥50% were present in 60 patients, with a coronary artery narrowing ≥70% in 32 of them. The patients with CS had higher TyG ($p<0.05$). The association of TyG with CS remained significant in a multivariate analysis including confounding risk factors. The number of narrowed vessels and the degree of stenosis were associated with higher TyG levels ($p=0.04$ and $<0.005$). TyG was significant in identifying patients with CS with an area under the ROC curve of 0.678 (95%CI: 0.582-0.775, $p=0.002$), a cut-off point of 9.63 offering 75% sensitivity and 44% specificity. In subgroup analysis the association TyG-CS was stronger in patients ≥60 yrs, with HbA1c≥7%, on statin or anti-platelet therapy. The AROC was higher with the triple criterion age-HbA1c-TyG than with age or HbA1c alone ($p<0.001$ for both comparisons).

Conclusion More than one third of asymptomatic patients with type 2 diabetes had CS on CCTA. TyG may be considered as a marker of insulin resistance and allows to identify patients with high risk of coronary stenoses, particularly in those ≥ 60 yrs with poor glycemic control, and is associated with the number and the severity of narrowed branches.


# Background

Diabetes is one of the major risk factors for coronary artery disease. It is estimated that 20–30% of patients with coronary disease have known diabetes, and among the others up to 70% have newly detected diabetes or prediabetes when investigated with an oral glucose tolerance test (1). Patients with diabetes are at substantially increased risk of fatal and non fatal coronary events (2).

In the diabetic population coronary disease is often silent without any cardiac symptom. In asymptomatic diabetic patients the prevalence of silent myocardial ischemia as detected by a stress test varies depending on several factors including the diagnostic test performed, combined or not with cardiac imaging, the number of additional cardiovascular risk factors, the presence of diabetic complications, in particular nephropathy or cardiac autonomic neuropathy (3,4). The prevalence of silent ischemia which

was 20–30% in the 90's (4) was reported to sharply decrease in the last decade (5). Some recent studies have shown that coronary computed tomography angiography (CCTA) may detect coronary artery stenoses in a large proportion of asymptomatic patients with diabetes (6,7).

Insulin resistance is one of the pivotal risk factors for cardiovascular disease. Various associated disorders are involved including hyperglycemia, lipid alterations, hypertension and the production of clotting and inflammatory factors that may promote atherothrombotic changes. An independent association has been reported between insulin resistance evaluated using HOMA-IR and cardiovascular disease (8–10). Some studies have shown that the Triglyceride Glucose index (TyG) calculated simply using fasting glucose and triglyceride measurements may be used as a surrogate for insulin resistance (11–13). In addition TyG index was shown to predict cardiovascular events (14), to be a marker of subclinical atherosclerosis (15), and in a recent Korean study to be associated with an increased risk of coronary artery stenoses in patients with type 2 diabetes (7).

Vietnam is a low-middle income country, which is undergoing an important epidemiological transition. The prevalence of Vietnamese people with multiple comorbidities is increasing (16) with a rapid rise in the overall morbidity and mortality from non-communicable diseases over the last two decades. The prevalence of silent coronary disease in the diabetic population is expected to be greater than in higher income countries as a result of poorer control of cardiovascular risk factors.

The aim of the present study performed in Vietnam was in patients with type 2 diabetes and no symptom or history of cardiovascular disease, to assess the prevalence of coronary artery stenoses (CS) on CCTA and investigate the association between TyG index and cardiovascular risk factors and the presence and severity of CS.

## Methods

# Study Population And Design

In this cross-sectional observational study we included 166 patients with type 2 diabetes diagnosed according to the American Diabetes Association criteria (17), who were examined at Ninh Thuan General Hospital from April 2017 to May 2018. None of them had any history or symptom of cardiac disease.

Each patient was asked about the medical history, doing physical activity, taking medications for diabetes, statins or antiplatelet therapy. Blood pressure, body weight and waist circumference were measured.

# Biological Measurements

Plasma glucose, HbA1c, total cholesterol, triglycerides, HDL-cholesterol, and insulin were measured at fasting using HUMA STAR 600, Germany. LDL-cholesterol was calculated using Friedwald formula, and

non-HDL cholesterol by subtracting HDL-cholesterol from total cholesterol.

Indicators of insulin resistance were calculated: TyG index = Ln [Triglyceride x Glucose / 2] (11), and HOMA-insulin resistance (HOMA-IR) index (Insulin (mU/L) × plasma glucose (mmol/L) / 22.5) (18). Metabolic syndrome was diagnosed according to NCEP-ATP III criteria (19).

# Coronary Computed Tomography Angiography Imaging

Imaging was obtained by using a 64-slice scanner (Optima CT660, GE Healthcare, USA). Diameter stenosis (percentage) was defined from detected lumen contours at the minimal lumen area, and corresponding reference diameter values were obtained from an automatic trend analysis of the vessel areas within the artery. The principles of coronary artery interpretation include (1) systematic review of each coronary segment from multiple planes and in transverse section, (2) awareness of relevant artifacts, and (3) assessment of stenosis severity using high resolution images (including multiplanar reformation format) in views both longitudinal and transverse to the vessel. An image review in the frontal and lateral planes could aid in the identification of artifacts. Experienced readers reviewed the arterial tree in detail beginning in the axial (caudal) view since the trans-axial data are more robust as they are the less processed. CS was considered as significant when ≥ 50%.

# Statistical Analyses

Results were expressed as mean ± SD values or percentages. Comparisons between groups were performed by one-way ANOVA test for quantitative parameters and chi-2 test for categorical parameters. Correlations between quantitative parameters were performed by using Pearson test. ROC curve analysis was used to evaluate the accuracy of TyG index in detecting CS. Multivariate logistic regression analyses were performed in order to examine the association of TyG index with CS after adjustment for confounding risk factors. Odds ratios with 95% confidence intervals (95% CI) for the risk of CS are reported. In subgroup analysis odds ratios were compared between the highest and lowest TyG tertiles. Statistical analyses were carried out using SPSS (Statistical Product and Services Solutions) software version 20.0.

## Results

# Main Clinical Characteristics Of The Study Population

In the total population of 166 patients, 62% were male, mean age was 58.9 ± 10.8 years, BMI 24.8 ± 2.6 kg/$m^2$, and HbA1c 7.8 ± 1.0%. TyG index was between 7.80 and 10.96, with a mean value of 9.64 ± 0.63.

# Clinical and biochemical characteristics according to TyG tertiles

Table 1

Clinical and biological characteristics according to the TyG tertiles

| | Lowest tertile (7.80–9.37) (n = 56) | Mid tertile (9.38–9.99) (n = 55) | Highest tertile (10.00- 10.96) (n = 55) | p value |
|---|---|---|---|---|
| Age (years) | 58.5 ± 10.1 | 60.6 ± 11.4 | 57.5 ± 11.0 | 0.306 |
| Gender (M/F) | 36/20 | 34/21 | 33/22 | 0.897 |
| BMI (kg/m$^2$) | 23.6 ± 2.8 | 25.0 ± 2.5 | 25.8 ± 2.1 | < 0.001 |
| Waist circumference (cm) | 86.0 ± 11.7 | 91.2 ± 10.9 | 94.0 ± 9.9 | 0.001 |
| Male | 90.2 ± 11.9 | 94.9 ± 9.9 | 96.4 ± 9.1 | 0.041 |
| Female | 78.4 ± 6.1 | 85.2 ± 10.2 | 90.4 ± 10.2 | < 0.001 |
| Systolic blood pressure (mmHg) | 138.9 ± 21.3 | 139.2 ± 22.9 | 143.7 ± 23.1 | 0.456 |
| Diastolic blood pressure (mmHg) | 85.9 ± 13.4 | 85.4 ± 14.1 | 85.6 ± 14.0 | 0.975 |
| Duration of diabetes (years) | 4.7 ± 2.8 | 5.8 ± 4.2 | 5.9 ± 4.1 | 0.006 |
| Practicing physical activity | 24 (42.9%) | 12 (21.8%) | 7 (12.7%) | 0.001 |
| Smoking | 15 (26.8%) | 22 (40%) | 24 (43.6%) | 0.152 |
| Metabolic syndrome | 23 (41.1%) | 42 (76.4%) | 44 (80.0%) | < 0.001 |
| Total cholesterol (mg/dL) | 207.1 ± 46.3 | 224.1 ± 55.2 | 232.8 ± 52.7 | 0.03 |
| Triglycerides (mg/dL) | 146.9 ± 42.2 | 209.9 ± 44.2 | 330.8 ± 70.4 | < 0.001 |
| HDL-cholesterol (mg/dL) | 50.0 ± 12.4 | 41.9 ± 8.2 | 40.1 ± 7.8 | < 0.001 |
| LDL-cholesterol (mg/dL) | 126.1 ± 36.7 | 130.4 ± 44.0 | 146.0 ± 51.5 | 0.042 |
| Non-HDL cholesterol (mg/dl) | 157.1 ± 43.3 | 182.2 ± 54.6 | 192.7 ± 51.5 | < 0.001 |
| Fasting plasma glucose (mg/dL) | 111.9 ± 27.7 | 159.7 ± 29.3 | 189.0 ± 43.2 | < 0.001 |
| HbA1c (%) | 7.3 ± 0.6 | 8.0 ± 0.9 | 8.3 ± 1.0 | < 0.001 |
| TyG index | 8.95 ± 0.37 | 9.67 ± 0.19 | 10.33 ± 0.23 | < 0.001 |
| Insulin (mU/L) | 20.3 ± 11.6 | 27.7 ± 13.0 | 28.1 ± 12.5 | < 0.001 |
| HOMA-IR index | 5.43 ± 3.36 | 10.50 ± 5.57 | 13.04 ± 6.84 | 0.001 |
| eGFR (mL/min/1.73 m$^2$) | 110.7 ± 162.0 | 91.2 ± 70.5 | 86.2 ± 31.7 | 0.46 |
| Coronary artery stenosis (%) | 16 (28.6) | 16 (29.1) | 28 (50.9) | 0.021 |

| | Lowest tertile (7.80–9.37) (n = 56) | Mid tertile (9.38–9.99) (n = 55) | Highest tertile (10.00- 10.96) (n = 55) | p value |
|---|---|---|---|---|
| Drug therapy | | | | |
| Metformin | 55 (98.2%) | 53 (96.4%) | 55 (100%) | 0.359 |
| Sulphonylurea | 50 (89.3%) | 51 (92.7%) | 48 (87.3%) | 0.634 |
| Thiazolidinedione | 1 (1.8%) | 0 (0%) | 0 (0%) | 0.372 |
| DPP-4 inhibitors | 1 (1.8%) | 1 (1.8%) | 3 (5.5%) | 0.432 |
| α-glucosidase inhibitor | 4 (7.1%) | 12 (21.8%) | 14 (25.5%) | 0.029 |
| Insulin | 2 (3.6%) | 0 (0%) | 1 (1.8%) | 0.369 |
| Antiplatelet | 30 (53.6%) | 32 (58.2%) | 32 (58.2%) | 0.852 |
| Statin | 33 (58.9%) | 32 (58.2%) | 31 (56.4%) | 0.961 |

We separated the population in tertiles of TyG index. Among the patients in the highest tertiles, BMI, waist circumference, total cholesterol, triglycerides, LDL-cholesterol, non-HDL cholesterol, plasma glucose and HbA1c levels were higher, HDL-cholesterol levels were lower, and lesser patients practiced physical activity. There was no significant difference for the current treatments across TyG tertiles.

# Association of TyG index with the metabolic syndrome and HOMA-IR index

A metabolic syndrome affected 109 patients (65.7%). The percentage of patients with the metabolic syndrome was higher in the highest TyG tertiles (Table 1). TyG index was significant in detecting a metabolic syndrome with an area under the ROC curve of 0.745 (95% CI: 0.660–0.830, $p < 0.001$) (Fig. 1). The cut-off point of 9.145 for TyG index offered a sensitivity of 93.6% and specificity of 52.6%, positive and predictive values of 77.3% and 79.4%, respectively. TyG index correlated significantly with HOMA-IR index ($r = 0{,}569$, $p < 0.001$) (Fig. 2).

# Results of coronary computed tomography angiography and association with TyG index

Among the 166 patients, 60 had CS ≥ 50%, including 32 with CS ≥ 70%. Twenty-one patients had 2- or 3-vessel disease (with stenosis ≥ 50%).

Compared to the patients without significant CS, the patients with CS ≥ 50% were older, had a longer diabetes duration, higher waist circumference, blood pressure, HbA1c and TyG index without significant difference for HOMA-IR, and more of them had a metabolic syndrome, were smokers, and were on statin or antiplatelet treatments (Table 2).

Table 2

Comparison between the patients with and without coronary artery stenosis (CS)

| | No significant CS (n = 106) | Significant CS (n = 60) | p value |
|---|---|---|---|
| Age (years) | 57.2 ± 10.7 | 61.9 ± 10.4 | 0.007 |
| Gender (M/F) | 63/43 | 40/20 | 0.356 |
| BMI (kg/m$^2$) | 24.5 ± 2.7 | 25.3 ± 2.4 | 0.061 |
| Waist circumference (cm) | 88.8 ± 11.3 | 93.1 ± 11.0 | 0.020 |
| Systolic blood pressure (mmHg) | 130.2 ± 18.5 | 158.9 ± 16.2 | 0.001 |
| Diastolic blood pressure (mmHg) | 80.3 ± 11.1 | 95.2 ± 12.8 | 0.001 |
| Duration of diabetes (years) | 3.9 ± 3.0 | 9.3 ± 3.3 | 0.001 |
| Practicing physical activity | 30 (28.3%) | 13 (21.7%) | 0.349 |
| Smoking | 27 (25.5%) | 34 (56.7%) | < 0.001 |
| Metabolic syndrome | 60 (56.6%) | 49 (81.7%) | < 0.001 |
| Total cholesterol (mg/dl) | 222.7 ± 53.3 | 218.6 ± 50.9 | 0.624 |
| Triglycerides (mg/dl) | 218.3 ± 94.3 | 247.2 ± 89.5 | 0.055 |
| HDL-cholesterol (mg/dl) | 45.2 ± 11.3 | 42.0 ± 8.9 | 0.061 |
| LDL-cholesterol (mg/dl) | 130.5 ± 44.9 | 141.1 ± 44.9 | 0.146 |
| Non-HDL cholesterol | 177.5 ± 52.7 | 176.6 ± 50.9 | 0.910 |
| Fasting plasma glucose (mg/dl) | 146.9 ± 43.5 | 165.3 ± 50.3 | 0.015 |
| HbA1c (%) | 7.57 ± 0.78 | 8.45 ± 1.08 | 0.001 |
| TyG index | 9.56 ± 0.61 | 9.78 ± 0.63 | 0.028 |
| HOMA-IR index | 9.12 ± 6.17 | 10.54 ± 6.41 | 0.163 |
| Drug therapy | | | |
| Metformin | 104 (98.1%) | 59 (98.3%) | 0.919 |
| Sulphonylurea | 91 (85.8%) | 58 (96.7%) | 0.027 |
| Thiazolidinedione | 1 (1%) | 0 (0%) | 0.450 |
| DPP4 inhibitors | 0 (0%) | 5 (8%) | 0.003 |
| Alpha glucosidase inhibitor | 5 (4.7%) | 25 (41.7%) | 0.001 |

| | No significant CS (n = 106) | Significant CS (n = 60) | p value |
|---|---|---|---|
| Insulin | 0 (0.0%) | 3 (5.0%) | 0.02 |
| Antiplatelet | 46 (43.4%) | 48 (80%) | 0.001 |
| Statin | 47 (44.3%) | 49 (81.7%) | 0.001 |

The prevalence of CS ≥ 50% was higher in the patients of the highest TyG tertiles (50.9% vs 28.6 and 29.1% in the lowest and mid tertiles, p = 0.021) (Table 1). In multivariate logistic regression analyses, TyG index was associated (p < 0.05) with CS independently of duration of diabetes, systolic blood pressure, waist circumference, LDL-cholesterol and HbA1c (Table 3).

Table 3
Multivariate regression analysis for significant coronary artery stenosis

| | Odds ratio (95% CI) | p value |
|---|---|---|
| Waist circumference > 90 cm male, > 80 cm female* | 0.637 (0.242–1.675) | 0.361 |
| HbA1c > 7% | 1.725 (0.455–6.550) | 0.423 |
| Duration of diabetes > 10 years | 10.463 (2.963–36.946) | 0.0001 |
| TyG index > 10 | 2.831 (1.050–7.633) | 0.040 |
| LDL-cholesterol > 100 mg/dL | 2.957 (1.042–8.394) | 0.042 |
| Systolic blood pressure > 140 mmHg | 23.596 (7.526–73.978) | 0.0001 |
| * Thresholds for abdominal obesity in the Asian population according to the IDF (20) | | |

TyG index was significant in predicting the presence of CS with an area under the ROC curve of 0.678 (95% CI: 0.582–0.775, p = 0.002) (Fig. 3). The cut-point of 9.63 offered 75% sensitivity, 44% specificity, 34% positive predictive value and 56% negative predictive value. When adding TyG index to age and HbA1c in the prediction model, the AROC was higher (0.780) than considering age or HbA1c alone (0.622 and 0.748, respectively) (p < 0.001 for both comparisons).

A higher number of diseased vessels (p = 0.04) and the degree of CS (p < 0.005) were associated with a higher level of TyG index (Tables 4 and 5).

Table 4
TyG index according to the number of coronary vessels with stenosis ≥ 50%

| Number of vessels with stenosis | Number of patients | TyG index | 95% CI | p value |
|---|---|---|---|---|
| 0 | 106 | 9.56 ± 0.62 | 9.44–9.68 | 0.04 |
| 1 | 39 | 9.72 ± 0.71 | 9.49–9.95 | |
| 2 or 3 | 21 | 9.92 ± 0.44 | 9.72–10.12 | |

Table 5
TyG index according to the degree of coronary artery stenosis

| Degree of stenosis | Number of patients | TyG index | 95% CI | p value |
|---|---|---|---|---|
| < 50% | 106 | 9.56 ± 0.61 | 9.45–9.68 | < 0.005 |
| 50–69% | 28 | 9.58 ± 0.71 | 9.30–9.85 | |
| ≥ 70% | 32 | 9.97 ± 0.49 | 9.79–10.15 | |

Subgroup analyses showed that TyG index was associated with CS in the patients aged ≥ 60 years, with HbA1c ≥ 7%, on statin or antiplatelet therapy (Fig. 4).

# Discussion

In the current study we included patients with type 2 diabetes without any symptom or history of cardiac disease but with rather poor control of hypertension and lipid disorders. TyG index correlated with HOMA-IR. The patients with highest TyG index had more marked metabolic disorders. More than one third of our patients had coronary stenoses on CCTA. The patients with CS had higher TyG index with no significant difference for HOMA-IR. The predictive value of TyG index for CS was additional to classical risk factors. In addition, for the first time in an asymptomatic population we showed that the number of narrowed vessels and the degree of coronary stenosis were associated with higher TyG levels. Our results suggest that in patients with type 2 diabetes TyG index may be considered as a marker of insulin resistance and allows to identify patients with high coronary risk.

TyG index, a composite indicator composed of triglycerides and fasting plasma glucose, was shown to correlate with insulin resistance as assessed by the hyperinsulinemic euglycemic clamp or HOMA-IR (11–13) and may thus be used as a surrogate marker of insulin resistance. When compared to clamp TyG index would even perform better than HOMA-IR (21). TyG index was also reported to be a marker of metabolic disorders (7,12,22) and a good predictor of incident type 2 diabetes (23–25). In our population of patients with type 2 diabetes TyG index was associated strongly with higher HOMA-IR and more marked metabolic disorders including higher BMI, waist circumference, total cholesterol, triglycerides,

LDL-cholesterol, non-HDL cholesterol, plasma glucose and HbA1c levels, lower HDL-cholesterol levels and also less physical activity. TyG index offered good performances to identify the patients with a metabolic syndrome. This index was not associated with current glucose lowering treatments except for α-glucosidase inhibitors (only 30 patients on this treatment) nor with lipid lowering treatment. Of note none of our patients was on fibrate which might have altered TyG. Interestingly, TyG index was significant in detecting metabolic syndrome with rather good performances for the cut-off point of 9.145.

Several studies suggest that TyG index might be recognized as a risk factor for cardiovascular complications and a marker of atherosclerosis. TyG index was shown to be an independent predictor of risk of cardiovascular events in an healthy population (14) and associated to a higher incidence of cardiovascular outcomes in patients with stable CAD (26) including those with type 2 diabetes (27), in patients with non-ST-segment elevation acute coronary syndrome (28) and in those with acute ST-elevation myocardial infarction after percutaneous coronary intervention (29). This index was reported to be a marker of subclinical carotid atherosclerosis in the general population, better than HOMA-IR (30), and of carotid atherosclerosis and arterial stiffness in lean postmenopausal women (15). In an healthy population TyG index was more independently associated with coronary artery calcifications than was HOMA-IR (22).

Cardiovascular disease is becoming a major cause of deaths in Vietnam like in other low-middle income countries. In the setting of acute myocardial infarction the incidence of in-hospital death rates is higher in patients with multiple cardiac comorbidities (31) with a need to improve guideline adherence (32). The proportion of diabetic patients with silent coronary artery disease is expected to be greater than in higher income countries. In the present study CCTA detected coronary stenoses ≥ 50% in 36% and ≥ 70% in 19% of the patients. In two previous studies which similarly performed CCTA in asymptomatic individuals the proportion of patients with CS ≥ 70% was found lower, 6.3% in an US population of patients with type 1 or type 2 diabetes deemed to be at high cardiovascular risk (6) and 12.3% of a Korean population of patients with type 2 diabetes (7). Compared to the latter study, our population had some similarities but exhibited a more marked risk related to higher blood pressure, triglycerides and LDL-cholesterol levels, and TyG index was also higher. The levels of these risk factors were clearly higher than the goals to be achieved according to the recent guidelines (1).

Our data showed that TyG index was associated with an increased risk of CS on CCTA as previously reported (7). The risk was independent of duration of diabetes, waist circumference, systolic blood pressure, HbA1c levels and LDL-cholesterol. Additionnally, since coronary artery disease is more extended and severe in diabetic patients than in non-diabetic individuals, for the first time we evaluated the severity of CS and found that higher levels of TyG index were associated with the number of diseased vessels and the degree of coronary narrowing. This result is consistent with a previous study performed in patients with non-ST-segment elevation acute coronary syndrome which reported an independent association of TyG index with the number of diseased vessels and the SYNTAX score (28). This suggests that insulin resistance as expressed by TyG may contribute to atherosclerosis in addition to cardiovascular risk factors. Our data based on subgroup analyses showing that TyG index was associated with an increased

risk of CS in the patients ≥ 60 years, with poor glycemic control (HbA1c ≥ 7%), on statin or antiplatelet therapy, indicate that TyG might account for a residual risk despite these treatments.

Our study has some limitations. First, its cross-sectional design cannot definitely allow to consider the results in a causality relationship. Thus, the mechanisms behind the association of TyG index with CS remain to be clarified. Second, our study population was relatively small. Third, we compared TyG index with HOMA-IR and not with the hyperinsulinemic euglycemic clamp, the gold standard method for measuring insulin resistance. However several studies have previously shown similar associations of TyG with the clamp test. Fourth, we did not record nutritional data and we were so unable to adjust for diet habits which can change triglyceride levels. Fifth, the participants were recruited at one hospital center, which may limit the generalizability of our results. One strength of the current study was to perform CCTA in a relatively homogeneous population of patients with type 2 diabetes and without evidence of cardiovascular disease.

# Conclusion

Our results support that in patients with type 2 diabetes TyG index may be used as a reliable tool to assess insulin resistance and to identify patients with a metabolic syndrome. This simple and cheap tool may be easily used in low-middle income countries. More than one third of our patients had CS on CCTA. TyG index was able to identify patients at high risk of silent coronary disease independently from classical risk factors and did it better than HOMA-IR. Higher TyG index was associated with the number of narrowed vessels and the degree of stenosis. The predictive value of TyG index seems to be additional to classical risk factors and remains significant even in the patients on statin or antiplatelet therapy. Insulin resistance might thus be involved in the residual cardiovascular risk. Finally, TyG index might be beneficial for stratification and intervention to prevent major cardiac events. Further studies in larger populations are needed to assess the importance of these results.

# Abbreviations

CCTA
computed tomography angiography
CS
coronary stenoses
HOMA-IR
HOMA-insulin resistance index
TyG
Triglyceride Glucose index

# Declarations

### Acknowledgements

None.

### Authors' contributions

All authors have made substantial contributions. HVM conceived the study and designed the study protocol. PVT, HAT and HVM organized, performed the study investigations and supported the recruitment of the patients. HAT performed statistical analyses. PVT, HVM and PV wrote the first draft of the manuscript. All authors critically revised the manuscript for important intellectual content. They all read and approved the final manuscript.

### Competing interests

The authors declare they have no competing interests.


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### Availability of data and materials

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

### Ethics approval and consent to participate

The study protocol was approved by our institution's ethics commiette, and informed consent for the procedure was obtained from each participant.

### Consent for publication

Not applicable.

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# Figures

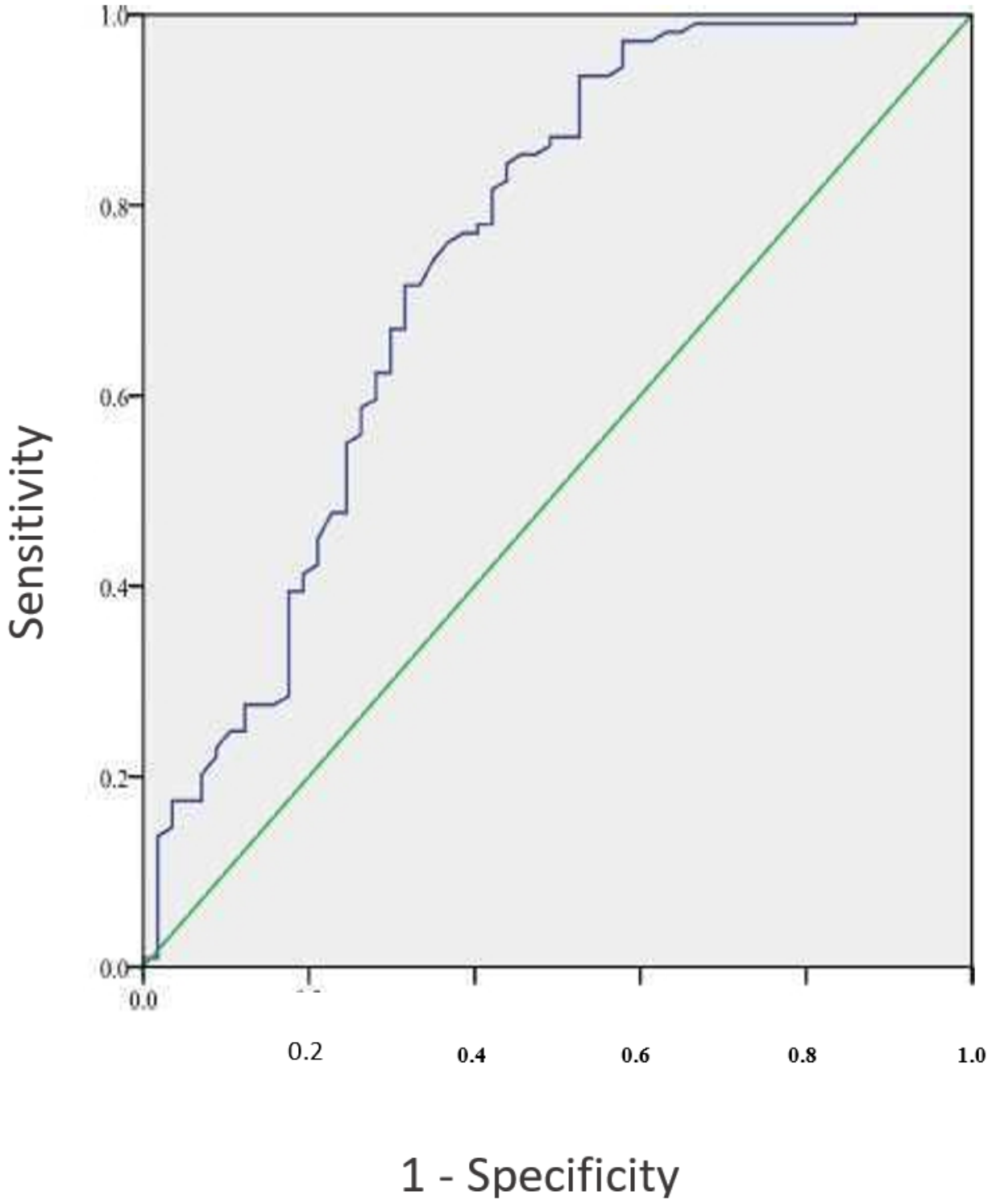



**Figure 1**

ROC curve of TyG index for detecting a metabolic syndrome

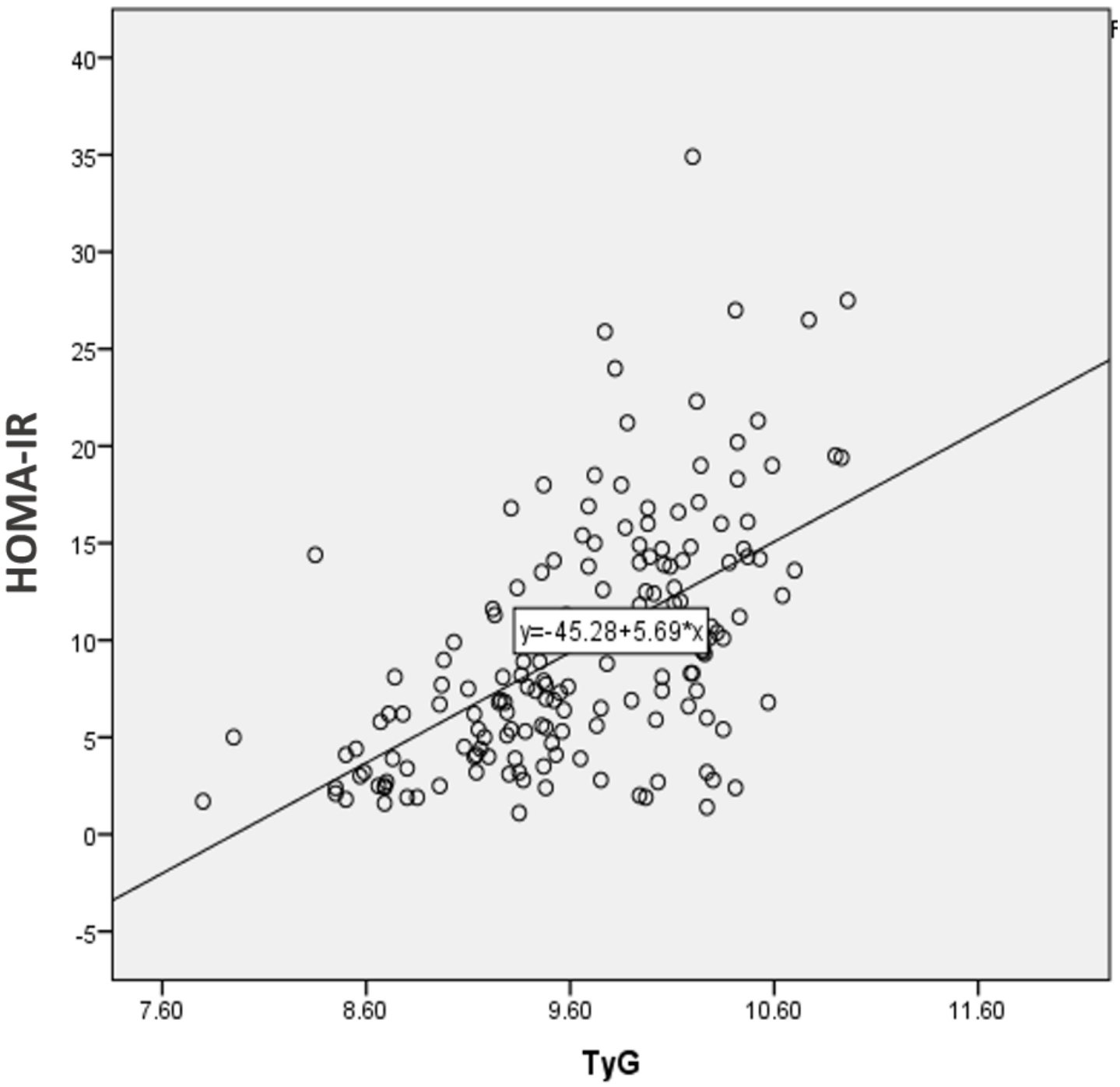



**Figure 2**

Correlation between TyG index and HOMA-IR index

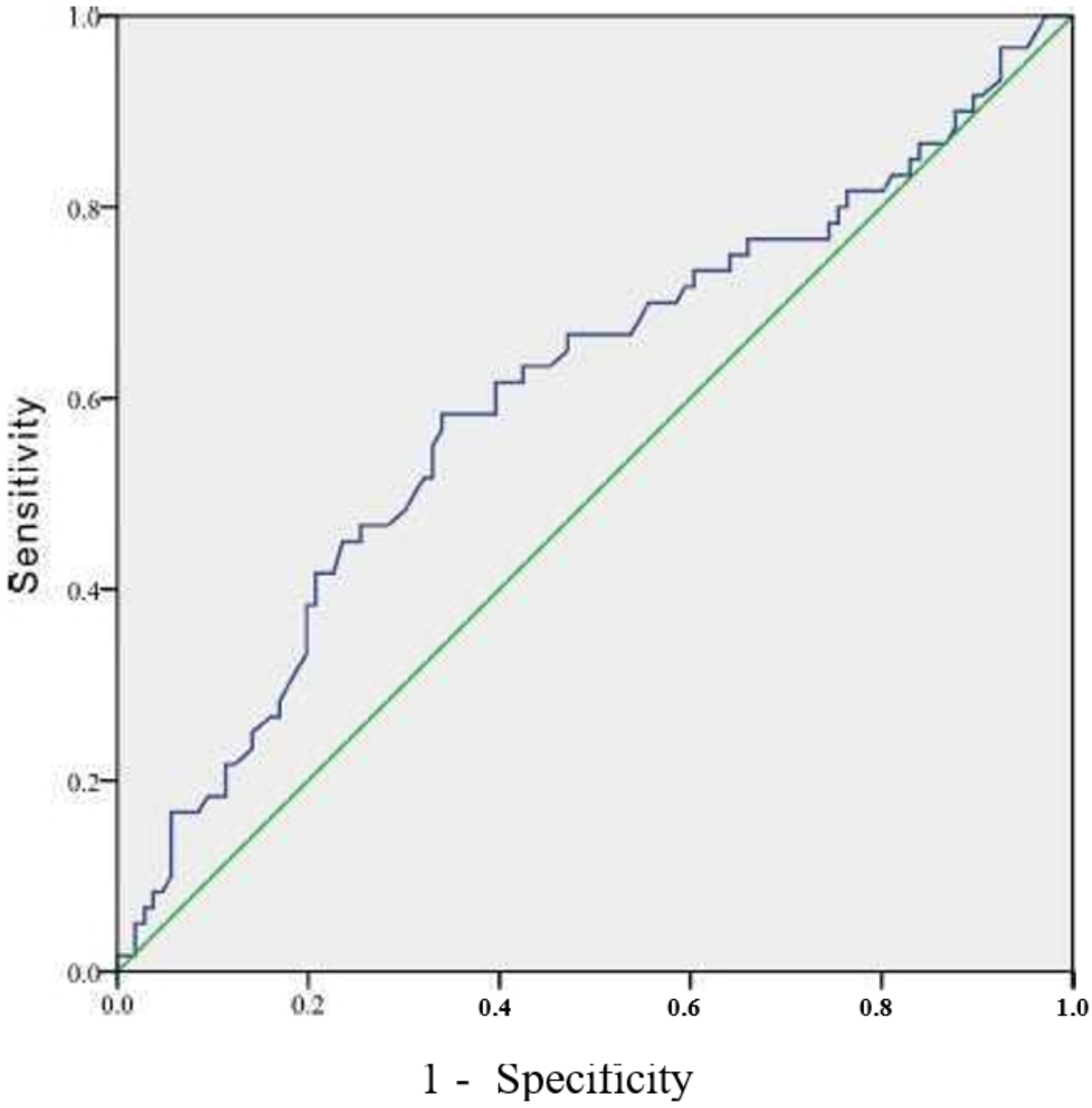
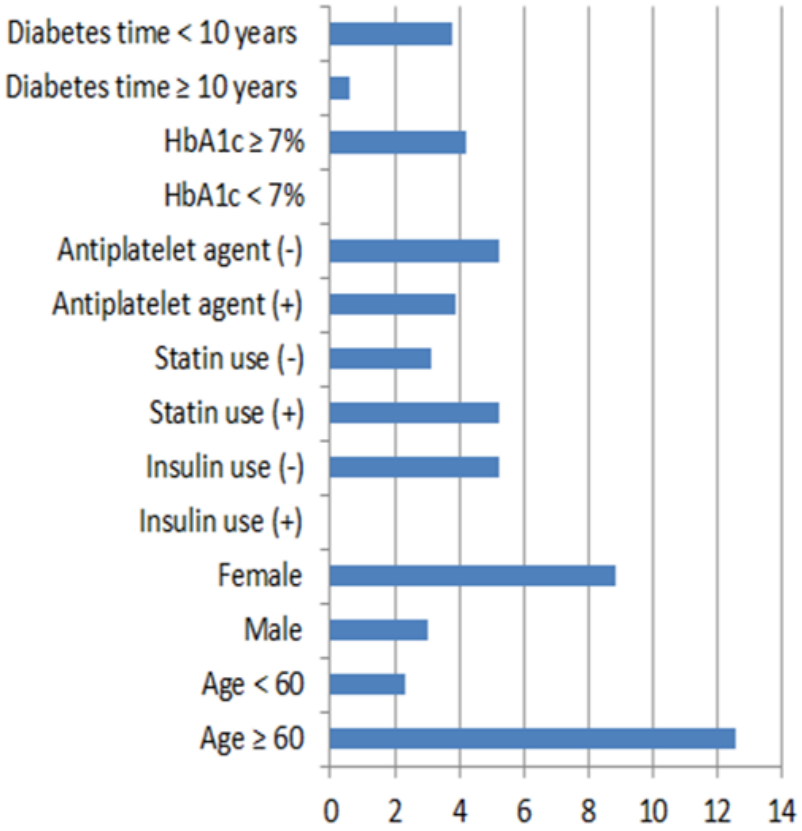



**Figure 3**

ROC curve of TyG index for the prediction of coronary artery stenosis




| | OR | 95%CI | p |
|---|---|---|---|
| Diabetes time < 10 years | 3.788 | 0.694-20.687 | 0.124 |
| Diabetes time ≥ 10 years | 0.611 | 0.052-7.240 | 0.696 |
| HbA1c ≥ 7% | 4.229 | 1.288-13.888 | 0.017 |
| HbA1c < 7% | 0 | 0 | 0.999 |
| Antiplatelet agent (-) | 5.263 | 0.453-50.998 | 0.152 |
| Antiplatelet agent (+) | 3.9 | 1.092-13.928 | 0.036 |
| Statin use (-) | 3.143 | 0.30232.654 | 0.338 |
| Statin use (+) | 5.236 | 1.477-18.563 | 0.01 |
| Insulin use (-) | 5.263 | 1.267-17.027 | 0.006 |
| Insulin use (+) | 0 | 0 | 1 |
| Female | 8.867 | 0.981-80.177 | 0.052 |
| Male | 3 | 0.825-10.912 | 0.095 |
| Age < 60 | 2.32 | 0.623-8.633 | 0.209 |
| Age ≥ 60 | 12.571 | 1.415-111.677 | 0.023 |

## Figure 4

Subgroup analysis showing the odds ratios for the highest compared to the lowest tertile of TyG index for coronary artery stenosis.