Control of cardiometabolic risk factors and their association with carotid intima media thickness among patients with type 2 diabetes mellitus - single center experience in a developing country

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The authors declare no competing interests.

Informed consent

The study protocol was approved by the Ethical Review Committee, Faculty of Medicine, University of Ruhuna, Sri Lanka (ERC 11/12/12). At the commencement of the study, all the study participants signed an informed consent.

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Abstract

Background/aim: Type 2 diabetes mellitus (T2DM) is closely linked with atherosclerotic cardiovascular diseases (ASCVD). We aimed to describe the degree of ASCVD risk factor control and their association with carotid intima media thickness (CIMT) in T2DM patients followed-up at a diabetes clinic in Southern, Sri Lanka.

Materials and methods: We analyzed 300 T2DM patients for CIMT and nonalcoholic fatty liver disease (NAFLD), both ultrasonically in the present cross sectional study. CIMT and its associations with modifiable cardiometabolic risk factors were examined. Recommended optimal targets of risk factors were defined as glycated hemoglobin (HbA_{1C}) < 7 %, absence of NAFLD, albumin creatinine ratio (ACR) < 30 mg, triglyceride (TG) < 150 mg/dL, low density lipoprotein cholesterol (LDL-C) < 100 mg/dL, high density lipoprotein cholesterol (HDL-C) in men > 40 and in women > 50 mg/dL, systolic blood pressure (SBP) < 130 mmHg, and diastolic blood pressure (DBP) < 80 mmHg.

Results: SBP, DBP, LDL-C, TG, HDL-C, HbA_{1C}, and ACR were optimally controlled in 59.3, 75.0, 46.7, 84.3, 46.0, 33.0, and 18.7% patients, respectively and nearly half of the study subjects haven't NAFLD. Only three patients (1%) had achieved all therapeutic targets. There were statistically significant differences in CIMT between optimally controlled TG and sub optimally controlled TG group (p=0.027) and between the groups with and without NAFLD (p=0.045) when adjusted for age and duration of diabetes. CIMT showed significant and positive associations with LDL-C (p=0.024), TG (p=0.026), and NAFLD (p=0.005). The

presence of NAFLD had the highest odds of having higher CIMT when compared to LDL-C and TG.

Conclusion: The majority of patients have not achieved the recommend targets of ASCVD risk factors and at high risk of ASCVD. Attempts must be made to identify reasons for not achieving the treatment targets and thereby reduce ASCVD burden by controlling LDL-C, TG, and NAFLD.

Key words: Atherosclerotic cardiovascular diseases, cardiometabolic risk factors, carotid intima media thickness, type 2 diabetes mellitus

1. Introduction

On the far side of last few decades, there has been an exponential rise in morbidity and mortality caused by atherosclerotic cardiovascular diseases (ASCVD) and the pandemic of diabetes mellitus has substantially contributed to this upsurge [1,2]. Cardiovascular disease (CVD) account for nearly three fourths of deaths in patients with type 2 diabetes mellitus (T2DM) [3]. To date, it is shown that patients with T2DM are at a twofold multiple risk for CVD compared to those without diabetes mellitus [4]. In the prospective atherosclerosis risk in communities study, which followed up 13,790 patients over a two-year period, it was revealed that a patient with T2DM without established CVD has the same risk of developing a myocardial infarction as an individual who has already developed a myocardial infarction [5]. These observations have led to the notion that T2DM is a major determinant of CVD.

Several metabolic derangements seen in diabetes are responsible for both initiation and progression of arterial injury and thereby high risk of ASCVD observed among them. Hyperglycemia, insulin resistance coupled with hyperinsulinemia, atherogenic dyslipidemia, elevated systolic and diastolic blood pressures, and microalbuminuria operate at different molecular and cellular levels increase arteriopathy and the ASCVD risk in patients with T2DM [6]. Furthermore, chronic kidney disease resulting from diabetic nephropathy and comorbidities such as nonalcoholic fatty liver disease (NAFLD) are potential contributors for increased ASCVD risk in patients with T2DM [6].

Epidemiological studies conducted in multiethnic settings have shown that patients with T2DM of South Asian ethnicity have a significantly higher risk of ASCVD compared to other ethnic groups [7]. Although several genetic, environmental, and behavioral factors have been

postulated to explain the reported high risk of ASCVD among South Asian T2DM patients, the underlying mechanisms for this observation remain largely obscure.

Health authorities and professional organizations have embarked on several strategies to combat the rising incidents of death in patients with T2DM especially due to ASCVD. They mainly focus on lifestyle and pharmacological manipulations of modifiable risk factors including dyslipidemia, microalbuminuria, hyperglycemia, and high blood pressure. Based on major prospective observational and interventional studies, optimal levels for these risk factors have been laid down as recommended therapeutic targets [8]. Major clinical trials and real-life studies provide evidence on the fact that adhering to these recommended therapeutic targets reduce adverse cardiovascular events in patients with T2DM [9]. The other primary prevention strategies include an early identification of arterial injury and implementation of appropriate therapeutic interventions to delay its progression. The impact of these strategies on the rising ASCVD burden, however, depends on several factors including the awareness of caregivers to recommend appropriate interventions, readiness of patients to follow them and achieve the recommended treatment targets, and wider availability of resources to screen ASCVD at asymptomatic stages. Due to the variation of above factors, the degree of the achievement of endorsed targets of ASCVD risk factors vary among T2DM patients who are living in different localities in the world [10].

Developing countries like Sri Lanka are facing rising burden from T2DM and its related complications. These are reflected in the recent trends in community survey-based data, country's hospital admissions, and morbidity and mortality data [11,12]. Although, these data have highlighted the rising burden of diabetes and related ASCVD on the healthcare settings

and the community in Sri Lanka, there is paucity of literature on the degree of cardiometabolic risk factor control and their associations with carotid intima media thickness (CIMT), as a surrogate of chronic arterial injury, in patients with T2DM. Knowledge on the intensity of control and strengths of associations of major modifiable ASCVD risk factors would enable clinicians to focus more on the most pivotal risk factors with strong associations to reduce morbidity and mortality in T2DM patients, especially in the resource poor settings in developing countries. Herein, we aimed to describe the degree of control of cardiometabolic risk factors and study their associations with CIMT in a cohort of patients with T2DM followed up at a tertiary care diabetes clinic in Southern, Sri Lanka.

2. Materials and methods

2.1. Study design and setting

Present study was designed as a single center cross-sectional study. The study was conducted in the university medical clinic at the Teaching Hospital Karapitiya in Southern, Sri Lanka during January and June in 2021. Teaching Hospital Karapitiya, the largest tertiary care center in Southern, Sri Lanka, serve as the main training facility center for the Faculty of Medicine, University of Ruhuna, Sri Lanka. The university medical clinic receives referrals from other subspecialties in the hospital, outpatients' departments, and primary and secondary care services in the area. All services including drugs and investigations are sponsored by the state and the hospital service area includes all ethnicities, almost to the same proportions found in the country.

2.2. Sample size and patients

The sample size was determined with the prevalence of CIMT among patients with T2DM as 57% and the margin of error of 6% [13].

$n = Z^2P (1-P) / W^2$

where, n = minimum sample size, Z = 1.96 (for 95% confidence interval). The calculated minimum sample size was 262, hence the final sample size was kept at 300 to make allowance for missing data and incomplete questionnaire.

A total number of 300 patients with T2DM aged 18 – 70 years and attending the outpatient clinic of the University medical unit at the Teaching Hospital Karapitiya in Southern, Sri Lanka were enrolled for the study. Patients with established ASCVD, previous myocardial ischemia, stroke, transient ischemic attacks, peripheral arterial disease, vascular dementia, and type 1 diabetes mellitus were excluded from the study. Pregnant women were also excluded. An identification number was given to each study subject at the time of data collection. All the data collected during the study were stored in the principal investigator's laptop and in a data repository with respect to their identification numbers. Data were not shared with persons other than the investigators of the study and all the investigators had access for the data repository.

2.3. Variables

According to the objectives of the present study, primary outcome was to determine degree of control of cardiometabolic risk factors including glycated hemoglobin (HbA_{1C}), absence of NAFLD, albumin creatinine ratio (ACR), triglyceride (TG), low density lipoprotein cholesterol (LDL-C), high density lipoprotein cholesterol (HDL-C), systolic blood pressure (SBP), and diastolic blood pressure (DBP) in T2DM patients. The secondary outcome was

to estimate associated cardiometabolic risk factors with CIMT in a cohort of patients with T2DM. Age, gender, and the duration of T2DM were the potential confounders for outcomes.

2.4. Laboratory and demographic measurements

A fasting venous blood sample (5 cc) was collected and HbA_{1C}, serum creatinine, serum albumin, and lipid profile including LDL-C, TG, and HDL-C were measured. HbA_{1C} was measured by HPLC method using an automated analyzer (BIO RAD D analyzer, USA) while lipid profile, serum creatinine and albumin were measured by a fully automated analyzer based on spectrophotometric principles (Huma star -600 HS- Germany). Estimated globular filtration rate (eGFR) was calculated in mL/min/1.73 m^2 using the Chronic Kidney Disease-Epidemiology Collaboration equation. ACR was used to measure the amount of albumin in the urine. All the biochemical estimations were performed at the same laboratory with periodic *in-vitro* quality control measures and results were entered into a data entry form.

Demographic data including gender, age, duration of diabetes were collected. Body weight, height, and waist circumference (WC) were measured and thereby body mass index (BMI) was calculated as body weight (kg) divided by height squared (m^2). Both SBP and DBP were mentioned as an average of three readings.

Ultrasonographic assessment of the liver was performed by a specialist radiologist (IK) using the curvilinear probe (3.5MHz) of the high-end ultrasound unit (GE LOGIQ E9 XD clear-Seognam, Gyeonggi, Korea) to detect NAFLD. Upon the diagnosis of fatty liver, the increment of liver echogenicity was observed compared to renal cortex and the spleen, loss of definition of the diaphragm, and poor delineation of the intrahepatic portal venous architecture. One or two of the mentioned criteria were required to be achieved to prevent false positive results. The status of NAFLD was documented as present or absent.

Ultrasonographic measurement of CIMT was performed using the linear transducer (3 - 11 MHz) of GE LOGIQ E9 XD clear-Seognam, Gyeonggi, Korea scanner. Best quality images were collected via adjusting the time gain compensation curve and amplifying the greyscale. A single focus point was adjusted at the level of the posterior wall of the carotid artery and in optimum magnification, the measurements were taken from the posterior wall. Both common carotid arteries in a plaque-free segment were used to measure CIMT and the average of three measurements was taken as the CIMT. The mean value of both CIMT measurements was taken for the analyses.

2.5. Statistical analysis

After having check the data sets for distribution, the normally distributed data sets were expressed as mean ± standard deviation (SD). Skewed data sets were represented in median value with the interquartile range. All the categorical data were reported as number with the percentage. Optimal levels of cardiometabolic risk factors were defined according to the American Diabetes Association (ADA) clinical practice guidelines (HbA_{1C} < 7 %, absence of NAFLD, ACR < 30 mg, TG < 150 mg/dL, LDL-C < 100 mg/dL, HDL-C in males > 40 and in females > 50 mg/dL, SBP < 130 mmHg, and DBP < 80 mmHg). The one-way ANCOVA was applied to determine whether there were significant differences of CIMT between each optimally and suboptimaly controlled groups, separately. In the one-way ANCOVA, age and the duration of T2DM were used as the covariates. The strength of correlations between CIMT and the risk factors were determined using either Pearson correlation coefficient or Spearman rank correlation coefficient. A point-biserial correlation was applied to measure the correlation between CIMT and NAFLD. Association between CIMT and the risk factors was assessed through multiple linear regression at 95% CI with

the adjustment for age, gender, and the duration of T2DM. Missing values were not inferred for the study analysis. A significance level of $p \leq 0.05$ was considered. All the analysis were carried out using SPSS V 25.0.

3. Results

A total number of 330 T2DM patients were eligible for the study and among them, 300 patients (209 women) were enrolled for the study (Figure 1). Table 1 includes basic characteristics of the study subjects.

Of all 300 patients, only three patients (1%) had controlled all cardiometabolic risk factors at optimal level. The therapeutic targets of risk factors such as SBP, DBP, LDL-C, TG, HDL-C, HbA_{1C}, and ACR were achieved by 59.3, 75.0, 46.7, 84.3, 46.0, 33.0, and 18.7% patients, respectively. Nearly half of the study subjects were detected to have NAFLD (Table 2). Furthermore, mean CIMTs were significantly different between those with optimally controlled TG and those without and also between those with and without NAFLD when adjusted for age and the duration of T2DM (Table 2).

In study subjects, TG and LDL-C showed significant and positive correlations with CIMT (Figures 2a and 2b) while HDL-C showed an inverse correlation (Figure 2c). SBP, DBP, HbA_{1C}, ACR, and as well as duration of T2DM, however, showed no significant correlations with CIMT in these patients. Furthermore, a positive correlation was seen between NAFLD and CIMT ($r=0.161$, $p=0.005$).

As revealed by multiple linear regression analysis (Table 3), CIMT showed significant and positive associations with LDL-C ($p=0.024$), TG ($p=0.026$), and NAFLD ($p=0.005$). The presence of NAFLD had the highest odds of having higher CIMT when compared to LDL-C and TG.

4. Discussion

This single center investigation exposed several important facts regarding the control of major amendable cardiometabolic risk factors and their association with CIMT in a cohort of adults with T2DM without established cardiovascular disease, in a developing South Asian country.

Firstly, these findings exposed the alarming suboptimal control of major amendable ASCVD risk factors among patients with T2DM in a tertiary care center in Sri Lanka, the country having rising burden of CVD. Only about one third (33%) of patients have achieved the recommended therapeutic targets of glucose control determined by HbA_{1C} while only 46% achieved the LDL-C optimal target. In contrast, high proportion of patients had achieved systolic and diastolic blood pressures targets (75% and 59%, respectively). Furthermore, the optimal control of HbA_{1C}, all major lipid, and blood pressure parameters was achieved by only a small fraction (1%) of study participants. Secondly, these findings reconfirm the established associations of high LDL-C, TG, and low HDL-C with CIMT. The stronger association of NAFLD with CIMT, compared to LDL-C, TG, and HDL-C, however, is a somewhat novel finding emerging from this analysis.

In the real world setting, only small faction of diabetic patients achieve the recommended targets for the control of major CVD risk factors. According to a multi-center survey conducted in China involving T2DM patients, the optimal glycemic control was seen in only 32.6% of patients and the control of lipids, glycemia, and blood pressure in together was seen in only 11.2% [14]. Wong et al. (2013) reported that only 24% US adults with T2DM control all three CVD risk factors including LDL-C, HbA_{1C}, and blood pressure [15]. In a recent meta-analysis, achievement rates of the control of CVD risk factors; glycemic control, blood

pressure, LDL-C, HDL-C, and TG were 42.8, 29, 49.2, 58.2, and 61.9% respectively [16]. During 2013 and 2017, control rates of HbA_{1C}, LDL-C, and blood pressure had increased among hospitalized T2DM patients in Tianjin, China [17]. A cross-sectional study conducted in a tertiary care teaching hospital in Wardha District, India demonstrated that only one-fourths of T2DM patients have the optimal control of one or more risk factors for CVD including physical inactivity, tobacco use, hypertension, obesity, dyslipidemia, and dietary risk factor [18]. A previous cross-sectional study carried out at a private diabetes center in Sri Lanka showed that the percentage of patients attaining the recommended therapeutic targets of CVD risk factors as 25.2% for HbA_{1C}, 24.3% for LDL-C, 32% for SBP, and 56.7% for DBP [19].

Atherosclerosis is a chronic process initiated by arterial injury due to a variety of factors progressing over decades. There is an imperative need of a low-cost, convenient, and non-invasive screening tool to detect progressive arteriopathy before its adverse clinical outcomes occur especially among at-risk population such as those with T2DM. CIMT is a reliable and non-invasive indicator of chronic arterial injury [20]. Similar to the current study findings, Li et al. [21] found a significant association between TG with CIMT among 1,476 T2DM patients in Affiliated Hospital of Southwest Medical University. Even though, they found an association between blood glucose and CIMT in diabetic patients, our analysis did not find such association between HbA_{1C} and CIMT. Concordant with our data, Kowall et al. [22] also did not find different measures of glycaemia to be associated with CIMT in diabetic and non-diabetic subjects in Southern Germany (n=2,663). However, HbA_{1C} was a significant determinant of CIMT in non-diabetic community dwelling individuals [23]. Even though, some studies found significant associations of CIMT with SBP, DBP, and ACR [21,23-25],

our study failed to observe such associations. It could partly be due to obtaining office measurement of SBP, DBP, and ACR in our study. Office blood pressure measurement often does not reflect the control of blood pressure over a period and patients may have been more compliant with medication before the scheduled clinic visit.

South Asians possess a lipid profile favoring chronic arterial injury especially with high TG and low HDL-C than other ethnicities [26-28]. We observed a significantly higher CIMT in T2DM patients with sub-optimally controlled TG. However, there were no significant associations between CIMT and other lipids namely LDL-C and HDL-C and this can be due to several reasons.

South Asians are reputed to have arterial injuries at relatively lower levels of LDL-C [26]. Even though, South Asians have a high HDL-C level as >40 mg/dL, its considerable percentage is dysfunctional. Indeed, dysfunctional HDL-C has less defensive aptitudes and pro-inflammatory effects and thereby link with the progression of CVD [29].

There is increasing prevalence of NAFLD in the globe and it is estimated to affect more than half of T2DM patients [30]. The leading cause of mortality in patients with NAFLD is CVD. Recently carried out study involving 3,000 patients demonstrated significant higher prevalence of CVD in T2DM patients with ultrasound-diagnosed NAFLD than those without NAFLD [31]. It was reported 90% increment of CVD risk in T2DM patients with NAFLD diagnose on ultrasonography [32]. A large–meta-analysis reconfirmed that NAFLD is a risk factor of fatal and non-fatal cardiovascular events among patients with T2DM [33]. An investigation undertaken in China involving study participants (n=71,852) who hadn't previous cardiovascular events demonstrated that NAFLD is an independent predictor of CVD in not only patients with T2DM but also with pre-diabetes [34]. A prospective pilot

study including 529 T2DM outpatients with no history of CVD has further reported that NAFLD detected via non-enhanced computed tomography could be used to identify T2DM patients at high risk for CVD [35]. In addition to the aforementioned studies, several investigations have highlighted the association between NAFLD and CVD in patients with T2DM [36,37].

Of note, it is reported that CVD accompanied by NAFLD exert more adverse metabolic burden than CVD alone [38]. In actual fact, the strong association between NAFLD and CVD is governed by numerous pathophysiological mechanisms including oxidative stress, inflammation, lipid metabolism, gut microbiota etc. [39-41]. In NAFLD patients, higher level of TG, LDL-C, and VLDL-C, which are established ASCVD risk factors, could be seen due to increased lipogenesis and overflow of free fatty acid to the liver [42-44]. Furthermore, increased overflow of free fatty acids to the liver lead for oxidative stress which induces endothelial dysfunction, and ultimately the whole process enhances CVD events [45,46]. Also, hepatic insulin resistance and inflammation accelerate CVD risk [47,48]. Moreover, the increase intestinal microbiota could influence lipid metabolism, adipose inflammation, and insulin resistance that are collective mechanisms between NAFLD and CVD events [49]. In the present study, NAFLD was found to be a more significant marker of chronic arterial injury measured with CIMT over other conventional risk factors; LDL-C and TG.

The main strength of the present study is assessing CIMT in patients before the onset of adverse ASCVD clinical outcomes such as myocardial and cerebrovascular disease. Furthermore, we considered all major modifiable ASCVD risk factors to draw the final conclusions. However, some limitations have to be addressed in here. This study was a single center, cross-sectional study involving only 300 T2DM patients and that limits the

generalizability of our findings. We propose further studies with a wider inclusion of study centers and more study participants. It should also be noted that we assessed severity of chronic arterial injury in these patients by measuring their CIMT, which is considered as a less robust indicator of atherosclerosis compared to other measurements like quantification of plaque burden or coronary artery calcium score. But in the low resource setting we were compelled to use CIMT as a surrogate of arterial injury. The potential confounding effects of antidiabetic, antihyperlipidemic, and antihypertensive treatments on our findings were also not investigated in this study. Furthermore, NAFLD was detected in dichotomous manner; present or absent, disregarding the different stages of the fat content. Also ultrasonography, compared to MRI has low sensitivity and specificity in differentiating different stages of fatty liver.

In conclusion, control of major modifiable ASCVD risk factors; SBP, DBP, LDL-C, TG, HDL-C, HbA_{1C}, and ACR, by patients with T2DM is grossly suboptimal in the present cohort. Significantly higher CIMT was observed in T2DM patients with suboptimal control of TG than optimal control of TG. Importantly, T2DM patients with NAFLD had higher CIMT than patients without NAFLD. Lipid profile parameters including HDL-C, LDL-C, and TG and NAFLD were significantly correlated with CIMT in these study subjects. This study indicates that LDL-C, TG, and presence of NAFLD are significant predictors of chronic arterial injury in patients with T2DM. In general, these findings could be utilized to strengthen the current care delivered by the study center by educating patients as well as doctors involved in patient care. Furthermore, these data could be used as a platform in designing future studies.

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Table 1. Patient and disease related variables of 300 patients included in the analysis.

Variable	**Results**
Number (%) of women	209 (69.7)
Mean ± SD age (years)	62 ± 10
Median (IQR) of the duration of T2DM (years)	7 (4 – 11)
Mean ± SD BMI (kg/m^2)	24.4 ± 3.8
Median (IQR) WC (cm)	87.0 (82.0 – 95.0)
Median (IQR) systolic pressure mmHg	126.0 (114.0 – 140.0)
Median (IQR) diastolic pressure mmHg	72.0 (63.0 – 80.8)
Median (IQR) TG (mg/dL)	96.0 (71.0 – 133.8)
Median (IQR) HDL-C (mg/dL)	45.0 (39.3 – 51.0)
Median (IQR) LDL-C (mg/dL)	104.6 (79.0 – 140.0)
Median (IQR) HbA_{1C} (%)	7.65 (6.80 – 9.00)
Mean ± SD eGFR (mL/min/1.73 m^2)	73.4 ± 23.6
Median (IQR) ACR (mg/mmol)	68.8 (35.1 – 120.1)
Mean ± SD CIMT (mm)	0.70 ± 0.14
Number (%) with NAFLD	147 (49.0)

ACR, urine albumin to creatinine ratio; BMI, body mass index; CIMT, carotid intima-media thickness; eGFR, estimated glomerular filtration rate; $HbA_{1C,}$ glycated hemoglobin; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; NAFLD, nonalcoholic fatty liver disease; TG, triglyceride; T2DM, type 2 diabetes mellitus; WC, waist circumference.

Table 2. Mean differences of CIMT based on the control of cardiometabolic risk factors.

Factor	**State**	**No. of study subjects (%)**	**CIMT /mm** **Mean ± SD**	**p value**
SBP	Optimal	178 (59.3)	0.69 ± 0.14	0.87
	Suboptimal	122 (40.7)	0.71 ± 0.14	
DBP	Optimal	225 (75.0)	0.70 ± 0.14	0.70
	Suboptimal	75 (25.0)	0.69 ± 0.13	
LDL-C	Optimal	140 (46.7)	0.69 ± 0.13	0.11
	Suboptimal	160 (53.3)	0.70 ± 0.15	
TG	Optimal	253 (84.3)	0.69 ± 0.13	0.027
	Suboptimal	47 (15.7)	0.74 ± 0.17	
HDL-C	Optimal	140 (46.7)	0.68 ± 0.13	0.18
	Suboptimal	160 (53.3)	0.71 ± 0.15	
HbA_{1C}	Optimal	99 (33.0)	0.69 ± 0.15	0.28
	Suboptimal	201 (67.0)	0.70 ± 0.14	
ACR	Optimal	56 (18.7)	0.67 ± 0.13	0.16
	Suboptimal	244 (81.3)	0.70 ± 0.14	
NAFLD	Absent	153 (51.0)	0.68 ± 0.14	0.045
	Present	147 (49.0)	0.72 ± 0.14	

ACR, urine albumin to creatinine ratio; CIMT, carotid intima-media thickness; HbA_{1C}, glycated hemoglobin; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; NAFLD, nonalcoholic fatty liver disease; TG, triglyceride; WC, waist circumference.

Table 3. Associated risk factors with CIMT in patients with T2DM.

	OR (95% CI)	**p value**
HDL-C	-0.074 (-0.003 – 0.001)	0.20
LDL-C	0.131 (0.000 – 0.001)	0.024
TG	0.131 (0.000 – 0.001)	0.026
NAFLD	0.156 (0.014 – 0.074)	0.005

HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; NAFLD, nonalcoholic fatty liver disease; TG, triglyceride.

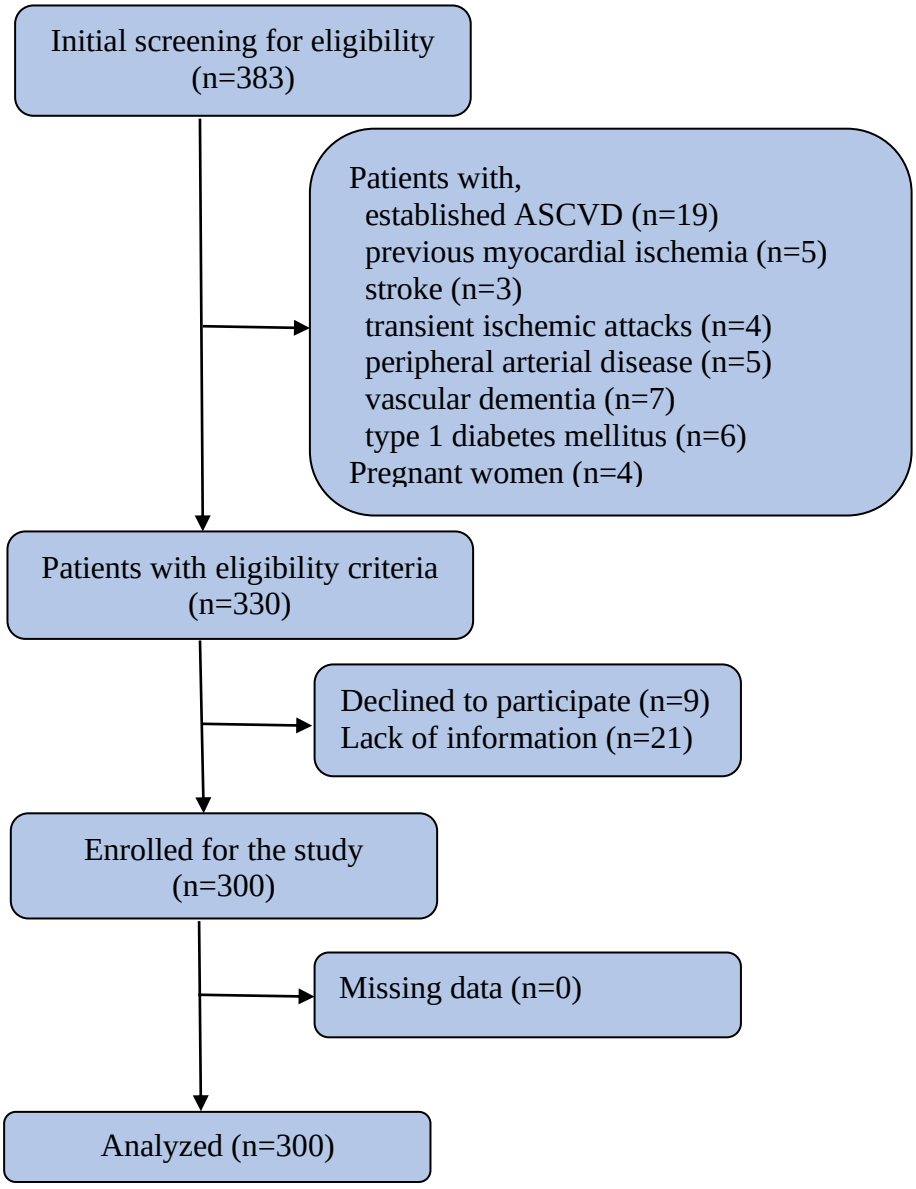

Figure 1. Study participants' flow diagram, from recruitment to analysis.

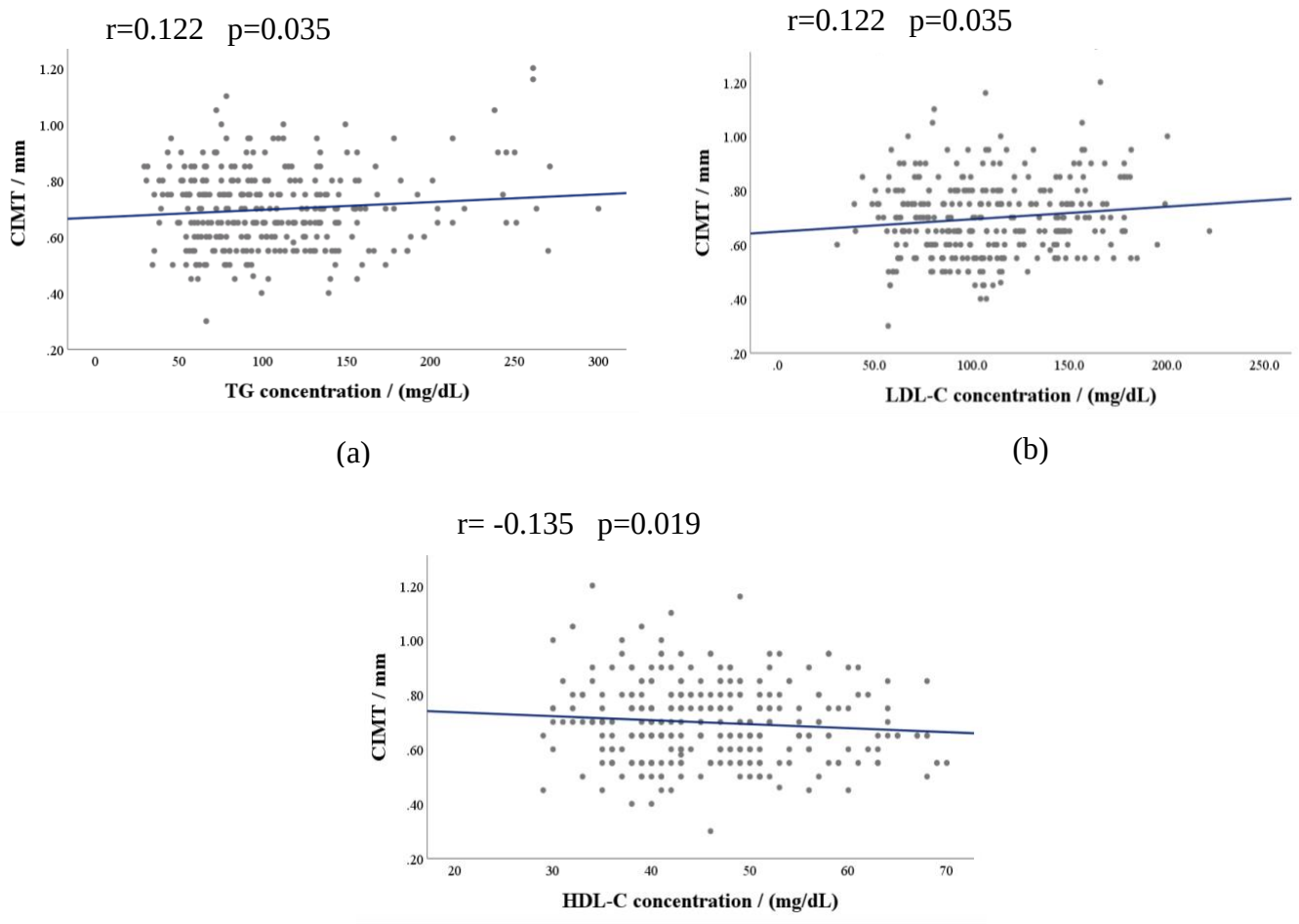

Figure 2. Correlation matrix plots of CIMT with (a) TG, (b) LDL-C, and (c) HDL-C.

CIMT: carotid intima-media thickness, HDL-C: high density lipoprotein cholesterol, LDL-C: low density lipoprotein cholesterol, TG: triglyceride