Annals of Medicine and Surgery 75 (2022) 103368

Contents lists available at ScienceDirect

Annals of Medicine and Surgery

journal homepage: www.elsevier.com/locate/amsu

Cross-sectional Study

Profile of cardiovascular disease risk in type 2 diabetes mellitus patients receiving statin therapy: A cross-sectional study

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ARTICLE INFO

Keywords:
Atherosclerosis vascular disease
Framingham risk score
Type 2 diabetes mellitus

ABSTRACT

Background: Cardiovascular disease is still the number 1 cause of death globally. Meanwhile, type 2 diabetes mellitus (T2DM) is a risk factor for atherosclerosis vascular disease (ASCVD), so an assessment using Framingham Risk Score (FRS) is needed to predict the risk of ASCVD in the future.
Objective: Analyzing the risk factor of ASCVD using the Framingham Risk Score (FRS) in T2DM patients.
Methods: This study was conducted from July 2020 to July 2021, which the participants were measured for FRS including age, gender, current smoking, diabetes, blood pressure (systolic), high-density lipoprotein (HDL) cholesterol, total cholesterol (TC), and ASCVD risk score. The analysis employed multiple linear tests and ANOVA tests with $p < 0.05$.
Results: Several ASCVD risk factors in T2DM patients were found, including gender ($t = 6.015$; $p < 0.001$), age ($t = 6.901$; $p < 0.001$), HDL level ($t = 2.287$; $p = 0.024$), CT level ($t = 5.273$; $p < 0.001$), blood pressure ($t = 5.850$; $p < 0.001$), and current smoking ($t = 2.638$; $p = 0.009$). The results of analysis between ASCVD risk factor and level of ASCVD risk obtained a significant association ($F = 36{,}642$; $p < 0.001$).
Conclusion: Risk factors of ASCVD in T2DM patients such as gender, age, HDL level, CT level, blood pressure, and current smoking.

1. Introduction

Cardiovascular disease (CVD) is the number one death for non-communicable diseases each year globally. Around 17.9 million people in the world die from this disease, and it is 31% of the causes of death worldwide [1]. Data from WHO shows that in Indonesia in 2012, ischemic heart disease (IHD) placed second as the disease that can cause death in sufferers by 8.9% or around 138.4 thousand population, where one of the main causes is atherosclerosis and diabetes [2]. Overall, an estimated 2.6 million deaths are caused by elevated cholesterol and another 29.7 million people experience disability each year. The prevalence of coronary heart disease is 1.5% that increases with age, where the highest group is at the age of 65–74 years [3].

Diabetes mellitus is a metabolic disorder caused by genetic and environmental factors. Type 2 diabetes mellitus (T2DM) is a major risk factor affecting coronary artery disease (CAD) which approximately 75% of T2DM patients die as a consequence of atherosclerosis vascular disease (ASCVD) [4]. In T2DM patients there is insulin resistance which triggers hyperglycemia which causes multiple metabolic abnormalities that increase the risk of ASCVD [5,6]. The gold-standard treatment for the prevention of primary and secondary ASCVD used statins [7] which statins have been shown to reduce the risk of CVD in T2DM [8]. This study aimed to analyze the profile of the risk factors for ASCVD in T2DM patients.

2. Methods

2.1. Participants

Participants in this study were patients diagnosed with T2DM [9,10]. Participant inclusion criteria included patients diagnosed with T2DM (HbA1c of ≥6.5%, fasting plasma glucose of ≥126 mg/dL, 2-h plasma glucose & random plasma glucose ≥200 mg/dL) [11,12], and consuming statins. Meanwhile, participant exclusion criteria included

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https://doi.org/10.1016/j.amsu.2022.103368
Received 17 December 2021; Received in revised form 4 February 2022; Accepted 10 February 2022
Available online 15 February 2022

patients with a history of CVD, patients who had received nicotinic acid therapy, bile acid sequestrants, fibrates, ezetimibe, and PCSK9 inhibitors. Participants were required to fill out an informed consent before starting the study.

2.2. Study design

A cross-sectional study was conducted using purposive sampling from July 2020 to June 2021 with 124 T2DM patients. This study was conducted based on Strengthening the Reporting of Cohort Studies in Surgery (STROCSS) 2021 Guideline [13]. Measurement of ASCVD risk score was calculated based on the Framingham score (FRS), of which the calculation was based on ASCVD risk factors including age, TC, HDL, blood pressure (systolic), current smoking, and diabetes [14]. The measurement results were categorized into 3, namely low risk (<10%), middle risk (11–19%), and high risk (≥20%). This measurement was used to predict that participants are likely to experience ASCVD disorders during the next 10 years [15].

2.3. Blood pressure examination

Blood pressure is a vital sign measured by a tensimeter that is used to make a clinical decision. It is divided into two, systolic and diastolic, with a measurement unit of mmHg. Blood pressure used in this study was only systolic, which are categorized into hypertension (>140 mmHg), normal (100–140 mmHg), and hypotension (systolic <100 mmHg) [16]. The categorization of blood pressure used in this study was <120 mmHg, 120-29 mmHg, 130–139 mmHg, 140–149 mmHg, 150–159 mmHg, and ≥160 mmHg.

3. Cholesterol examination

Cholesterol levels in this study were measured using a chemical autoanalyzer (Toshiba, Japan) [17], in which the cholesterol used in this study included TC and HDL cholesterol [18]. Measurement of TC in this study was in mg/dL, which was categorized into <160 mg/dL, 160–199 mg/dL, 200–239 mg/dL, 240–279 mg/dL, and ≥280 mg/dL. Meanwhile, HDL level measurements were categorized as follows <35 mg/dL, 35–44 mg/dL, 45–49 mg/dL, 50–59 dL, and 60 mg/dL.

3.1. Statistical analysis

The measurement data were collected and analyzed using the statistical package for the social science (SPSS) version 24.0 software (IBM Corp., Armonk, NY, USA). The data were presented in the form of tables or figures. Analysis to determine the risk factors for ASCVD in patients with diabetes mellitus used the ANOVA test which was declared significant if $p < 0.05$. In addition, this study used multiple linear regression with $p < 0.05$.

4. Results

4.1. Characteristic of participant

Most participants were female as many as 85 participants (65.8%), and all participants had T2DM. Most participants were non-smokers as many as 89 participants (71.8%). The participants' average age was 56.15 ± 9.01, with a median value of 57.00 (51.00–62.25) years. The youngest and oldest participants were 30 years old and 75 years old, respectively. Most participants were in the age range of 50–54 years as much as 27 participants (21.7%). The participants' average HDL levels were 56.43 ± 17.42 mg/dL, with a median value of 52.00 (45.00–61.00) mg/dL. The lowest and highest HDL levels were 34.00 mg/dL and 124.00 mg/dL, respectively. Meanwhile, the participants' HDL levels ranged from 50.00 to 59.00 mg/dL and 60.00 mg/dL, each of which has a total of 37 participants (29.8%). The participants' average CT value was 205.19 ± 36.47 mg/dL, with a median value of 199.00 (178.00–225.25) mg/dL. The highest and lowest CT scores were 303.00 mg/dL and 129 mg/dL, respectively. Most participants had CT values ranging from 160.00 to 199.00 mg/dL as many as 53 participants (42.7%). The participants' average blood pressure was 123.98 ± 11.36 mmHg, with a median value of 120.00 (120.00–130.00) mmHg. The participants' lowest and highest blood pressures were 100.00 mmHg and 181 mmHg, respectively. Most participants had blood pressure ranging from 120.00 to 129.00 mmHg as many as 53 participants (42.7%; Table 1).

4.2. Risk factor of atherosclerotic cardiovascular disease in type 2 diabetes mellitus patient

The FRS participant measurement showed that 26 participants (21%) had low risk of ASCVD, 52 participants (42%) had middle risk of ASCVD, and 46 participants (37%) had high risk of ASCVD. Based on the analysis, several risk factors for ASCVD in T2DM patients were found, including gender ($t = 6.015$; $p < 0.001$), age ($t = 6.901$; $p < 0.001$), HDL level ($t = 2.287$; $p = 0.024$), CT level ($t = 5.273$; $p < 0.001$), blood pressure ($t = 5.850$; $p < 0.001$), and current smoking ($t = 2.638$; $p = 0.009$; Table 2). There was a significant relationship between ASCVD risk factor and ASCVD risk level ($F = 36{,}642$; $p < 0.001$).

5. Discussion

Age is a risk factor for ASCVD because increasing age will increase the risk of atherosclerotic cardiovascular disease [19]. Age is a risk

Table 1
Characteristic of participant.

Variable	n (%)
Gender	
Male	39 (31.4)
Female	85 (68.5)
Age (years old)	
30-34	3 (2.4)
35-39	3 (2.4)
40-44	6 (4.8)
45-49	14 (11.2)
50-54	27 (21.7)
55-59	23 (18.5)
60-64	22 (17.7)
65-69	22 (17.7)
70-74	3 (2.4)
>75	1 (0.8)
HDL level (mg/dL)	
<35	1 (0.8)
35-44	25 (20.1)
45-49	24 (19.3)
50-59	37 (29.8)
≥60	37 (29.8)
Cholesterol total (mg/dL)	
<160	10 (8.0)
160-199	53 (42.7)
200-239	37 (29.8)
240-279	22 (17.7)
≥280	2 (1.6)
Blood pressure (mmHg)	
<120	23 (18.5)
120-129	53 (42.7)
130-139	41 (33.0)
140-149	1 (0.8)
150-159	4 (3.2)
≥160	2 (1.6)
Diabetes mellitus	
Yes	124 (100.0)
No	0 (0.0)
Current smoking	
Yes	35 (28.2)
No	89 (71.8)

Table 2
Risk factor of atherosclerotic cardiovascular disease in type 2 diabetes mellitus.

	FRS			*t*	*p*
	Low	Middle	High		
Gender				6.015	<0.001**
Male	4 (10.2)	6 (15.3)	29 (74.3)		
Female	22 (25.8)	46 (54.1)	17 (20.0)		
Age (years old)				6.901	<0.001**
30–34	3 (100.0)	0 (0.0)	0 (0.0)		
35–39	1 (33.3)	2 (66.7)	0 (0.0)		
40–44	4 (66.7)	2 (33.3)	0 (0.0)		
45–49	8 (57.1)	3 (21.4)	3 (21.4)		
50–54	5 (18.5)	15 (55.5)	7 (26.0)		
55–59	4 (17.4)	12 (52.1)	7 (30.4)		
60–64	1 (4.5)	8 (36.5)	13 (59.0)		
65–69	0 (0.0)	10 (45.5)	12 (54.5)		
70–74	0 (0.0)	0 (0.0)	3 (100.0)		
>75	0 (0.0)	0 (0.0)	1 (100.0)		
HDL level (mg/dL)				2.287	0.024*
<35	0 (0.0)	0 (0.0)	1 (100)		
35–44	3 (12.0)	7 (28.0)	15 (60.0)		
45–49	5 (20.8)	10 (41.6)	9 (37.5)		
50–59	9 (24.3)	16 (43.2)	12 (32.4)		
≥60	9 (24.3)	19 (51.3)	9 (24.3)		
Cholesterol total (mg/dL)				5.273	<0.001**
<160	3 (30.0)	3 (30.0)	4 (40)		
160–199	17 (32.0)	22 (41.6)	14 (26.4)		
200–239	6 (16.2)	17 (46.0)	14 (37.8)		
240–279	0 (0.0)	9 (41.0)	13 (59.0)		
≥280	0 (0.0)	1 (50.0)	1 (50.0)		
Blood pressure (mmHg)				5.850	<0.001**
<120	13 (56.5)	7 (30.5)	3 (13.0)		
120–129	8 (15.0)	25 (47.1)	20 (37.7)		
130–139	5 (21.1)	20 (48.7)	16 (39.0)		
140–149	0 (0.0)	0 (0.0)	1 (100.0)		
150–159	0 (0.0)	0 (0.0)	4 (100.0)		
≥160	0 (0.0)	0 (0.0)	2 (100.0)		
Diabetes mellitus				–	–
Yes	26 (21.0)	52 (42.0)	46 (37.0)		
No	0 (0.0)	0 (0.0)	0 (0.0)		
Current smoking				2.638	0.009*
Yes	5 (14.3)	7 (20.0)	23 (65.7)		
No	21 (23.5)	45 (50.5)	23 (26.0)		

Note: FRS = Framingham risk score; HDL = high-density lipoprotein; *significant <0.05; **significant <0.001.

factor for CAD as increasing age will increase the risk of CVD. The older the age, the greater the possibility of atheroma plaques sticking to the walls and disrupting blood flow to the tissues [20]. ASCVD is more common in men than women as supported by previous research, stating that the majority of patients with ASCVD are men [21]. The latest study in Indonesia stated that ASCVD was found in men as much as 61% with a prevalence ratio of 2:1 between men and women [3].

Lower HDL cholesterol levels are associated with a higher risk of cardiovascular disease. Several studies have also shown that people with HDL levels of <35 mg/dL are more likely to experience ASCVD [18,22]. HDL will carry cholesterol from tissues including coronary arteries to be catabolized in the liver. The newly formed HDL from its precursors, namely apo a-1, apo a-2, and apo a-milano proteins, will attract cholesterol with the help of the ATP binding cassette transporter A1 (ABCT A1) enzyme. This HDL cholesterol will later increase in size and can attract more fat and cholesterol in the body for catabolism [23]. In addition, high CT levels lead to deposition, narrowing, and plaque in blood vessels and increase the risk of ASCVD [18,24]. Hypertension is a major risk factor contributing to ASCVD, which has been mentioned in several kinds of literature and studies [25]. Recent studies have also stated that patients with hypertension have a 10 times risk of developing ASCVD including coronary heart disease [26].

Meanwhile, current smoking increases the risk of ASCVD which mechanisms that cause atherosclerosis are direct endothelial injury due to agents in cigarettes such as carbon monoxide and nicotine that cause blebs on the lumen surface, microphile formation, and release of endothelial cells (endothelial damage), changes in platelets, increased fibrinogen and C-reactive protein levels and induce proinflammatory cytokines [27]. Type 2 DM is a disease related to glucose in the blood, in which when hyperglycemia occurs, the blood will experience a viscosity so that the blood supply to the tissue is blocked and has a high risk of ASCVD [2].

Nevertheless, this study has a limitation as it only included data components of the Framingham risk scoring risk factors such as gender, age, HDL cholesterol levels, total cholesterol levels, blood pressure, type 2 diabetes mellitus status, and smoking status. Data such as body weight, family history, low-density lipoprotein cholesterol levels, triglyceride levels, and physical activity were not included in this study. In addition, the method used was FRS, in which the score is only based on data from the white population. These considerations are expected to become an evaluation for further research.

6. Conclusion

Based on the results of the patients' risk score, the highest percentage of atherosclerotic cardiovascular disease risk using FRS is patients with a moderate-risk level, followed by a high-risk level and a low-risk level. The analysis shows that T2DM participants are at risk for ASCVD that is influenced by gender, age, current smoking, diabetes, blood pressure, HDL cholesterol, and TC.

Ethical approval

We have conducted an ethical approval based on the Declaration of Helsinki with registration research at the Health Research Ethics Committee in Dr. Soetomo General Academic Hospital, Surabaya, Indonesia.

Funding

None.

Author contributor

All authors contributed toward data analysis, drafting and revising the paper, gave final approval of the version to be published and agree to be accountable for all aspects of the work.

Registration of research studies

Name of the registry: Health Research Ethics Committee in the Dr. Soetomo General Academic Hospital, Surabaya, Indonesia.

Unique identifying number or registration ID: 0181/LOE/301.4.2/XI/2020.

Hyperlink to your specific registration (must be publicly accessible and will be checked): .

Guarantor

Soebagijo Adi Soelistijo.

Consent

Written informed consent was obtained from the patient.

Provenance and peer review

Not commissioned, externally peer-reviewed.

Declaration of competing interest

The authors declare no conflict of interest.

Acknowledgment

We thank our editor “Fis Citra Ariyanto”.

Abbreviations

ASCVD	atherosclerosis vascular disease
ABCT A1	ATP binding cassette transporter A1
CAD	coronary artery disease
CVD	Cardiovascular disease
FRS	Framingham Risk Score
HDL	high-density lipoprotein
IHD	ischemic heart disease
LDL	low-density lipoprotein
STROCSS	Strengthening the Reporting of Cohort Studies in Surgery
T2DM	type 2 diabetes mellitus
TC	total cholesterol

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