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Original Research

The Correlation between Serum TG/HDL-c ratio and Arterial Stiffness Using the Cardio-ankle Vascular Index in Overweight or Obese Patients

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ABSTRACT

Background. The effect of increasing TG/HDL-c serum ratio, as a result of insulin resistance, is considered to have an important role in the occurrence of arterial stiffness. Increased arterial stiffness is an important marker in the development of cardiovascular disease and is a predictor of heart attack and stroke. **Aims.** This research was conducted to determine the relationship between the arterial stiffness assessed through non-invasive cardio-ankle vascular index (CAVI) examination and the TG/HDL-c ratio in overweight and obese individuals. Cardio-Ankle Vascular Index (CAVI) is a non-invasive clinical measurement to evaluate arterial stiffness manner and independent of blood pressure. **Methods.** This study is considered as correlational study using purposive sampling as the technique. Thirty-two subjects participated in this research and each of them was subjected a CAVI examination to assess arterial stiffness. Their blood samples were collected for lipid profile measurement. The data were analyzed using Pearson Correlation Test. **Results.** The correlation between TG/HDL-c serum level and arterial stiffness using CardioAnkle Vascular Index (CAVI) in overweight or obese patients (p <0,01) proved to be positive and significant.

Introduction

Overweight or obesity could change the structure and function of the blood vessels that lead to an increase in the blood vessels stiffness (arterial stiffness). Arterial stiffness occurs in the early phase and contributes to the process of cardiovascular premature dysfunction [1,2]. The mechanism of arterial stiffness in overweight or obese populations involving some complex process has not been known completely. Furthermore, the last study is still controversial and advanced research is needed to clarify the factors that initiate and hasten the progression of this phenomenon. Therefore, a deeper understanding of the mechanism of arterial stiffness in overweight/obesity has a great clinical significance [1]. In this research, we will discuss the relationship between the arterial stiffness assessed through non-invasive cardio-ankle vascular index (CAVI) examination and the TG/HDL-c ratio in overweight and obese individuals, to give understanding about the management [1,2].

Methods

This research used analytic correlational design. The samples of this research were overweight or obese individuals gathered during October 2016 until December 2016, who met the research criteria. Inclusion criteria in this research were overweight or obese man or woman, aged 20-60 years, and willing to participate by signing the informed consent. Exclusion criteria in this research were patient with a history of cardiovascular disease, coronary atherosclerotic disease, stroke, peripheral arteries disease/PAD), history of diabetes mellitus, history of chronic kidney disease, or history of smoking. CAVI examination used an automatic machine called VaSera VS-1500 (Fukuda Denshi, Tokyo, Japan). Thirty-two subjects participating in this research underwent CAVI examination to assess arterial stiffness and their blood sample were collected for lipid profile measurement. Relationship between serum TG/HDL-c ratio and the arterial stiffness was analyzed using the Pearson correlation test if the data were distributed normally, or the Spearman rank correlation test as an alternative.

The study was done in Cardiology Clinic Dr. Soetomo Hospital, Surabaya, during September 2016- December 2017. We enrolled 32 overweight or obese subjects who fulfilled the research criteria. The subjects' ages were ranging from 20 to 60 years old, with the mean age of 42.69 ± 8.42 years old. Based on sex, subjects were mostly female (75%). The average of subject's body mass index (BMI) was 30.83 ± 5.07, with the lowest was 25.8 kg/m2 and the highest was 47.8 kg/m2. Based on the BMI category, 18 subjects were overweight (56,3%), meanwhile 14 subjects were obese (43,7%). There were 7 subjects with obese grade I (21,9%), 6 subjects with obese grade II (18,8%), and 1 subject with extreme obese (3,0%). There were 30 subjects (93,7%) with abnormal waist circumference. The subject with increasing TG (>150 mg/dL) were 16 subjects (50,0%), meanwhile subject with low HDL-c (<35 mg/dL) was 16 subjects (50,0%). The lowest ratio of TG/ serum HDL-c was 1.39, and the highest was 7.47, with an average of 3.83 ± 1.39. There were 2 subjects (6,3%) with normal TG/HDLc ratio (≤2.0), 17 subjects (53,1%) with high TG/HDL-c ratio (2.0–4.0), and 13 subjects (40,6%) with high TG/HDL-c ratio (>4). We also collected the blood pressure, fasting blood glucose, and 2 hours postprandial blood glucose data. The baseline characteristics were shown in Table 1.

Results

Table 1. Baseline characteristic of the subject (N=32).

Variable	n (%) or Mean ± SD
Age(years old)	42.69 ± 8.42
20 – 29	4 (12.5)
30 – 39	5 (15.6)
40 – 49	15 (46.9)
50 – 59	8 (25.0)
Sex	
Male	8 (25.0)

Female	24 (75.0)
Height (cm)	158.84 ± 7.48
Weight (kg)	78.37 ± 17.35
Body Mass Index (kg/m^2)	30.83 ± 5.07
Overweight (25 – 29,9)	18 (56.3)
Obese grade I (30 – 24,9)	7 (21.9)
Obese grade II (35 – 39,9)	6 (18.8)
Extremely Obese (≥ 40)	1 (3.1)
Waist Circumference (cm)	101.36 ± 14.81
Systolic Blood Pressure (mmHg)	122.50 ± 10.98
Diastolic Blood Pressure (mmHg)	80.06 ± 8.01
Right-Ankle Brachial Index	1.04 ± 0.12
Left-Ankle Brachial Index	1.05 ± 0.13

The study found that the lowest TG/ HDL-c ratio was 1.39, meanwhile the highest was 7.47 with the average number of 3,83 ± 1,39. TG/serum HDL-c ratio is classified into three categories: normal if the TG/ serum HDL-c ratio is ≤ 2, high TG/ serum HDL-c if it is in the range 2,0 - ≤ 4, and very high if it is >4. About 6,3% of subjects have normal TG/ HDL-c ratio and the rest have high TG/serum HDL-c ratio. CAVI is classified based on the index score: <8 is categorized as normal; >8– <9 as borderline; and >9 as abnormal/atherosclerotic suspected. In this study, the minimum index score for Right-CAVI (R-CAVI) was 3.40 and the maximum was 11.10, with the mean score of 6,69 ± 2,24. Meanwhile, the minimum index score for Left-CAVI (L-CAVI) was 3.30 and the maximum was 11.60, with the mean score of 6.45 ± 2.26. Mean-CAVI (M-CAVI) was obtained by calculating the mean index score of RCAVI and L-CAVI for each subject.

Distribution of normality tests was done for the R-CAVI, L-CAVI, M-CAVI, and TG/HDL-c ratio by using Kolmogorov-Smirnov test. The result of normality test showed p value of ≥0.05. The Pearson correlation test found that there were positive and significant correlations between the TG/HDL-c ratio and the CAVI scores, as shown in Table 2. The TG/HDL-c ratio had a positive and significant correlation with the R-CAVI score (r=0.455, p=0.004). The TG/HDL-c ratio had a positive and significant correlation with the L-CAVI score (r=0.528, p=0.001). The TG/HDL-c ratio had a positive and significant correlation with the M-CAVI score (r=0.497, p=0.002).

Table 2. Correlation results using Spearman analysis

Variable	p	r
TG/HDL-c serum ratio and R-CAVI	0,004	0,455
TG/HDL-c serum ratio and L-CAVI	0,001	0,528
TG/HDL-c serum ratio and M-CAVI	0,002	0,497

[a]TG/HDL-c : Triglyceride/High density lipoprotein-c
[b]R: right

Discussion

Obesity was already a health epidemic in the last two decades. Some studies said that the increase of BMI is correlated with increasing risk of morbidity and mortality of the cardiovascular diseases. Although the correlation is clearly showed, most of the studies did not give the clear pathophysiology about BMI increase contributing to the increase of cardiovascular diseases incidence. However, some of the literature said that the correlation of overweight or obesity with cardiovascular diseases occurs through metabolic profile changes or cardiac and blood vessel's structural and functional changes. The metabolic profile changes include glucose intolerant, insulin resistant, increasing of inflammation marker, and the lipid metabolism changes. Meanwhile, the structure changes, also the cardiac and blood vessel function changes, occur through the increasing of the arterial stiffness and left ventricle hypertrophy. Wang et al. and Di Bonito et al. studies found a strong correlation between arterial stiffness with the proatherogenic lipid ratio in teenagers or adults [3,4]. Our study was intended to evaluate the correlation between TG/serum HDL-c ratio with arterial stiffness assessed with CardioAnkle Vascular Index (CAVI) in overweight or obese patient.

a. Basic characteristics of the subject

The subjects in this study were overweight or obese patient who visited the cardiology clinic during October 2016 – December 2016. We enrolled 32 subjects with overweight or obese who were selected by consecutive sampling. Most of the respondent is female (75%), with the average age in the fourth decade, and mean BMI of 30.83 ± 5.07 kg/m2. Almost all of the subject had abnormal waist circumference (93,7%). The increased CAVI value above normal was found in 9 subjects, and all of them were older than 40 years old. In the subject with abnormal CAVI (>8), only one subject (11,1%) had a normal TG/serum HDL-c ratio, while the others had TG/serum HDL-c ratio above normal.

The previous study had shown that there was an effect from some of the risk factors which correlated to the arterial stiffness progressivity, such as age, hypertension, smoking, and diabetes. However, other factors such as dyslipidemia and obesity also play a role in the arterial stiffness. The study by Holewijn et al., showed that non-HDL-c usage is a predictor in the identification of arterial stiffness compared to the LDL-c. The study by Di Bonito et al., said that TG/serum HDL-c ratio is the independent risk factor of the arterial stiffness in teenagers and adults population [3]. In this study, from all of the subject with normal BMI, there were 16 subjects (50,0%) with increasing TG, while 16 subjects (50,0%) had low HDL levels.

b. TG/serum HDL-c ratio

The study by Gaziano et al., was the first that reported 16 times increase of the risk to a myocardial infarction in the highest TG/serum HDL-c ratio quartile group compared to the lowest quartile [5]. Another study reported that high TG/serum HDL-c ratio is correlated independently with coronary artery disease, which is assessed by angiography (defined as stenosis >50%) and cardiovascular mortality. The latest study by Yuji, et al., said that high TG/HDL-c ratio is the risk to atherosclerosis and significantly increases the arterial stiffness in Japanese male population with diabetes, which was assessed by carotid artery intima-media thickness (CIMT) examination and CAVI.

Based on the data from Wan et al., TG level is an independent variable which inversely proportional to predict LDL particle size. Meanwhile, HDL-c level is an independent variable which directly proportional to the LDL particle size. Because of that, TG/ HDL-c ratio can be more accurate to predict small sd-LDL. Low TG/ HDL-c ratio presents big size LDL particle or non-atherogenic LDL particle. However, high TG/ HDL-c ratio present small size pro-atherogenic LDL particle, which is very correlated to the atherosclerosis initiation and progression.

Dobiasova et al., found that the increasing of TG/ HDL-c log parameter as the atherogenic index showed the high concentration of plasma triglyceride-rich lipoprotein and small size LDL-c particle [4,6]. The study by Shimizu et al., involving 2.431 subjects in Japan, showed that BMI has a positive correlation to the TG/serum HDL-c ratio, also the correlation between BMI and diabetes is influenced by the role of TG/serum HDL-c ratio [7].

In this study, we obtained the minimum the TG/serum HDL-c ratio of 1.39 and the maximum of 7.47, with the mean ratio of 3.83 ± 1.39. From this result, we did not find any significant correlation between TG/serum HDL-c ratio with LDL-c level. This can be caused by quantitatively measured LDL-c level without considering the quality of the LDL-c particle size, such as mentioned in the study by Wan et al. This study also found that there was no correlation between TG/serum HDL-c ratio with BMI. This phenomenon can be explained by Grundy et al. and Festa et al. studies, where they found that insulin resistant prevalence in the overweight or obese population was about 30-37% [8]. However, the interesting finding here was that we obtained a significant correlation between BMI and LDL-c level ($p<0,05$; $r=0,395$). This finding supports the study by Lauvicius et al., which showed that the proatherogenic profile lipid metabolism changes and the increase of the cardiovascular incidence are in line with the increasing of BMI [9].

c. Cardio-ankle vascular index (CAVI) number

Arterial stiffness is one of the cardiovascular morbidity and mortality predictor. A study by Luo et al., showed that there was a significant positive correlation between arterial stiffness with the risk of coronary heart disease incident [10]. The progressive structural changes, such as elastin fragmentation and degeneration, increasing of collagen, artery wall thickness, and endothelium damage cause the increase of arterial stiffness incidence.

In this study, CAVI examination was done in all subjects using VaSera VS-1000 machine. CAVI was used to assess the arterial stiffness and to evaluate the risk of cardiovascular disease incidence. From 32 subjects, there were nine subjects (28,2%) with abnormal CAVI. The increased CAVI score showed the progressivity of the arterial stiffness. However, from this data, we could not find the significant correlation between CAVI and the blood pressure, neither systolic ($p=0.686$) nor diastolic ($p=0.408$), also the correlation between CAVI with ABI ($p=0.504$).

These results were in line with the study by Kotani et al., which proved that the benefit of arterial stiffness measurement with CAVI depended on the stiffness-β parameter and was not influenced by blood pressure [11].

d. Correlation between TG/serum HDL-c ratio with arterial stiffness which is assessed by CAVI

This study showed that there was a positive and significant correlation between TG/serum HDL-c ratio level and the arterial stiffness assessed with CAVI in overweight or obese patient. The higher the TG/serum HDL-c ratio means the higher the arterial stiffness is.

Some potential mechanism can explain the correlation between TG/serum HDL-c ratio and arterial stiffness. Insulin resistant is believed to have a significant role in cardiovascular disease pathogenesis and has been correlated independently with brachial-ankle Pulse Wave Velocity, even in a healthy person. Insulin resistant causes the increasing of synthesis and secretion of TRL, whilst decreasing the HDL cholesterol. McLaughlin et al., said that TG/serum HDL-c ratio could be identified if there is insulin resistant in overweight person with normal glucose tolerant and it serves as an insulin resistant marker that has the same sensitivity and specificity with the plasma insulin concentration in fasting condition [12]. In a cross-sectional study from 6.546 Korean adults who had done the routine health examination, it was found that TG/serum HDL-c ratio had a significant correlation with the insulin resistant in person without metabolic syndrome abnormality. Because the TG/HDL-c ratio examination is a simple clinical examination used as an indicator of insulin resistance, this examination can predict arterial stiffness related to insulin resistance.

Next, the correlation between TG/ serum HDL-c ratio and arterial stiffness may be related to the increased of small dense-LDL (sd-LDL) particle, which is considered as more atherogenic than normal size LDL particle because the sd-LDL particle is easier to enter the blood vessel wall, as well as more vulnerable to oxidative modification, which in turn will be increasing its atherogenicity [12]. These findings showed that high TG/serum HDL-c ratio could be used as the clinical indicator of insulin resistance and the increasing of sd-LDL particle can be used to evaluate the early damage phase of vascular. Further study is needed to explain the right mechanism responsible for that correlation.

This study was in line with the study in 2012 by Urbina et al. that showed TG/serum HDL-c ratio was positively correlated to the arterial stiffness in healthy teenagers and adults population. In the study by Laucevicius et al., it was showed that subject group with high CAVI had worse metabolic profile compared to the subject group with normal CAVI, and after further follow up (average 3.8 ± 1,7 years) CAVI was correlated significantly to the cardiovascular and myocardial infarction incidence [9]. With the data above and based on the literature, CAVI measurement can be used to evaluate the subclinical cardiovascular disease that can predict the cardiovascular incidence in the future. The correlation between obesity and CAVI is strengthened by the study that showed that weight loss in the obesity subject can improve the arterial stiffness assessed with CAVI [13]. Therefore, healthy lifestyle changes to achieve the ideal weight can decrease the cardiovascular risk. Some of the limitations in this study were its sampling technique and small scope population. Samples were taken by purposive sampling because of the time limit, number of patients, and the budget. This study conducted in a small scope of population and non-multicentre.

Conclusion

There is a positive and meaningful correlation between TG/serum HDL-c ratio level and arterial stiffness which is assessed by Cardio-Ankle Vascular Index (CAVI) in overweight or obese patients ($p<0,01$; r= 0,455 – 0,528). Further study about the correlation between TG/ serum HDL-c ratio and arterial stiffness is needed for an overweight or obese patient with the bigger numbers of sample to get the result that can be generalized.

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There is no conflict of interest.

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