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Carotid Intima Media Thickness as a Predictor for the Severity of Coronary Artery Disease

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ABSTRACT

Background: Coronary artery disease is the chief cause of non infection cause of death in the developing country, carotid intima-media thickness evaluation are used for over three decade to asses atherosclerotic burden, this study aimed to seek correlation between carotid intima-media thickness with coronary artery disease severity.

Methods: This was a cross-sectional study involving 63 patients diagnosed with stable angina pectoris in Haji Adam Malik General Hospital Medan from November 2018 to December 2018. Carotid Doppler USG and Angiography were performed for each patients. Chi-Square test will be performed to analyze correlation between internal carotid intima-media thickness with Gensini score.

Results: From 63 subjects, 23 subjects (82.1%) with internal carotid intima-media thickness ≥ 0.75mm have Gensini score ≥20 while patients with carotid intima-media thickness <0.75mm 8 (22.9%) have Gensini score ≥20 (p<0.001). Cut-off point 0.55 mm (Sensitivity: 93.5% and Specificity: 87.5%) was a marker for high Gensini score.

Conclusion: Internal Carotid intima-media thickness with cut-off point 0.55 mm can be used to predict the severity of coronary artery disease measured by Gensini Score in stable coronary artery disease patients.

INTISARI

Latar Belakang: penyakit jantung koroner merupakan penyebab kematian non infeksi terbesar di negara berkembang. Pengukuran tebal intima-media arteri karotis telah digunakan lebih dari tiga dekade untuk mengukur beban aterosklerosis, penelitian ini bertujuan untuk mengetahui hubungan antara ketebalan intima-media arteri karotis dengan derajat keparahan penyakit jantung koroner pada pasien angina pektoris stabil.

Metode: penelitian ini merupakan penelitian potong lintang terhadap 63 pasien dengan diagnosa angina pektoris stabil yang datang ke poliklinik rawat jalan RSUP HAM sejak November 2018 sampai dengan Desember 2018. Pasien dilakukan pemeriksaan USG doppler untuk mengukur tebal intima-media arteri karotis interna kemudian dilanjutkan dengan pemeriksaan angiografi koroner dan dihitung derajat keparahan lesi koroner dengan skor Gensini. Dilakukan analisa bivariat dengan Chi-Square pada skala kategorik skor Gensini untuk menilai hubungan antara ketebalan intima-media arteri karotis dengan derajat keparahan.

Hasil: Dari 63 subjek penelitian, 23 (82.1%) subjek dengan ketebalan intima-media arteri karotis ≥ 0.75 mm memiliki skor Gensini ≥ 20 dan pada subjek dengan ketebalan intima-media arteri karotis < 0.75 mm hanya 8 (22.9%)

subjek dengan nilai Gensini ≥ 20 (p < 0.001). Didapatkan nilai cut-off 0.55 mm (sensitivitas : 93.5% dan spesifisitas 87.5%) sebagai penanda skor Gensini ≥ 20 pada pasien angina pektoris stabil.

Kesimpulan: Tebal intima-media arteri karotis interna dengan nilai cut-off 0.55 mm dapat digunakan sebagai penanda derajat keparahan penyakit jantung koroner yang diukur dengan skor Gensini.

Introduction

Atheroschlerotic process has been started since childhood and continued until decades before giving any symptoms. Only a few parts of the population show any symptoms when the blood flow become obstructed due to atheroschlerotic plaque or thrombus formed by a ruptured intimal artery wall. The severity of atherosclerotic artery is associated with future cardiovascular events, such as sudden cardiac death. Interest in identifying atheroschlerosis burden in patients without symptoms are rapidly increasing and any available data could be used as a pivotal data to make a medical intervention decision.1

Previous study showed that risk factors such as sex, age, hypertension, dyslipidemia, type 2 diabetes mellitus (T2DM) clearly affects the intima-media artery thickness but the correlation between artery intima-media and coronary atherosclerosis is yet to be confirmed.2

Simon et al stated that carotid intima-media thickness (CIMT) gives a complete view about any change caused by any risk factor exposed to arterial wall. Prospective study as a mean to prevent primary and secondary artery coronary disease had found that increase in CIMT is a strong predictor for coronary artery complications, but standardized methods to measure the CIMT should be further implemented before it can be used in clinical practise.3

Imaging approach that could help to conduct diagnostic process should be easy to conduct, relatively cheap, sensitive and widely available (murari).1 Carotid ultrasonography (USG) are widely available in Indonesia, it was used not only as a diagnostic instrument but also as an evaluation to certain disease.4

Methods

Study Design and Population

This study was a cross-sectional study in Haji Adam Malik General Hospital with permission from the Research Ethics Committee of the Faculty of Medicine University of North Sumatera and Haji Adam Malik General Hospital. The study was conducted on patients with stable coronary artery disease (SCAD) or stable angina pectoris (SAP) diagnosis at Haji Adam Malik General Hospital from November 2018 to December 2018 scheduled to underwent coronary angiography.

The inclusion criteria for this study were patients with SCAD/SAP diagnosis, patients with T2DM, and have no history of acute coronary syndrome (ACS). The exlusion criteria were patients with myocardial bridging and poor doppler internal carotid artery view.

Patients with SCAD/APS and willing to participate in the study was assessed by history taking, physical examination, ECG and blood sampling. Patients then underwent a Doppler USG mode-B to measure the internal carotid IMT and patients proceeded to cath-lab to underwent coronary angiography as scheduled. The result of the angiography was used to measure the severity of CAD lesion using Gensini Score. Gensini score ≥ 20 was regarded as high score (severe CAD). After all data were collected, statistical analysis of internal CIMT as a predictor for the severity of CAD were conducted with computer statistical software.

Data Analysis

The Kolmogorov-Smirnov and Saphiro-Wilk tests were used to determine the normality of data distribution. Categorical variables were presented as percentage (%) while numeric variables with normal distribution was presented as mean ± standard deviation (SD), and mean ± standard error (SE) if the data was not normally distributed. Categorical variables were compared using the Chi-Square test (normally distributed data) or the Fischer Exact test (not normally distributed). Pearson correlation test (normally distributed data) and Spearman (not normally distributed data) were used to assess the correlation between internal carotid intima-media thickness and high Gensini score. Significantly different statistics were defined as $p<0.05$.

Result

The study was conducted in the Department of Cardiology and Vascular Medicine Haji Adam Malik General Hospital Medan from November 2018 to December 2018 with a total sample of 63 eligible stable CAD patients. Basic characteristics were shown in the following table.

The majority of the subjects were male; n: 43 (68.3%), mean subjects age were 54 years old, 48 (76.2%) subjects have hypertension, 13 (20.6%) subjects have T2DM, 34 (54%) subjects were smokers and only 10 (15.9%) people have dyslipidemia. From doppler USG for ICA-IMT, 28 (44.4%) subjects have IMT ≥ 0.75 mm. Coronary angiography resulted in 29 (46.0%) subjects with multivessels disease, 12 (19%) with single vessel disease while 22 (34.9%) subjects have normal angiograph result. High Gensini score were found in 31 (49.2%) subjects

Bivariat analysis was performed for table 2 to correlates between ICA-IMT and baseline characteristic. It was found that hypertension, smokers, dyslipidemia, total cholesterol value and HDL have significant correlation with intima-media thickness in SCAD patients ($p < 0.05$).

Correlation between Baseline characteristics and Gensini score was showen in Table 3. Bivariat analysis showed a statistically significant correlation between dyslipidemia, smoking habit (smoker), platelets count and number of CAD lession (p<0.05)

Table 1.
Baseline Characteristics

Characteristic	N=63
Sex, n(%)	
Male	43 (68.3%)
Female	20 (31.7%)
Age (Year), Mean±SD	54.48±7.569
Comorbid and Risk Factor, Yes, n (%)	
Hypertension	48 (76.2%)
Diabetes Mellitus	13 (20.6%)
Dyslipidemia	36 (57.1%)
Smoker	45 (71.4%)
Body Mass Index Median (Min-Max)	25.240 (19.2-34.08)
CAD, n%	
Single	12 (19.0%)
Multiple	29 (46.0%)
No CAD	22 (34.9%)
Laboratory	
Leukocyte (sel/mm^3), Media (Min-Max)	8,590 (5,800-19,800)
Trombocyte (sel/mm^3), Mean±SD	269,349±67,469
Random Blood Glucose, Media (Min-Max)	109 (71-569)
Total Cholesterol, Median (Min-Max)	198 (95-304)
Trigliseride, Median (Min-Max)	120 (48-356)
HDL, Median (Min-Max)	45 (19-60)
LDL, Median (Min-Max)	110 (50-276)
CIMT, Median (Min-Max)	0.6 (0.30-1.00)
Gensini Score, Median (Min-Max)	16.0 (0.00-124.00)
ICA-IMT , n(%)	
<0.75	35 (56.6%)
≥0.75	28 (44.4%)
Gensini Score, n(%)	
< 20	32 (50.8%)
≥ 20	31 (49.2%)

Table 2.
Correlation between baseline characteristic and ICA-IMT

Characteristic	*ICA-IMT*		*P*
	<0.75 (n=35)	≥0.75 (n=28)	
Sex			
Male	21 (60.0%)	22 (78.6%)	0.116
Female	14 (40.0%)	6 (21.4%)	
Age (Year), Mean ±SD	54.45±7.805	54.52±7.310	0.971
Comorbid and Risk Factor,			
Hypertension	31 (88.6%)	17 (60.7%)	0.010
Diabetes Mellitus	7 (20.0%)	6 (21.4%)	0.889
Dyslipidemia	13 (37.1%)	23 (82.1%)	<0.001
Smoker	25 (62.5%)	20 (87.0%)	0.039
Body Mass Index	25.31 (19.20-34.04)	25.24 (22.77-33.33)	0.792
Vessels CAD, n%			
Single	12 (34.0%)	5 (17.9%)	<0.001
Multiple	6 (17.1%)	23 (82.1%)	
No CAD	17 (48.6%)	0 (0.0%)	
Laboratory			
Leukocyte (cell/mm^3)	8,825 (5,820-19,800)	8,520 (5,800-14,020)	0.281
Trombosite (cell/mm^3	280,000±73,433	250,826±52,004	0.099
Random Blood Glucose (g/dl)	107 (72-325)	110 (71-569)	0.568
Total Cholesterol (mg/dl)	253 (95-276)	173 (118-304)	0.024
Trigliseride (mg/dl)	121.5 (48-315)	117 (62-356)	0.870
HDL (mg/dl)	46 (23-58)	41 (19-60)	0.028
LDL (mg/dl)	110 (50-149)	106 (83-276)	0.449

Table 3.
Corellation Between Baseline Characteristics and Gensini Score

Characteristic	*Gensini Score*		*P*
	<20 (n=32)	≥20 (n=31)	
Sex			
Male	19 (59.4%)	24 (77.4%)	0.124
Female	13 (40.6%)	7 (22.6%)	
Age (Year), Mean ±SD	53.31±7.998	55.68±7.026	0.218
Comorbid and Risk Factor,			
Hypertension	27 (84.4%)	21 (67.7%)	0.121
Diabetes Mellitus	6 (18.8%)	7 (22.6%)	0.707
Dyslipidemia	13 (40.6%)	23 (74.2%)	0.007
Smoker	17 (53.1%)	28 (90.3%)	0.001
Body Mass Index	25.39 (19.20-34.08)	25.35 (22.58-33.33)	0.531
Vessels CAD, n%			
Single	10 (31.3%)	2 (6.5%)	
Multiple	0 (0.0%)	29 (93.5%)	<0.001
No CAD	22 (68.8%)	0 (0.0%)	
Laboratory			
Leukocyte (cell/mm^3)	8,825 (5,820-19,800)	8,520 (5,800-14,020)	0.280
Trombocyte (cell/mm^3)	289.250±75.494	248.806±51.573	0.016
Random Blood Glucose (g/dl)	103.5 (72-325)	112 (71-569)	0.151
Total Cholesterol (mg/dl)	276 (95-276)	173 (118-304)	0.010
Trigliseride (mg/dl)	126 (48-225)	117 (62-356)	0.891
HDL (mg/dl)	45.46±8.864	40.61±11.359	0.063
LDL (mg/dl)	110 (50-149)	106 (69-276)	0.842

Table 4.
Mean Value Between ICA- IMT and Gensini Score

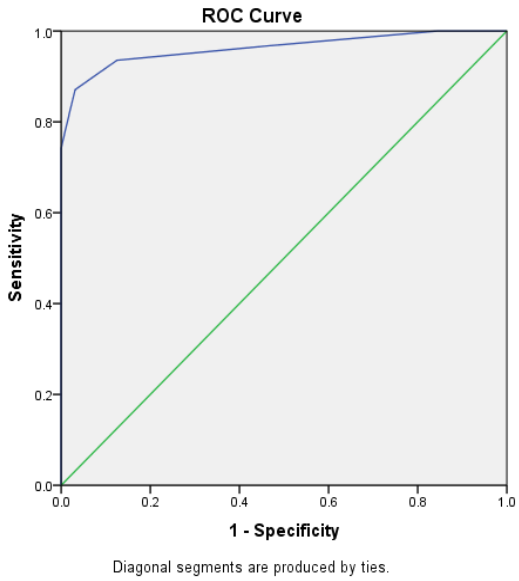
	Coronary Lession		*P*
	Single	*Multiple*	
ICA- IMT	0.475±0.105	0.837±0.111	<0.001
Gensini Score	17.166±7.837	79.689±24.548	<0.001

Table 4 showed mean value of ICA-IMT between single and multiple CAD and Gensini score between single and multiple CAD. It also shows that there is a strong correlation between ICA-IMT and the number of CAD (p<0.001) and Gensini Score with the number of CAD lession (p<0.001).

Table 5
Correlation Between ICA-IMT and Gensini Score

	ICA		*P*
	< 0.75	≥ 0.75	
Gensini Score			
< 20	27 (77.1%)	5 (17.9%)	<0.001
≥ 20	8 (22.9%)	23 (82.1%)	
Total	35 (100.0%)	28 (100.0%)	

Correlation between ICA-IMT and Gensini Score were shown in Table 5. A strong correlation was found between ICA-IMT value ≥ 0.75 mm and a high (≥ 20) Gensini score in SCAD patients (p<0.001).

Area Under Curve	Cut off	p	IK 95%
	0,55 mm Sensitivity : 93.5% Specificity : 87.5%	<0.001	0.914 – 1.000
AUC: 96.2%			

Diagnostic value of ICA-IMT were analyzed in Table 6 and a cut-off point of 0.55 mm (sensitivity 93.5% & specificity 87.5%) could indicate a SCAD patients will have a high Gensini score on coronary angiography.

Discussion

In this study, all USG doppler data and Gensini Score were confirmed by the respective division (vascular and intervention cardiologist) before statistical analysis. In this study, patients with hypertension have higher CIMT value compared to patients without hypertension. This result were confirmed by previous study by Armentano et al.[5] were T2DM have a correlation with high CIMT and High Gensini score. In the present study however, such results were not found, possibly due to low number of T2DM patients involved in this study (n=13, 20.6%).[6]

Cigarette smoking will rapidly alter atherosclerosis process. Oxidant content in the cigarette will damage artery endothelial cell. This theory and previous study conduct by Bin et al, confirmed the finding on this study.[7] High total cholesterol and low value of high densitiy lipoprotein (HDL) were associated with increasing CIMT.[8]

Oliver et al, conducted a study that results in similar fashion with this study where high CIMT and Femoral artery intima-media thickness had a strong correlation with the severity of coronary artery disease.[9]

Other study used CIMT to predict a SYNTAX score to asses the complexity of coronary artery disease using CIMT with cut-off point of 0.71 mm found that higher CIMT was associated with high SYNTAX score.[10]

Previous 27 cohort diagnostic studies about internal carotid intima-media thickness to predict the severity of coronary artery disease lession found sensitivity: 79%; specificity: 74.4%; odd ratio: 7.9 while IMT in common carotid artery had sensitivity: 68%; specificity: 61.5%; odd ratio: 3.2. Measuring the internal carotid artery was found to be more accurate in predicting the severity of coronary artery disease lessions.[11]

Turk et al, conducted a study about the correlation of platelet counts. The results showed that platelet counts have a strong correlation in predicting the severity of coronary artery lession and this study repeated this finding.[12]

Conclusion

Internal carotid intima-media thickness can be used as a tool to predict the severity of coronary artery disease in

stable coronary artery disease patient with cut-off point 0.55 mm. Further study with more subjects should be conducted to obtain more representative result.

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