Relationship Between Risk Factors and Carotid Artery Stenosis Prevalence in Patients With Lower Extremity Peripheral Arterial Disease

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Introduction: One of degenerative disease is atherosclerosis. Peripheral artery disease (PAD) and carotid artery stenosis (CS) broadly covers vascular disease, both of which can be caused by atherosclerosis. Given the general etiology of peripheral atherosclerosis that can occur in different vascular locations, the presence of disease in one place increases the frequency of symptomatic and asymptomatic disease in another. Because both have the same cause, there is a hypothesis that the two are correlated. The purpose of this study was to determine the risk factors associated with carotid artery stenosis (CS) in patients with lower extremity peripheral artery disease (PAD) and to determine the prevalence of carotid artery stenosis (CS) and the thickness of intimal media thickness (IMT) in patients with lower extremity peripheral artery disease (PAD).

Method: This research was conducted at Cipto Mangunkusumo General Hospital during February-May 2018. This study was prospective. Data were taken from secondary data based on history and laboratory results, while the degree of stenosis and intimal media thickness were carried out by carotid duplex ultrasound (DUS) with united imaging ultrasound using a probe 8.5 Mhz. The receiver operating characteristic curve was used to assess the best cut point with sensitivity, specificity, positive predictive value, and negative predictive value.

Results: A total of 50 subjects with an age range between 49-80 years (63.8 ± 8.8 years), of which there were 31 male males (62%) and 19 females (38%). There was a correlation between hypercholesterolemia and smoking history with the degree of carotid stenosis ($p < 0.05$), while risk factors for the degree of IMT was not found. The prevalence of mild carotid artery stenosis (CS) was 26 (52%), moderate carotid artery stenosis 15 (30%), severe carotid artery stenosis 9 (18%). In comparison, the IMT value in this study obtained 9 (18%) mild IMT, 22 (44%) moderate IMT, and 19 (38%) severe IMT.

Conclusion: In patients with severe PAD, the highest incidence of carotid artery stenosis (CS) was in the mild category (52%). The highest rate of intimal media thickness (IMT) was a medium-size IMT (44%). Carotid artery stenosis (CS) was associated with hypertension, diabetes, hypercholesterolemia, smoking, and a family history of atherosclerosis. In statistical analysis, hypercholesterolemia and smoking history had a relationship with the severity of carotid stenosis.

Keywords: Atherosclerosis, carotid artery stenosis (CS), carotid duplex ultrasound (DUS), intimal media thickness (IMT), peripheral arterial disease (PAD)

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INTRODUCTION

As a degenerative disease, peripheral artery disease (PAD) and carotid artery stenosis (CS) broadly include vascular disease, both of which can be caused by atherosclerosis, a systemic disease. Given the general etiology of peripheral atherosclerosis that can occur in different vascular locations, the presence

of disease in one place increases the frequency of symptomatic and asymptomatic disease in another. Because both have the same cause, there is a hypothesis that the two are correlated with each other. Another studies already identified a relationship between the prevalence of peripheral artery disease (PAD) and carotid artery stenosis (CS).^{1,2}

Caused by atherosclerotic process, carotid artery stenosis (CS) is one of the leading causes of fatal complication in vascular disease. It can developed into cerebrovascular stroke (CVS) and transient ischemic attack (TIA). Ischemic stroke has a significant public health impact as the main cause of long-term disability in people. In the world, it becomes the third leading cause of death. As many as 20% of all ischemic strokes are large arterial atherosclerosis and specifically internal carotid artery stenosis. In most cases, atherosclerosis caused the carotid artery stenosis.¹

For examination, CS is usually diagnosed by carotid duplex ultrasound (DUS) in both carotid arteries. It is very important to do screening, because early detection of carotid occlusion will help control cerebrovascular events, such as for every 10% increase in the degree of carotid stenosis.³

Each manifestation of atherosclerosis has different predominant risk factors. There are several risk factors that already identified for carotid artery stenosis (CS) that cause ischemic stroke, such as hypercholesterolemia, smoking, diabetes, hypertension, and a family history of atherosclerosis. Meanwhile, peripheral artery disease (PAD) risk factors are found in smokers, black race, diabetes, hypertension, decreased kidney function, and hypercholesterolemia.⁴

Various studies using several types of research designs has been evaluated in the relationship between manifestations of atherosclerotic disease in various arterial systems. The rationale for knowing the correlation between different arterial systems is the systemic nature of atherosclerosis. Specifically, PAD and CS have been evaluated to determine how the relationship is linked or as a manifestation of atherosclerosis.^{5,6}

METHOD

from February to May 2018. Patients with a diagnosis of severe lower extremity PAD, where an ABI score of <0.9 was obtained, severe ischemic to necrosis of both unilateral and bilateral limbs according to the Rutherford III category and from CT Angiography examination obtained stenosis >50 %, and requires limb salvage, both angioplasty and amputation. Patients with a history of CS, carotid endarterectomy, a history of cerebrovascular stroke or TIA, patients who are contraindicated for CT angiography such as allergic with contrast, and patients with only mild PAD were excluded from the study.

All severe lower-extremity PAD patients underwent carotid duplex ultrasound scanning (DUS) examination to detect carotid artery stenosis (CS). Data were collected on known risk factors (sex, hypertension, diabetes, hypercholesterol, smoking history, family history of atherosclerosis). Carotid Artery Stenosis (CS) was defined as mild stenosis <50%, moderate 50-69%, and weight ≥70%, and Intimal Media Thickness (IMT) thickness is defined as mild stenosis <1 mm, moderate 1-1.99 mm, and severe ≥2 mm.

The ultrasound used was United Imaging iuStar100™, a carotid examination with a high resolution (8.5 MHz). Three modes were used in B-mode grayscale imaging, doppler color flow, both in the transverse and longitudinal fields, and spectral Doppler velocities in the longitudinal plane.

The examination begins in the lower neck by visualizing the common carotid artery along its longitudinal axis, followed by an examination of the internal carotid artery. Plaque thickness was measured and recorded at each level. B-mode images were examined for acoustic shadows, the brightness of shadows from plaque and calcified locations, with plaques defined as shadow structures that enter the lumen of the arteries and detect the level of stenosis <50% as mild stenosis, 50% to 69% as moderate

Tabel 1. Characteristics of research subjects

	Descriptive	
Age (mean ± SD)	63,8±8,8	(49-80)
Gender (n,%)		
Male	31	62,0%
Female	19	38,0%
Hypertension (n,%)		
Positive	30	60,0%
Negative	20	40,0%
Diabetes (n,%)		
Positive	41	82,0%
Negative	9	18,0%
Hypercholesterolemia (n,%)		
Positive	26	52,0%
Negative	24	48,0%
Smoker (n,%)		
Positive	15	30,0%
Negative	35	70,0%
Family history of atherosclerosis (n,%)		
Positive	9	18,0%
Negative	41	82,0%
Carotid stenosis (CS) (n,%)		
Mild	26	52,0%
Moderate	15	30,0%
Severe	9	18,0%
Intimal media thickness (IMT)(n,%)		
Mild	9	18,0%
Moderate	22	44,0%
Severe	19	38,0%

The study took place at the Cipto Mangunkusumo General Hospital for four months

stenosis, 70% to 99% as severe stenosis and >99%

Table 2. Relationship of age to carotid stenosis degrees

Degree of CS	N	Mean	SD	Minimum	Maximum	p
Mild	26	66,08	8,158	53	80	Reference
Moderate	15	62,47	8,839	49	77	0,601
Severe	9	59,33	9,327	49	79	0,143
Total	50	63,78	8,800	49	80	

*) Bonferonni Anova Post hoc Test

Table 3. Relationship of subject age to IMT degrees.

Degree of IMT	N	Mean	SD	Minimum	Maximum	p
Mild	9	63,67	8,944	53	77	Reference
Moderate	22	68,14	7,246	53	80	0,472
Severe	19	58,79	8,032	49	79	0,396
Total	50	63,78	8,800	49	80	

*) Bonferonni Anova Post hoc Test

as total occlusion. IMT thickness was measured and defined as <1 mm mild stenosis, 1-1.99 mm moderate stenosis, and ≥ 2 mm as severe stenosis (plaque). The doppler peak sample volume at each point was positioned in the middle of the artery or, at the point, gives the greatest change in speed that can be heard. During the inspection, the sound characteristics of the speed signal were recorded. This characteristic was useful in detecting changes in speed associated with flow disturbance. Peak systolic velocity (PSV) was measured in the common carotid artery and an internal carotid artery to detect CS significance (Table 1). Significant carotid stenosis was defined as stenosis of 70% or more in the internal carotid arteries.

Data were collected, revised, coded, and entered into a statistical package for social science (SPSS) version 20. Qualitative data was presented as a sum and percentage, while quantitative data was presented as averages, standard deviations, median ranges, and interquartile. The receiver operating characteristic curve was used to assess the best cut point with sensitivity, specificity, positive predictive value, and negative predictive value.

RESULTS

This study included fifty subjects, with an age range between 49-80 years (63.8 ± 8.8 years). As much as 31 (62%) was male, and female sex as much as 19 (38%). Research subjects who had hypertension were 30 (60%), diabetes 41 (82%), hypercholesterolemia 26 (52%), smokers 15 (30%), and family history of atherosclerosis 9 (18%). The incidence of mild carotid artery stenosis (CS) was 26 (52%), moderate carotid artery stenosis (CS) 15 (30%), severe carotid artery stenosis (CS) 9 (18%) while the IMT value in this study was 9 (18%) mild IMT, 22 (44%) IMT, and 19 (38%) IMT (Table 1).

Based on the relationship between age and carotid stenosis in 50 research subjects, 26 (52%) of them were recorded as having mild carotid stenosis, 15 (30%) had moderate carotid stenosis, while 9 (18%) were recorded as having severe carotid stenosis. No significant relationship was found between age and degree of moderate carotid stenosis ($p=0.601$) nor the relationship between age and degree of severe carotid stenosis ($p=0.413$) (figure 1 and table 2).

Figure 1. Relationship of Age to the degree of stenosis

Based on the relationship between age and IMT, nine subjects (18%) were recorded as having a mild IMT, 22 subjects (44%) were recorded as having a moderate IMT, while 19 subjects (38%) were recorded as having a severe IMT. No significant relationship was found between age and degree of moderate carotid stenosis ($p=0.472$) nor the relationship between age and degree of severe carotid stenosis ($p=0.396$) (figure 2 and table 3).

Figure 2. Relationship of subject age to IMT degree.

Based on the results of this study, it was found that the majority of male subjects experienced mild type of carotid stenosis, namely 14 subjects (35.5%), six types of severe subjects (19.4%), and 11 types of moderate subjects (45.2%) whereas female subjects experienced a mild type of carotid stenosis, which was 12 (63.2%). No significant

Table 4. Gender relationship to carotid stenosis.

	Carotid stenosis			p
	Mild	Moderate	Severe	
Gender				
Male	14 (45,25%)	11 (35,5%)	6 (19,4%)	0,442
Female	12 (63,2%)	4 (21,1%)	3 (15,8%)	
Total	26 (52,0%)	15 (30,0%)	9 (18,0%)	

Table 5. Relationship of hypercholesterolemia to carotid stenosis

	Carotid stenosis		p
	Mild	Moderate-severe	
Hypercholesterolemia			
Positive	6 (30,0%)	14 (70,0%)	0,011
Negative	20 (66,7%)	10 (33,3%)	
Total	26 (52,0%)	24 (48,0%)	

Table 6. Relationship of smoking to carotid stenosis.

	Carotid stenosis		p
	Mild	Moderate-severe	
Smoke			
Positive	4 (26,7%)	11 (73,3%)	0,019
Negative	22 (62,9%)	13 (37,1%)	
Total	26 (52,0%)	24 (48,0%)	

Table 7. Relationship of sex with IMT

	IMT			P
	Mild	Moderate	Severe	
Gender				
Male	7 (22,6%)	11 (35,5%)	13 (41,9%)	0,269
Female	2 (10,5%)	11 (57,9%)	6 (31,6%)	
Total	9 (18,0%)	22 (44,0%)	19 (38,0%)	

differences were found between gender and the degree of stenosis ($p=0.442$) (table 4).

Carotid stenosis mild type was more common in the positive hypertension group, as many as 16 subjects (53.3%) while in moderate-severe carotid stenosis were found in 14 subjects (46.7%). Statistically, there was no significant difference between mild and moderate-severe carotid stenosis in the hypertension group ($p=0.817$).

The positive diabetes group also found that more experienced mild type of carotid stenosis, namely 22 subjects (53.7%), while carotid stenosis was moderate-severe in 19 subjects (46.3%). No statistically significant differences were found between mild carotid stenosis and moderate-severe carotid stenosis in the diabetes group ($p=0.616$).

The positive hypercholesterol group was found more in moderate-severe type of carotid stenosis, namely as many as 14 subjects (70%), whereas the mild type of carotid stenosis was six subjects (30%), this showed a significant difference between moderate-severe carotid stenosis and carotid stenosis mild in the hypercholesterolemia group ($p=0.011$) (table 5).

Correspondingly, in the positive smoking group, subjects were found with moderate-severe type of carotid stenosis by 11 subjects (73.3%), whereas carotid stenosis was mild by four subjects (26.7%). This showed a statistically significant difference between moderate-severe carotid stenosis and mild carotid stenosis in the smokers group ($p=0.019$) (table 6).

Mild type of carotid stenosis was common in the group with a family history of atherosclerosis, namely as many as six subjects (66.7%) and moderate-severe carotid stenosis by three subjects (33.3%). No statistically significant differences were found between mild carotid stenosis and moderate-

severe carotid stenosis in the group with a family history of atherosclerosis. ($p=0.33$; CI95% 0.3-9.0).

Based on the results of this study, it was found that the majority of male sex subjects experienced severe type IMT, as many as 13 subjects (41.9%), moderate type with 11 subjects (35.5%), and mild type with seven subjects (22.6%). While in the female group, who experienced severe type of IMT, as many as six subjects (31.6%), 11 with moderate types (57.9%), and two mild subjects (10.5%). There were no statistically significant differences between sexes with the incidence of IMT ($p=0.269$) (table 7).

While risk factors such as diabetes, hypertension, cholesterol, smoking, and family history were associated with moderate-severe IMT did not find any significant differences.

DISCUSSION

In this study, patients with peripheral artery disease (PAD) found a relationship between risk factors for hypercholesterolemia and smoking history to the degree of carotid artery stenosis (CS). The highest incidence of carotid artery stenosis (CS) was in the mild category (52%). The highest incidence of intimal media thickness (IMT) in this study was medium IMT (44%). Carotid artery stenosis (CS) was associated with hypertension, diabetes, hypercholesterolemia, smoking, and a family history of atherosclerosis. In statistical analysis, hypercholesterolemia and smoking history appear to had independent effects.

Risk factors such as hypercholesterolemia and a positive smoking history were found in subjects with moderate-severe type of carotid artery stenosis (CS) with significant differences while the risk factors

associated with the incidence of moderate-severe IMT were not found to be significant differences.

CONCLUSION

In patients with severe PAD, the highest incidence of carotid artery stenosis (CS) was in the mild category (52%). The highest incidence of intimal media thickness (IMT) was a medium-size IMT (44%). Carotid artery stenosis (CS) was associated with hypertension, diabetes, hypercholesterolemia, smoking, and a family history of atherosclerosis. In statistical analysis, hypercholesterolemia, and smoking history had a relationship with the severity of carotid stenosis.

CONFLICT OF INTEREST

The author states the original work, and there is no conflict of interest in doing this research.

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