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Original Article

The Relationship Between Renal Artery Stenosis and Degree of Angio Score on the Lower Extremity Peripheral Arterial Disease in Cipto Mangunkusumo Hospital

Hippocrates Kam[a], Alexander Jayadi Utama[b], Aria Kekalih[c]

Introduction: The most common cause of the peripheral arterial disease (PAD) is atherosclerosis. PAD is associated with other atherosclerotic diseases such as renal artery stenosis (RAS). Life expectancy decreases in patients with RAS, especially those whose stenosis is above 60% but has not reached the stage of chronic kidney failure. This study aims to determine the prevalence of RAS in PAD patients, the relationship between angiographic scoring system (ANGIO Score), history of hypertension, and diabetes mellitus with the degree of RAS.

Method: This research was a cross-sectional study conducted at Cipto Mangunkusumo Hospital from February to May 2019. Patients with a diagnosis of lower extremity PAD and had been assessed with CT angiography examination, were included in this study. The degree of RAS and ANGIO Score were calculated. Sampling was done by the total sampling method.

Results Most patients were women 33 (50.8%), while men were 32 (49.2%). 90.8% of the patients had diabetes, while 61.5% of the sample had hypertension. Grade 1 RAS was the most found. There was no correlation between ANGIO Score on age, sex, and diabetes mellitus, but there was a significant relationship with hypertension. There was a relationship between RAS with age and hypertension, but there was no relationship with diabetes mellitus and gender. ANGIO Score and RAS had a significant relationship (p <0.001).

Conclusion: There was a relationship between the ANGIO Score and the severity of RAS. The cut-off score of 9 for the ANGIO Score had a sensitivity of 85.7% and a specificity of 61.4% for predicting RAS.

Keywords: peripheral arterial disease, angiographic scoring system, renal artery stenosis, CT angiography
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*Correspondence: hippocrateskam@yahoo.com
[a]M.D., Department of Surgery, Dr. M. Djamil Hospital, Padang, Indonesia
[b]M.D., Vascular and Endovascular Division, Department of Surgery, Cipto Mangunkusumo Hospital - Faculty of Medicine, Universitas Indonesia, Jakarta, Indonesia
[c]M.D., M.T.I., Ph.D., Department of Community Medicine, Faculty of Medicine Universitas Indonesia, Jakarta, Indonesia

INTRODUCTION

Peripheral artery disease (PAD) is a disease of the arteries that affects the blood vessels other than the heart and brain. The most common cause of PAD is atherosclerosis; and other causes such as inflammatory disorders of arterial walls (vasculitis) and non-inflammatory arteriopathies, such as fibromuscular dysplasia.[1] The prevalence of PAD is estimated at 8.5 million people in the United States[2], and more than 200 million people worldwide suffer from PAD. Risk factors for PAD are similar to other atherosclerosis diseases, such as smoking and diabetes mellitus.[3] Inflammatory markers, thrombosis, increased lipoprotein and homocysteine levels, and chronic kidney disease are also associated with PAD.[2]

PAD is associated with other atherosclerotic diseases such as renal artery stenosis (RAS). Renal artery stenosis is defined as the narrowing of one or both renal arteries or their branches and, most often, is caused by atherosclerosis. Atherosclerotic-type RAS is more commonly found in elderly patients and has multiple cardiovascular risk factors. Atherosclerosis has often been systemic and does not only occur in the renal artery.[4] A study conducted by Aboyans et al.[5] found that the RAS accidentally diagnosed at the time of the PAD examination was 14%. Research by Wollenweber et al.[4] states that 31% of patients with mild atherosclerotic narrowing (<50% occlusion) in RAS

have symptoms of coronary, cerebrovascular, or peripheral arterial disease. A prospective study involving renal artery disease patients showed that they also had a prevalence of poor ABI scores.

RAS is closely related to three main clinical symptoms, which are ischemic nephropathy, hypertension, and destabilizing cardiac syndromes. Often, the diagnosis of RAS was made due to incidental findings of other diseases. RAS is a progressive disease characterized by worsening of stenosis and followed by occlusion that affects the physiological function and the patient's prognosis. Life expectancy decreases in patients with RAS, especially those whose stenosis is above 60%, but has not yet reached the stage of chronic kidney failure. The majority of these patients die from cardiovascular failure. However, life expectancy will be more decreased if the patient's kidney reaches the stage of chronic kidney failure or commonly referred to as End-Stage Renal Disease (ESRD).

The angiographic scoring system, called the ANGIO score, is created to be used for CT angiography and conventional angiography examinations. ANGIO score is a simple scoring system that can be assessed repeatedly and relatively quick. The score correlates with the severity of lower limb ischemia as measured by ABPI, and predicts impending major amputation of lower limbs and cardiovascular events.[6] This study aims to determine the prevalence of RAS in PAD patients, the relationship between ANGIO score, history of hypertension, and diabetes mellitus with the degree of RAS.

METHOD

This was a cross-sectional study that was conducted at Cipto Mangunkusumo National Hospital from February to May 2019 with patients who is diagnosed with lower extremity PAD (ABI score <0.9), severe ischemic to necrosis of the limbs, and from CT angiography examination obtained degree of stenosis of lower leg arteries, as well as renal artery assessment with CTA on these patients. PAD patients who have been diagnosed with chronic kidney failure and undergoing hemodialysis were excluded from the study.

The degree of stenosis of the renal artery was assessed using the OSIRIX program and divided into a value of 0 (degree of stenosis 0-10%), value of 1 (degree of stenosis 11-30%), value of 2 (degree of stenosis 31-50%), value of 3 (degree of stenosis 51-70%), value of 4 (degree of stenosis >70%), and value of 5 for total occlusion. ANGIO Score consists of evaluating the ten main of the lower extremity. Arteries are given ratings 0, 1, and 2 based on the degree of stenosis or occlusion. A value of 0 is given if there is no stenosis or below 50%, a value of 1 is given for non-occlusive stenosis (<50%), and a value of 2 for total occlusion of the artery. Because of limited spatial resolution, the infra-popliteal artery is rated as 0 or 2. The assessment of the ANGIO score will be divided into three groups, namely the ANGIO score ≤4, ANGIO score 5-9, and the ANGIO score ≥10.

The analysis of this study were done using SPSS version 20. Analysis of the relationship would be assessed by the chi-square test with a significance value of $p < 0.05$.

RESULTS

A total of 65 patients were included in this study. The results showed that most samples were women, (50.8%), while men were 32 (49.2%). As many as 90.8% of the patients had diabetes while 61.5% of the sample had hypertension (table 1).

Table 1. Characteristic of Gender, Hypertension and Diabetes Mellitus in PAD Patients

		n	%
Gender	L	32	49.2%
	P	33	50.8%
Diabetes	-	6	9.2%
	+	59	90.8%
Hypertension	-	25	38.5%
	+	40	61.5%

In categorizing the degree of stenosis, it was found in this study that the most degree was the degree of 1, which was 27.7%. Degrees of 0 and 2 were both 20% of the total sample, while degrees of 3 and 4 were 16.9% and 15.4% of samples (table 2).

Table 2. Overview of Degree of Renal Artery Stenosis in PAD Patients (n = 65).

Stenosis degree	n	%
0	13	20.0%
1	18	27.7%
2	13	20.0%
3	11	16.9%
4	10	15.4%

At a stenosis degree of 0, the mean ANGIO score was 4.38 ± 2.96. With the greater the degree of stenosis, the higher the average of the ANGIO score. This was seen from the increase of the ANGIO score of the degree of stenosis of 1 (8.83 ± 3.57),

Table 3. Comparison of ANGIO Score based on Degree of Renal Artery Stenosis.

Stenosis degree	Mean ANGIO Score	SD	Median	Min	Max	p
0	4.38	2.96	3	1	12	<0,001*
1	8.83	3.57	9	3	16	<0,001^T
2	9.54	4.27	10	2	17	<0,001^T
3	11.55	4.78	10	4	21	<0,001^T
4	20.50	5.54	21	10	31	<0,001^T

*Kruskall Wallis, ^{T}Mann-Whitney

Table 4. Comparison of ANGIO Score based on stenosis degrees 0-2 and 3-4

Stenosis degree	Mean ANGIO Score	Standard Deviation	Median	Minimum	Maximum	p
0-2	7.73	4.18	7	1	17	< 0,001
3-4	15.81	6.80	15	4	31	

the degree of stenosis of 2 (9.54 ± 4.27), the degree of stenosis of 3 (11.55 ± 4.78) and the highest was the degree of stenosis of 4 which is 20.5 ± 5.54. From the figure, it appeared that there was still overlapping ANGIO score in the degree of stenosis of 1, 2, and 3. However, when compared to the degree of stenosis of 0 with 1 and 3 with 4, there appeared to be no overlapping of ANGIO score against the degree of stenosis. Kruskall-Wallis test was performed and obtained p values of <0.001 and continued with the Mann-Whitney test found that differences had occurred when comparing the degree of stenosis of 0 to 1, and so on (p <0.001) (table 3, figure 1).

The degree of stenosis, which was considered to cause clinical symptoms in patients, was degrees of 3 and 4. In table 4, the category of stenosis degrees was divided into two categories, 0 (degree of stenosis <3) and 1 (degree of stenosis 3-4). The stenosis degree of 0-2 had an average ANGIO score of 7.73 ± 4.18, while the degree of stenosis 3-4 had an average ANGIO score of 15.81 ± 6.80 (table 4, figure 2).

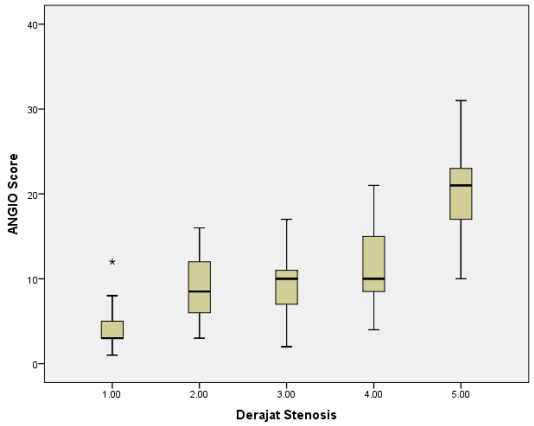

Figure 1. Comparison of ANGIO Score based on the degree of renal artery stenosis

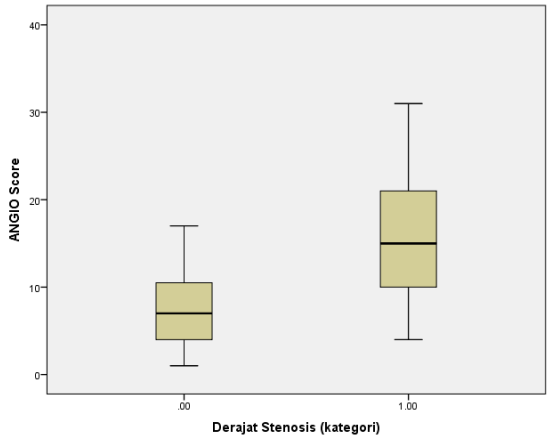

Figure 2. Comparison of ANGIO Score based on Stenosis Degrees 0-2 and 3-4

In the comparison of the ANGIO Score cut-off option to determine the degree of stenosis (0-2 vs. 3-4), a diagnostic test was performed. An increase in specificity scores was found along with an increase in the ANGIO score cut-off. However, this applies in contrast to sensitivity figures. At the ANGIO cut-off score of 9, a sensitivity of 0.857 and a sensitivity of 0.614 was obtained. However, in the ANGIO cut-off score of 15, a sensitivity of 0.619 and a specificity of 0.932 was obtained (table 5).

Table 5. Comparison of Cut-Off for ANGIO Score to Determine the Degree of Stenosis.

Cut-off ANGIO Score	Sensitivity	Specificity
9.00	.857	0.614
10.00	.810	0.636
11.00	.667	0.750
12.00	.667	0.773
13.00	.667	0.886
14.00	.619	0.909
15.00	.619	0.932

DISCUSSION

Many factors are associated with PAD, but in this study, we assessed the relationship with age, hypertension, diabetes mellitus, and gender. The PAD can be assessed for its severity by looking at the amount of involvement of the affected leg blood vessels. In this study, the assessment was carried out using the ANGIO Score after the CT angiography had been performed on the limbs of patients diagnosed with PAD. The difference was that the ANGIO Score sums the scores of all blood vessels involved, both in healthy and diseased limbs.

This study found that there was no significant relationship between age and the ANGIO Score. When compared with research by Wang et al.[7] showed that age was correlated with more severe PAD, as in the old age group, the likelihood of someone suffering from PAD is higher than the younger age group. The diagnosis of PAD in this study might have been assessed, but the blood vessels involved were not analyzed and grouped based on the severity of the PAD. The leading cause of problems in PAD is atherosclerosis, which is a disease caused by aging. In addition, with increasing age the blood vessels also physiologically will become poor, and their elasticity decreases.[7,8]

ANGIO Score is a scoring system to assess the severity of a PAD by looking at the condition of the blood vessels in both legs. In this study, there was also no relationship between ANGIO Score and gender. Female were suffered more in the ANGIO Score 1-9 group, while male were suffered in the group >10. In a study conducted by Wang et al.[8] it was found that the incidence of women suffering from PAD was higher than that of men. Young women were higher than in men for the risk of suffered from PAD, but in the age >70 years, this risk was the same between the two sex groups.

According to Anderson et al., the significance of stenosis was considered to gave clinical symtopms if the degree was in category >3 (stenosis degree >51%) Therefore, in this study we categorized into 2 group, which were 0 to 2 (no symptom), and 3 to 4 (symptomatic).

In this study, the incidence of hypertension had a statistically significant relationship with renal artery stenosis, but not with diabetes. In other words, with hypertension, it was likely that someone would experience stenosis of the renal artery. In a study conducted by Missouris et al., there was a significant relationship between the incidence of RAS

and hypertension (p = 0.0065).[9] According to Sowers et al.[10] between diabetes and hypertension, although they are two different diseases, they were related to each other.

Diabetes mellitus also had no statistically significant relationship to the ANGIO Score. In other words, diabetes mellitus would not affect the results of the ANGIO Score. The dominance of diabetes mellitus patients in this study caused the sample to become more homogeneous toward diabetes mellitus. This could be the cause of the absence of a relationship between diabetes mellitus and RAS or ANGIO Score.

As the ANGIO Score increased, so was the degree of renal artery stenosis. Hypertension was a typical symptom in patients with renal artery stenosis, and according to Wang, it also stimulates the emergence of atherosclerotic.[7,10-12] Renal artery stenosis that occurred in old age was also most often caused by atherosclerotic. PAD also predominantly occurs in diabetes mellitus, and this also triggers atherosclerotic development.[11] Looking at the relationship that caused atherosclerosis was a critical factor in the relationship between ANGIO Score and RAS.

This study had a limitation as the number of samples was small. Besides, it was necessary to conduct a CT scan assessment by at least two people.

CONCLUSION

There was a relationship between the ANGIO Score and the severity of RAS, with hypertension as a significant risk factor. The cut-off ANGIO Score of 9 had a sensitivity of 85.7% and a specificity of 61.4%.

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ORCID ID OF AUTHORS

Hippocrates Kam
https://orcid.org/0000-0003-0397-6108

Alexander Jayadi Utama
https://orcid.org/0000-0003-2922-6487

Aria Kekalih
https://orcid.org/0000-0001-7811-097X

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