

# The Difference of Mean WSS Value on The Carotid Bifurcation and The Medial Segment of Common Carotid Artery Using Vector Flow Ultrasonography in Hypertensive Patients at Prof Dr. I.G.N.G Ngoerah General Hospital February-April 2022

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## ABSTRACT

**Background:** Hypertension is a risk factor for atherosclerosis which increases the risk of stroke. Transitions in blood vessels such as bifurcations are associated with changes in the velocity and pattern of blood flow that decrease wall shear stress (WSS) and is believed to be a risk factor for atherosclerosis. Shear stress on the common carotid artery also decreased with increasing blood pressure. This study aims to determine the difference of mean WSS value on the carotid bifurcation and the medial segment of common carotid artery using vector flow ultrasonography in hypertensive patients. **Methods:** This study used a cross-sectional design with the research location at the Radiology Installation of Prof. Dr. I.G.N.G Ngoerah Hospital Denpasar in February-April 2022. The sample of this study was hypertensive patients who came to the Radiology Installation of Prof. Dr. I.G.N.G Ngoerah Hospital and met the inclusion criteria as many as 32 people. The examination was carried out by a consultant of head and neck radiology, using an ultrasound device with a linear transducer probe that has a probe frequency range of 3-9 Mhz. **Results:** The average age of the sample in this study was 50 years, with 9 males (28.1%), 23 females (71.9%). The results showed that the average maximum WSS value on the carotid bifurcation ( $3.37 \pm 0.96$ ) Pa, the mean value ( $1.15 \pm 0.45$ ) Pa, while the average maximum WSS value on the medial segment of the common carotid artery ( $4.41 \pm 1.45$ ) Pa, the mean value ( $1.78 \pm 0.54$ ) Pa. The average maximal and mean WSS value on carotid bifurcation were lower than the medial segment of the common carotid artery in hypertensive patients ( $p < 0,05$ ). The results of multivariate analysis on WSS values after controlling for confounding variables, obtained the average maximal and mean WSS value on carotid bifurcation, remained lower than the medial segment of the common carotid artery ( $p < 0,05$ ). **Conclusion:** there were significant differences in the mean wall shear stress (WSS) of the carotid bifurcation and the medial segment of the common carotid artery in hypertensive patients. Suggestions that can be done next are in facilities that have vector flow ultrasonography facilities, it is recommended to measure the WSS value in hypertensive patients as additional information as a predictor of atherosclerosis.

**Keywords:** Wall shear stress; carotid bifurcation; medial segment of the common carotid artery; vector flow ultrasonography.

## INTRODUCTION

Stroke is a rapidly developing clinical symptom resulting from cerebral dysfunction, where the symptoms last for more than 24 hours or cause death, without any other cause except for vascular disturbances [1]. Stroke is the second leading cause of death globally and the third leading cause of disability [2]. The global prevalence of stroke in 2019 was 101.5 million people, with ischemic stroke accounting for 77.2 million, intracerebral hemorrhage 20.7 million, and subarachnoid hemorrhage 8.4 million.

In 2019, globally, 3.3 million people died from ischemic stroke, 2.9 million from intracerebral hemorrhage, and 0.4 million from subarachnoid hemorrhage. Several countries in Eastern Europe, Central and Southeast Asia, and Oceania have the highest stroke mortality rates [3].

Many risk factors for stroke have been identified, including age and gender, hypertension, serum cholesterol, fibrinogen; lifestyle factors such as smoking, diet, alcohol consumption, physical inactivity;

social factors such as education, social class, and ethnicity; and physical environmental factors (temperature, altitude), geographic, or psychosocial factors [1]. Among these factors, hypertension is the most frequent cause of stroke [2].

Hypertension is a vascular disease where a person has blood pressure elevated above normal after repeated examinations [4]. Hypertension or elevated blood pressure remains the leading cause of death globally, accounting for 10.4 million deaths per year [4]. According to the World Health Organization (WHO) in 2021, 1.28 billion adults aged 30-79 years worldwide suffer from hypertension, with most (two-thirds) living in low- and middle-income countries. About 46% of people are unaware that they have hypertension. Only about 1 in 5 people with hypertension are receiving treatment [5]. In Indonesia, the incidence of hypertension increased from 25% in 2013 to 34.1% in 2018 [6]. The 2018 Riskesdas explains that the incidence of hypertension is higher in women than in men and increases with age [7]. In Bali, there are approximately 728,192 people with hypertension [8].

Hypertension will cause damage to the endothelial cells of the blood vessels. Once endothelial damage occurs, atherosclerosis and plaque buildup begin to form. Therefore, hypertension is known as a major risk factor for the formation of atherosclerosis. When plaques become vulnerable and rupture, the ruptured plaques will cause blood clots that will block blood flow and move to other body organs. If the plaque blocks the blood vessels supplying blood to the brain, it will cause a stroke [9].

The process of atherosclerosis itself more often affects the bifurcation of blood vessels. The focal nature of atherosclerosis may be due to local hemodynamic factors such as shear stress [10]. Transitions in blood vessels such as at bifurcations are associated with changes in blood flow velocity and pattern, leading to disrupted laminar flow and affecting the reduction of wall shear stress (WSS) values, which are believed to be a risk factor for the formation of atherosclerosis [11]. Another study by Marfella et al. explained that shear stress in the common carotid artery also decreases with increasing blood pressure, age, and body mass index [12]. In a study by Oshinski et al., it was explained that the average WSS value in the common carotid artery could not be used to predict abnormalities at the bifurcation of the carotid artery [13].

There are many imaging modalities to evaluate carotid arteries and WSS, including Ultrasound Echo Color Doppler (US-ECD), Computed Tomography Angiography (CTA), and Magnetic Resonance Angiography (MRA). One of the latest methods to assess shear stress in the carotid artery is using ultrasound with vector flow technology (V flow). Vector Flow displays easy-to-read arrows to visualize blood flow movements, showing complex movements within the flow to better understand hemodynamic changes.

Considering that this is a new technique and there is still limited research on its use in assessing WSS, which can aid in hypertension management, this study aims to determine the difference in mean WSS values using V flow technology at four bifurcations of the common carotid artery and the medial segment of the common carotid artery using vector flow ultrasound in hypertensive patients.

## METHOD

The study used a cross-sectional design to determine the difference in wall shear stress (WSS) values at the bifurcation of the common carotid artery and the medial segment of the common carotid artery. This study was conducted in the ultrasound examination room of the Radiology Department of Prof. Dr. I.G.N.G Ngoerah General Hospital, Denpasar, from February to April 2022. The study sample was obtained through consecutive sampling. Inclusion criteria: 1. Male or female patients aged > 30 years; 2. Patients with systolic blood pressure > 140 mmHg, diastolic > 90 mmHg, and/or on antihypertensive medication; 3. Patients willing to participate after signing informed consent. Exclusion criteria: 1. Stroke and post-stroke patients; 2. Intima-media thickness > 1 mm and/or carotid artery plaque causing  $\geq$  50% carotid artery stenosis.

The study received approval from the Research and Development Unit (Litbang) of the Faculty of Medicine, Udayana University, Prof. IGNG Ngoerah General Hospital, Denpasar. Blood pressure was measured using a sphygmomanometer. The examiner recorded the numbers shown on the sphygmomanometer. All ultrasound examinations were performed using the Mindray Resona 7 ultrasound equipped with V flow technology, using a linear transducer L9-3U (3-9 MHz). Patients then lay down with their neck supported by a pillow. First, locate the common carotid artery, starting from the initial segment to the bifurcation of the common carotid artery using B-mode ultrasound in longitudinal and transverse positions. Then switch the ultrasound to V flow mode, where the frequency ranges between 4.4-9 MHz, depth 2 cm, arrow life cycle 25 ms, arrow density 10%. The right and left common carotid arteries were evaluated in the medial segment using V flow ultrasound. The medial segment was evaluated between the initial segment and the near bifurcation segment (the initial segment was counted about 1 cm from the start of the common carotid artery, and near bifurcation about 1 cm from the bifurcation of the common carotid artery). The WSS values of the medial segment of the common carotid artery were measured automatically by the ultrasound. Then the bifurcation of the carotid artery was evaluated and its WSS measured. The WSS values were averaged over six points, including both maximum and mean values. All carotid artery WSS measurements in the study sample were conducted by one neuro-head and neck radiology consultant.

Statistical analysis was performed using IBM SPSS version 25.0, including descriptive analysis, dependent t-test, and multivariate ANCOVA analysis, with a significance level ( $\alpha$ ) determined by a P-value < 0.05.

**RESULT**

This study involved a sample size of 32 hypertensive patients who came to the Radiology Department of Prof. Dr. I.G.N.G Ngoerah General Hospital, meeting

the inclusion criteria and having received explanations about the study and signed informed consent as a preliminary study. Basic sample characteristics are shown in Table 1.

**TABLE 1:** Characteristics of Research Subjects (n=32).

Variables	Mean ± SD	N (%)
Age (years)	50.53 ± 11.23	
Gender		
Man		9 (28.1%)
Woman		23 (71.9%)
Nutritional status		
Underweight		0 (0%)
Normal		15 (46.9%)
Overweight		14 (43.8%)
Obese		3 (9.4%)
Duration of Antihypertensive Therapy		
Not therapy		12 (37.5%)
≤ 5 years		18 (56.3%)
6-10 years		1 (3.1%)
≥ 10 years		1 (3.1%)
Diabetes mellitus		0 (0%)
Dyslipidemia		0 (0%)
Smoke		0 (0%)

The measurement results of wall shear stress (WSS; in Pa) values at the bifurcation of the common carotid artery and the medial segment of the common carotid artery using vector flow ultrasonography revealed that the mean maximum WSS value at the bifurcation of the right common carotid artery was 3.35 ± 1.40 with a minimum value of 1.50 and a maximum value of 6.3. The mean maximum WSS value at the bifurcation of the left common carotid artery was 3.39 ± 1.18 with a minimum value of 1.29 and a maximum value of 7.67. The mean average WSS value at the bifurcation of the right common carotid artery was 1.12 ± 0.59 with a minimum value of 0.20 and a maximum value of 2.41. The mean average WSS value at the bifurcation of the left common carotid artery was 1.18 ± 0.59 with a

minimum value of 0.10 and a maximum value of 2.36 (Table 2).

The mean maximum WSS value at the medial segment of the right common carotid artery was 4.30 ± 1.79 with a minimum value of 1.51 and a maximum value of 12.12. The mean maximum WSS value at the medial segment of the left common carotid artery was 4.51 ± 1.45 with a minimum value of 2.73 and a maximum value of 9.82. The mean average WSS value at the medial segment of the right common carotid artery was 1.74 ± 0.64 with a minimum value of 0.63 and a maximum value of 3.31. The mean average WSS value at the medial segment of the left common carotid artery was 1.83 ± 0.64 with a minimum value of 1.03 and a maximum value of 3.72.

**TABLE 2:** Differences in Mean Wall Shear Stress (WSS) Values at the Bifurcation of the Common Carotid Artery and the Medial Segment of the Common Carotid Artery.

WSS Value (Pa)	Measurement Location		Mean difference ± SD	95%CI	P value
	Bifurcation mean±SD	Medial Segment mean±SD			
Maximum right	3.35 ± 1.40	4.30 ± 1.79	0.95±2.21	0.15-1.75	0.021
Right mean	1.12 ± 0.59	1.74 ± 0.64	0.62±0.88	0.30-0.94	<0.001
Maximum left	3.39 ± 1.18	4.51 ± 1.45	1.12 ± 1.79	0.47-1.77	0.001
Left mean	1.18 ± 0.59	1.83 ± 0.64	0.64 ± 0.68	0.40-0.89	<0.001
Maximum right and left	3.37 ± 0.96	4.41 ± 1.45	1.03 ± 1.65	0.44-1.63	0.001
Right and left average	1.15 ± 0.45	1.78 ± 0.54	0.63±0.60	0.41-0.85	<0.001

In addition to hypertension, several variables are suspected to affect WSS values, including age, gender, nutritional status measured by BMI, diabetes mellitus, dyslipidemia, smoking, and duration of antihypertensive therapy.

In this study, there were no subjects with diabetes mellitus, dyslipidemia, or smoking. Therefore, only age, gender, nutritional status measured by BMI, and duration of antihypertensive therapy were evaluated using multivariate ANCOVA analysis.

The analysis results for these variables showed that age, gender, nutritional status, and duration of therapy had a significance value >0.05.

The results of the multivariate ANCOVA analysis are shown in Tables 3, 4, and 5.

**TABLE 3:** Multivariate ANCOVA Test Results on Maximum and Average Wall Shear Stress (WSS) Values at the Bifurcation of the Common Carotid Artery and the Medial Segment of the Right Common Carotid Artery.

Variable	Maximum Value			Average value		
	F	p value	R2	F	p value	R2
Bifurcation vs Medial Segment	5.59	0.02	0.08	17.59	<0.001	0.23
Age (Years)	2.90	0.09	0.04	4.18	0.04	0.06
Gender	0.97	0.32	0.01	1.54	0.21	0.02
Nutritional status (Kg/m <sup>2</sup> )	0.01	0.90	<0.001	3.75	0.057	0.06
Duration of antihypertensive therapy (Years)	0.36	0.55	0.006	0.43	0.51	0.007

The multivariate ANCOVA test results in the above table show a significant difference in the mean maximum values at the bifurcation of the common carotid artery and the medial segment of the right common carotid artery with a p-value of 0.02. Factors such as age, gender, nutritional status, and duration of therapy did not affect WSS values at these measurement locations.

There was a significant difference in the mean average values at the bifurcation of the common carotid artery and the medial segment of the right common carotid artery with a p-value of <0.001. The F-test results in the multivariate ANCOVA for age showed an F-value (4.139) lower than the calculated F-value (4.18) with a significance (p=0.04). This indicates that age affects WSS values. Additionally, age affects WSS values at these measurement locations by 6%.

**TABLE 4:** Multivariate ANCOVA Test Results on Maximum and Average Wall Shear Stress (WSS) Values at the Bifurcation of the Common Carotid Artery and the Medial Segment of the Left Common Carotid Artery.

Variable	Maximum Value			Average value		
	F	p value	R2	F	p value	R2
Bifurcation vs Medial Segment	5.59	0.02	0.08	17.59	<0.001	0.23
Age (Years)	2.90	0.09	0.04	4.18	0.04	0.06
Gender	0.97	0.32	0.01	1.54	0.21	0.02
Nutritional status (Kg/m <sup>2</sup> )	0.01	0.90	<0.001	3.75	0.057	0.06
Duration of antihypertensive therapy (Years)	0.36	0.55	0.006	0.43	0.51	0.007

The results in Table 4 show a significant difference in the mean maximum values at the bifurcation of the common carotid artery and the medial segment of the left common carotid artery with a p-value of 0.001. The F-test results in the multivariate ANCOVA for age showed an F-value (4.139) lower than the calculated F-value (9.99) with a significance (p=0.002). This indicates that age affects WSS values. The r<sup>2</sup> value for age was 0.14, meaning age affects WSS values at these measurement locations by 14%.

The F-test results in the multivariate ANCOVA for age showed an F-value (4.139) lower than the calculated F-value (5.23) with a significance (p=0.02). The F-test results for gender showed an F-value (4.139) lower than the calculated F-value (8.14) with a significance (p=0.006). The F-test results for nutritional status showed an F-value (4.19) lower than the calculated F-value (4.53) with a significance (p=0.03). This indicates that age, gender, and nutritional status affect WSS values. The r<sup>2</sup> value for age was 0.08, meaning age affects WSS values at these measurement locations by 8%. The r<sup>2</sup> value for age was 0.12, meaning age affects WSS values at these measurement locations by 12%. The r<sup>2</sup> value for nutritional status was 0.07, meaning age affects WSS values at these measurement locations by 7%.

There was a significant difference in the mean average values at the bifurcation of the common carotid artery and the medial segment of the left common carotid artery with a p-value of <0.001.

**TABLE 5:** Multivariate ANCOVA Test Results on Maximum and Average Wall Shear Stress (WSS) Values at the Bifurcation of the Common Carotid Artery and the Medial Segment of the Right and Left Common Carotid Arteries.

Variable	Maximum Value			Average value		
	F	p-value	R <sup>2</sup>	F	p-value	R <sup>2</sup>
Bifurcation vs Medial Segment	12.17	0.001	0.17	31.05	<0.001	0.34
Age (Years)	7.81	0.007	0.11	7.76	0.007	0.11
Gender	1.86	0.17	0.03	6.87	0.01	0.10
Nutritional status (Kg/m <sup>2</sup> )	0.09	0.76	0.002	6.84	0.01	0.10
Duration of antihypertensive therapy (Years)	0.19	0.66	0.003	0.01	0.92	<0.001

From Table 5, there is a significant difference in the mean maximum values at the bifurcation of the common carotid artery and the medial segment of the right and left common carotid arteries with a p-value of 0.001. The F-test results in the multivariate ANCOVA for age showed an F-value (4.139) lower than the calculated F-value (7.81) with a significance ( $p=0.007$ ). This indicates that age affects WSS values. The  $r^2$  value for age was 0.11, meaning age affects WSS values at these measurement locations by 11%.

There was a significant difference in the mean average values at the bifurcation of the common carotid artery and the medial segment of the right and left common carotid arteries with a p-value of  $<0.001$ . The F-test results in the multivariate ANCOVA for age showed an F-value (4.139) lower than the calculated F-value (7.76) with a significance ( $p=0.007$ ). The F-test results for gender showed an F-value (4.139) lower than the calculated F-value (6.87) with a significance ( $p=0.01$ ). The F-test results for nutritional status showed an F-value (4.139) lower than the calculated F-value (6.84) with a significance ( $p=0.01$ ). This indicates that age, gender, and nutritional status affect WSS values. The  $r^2$  value for age was 0.11, meaning age affects WSS values at these measurement locations by 11%. The  $r^2$  value for age was 0.10, meaning age affects WSS values at these measurement locations by 10%. The  $r^2$  value for nutritional status was 0.10, meaning age affects WSS values at these measurement locations by 10%.

## DISCUSSION

The subjects in this study comprised 32 hypertensive patients who visited the Radiology Department of Prof. Dr. I.G.N.G Ngoerah General Hospital for vector flow ultrasonography procedures. The mean age (years) of the patients in this study was  $50.53 \pm 11.23$ , with 9 male patients (28.1%) and 23 female patients (71.9%). This is consistent with the 2018 Riskesdas data, which shows that women are more likely to suffer from hypertension than men, and the incidence of hypertension increases with age [7].

Nutritional status, as assessed by body mass index (BMI), showed that 15 subjects had normal BMI (46.9%), 14 subjects were overweight (43.8%), and 3 subjects were obese (9.4%). BMI is associated with metabolic syndrome, where a higher BMI, especially in obese patients, leads to inflammation underlying the occurrence of atherosclerosis [14].

The history of antihypertensive therapy among study subjects showed that 12 people were not on therapy (37.5%), 18 people had been on therapy for  $\leq 5$  years (56.3%), 1 person had been on therapy for 6-10 years (3.1%), and 1 person had been on therapy for  $\geq 10$  years (3.1%). Antihypertensive drugs function to control blood pressure, thereby potentially delaying the progression of vascular disease.

The mean maximum WSS value (in Pa) at the bifurcation of the right common carotid artery was  $3.35 \pm 1.40$ . The mean maximum WSS value at the bifurcation of the left common carotid artery was

$3.39 \pm 1.18$ . The mean average WSS value at the bifurcation of the right common carotid artery was  $1.12 \pm 0.59$ . The mean average WSS value at the bifurcation of the left common carotid artery was  $1.18 \pm 0.59$ .

The mean maximum WSS value at the medial segment of the right common carotid artery was  $4.30 \pm 1.79$ . The mean maximum WSS value at the medial segment of the left common carotid artery was  $4.51 \pm 1.45$ . The mean average WSS value at the medial segment of the right common carotid artery was  $1.74 \pm 0.64$ . The mean average WSS value at the medial segment of the left common carotid artery was  $1.83 \pm 0.64$ .

There were significant differences in WSS values between the bifurcation of the common carotid artery and the medial segment of the common carotid artery on both sides with  $p<0.05$ . WSS values reflect the shear stress on the vessel wall when blood flows, where lower WSS values indicate an increased risk of atherosclerosis. This is consistent with literature showing that the process of atherosclerosis more frequently affects the bifurcation of blood vessels. Transitions in blood vessels, such as at bifurcations, are associated with changes in blood flow velocity and pattern, leading to disrupted laminar flow and affecting the reduction of wall shear stress (WSS) values, which are believed to be risk factors for atherosclerosis formation [11]. This is due to the sudden change in the direction of blood flow from pure axial to branching directions, causing flow separation and the formation of secondary flow patterns, such as vortices [11]. Blood flow-induced shear stress and the relationship between carotid artery bifurcation geometry are important factors in the occurrence of atherosclerosis at bifurcations [15,16].

In addition to hypertension, several variables are suspected to affect WSS values, including age, gender, nutritional status measured by BMI, diabetes mellitus, dyslipidemia, smoking, and duration of antihypertensive therapy. In this study, there were no subjects with diabetes mellitus, dyslipidemia, or smoking. Therefore, only age, gender, BMI, and duration of antihypertensive therapy were evaluated using multivariate ANCOVA analysis. The analysis results for these variables showed that age, gender, and nutritional status could affect WSS values. The study by Qiu et al. explained that WSS values in females and males slightly differ. This could be due to differences in carotid artery diameter, with females having smaller diameters than males. Additionally, age can affect WSS values, where older age is associated with lower WSS values, and lower WSS values indicate an increased risk of atherosclerosis [17]. Nutritional status, especially obesity, is linked to several underlying mechanisms between obesity and atherosclerosis. Important factors linking obesity and atherosclerosis include changes in adipokines, inflammation, and activation of gut microbiota inflammasome, oxidative stress, and endothelial dysfunction [14].

This study has limitations in determining WSS values at the bifurcation of the common carotid artery and the medial segment of the common carotid artery due to a limited sample size. Other factors outside of this study that were not evaluated may also influence the results. Further evaluation of these factors is necessary to improve the study's results.

### CONCLUSION

There are significant differences in the mean wall shear stress (WSS) values at the bifurcation of the common carotid artery and the medial segment of the common carotid artery in hypertensive patients, and factors such as age, gender, and nutritional status may be associated with WSS values.

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### DECLARATIONS

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