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3-Years of Cerebral Angiography Profiles in Recurrent Ischemic Stroke at Pelni Hospital Jakarta

Fritz Sumantri Usman[1], Yudistira[2], Windi Christianti M[3], Seri Ulina[4], Merlin Pricilla K[1], Leny Kurnia[1]

[1]Interventional Neurologist, Department of Neurology, Pelni Hospital Jakarta
[2]Neurologist, Department of Neurology, Pasar Minggu General Hospital Jakarta
[3]Neurologist, Department of Neurology, Sele Be Solu General Hospital Sorong
[4]Neurologist, Department of Neurology, Tarutung General Hospital Medan, Indonesia.

Corresponding Author: Yudistira

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ABSTRACT

Background: Recurrent ischemic stroke is a leading cause of high morbidity and mortality in Indonesia, with a consistently increasing prevalence in recent years. Cerebral angiography using Digital Subtraction Angiography (DSA) plays a crucial role in assessing underlying vascular abnormalities, such as stenosis caused by atherosclerotic plaque. This study aimed to determine the cerebral angiographic characteristics of patients with recurrent ischemic stroke at Pelni Hospital, Jakarta, between 2022 and 2024.

Methods: This study employed a cross-sectional design using secondary data. The sample consisted of patients diagnosed with recurrent ischemic stroke who underwent angiography at the catheterization laboratory of Pelni Hospital between 2022 and 2024. Data were collected from medical records, including age, gender, hypertension, diabetes mellitus, dyslipidemia, plaque type, and the degree and location of stenosis. Data were analyzed descriptively, and differences between groups were assessed using the Mann–Whitney U test.

Results: Of the 141 patients who met the eligibility criteria, the median age was 52 years (range 40–72), and most were male (80 of 141). Stenosis was most commonly found in the anterior circulation, particularly in the internal carotid artery (especially the distal segment) (n = 37) and the middle cerebral artery (M1 segment) (n = 32). The severity of stenosis was associated with unstable atherosclerotic plaque (p = 0.01) and the risk factors diabetes mellitus (p = 0.024) and dyslipidemia (p = 0.017).

Conclusion: The severity of stenosis in patients with recurrent ischemic stroke was associated with unstable atherosclerotic plaque, diabetes mellitus, and dyslipidemia. The most common stenosis locations were the distal ICA and the M1 segment of the MCA. Cerebral angiography is important for evaluating recurrence risk and guiding further therapeutic strategies.

Keywords: atherosclerosis, cerebral angiography, plaque, recurrent ischemic stroke, stenosis.

INTRODUCTION

Stroke is a leading cause of death and disability in Indonesia, with prevalence rates trending upward in recent years.[1,2] The 2019 Global Burden of Disease (GBD) data for Southeast Asia shows Indonesia ranked second in stroke sufferers after India, with an incidence and prevalence of 642,943 new cases and 4,918,487 identified stroke

sufferers.[2] Stroke requires high-quality, rapid, and appropriate treatment to prevent and avoid disability and death. One preventative measure is adequate risk factor management and promoting a healthy lifestyle. Implementing community-level health promotion programs, distributing expert personnel (neurologists, radiologists, rehabilitation specialists, and interventional specialists), and supporting equipment (Computed Tomography (CT) Scans or Magnetic Resonance Imaging (MRI)) in peripheral areas are also needed to improve an integrated acute stroke management system.[1,2]

Most people with ischemic stroke or Transient Ischemic Attack (TIA) are at risk of recurrent stroke, especially within the first week after onset. Patients with TIA and a first stroke have a 19% risk of recurrent stroke within 10 years, increasing to 43% if they have other vascular risks such as myocardial infarction.[3] Recurrent strokes lead to poor functional outcomes (physical, mental, cognitive), high dependency, prolonged hospitalization, and increased mortality, making stroke management a challenge for medical personnel and the community.[2,3] Risk factors for ischemic stroke are divided into two categories: modifiable and nonmodifiable. Nonmodifiable factors include age, gender, and family history of stroke. Modifiable factors include hypertension, coronary heart disease, diabetes mellitus, hypercholesterolemia, atherosclerotic plaque, and carotid artery stenosis.[3,4]

Cerebral vascular abnormalities, particularly atherosclerotic stenosis and plaque, are key factors in the recurrence of ischemic stroke, affecting both extracranial and intracranial vessels, such as the internal carotid artery (ICA) and middle cerebral artery (MCA). Symptomatic intracranial stenosis (50-99%) treated medically still carries a 30-day risk of recurrent stroke of up to 20.6%. This is associated with the use of single antiplatelet therapy (SAPT) and the risk of hypoperfusion.[3,5] Chronic stenosis is thought to cause hypoperfusion, which facilitates the formation of micro emboli and contributes to recurrent cerebral ischemic.[6-8] Furthermore, the incidence of recurrent ischemic stroke is also closely related to atherosclerotic plaque status, as plaque rupture can lead to thrombus formation in more distal intracranial arteries. The morphology of atherosclerotic plaque, whether stable or unstable (vulnerable plaque), also influences the risk of recurrence through mechanisms of hypoperfusion, stenosis progression, and artery-to-artery embolism release. Therefore, accurate assessment of atherosclerotic plaque is crucial for predicting the likelihood of future recurrent ischemic stroke.[9-12]

Cerebral angiography, including digital subtraction angiography (DSA), computed tomography angiography (CTA), and magnetic resonance angiography (MRA), is an important examination for evaluating the anatomy and pathology of cerebral blood vessels. Angiographic images can demonstrate the location of stenosis, the degree of narrowing, the pattern of occlusion, the quality of collaterals, and the flow characteristics that are closely related to the risk of recurrent stroke. Identification of certain angiographic patterns, such as significant stenosis of the distal ICA, stenosis of the MCA segment M1–M2, collateral insufficiency, or the presence of tandem lesions, is crucial in assessing the mechanism of stroke and determining appropriate secondary prevention strategies. CTA is superior because it is fast, has high resolution, and is excellent for viewing calcification and luminal anatomy, especially in emergency situations. However, it involves radiation and iodinated contrast, which pose a risk to the kidneys. MRA, on the other hand, is better at assessing the lumen and vessel wall, especially with HR-VWI (High-Resolution Vessel Wall Imaging), but is susceptible to flow artifacts, is less accurate in high stenoses, and has lower resolution than CTA. However, in the context of atherosclerotic plaque and stenosis in

patients with recurrent ischemic stroke, DSA examination is considered more informative in quantitatively demonstrating the degree of stenosis, along with crucial hemodynamic features as an assessor of the risk of ipsilateral ischemic events. DSA procedures are the gold standard for assessing intraluminal stenosis in both intracranial and extracranial vessels. Furthermore, they can evaluate collateral vessels directly or in real time, enabling intervention.[6,13-15]

However, data on cerebral angiography using DSA in patients with recurrent ischemic stroke, especially in the Indonesian population, is still limited. Understanding cerebral vascular abnormalities, including atherosclerotic plaques and the degree and location of stenosis, is necessary to improve diagnostic and therapeutic strategies, including evaluating the intensity of medical therapy, the role of revascularization, and monitoring the risk of recurrence. Based on this background, this study aimed to determine the cerebral angiography in recurrent ischemic stroke at Pelni Hospital, Jakarta, from January 2022 to December 2024, as a representative sample of data in Indonesia.

MATERIALS & METHODS

This cross-sectional study used secondary data from the medical records of stroke patients at Pelni Hospital from January 2022 to December 2024. After the research team developed a proposal and received approval from the ethics committee (No. 157/EC-04/FK-06/UNIZAR/X/2025), researchers collected data on age, gender, risk factors (hypertension, diabetes mellitus, and dyslipidemia), atherosclerotic plaque, and the degree and location of stenosis in patients with recurrent ischemic stroke from the catheterization laboratory of Pelni Hospital, Jakarta. Inclusion criteria included recurrent ischemic stroke patients with carotid atherosclerotic plaque confirmed by DSA examination. Exclusion criteria included stroke patients without complete medical record documentation, recurrent ischemic stroke patients without atherosclerotic plaque, or those with massive steno-occlusive abnormalities resembling moyamoya on DSA.

Age and gender data were obtained from patient identification data in the patient's medical record. Atherosclerotic plaque is defined as a condition of impaired fat metabolism that causes lipoprotein deposition on the artery wall with an inflammatory reaction that results in thickening of the blood vessel wall.[11,12] From DSA, it will be concluded that there is a stable or unstable atherosclerotic plaque in the form of IPH (intraplaque haemorrhage) and ulcerative plaque. Carotid artery stenosis is defined as narrowing or blockage of blood flow in the carotid artery caused by plaque buildup. Stenosis that occurs is divided based on the severity of the blockage into mild (<30%), moderate (30-69%) and severe (70-99%).[7,16,17] Other risk factors such as hypertension, diabetes mellitus or dyslipidemia are taken from the patient's medical history data or in the examination data listed systolic blood pressure ≥140 mmHg and or diastolic ≥90 mmHg for hypertension.[18] Meanwhile, in diabetes mellitus, laboratory tests reveal an increase in fasting blood sugar levels >126 mg/dL or 2-hour post-prandial blood sugar >200 mg/dL or HbA1c >7%.[19] Furthermore, in dyslipidemia, total cholesterol levels are >200 mg/dL, triglycerides >150 mg/dL, HDL <40 mg/dL, or LDL >100 mg/dL.[20] These three risk factors are categorized as present or absent.

STATISTICAL ANALYSIS

Statistical analysis was performed using SPSS (Statistical Product and Science Service) version 29. Age data was numeric, while other categorical data included characteristics of carotid atherosclerotic plaque, degree of carotid stenosis, hypertension, diabetes mellitus, and dyslipidemia. Data are presented in frequency distributions and percentages. Eligible hypotheses were tested using the Chi-square test or the Fischer's exact test, as

appropriate. If it does not meet the requirements, the Mann Whitney test will be applied with a significant value if $p < 0.05$.[21]

RESULT

A total of 2,039 patients underwent digital cerebral angiography during the period January 2022-December 2024, of which 1,856 (91%) patients had ischemic stroke while the remaining 183 (9%) did not (haemorrhagic stroke, tumour, AVM, etc.). Of the 1,856 patients who experienced ischemic stroke, 141 patients had recurrent ischemic stroke who met the eligibility criteria in this study with a median age of 52 (40-72) years. Gender was predominantly male at 56.7% compared to female (43.3%), with a history of hypertension, diabetes mellitus type 2, and dyslipidemia at 83%, 36.2%, and 14.2%, respectively. In addition, the majority of patients had mild stenosis (78 people) compared to moderate (54 people) and severe (9 people). The most common locations of stenosis were in the anterior segment (135 individuals), namely the distal ICA, followed by the MCA M1, MCA M2, proximal ICA, and bifurcation. In the posterior segment, the most common location was the vertebrobasilar junction (3 out of 6 individuals). The most common plaque type in this study was stable plaque (n = 110, 78%) compared to unstable plaque (Table 1).

The Mann-Whitney test was used to compare the rankings between groups. The unstable atherosclerotic plaque group had a significantly higher ranking ($p = 0.01$) for severe stenosis compared to the stable atherosclerotic plaque group (89.29 vs. 65.85) (Table 2). Other confounding factors such as hypertension, diabetes mellitus, and dyslipidemia also had higher rankings compared to the group without these risk factors, with mean rankings of 71.82, 80.06, and 88.70, respectively. Of the three confounding factors, diabetes mellitus ($p = 0.024$) and dyslipidemia ($p = 0.017$) had significant results for involvement in the occurrence of more severe stenosis (Table 3).

Table 1. Subject characteristic

Characteristic Data	Recurrent Ischemic Stroke n = 141
Age	52 (40-72)
Gender	
Male	80 (56.7)
Female	61 (43.3)
Hypertension	
Yes	117 (83)
No	24 (17)
Diabetes Mellitus type 2	
Yes	51 (36.2)
No	90 (63.8)
Dyslipidemia	
Yes	20 (14.2)
No	121 (85.8)
Stenosis Degree	
Mild	78 (55.3)
Moderate	54 (38.3)
Severe	9 (6.4)
Anterior Circulation (n = 135)	
Stenosis CCA/ICA bifurcation	17 (12.1)
Stenosis ICA proximal	22 (15.6)
Stenosis ICA distal/terminal	37 (26.2)
Stenosis MCA M1	32 (22.7)
Stenosis MCA M2 superior/inferior truncus	27 (19.1)
Posterior Circulation (n = 6)	
Stenosis ostium vertebral	2 (1.4)
Stenosis v1-v4 vertebral	1 (0.7)
Stenosis vertebrobasilar junction	3 (2.1)

Atherosclerosis Plaque	
Stable	110 (78)
Unstable	31 (22)
- Ulcerative	13 (9.2)
- IPH (*intraplaque hemorrhage*)	18 (12.8)

Table 2. Bivariate analysis of atherosclerotic plaque by degree of stenosis (Mann Whitney)

	Stenosis Degree			Mean Rank	P value
	Mild	Moderate	Severe		
Atherosclerosis Plaque					
Unstable	10 (32.3)	16 (51.6)	5 (16.1)	89.29	0.01*
Stable	68 (61.8)	38 (34.5)	4 (3.6)	65.85	

***p value significant (<0.05)**

Table 3. Bivariate analysis of confounding factors with degree of stenosis (Mann Whitney)

	Stenosis Degree			**Mean Rank**	**P value**
	Mild	**Moderate**	**Severe**		
Hypertension					
Yes	64 (54.7)	44 (37.6)	9 (7.7)	71.82	0.550
No	14 (58.3)	10 (41.7)	0 (0)	67.00	
Diabetes Mellitus type 2					
Yes	23 (45.1)	21 (41.2)	7 (13.7)	80.06	0.024*
No	55 (61.1)	33 (36.7)	2 (2.2)	65.87	
Dyslipidemia					
Yes	7 (35)	9 (45)	4 (20)	88.70	0.017*
No	71 (58.7)	45 (37.2)	5 (4.1)	68.07	

*** p value significant (<0.05)**

DISCUSSION

Factors contributing to the high risk of recurrent stroke in Indonesia are similar to global findings, including uncontrolled hypertension, diabetes mellitus, dyslipidemia, smoking, obesity, and heart disease (including atrial fibrillation) as the main determinants. However, in this study, researchers only assessed the risk of hypertension, diabetes mellitus, and dyslipidemia, and focused on vascular abnormalities. One systematic review found that most recurrences occurred within the first 90 days of onset, while other studies report large variations between populations (reported recurrences range from approximately 5–20% in the first year to higher cumulative rates at 5–10 years, depending on the study setting).[22] This study did not include the time to recurrence because it aimed to assess vascular abnormalities in recurrent ischemic stroke and did not allow for a temporal analysis due to the lack of structured follow-up data in the secondary data.

Demographically, the patients in this study were predominantly aged 52 (40–72) years. This middle and older age group demonstrates a tendency toward increased stenosis and plaque formation, possibly related to the aging process. With increasing age, changes in endothelial dysfunction, decreased arterial elasticity, and the progression of atherosclerotic plaques increase susceptibility to luminal narrowing and turbulent blood flow, thus facilitating the occurrence of local emboli and recurrent focal perfusion disorders. Mechanisms of distal hypoperfusion, microemboli formation, and gradual stenosis progression increase the risk of recurrent stroke in this age group despite standard medical therapy.[2,3,5,23]

The study found a male predominance (56.7%) compared to females (43.3%). This predominance of men with stenosis and plaque on angiography may be related to a higher risk of atherosclerosis due to lifestyle factors such as alcohol consumption and smoking. Women are more likely to have metabolic disorders such as weight gain and

other vascular risk factors (hypertension, diabetes mellitus, dyslipidemia) due to hormonal influences [24,25]. Men are considered to be at greater risk for atherosclerotic plaque formation and large artery stenosis due to the lack of estrogen hormonal protection, a more atherogenic lipid profile, and higher levels of vascular inflammation. Lifestyle factors such as smoking and uncontrolled hypertension also contribute to accelerating the atherosclerotic process. The combination of severe stenosis, distal hypoperfusion, microemboli release from eccentric plaques, and progressive arterial narrowing puts men at greater risk of recurrent ischemic stroke than women.[24,26,27]

Risk factors: hypertension, diabetes mellitus, dyslipidemia

The confounding factors analysed in this study were hypertension, diabetes mellitus, and dyslipidemia, with higher scores in the group with risk factors than in the group without, with mean scores of 71.82, 80.06, and 88.70, respectively. Biologically, hypertension is known to play a role in plaque formation and stenosis through mechanisms of endothelial damage, chronic inflammation, and vascular remodeling.[28] However, this study did not find a statistically significant association with a p-value of 0.550. This may be due to the high prevalence of hypertension in almost all subjects (117 (83%) of the 141 subjects), thus reducing intergroup variation. Furthermore, hypertension tends to produce more stable fibrotic plaques, making its contribution to recurrent ischemic stroke less statistically significant.[29]

Dyslipidemia causes stenosis through the accumulation of low-density lipoprotein (LDL) in the arterial intima, which undergoes oxidation and triggers chronic inflammation, foam cell formation, and the growth of atherosclerotic plaques with lipid cores protruding into the lumen. In this study, dyslipidemia was found in 20 of 141 subjects (14.2%) with a mean significant score of 88.70 ($p = 0.017$) which resulted in a more severe degree of stenosis. At the site of turbulence, this process accelerates eccentric plaque formation and negative remodelling, resulting in further narrowing of the lumen. Stenosis due to dyslipidemia causes stroke through distal hypoperfusion, microemboli from irregular plaque surfaces, progression of chronic stenosis, and in some cases, plaque rupture.[30,31]

Atherosclerotic plaque and stenosis in recurrent ischemic stroke

This study demonstrates the importance of vascular structural abnormalities in the development of recurrent ischemic stroke, particularly intracranial stenosis and atherosclerotic plaques in large arteries. These findings align with evidence that atherosclerotic stenosis is a major risk factor for recurrent stroke, particularly in Asian populations, which have a higher prevalence of intracranial stenosis than Western populations.[32] Atherosclerotic plaques are divided into stable and unstable/vulnerable plaques. In this study, stable atherosclerotic plaques were more common in the population (110%, 78%) than unstable plaques. Stable plaques can contribute to recurrent stroke due to chronic stenosis that reduces distal perfusion, recurrent microemboli, endothelial dysfunction that results in mild segmental thrombosis, progression of fibrotic stenosis that narrows the lumen, and vulnerable or inadequate hemodynamic from the collateral side. Therefore, in the absence of rupture, the combination of hypoperfusion and microemboli from stable plaques can also contribute to the likelihood of recurrent stroke.[33-36] Therefore, plaque identification in stroke cases is essential for determining patient prognosis.

Most vulnerable plaques remain clinically inapparent, but can contribute to ischemic stroke. The use of DSA is considered superior to MRI for identifying plaque morphology of the atherosclerotic components of the intracranial carotid artery and its hemodynamics.[10,12] The unstable atherosclerotic plaque group had a

significantly higher (p = 0.01) score for severe stenosis compared to the stable atherosclerotic plaque group (89.29 vs. 65.85) in this study. Morphologically unstable atherosclerotic plaques have a lipid-rich necrotic core (LRNC), intraplaque haemorrhage (IPH), a thin fibrous cap, and plaque surface damage/ulceration, accelerating plaque progression, increasing fragility, and strongly associated with subsequent ipsilateral ischemic events. High inflammation and fragile neovascularization make plaques prone to rupture and generate large thrombi that suddenly worsen the degree of stenosis. Evidence from cohort studies and meta-analyses suggests that the presence of IPH visible on plaque MRI substantially increases the risk of recurrent ischemic events compared with plaques without IPH; some studies report a significant hazard ratio for IPH with respect to ipsilateral stroke/TIA. Therefore, assessing plaque components via imaging modalities provides additional prognostic information beyond stenosis size, which will help identify high-risk patients and thus facilitate more aggressive and personalized prevention strategies.[6,35,36]

The presence of carotid stenosis ≥50% in high-risk patients with ischemic stroke or TIA significantly increases the risk of recurrent ischemic stroke despite dual antiplatelet therapy (DAPT). Therefore, secondary prevention strategies are crucial.[9,27,37-39] Based on the North American Symptomatic Carotid Endarterectomy Trial (NASCET) and European Carotid Surgery Trial (ECST) criteria, the degree of carotid stenosis is divided into 3 criteria, namely mild stenosis (<30%), moderate stenosis (30-69%), and severe stenosis (70-99%).[7] The majority of patients in this study experienced mild stenosis (78 people) compared to moderate (54 people) and severe (9 people). The most common location of stenosis was in the anterior segment, namely the distal ICA, then MCA M1, MCA M2, proximal ICA, and bifurcation. The ICA is susceptible to stenosis, possibly due to its large caliber with turbulent flow patterns, especially in the carotid bifurcation, so this area experiences high shear stress that triggers focal endothelial dysfunction. The distal ICA location has high flow turbulence, increasing the susceptibility to rupture and resulting in more severe stenosis than other areas. The next impact occurs in the distal flow, namely MCA M1, so that severe stenosis in the distal ICA or M1 is generally associated with unstable plaque morphology and can cause emboli that spread distally.[17,34,36] Furthermore, in the posterior segment of this population, the most common was found in the vertebrobasilar junction (3 of 141 subjects). Posterior circulation stroke is known to have a lower prevalence with a worse prognosis than stenosis or plaque in the anterior circulation area. In another study, atherosclerosis in the vertebrobasilar was associated with a high risk of recurrent stroke despite medical therapy, amounting to 10-15% of patients within 3 years.[40]

Conversely, diabetes was found in 51 (36.2%) of the 141 subjects, which was assessed to cause a more severe degree of stenosis compared to subjects without diabetes, with a mean score of 80.06 (p = 0.024). These results align with previous studies that assessed that diabetes accelerates arterial stenosis through mechanisms of chronic hyperglycemia, endothelial dysfunction, atherogenic dyslipidemia, and inflammation, leading to the formation of diffuse and progressive atherosclerotic plaques. Stenosis in patients with diabetes tends to be longer and thinner, resulting in relatively stable plaque morphology. However, the resulting plaques produce poorer collaterals due to low perfusion and impaired autoregulation, facilitating the formation of microemboli, which increase the risk of recurrent stroke.[29]

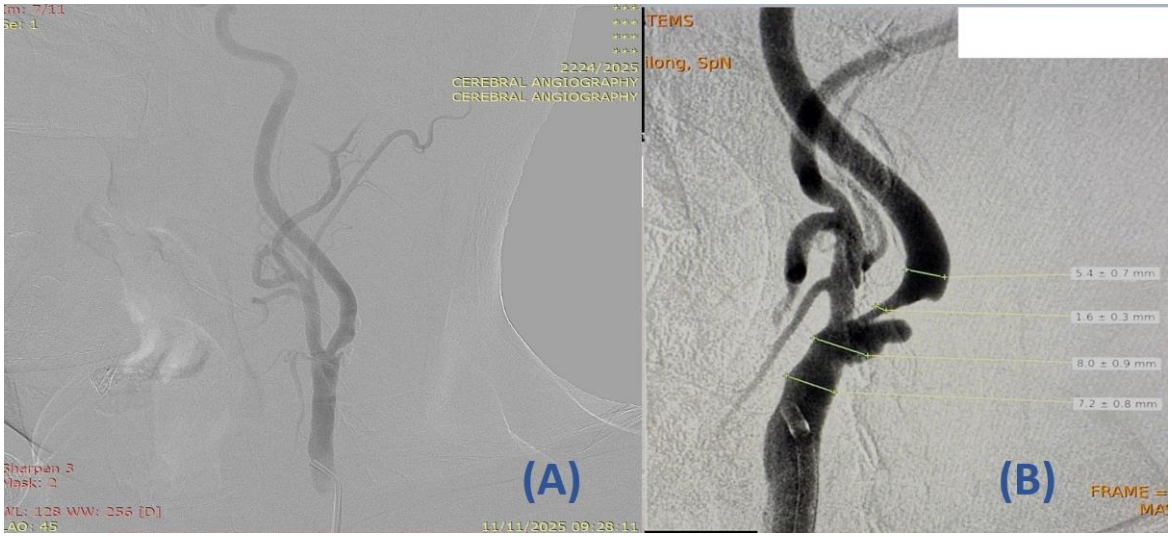

Figure 1. Plaque profile:
(A) Ulcerative plaque at the LICA/LCCA bifurcation; (B) Calcified plaque at the RICA/RCCA bifurcation

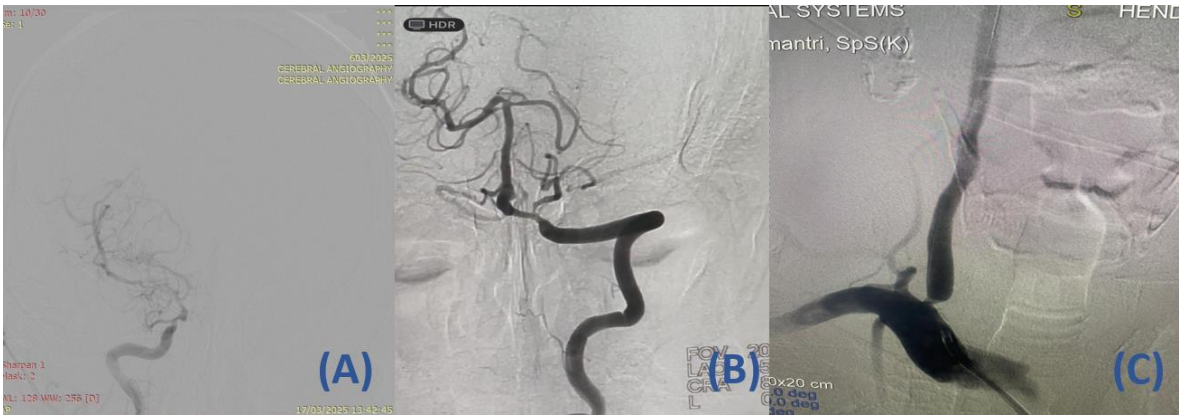

Figure 2. Stenosis profile:
(A) Severe stenosis in the Right ICA supraclinoid segment; (B) Stenosis with atherosclerotic plaque at the Vertebrobasilar Junction; (C) Severe Stenosis with Calcified Plaque in the Right Vertebral Artery Ostium

Dyslipidemia causes stenosis through the accumulation of low-density lipoprotein (LDL) in the arterial intima, which undergoes oxidation and triggers chronic inflammation, foam cell formation, and the growth of atherosclerotic plaques with lipid cores protruding into the lumen. In this study, dyslipidemia was found in 20 of 141 subjects (14.2%) with a mean significant score of 88.70 ($p = 0.017$), leading to more severe stenosis. At sites of turbulence, this process accelerates eccentric plaque formation and negative remodeling, resulting in further narrowing of the lumen. Stenosis due to dyslipidemia causes stroke through distal hypoperfusion, microemboli from irregular plaque surfaces, progression of chronic stenosis, and in some cases, plaque rupture.[30,31]

Overall, the cerebral angiographic findings in this study reinforce the understanding that recurrent ischemic stroke is generally associated with atherosclerotic vascular abnormalities, particularly stenosis of large intracranial arteries. Early identification through angiography is crucial for determining secondary prevention strategies, including optimizing antiplatelet therapy, controlling risk factors, and considering revascularization interventions in cases of severe stenosis. Therefore, cerebral angiography remains an essential modality for assessing the etiology and risk

of recurrence in patients with recurrent ischemic stroke.

Strengths and Weaknesses of the Study

To the best of the authors' knowledge, this study is the first pilot study to present cerebral angiographic findings using DSA in patients with recurrent ischemic stroke in Indonesia. However, because the study variables are limited in describing the overall DSA profile of recurrent ischemic stroke patients treated at a single stroke referral center, further multicenter studies incorporating additional variables are needed to explore relationships between variables and identify independent factors that may influence recurrent ischemic stroke.

CONCLUSION

Unstable atherosclerotic plaque, diabetes mellitus, and dyslipidemia were associated with a higher risk of severe stenosis in the population of this study. Cerebral evaluation using DSA should be considered in all stroke survivors to identify stenosis due to atherosclerotic plaque, which is a risk factor for recurrent stroke. Controlling other vascular risk factors, such as diabetes mellitus and dyslipidemia, is also crucial for preventing recurrent stroke and improving the patient's quality of life.

Declaration by Authors

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