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Short Communication

Cerebral artery stenosis and neurological outcomes after anticoagulant and antiplatelet therapy in acute ischemic stroke: A digital subtraction angiography-based study in Indonesia

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Abstract

Acute ischemic stroke (AIS) is a leading cause of morbidity and mortality, with cerebral artery stenosis serving as an important prognostic factor. While revascularization therapies benefit selected patients, most rely on pharmacological strategies. However, evidence regarding the effect of sequential anticoagulant–antiplatelet therapy on vascular stenosis and neurological outcomes remains limited. The aim of this study was to evaluate changes in cerebral artery stenosis, assessed using digital subtraction angiography (DSA), and neurological deficits, assessed by the National Institutes of Health Stroke Scale (NIHSS), in patients with first-onset AIS treated with anticoagulant and antiplatelet therapy. A prospective cohort study was conducted involving 35 patients who received low-molecular-weight heparin or warfarin for seven days, followed by 90 days of oral antiplatelet therapy (aspirin or clopidogrel). Sixteen patients consented to repeat DSA at 90 days. Among these, the median stenosis decreased from 44.5% (30–90%) to 44.0% (20–90%) (p=0.003). In the full cohort (n=35), the median NIHSS improved from 10 (5–17) at baseline to 9 (2–14) at 90 days (p<0.001). Correlation analysis demonstrated a positive but non-significant association between stenosis reduction and NIHSS improvement (r=0.474, p=0.064). These findings suggest that sequential anticoagulant–antiplatelet therapy in first-onset AIS was associated with a modest but statistically significant reduction in arterial stenosis and meaningful improvement in neurological function. Although vascular and clinical outcomes were not significantly correlated, the observed trend highlights the importance of structured pharmacological therapy and the potential role of serial vascular imaging in follow-up care.

Keywords: Acute ischemic stroke, anticoagulant, antiplatelet, NIHSS, cerebral artery stenosis

Introduction

Stroke continues to represent a major global health problem. According to the Global Burden of Disease (GBD) 2019, stroke accounted for more than 12 million incident cases and 6.5 million deaths worldwide, making it the second leading cause of mortality and the third leading cause of disability-adjusted life years (DALYs) lost [1]. The burden is particularly heavy in low- and

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middle-income countries (LMICs), where more than 80% of cases and deaths occur [2]. In Indonesia, stroke ranks as the leading cause of death, with age-standardized mortality exceeding 190 per 100,000 population, one of the highest in Southeast Asia [3]. These data highlight the urgent need for effective diagnosis and treatment strategies in acute ischemic stroke (AIS).

Cerebral artery stenosis plays a pivotal role in the pathogenesis and recurrence of AIS [4,5]. Intracranial atherosclerotic stenosis is a major AIS mechanism and is associated with high recurrence risk and mortality [5]. The severity of arterial narrowing is not only a predictor of outcome but also an important factor guiding therapeutic decisions, with severe stenosis repeatedly associated with higher recurrence risk [6]. Accurate assessment of stenosis severity is therefore crucial in both clinical management and prognostication. Among available imaging modalities, digital subtraction angiography (DSA) remains the gold standard for evaluating both intracranial and extracranial vessels [7]. Although non-invasive techniques such as computed tomography (CT) angiography and magnetic resonance (MR) angiography are widely used, DSA remains the reference standard due to its superior accuracy in quantifying stenosis, detecting vessel wall abnormalities, and guiding endovascular interventions [7,8].

The degree of neurological deficit remains the most immediate and clinically relevant measure of stroke severity [9]. The National Institutes of Health Stroke Scale (NIHSS) is the most widely adopted tool for assessing neurological impairment, offering a standardized method to quantify motor, sensory, and cognitive functions [9-11]. Baseline NIHSS scores correlate strongly with long-term functional outcomes, and changes in NIHSS scores over time are sensitive markers of treatment response [12]. Several studies have shown that NIHSS measurements within the first 24 hours after therapy serve as the strongest predictors of 90-day functional status, outperforming baseline scores alone [12-14].

Antithrombotic therapy is the cornerstone of AIS management [15]. Anticoagulants act by inhibiting the coagulation cascade, while antiplatelet agents reduce platelet aggregation, both aiming to prevent clot propagation and recurrent ischemia [16]. Current literature has shown that routine use of anticoagulation in acute stroke does not provide a significant net benefit and increases the risk of bleeding [17]. Conversely, antiplatelet therapy, especially dual regimens initiated in the acute phase of minor ischemic stroke or transient ischemic attack, has demonstrated efficacy in reducing recurrent stroke [18-20]. Clinical guidelines therefore recommend individualized use of anticoagulants and antiplatelets depending on stroke etiology, vascular imaging findings, and risk of hemorrhage [21-23].

Despite advances in stroke management, gaps remain in understanding how radiological and clinical parameters change after antithrombotic therapy. Evidence integrating DSA-based evaluation of cerebral artery stenosis with NIHSS-based neurological assessment following anticoagulant and antiplatelet therapy remains scarce. Such an approach may provide a more comprehensive picture of treatment effects by linking vascular improvement with functional recovery. Therefore, the aim of this study was to evaluate changes in cerebral artery stenosis, assessed using DSA, and neurological deficits, assessed using NIHSS, in patients with acute ischemic stroke treated with anticoagulant and antiplatelet therapy.

Methods

Study design and setting

An observational prospective cohort study was conducted in the Department of Neurology, Dr. Zainoel Abidin Hospital, Banda Aceh, Indonesia. The study enrolled adult patients (≥18 years) with first-ever AIS who underwent DSA to assess cerebral artery stenosis. Eligible participants demonstrated measurable intracranial or extracranial arterial stenosis on DSA, classified using the North American Symptomatic Carotid Endarterectomy Trial (NASCET) criteria [24]. All patients received a standardized antithrombotic protocol consisting of low-molecular-weight heparin or warfarin for seven days, followed by a 90-day course of oral antiplatelet therapy (aspirin or clopidogrel). Neurological status was assessed using the NIHSS at admission (day 0) and at day 90 to monitor clinical outcomes.

Sample size and patients' criteria

Consecutive sampling was used to reflect the center caseload during the recruitment window (feasibility-based sample size). No a priori power calculation was performed, given the exploratory design. With the available sample and α=0.05 (two-sided), the study provides approximately 80% power to detect a within-subject standardized mean change of ~0.5 in NIHSS (paired comparison) and a correlation of ~0.45 between change in stenosis and change in NIHSS. Inclusion criteria were: (1) AIS patients aged ≥18 years; (2) first-ever ischemic stroke; (3) no prior history of stroke or hemorrhagic events; (4) initiation of anticoagulant or antiplatelet therapy during admission; and (5) confirmed diagnosis of AIS based on clinical and radiological findings. Patients who had contraindications to antithrombotic therapy were excluded.

Study procedure and data collection

At baseline (day 0), all participants underwent DSA using a biplane digital subtraction angiography system Philips Allura Xper FD20 (Philips Healthcare, Best, The Netherlands) following standard institutional protocol. Nonionic contrast medium was administered intra-arterially, and angiographic projections were obtained in at least two planes to ensure accurate lumen visualization. The degree of cerebral artery stenosis was calculated according to the NASCET criteria [24].

Neurological deficits were assessed using NIHSS scale at baseline and at day 90. Eligible patients received low-molecular-weight heparin (1 mg/kg twice daily, subcutaneous) or warfarin (dose titrated to INR 2.0–3.0) for seven days, followed by a 90-day course of single antiplatelet therapy with either aspirin 80–100 mg daily or clopidogrel 75 mg daily. To ensure data completeness, a standardized follow-up protocol was implemented. Patients were scheduled for outpatient visits on day 90, during which NIHSS scoring was repeated. Participants who missed appointments were contacted by telephone and reminded of their scheduled evaluation.

Study variables

The primary independent variable was the use of a sequential anticoagulant–antiplatelet regimen, defined as administration of low-molecular-weight heparin (enoxaparin 1 mg/kg subcutaneously every 12 hours) or warfarin (oral, titrated to achieve INR 2.0–3.0 with daily monitoring) for seven days, followed by a 90-day course of oral antiplatelet therapy with either aspirin 80–100 mg once daily or clopidogrel 75 mg once daily. The dependent variables consisted of neurological and radiological outcomes. Neurological outcome was assessed using the NIHSS scale at admission (day 0) and at day 90, with the change in NIHSS (ΔNIHSS) representing clinical improvement over time. NIHSS scale is a standardized 15-item scale that quantifies stroke-related neurological deficits. Scores range from 0 to 42, where 0 indicates no neurological deficit and 42 represents the most severe deficit [25]. Higher scores reflect greater stroke severity, while lower scores indicate milder deficits or clinical improvement [25]. The radiological outcome was measured as the degree of cerebral artery stenosis on DSA, expressed as a percentage, and classified according to the NASCET criteria [24].

Statistical analysis

Continuous variables were expressed as mean and standard deviation (SD) or median (min-max) depending on distribution, and categorical variables as frequencies and percentages. Changes in stenosis and NIHSS scores were analyzed using paired t-test or Wilcoxon signed-rank test. Comparisons between treatment groups were performed with independent t-test, Mann-Whitney U test, or chi-square test, as appropriate. Correlation between changes in stenosis and NIHSS improvement was assessed using Pearson or Spearman correlation test. A p-value<0.05 was considered statistically significant. Data were analyzed using SPSS version 26 (IBM SPSS, New York, USA).

Results

Characteristics of the included patients

A total of 35 patients were included, and their characteristics are presented in **Table 1**. The mean age was 54.1±10.0 years, and most participants were male (74.3%). Hypertension (60.0%) was

the most common comorbidity, followed by dyslipidemia (40.0%) and diabetes mellitus (31.4%); 37.1% had a smoking history. The median baseline NIHSS score was 10 (5–17). Stroke locations included the left vertebral artery (25.7%), left middle cerebral artery (MCA) (20.0%), right MCA (14.3%), left internal carotid artery (ICA) (11.4%), and others such as anterior cerebral artery (ACA), or posterior cerebral artery (PCA) (28.6%) (**Table 1**). Repeat DSA at day 90 was successfully completed in 16 of 35 patients (45.7%), with the remainder declining the procedure.

Table 1. Characteristics of acute ischemic stroke (AIS) patients included in the study (n=35)

Variable	Frequency (%)
Age (years), mean±SD	54.14±10.03
Sex	
Male	26 (74.3)
Female	9 (25.7)
Comorbidities	
Hypertension	21 (60.0)
Dyslipidemia	14 (40.0)
Diabetes mellitus	11 (31.4)
Smoking history	
Yes	13 (37.1)
No	22 (62.9)
Initial NIHSS score, median (min-max)	10 (5–17)
Stroke location	
Left vertebral artery	9 (25.7)
Left middle cerebral artery	7 (20.0)
Right middle cerebral artery	5 (14.3)
Left internal carotid artery	4 (11.4)
Others (anterior cerebral artery, posterior cerebral artery, and others)	10 (28.6)

NIHSS: National Institutes of Health Stroke Scale

Cerebral artery stenosis and neurological outcomes after anticoagulant and antiplatelet therapy in acute ischemic stroke

Among the 16 AIS patients who consented to repeat DSA, the median degree of cerebral artery stenosis significantly decreased from 44.5% (30–90%) to 44.0% (20–90%) (p=0.003) (**Table 2**). In the full cohort of 35 patients, the median NIHSS score improved from 10 (5–17) to 9 (2–14) after 90 days of therapy (p<0.001), indicating significant neurological recovery (**Table 2**).

Table 2. Comparison of cerebral artery stenosis and National Institutes of Health Stroke Scale (NIHSS) score before and after anticoagulant-antiplatelet therapy.

Variable	Before therapy Median (min-max)	After therapy Median (min-max)	p-value [a]
Cerebral artery stenosis (%) (n=16)	44.5% (30–90)	44.0% (20–90)	0.003
NIHSS score (n=35)	10 (5–17)	9 (2–14)	<0.001*

[a] Analyzed using Wilcoxon signed-rank test
*Statistically significant at p<0.05

Correlation between changes in cerebral artery stenosis and neurological outcomes after anticoagulant and antiplatelet therapy in acute ischemic stroke

Spearman correlation analysis was performed in 16 patients with complete DSA and clinical data to assess the association between changes in cerebral artery stenosis and NIHSS improvement. The results demonstrated a positive but non-significant correlation (r=0.474, p=0.064), indicating that vascular changes may contribute to, but do not fully account for, neurological recovery.

Discussion

Anticoagulation was initiated selectively, guided by imaging findings and clinical risk assessment. Patients with evidence of high-grade arterial stenosis, intraluminal thrombus, or cardioembolic sources with high early recurrence risk (e.g., atrial fibrillation, intracardiac thrombus) were prioritized for anticoagulation during the first seven days, based on individualized clinical decision-making. This targeted approach reflects guideline recommendations that discourage

routine anticoagulation for all AIS patients but allow for short-term use in select high-risk situations to prevent clot propagation and early recurrent ischemia [22].

This study demonstrated that a sequential antithrombotic regimen, consisting of short-term anticoagulation followed by antiplatelet therapy, may provide measurable vascular and clinical benefits in patients with first-onset AIS. The finding of a statistically significant reduction in arterial stenosis, though modest in magnitude (44.5% to 44.0%), suggests that early medical therapy can influence vascular remodeling processes. Importantly, clinical improvement, reflected in the significant reduction of NIHSS scores over 90 days, was observed in parallel. Together, these findings indicated that pharmacological therapy has the potential to contribute not only to secondary prevention but also to vascular stabilization and functional recovery in AIS.

The observed vascular improvement can be plausibly attributed to the complementary actions of anticoagulant and antiplatelet therapy. Anticoagulants such as low-molecular-weight heparin or warfarin act by reducing fibrin generation and inhibiting thrombus propagation, thereby facilitating the resolution of acute or superimposed thrombus [26]. Antiplatelet agents, such as aspirin or clopidogrel, inhibit platelet aggregation and prevent further microthrombus formation at sites of endothelial disruption [27]. This sequential strategy may provide a synergistic effect, allowing initial stabilization of the acute thrombotic process followed by long-term suppression of platelet-mediated arterial occlusion. The fact that measurable stenosis reduction was captured by DSA strengthens the argument that these pharmacological agents can exert structural effects on diseased vessels, particularly in patients with non-occlusive lesions.

The significant decrease in NIHSS scores supports the concept that hemodynamic stability achieved by medical therapy can contribute to functional recovery [28]. Although the correlation between stenosis reduction and neurological improvement did not reach statistical significance (r=0.474, p=0.064), the positive trend suggests that vascular healing may partly underpin clinical gains. Larger studies with higher statistical power and adjunctive imaging modalities, such as CT-scan or magnetic resonance imaging (MRI) perfusion, could better elucidate the relationship between anatomical improvement and functional outcomes [29,30]. It is also important to recognize that neurological recovery after stroke is influenced by multiple factors beyond proximal vessel patency [29,30]. Collateral circulation, infarct topography, lesion volume, and intrinsic neuroplastic processes play pivotal roles in determining the trajectory of recovery [29-32]. Patients with robust collateral networks and smaller infarct cores have been shown to recover more favorably, even when significant stenosis persists [32].

The discrepancy between anatomical and clinical improvements observed in this study highlights the complex interplay between vascular and neural factors. Clinical improvement in some patients may occur despite minimal anatomical change, likely mediated by compensatory mechanisms such as angiogenesis, microvascular remodeling, synaptic reorganization, and enhanced neuroplasticity [29,31,33]. Conversely, failure of neurological recovery in the presence of improved patency may be explained by factors such as large infarct size, impaired collaterals, or irreversible neuronal injury [32,34]. These findings reinforce the importance of interpreting stenosis regression and neurological improvement as complementary but distinct domains of stroke recovery [35].

The present study findings are consistent with prior evidence supporting intensive medical management in stroke. The Stenting and Aggressive Medical Therapy for Intracranial Artery Stenosis (SAMMPRIS) trial demonstrated that aggressive pharmacological therapy significantly reduced recurrent stroke risk compared to endovascular stenting in patients with high-grade intracranial stenosis [36]. While the SAMMPRIS trial focused primarily on clinical outcomes [36], the present study added nuance by showing that anatomical changes in stenosis may also be observed following medical therapy. This observation aligns with emerging evidence that antithrombotic regimens can contribute not only to secondary prevention but also to dynamic vascular remodeling and stabilization [18-20].

Another notable aspect of this study is the use of DSA for serial vascular assessment. Although computed tomography angiography (CTA) and magnetic resonance angiography (MRA) are more widely used in clinical practice due to their safety and accessibility, DSA remains the reference standard for evaluating vascular anatomy [7]. Its superior spatial and temporal resolution allows for detailed visualization of luminal changes, vessel wall irregularities, and

mural thrombi [7,8]. This makes DSA uniquely suited to research settings where subtle anatomical changes must be documented. The ability to capture such changes strengthens the validity of the present study findings, although it is acknowledged that the invasiveness of DSA limits its utility in routine follow-up.

Despite its contributions, this study has several limitations. The small sample size, particularly the 16 patients who underwent repeat DSA, restricts the generalizability of the vascular findings. It should be acknowledged that although DSA is the gold standard for assessing cerebrovascular stenosis, it is invasive and may not be feasible for routine follow-up, highlighting the need for less invasive modalities such as CTA or MRA for longitudinal monitoring. Moreover, important variables such as statin use, blood pressure control, and glycemic management were not stratified, despite their known impact on vascular remodeling and endothelial function. It is therefore possible that the observed vascular improvements were influenced by unmeasured confounders. Furthermore, the 90-day follow-up period may have been insufficient to capture the full trajectory of vascular and neurological recovery.

Future research should address the limitations of this study by including larger multicenter cohorts, extending follow-up duration, and integrating multimodal imaging approaches. High-resolution vessel wall MRI could provide additional information on plaque composition and stability, while perfusion studies could clarify the relationship between anatomical changes and cerebral hemodynamics. Furthermore, biomarker studies investigating endothelial dysfunction, inflammation, and neuroplasticity may help identify biological pathways through which medical therapy contributes to recovery. Such integrative approaches could refine patient selection, optimize therapeutic regimens, and guide personalized treatment strategies in AIS.

Conclusion

Sequential anticoagulant followed by antiplatelet therapy in AIS patients was associated with modest but statistically significant reductions in stenosis and improvement in NIHSS scores. Although the correlation between anatomical and clinical outcomes did not reach statistical significance, the observed trend suggests potential benefit. Given the small sample size and modest vascular changes, these findings should be interpreted with caution and considered hypothesis-generating, highlighting the need for larger studies with serial vascular imaging to confirm these results.

Ethics approval

The protocol of the present study was reviewed and approved by Ethical Committee for Health Research, Dr. Zainoel Abidin Hospital, Banda Aceh, Indonesia (Approval number: 197/ETIK-RSUDZA/2024).

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Competing interests

All authors declare that there are no conflicts of interest.

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Underlying data

Derived data supporting the findings of this study are available from the corresponding author on request.

Declaration of artificial intelligence use

This study used artificial intelligence (AI) tool and methodology of which AI-based language model ChatGPT was employed in the language refinement (improving grammar, sentence structure, and readability of the manuscript). We confirm that all AI-assisted processes were critically reviewed by the authors to ensure the integrity and reliability of the results. The final decisions and interpretations presented in this article were solely made by the authors.

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