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Original article

Serum vascular endothelial growth factor (VEGF) levels and neuroimaging markers in acute ischemic stroke: A cross-sectional analysis of hounsfield units, infarct volume, and clinical severity

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Abstract. *Background and aim:* Vascular Endothelial Growth Factor (VEGF) is a key mediator of angiogenesis, neurogenesis, and blood–brain barrier (BBB) regulation in acute ischemic stroke (AIS). While elevated VEGF may represent a compensatory response, excessive expression can exacerbate tissue injury and cerebral edema. This study investigated the relationship between serum VEGF levels, Hounsfield units (HU), infarct volume, and neurological severity using the National Institutes of Health Stroke Scale (NIHSS). *Methods:* This observational, analytical, cross-sectional study was conducted at Dr. Wahidin Sudirohusodo Hospital and affiliated teaching hospitals in Makassar, Indonesia, from September 2025 until sample completion. Thirty-two AIS patients aged 18–65 years, with symptom onset <7 days, were included. Serum VEGF was measured using ELISA, HU values using region-of-interest (ROI) analysis, and infarct volume with the Broderick ABC/2 method on non-contrast CT. Demographics, vascular risk factors, stroke onset, and NIHSS were recorded at admission. Correlations were assessed with Spearman's rho; $p < 0.05$ was considered significant. *Results:* The mean age was 56.7 ± 8.8 years, with 59.4% male. Most patients presented on day 1 (50%). Common risk factors were dyslipidemia (87.5%), hypertension (68.8%), and smoking (40.6%). Median values were VEGF 213 pg/ml, HU 19, infarct volume 15.4 cm^3, and NIHSS 7. VEGF showed a moderate negative correlation with HU ($r = -0.419$, $p = 0.016$), a moderate positive correlation with infarct volume ($r = 0.447$, $p = 0.010$), and a weak positive correlation with NIHSS ($r = 0.358$, $p = 0.044$). *Conclusions:* Higher VEGF levels are associated with larger infarct volumes and lower HU values, suggesting greater tissue damage and BBB disruption. The weak correlation with severity highlights the influence of lesion site, collateral flow, and compensatory responses. VEGF may serve as a biomarker for tissue injury progression, supporting integrated imaging and clinical evaluation in early AIS management. (www.actabiomedica.it)

Key words: acute ischemic stroke, biomarker, blood brain barrier, hounsfield unit, infarct volume, nihss, vascular endothelial growth factor

Introduction

Stroke is the second leading cause of death and the third leading cause of disability worldwide, with 12.2 million new cases of stroke each year. In Europe, projections estimate an increase in the number of stroke survivors, which will reach 4,631,050 people by 2035 (1). The need for robust, non-invasive biomarkers that can be used to diagnose and predict functional outcomes of stroke is increasing (2). In Southeast Asia, the incidence of ischemic stroke per 100,000 population in 13 countries continues to increase every year. Indonesia initially ranked third in terms of the highest incidence rate and then experienced significant growth. Based on the 2023 Indonesian Health Survey, the prevalence of stroke reached 8.3%, with the highest prevalence in the province of D.I. Yogyakarta (11.4%) and the province of South Sulawesi in 12th place (7.9%) (3,4). Ischemic stroke occurs due to blockages in the cerebral arteries that inhibit blood and oxygen flow to the brain, triggering tissue damage through mechanisms of excitotoxicity, oxidative stress, inflammation, and neuronal apoptosis (5,6). Ischemic injury to the nerve compartment is accompanied by blood vessel leakage, microvascular inflammation, and endothelial apoptosis. The reformation of functional microvasculature will promote stroke recovery. Angiogenesis and vascular maturation are regulated by Vascular Endothelial Growth Factor (VEGF) and Angiopoietin 1 (7). VEGF is a protein biomolecule that plays an important role in the body's response to ischemic injury (hypoxic conditions). VEGF plays a role in the processes of angiogenesis and neurogenesis, which can improve blood supply to the infarct area, but on the other hand, it can cause blood-brain barrier (BBB) disruption, which has the potential to aggravate cerebral edema, increase infarct volume, and worsen the patient's condition. Increased VEGF levels after ischemic stroke reflect the activation of the biological compensation system against cerebral hypoxia (8). A study by Hu et al. showed that higher serum VEGF levels were found in the acute phase of ischemic stroke and correlated with the formation of neovascularization in the infarct area, although the effect can be both protective and worsening edema, depending on the level of expression and the phase of stroke (9). Therefore, VEGF is considered a potential biomarker candidate for assessing the progression and prognosis of ischemic stroke. Biological changes such as fluctuations in VEGF levels need to be combined with radiological parameters to comprehensively assess brain tissue damage, for example by using non-contrast computed tomography (CT) to measure Hounsfield Units (HU) to quantify the degree of ischemia and predict infarct volume and severity. CT measures the level of X-ray attenuation of brain tissue in HU, where decreased HU in ischemic areas indicates edema and loss of cellular integrity, so that changes in HU can be used as an early prognostic indicator of stroke (10,11). Infarct volume, measured through volumetry on CT or MRI, is a measure of the extent of brain tissue damage due to blood flow obstruction. This volume correlates positively with the degree of disability and mortality, so it is often used as a quantitative endpoint in acute stroke research (2). Systematic analysis shows a significant positive correlation between VEGF levels and national institutes of health stroke scale (NIHSS) scores in the acute phase of stroke. Research indicates that increased VEGF levels in the acute phase of ischemic stroke are associated with higher NIHSS scores, indicating more severe neurological deficits (12). Given the important role of VEGF in angiogenesis, neuroprotection, neurogenesis, and vascular permeability regulation in the acute phase of ischemic stroke, this study aims to evaluate the relationship between VEGF levels and HU values, infarct volume, and stroke severity, to support its use as a potential biomarker in more personalized diagnostic and therapeutic strategies.

Material and methods

Study design

This study is an analytical observational study with a cross-sectional design conducted at Wahidin Sudirohusodo General Hospital and affiliated teaching hospitals in Makassar, with a total sample of 32 patients who met the inclusion and exclusion criteria. The inclusion criteria for sampling were: patients with acute ischemic stroke (AIS) with onset within 1-7 days; individuals aged 18-65 years who had experienced their

first ischemic stroke and were willing to participate in the study and sign an informed consent form. The diagnosis of AIS was confirmed based on neurological physical examination and neuroimaging, enabling accurate case identification for further analysis.

Sample criteria

The population in this study consisted of all patients with AIS based on the results of neurological physical examinations and neuroimaging examinations (head CT scan without contrast) who were hospitalized in the neurology ward of Dr. Wahidin Sudirohusodo General Hospital in Makassar and other educational network hospitals in the city of Makassar. The variables in this study included serum VEGF and neuroimaging indicators, namely HU and infarct volume, as well as stroke severity using the NIHSS scale to assess the severity of stroke upon admission to the hospital. Patients were recruited based on strict inclusion criteria to obtain a relatively homogeneous study population. To minimize confounding factors that could affect serum VEGF levels, imaging findings, and clinical stroke outcomes, exclusion criteria were established, including patients with recurrent ischemic stroke, hyperacute stroke, a history of infectious diseases, malignancies, autoimmune diseases, and neurodegenerative diseases.

Research procedure

The diagnosis of AIS is based on physical examination of clinical signs and symptoms, as well as a non-contrast CT scan of the head showing hypodense lesions. Venous blood samples are collected within the first 24 hours after the patient is admitted to the hospital, then processed to obtain serum which is subsequently analyzed using the enzyme-linked immunosorbent assay (ELISA) method.

ELISA test

Venous blood serum samples were examined using the ELISA method at the Hasanuddin University Medical Research Center Laboratory of Hasanuddin University to measure serum VEGF levels. VEGF levels were measured using a product from Thermo Fisher Scientific Inc. (Waltham, MA, USA) with catalog number KHG0111, in accordance with the manufacturer's guidelines. The results were read using an ELISA Microplate Reader 357 from Thermo Fisher Scientific Inc. (Shanghai, China) at a wavelength of 450 nm.

Severity assessment

Assessment of stroke severity upon admission was performed using the NIHSS scale in patients with acute ischemic stroke. The NIHSS score was assessed within the first 24 hours after the patient was admitted. Interpretation of the NIHSS score was divided into four groups: mild 0-4, moderate 5-14, severe 15-25, and very severe >25.

Imaging methodology

A non-contrast head CT scan is used to evaluate HU values and infarct volume. HU measurements are taken by placing three oval-shaped regions of interest (ROI) on the infarct area that is clearly visible on the axial slice; the average value of the three measurements is recorded to improve accuracy (Figure 1). Infarct volume is calculated using the ABC/2 method on axial slices, with additional manual tracing of the infarct perimeter when necessary to improve measurement accuracy (Figure 2). Two independent assessors performed the HU value and volume measurements, and inter-rater reliability was evaluated using the intraclass correlation coefficient (ICC). The type of CT scan used was a GE (General Electric) High-Speed dual slice multi-detector CT scan, with model number 5114671-2 and serial number 139669HM6; Siemens Somatom Go Top 128 Slice CT scan; Varex GS-4570 CT scan, with tube serial number 18525-M8, 64 slices, and Canon TSX 303A CT scan with serial number BCD 1942544, 64 slices. The research flowchart is shown in Figure 3, which outlines the methodology used in this study.

Data and statistical analysis

Statistical data analysis was performed to assess the relationship between serum VEGF and HU values, infarct volume, and severity using the NIHSS score.

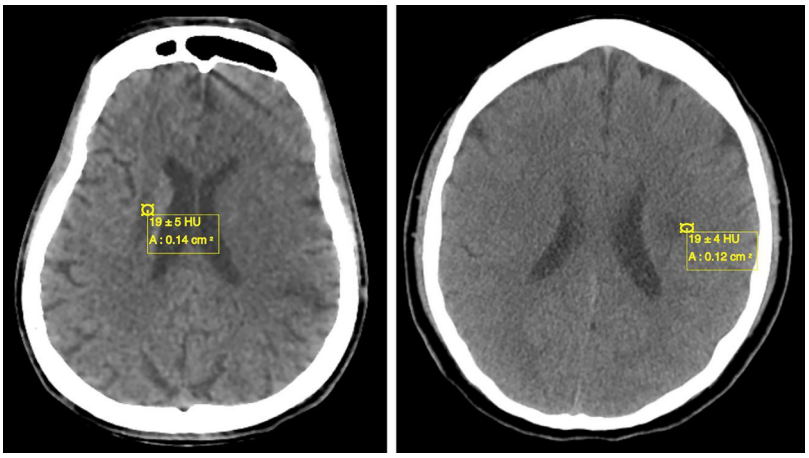

Figure 1. Illustration of a non-contrast computed tomography (CT) scan demonstrating the assessment of hypodense regions consistent with cerebral infarction. The degree of tissue attenuation within these areas is quantified through Hounsfield Unit (HU) measurement, obtained by placing a yellow-colored region of interest (ROI) marker directly over the affected zone for precise evaluation.

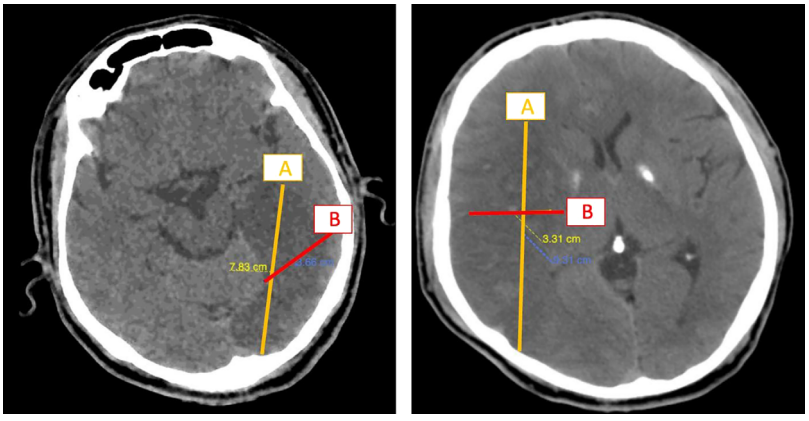

Figure 2. Depiction of the method used to calculate infarct volume on axial computed tomography (CT) images. The measurement is performed by applying the commonly used formula (A×B×C)/2(A \times B \times C) / 2(A×B×C)/2, where dimension *A* represents the greatest diameter of the lesion, *B* is the diameter perpendicular to *A*, and *C* corresponds to the vertical extent of the infarct across the involved slices. This formula provides a practical approximation of the total infarct volume, allowing clinicians and researchers to quantify the burden of ischaemic injury in a reproducible manner.

Data distribution was tested for normality (Shapiro-Wilk test, which is recommended for small sample sizes (n < 50), before correlation analysis). All data were found to be non- normally distributed, and Spearman's rank correlation test was used to examine non- parametric relationships. Statistical analysis was performed using IBM Statistical Package for the Social Sciences (SPSS) version 2.7 (IBM Corp., Armonk, NY, USA). Statistical significance was set at a p-value <0.05, meaning that the relationship between the variables studied could be considered statistically significant. Demographic, clinical characteristics, and laboratory findings data were summarized using descriptive statistics, and inferential statistical tests were used to determine the strength and

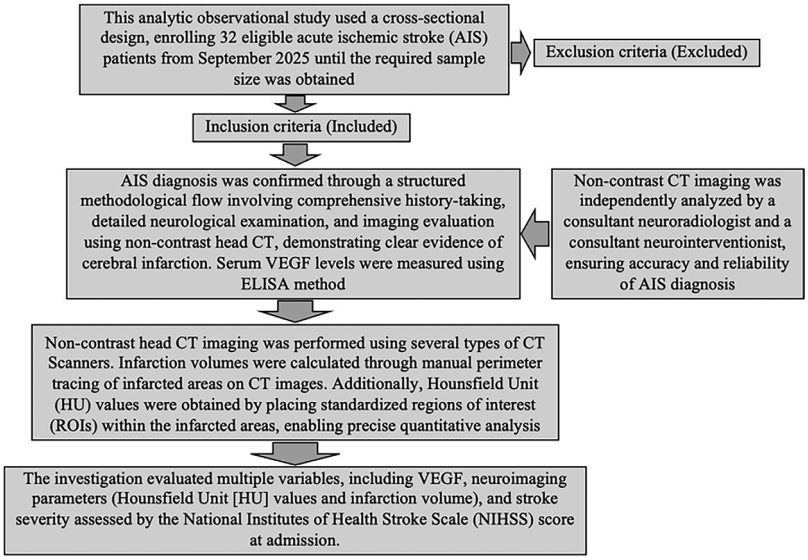

Figure 3. Study Flow Diagram: VEGF Biomarkers and Neuroimaging in Acute Ischemic Stroke.

direction of the correlations between VEGF, HU, infarct volume, and NIHSS scores.

Results

Baseline characteristics of the study population

This study aimed to evaluate the relationship between serum VEGF and HU values, infarct volume, and severity in patients with acute ischemic stroke. A total of 32 patients with AIS were included in this study. The demographics and examination results of the patients are presented in Table 1. Based on gender distribution, men were more common than women (59.4% vs. 40.6%). The mean age of the study sample was 56.66 years (SD ± 8.783). Based on onset, most patients arrived on day 1 (50.0%), followed by day 2 (25.0%),

Primary data sources

Correlation of vascular endothelial growth factor (VEGF) to HU

The relationship between VEGF and HU is summarized in Table 2. Since the data were not normally

Table 1. Basic characteristics of the research subject

Characteristic	Total (n=32); n (%); Mean ± SD; Median (min-max)
Gender	
• Male	19 (59.4%)
• Female	13 (40.6%)
Onset (day)	
• 1	16 (50.0%)
• 2	8 (25.0%)
• 3	1 (3.1%)
• 4	5 (15.6%)
• 5	2 (6.3%)
Age	56.66 (SD+/- 8.783)
Risk factors	
• Hypertension	22 (68.8%)
• Smoking	13 (40.6%)
• Dyslipidemia	28 (87.5%)
Vascular Endothelial Growth Factor (VEGF)	213 (55.08–517.09)
Hounsfield Unit (HU)	19 (10–23)
Infarct Volume, cm^3	15.36 (1.28–138)
NIHSS	7 (5-18)

distributed, Spearman's rank correlation test was applied. A moderate negative correlation was observed between VEGF and HU (r = –0.419, 95% CI –0.706 to –0.049, p = 0.016), indicating that higher VEGF levels are associated with lower HU values. As illustrated in Figure 4, there was a downward trend in HU values as VEGF levels increased, reinforcing the statistical findings (r = –0.419, p = 0.016). This graphical representation shows a moderate negative correlation, indicating that patients with higher VEGF levels tended to have lower HU values.

Correlation of Vascular Endothelial Growth Factor (VEGF) to Infarct Volume

Table 3. shows a moderate positive correlation between VEGF and infarct volume (r = 0.447, 95% CI 0.052–0.712, p = 0.010), indicating that higher VEGF levels are associated with larger infarct volumes. Figure 5 illustrates the correlation between VEGF levels and infarct volume in patients with acute ischemic stroke. The scatter plot shows a moderate positive correlation (r = 0.447, p = 0.010). As VEGF levels increase, there is a tendency for infarct volume to increase. This relationship suggests that higher VEGF concentrations may be associated with more extensive brain tissue damage. The upward trend line in the figure visually supports this correlation, suggesting that VEGF may potentially serve as a biomarker for stroke severity and infarct size.

Correlation of vascular endothelial growth factor (VEGF) to NIHSS

Table 4 shows the relationship between NIHSS scores and in addition, a weak positive correlation between VEGF and NIHSS scores was identified (r = 0.358, 95% CI -0.006–0.668, p = 0.044). Although this correlation is statistically significant, the small effect size indicates limited clinical

Table 2. Correlation between Vascular Endothelial Growth Factor (VEGF) and HU values

Variable	Vascular Endothelial Growth Factor (VEGF)			
	r	95% CI	*p*	Strength
Hounsfield Unit (HU)	-0.419	-0.706 – -0.049	0.016**	Moderate

*(Spearman Correlation Test) *P<0.05; **P< 0.01*

Table 3. Correlation between Vascular Endothelial Growth Factor (VEGF) and infarct volume

Variable	Vascular Endothelial Growth Factor (VEGF)			
	r	95% CI	*p*	Strength
Infarct Volume	0.447	0.052–0.712	0.010**	Moderate

*(Spearman Correlation Test) *P<0.05; **P< 0.01*

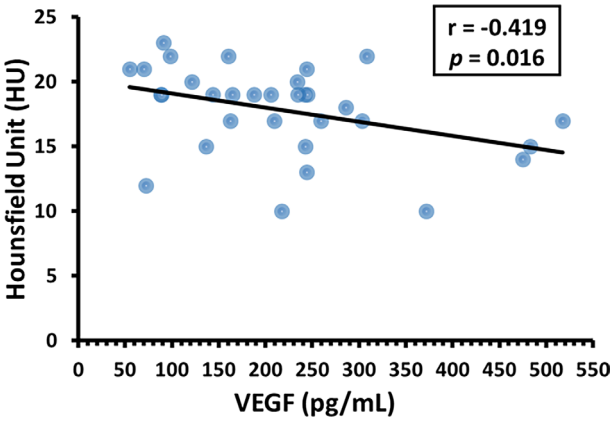

Figure 4. Graph of Correlation of Vascular Endothelial Growth Factor (VEGF) to HU.

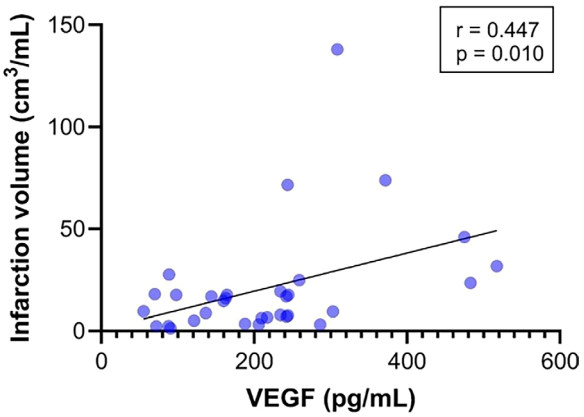

Figure 5. Graph of Correlation of Vascular Endothelial Growth Factor (VEGF) to Infarct Volume.

significance. These findings suggest that VEGF has a meaningful relationship with HU and infarct volume, but its relationship with NIHSS is relatively weaker. Figure 6 shows the correlation between VEGF levels and NIHSS scores. The scatter plot shows a weak positive correlation (r = 0.358, p = 0.043). This indicates that higher VEGF levels are slightly associated with higher NIHSS scores, reflecting greater neurological impairment. Although the correlation is statistically significant, the relatively low r value suggests that VEGF alone may not strongly predict the severity of stroke as measured by the NIHSS. The upward trend line on the graph illustrates this relationship, suggesting that VEGF may play a role in the pathophysiological processes that influence neurological outcomes, but most likely in combination with other factors.

To provide a comprehensive comparison, all correlation results are summarized in Table 5. This highlights that VEGF shows the strongest positive relationship with infarct volume, followed by a moderate positive correlation with HU, and a weaker positive correlation with NIHSS. These findings suggest that higher VEGF levels are more closely associated with larger infarct size, with a smaller but still significant relationship with tissue density changes and neurological severity. The clinical implications of these results are discussed below.

Table 4. Correlation of Vascular Endothelial Growth Factor (VEGF) with NIHSS

	Vascular Endothelial Growth Factor (VEGF)			
Variable	***r***	**95% CI**	***p***	**Strength**
NIHSS	0.358	−0.006–0.668	0.043	Weak Positive

*(Spearman Correlation Test) *P<0.05; **P< 0.01*

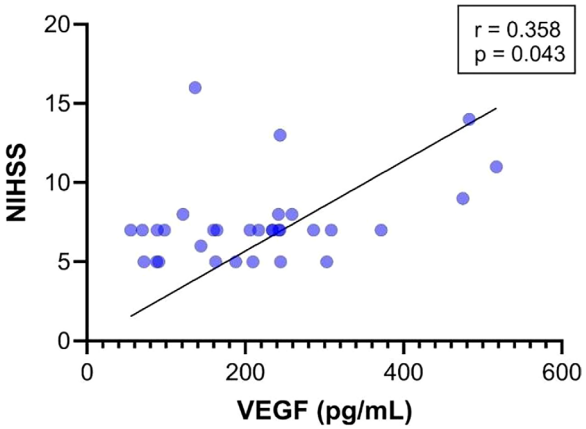

Figure 6. Graph of Correlation of Vascular Endothelial Growth Factor (VEGF) to NIHSS.

Discussion

In this study, we evaluated the relationship between VEGF levels and HU values, infarct volume, and NIHSS scores in patients with AIS. A total of 32 patients met the inclusion criteria, with men being more frequently affected than women (59.4% vs. 40.6%) with an average age of 56.66 years, in line with the study by Akbar et al., which found a predominance of stroke in men with an average age of 64.5 ± 10.1 years (7,12-14). The higher prevalence of stroke in men can be explained by constitutional hormonal factors, combined with higher smoking rates and higher stress levels in men compared to women (15,16). These

Table 5. Summary of correlation comparisons between VEGF, imaging markers, and clinical severity in AIS

Variable	**HU (Spearman *r*, 95% CI, *p*)**	**Infarct volume (Spearman *r*, 95% CI, *p*)**	**NIHSS (Spearman *r*, 95% CI, *p*)**	**Interpretation**
Vascular Endothelial Growth Factor (VEGF)	-0.419 (−0.706 - −0.049), p = 0.016	0.447 (0.052 - 0.712), p = 0.010	0.358 (−0.00–0.668), p = 0.043	Moderate negative with HU; moderate positive with infarct volume; weak positive with NIHSS

demographic findings reinforce the understanding that gender and age remain important determinants in the epidemiology of acute ischemic stroke. The most common risk factors are dyslipidaemia (87.5%), hypertension (68.8%), followed by smoking (40.6%), supporting the findings of Akbar et al., which identified hypertension and dyslipidaemia as the most dominant risk factors for AIS (7). A median HU value of 19 indicates hypoattenuation in brain tissue, reflecting ionic oedema and permanent damage. This is in line with the findings of Govind et al., who reported that HU < 19.13 indicates acute infarction (17). Hypo attenuated brain parenchyma reflects ischemic tissue with ionic oedema, followed by vasogenic oedema and permanent damage, thus accurately representing infarction (18). In this study, a moderate negative correlation was found between VEGF levels and HU values ($r = -0.419$, $p = 0.016$), indicating that increased VEGF is associated with decreased brain tissue density on CT scans. These findings support the hypothesis that VEGF plays a role in structural brain damage through inflammatory and vascular mechanisms. VEGF plays a complex role in the pathophysiology of ischemic stroke. VEGF functions as an angioneurin that supports angiogenesis, neurogenesis, and neuroprotection, which are important in post-ischemic tissue recovery. However, on the other hand, in the acute phase of stroke, increased VEGF expression can worsen damage by increasing the permeability of the BBB. Other studies show that VEGF, together with Angiopoietin-2, contributes to BBB disruption through the activation of matrix metalloproteinase-9 (MMP-9), which causes degradation of the neurovascular matrix and displacement of tight junction proteins, thereby triggering cerebral oedema and the risk of haemorrhage (19). Activation of VEGF-A and its receptor (VEGFR-2) in the penumbra area has been associated with increased vascularization and functional improvement (20). Research by Valable et al. shows that co-administration of VEGF with Angiopoietin- 1 (Ang-1) can suppress the destructive effects of VEGF on the BBB. This combination reduces oedema volume by up to 42% and strengthens the formation of more stable neovascularization, with modulation of MMP-9 activity as the main mechanism (21). This indicates that increased VEGF expression in the acute phase of stroke can worsen tissue damage. Thus, although VEGF has therapeutic potential in the subacute and chronic phases of stroke, its use in the acute phase must be carefully considered. A combination approach or appropriate timing of administration is key to maximizing angiogenic benefits without worsening vascular damage (22,23). Conversely, a moderate positive correlation between VEGF and infarct volume ($r = 0.447$, $p = 0.010$) indicates that higher VEGF levels are associated with more extensive brain tissue damage. A study by Fakhri et al. showed that serum VEGF levels were negatively correlated with ASPECTS scores, where higher VEGF levels were associated with more extensive ischemic lesions in the middle cerebral artery territory (24). These findings are also consistent with a study by Prodjohardjono et al., which showed that patients with VEGF ≥519.8 pg/ml and infarct volume ≥0.054 ml had a higher risk of post-stroke cognitive impairment (25). In addition to cognitive impairment, large infarct volume is also associated with various poor clinical outcomes, such as increased functional disability, risk of cerebral oedema, haemorrhagic transformation, worsening neuroinflammation, causing reactive gliosis around the infarct area, and higher mortality. Increased VEGF in this condition likely reflects the severity of ischemia and more severe vascular damage (20,26,27). The weak correlation between VEGF and NIHSS scores ($r = 0.358$, $p = 0.044$) indicates that although VEGF is associated with the degree of neurological deficit, its predictive power for clinical stroke severity is lower than that of infarct volume. In the acute phase of ischemic stroke, VEGF levels do not always show a linear relationship with NIHSS scores. This differs slightly from previous studies showing that increased VEGF levels in the acute phase of ischemic stroke are associated with higher NIHSS scores, indicating more severe neurological deficits. This may be due to the dominance of neuroanatomical and hemodynamic factors in determining the degree of acute neurological deficit. The NIHSS better reflects the location of the lesion, the extent of the affected eloquent area, and the presence of collateral circulation and early cerebral oedema, compared to molecular responses such as VEGF expression. For example, a small lesion in the internal capsule can result in a high NIHSS

score, while an extensive lesion in a non-eloquent area with good collaterals may show a low score, even though VEGF levels are elevated due to tissue hypoxia (28,29,30). Several studies have shown that VEGF expression increases in the acute phase of ischemic stroke and correlates with stroke severity, including NIHSS scores in univariate analysis. However, the strength of this correlation is generally lower than that of direct clinical factors, such as level of consciousness, presence of hemiplegia, or aphasia. This can be explained by the fact that the NIHSS score is not only influenced by molecular responses but is also highly determined by lesion location, involvement of eloquent areas, and collateral circulation status (28,29,31). This indicates that VEGF is not the sole determinant in the clinical manifestation of acute stroke, but rather part of a complex mechanism involving inflammation, disruption of the BBB, and neurovascular response. Overall, these results show that VEGF has a stronger association with infarct volume than HU and NIHSS. This reinforces the potential of VEGF as a biomarker for the extent of brain tissue damage, although its use as a single indicator of neurological severity is still limited and requires a multimodal approach.

Clinical relevance and practical implications

These findings confirm the role of VEGF as a blood biomarker associated with the degree of brain tissue damage and clinical severity in acute ischemic stroke. The strong correlation between VEGF and infarct volume suggests that increased VEGF levels may reflect the extent of ischemic damage, while the relationship with HU and NIHSS illustrates its involvement in pathophysiological processes that affect tissue integrity and neurological deficits. Practically, VEGF measurement can be performed routinely, quickly, and relatively affordably, making it a potential clinical tool in various healthcare facilities, including those with limited access to advanced imaging. Integrating VEGF levels with neuroimaging parameters (HU and infarct volume) and clinical scores (NIHSS) can improve accuracy in identifying patients at high risk for poor neurological outcomes, thereby supporting clinical decision-making regarding the need for close monitoring, more aggressive therapeutic interventions, and more individualized rehabilitation planning.

Limitations

This study has several limitations. First, the cross-sectional study design only allows for the assessment of relationships at a single point in time, thus it cannot describe the dynamic changes in VEGF levels or their relationship with long-term outcomes in patients with AIS. Second, the assessment of infarct volume only used CT scans without multimodal imaging such as diffusion or perfusion MRI, which can provide higher accuracy. Third, the sample size was relatively small, which may reduce the statistical power and relevance of the findings for a more diverse population and for detecting subtle relationships. Fourth, this study did not stratify patients based on ischemic stroke subtypes (e.g., large artery atherosclerosis, cardio embolism, lacunar), so differences in etiology that could affect VEGF levels and imaging patterns could not be evaluated. Fifth, this study did not establish a cut-off value for VEGF levels that could predict the occurrence of hemorrhagic transformation, so further research with a larger population is needed to determine the VEGF level threshold that has clinical implications for the risk of this complication. Finally, although this study found a moderate negative correlation between VEGF and HU, a moderate positive correlation with infarct volume, and a weak positive correlation with NIHSS score, these findings need to be interpreted with caution. The limitations of the study design and the small sample size emphasize the need for prospective studies with larger sample sizes and longitudinal follow-up to strengthen the evidence of the relationship between VEGF, imaging parameters, and the severity of AIS (32,33).

Conclusions

This study shows a multifaceted relationship between serum VEGF levels, neuroimaging parameters, and clinical severity in patients with acute ischemic stroke. Increased VEGF was found to be negatively correlated with HU values, which describe a decrease

in brain tissue density due to inflammatory processes and vascular disruption. Conversely, higher VEGF levels positively correlate with infarct volume, indicating VEGF's role in more extensive tissue damage and the risk of complications such as cerebral oedema and haemorrhagic transformation. However, the relationship between VEGF and NIHSS scores was only weak, indicating that clinical severity is determined more by neuroanatomical factors, lesion distribution, and collateral circulation conditions than by molecular expression alone, such as VEGF expression. These findings confirm the dual nature of VEGF in the acute phase of stroke, where this molecule on one hand supports angiogenesis and neuroprotection, but on the other hand has the potential to worsen damage through increased BBB permeability. Therefore, although VEGF has therapeutic potential in the subacute and chronic phases, its use in the acute phase must be carefully considered. Overall, this study emphasizes that VEGF can be a potential biomarker for assessing the degree of brain tissue damage and the risk of extensive infarction, but its interpretation must be combined with other radiological and clinical parameters to determine the prognosis and management strategy for AIS.

Ethic Approval: All research designs were reviewed and approved by the Health Research Ethics Committee of Dr Wahidin Sudirohusodo Hospital – Faculty of Medicine, Hasanuddin University (892/UN4.6.4.5.31/PP36/2024).

Conflict of Interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article.

Authors Contribution: Conceptualization, JAG, MYA, and MA; Methodology, JAG, MYA and MA; Software, JAG; Validation, JAG, MYA, MA, and GVA; Formal analysis, JAG; Investigation, JAG; Resources, JAG, DAN, MI and MYA; Data Curation, JAG, and MYA; Writing—Original Draft Preparation, JAG, MYA and MA; Writing Review and Editing, JAG, MYA, MA, and GVA; Visualization, JAG, MYA, MA, and GVA; Supervision, MA and MYA; Project Administration, JAG. All authors have read and agreed to the published version of the manuscript.

Declaration on the Use of AI: None.

Consent for Publication: All subjects have provided consent for publication.

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Data Availability Statement: All the data are available from the corresponding author upon a reasonable request (MYA).

Abbreviations

AIS	– Acute Ischemic Stroke
Ang-1	– Angiopoietin-1
BBB	– Blood Brain Barrier
CBF	– Cerebral Blood Flow
CBV	– Cerebral Blood Volume
CT	– Computed Tomography
ELISA	– Enzyme-Linked Immunosorbent Assay
HU	– Hounsfield Unit
ICC	– Intraclass Correlation Coefficient
IQR	– Interquartile Range
mRS	– Modified Rankin Scale
MRI	– Magnetic Resonance Imaging
NIHSS	– National Institutes of Health Stroke Scale
NCCT	– Non-Contrast Computed Tomography
ROI	– Region of Interest
SPSS	– Statistical Package for the Social Sciences
TIA	– Transient Ischemic Attack
VEGF	– Vascular Endothelial Growth Factor
VEGFR-2	–Vascular Endothelial Growth Factor Receptor-2

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