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ORIGINAL RESEARCH

Inverse Association Between D-Dimer Levels and Glasgow Coma Scale Scores in Hemorrhagic Stroke Patients: A Cross-Sectional Study

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Aim: Hemorrhagic stroke (HS) represents one of the major causes of death in China. The research work focuses on the correlation between Glasgow Coma Scale (GCS) score and D-dimer level, and the role of modified factors such as platelet count in HS patients.
Methods: This was a cross-sectional study that was conducted at the First People's Hospital of Lianyungang, Lianyungang City, China. HS Patients were divided into three groups according to their GCS scores: GCS < 9 (severe, n = 43), 9 ≤ GCS < 13 (moderate, n = 97), and GCS ≥ 13 (mild, n = 487).
Results: The analysis comprised 627 participants. D-dimer levels were 142.0 ng/mL on average. The average GCS score was 13.6, and the average age was 61.0 years. The three GCS groups showed significant differences in D-dimer concentrations, diastolic blood pressure (DBP), and systolic blood pressure (SBP) (P < 0.001, P = 0.028, and P = 0.005, respectively). Among severe GCS scores (<9), the D-dimer level was the highest at 237.0 ng/mL. After adjustment for possible confounders, the D-dimer concentrations were significantly lower in the moderate and mild GCS groups than in the severe group (P = 0.030 and P = 0.038, respectively). In the stratified analysis, the association between GCS categories and D-dimer levels was stronger among participants with low platelet counts (<194 × 10^9/L; P for interaction = 0.017).
Conclusion: This study reveals a significant inverse association between D-dimer levels and GCS scores in HS patients, especially those with lower platelet counts. Elevated D-dimer levels may reflect coagulation and fibrinolysis activation, contributing to worse outcomes. Clinically, more attention and monitoring should be paid to the HS patients with elevated D-dimer levels.
Keywords: D-dimer, Glasgow coma scale, hemorrhagic stroke, platelet count, epidemiology, neurology

Introduction

Stroke is the most common cause of death in China.[1] Two million cases of hemorrhagic stroke (HS) occur worldwide every year.[2,3] The reported 30-day mortality rate of HS is between 35% and 50%.[4–7] Consequently, the early risk assessment and intervention for stroke may prevent further advancement and complications associated with the disease.

D-dimer is a specific degradation product of cross-linked fibrin lysed by plasmin and represents a molecular marker of active thrombosis and subsequent fibrinolysis. Cerebral thrombosis, where in acute ischemic stroke, the D-dimer level is elevated due to spontaneous thrombolysis and secondary fibrinolysis; and disseminated intravascular coagulation, where wide microthrombosis with subsequent fibrinolysis results in significantly raised D-dimer levels.[8,9] Therefore, D-dimer is an important factor in the evaluation of coagulation function in intracerebral hemorrhage, ischemic stroke, traumatic brain injury, and post-surgical states.

The up-regulation of the coagulation, fibrinolysis, and inflammation systems following an HS may lead to an increase in D-dimer concentrations.[10,11] Prior research has shown that in individuals with HS, higher D-dimer levels are linked to more severe clinical symptoms, and poor prognosis.[12,13] Johansson et al identified that higher plasma concentrations of D-dimer are significantly associated with an increased risk of intracerebral hemorrhage (ICH).[14] In a study conducted by

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Yao et al[15] involving a cohort of 877 Chinese patients with acute ischemic stroke, it was determined that elevated plasma D-dimer levels, particularly those in the highest quartile (>1.78 mg/L), were significantly correlated with a 34.4% incidence of poor short-term outcomes as assessed by the modified rankin scale (mRS) at 90 days. The Glasgow Coma Scale (GCS) provides a practical method of assessing the level of consciousness. The scale evaluates three different response aspects: eye-opening, verbal response, and best motor response. Each response level is given a score, with lower scores indicating worse responses. GCS is broadly applied in the screening evaluations and the supporting evidence for the prognosis for the stroke patients.[16]

However, the mechanism of hemorrhagic stroke (HS) is complex, it is still necessary to find the early screening factors related to stroke. Moreover, few researches have been done on the connection between D-dimer concentration and the clinical severity of general HS.

To this effect, the current study was conducted to explore the correlation between GCS scores and D-dimer concentrations in patients presenting with HS and to explore and the role of the possible effect modifiers such as platelet count.

Methods

Study Design and Participants

The cross-sectional study was conducted at the First People's Hospital of Lianyungang, China, between October 14th, 2015, and August 9th, 2018. It was performed with the aim of investigating the association of GCS scores as the independent variable and D-dimer levels as the dependent variable in patients diagnosed with HS.

Eligibility Criteria

Participants were eligible if they fulfilled the following criteria: (1) total homocysteine (tHcy) levels ≥15 μmol/L (tHcy < 15 μmol/L means healthy body),[17] (2) HS confirmed by non-contrast CT and diagnosed in compliance with WHO criteria.[18]

Exclusion Criteria

Participants were excluded in cases of: (1) secondary hemorrhages caused by trauma, venous sinus thrombosis, hemorrhagic transformation of ischemic infarction, tumors, or postoperative complications; (2) recent use of anticoagulants or antiplatelet drugs; and (3) non-agreement for participating this study.

All included participants provided written informed consent; While the patients were in severe state of stroke and was in unconsciousness, their legal guardians signed the written informed consent on behalf of the patients. The First People's Hospital of Lianyungang's Ethics Committee gave its approval to the study (No.20200310).

Data Collection Procedures

Baseline data collection, including GCS, was performed under a blinded way by the same groups of research staff who were trained to follow standardized protocols. These research staff were blinded to this research and blinded to the participants. For GCS scoring, a double-person review mechanism was adopted for key indicators (such as pupillary reflex and motor response) to ensure the objectivity of the scoring. Anthropometric measures included height and weight measured using standard procedures. While participants wore light indoor clothing, their weight was measured on a digital scale to the nearest 0.1 kg, and their height, measured without shoes, was taken to the nearest 0.1 cm using a portable stadiometer. Weight in kilograms divided by height in meters squared was used to compute BMI. After ten minutes of relaxation, seated blood pressure was taken using a mercury sphygmomanometer and cuffs of the proper size.

If the patients fell into a coma or (GCS < 9), the clinical data such as smoke status, alcohol drinking status were collected from his/her legal guardian.

Scoring Neurological Deterioration Using the GCS: Physiological Scales and Clinical Correlation

The three individual components of the GCS,[19] including eye, verbal, and motor responses, together estimate the level of consciousness in a patient. The eye responses are scored from 1 - no response to 4 - spontaneous opening, the verbal responses range from 1 - no verbal response to 5 - appropriate conversation, and the motor responses range from 1-no movement to 6-purposeful movement. The total GCS score, which ranges between 3 and 15, reflects the severity of neurological impairment and guides clinical decisions and predictions of outcomes. The patients were divided at the time of admission into three groups according to their GCS scores: severe impairment (GCS < 9), which is indicative of grave injury of the brain and a state of high unresponsiveness or coma; moderate impairment (9 ≤ GCS < 13), which indicates intermediate states of consciousness or cognitive function; and mild impairment (GCS ≥ 13), with minimal impairment and higher functional capacity.

Subgroups

The interaction between GCS and D-dimer was compared between different subgroups, based on age (<60 vs ≥60 years), gender, BMI (<24 vs ≥24 kg/m²), SBP (<160 vs ≥160 mmHg), alcohol consumption (ever vs never), smoking (ever vs never), tHcy (<15 vs ≥15 μmol/L), platelet count (<194 vs ≥194 × 10^9/L), and fibrinogen.

Laboratory Assays

Blood samples were collected soon after admission. A total of 10–15 mL venous blood were drawn from each participant and placed in blood collection tube containing anticoagulant. The serum or plasma was separated immediately and stored at a low temperature of 4°C ± 2°C. The detection of plasma tHcy was completed within 2 hours by chemiluminescence immunoassay at the automated clinical analyzers (Cobas c702, Roche, Switzerland) in our hospital's central laboratory. The fluorescence immunochromatography was used to detect D-dimer levels. Total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), creatinine (CR), platelet count, fibrinogen, and international normalized ratio (INR) were analyzed at the automated clinical analyzers.

Statistical Analysis

The distributions of D-dimer levels were skewed; therefore, the Box-Cox transformation was used to approximate normality. The D-dimer was converted using the formula (D-dimer^0.21–1)/0.21 (Figure 1). Baseline characteristics were expressed as means (SDs) for continuous variables and proportions for categorical variables. Baseline characteristics were compared between GCS groups [GCS < 9 (severe), 9 ≤ GCS < 13 (moderate), and GCS ≥ 13 (mild)] using ANOVA, followed by post-hoc or chi-squared testing. In both unadjusted and adjusted multivariable linear regression models for age, sex, BMI, smoking

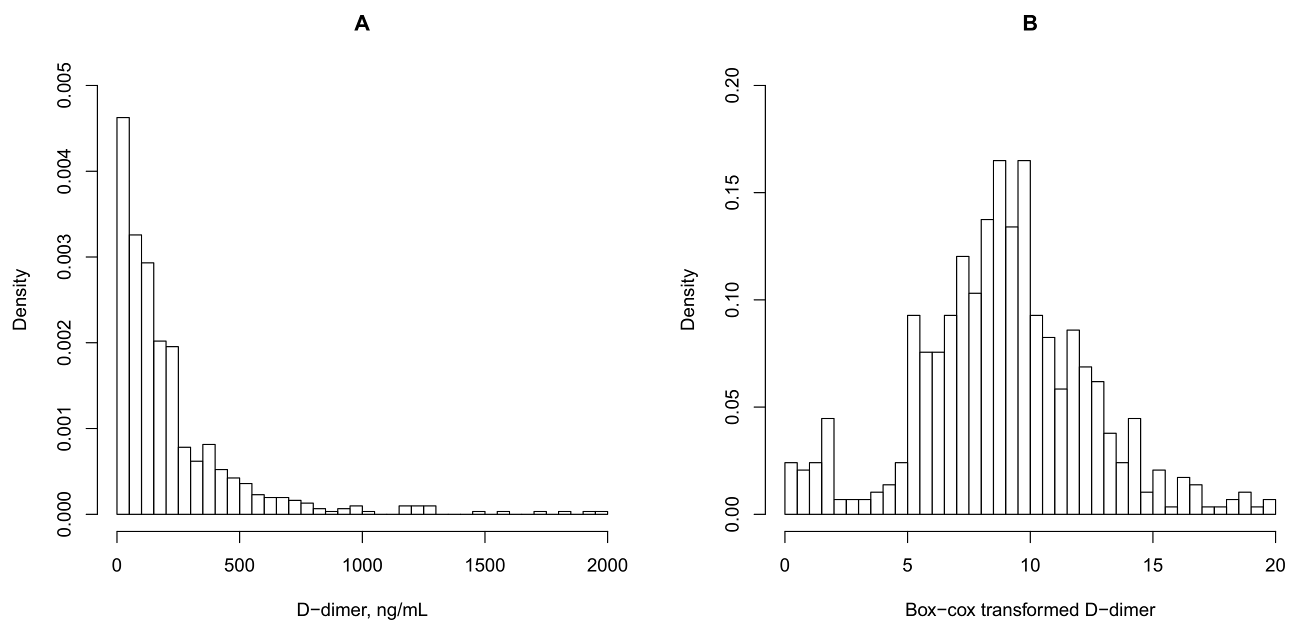

Figure 1 The distribution of D-dimer before and after Box-Cox transformation. (**A**) The distribution of D-dimer before Box-Cox transformation; (**B**) The distribution of D-dimer after Box-Cox transformation.
Notes: Box−cox transformed formula: ((X^lambda) − 1)/lambda lambda = 0.210.

status, alcohol intake, SBP, INR, fibrinogen, platelet count, and tHcy, the dependent variable was D-dimer level. Exploratory analyses compared the interaction between GCS and D-dimer based on age (<60 vs ≥60 years), gender, BMI (<24 vs ≥24 kg/m²), SBP (<160 vs ≥160 mmHg), alcohol consumption (ever vs never), smoking (ever vs never), tHcy (<15 vs ≥15 μmol/L), platelet count (<194 vs ≥194 × 10^9/L), and fibrinogen. All tests of significance were two-tailed, and P values less than 0.05 were considered significant. The statistical analyses were carried out with R 3.3.2.

Results

A total of 627 patients were included (Figure 2), of which, there were 93 cases of subarachnoid hemorrhage and 534 cases of intracerebral hemorrhage. Among these 627 patients, there were 43 cases in the GCS < 9 group, 97 in the 9 ≤ GCS < 13 group, and 487 in the GCS ≥ 13 group. The age range of patients was between 59.7 and 61.9 years, with no significant difference among the three groups (P = 0.582). There were 218 female patients, accounting for 34.8% (44.2% in the GCS < 9 group, 38.1% in the 9 ≤ GCS < 13 group, and 33.3% in the GCS ≥ 13 group), with no significant difference in gender distribution (P = 0.265). BMI ranged from 24.3 to 25.3 kg/m², showing no significant difference among the groups (P = 0.175). The median D-dimer concentration was 142.0 ng/mL, with an interquartile range of 60.0–273.5 ng/mL. After data transformations, the mean (SD) age of the participants was 61.0 years (12.0), with ages typically ranging within 12 years of the mean. The mean GCS score was 13.6 ± 2.5; values were usually above and below the mean by a factor of 2.5. The mean (SD) D-dimer concentration was 8.5 ng/mL (4.3); values were usually changing by 4.3 ng/mL from the mean.

The baseline characteristics of participants, stratified by GCS categories, are presented in Table 1. Significant differences were seen between the three GCS groups in SBP (P < 0.001), DBP (P = 0.028), and D-dimer concentrations (P = 0.05). In particular, the severe cases of GCS scores (<9) were associated with higher D-dimer levels [237.0 ng/mL

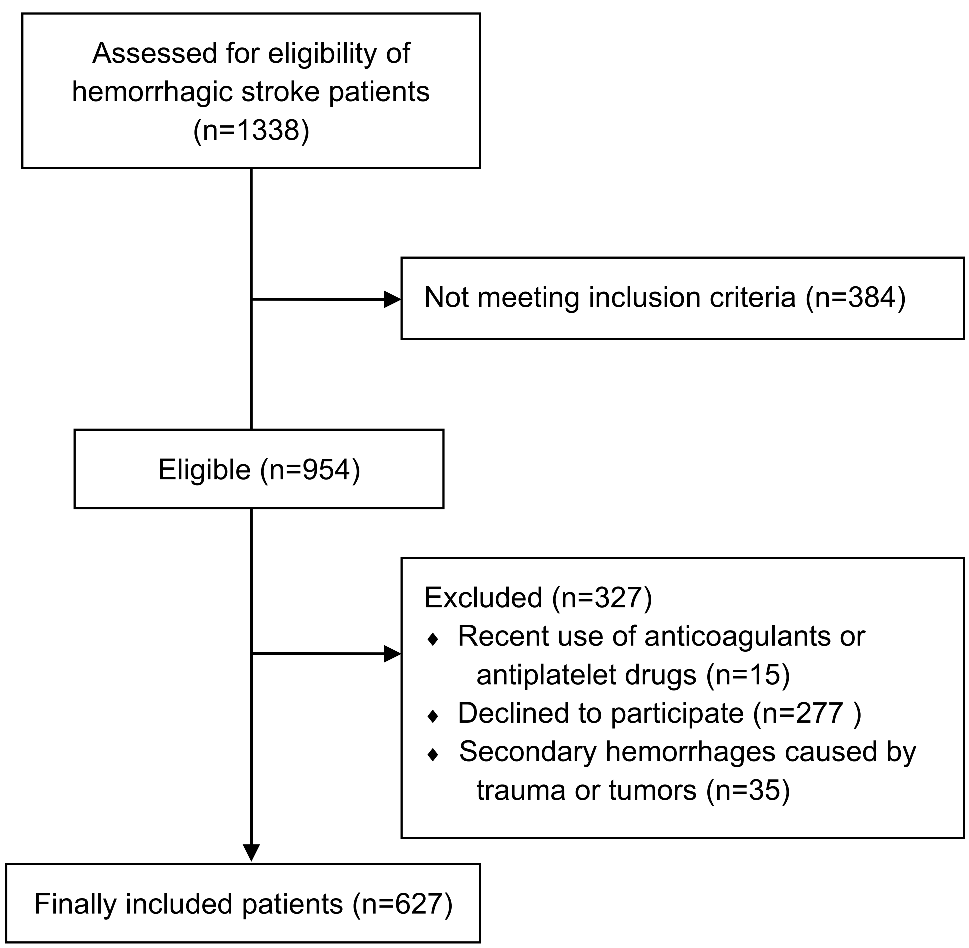

Figure 2 The flow chart of the patients' inclusion.

Table 1 The Comparisons of the Baseline Characteristic of Different Subgroups Classified by Glasgow Coma Scale Groups*

	GCS Groups			***P Value***
	GCS < 9	**9 ≤ GCS < 13**	**GCS ≥ 13**	
Patient number	43	97	487	
Age, years	59.7 (13.1)	61.9 (12.8)	61.0 (11.7)	0.582
Sex				0.265
Female [n (%)]	19 (44.2)	37 (38.1)	162 (33.3)	
Male [n (%)]	24 (55.8)	60 (61.9)	325 (66.7)	
BMI, kg/m^2	25.3 (2.8)	24.3 (3.0)	24.7 (3.2)	0.175
Smoking status				0.329
Current	3 (7.0)	19 (19.6)	83 (17.0)	
Former	14 (32.6)	23 (23.7)	112 (23.0)	
Never	26 (60.5)	55 (56.7)	292 (60.0)	
Alcohol drinking				0.777
Current	6 (14.0)	21 (21.6)	107 (22.0)	
Former	8 (18.6)	18 (18.6)	80 (16.4)	
Never	29 (67.4)	58 (59.8)	300 (61.6)	
SBP, mmHg	172.7 (24.4)	167.6 (27.2)	156.9 (24.2)	<0.001
DBP, mmHg	97.0 (20.3)	99.8 (16.7)	95.4 (14.1)	0.028
CR, mmol/L	69.9 (21.3)	70.3 (19.9)	72.4 (44.8)	0.861
tHcy, μmol/L	18.9 (11.5)	18.0 (12.0)	16.3 (8.5)	0.081
TC, mmol/L	4.7 (1.1)	4.8 (1.0)	4.8 (2.0)	0.935
TG, mmol/L	1.5 (0.8)	1.3 (0.7)	1.9 (6.0)	0.661
HDL-C, mmol/L	1.2 (0.4)	1.2 (0.3)	1.3 (0.4)	0.258
Platelet count$^{\#}$, 10$^{\wedge 9}$/L	190.0 (159.5, 243.0)	200.0 (164.5, 235.5)	193.0 (159.0, 234.0)	0.678
Fibrinogen, g/L	3.3 (0.9)	3.2 (1.0)	3.2 (1.3)	0.683
INR	1.0 (0.1)	1.1 (0.2)	1.0 (0.2)	0.318
D-dimer$^{\#}$, ng/mL	237.0 (131.0, 456.0)	123.0 (48.0, 317.0)	140.0 (60.5, 256.0)	0.05

Notes: *Values are presented as means (SD); $^{\#}$Values are presented as median (IQR).
Abbreviations: tHcy, total homocysteine; TC, total cholesterol; TG, triglycerides; HDL-C, high density lipoprotein cholesterol; CR, creatinine; SBP, systolic blood pressure; DBP, diastolic blood pressure; BMI, body mass index; INR, international normalized ratio.

(131.0, 456.0)] compared with the moderate ones (9 ≤ GCS < 13) [123.0 ng/mL (48.0, 317.0)] and mild scores (≥13) [140.0 ng/mL (60.5, 256.0)].

There were no significant differences in smoking status (P = 0.329), alcohol use (P = 0.777), CR (P = 0.861), tHcy (P = 0.081), TC (P = 0.935), TG (P = 0.661), HDL-C (P = 0.258), platelet count (P = 0.678), fibrinogen (P = 0.683), and INR (P = 0.318).

Table 2 highlights the correlation between GCS groups and D-dimer concentration. Crude models indicated that severe GCS scores (<9) were associated with higher D-dimer concentrations compared to moderate (9 ≤ GCS < 13) and mild (GCS ≥ 13) groups. In particular, in the moderate group, the difference in D-dimer concentration was −2.04 [β = −2.04; 95% confidence interval (CI): −3.61, −0.47; P = 0.030], and in the mild group, −1.91 (β = −1.91; 95% CI: −3.27, −0.55; P = 0.038). The respective differences in D-dimer concentration for the moderate and mild groups were −1.64 (β = −1.64; 95% CI: −3.11, −0.16; P = 0.030) and −1.37 (β = −1.37; 95% CI: −2.67, −0.08; P = 0.038) after adjustment for the potential confounders. Further, when stratified into two groups (<9 vs ≥9), the difference in D-dimer concentration was −1.93 (β = −1.93; 95% CI: −3.28, −0.58; P = 0.029) in the crude model and −1.43 (β = −1.43; 95% CI: −2.71, −0.15; P = 0.029) in the adjusted model.

Among stratified analysis, a higher negative correlation between GCS categories (≥9 vs <9) and D-dimer concentrations among patients with lower platelet counts (<194 × 10^9/L vs ≥194 × 10^9/L; P for interaction = 0.017) was detected (Figure 3).

Table 2 The Correlation Between Glasgow Coma Scale Subgroups and D-Dimer Concentrations

GCS	N	Transformed# D-dimer	Crude Models	Adjust Models*	
		Means (SD)	(95% CI)	(95% CI)	*P* Value
Three groups					
GCS < 9 (severe)	43	10.3 (4.8)	ref	ref	
9 ≤ GCS < 13 (moderate)	97	8.3 (4.9)	−2.04 (−3.61, −0.47)	−1.64 (−3.11, −0.16)	0.030
GCS ≥ 13 (mild)	487	8.4 (4.2)	−1.91 (−3.27, −0.55)	−1.37 (−2.67, −0.08)	0.038
Two groups					
<9 (severe)	43	10.3 (4.8)	ref	ref	
≥9 (non-severe)	584	8.4 (4.3)	−1.93 (−3.28, −0.58)	−1.43 (−2.71, −0.15)	0.029

Notes: *Adjust models adjusted for age, sex, BMI, smoking status, alcohol drinking, SBP, INR, fibrinogen, platelet count, tHcy. #D-Dimer was transformed to (D-Dimer$^{0.21-1}$)/0.21.

Abbreviations: SD, standard deviation; CI, confidence interval; GCS, Glasgow Coma Scale; tHcy, total homocysteine; SBP, systolic blood pressure; BMI, body mass index; INR, international normalized ratio.

Discussion

The current study found a negative connection between D-dimer levels and GCS scores in HS patients, particularly those with low platelet counts.

Subgroup	No.	D−dimer with GCS<9,ng/mL	D−dimer with GCS>=9,ng/mL	Beta (95%CI)	P for interaction
Age, yrs					0.603
<60	265	10.1 (4.5)	7.7 (3.8)	−1.98 (−3.63,−0.33)	
>=60	362	10.6 (5.2)	8.9 (4.6)	−1.16 (−3.11,0.79)	
Sex					0.258
Male	409	10.3 (4.7)	8.0 (4.3)	−2.22 (−3.92,−0.52)	
Female	218	10.3 (5.1)	9.1 (4.2)	−0.10 (−2.15,1.95)	
BMI, kg/m^2					0.701
<24	265	11.0 (5.5)	8.2 (4.7)	−1.50 (−3.91,0.91)	
>=24	362	10.0 (4.6)	8.5 (4.0)	−1.33 (−2.79,0.13)	
SBP, mmHg					0.105
<160	331	11.0 (6.2)	7.9 (4.2)	−2.98 (−5.31,−0.64)	
>=160	296	10.1 (4.3)	9.0 (4.4)	−0.35 (−1.89,1.19)	
Smoking status					0.269
ever	254	10.8 (4.3)	8.0 (4.5)	−2.58 (−4.67,−0.48)	
never	373	10.0 (5.2)	8.7 (4.2)	−0.89 (−2.52,0.74)	
Alcohol drinking					0.505
ever	240	10.1 (4.2)	7.7 (4.5)	−2.30 (−4.50,−0.09)	
never	387	10.4 (5.2)	8.8 (4.2)	−1.00 (−2.56,0.56)	
tHcy, µmol/L					0.591
<13.5(median)	313	10.4 (5.7)	8.3 (4.1)	−1.83 (−3.64,−0.02)	
>=13.5	313	10.2 (4.2)	8.5 (4.5)	−1.21 (−3.06,0.63)	
Platelet count, 10^9/L					0.017
<194(median)	303	11.7 (4.9)	8.5 (3.9)	−2.61 (−4.22,−1.00)	
>=194	304	8.6 (4.2)	8.5 (4.5)	0.32 (−1.72,2.37)	
Fibrinogen, g/L					0.284
<3.1(median)	313	10.2 (6.2)	7.6 (4.1)	−2.15 (−4.36,0.05)	
>=3.1	313	10.4 (4.2)	9.2 (4.4)	−0.95 (−2.62,0.71)	
INR					0.070
<1.0(median)	287	9.3 (4.8)	8.1 (4.2)	−0.34 (−2.00,1.32)	
>=1.0	340	11.5 (4.8)	8.6 (4.4)	−2.61 (−4.59,−0.64)	

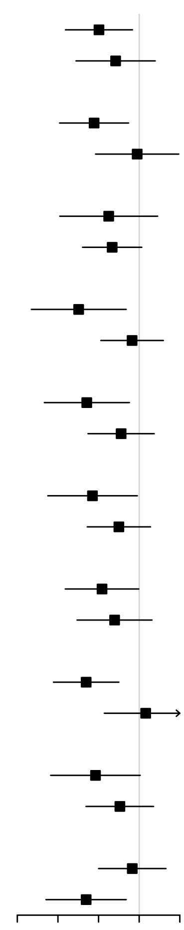

Figure 3 The association between Glasgow Coma Scale and D-dimer in subgroups. A higher negative correlation between GCS categories (≥9 vs <9) and D-dimer concentrations among patients with lower platelet counts was detected.

Previous studies looked at the link between D-dimer concentrations and the risk of HS, as well as the prognosis of the HS.[12–15,20] Ilveskero et al found that plasma D-dimer levels after surgery predicted severe disability, vegetative state, or death in aneurysmal subarachnoid hemorrhage patients, with an OR of 1.63 per mg/L (95% CI: 1.03, 2.60; P = 0.038).[20] Greater D-dimer levels are linked to a higher chance of having higher risk of recurrence stroke.[21,22] Xiao et al[23] enrolled 557 patients with spontaneous supratentorial ICH and found significant differences in the age group, Glasgow Coma Score at the time of admission, high D-dimer levels, and bleeding. Nevertheless, the association between D-dimer and clinical severity of general hemorrhagic stroke has not been fully investigated. Our results represent new evidence in this field.

First, we found that plasma D-dimer levels were inversely associated with GCS scores: The lower GCS score, the higher D-dimer levels. Although the biological basis for this association is unknown, several possibilities are biologically plausible. (1) High concentrations of D-dimer reflect activation of the systemic coagulation and fibrinolytic systems. When the blood vessels rupture, the tissue factors from brain tissue enter the circulation, thus activating the hemostatic system that may lead to accumulation of thrombin, cross-linked fibrin, and fibrinolysis, hence increasing D-dimer levels.[24] (2) HS triggers the release of inflammatory cytokines contributing to a hypercoagulable state.[25] This in turn activates the fibrinolytic system, raising D-dimer levels. D-dimer may promote pro-inflammatory cytokines, including interleukin-6 (IL-6), that is secreted by monocytes, thus enlarging hematoma size.[26–28] This D-dimer, being a product of fibrinolysis, could present an indirect evidence for hematoma size enlargement. Thereby, higher hematoma enlargement leads to worse GCS presentations. Severe outcomes for patients with HS might be highly explained by such highly activated inflammation, coagulation, and fibrinolysis.

Second, we found higher D-dimer levels in patients with low GCS and platelet count. We suspected that the correlation of GCS categories and the level of D-dimer can probably be moderated by platelet count. Suehiro demonstrated low platelet count and high D-dimer level in the acute stage, which was associated with hematoma expansion resulting in a worse GCS score.[29] Our study showed that, in the stratified analysis, the association between GCS categories and D-dimer levels was stronger among participants with low platelet counts, which is consistent with the study by Suehiro.[29] However, the exact mechanisms for the correlation of D-dimer and platelet counts with GCS scores are not fully known.

This study has several limitations. First, this is a cross-sectional study in which we could not assess the dynamic changes in D-dimer concentration and GCS over time. Second, FDP, mean platelet volume, and platelet-activating factors were not measured, all of which would add further value to understanding the underlying pathophysiology between D-dimer levels and platelet count. Our findings are therefore hypothesis-generating, and confirmation of these results will be necessary in future studies. Third, hematoma volume and intraventricular hemorrhage are closely related with GCS, which are not analyzed in the multivariate regression model, which may lead to some bias on the results. Fourth, this study did not analyze the correlation between D-dimer, GCS and the subtypes of hemorrhagic stroke (subarachnoid hemorrhage and ICH) because the case numbers of the two types are significantly different. This correlation between D-dimer, GCS and the subtypes of hemorrhagic stroke need further validations.

Future Directions

In the future, the prognostic evaluation value of the combined application of GCS score and D-dimer in patients with cerebral hemorrhage can be explored, especially for elderly patients with hypertensive cerebral hemorrhage complicated with underlying diseases. Their conditions progress rapidly and have a high mortality rate, and more accurate predictive models are needed to assist clinical decision-making. The predictive value of the dynamic changes of GCS score and D-dimer for poststroke complications such as rebleeding and infection in stroke patients can be analyzed. Especially in the intensive care stage, explore the guiding significance of changes in dynamic monitoring indicators for the optimization of clinical pathways.

Conclusion

The present study showed a significant inverse correlation between D-dimer levels and GCS scores in HS patients, mainly those with lower platelet count. High levels of D-dimer may reflect the activation of systemic coagulation and fibrinolysis that lead to poor outcome such as hematoma enlargement and low GCS score. Platelet count might modify the correlation between D-dimer levels and stroke severity, suggested by our finding. Nevertheless, the association between D-dimer and the clinical severity of general hemorrhagic stroke has not been fully investigated. Routine assessment of D-dimer and platelet count may aid early risk stratification in HS patients. For patients with more severe conditions or low GCS scores, close monitoring on D-dimer levels and platelet counts is necessary for providing further treatment on these patients.

Abbreviation

GCS, Glasgow Coma Scale; tHcy, total homocysteine; TC, total cholesterol; TG, triglycerides; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; CR, creatinine; SBP, systolic blood pressure; DBP, diastolic blood pressure; BMI, body mass index; INR, international normalized ratio; SD, standard deviation; CI, confidence interval; HR, hazard ratio; OR, odds ratio; mRS, modified rankin scale; RR, risk ratio.

Data Sharing Statement

The data are available from the corresponding author, AL, upon reasonable request.

Ethics Approval and Informed Consent

The study was approved by the Ethical Committee of the First People's Hospital of Lianyungang (No.20200310) and was conducted in compliance with the Declaration of Helsinki. All included participants provided written informed consent; While the patients were in severe state of stroke and was in unconsciousness, their legal guardians signed the written informed consent on behalf of the patients.

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Disclosure

The authors report there are no competing interests to declare for this work.

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