Prevalence and Risk Factors of Deep Vein Thrombosis with Acute Stroke: A Cross-sectional Study

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

Original Research Article

ABSTRACT

Background: Deep vein thrombosis (DVT) is a serious complication in stroke patients and may lead to the devastating consequences of a pulmonary embolism. The risk factors for DVT in acute stroke are advanced age, high National Institute of Health Stroke Scale (NIHSS) score, hemiparesis, immobility, female gender, atrial fibrillation. The present study is aimed at identifying the prevalence and risk factors for DVT in acute stroke patients.

Methods: This was a prospective cross sectional study conducted in of Dhaka Medical College and Hospital from January 2022 to December 2023. Data was collected in a preformed questionnaire. Statistical analysis was performed using IBM SPSS version 26.0. Continuous

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variables were analyzed in the form of the means with standard deviations (Mean ± SD). Categorical variables were shown as numbers and proportions. Continuous data were analyzed using the independent samples t-test. Categorical data were analyzed using the chi-squared test. Univariate variables with a p-value of <0.05 were retained in a binary logistic regression model. Receiver operating characteristic (ROC) curve analysis was performed by identifying the area under the ROC curve (AUC) to evaluate the performance of the logistic regression model. Statistical significance was defined as a p-value of < 0.05.

Results: A total of 106 patients with acute stroke (AS) were included in the study. The included patients were divided into two groups: DVT and non-DVT group. Out of 106 patients, 34(32.07%) patients presented with DVT. Patients with DVT were older than those without DVT (62.7 ± 10.7 vs. 56.5 ± 11.9 years, p < 0.05). Females were more affected by DVT (58.88% vs. 26.85%, p<0.05). In the DVT group, the level of D-dimer was significantly higher than that in the non- DVT group (2.2 ± 1.7 vs. 0.45 ± 1.1, p < 0.05). Elevated CRP and low serum albumin level were also observed in DVT group which was statistically significant. (p<0.05). Multiple logistic regression analysis showed that age>60years, NIHSS score>25 and a D-dimer level of ≥ 1.52 μg/mL and caprine score >6 were independent factors for the presence of DVT at the time of stroke admission. Odds ratio for age, Caprini RAM score, NIHSS score and elevated d-dimer were 1.043(1.000–1.075, p=0.029),1.43(0.85-0.1.96, p=0.001),1.266(1.168-1.284, p=0.008) and1.446 (1.130–1.849, p=0.003) respectively.

Conclusion: The present study has showed that advanced age, high NIHSS and caprini score and raised serum D-dimer levels are independent predictors of DVT in stroke patients. A further large multicenter study should be done to provide a better management to the patients of DVT in stroke patients.

1. INTRODUCTION

"Deep vein thrombosis (DVT) is a serious complication in stroke patients and may lead to the devastating consequences of a pulmonary embolism". (Powers et al., 2018) "Though majority of morbidity arises within one week of stroke, complications like pulmonary embolism (PE) occurs between the second to fourth weeks of an ischemic and hemorrhagic stroke which is also the leading cause of mortality in the post stroke period". (Winstein et al., 2016) "PE generally arise from venous thromboembolism that develops in a paralyzed lower extremity or pelvis. It has been reported in studies from Western societies that DVT occurred in up to 80% of patients with ischemic stroke who did not receive prophylactic therapy". (Ha et al., 2020) "In general, studies have estimated the overall prevalence of clinically evident DVT after acute stroke to be around 2–20%". (Wu et al., 2019) "Data from the CLOTS trials, the largest observational report, which evaluated 5632 immobile patients with acute stroke using duplex ultrasound showed detection of DVT within 10 days of enrollment in 11 percent and within 30 days in 15% of patients". (Dennis et al., 2019) Apart of PE, DVT can lead to chronic venous insufficiency which may lead to further complications.

"The risk factors for DVT in acute stroke are advanced age, high National Institute of Health Stroke Scale (NIHSS) score, hemiparesis, immobility, female gender, atrial fibrillation." (Tondel et al., 2020) "A recent large prospective study based on a cohort of 30,000 members of a general population in Norway demonstrated that DVT was independent of traditional cardiovascular risk factors, implying that stroke and related conditions mainly immobility are the main contributors to the venous thromboembolism (VTE)". (Tondel et al., 2020) "Besides the risk of DVT/pulmonary embolism (PE) may even be higher in patients with sub-arachnoid hemorrhage and intracranial hemorrhage then ischemic stroke". (Liu et al., 2021)

"The initial test of choice for diagnosing peripheral venous thrombosis is duplex ultrasound due to its accuracy, low cost, portability and safety. In addition, Doppler techniques provide direct information regarding flow physiology". (Maufus et al., 2018) CT or MR venography are also good alternatives to duplex ultrasound.

"The options for lowering the risk of DVT has been documented quite extensively in the literature. Early mobilization, administration of antithrombotic agents, and the use of external

compression devices are well known methods to prevent DVT. However, in clinical medical practice, VTE prophylaxis in acutely stroke patients has been found to be suboptimal" (Liu et al., 2020) "Several studies have also validated this observation by showing a gap that exists between evidence-based guidelines/ recommendations and actual practice in the hospital setting". (Kong et al., 2019) "Besides the National Institute for Health and Clinical Excellence (NICE) guidelines recommend that routine prophylactic anticoagulation should not be used (grade A) for prevention of venous thromboembolism (VTE) after stroke as it may lead to hemorrhagic complications". (Khan et al., 2017) "Though Well's criteria is widely used too to diagnose and assess DVT, risk stratification is can be poorly identified in the immediate stroke period". (Liu et al., 2014) So the present study is aimed at identifying the prevalence and risk factors for DVT in acute stroke patients.

2. MATERIALS AND METHODS

This was a prospective cross sectional study conducted in of Dhaka Medical College and Hospital, Bangladesh from January 2022 to December 2023. The inclusion criteria were as follows:

1. Patient age>18 years
2. Patient presented with acute onset of stroke (within 7 days)
3. Patient diagnosed with DVT within 14 days of stroke

Following patients were excluded from study

1. Recurrent stroke
2. Past history of venous thromboembolism (VTE)
3. Incomplete medical records
4. Age< 18 years

Deep-vein thrombosis was diagnosed according to the clinical examination findings like unilateral swollen limb with pain and erythema of lower extremity aided ultrasonography, performed by trained ultrasound physicians. DVT was defined based on the following ultrasonic findings:

- Heterogeneous thrombus was present inside any of the screened veins on B-mode
- Presence of a non-compressible segment
- Flow impairment on color Doppler imaging.

Demographic variables including age, sex, BMI, history of smoking, co-morbidities (hypertension, hyperlipidemia, diabetes, coronary heart disease, atrial fibrillation, and malignant tumor), and infections (pneumonia and urinary tract infection) were measured. Clinical data like time of onset of stroke, type of stroke, site of stroke, neurological deficit were recoded. Laboratory data were obtained with blood samples collected within 24 hours after hospitalization: The National Institutes of Health Stroke Scale (NIHSS) score calculated to objectively quantify the impairment caused by a stroke. The NIHSS is composed of 11 items, each item is scored between a 0 and 4. The maximum possible score is 42 with the minimum score being a 0. Never the less, Caprini risk assessment model (RAM) score of VTE was also calculated. Originally developed for surgical patients, the Caprini RAM facilitates the derivation of VTE risk by summing individual risk factors so as to place patients into four categories: "low risk" (0-1 points), "moderate risk" (2 points), "high risk" (3-4 points), and "highest risk" (≥5 points).

Data was collected in a preformed questionnaire. Prevalence of DVT among the ischemic stroke patients was investigated. Then, the clinical characteristics and laboratory results were compared between those with and without DVT. Statistical analysis was performed using IBM SPSS version 26.0. Continuous variables were analyzed in the form of the means with standard deviations (Mean ± SD). Categorical variables were shown as numbers and proportions. Continuous data were analyzed using the independent samples t-test. Categorical data were analyzed using the chi-squared test. Statistical significance was defined as a p-value of < 0.05. Multivariable analysis using a binary logistic regression model was used to verify the independent risk factors for DVT in acute ischemic stroke patients. Variables identified as having a potential association ($p < 0.05$) in a univariate analysis were entered into each multivariable analysis model. Receiver operating characteristic (ROC) curve analysis was performed by identifying the area under the ROC curve (AUC) to evaluate the performance of the logistic regression model.

3. RESULTS

A total of 106 patients with acute stroke (AS) were included in the study. The included patients were divided into two groups: DVT and

non-DVT group. Out of 106 patients, 34 (32.07%) patients presented with DVT. The general characteristics of the patients are demonstrated in Table 1.

There was no significant difference in BMI, smoking, history of surgery, comorbidities, and infections between the two groups. Patients with DVT were older than those without DVT (62.7 ± 10.7 vs. 56.5 ± 11.9 years, p < 0.05). Females were more affected by DVT (58.88% vs. 26.85%, p<0.05)

Table 3 shows the results of laboratory factors in patients with DVT vs. those without DVT. In the DVT group, the level of D-dimer was significantly higher than that in the non- DVT group (2.2 ± 1.7 vs. 0.45 ± 1.1, p < 0.05). Elevated CRP and low serum albumin level were also observed in DVT group which was statistically significant. (p<0.05).

Multiple logistic regression analysis showed that age, NIHSS score and D-dimer levels were independent variables for the presence of DVT in acute stroke patients.

Odds ratio for age, Caprini score, NIHSS score and elevated d-dimer were 1.043(1.000–1.075, p=0.029),1.43(0.85-0.1.96,p=0.001),1.266(1.168-1.284, p=0.008) and1.446 (1.130–1.849, p=0.003) respectively (Table 4).

Receiver operating characteristic curves demonstrated that age>60years, NIHSS score>25 and a D-dimer level of ≥ 1.52 μg/mL were independent factors for the presence of DVT at the time of stroke admission. (Fig. 1) Sensitivity for age>60 years, D-dimer>1.52 μg/mL,Caprini score >6 and NIHSS score >25 were 86.04%, 88.09%,87.06% and 92.17% respectively. Besides, specificity of these parameters were 87.45%, 85.02%, 76.83%and 78.04% respectively (Table 5).

4. DISCUSSION

Different studies had showed different risk factors for DVT in patients after AS. In our study, older age, higher NIHSS score, and higher D-dimer were identified as independent factors associated with the occurrence of DVT in patients with AS.

Table 1. Showing demographic characteristics of patients

Characteristics	Non-DVT(n=72)	DVT(n=34)	P-value
Age (years)	56.5 ± 11.9	62.7 ± 10.7	0.004
Male n (%)	54(75.00%)	14(41.12%)	0.118
Female n (%)	18(25.00%)	20(58.88%)	0.002
BMI (kg/m^2)	24±1.2	26±3.2	0.125
Smoking, n (%)	65(90.72%)	32(94.11%)	0.43
Comorbidities			
Hypertension, n (%)	68(94.44%)	30(88.23%)	0.085
Hyperlipidemia, n (%)	58(80.55%)	30(88.23%)	0.664
Diabetes, n (%)	71(98.86%)	32(94.11%)	0.862
Coronary heart disease n (%)	45(62.50%)	28(82.35%)	0.068
Atrial fibrillation n (%)	6(.8.33%)	2(5.88%)	0.488
Malignant tumor n (%)	4(5.55%)	2(5.88%)	0.269
Infections			
Pneumonia, n (%)	23(31.94%)	6(17.64%)	0.182
Urinary tract infection, n (%)	18(25.00%)	11(32.35%)	0.218
NIHSS score	18±4.2	34±8.2	0.003
Caprini RAM score	2±1.2	7±1.62	0.001

Table 2. Showing pattern of stroke of study population

Variable	DVT	Non-DVT	P value
Onset-to-admission time (days)	2±1.6	1.6±2.1	0.165
Site of stroke			
Cerebral hemisphere n (%)	30(88.23%)	56(77.77%)	0.983
Brainstem, n (%)	4(11.76%)	13(18.05%)	0.335
Both, n (%)	0	3(4.16%)	0.467
Type of stroke			
Ischemic n (%)	28(82.35%)	60(83.33%)	0.076
Haemorrhagic n (%)	6 (17.64%)	12(16.66%)	0.087

Table 3. Showing laboratory variables of the patients

| Parameter	DVT	Without DVT	p-value
WBC (10^9/L)	8.6 ± 3.6	7.8 ± 4.6	0.178
Hematocrit (%)	43.7 ± 3.9	42.6 ± 4.8	0.351
RBC (10^12/L)	4.5 ± 0.5	4.8 ± 1.2	0.243
Hb (g/L)	12.6±0.78	12.6±0.32	0.285
PLT (10^9/L)	254.2 ±84.0	236.7 ±76.2	0.182
Alb (g/L)	29.3 ± 3.9	38.5 ± 3.5	0.004
TG (mmol/L)	1.4 ± 0.7	1.6 ± 0.6	0.814
Totalcholesterol (mmol/L)	3.6 ± 0.8	3.8 ± 0.7	0.367
HDL-C (mmol/L)	0.8 ± 0.2	0.7 ± 0.2	0.590
LDL-C (mmol/L)	1.8± 0.6	1.6 ± 0.4	0.329
Random Blood glucose (mmol/L)	8.8 ± 1.9	7.45 ± 2.4	0.729
CRP	16±4.3	10±1.6	0.047
AST (IU/L)	30.8 ±14.3	28.4 ±12.1	0.638
ALT (IU/L)	36.2 ±12.4	35.6 ±18.0	0.470
D-dimer (ug/mL)	2.2 ± 1.7	0.45 ± 1.1	0.002
FDP	11.3 ± 1.2	9.0 ± 1.3	0.068
APTT (s)	38.6 ± 4.3	36.6 ± 4.6	0.764
PT (s)	12.4 ± 0.6	12.2 ± 0.5	0.675
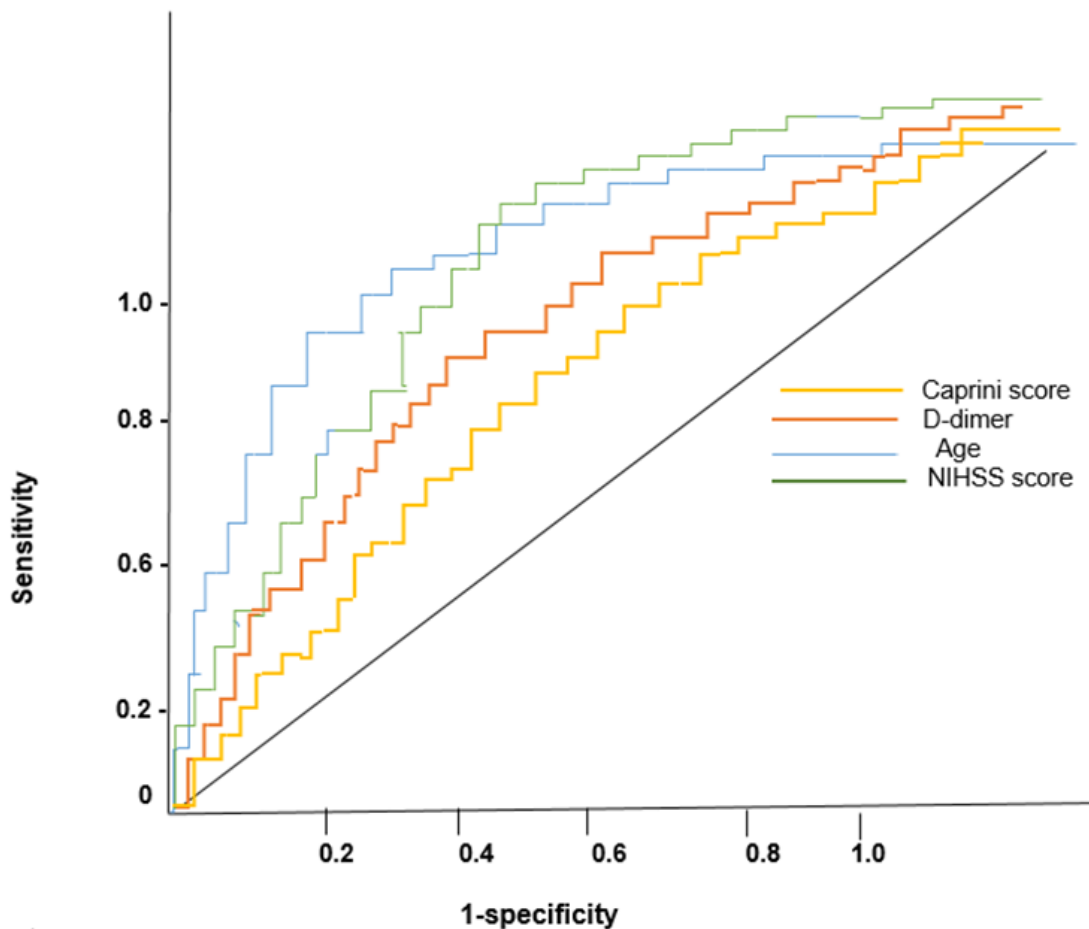
Fig. 1. ROC curve of NIHSS, Caprini score, D-dimer and age for predicting DVT in post stroke patients

Table 4. Showing Multivariate logistic regression model correlated to DVT

Variable	Odd ratio	95% CI	P value
Age	1.043	1.000–1.075	0.029
Female sex	0.852	0.713–0.993	0.071
D dimer	1.446	1.130–1.849	0.003
NIHSS	1.266	1.168-1.284	0.008
CRP	0.882	0.778-0.912	0.213
Serum Albumin	0.654	0.613-0.734	0.084
Caprini RAM score	1.43	0.85-0.1.96	0.001

Table 5. Predictive values of D-dimer, caprini score, NIHSS score and age for development of DVT in stroke patients

variable	Cut-off	Sensitivity	specificity	Area under curve (AUC) of ROC	95%CI
D-dimer(ug/mL)	1.52	88.09%	85.02%	0.618	0.510–0.726
NIHSS score	25	92.17%	78.04%	0.730	0.643–0.818
Age(years)	60	86.04%	87.45%	0.819	0.744–0.894
Caprini score	6	87.06%	76.83%	0.715	0.695-0.7146

"The present study showed 32.04% presented with DVT in AS patients which is higher than other studies". (Kelly et al., 2004) "In another study, stroke patients admitted to a rehabilitation unit in Singapore was 9%, which was lower than ours". (Kawase et al., 2015) The higher rate of DVT may be due to delayed presentation and lack of proper guideline for rehabilitation after AS. Besides de-ambulation by physiotherapists and use of compression therapy by intermittent pneumatic compression is not routinely advised in the current center for stroke patients.

"Previous studies have shown that advanced age was significantly associated with DVT, Particularly, the age ≥65 years was closely related to the occurrence of DVT" (Holst et al., 2018). In the present study, age at a cutoff of ≥60 years should raise clinical suspicion and could be used as an independent factor to predict DVT risk.

"CRP is a proven clinical marker of systemic inflammation which potentially affects all stages of the coagulation pathway". (Liu et al., 2015) "After acute inflammation, the coagulation cascade is triggered, contributing to thrombotic events. During the immediate aftermath of an AS episode, it induces a systemic inflammatory response, leading to increased peripheral blood inflammatory indicators. like CRP". (Bembenek et al., 2011) In our study raised CRP was significantly related to development of post stroke DVT which coincides with previous studies. But in regression model, it failed to show

as an independent risk factor of post stroke DVT formation.

"Low albumin concentration is considered an integrative index for inflammation, hypercoagulability, or disease states that predispose patients to thrombosis". (Khan et al., 2017) "Several previous studies have described an association between hypoalbuminemia and VTE". (Khan et al., 2017; Heit, 2015) Gyamlani, and Molnar showed that serum albumin <2.5 g/dL at presentation was a significant risk factor for recurrence of venous thromboembolism (40 versus 2.7%, P < 0.01). (Gyamlani et al., 2017) In our study we found low albumin level was significantly associated with DVT in stroke patients. But logistic regression analysis model showed not significant association between DVT and serum albumin (p=0.084).

"High level of D-dimer is risk factor of DVT. Previous studies reported that D-dimer had a sensitivity of 85–95% and a specificity of 25–50% for DVT in patients with AS during hospitalization". (Soomro et al., 2016) "Besides, Smith et al reported that D-dimer could predict incident stroke in the general population within 24 hours". (Smith et al., 2015) Our findings were consistent with results of previous prospective studies showing that D-dimer levels were elevated in the acute phase of AS compared with the healthy control population. Our study showed similar findings indicating routinely d-dimer should be advocated for early detection of DVT on the background of AS.

In the present study a higher NIHSS score (>25) has demonstrated to be a significant risk factor for developing DVT. The prevalence of DVT or pulmonary embolism is lower in Asians than in non-Asian subjects, and coagulopathy is less associated with ischemic stroke in Asian patients. (Adams et al., 2019) Therefore, the relative importance of systemic coagulopathy may be less important in Asian patients with ischemic stroke, and immobilization and severe neurological deficit may be more important in the development of DVT in Asian patients with acute ischemic stroke. (De et al., 2006) So NIHSS score plays an important role to predict post stroke DVT formation as an indicator of stroke severity especially in our region. Therefore, NIHSS score should be analyzed to predict DVT development in stroke patients.

"The Caprini RAM is the most widely used and guideline recommended tool for VTE risk prediction, also well-validated in stroke patients". (Chopard et al., 2020) "In a recent retrospective Chinese study assessed the Caprini RAM inpatients who developed image-confirmed VTE and found a score more than 6 was strongly associated with post stroke DVT which was similar to our findings" (Zhu et al., 2020).

Our study has several limitations. First, this study was a single- center study with a small sample size. Second, this study did not distinguish between newly developed DVT and asymptomatic DVT that had not been found prior to stroke. Third, the study period was very short.

5. CONCLUSION

The present study has showed that advanced age, high NIHSS and Caprini score and raised serum D-dimer levels are independent predictors of DVT in stroke patients. Besides routine physiotherapy and compression therapy should be administered to reduce the burden of DVT in stroke patients in our country. A further large multicenter study should be done to provide a better management to the patients of DVT in stroke patients.

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Authors hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators have been used during the writing or editing of this manuscript.

CONSENT

Patient's informed written consent was taken to publish her case for academic purpose.

ETHICAL APPROVAL

As per international standards or university standards written ethical approval has been collected and preserved by the authors.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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Peer-review history:
The peer review history for this paper can be accessed here:
https://www.sdiarticle5.com/review-history/129652