ORIGINAL ARTICLE

J Neurocrit Care 2018;11(2):102-109
https://doi.org/10.18700/jnc.180068

Journal of Neurocritical Care

eISSN 2508-1349

Venous Thromboembolism Following Acute Ischemic Stroke: A Prospective Incidence Study

Keun Hyuk Ko, MD[1], Ji-Hoon Kang, MD, PhD[1], Sa-Yoon Kang, MD[1], Jung Seok Lee, MD[1], Sook-Keun Song, MD[1], Jung-Hwan Oh, MD[1], Joong-Goo Kim, MD[1], Eun Young Han, MD[2], Ho Kyu Lee, MD[3], Jay Chol Choi, MD, PhD[1]

Departments of [1]Neurology, [2]Rehabilitation Medicine, [3]Radiology, Jeju National University School of Medicine, Jeju, Korea

Background: Asians were known to have a relatively lower incidence of venous thromboembolism (VTE), and there is insufficient evidence to suggest a specific D-dimer threshold level for screening VTE in patients with acute stroke.

Methods: We prospectively enrolled patients with acute ischemic stroke admitted to Jeju National University Hospital. The inclusion criteria were: 1) aged ≥18 years, 2) admission within seven days of symptom onset, and 3) an initial National Institute of Health Stroke Scale (NIHSS) score >1 for the affected lower limb. Ultrasound scans of the lower limbs and plasma D-dimer assays were performed on days 7-14 and 15-28 after stroke onset.

Results: Of 285 patients admitted during the study period, 52 patients met inclusion criteria (mean age 74.5, male 40.4%, median initial NIHSS score 12, and unable to walk unassisted at discharge 76.9%). During 7-14 days, 23 of 52 patients (44.2%) had a D-dimer level above 1.57 mg/L, and 9.6% had a level above 5.50 mg/L. Proximal deep vein thrombosis (DVT) was detected in 3 patients (5.8%, 95% confidence Interval 1.2-16.0%) on ultrasound examination. All DVTs were found in elderly female patients with severe leg weakness. No patient was diagnosed with pulmonary embolism during the study period.

Conclusion: The incidence of VTE seems to be very low among Korean patients with acute ischemic stroke. Advanced age, female sex, and severe leg weakness were important risk factors for developing DVT in this study.

J Neurocrit Care 2018;11(2):102-109

Key words: Venous thromboembolism; Stroke; Venous thrombosis

Received November 13, 2018
Revised December 12, 2018
Accepted December 18, 2018

Corresponding Author:
Jay Chol Choi, MD, PhD
Department of Neurology, Jeju National University School of Medicine, 15 Aran 13-gil, Jeju 63241, Korea
Tel: +82-64-754-8160
Fax: +82-64-717-1131
E-mail: jaychoi@jejunu.ac.kr

INTRODUCTION

Studies have shown that, without prophylaxis approximately 33-50% of Caucasian acutely immobilized stroke patients developed deep vein thrombosis (DVT) within two weeks after the onset of stroke.[1,2] Although the DVT rates varied significantly with different diagnostic tests, it occurred most frequently between 2 and 7 days after the

stroke.[3] Also, pulmonary embolism (PE) was found among 1% of acute stroke patients,[4] and it was responsible for up to 13% of early mortality among stroke patients in an autopsy study.[5] As a result, the current stroke management guidelines strongly suggest the use of subcutaneous anticoagulation to prevent venous thromboembolism (VTE) in immobilized stroke patients.[6]

Interestingly, previous studies have suggested racial differences in VTE incidence, and Asians were found to have up to 70% lower VTE rates compared to Caucasians.[7,8] Because of this difference, the use of prophylactic anticoagulation to prevent VTE among stroke patients has shown vast practice variation, as well. For example, 95% of the US hospitals used VTE prophylaxis according to the 2015 annual report.[9] However, studies report prophylactic anticoagulation was used in less than 5% of stroke patients in Korea and China.[10,11]

The D-dimer assay has been used to screen for VTE among various patient populations with a high diagnostic sensitivity, but a limited specificity for VTE at a cutoff level of 0.5 mg/L.[12] Because acute phase stroke patients can frequently have a high D-dimer level, the same threshold level cannot be used for these patients.[13,14] Only a few studies on the incidence of VTE and the possible role of the D-dimer assay in screening for VTE in Asian acute stroke patients have been conducted. Therefore, we investigated the frequency of VTE and usefulness of the D-dimer assay for screening VTE in Korean acute stroke patients using a prospective research design.

METHODS

Study participants

We prospectively and consecutively enrolled patients with acute ischemic stroke admitted to the Department of Neurology of Jeju University Hospital from May 2016 to April 2017. The inclusion criteria were: 1) aged ≥18 years with acute ischemic stroke, 2) hospital admission within seven days of symptom onset, and 3) an initial National Institute of Health Stroke Scale (NIHSS) score >1 for the lower limb affected by the acute ischemic stroke at the time of admission. Patients with significant pre-stroke disability (i.e., a modified Rankin Scale [mRS] score ≥4) or patients with a past history of DVT were excluded. This study was approved by a local ethics committee and written informed consent was obtained from all the patients or their legal representative.

Sonographic examination

Ultrasound scans of lower limbs were performed during the time periods of 7 to 14 days and 15 to 28 days after stroke onset. The examinations were performed at least 14 days apart. Compression tests were performed on the common femoral vein, femoral vein, and popliteal vein using a Voluson E ultrasound (General Electric Healthcare, Pittsburgh, PA, USA) with a 10-14 MHz linear transducer.[15] The examinations were performed by a trained ultrasonographer blinded to patients' clinical information. The study results were considered positive for DVT when vein compression failed. Results of the ultrasound studies were independently interpreted by two researchers (J.C.C. and H.K.L.) who were also blinded to the patient's clinical information, and any disagreement was resolved by consensus.

Clinical and laboratory assessment

All patients were rated by the Wells score at the time of the ultrasound examination, and it was used to classify the patient's probability of DVT as low (≤0), moderate (1 or 2), or high (>2).[16,17] PE was confirmed by chest computed tomography in patients with symptoms suggestive of PE, such as sudden dyspnea, hypoxemia, chest pain, or hemoptysis. Plasma D-dimer assays were performed on the same day as the ultrasound examination. D-dimer was measured by a particle-enhanced immunoturbidimetric assay for the quantitative determination of cross-linked fibrin degradation products using the INNOVANCE® (Siemens AG, Munich, Germanry) D-Dimer reagents on the automatic coagulation analyzer, Sysmex® CA-1500 System (Siemens Healthcare, Tokyo, Japan). The results of D-dimer testing were examined for sensitivity and specificity using cutoff values of 1.57 mg/L and 5.50 mg/L, as suggested in previ-

ous reports on patients with acute stroke.[13,14] Administration of antiplatelet agents or anticoagulants, use of elastic stockings or intermittent pneumatic compression devices to prevent DVT were also assessed at the time of ultrasound examination. Other clinical information, such as detailed stroke characteristics, vascular risk factors, other medications used during admission, and clinical outcomes at discharge were collected using an ongoing prospective stroke registry.[18] The primary outcome of this study was the incidence of DVT or PE within 28 days after stroke onset.

Statistical analysis

Univariate analysis was performed to evaluate the distribution of baseline characteristics of the patients. For bivariate analyses, Chi-square tests, Fisher's exact test, Student's *t*-test or Wilcoxon's rank sum test were applied where appropriate. Kappa statistics were used to measure the degree of inter-rater agreement for the presence or absence of DVT on the ultrasound examination. Sensitivity and specificity of the D-dimer test were calculated according to the aforementioned threshold values. For all analyses, a two-sided *P* value less than 0.05 was considered to be statistically significant. All analyses were performed using STATA version 15.0 software (Stata Corporation, College Station, TX, USA).

RESULTS

Patients

During the recruitment period of 12 months, a total of 285 acute ischemic stroke patients were admitted to the hospital within seven days from onset of stroke symptoms. Of the 285 patients, 52 patients met the eligibility criteria and underwent a first ultrasound examination during the time periods of 7 to 14 days after stroke onset. After the first ultrasound examination, four patients declined participation in the second study, one patient showed a critical condition that precluded the ultrasound examination, and one patient was transferred to another hospital before the second examination. As a result, 46 patients (46/52, 88.5%) received the second ultrasound examination dur-

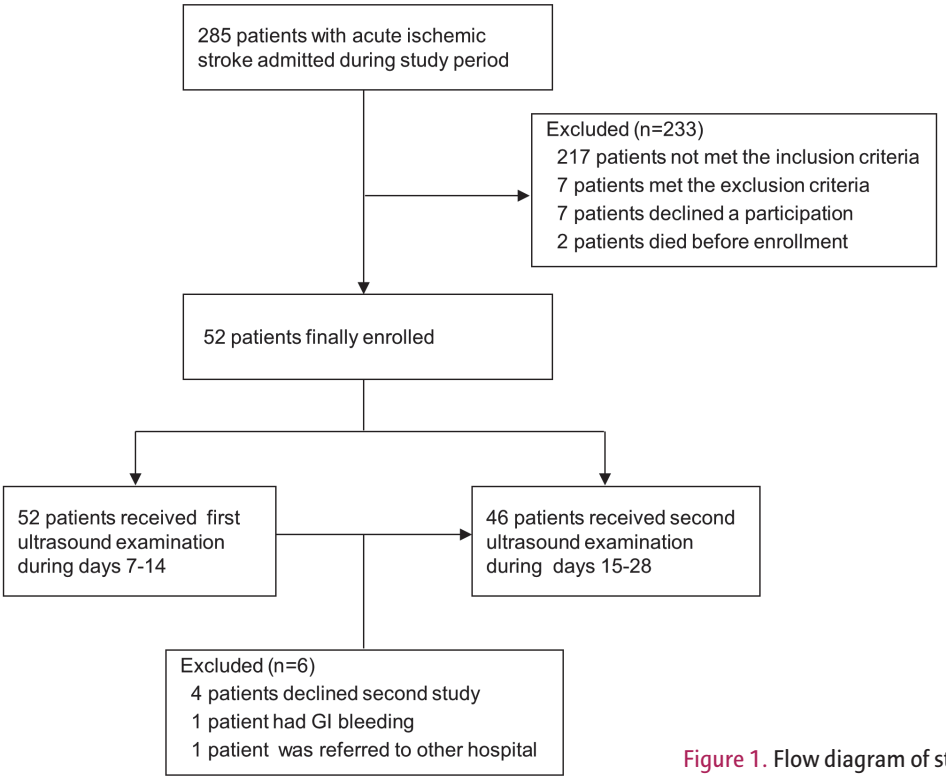

Figure 1. Flow diagram of study inclusion. GI, gastrointestinal.

https://doi.org/10.18700/jnc.180068

ing the time periods of 15 to 28 days (Fig. 1). Compared with the 233 acute ischemic stroke patients who were not enrolled, the 52 patients enrolled in this study were more likely to be older, female, and have higher stroke severity, atrial fibrillation, worse clinical outcomes. Of the 233 patients, six patients died during hospitalization, and the cause of death for four of them was directly related to the stroke. Of the remaining two patients, one died of asphyxia and the other died of myocardial infarction (Supplementary Table 1).

Table 1. Baseline characteristics of the patients

Characteristic	Study participants (n=52)
Age (years)	74.5±12.4
Sex (male)	21 (40.4)
TOAST classification	
Large artery atherosclerosis	17 (32.7)
Cardiac embolism	8 (15.4)
Small vessel occlusion	18 (34.6)
Undetermined or other determined etiology	9 (17.3)
Initial NIHSS score	12.2 (7-16.5)
Mild (0-4)	6 (11.5)
Moderate (5-14)	28 (53.8)
Severe (≥15)	18 (34.6)
NIHSS score of affected lower limb	
1	16 (30.8)
2	17 (32.7)
3	19 (36.5)
Treatment	
Intravenous thrombolysis	5 (9.6)
Antiplatelet	37 (71.1)
Aspirin	35 (67.3)
Clopidogrel	21 (40.4)
Anticoagulation	13 (25.0)
Warfarin	4 (7.7)
NOAC	5 (9.6)
Early rehabilitation	47 (90.4)
Elastic stocking	3 (5.8)
Intermittent pneumonic compression	12 (23.1)
Plasma D-dimer level (mg/L)	1.64 (0.8-3.9)

TOAST, the trial of ORG 10172 in acute stroke treatment; NIHSS, National Institutes of Health Stroke Scale; NOAC, non-vitamin K antagonist oral anticoagulants.
Values are presented as mean±standard deviation, number (%), or median (interquartile range).

Table 1 shows the baseline characteristics of the 52 patients enrolled in this study. The mean age was 74.5 years, and 40.4% were men. Hypertension (71.1%) was the most frequent risk factor for stroke, followed by atrial fibrillation (38.6%), diabetes mellitus (30.8%), hypercholesterolemia (23.1%), and smoking (17.3%). More than half of the patients had moderate stroke severity (i.e., baseline NIHSS score 5-14) and lower limb NIHSS scores were distributed almost evenly among scores between one and three. All patients had previous mRS score ≤3 and no history of DVT or PE. Antiplatelet agents were administered to 71.1% of the patients, and anticoagulants were used in 25% of the patients. Intermittent pneumatic compression devices were used in 23.1% of the patients, and early rehabilitation was performed in 90.4% of patients. However, compression stockings were used in only 5.8% of the patients. Of the 52 patients, one patient had active cancer at the time of the admission.

Ultrasound examination

Agreement between two researchers on the diagnosis of DVT by ultrasound examination was moderate (kappa=0.58). DVT at proximal lower limbs was detected in three patients (5.8%, 95% confidence Interval 1.2-16.0%) on the first ultrasound examination and no new DVTs were found in patients at the second examination. All DVTs were found in elderly female patients, with an NIHSS score of three (i.e., no effort against gravity) for the lower limb affected by the stroke. Although the analyses were limited by the small number of patients with DVT, patients with DVT appeared to have greater stroke severity and more severe leg motor weakness, compared to patients without DVT (Supplementary Table 2). Two patients had DVT, even though they were receiving oral anticoagulants at the time of the ultrasound examination (Table 2). None of the three patients were using intermittent pneumonic compression devices at the time of DVT diagnosis, though one patient was wearing compression stockings, and two were receiv-

Table 2. Characteristics of three patients with DVT

No.	Patient 1	Patient 2	Patient 3
Sex/age	F/81	F/75	F/95
Initial NIHSS score	7	26	28
Leg motor scale (Rt/Lt)	3/0	3/1	3/3
Infarct location	Lt. ACA	Lt. MCA	Rt. MCA/ACA
TOAST classification	LAA	ODE	CE
Antithrombotics	Aspirin+clopidogrel	Warfarin	Apixaban
Wells score	1	3	1
DVT location	Rt. FV	Rt. CFV	Rt. CFV
D-dimer level (mg/L)	2.0	35.0	3.6
Discharge mRS	4	5	5
Cancer history	No	Yes	No
Intravenous thrombolysis	No	No	No
Laboratory parameter			
WBC ($\times 10^3$/uL)	6.0	6.8	10.5
Hemglobin (g/dL)	12.5	8.5	14.6
Platelet ($\times 10^3$/uL)	259	111	209
PT INR	0.91	1.34	1.05
PT (sec)	10.2	15.2	11.8
aPTT (sec)	Not done	31	29

DVT, deep vein thrombosis; F, female; NIHSS, National Institutes of Health Stroke Scale; Rt, right; Lt, left; ACA, anterior cerebral artery, MCA, middle cerebral artery; TOAST, the trial of ORG 10172 in acute stroke treatment; LAA, large artery atherosclerosis; ODE, other determined etiology; CE, cardiac embolism; FV, femoral vein; CFV, common femoral vein; mRS, modified Rankin Scale; WBC, white blood cells; PT INR, prothrombin time international normalized ratio; PT, prothrombin time; aPTT, activated partial thromboplastin time.

ing early rehabilitation. Patient 2, who showed the highest D-dimer value had been diagnosed with gallbladder cancer with metastasis before hospital admission. The incidence of DVT was 9.68% (3/31) in female patients, 11.1% (2/18) in severe stroke patients (NIHSS ≥15), and 15.8% (3/19) in patients with a lower limb NIHSS score of three. No patient was diagnosed with PE during the study period. Of 52 patients, only eight (15.4%) had favorable outcomes at discharge. However, no one died during the study period.

Plasma D-dimer & Wells score

Plasma D-dimer levels were available for all patients at the time of the first ultrasound examination, and in 35 patients (35/46, 76.1%) at the time of the second ultrasound examination. During the time periods of 7 to 14 days, 23 of 52 patients (44.2%) had a D-dimer level above 1.57 mg/L, and 9.6% had levels above 5.50 mg/L. During the time periods of 15 to 28 days, 32.5% of the patients had a D-dimer level above 1.57 mg/L, and 8.7% had levels above 5.50 mg/L (Fig. 2). At the maximal D-dimer value, sensitivity and specificity were 100% (3/3) and 53.1% (26/49), respectively, for a cutoff value of 1.57 mg/L; and 33.3% (1/3)

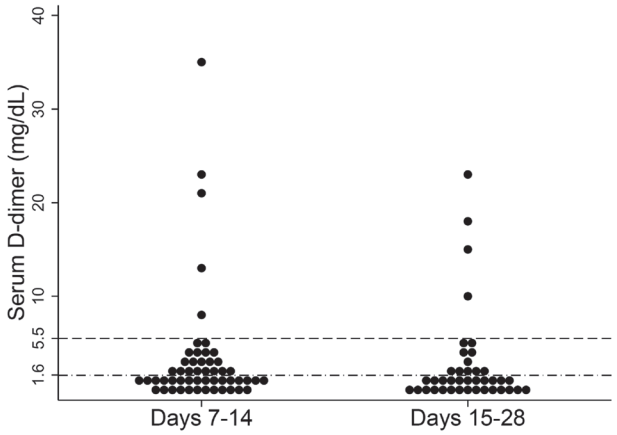

Figure 2. Distribution of the plasma D-dimer levels

https://doi.org/10.18700/jnc.180068

and 87.8% (43/49), when the cutoff value was 5.50 mg/L, respectively.

At the time of the first ultrasound examination, the probability of DVT based on total Wells score of 52 patients was moderate (1-2) in 50 patients (96.2%), and high (>2) in two patients (3.9%), and 11.5% (6/52) of these patients had a score of 2 or more. The probability at the second examination was moderate or high in 91.3% of patients. The Wells score of patients diagnosed with DVT was 3 in one patient and 1 in two patients (Table 2).

DISCUSSION

In this study, we found that the incidence of VTE was only 5.8% among Korean patients with ischemic stroke who were immobilized due to leg weakness. The risk seemed to be greatest for elderly female patients with severe lower extremity weakness due to stroke. This study also confirmed that the current reference value of plasma D-dimer was not helpful in screening for VTE among patients with acute ischemic stroke.

Vast variations in VTE prevalence among Asian stroke patients have been reported, depending on the research method.[19] In clinical studies, the prevalence rates were less than 1%, however the rates varied significantly from 4.8% to 45% in imaging studies. The highest reported rates were from a Doppler ultrasound study done in 111 acute stroke patients from Singapore.[20] DVT was found in 30% of the patients during the time period of 7 to 10 days and 45% during 25 to 30 days from stroke onset. However, the majority of the DVTs were in the distal part of a lower extremity, and only one patient had PE in that study due to limited risk of proximal extension on the distal DVT. Other ultrasound-based studies reported prevalence rates of DVT from 4.8 to 9.0%, which are similar to the current report.[21,22] Based on the current findings, the prevalence of clinically significant symptomatic DVT or PE seems to be quite low in Asian stroke patients.

The exact mechanisms underlying racial differences in VTE rates are not clear. Possible explanations may include variation in the prevalence of genetic and environmental risk factors and accessibility to medical care to provide a correct diagnosis of VTE.[7,23] Several researchers have also claimed that the lower VTE incidence in Asians may be due to lack of well-designed large clinical studies. Prospective studies in Asian patients have reported higher rates of VTE following major surgery, and rates that varied with different medical conditions.[24-26] Well-designed large multicenter research is required to investigate the accurate prevalence and risk factors for VTE, and evaluate optimal thromboprophylaxis in high-risk Asian patients.

Plasma D-dimer levels are useful for screening DVT in chronic stroke patients receiving rehabilitation.[27,28] However, stroke patients can have frequently higher D-dimer levels during the acute phase, so the same threshold level cannot be used during that phase.[29] Balogun et al.[13] found that a baseline D-dimer of 1.7 mg/mL had a sensitivity of 0.71 and a specificity of 0.74 in detecting ultrasound-verified DVT in patients with acute stroke. In another DVT screening study, Kuwashiro et al.[14] suggested an optimum D-dimer cut-off value of 5.50 mg/mL (sensitivity, 89%; specificity, 82%) as the maximum for definitive DVT. Because of the small number of DVT patients in the current study, we could not suggest a threshold level of D-dimer for the presence of DVT. In this study, sensitivity and specificity were 100% and 53.1% when the cutoff value was 1.57 mg/L, respectively, and 33.3% and 87.8% when the cutoff value was 5.50 mg/L, respectively. At present, there is a wide variation in plasma D-dimer levels among patients with acute stroke, and the level could change over time during the acute phase of stroke. Therefore, there is insufficient evidence to suggest a certain threshold D-dimer level for screening DVT in patients with acute stroke.

This study had several limitations. Because this was a single center study with a small number of patients, our findings may not apply to other populations or different clinical settings. In particular, usefulness of the D-dimer assay may be limited in this study due to the small number of patients diagnosed with DVT, as well as the presence of an active cancer patient among the DVT patients. However, we could evaluate the effect of various stroke character-

istics on the risk of VTE, including total NIHSS score and severity of leg motor weakness. We could not evaluate the incidence of VTE beyond four weeks after onset of stroke because a substantial number of patients had already been discharged from our institution by that time. Finally, active employment of intermittent pneumatic compression, early rehabilitation therapy, and the use of antiplatelet agents or anticoagulant as part of secondary stroke prevention may have contributed to the low incidence of VTE in the current study.

CONCLUSION

The incidence of VTE seems to be very low among Korean patients with acute ischemic stroke. Advanced age, female gender, and severe leg weakness due to stroke were important risk factors for developing DVT in this study. Large-scale multicenter research is needed to investigate the exact incidence, biomarkers, and risk factors for VTE in Asian stroke patients to identify high-risk patients and to provide safe and effective VTE prophylaxis.

Supplementary content

The online-only supplementary material is available with this article at https://doi.org/10.18700/jnc.180068.

REFERENCES

1. Brandstater ME, Roth EJ, Siebens HC. Venous thromboembolism in stroke: literature review and implications for clinical practice. *Arch Phys Med Rehabil* 1992;73(5-S):S379-91.
2. Kelly J, Rudd A, Lewis R, Hunt BJ. Venous thromboembolism after acute stroke. *Stroke* 2001;32:262-7.
3. Kamphuisen PW, Agnelli G, Sebastianelli M. Prevention of venous thromboembolism after acute ischemic stroke. *J Thromb Haemost* 2005;3:1187-94.
4. Pongmoragot J, Rabinstein AA, Nilanont Y, Swartz RH, Zhou L, Saposnik G, et al. Pulmonary embolism in ischemic stroke: clinical presentation, risk factors, and outcome. *J Am Heart Assoc* 2013;2:e000372.
5. Bounds JV, Wiebers DO, Whisnant JP, Okazaki H. Mechanisms and timing of deaths from cerebral infarction. *Stroke* 1981;12:474-7.
6. Jauch EC, Saver JL, Adams HP Jr, Bruno A, Connors JJ, Demaerschalk BM, et al. Guidelines for the early management of patients with acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke* 2013;44:870-947.
7. Zakai NA, McClure LA. Racial differences in venous thromboembolism. *J Thromb Haemost* 2011;9:1877-82.
8. White RH, Keenan CR. Effects of race and ethnicity on the incidence of venous thromboembolism. *Thromb Res* 2009;123 Suppl 4:S11-7.
9. The Joint Commission. America's hospitals: improving quality and safety. The joint commission's annual report 2015 [online]. Available at: https://www.jointcommission.org/assets/1/18/TJC_Annual_Report_2015_EMBARGOED_11_9_15.pdf. Accessed at October 1, 2017.
10. Zheng H, Liu L, Sun H, Wang X, Wang Y, Zhou Y, et al. Prophylaxis of deep venous thrombosis and adherence to guideline recommendations among inpatients with acute stroke: results from a multicenter observational longitudinal study in China. *Neurol Res* 2008;30:370-6.
11. Choi JC, Bae HJ, Lee SJ, Park JM, Park TH, Cho YJ, et al. Variation in prophylactic anticoagulation for venous thromboembolism among acute stroke patients. *J Clin Neurosci* 2017;45:330-1.
12. Stein PD, Hull RD, Patel KC, Olson RE, Ghali WA, Brant R, et al. D-dimer for the exclusion of acute venous thrombosis and pulmonary embolism: a systematic review. *Ann Intern Med* 2004;140:589-602.
13. Balogun IO, Roberts LN, Patel R, Pathansali R, Kalra L, Arya R. Clinical and laboratory predictors of deep vein thrombosis after acute stroke. *Thromb Res* 2016;142:33-9.
14. Kuwashiro T, Toyoda K, Oyama N, Kawase K, Okazaki S, Nagano K, et al. High plasma D-dimer is a marker of deep vein thrombosis in acute stroke. *J Stroke Cerebrovasc Dis* 2012;21:205-9.
15. Guideline developed in collaboration with the American College of Radiology, Society of Pediatric Radiology, Society of Radiologists in Ultrasound. AIUM practice guideline for the performance of peripheral venous ultrasound examinations. *J Ultrasound Med* 2015;34:1-9.
16. Wells PS, Anderson DR, Bormanis J, Guy F, Mitchell M, Gray L, et al. Value of assessment of pretest probability of deep-vein

https://doi.org/10.18700/jnc.180068

thrombosis in clinical management. *Lancet* 1997;350:1795-8.
17. Wells PS, Anderson DR, Rodger M, Forgie M, Kearon C, Dreyer J, et al. Evaluation of D-dimer in the diagnosis of suspected deep-vein thrombosis. *N Engl J Med* 2003;349:1227-35.
18. Kim BJ, Park JM, Kang K, Lee SJ, Ko Y, Kim JG, et al. Case characteristics, hyperacute treatment, and outcome information from the clinical research center for stroke-fifth division registry in South Korea. *J Stroke* 2015;17:38-53.
19. Tan KS, Rashid AR, Tan CT. Venous thromboembolism in ischaemic stroke in Asia. *Neurology Asia* 2008;13:95-101.
20. De Silva DA, Pey HB, Wong MC, Chang HM, Chen CP. Deep vein thrombosis following ischemic stroke among Asians. *Cerebrovasc Dis* 2006;22:245-50.
21. Tan SS, Venketasubramanian N, Ong PL, Lim TC. Early deep vein thrombosis: incidence in Asian stroke patients. *Ann Acad Med Singapore* 2007;36:815-20.
22. Kong KH, Chua SG, Earnest A. Deep vein thrombosis in stroke patients admitted to a rehabilitation unit in Singapore. *Int J Stroke* 2009;4:175-9.
23. Angchaisuksiri P. Venous thromboembolism in Asia--an unrecognised and under-treated problem? *Thromb Haemost* 2011;106:585-90.
24. Leizorovicz A, Turpie AG, Cohen AT, Wong L, Yoo MC, Dans A, et al. Epidemiology of venous thromboembolism in Asian patients undergoing major orthopedic surgery without thromboprophylaxis. The SMART study. *J Thromb Haemost* 2005;3:28-34.
25. Piovella F, Wang CJ, Lu H, Lee K, Lee LH, Lee WC, et al. Deep-vein thrombosis rates after major orthopedic surgery in Asia. An epidemiological study based on postoperative screening with centrally adjudicated bilateral venography. *J Thromb Haemost* 2005;3:2664-70.
26. Liew NC, Alemany GV, Angchaisuksiri P, Bang SM, Choi G, DE Silva DA, et al. Asian venous thromboembolism guidelines: updated recommendations for the prevention of venous thromboembolism. *Int Angiol* 2017;36:1-20.
27. Harvey RL, Roth EJ, Yarnold PR, Durham JR, Green D. Deep vein thrombosis in stroke. The use of plasma D-dimer level as a screening test in the rehabilitation setting. *Stroke* 1996;27:1516-20.
28. Akman MN, Cetin N, Bayramoglu M, Isiklar I, Kilinc S. Value of the D-dimer test in diagnosing deep vein thrombosis in rehabilitation inpatients. *Arch Phys Med Rehabil* 2004;85:1091-4.
29. Ageno W, Finazzi S, Steidl L, Biotti MG, Mera V, Melzi D'Eril G, et al. Plasma measurement of D-dimer levels for the early diagnosis of ischemic stroke subtypes. *Arch Intern Med* 2002;162:2589-93.

Supplementary Content

Ko KH, Kang JH, Kang SY, Lee JS, Song SK, Oh JH, et al. Venous Thromboembolism Following Acute Ischemic Stroke: A Prospective Incidence Study. J Neurocrit Care. Published online December 27, 2018. doi: 10.18700/jnc.180068

Supplementary Table 1. Characteristics of the patients by enrollment
Supplementary Table 2. Characteristics of the patients by deep vein thrombosis

This supplementary material has been provided by the authors to give readers additional information about their work.

Supplementary Table 1. Characteristics of the patients by enrollment

Characteristic	Enrolled (n=52)	Excluded (n=233)	*P* value
Age (years)	74.5±12.4	66.8±13.8	<0.001
Sex (male)	21 (40.4)	157 (67.4)	<0.001
Vascular risk factor			
Hypertension	37 (71.1)	148 (63.5)	0.297
Diabetes mellitus	16 (30.8)	76 (32.6)	0.797
Hypercholesterolemia	12 (23.1)	66 (28.3)	0.443
Smoking	9 (17.3)	87 (37.3)	0.006
Atrial fibrillation	18 (34.6)	41 (17.6)	0.006
TOAST stroke classification			0.136
Large artery atherosclerosis	17 (32.7)	85 (37.4)	
Cardiac embolism	8 (15.4)	51 (22.5)	
Small vessel occlusion	18 (34.6)	45 (19.8)	
Undetermined or other determined etiology	9 (17.3)	46 (20.3)	
Initial NIHSS score	12.2 (7-16.5)	5.5 (1-7)	<0.001
Initial NIHSS score, categorical			<0.001
Mild (0-4)	6 (11.5)	142 (60.9)	
Moderate (5-14)	28 (53.8)	67 (28.8)	
Severe (≥15)	18 (34.6)	24 (10.3)	
Treatment			
Intravenous thrombolysis	5 (9.6)	31 (13.3)	0.469
Anti-platelet	37 (71.1)	204 (87.5)	0.003
Aspirin	35 (67.3)	195 (83.7)	0.007
Clopidogrel	21 (40.4)	134 (57.5)	0.025
Anti-coagulation	13 (25.0)	29 (12.4)	0.021
Warfarin	4 (7.7)	15 (6.4)	0.743
NOAC	5 (9.6)	10 (4.3)	0.120
Discharge mRS			<0.001
Favorable (mRS 0-2)	8 (15.4)	161 (69.1)	
Unfavorable (mRS 3-6)	44 (84.6)	72 (30.9)	

TOAST, the trial of ORG 10172 in acute stroke treatment; NIHSS, National Institutes of Health Stroke Scale; NOAC, non-vitamin K antagonist oral anticoagulants; mRS, modified Rankin Scale.
Values are presented as mean±standard deviation, number (%), or median (interquartile range).

https://doi.org/10.18700/jnc.180068

Supplementary Table 2. Characteristics of the patients by deep vein thrombosis

Characteristic	No DVT (n=49)	DVT (n=3)	*P* value
Age (years)	74.0±12.3	83.7±10.3	0.215
Sex (male)	21(42.9)	0 (0.0)	0.264
Vascular risk factor			
Hypertension	36 (73.5)	1 (33.3)	0.196
Diabetes mellitus	15 (30.6)	1 (33.3)	1.000
Hypercholesterolemia	11 (22.4)	1 (33.3)	0.553
Smoking	9 (18.4)	0 (0.0)	1.000
Atrial fibrillation	17 (34.7)	1 (33.3)	1.000
TOAST stroke classification			0.592
Large artery atherosclerosis	16 (32.6)	1 (33.3)	
Cardiac embolism	8 (16.3)	0 (0.0)	
Small vessel occlusion	17 (34.7)	1 (33.3)	
Undetermined or other determined etiology	8 (16.3)	1 (33.3)	
Initial NIHSS	11.7±6.6	20.3±11.6	0.194
Lower motor scale, affected	2±0.8	3±0	0.039
D-dimer level	2.8±4.6	13.0±19.1	0.298
Well's score	1.1±0.5	0.7±1.1	0.190
Treatment			
Intravenous thrombolysis	5 (10.2)	0 (0.0)	1.000
Anti-platelet	35 (71.4)	2 (66.7)	1.000
Anti-coagulation	12 (24.5)	1 (33.3)	1.000
In-hospital rehabilitation	45 (91.8)	2 (66.7)	0.266
Elastic stocking	2 (4.1)	1 (33.3)	0.166
Intermittent pneumatic compression	12 (24.5)	0 (0.0)	1.000
Discharge mRS			1.000
Favorable (mRS 0-2)	8 (16.33)	0 (0.0)	
Unfavorable (mRS 3-6)	41 (83.67)	3 (100.0)	

DVT, deep vein thrombosis; TOAST, the trial of ORG 10172 in acute stroke treatment; NIHSS, National Institutes of Health Stroke Scale; mRS, modified Rankin Scale.
Values are presented as mean±standard deviation or number (%).