ปัจจัยที่ช่วยในการวินิจฉัยแยกโรคระหว่างหลอดเลือดดำอุดตันในสมอง ของโรงพยาบาลสุราษฎร์ธานี

พิชัย โรจนพิทยากร พ.บ., ว.ว.ประสาทวิทยา

Predicting diagnostic factors for cerebral venous sinus thrombosis in Suratthani Hospital

Abstract

Objective : To study the affecting factors for diagnosis of cerebral venous sinus thrombosis (CVST) and treatment.

Methods : A retrospective cross-sectional study was conducted in Suratthani Hospital, Thailand. All cases of CVST stroke patients, diagnosed by magnetic resonance imaging (MRI), MR-venography or computed tomography (CT), CT- venography between January 2013 and December 2018 were included. The sampling of cerebral arterial thrombosis (CAT) stroke cases during the same period as CTSV cases were randomly selected with one-to-one ratio. The key characteristics were abstracted from medical records, and were contrasted between the two groups with multivariable risk regression analyses.

Result : There were a total of 52 CVSTs and 52 random samples of CATs in the study. The median age were 44 years in CVST and 70 years in CAT. The most common sites of thrombosis were transverse sinus (59.62%) and superior sagittal sinus (51.92%). Prothrombotic risk identified were antithrombin III abnormal in 16 patients (40%), Beta2-Glycoprotein antibody in 9 patients (39.13%). In the multivariable risk regression analysis. The predicting factors favoring for CVST were; age <45 years (adjusted risk difference [aRD]) 16%, 95% confidence interval [CI]: 1-32%, p=0.039), headache (aRD 52%, 95%CI: 38-66%, p<0.001) and seizure (aRD 42%, 95%CI: 12-35%, p<0.001). The predicting factors favoring for CAT was history of previous stroke (aRD 22%, 95%CI: 7-37%, p=0.005).

Conclusion : The predicting factors favoring for CVST were; age <45 years, headache and seizure on presentation. The history of previous stroke was the only predicting factor favoring for CAT.

Key words : cerebral venous sinus thrombosis, Neurological manifestation, cerebral arterial thrombosis

Pichai Rojanapitayakorn MD.
Department of Medicine.
Suratthani Hopital
Suratthani 84000

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บทคัดย่อ

วัตถุประสงค์ การศึกษานี้เป็นศึกษาถึงปัจจัยที่มีผลในการวินิจฉัยแยกโรคหลอดเลือดดำอุดตันในสมอง

วิธีการ เป็นการศึกษาแบบตัดขวางย้อนหลังในโรงพยาบาล สุราษฎร์ธานี ประเทศไทย ช่วงเวลาระหว่างเดือนมกราคม พ.ศ. 2556 ถึง ธันวาคม พ.ศ. 2560 โดยศึกษาในกลุ่มประชากรหลอดเลือดดำอุดตันในสมอง วินิจฉัยโดยคลื่นแม่เหล็กไฟฟ้าสมอง หรือ เอ็กซ์เรย์คอมพิวเตอร์สมอง เปรียบเทียบกับกลุ่มประชากรหลอดเลือดแดงอุดตันในสมอง ในช่วงเวลาเดียวโดยการสุ่มเลือดแบบหนึ่งต่อหนึ่ง จากเวชระเบียน สนใจศึกษาในเรื่องอาการทางคลินิก ปัจจัยที่มีผลต่อการวินิจฉัยและการรักษา

ผลการศึกษา กลุ่มประชากรทั้งหมด 104 คน แบ่งเป็น กลุ่มหลอดเลือดดำอุดตันในสมอง 52 คน และหลอดเลือดแดงอุดตันในสมอง 52 คน อายุเฉลี่ยในกลุ่มหลอดเลือดดำ 44 ปี และหลอดเลือดแดงอายุเฉลี่ย70 ปีตำแหน่งหลอดเลือดดำอุดตันที่พบบ่อยที่สุดคือ transverse sinus (ร้อยละ59.62), ความผิดปกติของเลือดที่เสี่ยงต่อการเกิดอุดตันที่พบบ่อยที่สุด คือ ความผิดปกติของ antithrombin III (ร้อยละ40) รองลงมา beta2-Glycoprotein antibody ผิดปกติ (ร้อยละ39.13) ในการศึกษาหาความสัมพันธ์ระหว่างอาการทางคลินิกกับหลอดเลือดดำอุดตันในสมองพบว่าอายุที่น้อยกว่า 45 ปี มีความเสี่ยง ร้อยละ16 (adjusted risk difference [aRD]) 16%, 95% confidence interval [CI]: 1-32%, p=0.039), อาการปวดหัว ร้อยละ52 (aRD 52%, 95%CI: 38-66%, p<0.001) และอาการชักร้อยละ 42 (aRD 42%, 95%CI: 12-35%, p<0.001) ทั้งสามปัจจัยมีความสำคัญอย่างมีนัยทางสถิติ ในกลุ่มหลอดเลือดแดงอุดตันในสมองมีเพียงประวัติที่เคยเป็นโรคหลอดเลือดสมองที่มีความสัมพันธ์อย่างมีนัยทางสถิติ มีความเสี่ยง ร้อยละ 22 (aRD 22%, 95%CI: 7-37%, p=0.005)

บทสรุป ปัจจัยที่มีผลต่อการวินิจฉัยโรคหลอดเลือดดำอุดตันในสมอง คือ อายุน้อย 45 ปี อาการปวดหัว และอาการชัก ส่วนหลอดเลือดแดงอุดตันปัจจัยที่มีผลคือประวัติเคยมีโรคหลอดเลือดแดงอุดตันมาก่อน

คำรหัส :

Introduction

Cerebrovascular disease is the most common cause of acute neurological events, the majority of them are arterial strokes[1]. Cerebral venous sinus thrombosis (CVST) is a rare type of cerebrovascular disease[2]. The clinical manifestations are different among these two type of stroke, CVST often affects young adults, women of childbearing age. The patients mean age is 35 year and the common presentation are headache, seizures, sign of focal cerebral edema, and increase intracranial pressure[3-6]. Previously studies, the incidence were 1.32–1.57 per 100,000 person-years[7, 8]. The major causes of CVST were thrombophilia (56%), either genetic or acquired, obstetric and gynecological (50%), and sepsis (34%)[6]. Early diagnosis and anticoagulant treatment may decrease mortality and/or morbidity rates related with CVST in these patients[9]. The treatment consists of reversing the underlying cause, control of seizures and intracranial hypertension, and the use of antithrombotic drug. Heparin should be the first-line antithrombotic agent. Its safety even in patients with hemorrhagic

parenchymal lesions[10]. Sometime venous and arterial strokes manifest as acute neurological events that may similar clinical and radiological picture[1]. Resulting in difficult to diagnose of this disease. The purpose of this study were interested the affecting factors for diagnoses CVST and compare with the arterial stroke in clinical characteristics, laboratory, treatment and complication.

Methods

The study design was period cross-sectional retrospective study in Suratthani Hospital Thailand from January 2013 to December 2018. The study was approved by the Suratthani Hospital Institutional Review Board. All cases of CVST records were reviewed to collect demographic, clinical, laboratory finding, imaging, and treatment data. The following eligibility inclusion criteria were:

(1) All patients included in the study were diagnosed base on clinical presentation and confirmed by computed tomography (CT) or magnetic resonance imaging (MRI) or CT and computed tomography venography (CTV) or MRI and MR venography (MRV) or CT and MRI and MRV

(2)This study included adult onset, age more than 15 years

(3) In compared 1:1 random acute arterial ischemic stroke in similar period with CTSV, randomly selected by statisticians. To choose arterial stroke from the total number of patients 10,672 patients. Selected 52 patients, representing the ratio 0.5 % of total patients. The selected arterial stroke may not represent all arterial stroke but that should be compared with venous stroke.

Exclusion criteria was hemorrhagic stroke. All the data was collected in Microsoft excel, the Stata program was used for analysis. Fisher exact test used measure of association between two groups. Risk factor relation between predicting factor with clinical characteristic were analyzed by univariate risk regression analysis. Univariate logistic regression analyzed relationship between clinical manifestations, etiology with both type strokes. Significantly risk factors and symptoms related in CVST by univariate logistic regression analysis were sex, age , oral contraception, nephrotic syndrome, headache and seizure. In arterial group, significantly risk factors and symptoms were hypertension, old CVD, weakness and dysarthria. Selected significant clinical to analyzed multivariate logistic regression by selected in all significant ($p<0.1$) in both group and etiology possible in relationship. The significant cutoff value was set at 95% confidence interval and $P \leq 0.05$.

Results

This study analyzed data from 104 patients that were 52 CVST patients and 52 CAT patients. All cases were diagnosed by brain imaging technique. Classified arterial group in large cerebral vessel infraction (major vessel and main branch of major vessel) 31patients (40%) and small cerebral vessel infarction (perforating artery and small vessel) 21 patients (60%).The median age in arterial group was 70 (60-70) years, in venous group was younger than arterial group was 44 (30-52) years ($p<0.001$). The common symptoms manifestation in venous group were included headache (81%), seizures

(50%), altered of conscious (40%), and hemiparesis (35%). In arterial group, common symptoms were weakness (83%), dysarthria (44%), altered of consciousness (42%) and seizure (13%) were the major symptoms (p<0.001). The main risk factor of venous group were taking the oral contraceptive pill (10%) and nephrotic syndrome (10%). In arterial group were hypertension (65%) and old cerebrovascular disease (CVD) (27%). Modified Rankin scale on admission was not different between two groups. The number of deaths in this study were 11 patients (10.58%), by definition mRs = 6 (Table 1, 5)

The laboratory test had done both the venous group and the arterial group including complete blood count (CBC), lipid profiles and fasting blood sugar. This study found that the different in leukocytosis and polymorph nuclear cell predominantly were common in venous group (p0.002, p0.003). Cerebral venous sinus thrombosis blood glucose was higher (p=0.005). Others finding were not different between two group. Prothrombotic studies were done in venous group, only one arterial group patient was done. Most prothrombotic states in venous group identified were antithrombin III, which abnormal in 16 patients (40%) and Beta2-Glycoprotein antibody in 12 patients (39.13%). Computed tomography or magnetic resonance imaging of brain was abnormal in all patients with CVST, and the most common sinus involved were transverse sinus 31 patients (59.62%) and sagittal sinus 27 patients (51.92%). Lumbar punctures in the venous group were done 11 patients (21.15 %), we found that the mean open pressure was 29 ± 12, mononuclear cell pleocytosis in cerebrospinal fluid (CSF) mean 27 cell/cu.mm, nevertheless most patients (7 patients(63.64 %)) had normal cell count (<5 cell/cu.mm) in CSF. Mean protein in CSF in this study was mild elevation and all of them had normal glucose ratio in CSF. Not performed lumbar puncture in arterial group (Table 2,3)

The study showed that headache and seizure were highly significant in the venous group and the patient's age <45 years was slightly significant. History of previous CVD was only significant in the arterial group. (Table 4).

When consider treatment, in the venous group, 49 patients (95%) received anticoagulant therapy after diagnosed CVST, only 3 patients who did not received anticoagulant due to they had massive intracerebral hemorrhage and had condition that require surgery. Low molecular weight heparin (LMWH) treatment was most used to treat in CVST. In arterial group, most of them received antiplatelet agent 42 patients (80.77%), thrombolytic agent 11 patients (21%) in this study. The complication of treatment in the venous group found intracranial hemorrhage 5 patients (10%) but in the arterial group found only 1 patients (2%), the infectious complication found in arterial group 9 patients (18%) and in venous group 7 (13%). The complication in between the two groups were not any significant difference. (Table 5).

Discussion

Cerebral venous sinus thrombosis was a rare cause of stroke. In previous studies published in 2014 and 2016, there were 3.7–5.3 times more female than male patients[11, 12]and the mean age were 30-41 years[13-15]. This study in the venous group female more occurred than male. Median

age of the venous group was lower than the arterial group. The venous group was 44 years and in arterial group was 70 years old. We classified age group in the young age group (age<45 years) and the older group. We found that the young age group was significantly relate in the venous group, same as the previous studies. Many previous studies shown that combined oral contraceptive pills are associated with a twofold to sixfold increased risk of venous thrombosis[16-18]. This study had 5 patients (10%) had a history of using oral contraceptive drugs but in arterial group there was no use of contraceptive pill due to aging. This result was not significant due to limitation of number of venous data. Thrombosis was a common complication of nephrotic syndrome (NS). However, cerebral venous sinus thrombosis (CVST) secondary to NS may be one of the important etiology of CVST[19]. Causes of thrombosis risk of NS are the deficiency of coagulation factors, anomalies in platelet activation and aggregation, coagulation system activation; increased synthesis of coagulation factors V, VII, VIII, and X as well as von Willebrand factor, fibrinogen, and accumulation of α2-macroglobulin; reduction of endogenous anticoagulants (antithrombin III, C protein and S protein), decreased activity of the fibrinolytic system and imbalance of the plasmin formation system, changes in the glomerular hemostatic system, intravascular volume depletion and the use of diuretics[20-23]. This study had 5 patients with NS, 4 patients (80%) had protein S reduction and 2 patients (40%) had reduce thrombin III but in arterial group no one had nephrotic syndrome. When we find the relationship with CVST was slightly significant in univariate logistic regression when analyzed by multivariate logistic regression that not significant because of limitation of number of cases. Hypertension was the most commonly reported modifiable risk factors in arterial ischemic stroke[24-26]. Hypertension is the risk factor in this study, which significant related with the arterial group by univariate logistic regression but not significant by multivariate logistic regression, because hypertension was found in 43 patients (41.35%), in arterial ischemic stroke 34 patients (79%) and in venous group 9 patients (21%), the number of patients were not enough to make statistical implications when calculated by multivariate regression. And another reason was no data in 61 patients (58.65%). Clinical presentations of CVST were not specific[2] however some clinical was predominantly presentation. Headache, seizure and sign of focal neurodeficit were common manifestations in venous group[4, 6]. In arterial group, sign of focal neurodeficit and dysarthria were common symptoms.

The most common characteristics of headache of CVST was at firs time, paroxysmal, light and self-limited but then gradually developed into a persistent severe headache[27, 28]. In some studies, the headache was not related to the site of venous sinus thrombosis, however transverse sinus was the common sinus that frequently related to occipital region headache[29]. Previous studies have found that headaches are very common presentation and transverse sinus thrombosis is found 30 %. Headaches onset are acute 51.1%, subacute 42.6%, thunderclap 4.3%, and chronic 2.1%[30]. The mechanism of headache in CVT is not unclear. Several common mechanisms such

as a combination of raised intracranial pressure, subarachnoid hemorrhage, stretching of nerves in sinus walls and inflammation of sinus walls which are most likely responsible for variable patterns of headache among these patients[29]. This study has limitation in characteristics of headache, severity and location of headache. Because this study was a retrospective enrollment. In this series, 42 patients (81%) had headache. Measuring the relationship between headache and CVST by multivariate logistic regression headache had significant relationship. Seizures were a common symptoms of CVST and found 40-44% of CVST patients[31-33]. Predictors of early epileptic seizures were motor deficit, intracranial hemorrhage, sagittal sinus and cortical vein thrombosis[31-33]. This study found 26 patients (50%) CVST and 7 patients (13%) arterial stroke had seizures. Most of them treated with antiepileptic drugs (AEDs) and 4 patients (8%) of CVST with status epilepticus was a complication. This study found that the rate of seizure in CVST is slightly higher than others studies possibly the location of venous sinus thrombosis that sagittal and cortical vein thrombosis were found in 30 patients (57.69%) and focal neurodificit in 18 patients (35%). Therefore this venous group has the same risk of seizure as the other studies[4, 31, 33]. The relationship between seizure and CVST that were found to statistic significant correlation by multivariate logistic regression analysis.

The focal neurological symptoms, showed that there have statistic significant correlation in CAT more than CVST. Motor deficits in CVST patients were 19.1–39% in other studies[13, 34] . The mechanism of motor deficits was common in the arterial group because the arterial cerebral infarction had brain parenchymal lesion but neurodeficit in the venous group due to increase intracranial pressure effect, there was no parenchymal lesion[35]. This study found motor deficits 18 patients (35%) in the CVST group and 43 patients (83%) in the arterial cerebral infarction. The relationship between motor deficits, dysarthria and arterial cerebral infarction were statistic significant in univariate logistic regression but not significant in multivariate logistic regression analysis, due to the number of patients in study was too small, we need more patients in further study.

Altered consciousness was observed in previous studies 20–30.6% of patients with CVST[36,37] . This study the alteration of consciousness and severity while admission were not difference in both group.

Laboratory finding show leukocytosis and polymorphonuclear predominate was found in the venous group more than the arterial group. The possible reasons that the venous group may related with infection/ inflammation adjacent to the sinuses or in its drainage areas. Other studies mentioned to pregnancy/ postpartum period, polycythemias, thrombocytosis, obesity, diabetes, oral contraceptives, hormone replacement therapies, antiphospholipid antibodies, nephrotic syndrome and deficiency of Protein C, Protein S, antithrombin deficiency were related to CVST[38]. Other reason that CVST was prolonged causes dehydration and inflammatory process.

Thrombophilic state in CVST patients that may be the result of acquired cause such as protein S deficiency, oral contraceptive pills or hormone replacement therapy, Pregnancy, oral anticoagulants, DIC, nephrotic syndrome, inflammatory

conditions, after acute thromboembolism and other infections. Antithrombin3 deficiency may be the result of arterial and venous thrombosis and effect to resistance to heparin therapy too. Therefore after acute thrombosis, or while on heparin therapy that can be effect Antithrombin3 levels, were decline less than 50%, leading to wrong diagnosis, so it should be reevaluation after treatment. Others acquired causes of Antithombin3 deficiency were seen in liver disease, DIC, nephrotic syndrome (loss in urine) chemotherapy with L Asparaginase and preeclampsia[38].

CVST with thrombophilia in this study, most of them found thrombin III deficiency, maybe related with inflammation or consumption of thrombotic process. So we need repetitive laboratory later.

The most important treatment option in this study was anticoagulant therapy , which aim to arrest the thrombotic process. Most physicians suggested initial treatment with heparin as soon as the diagnosis is confirmed, even in the presence of hemorrhagic infarcts. In clinical trials show no increased or new cerebral hemorrhages developing after treatment with heparin. No comparative studies of fractionated heparin with unfractionated heparin but some scholars had proposed that LMWH was more appropriate, except when the patient may need a surgical intervention[39, 40] . This study used low molecular weight heparin treatment mainly in the venous group 45 patient (87%) and in arterial ischemic stroke the main treatment was use to antiplatelet 42 patients (81%). Intracerebral hemorrhage complications were found common in CVST, because the mechanism of CVST involved increase intracranial pressure and used anticoagulant. Althought there were intracranial hemorrhage, but there is a need to use anticoagulant anyway. The overall complications of treatment and mortality were not different in both groups.

Summary

Thrombosis of the cerebral venous sinuses can lead to a distinct arterial ischemic stroke. High index of suspicion and awareness of the clinical features and the predisposing factors helps in diagnosis such as young age onset disease, risk factor of thrombophilia such as oral contraction, nephrotic syndrome and onset symptom headache, present with seizure. Definite diagnosis was almost always by CVT or MRI, MRV. Laboratory studies were necessary to look for the various contributory factors for the prothrombotic state. Complete blood count might give evidence of inflammatory response.

If promptly diagnosed CVST and all the contributory factors are identified and corrected, anticoagulant was most the important treatment.

The author was suggested that next future research should to include more case or maybe prospective study that showed more detail of clinical characteristic findings, risk factor and outcome of disease that there were complete data but

CVST disease was rare, may be the limitation of study.

Table 1 Clinical characteristics of cerebral venous stroke (CVST) and acute arterial stroke (CAT) in Suratthani Hospital, January 2013 – December 2018 (n = 104). Thailand, January 2013 – De cember 2018 (n = 104)

Characteristics	CVST, n (%)	CAT, n (%)	P-value
Female	36 (69)	24 (46)	0.028
Age, years, median (IQR)	44 (30 - 52)	70 (60 - 79)	<0.001
Underlying diseases			
Hypertension	9 (17)	34 (65)	<0.001
Diabetic mellitus	4 (8)	7 (13)	0.530
Malignancy	2 (4)	2 (4)	1.000
Old cerebrovascular disease	0	14 (27)	<0.001
Nephrotic syndrome	5 (10)	0	0.057
Atrial fibrillation	0	2 (4)	0.500
Oral contraception	5 (10)	0	0.057
Pregnancy	3 (6)	0	0.240
Sign and Symptoms			
Headache	42 (81)	2 (4)	<0.001
Seizure	26 (50)	7 (13)	<0.001
Weakness	18 (35)	43 (83)	<0.001
Dysarthria	1 (2)	23 (44)	<0.001
Alteration of consciousness	21 (40)	22 (42)	1.000
Aphasia	1 (2)	5 (10)	0.200
Blurred vision	1 (2)	2 (4)	1.000
Vertigo	1 (2)	4 (8)	0.360
MRS on admission			0.037
1	0	0	
2	5 (10)	0	
3	22 (42)	20 (38)	
4	13 (25)	23 (44)	
5	12 (23)	9 (17)	

Abbreviation: IQR = interquartile range; MRS = Modified Rankin Scale

Table 2 Laboratory finding of cerebral venous stroke (CVST) and acute arterial stoke (CAT)

Laboratory finding	CVST	CAT	P-value
	median (IQR)	median (IQR)	
Complete blood count			
WBC, cell/cu.mm	12,100 (8,900 - 16,100)	8,315 (7,360 - 11,450)	0.002
PMN, %	79.1 (69.0 - 85.4)	70.3 (60.3 - 78.9)	0.003
Lymphocyte, %	13.3 (8.5 - 19.4)	20.6 (11.3 - 27.4)	0.008
Monocyte, %	5.7 (4.0 - 7.0)	6.2 (4.0 - 8.0)	0.700
Basophil, %	0 (0.0 - 0.4)	0 (0.0 - 0.3)	0.690
Eosinophil, %	0.2 (0.0 - 1.0)	1.1 (0.3 - 3.3)	<0.001
Hemoglobin, g/dL	13.1 (11.4 - 14.9)	12.1 (10.5 - 13.8)	0.059
Hematocrit, %	39.5 (34.0 - 45.6)	36.5 (32.1 - 41.7)	0.078
Platelet , cell/cu.mm	234,000 (184,000 - 303,000)	236,000 (177,500 - 288,000)	0.780
Lipid profiles, mg/dL			
Cholesterol	203 (180 - 228)	185 (149 - 207)	0.190
Triglyceride	98 (83 - 197)	103 (80 - 146)	0.730
HDL	50 (37 - 64)	40 (34 - 54)	0.220
LDL	141 (110 -165)	111 (92-138)	0.120
Fasting blood glucose, mg/dL	116 (99 - 134)	99 (93-120)	0.005

Abbreviation: IQR = interquartile range; WBC = white blood cell count; PMN = polymorphonuclear; HDL = high density lipoprotein; LDL = low density lipoprotein;

Table 3 specifically Laboratory finding of cerebral venous stroke (CVST)

Laboratory finding in cerebral venous sinus thrombosis	Not done (%)	Result finding	
		Abnormal n (%)	Normal n (%)
Hypercoagulable study,			
Protein C abnormality finding	8 (15)	1(2.27)	43(97.73)
Protein S abnormality finding	8 (15) (23)	12(27.27)	32(72.73)
Lupus anticoagulant finding	11 (21)6 (12)	6(14.63)	35(85.37)
Anticardiolipin finding	11 (21)	1 (2.44)	40 (97.56)
Beta2-Glycoprotein finding	29 (56)	9 (39.13)	14 (60.87)
Antithrombin 3 finding	12 (23)	16 (40)	24 (60)
Lumbar puncture; 11 (21.15)	41 (78.85)	Result finding; mean ± SD	
Open pressure, cmH_2O	-	29 ± 12	
WBC, cell/cu.mm	-	27 ± 52	
RBC, cell/cu.mm	-	98 ± 140	
Protein, mg/dL	-	76 ± 60	
Glucose, mg/dL	-	69 ± 15	
Brain imaging finding; n(%)			
Transverse sinus thrombosis	-	31 (59.62)	
Sagittal sinus thrombosis	-	27 (51.92)	
Others site thrombosis#	-	7 (13.46)	
Involve more than one site	-	13 (25)	

Abbreviation: WBC = white blood cell count; RBC = red blood cell count; # others site thrombosis consist of cortical vein thrombosis, deep venous thrombosis and cavernous sinus thrombosis

Table 4 Univariable and multiviable analysis of predicting factors associated with cerebral venous stroke (CVST) and acute arterial stroke (CAT)

Factors	Univariable analysis		Multivariable analysis	
	RD (95%CI)	P-value	aRD (95%CI)	P-value
Female	0.24 (0.05, 0.43)	0.015	-.026(-0.136, 0.084)	0.650
Age < 45 years	0.69(0.53, 0.85)	<0.001	0.16(0.01, 0.32)	0.039
Hypertension	- 0.49 (0.66, 0.91)	<0.001	-0.04(-0.16, 0.09)	0.590
Diabetic mellitus	- 0.15(-0.15, 0.16)	0.341	-	-
Old cerebrovascular disease	-0.58(-0.84, -0.32)	<0.001	-0.22(-0.37, -0.07)	0.005
Nephrotic syndrome	0.53 (0.08, 0.97)	0.020	0.13(-0.12, 0.39)	0.301
Atrial fibrillation	-0.51 (-1.21, 0.19)	0.153	-	-
Oral contraception	0.53 (0.08, 0.97)	0.020	0.01(-0.23, 0.25)	0.915
Pregnancy	0.51 (-0.06, 1.09)	0.077	-	-
Headache	0.79 (0.66, 0.91)	< 0.001	0.52(0.38, 0.66)	<0.001
Seizure	0.42 (0.23, 0.61)	<0.001	0.26(0.12, 0.35)	<0.001
Weakness	-0.50 (-0.67, -0.32)	<0.001	-0.10(-0.22, 0.01)	0.074
Alteration of consciousness	-0.02 (-0.22, 0.18)	0.844	-	-
Dysarthria	-0.60 (-0.80, -0.40)	<0.001	-0.13(-0.28, 0.01)	0.067
Aphasia	-0.35 (-0.76, 0.06)	0.091	-0.01(-0.22, 0.20)	0.925
Blurred vision	-0.17 (-0.75, 0.41)	0.561	-	-
Vertigo	-0.31 (-0.76, 0.14)	0.176	-	-
Antiphospholipid syndrome	0.50 (-0.48, 1.49)	0.317	0.21(-0.31, 0.72)	0.431

Abbreviation: RD = Risk difference; CI = confidence interval;

Table 5 Treatment, outcome and complication of cerebral venous stroke and acute arterial ischemic stroke

Treatment	Venous n (%)	Arterial n (%)	
LMWH	45 (87)	1 (2)	
UFH	4 (8)	0	
Oral anticoagulant	49 (94)	5 (10)	
Aspirin	0	39 (75)	
Clopidogrel	0	3 (6)	
Thrombolytic agent	0	11 (21)	
Surgery	4 (8)	2 (4)	
Antiepileptic drug	24 (46)	2 (4)	
Outcome	**Venous n (%)**	**Arterial n (%)**	**p-value**
MRS on discharge			0.070
1	2 (4)	0	
2	21 (40)	13 (25)	
3	13 (25)	19 (37)	
4	6 (12)	14 (27)	
5	4 (8)	1 (2)	
6	6 (12)	5(10)	
Complication	**Venous n (%)**	**Arterial n (%)**	**p-value**
Seizure	2 (4)	0	0.50
status epilepticus	4 (8)	0	0.12
Intracranial hemorrhage	5 (10)	1 (2)	0.11
pneumonia	7 (13)	5 (10)	0.76
UTI	0	4 (8)	0.12
Upper GI bleeding	0	3 (6)	0.24

Abbreviation: MRS = Modified Rankin Scale

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