

Stroke in young adults

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Summary

Objective: Stroke is an important cause of morbidity and mortality in young adults especially in developing countries. This study aimed at reviewing epidemiology, types, etiologies, risk factors in the young adults in 108 Military Central Hospital. **Subject and method:** This study retrospectively reviewed consecutive acute stroke patients aged 16-45 years admitted to the 108 Military Central Hospital between February 1, 2022, and September 18, 2023 to analyze epidemiology, types, etiologies, risk factors, compare the age groups of 16-30 and 31-45 years. **Result:** Among 319 young stroke patients (mean age at onset 36.4 ± 8.1 years; male 71.5%), there were nontraumatic spontaneous hemorrhagic stroke (including 156 intracerebral hemorrhage (ICH) and 47 subarachnoid hemorrhage, (SAH)), 106 ischemic stroke and 10 cerebral venous thromboses. Notably, ICH was more prevalent in patients aged 16-30 than in those aged 31-45 (63.2% vs 45.8%). Specifically, structural vasculopathy (e.g., arteriovenous malformation, cavernoma) was the most common etiologic subtype in patients aged 16-30 (80.6%), whereas hypertensive ICH was the most common subtype in patients aged 31-45 (57.1%). On the other hand, the top ischemic subtype for both age groups was other determined diseases (e.g., arterial dissection, autoimmune diseases, moyamoya disease, etc.) rather than large artery atherosclerosis. Hyperlipidemia, heart disease and cigarette smoking, excessive alcohol intake were more common risk factors for infarction than ICH. **Conclusion:** An aggressive approach to elucidate the etiology of stroke must be indicated for all young stroke patients. Structural vasculopathy was the most common etiology in patients aged 16-30, whereas hypertensive ICH was the most common in patients aged 31-45. For ischemic stroke, in addition to common causes such as cardiac embolism, atherosclerotic cerebrovascular disease... Other causes including arterial dissections, autoimmune diseases, moyamoya disease, cancer-related thromboembolisms, cerebral thrombosis venous complications, hematologic disease...

Keywords: Stroke, young adult, young stroke patient.

1. Background

Despite considerable improvement in primary prevention, diagnostic workup, and treatment, stroke is in second or third place on a mortality list, and projections indicate that it will remain so in the year 2025. Furthermore, stroke is a leading cause of disability. Strokes in young adults are reported as being uncommon, comprising 10%-15% of all stroke

patients [1]. Although published reports indicate that stroke is not common in young adults, in everyday clinical practice we are often faced with acute neurologic symptoms in this age group, and stroke should be considered as the differential diagnosis. Compared with stroke in older people, stroke in the young is particularly tragic because of the potential to create long-term disability, burden on the victims, their families, and the community at large. Despite this, there is limited data on stroke in young adults, and its risk factors in Vietnam. To gain further insight into the etiopathogenesis of young stroke, we analyzed a hospital based series of young adults (aged less than 45 years) with stroke, with

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particular focus on the etiologic subtype and the vascular risk profile at 108 Military Central Hospital.

2. Subject and method

This retrospective, single-centre, observational study included consecutive patients with acute stroke admitted to 108 Military Central Hospital between February 1, 2022, and September 18, 2023. The inclusion criteria for our stroke registry were acute hospitalized stroke patients whose symptom onset was within 3 days and evaluated by neurologists. This study reviewed data including demographics, risk factors, stroke subtypes, etiology, history of stroke in the patient, alcohol overconsumption, smoking.

Young patients (≤ 45 years old) with acute infarction, cerebral venous thrombosis (CVT), spontaneous ICH and subarachnoid hemorrhage (SAH), transient ischemic attack (TIA) were included. Ischemic infarction was classified according to The Trial of Org 10172 in Acute Ischemic Stroke (TOAST) into large artery atherosclerosis, small artery occlusion, cardioembolism, other determined diseases and undetermined causes (cryptogenic). Causes of spontaneous ICH were classified into

structural vasculopathy, medication, amyloid angiopathy, systemic diseases, hypertension, and undetermined causes (the SMASH-U system).

Data was analyzed using SPSS version 16.0.

3. Result

3.1. Basic demographics of the young stroke patient

After excluding patients with duplicate registration due to stroke recurrence, and 6 traumatic intracerebral haemorrhages, 3 due to bleeding tumours, 6 encephalitis, 1 functional neurological disorder, This study included a total of 319 young stroke patients (9.1%, $n = 3501$) between 8 and 45 years old. The mean age at onset was 36.4 ± 8.1 years, 229 males and 90 females giving a male: female ratio of 2.5:1. There were 314 patients with acute first-time stroke and 5 patients with acute recurrent stroke.

These patients had a higher percentage of hemorrhagic stroke ($n = 156$, 48.9%) than ischemic stroke ($n = 106$, 33.2%), and had 47 SAH (14.7%), 10 cerebral venous thrombosis (CVT) (3.1%).

3.2. Risk factors of stroke

Table 1. Risk factors of stroke

	Ischemic (n = 106)	ICH (n = 156)	CVT (n = 10)	SAH (n = 47)	Total (n = 319)
Hypertension	34 (32.0%)	65 (41.7%)	0	3	101 (31.6%)
Type 2 diabetes mellitus	5 (4.7%)	4 (2.6%)	0	0	9 (2.8%)
Hyperlipidemia	13 (12.3%)	11 (7.1%)	0	0	24 (7.8%)
Heart disease	15 (14.2%)	1 (0.6%)	0	0	16 (5.0%)
Heavy alcohol consumption	9 (8.5%)	15 (9.6%)	0	1	25 (7.5%)
Cigarette smoking	20 (18.8%)	17 (10.9%)	0	1	38 (11.9%)
Previous stroke	3 (2.8%)	2 (1.3%)	0	0	5 (1.6%)
Oral contraceptives	-	-	2 (20.0%)		2 (0.6%)
Post-partum period	-	-	3 (30.0%)		3 (0.9%)

Hypertension is the top risk factor for both ICH and infarction. Hypertension was responsible for 101 (31.6%) cases, smoking was present in 38 (11.9%) patients, diabetes mellitus was present in 9 (2.8%) cases, hyperlipidemia was reported in 24 (7.5%) cases, heart disease were reported in 16 (5.0%) cases, excessive alcohol intake 25 (7.5%) cases, oral contraception intake was verified present in 2 women, three patients presented their CVT during the postpartum period.

3.3. Stroke etiologic subtype

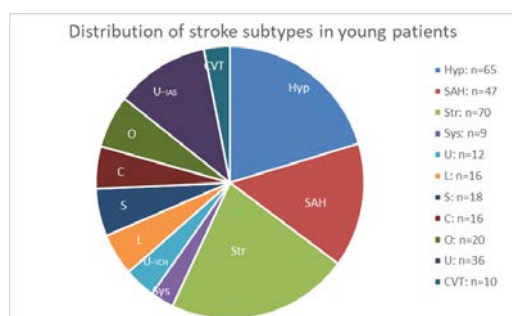


Figure 1. Pie chart for all etiologies of ischemic and hemorrhagic stroke.

Hyp = hypertension; Sys = systemic disease;

L = large artery atherosclerosis; C, cardioembolism;

CVT = cerebral venous thrombosis; Med = medication-related; O = other determined; S = small artery occlusion; SAH = subarachnoid hemorrhage;

Str = structural vasculopathy; U = undetermined (cryptogenic)

For SAH (n = 47), the most common cause was rupture artery (n = 37). No vascular abnormality on CTA and DSA in 10 patients.

For ICH (n = 156). This study, we included arteriovenous malformations (AVMs), cavernoma in the structural vascular lesions group, whenever present with intra-parenchymal ICH. 65 patients had hypertensive subtype (41.7%), 69 structural vasculopathy (44.2%), 10 systemic disease (6.4%), 12 undetermined ICH (7.7%), no patient with amyloid angiopathy or antithrombotic drugs. Specifically, the most common structural vasculopathy-induced ICH was arteriovenous malformation (48/70), followed by cavernoma (12/70). Regarding causes of cerebral infarction, 20 other determined diseases (18.9%), 16 large artery atherosclerosis (15.1%), 18 small artery occlusions (16.9%), 16 cardioembolic origin (15.1%) and the most common subtype was undetermined (33.9%). Among the other determined diseases (n = 20) including arterial dissections (n = 4), autoimmune diseases (n = 2), moyamoya diseases (n = 2), cancer-related thromboembolisms (n = 5), cerebral thrombosis venous complications (n = 3), hematologic diseases (n = 1), and others (n = 3).

3.4. Age of stroke onset ≤ 30 years vs 31-45 years

Table 2. Characteristic comparison between patients aged 16-30 years and 31-45 years

	16-30 (n = 57)	31-45 (n = 262)	Total (n = 319)	p
ICH	36 (63.2%)	120 (45.8%)	156 (48.9%)	<0.05
Structural vasculopathy	29 (80.6%)	40 (33.3%)	69 (21.6%)	<0.001
Hypertensive	3 (8.3%)	62 (51.7%)	65 (20.4%)	<0.001
Systemic disease	2 (5.5%)	8 (6.6%)	10 (3.2%)	>0.05
Undetermined	2 (5.5%)	10 (8.3%)	12 (3.8%)	>0.05
SAH	6 (1.0%)	41 (15.6%)	47 (14.7%)	<0.05
Infarction	13 (22.8%)	93 (35.5%)	106 (33.2%)	>0.05
LAA	0	16 (17.2%)	16 (5.0%)	

	16-30 (n = 57)	31-45 (n = 262)	Total (n = 319)	p
Small vessel occlusion	1 (7.7%)	17 (18.3%)	18 (5.6%)	>0.05
Cardioembolism	1 (7.7%)	15 (16.1%)	16 (5.0%)	<0.05
Other	7 (5.4%)	13 (13.9%)	20 (6.3%)	<0.05
Undetermined	4 (30.8%)	32 (34.4%)	36 (11.3%)	>0.05
CVT	2 (3.5%)	8 (3.0%)	10 (3.1%)	

LAA = large artery atherosclerosis.

This study compared patients aged 16-30 years (n = 57) with those aged 31-45 years (n = 262). Notably, ICH was particularly more prevalent in patients aged 16-30 years than in those aged 31-45 years (62.3% vs 45.8%). Specifically, structural vasculopathy was the most common etiologic subtype in patients aged 16-30 years ($p < 0.001$), whereas hypertensive ICH was the most common subtype in patients aged 31-45 years ($p < 0.001$). In contrast, cerebral infarction was more prevalent in patients aged 31-45 years. The overall subtype distribution differed between the groups. The top ischemic subtype for both age groups was other determined diseases rather than large artery atherosclerosis.

4. Discussion

Stroke is not uncommon among young people, as was previously assumed in early reports. There are many published series concerning stroke in young patients, but the data are conflicting. Comparison between studies is difficult for a number of reasons, including the methodology used, age groups, diagnostic criteria, time scale, and a change in the pathology. The proportion of first-ever stroke in young adults differs from country to country, ranging from < 5% to 20% of all strokes [2]. In this study showed that 319 patients (9.1% of 3501 patients) with stroke aged less than 45 years admitted to our stroke department between February 1, 2022, and September 18, 2023. This study found a male predominance with a male to female ratio of 2.5, this result is consistent with the general finding of previous studies. This may be due to differences in

certain risk factors such as smoking or alcohol overconsumption, which is much more prevalent among men in Vietnam compared with women.

The prevalence of stroke subtypes has specific considerations in young adults [3]. Several studies showed that ischemic stroke to be more prevalent than hemorrhagic stroke. A population-based stroke epidemiologic study in the Northern Kentucky region found that ischemic strokes represented about 65% of all strokes in young adults aged 20-44 years, while 17% were diagnosed with ICH and 16% with SAH [4]. George et al. have demonstrated that the national rate of hospitalization in the US for ischemic stroke in young adults aged between 18 and 44 years old has doubled between 2003 and 2012 while it remained stable for ICH and SAH [5].

Contrast, this study found a higher proportion of hemorrhagic stroke 63.6% (including ICH and SAH) than previously reported studies of young Asian populations, ranging from 20 to 40.0%. The proportion of hemorrhagic stroke in the present study are representative of hospital inpatients, but in spite of all the bias of such a study, important information can be gathered. In general, ischemic stroke occurs more commonly than hemorrhagic stroke, except in India and Vietnam, where the converse is observed [6]. This difference can be explain by the fact that etiological factors such as anormal vessel are frequent and the low prevalence of hypertension in these patients. Additionally, the different genetic and acquired risk factors may contribute to such differences and need further investigation.

The SMASH-U system is an aetiological based classification system for ICH by predefined criteria: Structural vascular lesions (S) (cavernomas, aneurysms, arteriovenous malformations (AVMs)), medication (M) (Vitamin K-Antagonists (VKAs), direct oral anticoagulants (DOACs), heparin and antiplatelet agents), amyloid angiopathy (A), systemic disease (S) (renal failure, liver disease, alcohol-related disease, coagulopathy, reversible vasospasm syndrome, systemic lupus erythematosus, cancer, ...), hypertension (H), or undetermined (U). This study used the definition of "Hypertensive aetiology" is: Most recent pre-ICH blood pressure $\geq 160/100$ mmHg, and on antihypertensive therapy or when pre-ICH blood pressure was not known, mention of pre-ICH elevated blood pressure by a patient or patient's family and medical records together with a left ventricular hypertrophy (as a biomarker of hypertension), or any pre-ICH use of blood pressure medication. This study, no patient included in the medication group (used DOACs or antiplatelet). In patient with many concomitant factors can lead to ICH, we have selected for classification the factor that we supposed to be the most likely and evincible aetiology. For instance, structural vascular lesions, coagulopathies, and systemic diseases (such as systemic lupus erythematosus) were preferred over hypertension and amyloid angiopathy.

This study revealed that the proportion of ICH was higher in patients aged between 16 and 30 years and among them, structural vasculopathy was the most common cause. This finding is similar to a Korean study in young adults aged under 40 [7]. In our patients aged between 31 and 45 years, hypertensive ICH was the most common subtype, which is concordant with previous reports [8]. This finding may be explained by the increase in the development of risk factors with advancing age. Tatlisumak et al (2018) showed that both hypertension and structural vasculopathy are the leading causes of ICH in young stroke patient [9]. Subarachnoid hemorrhage is common in young stroke. Cerebral venous sinus thrombosis may also

cause stroke, especially among young women use contraceptives drug.

For ischemic stroke: Despite a systematic diagnostic approach and more accurate diagnostic tools becoming available in the form of vascular imaging and hematologic and genetic studies, stroke of undetermined etiology was the most common etiology among young stroke patients. The high number of young stroke patients with undetermined etiology may be explained in part by the insufficient extent and timing of the investigations. Stroke of other determined etiology collectively account for 20%-30% of cases of young stroke. This study reported undetermined diseases as the most common causal subtype of ischemic stroke (33.9%) and followed by other determined 18.9%. Among those infarctions due to other determined causes, this study showed that arterial dissection accounted for 4/20. Cervical artery dissection accounts for 10-25% of all strokes in young adults, as opposed to 2% of all ischemic strokes in all age groups [10]. Most arterial dissections occur spontaneously, however, rarely, some are associated with trauma and several genetic and connective tissue disorders such as Marfan syndrome, and fibromuscular dysplasia. Several conditions that increase the risk of ischemic stroke include coagulation disorders, immunological and rheumatological disorders, and oral contraceptive drugs ...

Cardioembolism is another important cause of ischemic stroke in young adults. However, it is often more difficult to diagnose. The causes of cardiogenic embolism are different. Electrocardiogram monitoring is used to detect atrial dysrhythmias such as paroxysmal atrial fibrillation (AF), transesophageal and transthoracic echocardiograms are considered as important tools in diagnosing cardioembolic stroke. This procedure performed frequent in our hospital. This study reported cardioembolic stroke of patient accounts for up to one fourth of ischemic strokes in young adults.

Large artery atherosclerosis and small vessels diseases are a more common cause of stroke after

the age of 35-40 [11]. Of note, with the increased prevalence of traditional cardiovascular risk factors among young adults [12], these causes are expected to increase in proportion to other causes among patients with a stroke. As a consequence, currently those traditional cerebrovascular risk factors identified as relevant stroke in older populations also account for a large proportion of strokes in younger adults [13].

This study reported hypertension remains the most common medical risk factor for in young stroke patients aged ≤ 45 , whereas current smoking and over alcohol drinking are the most predominant among lifestyle-related risk factors. Initially, the risk factor profile in young stroke patients was unique when compared with the risk profile of elderly individuals: Strokes in young adults were infrequent, and attributed to characteristics such as hematologic diseases, vasculitis, malignancies, illicit drug use, pregnancy, thrombophilia, patent foramen ovale, and oral contraception use [12]. Nonetheless, recently there has been a shift in the risk factor profile of younger patients towards an increasing importance of traditional cardiovascular risk factors including hypertension, dyslipidemia, diabetes, smoking and others [14]. Additionally, traditional risk factors also have a role as underlying causes of thromboembolic ischemic strokes, for example hypertension, which causes left ventricle overload, left atrial enlargement and subsequent AF at relatively young ages.

5. Conclusion

This study provides the characteristic subtypes of etiologies, risk factors of young adult stroke patients from Stroke Department, 108 Military Central Hospital, a single medical center in Vietnam and showed that an aggressive approach to elucidate the etiology of stroke must be indicated for all young stroke patients. Structural vasculopathy was the most common etiology in patients aged 16-30, whereas hypertensive ICH was the most common in patients aged 31-45. For ischemic stroke, in addition to common causes such as cardiac embolism, atherosclerotic cerebrovascular disease... Other

causes including arterial dissections, autoimmune diseases, moyamoya diseases, cancer-related thromboembolisms, cerebral thrombosis venous complications, hematologic disease...

References

1. Ji R, Schwamm LH, Pervez MA, Singhal AB (2013) *Ischemic stroke and transient ischemic attack in young adults: Risk factors, diagnostic yield, neuroimaging, and thrombolysis*. JAMA Neurol 70: 51-57.
2. George MG, Tong X, Kuklina EV, Labarthe DR (2011) *Trends in stroke hospitalizations and associated risk factors among children and young adults, 1995-2008*. Ann Neurol 70: 713-721.
3. Marini C, Russo T, Felzani G (2011) *Incidence of stroke in young adults: A review*. Stroke Res Treat 2011:535672. doi: 10.4061/2011/535672.
4. Kissela BM, Khoury JC, Alwell K, Moomaw CJ, Woo D, Adeoye O, Flaherty ML, Khatri P, Ferioli S, De Los Rios La Rosa F, Broderick JP, Kleindorfer DO (2012) *Age at stroke: Temporal trends in stroke incidence in a large, biracial population*. Neurology 79(17): 1781-1787.
5. George MG, Tong X, Bowman BA (2017) *Prevalence of cardiovascular risk factors and strokes in younger adults*. JAMA neurology 74(6): 695-703.
6. Venketasubramanian N, Yoon BW, Pandian J, Navarro JC (2017) *Stroke epidemiology in south, east, and south-east Asia: A review*. Journal of stroke 19(3): 286.
7. Go GO, Park H, Lee CH, Hwang SH, Han JW, Park IS (2013) *The outcomes of spontaneous intracerebral hemorrhage in young adults-a clinical study*. Journal of cerebrovascular and endovascular neurosurgery 15(3): 214-220.
8. Lai SL, Chen ST, Lee TH, Ro LS, Hsu SP (2005) *Spontaneous intracerebral hemorrhage in young adults*. European journal of neurology 12(4): 310-316.
9. Tatlisumak T, Cucchiara B, Kuroda S et al (2018) *Nontraumatic intracerebral haemorrhage in young adults*. Nature Reviews Neurology 14(4): 237-250.

10. Hathidara MY, Saini V, Malik AM (2019) *Stroke in the young: A global update*. Current neurology and neuroscience reports 19: 1-8.
11. Cerrato P, Grasso M, Imperiale D, Priano L, Baima C, Giraudo M, Rizzuto A, Azzaro C, Lentini A, Bergamasco B (2004) *Stroke in young patients: etiopathogenesis and risk factors in different age classes*. Cerebrovascular Diseases 18(2): 154-159.
12. George MG, Tong X, Bowman BA (2017) *Prevalence of cardiovascular risk factors and strokes in younger adults*. JAMA neurology 74(6): 695-703.
13. Aigner A, Grittner U, Rolfs A et al (2017) *Contribution of established stroke risk factors to the burden of stroke in young adults*. Stroke 48(7): 1744-1751.
14. Kissela BM, Khoury JC et al (2012) *Age at stroke: temporal trends in stroke incidence in a large, biracial population*. Neurology 79(17): 1781-1787.