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ORIGINAL ARTICLE

Etiology and risk factors of intracranial hemorrhage and ischemic stroke in young adults

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Abstract

Background: Young stroke incidence has increased worldwide with lifestyle changes. Etiology and risk factors for both ischemic and hemorrhagic stroke in young Asians remain underexplored.

Methods: We retrospectively reviewed consecutive acute stroke patients aged 16–45 years admitted to the Taipei Veterans General Hospital between 2009 and 2019 to analyze etiologic subtypes, risk factors, and serial modified Rankin Scale scores for 1 year and compare the age groups of 16–30 and 31–45 years.

Results: Among 670 young Taiwanese patients (mean age at onset 37.5 ± 7.0 years; male 65.1%), there were 366 nontraumatic spontaneous hemorrhagic stroke (including 259 intracerebral hemorrhage [ICH] and 107 subarachnoid hemorrhage, SAH), 292 ischemic stroke and 12 cerebral venous thromboses. Notably, ICH was more prevalent in patients aged 16–30 than in those aged 31–45 (54.8% vs 36.8%). Specifically, structural vasculopathy (e.g., arteriovenous malformation, cavernoma) was the most common etiologic subtype in patients aged 16–30 ($p < 0.001$), whereas hypertensive ICH was the most common subtype in patients aged 31–45 ($p < 0.001$). 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, diabetes, and cigarette smoking were more common risk factors for infarction than ICH. Familial stroke patients whose first- or second-degree relatives had a stroke by age 80 (n = 104, 15.5%) had more infarctions than those without a familial stroke history. In multivariate analyses, initial stroke severity, and infarction type were important predictors of favorable outcomes after 3 months. At the 1-year follow-up, patients with ICH and SAH had worse functional outcomes and survival rates than those with infarction.

Conclusion: An aggressive approach to elucidate the etiology of stroke is indicated because structural vasculopathy-induced ICH and other determined infarction are distinctively prevalent in young adults, particularly those aged 16–30.

Keywords: Etiology; Outcome; Risk factor; Stroke; Subtype; Young adult

1. INTRODUCTION

Stroke incidence in young adults under the age of 45 has been rising worldwide possibly due to an increasing incidence of risk factors.[1–4] Overall incidence rates have been reported to range from 7 to 15 in 100,000 person/year, with higher rates reported in American blacks, Japanese, Libyans, and Hispanics.[5] Young stroke patients have a greater socioeconomic burden and an excess of mortality across all age groups of patients.[6,7] Two large consecutive series from Finland and the Netherlands reported a nonnegligible cumulative risk of recurrence in early-onset stroke survivors, ranging from 9.4% at 5 years to 19.4% at 20 years.[8,9] Hence, contemporary etiologic subtypes, risk factors, and prognosis of young stroke and ethnic differences between the Asian population and the Western population are important to elucidate. Hemorrhagic stroke has been found to be more common in Asian patients than Caucasian patients.[10,11] Different risk factor distributions have been proposed to account for these different stroke subtypes.[12] For example, in Chinese but not Caucasian patients, hypertension and alcohol overconsumption were more prevalent in intracerebral hemorrhage (ICH) than in ischemic infarction;[12] however, such complex etiologies and outcomes of both ICH and infarction have been underexplored in young Asian stroke patients (≤45 years old).[13] Here, we characterized etiologic subtypes, risk factors (including family history of stroke), and 1-year recurrence and outcomes of young Taiwanese stroke patients.

2. METHODS

2.1. Subjects and subtype classification

We retrospectively reviewed consecutive patients with acute stroke admitted to Taipei Veterans General Hospital between

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February 1, 2009, and December 31, 2019. The inclusion criteria for our stroke registry were acute hospitalized stroke patients whose symptom onset was within 10 days and evaluated by neurologists, including first-time and recurrent stroke, community-onset and in-hospital stroke. Two specialized nurses were responsible for data registry and monitoring. We reviewed data including demographics, risk factors, functional measures (National Institute of Health Stroke Scale, NIHSS, and modified Rankin scale, mRS) at admission baseline and at discharge, stroke subtypes, medical and interventional therapies, and regular follow-ups of mRS functional outcomes at 1, 3, 6, and 12 months after stroke onset by phone interviews. Patient death and the date of death were documented, if any, during follow-ups. The Institutional Review Board approved the study (2017-03-007AC).

Young patients (≤45 years old) with acute infarction, cerebral venous thrombosis (CVT), spontaneous ICH and subarachnoid hemorrhage (SAH) were included. We excluded patients with transient ischemic attack (TIA) to avoid diagnostic ambiguity with stroke mimics. 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).[14] Causes of spontaneous ICH were classified into structural vasculopathy, medication, amyloid angiopathy, systemic diseases, hypertension, and undetermined causes, that is, the SMASH-U system.[15] A positive family history of stroke was defined as at least a first-degree or second-degree family members having had a stroke by age of 80. Alcohol overconsumption was defined as more than 14 drinks per week for more than 6 months before stroke onset. Smoking was defined as smoking at least 0.5 packs per day for more than 6 months before stroke onset. Obesity was defined as a body mass index > 30.

The diagnostic algorithm for ischemic and hemorrhagic stroke subtypes is illustrated in Fig. 1. Brain computed tomography (CT) or magnetic resonance imaging (MRI), extra and intracranial Doppler ultrasound, 24-h Holter, transthoracic cardiac echogram, coagulation profile, autoimmune profile, tumor markers, and homocysteine were routinely examined. For advanced investigation of other unusual diseases, high-resolution (1 mm-section) contrast-enhanced vessel wall MR angiography of the brain or neck was reserved for patients suspected to have arterial dissection. Digital subtraction angiography was reserved for patients with intracranial vascular anomalies, such as moyamoya disease, arteriovenous malformation, and aneurysms. Transesophageal echocardiography was reserved for patients with suspected embolic stroke of undetermined source or patent foramen ovale. Toxicology screening, cerebrospinal fluid studies, and genetic studies were performed if there was suspicion of illicit drug use, infections of the central nervous system, or monogenic stroke diseases, respectively. Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL, *NOTCH3* gene mutation), mitochondrial encephalopathy, lactic acidosis, and stroke-like episodes (MELAS) syndrome (mtDNA), Fabry's disease (*GAL*), and Marfan's syndrome (*FBN1*) were confirmed by genetic diagnosis. Cryptogenic strokes were re-subtyped if a specific cause was identified by the 1-year follow-up.

2.2. Statistics

Patients classified as having ischemic versus hemorrhagic stroke and the presence versus absence of familial stroke were compared by the 2-sample independent t test, and proportions were compared by the χ^2 test. One-way analysis of variance (ANOVA) was performed to compare 3 groups of means. Risk factor scores were derived by summing the risk factors present in a stroke patient on admission, including hypertension, diabetes, hyperlipidemia, and cigarette smoking (0–4). Binary multivariate logistic regression analyses were performed with favorable outcome (mRS = 0–2) at 3 months as the dependent variable and with age, sex, initial NIHSS scores, and risk factor scores as prognostic predictors.[16] For 1-year survival analysis, a Kaplan-Meier plot was generated to measure the survival rate after stroke of various types, including infarction, ICH, and SAH. Age, sex, initial NIHSS scores and risk factor scores were adjusted using multivariate Cox proportional hazards (regression) model. Statistical significance was set at $p < 0.05$.

3. RESULTS

3.1. Stroke etiologic subtypes

After excluding patients with duplicate registration due to stroke recurrence, there were 670 young patients (6.6%) between 16 and 45 years old out of 10,112 consecutively registered stroke patients. The mean age at onset was 37.5 ± 7.0 years, and there were significantly more males than females. Six patients aged < 16 years were excluded from the study, including 3 children <

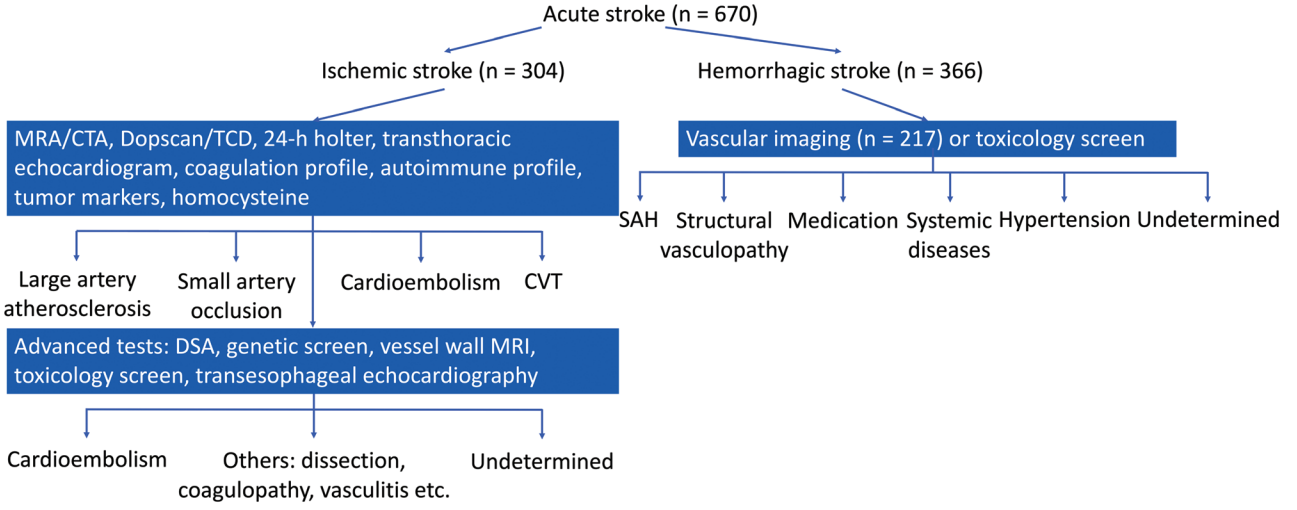

Fig. 1 Diagnostic algorithm and subtype classification in young stroke patients. MRA = magnetic resonance angiography; CTA = computed tomography angiography; TCD = transcranial doppler ultrasound; CVT = cerebral venous thrombosis; DSA = digital subtraction angiography; SAH = subarachnoid hemorrhage.

12 years (all had ICH caused by arteriovenous malformation) and 3 adolescents between 12 and 15 years (2 ICH due to arteriovenous malformation and 1 SAH). The basic demographics and outcomes of the study population are summarized and compared among stroke types in Table 1. There were 630 patients with acute first-time stroke and 40 patients with acute recurrent stroke. These patients had a higher percentage of hemorrhagic stroke (n = 366, 55.0%, including 259 ICH and 107 SAH) than ischemic stroke (n = 304, 45.0%, including 292 infarction and 12 cerebral venous thrombosis (CVT) (Table 1 and Fig. 2A). Note that the patients with CVT and ICH were younger than those with cerebral infarction and SAH. In addition, the proportions of females with CVT and SAH were higher than those with cerebral infarction and ICH.

For nontraumatic ICH (n = 259), 93.1% of the patients had either a hypertensive subtype (42.9%), structural vasculopathy (28.6%) or undetermined ICH (21.6%) (Fig. 2B). Specifically, the most common structural vasculopathy-induced ICH was arteriovenous malformation (70.3%), followed by cavernoma (18.9%) and aneurysm (4.1%). Regarding causes of cerebral infarction, other determined diseases (33.2%) was the most common subtype, followed by large artery atherosclerosis (25.7%), small artery occlusion (15.5%), and undetermined (15.1%) subtypes (Fig. 2C). Among the other determined diseases (n = 101), arterial dissection (n = 55, 54.5%) was the most common cause, followed by autoimmune diseases (n = 11), moyamoya diseases (n = 8), cancer-related thromboembolism (n = 7), and monogenic diseases (n = 7, 7.0%). Monogenic diseases included CADASIL (n = 2), MELAS (n = 3), Fabry disease (n = 1), and Marfan's syndrome (n = 1). Other unusual determined causes included central nervous system infection (n = 3), iatrogenic periprocedural complications (n = 3), hematologic diseases (n = 2), illicit drug use (n =2), and others (n = 3).

3.2. Age of stroke onset <30 years vs 31–45 years

We compared patients aged 16–30 years (n = 105) with those aged 31–45 years (n = 565) (Table 2). Notably, ICH was particularly more prevalent in patients aged 16–30 years than in those aged 31–45 years (54.8% vs 36.8%). Specifically, structural vasculopathy was the most common etiologic subtype in patients aged 16–30 years (χ^2 = 36.3, p < 0.001), whereas hypertensive ICH was the most common subtype in patients aged 31–45 years (χ^2 = 25.1, p < 0.001). In contrast, cerebral infarction was more prevalent in patients aged 31–45 years, and the overall subtype distribution did not differ between the groups (χ^2 = 4.1, p = 0.387). The top ischemic subtype for both age groups was other determined diseases rather than large artery atherosclerosis. Moreover, stroke caused by CVT was also more common in patients between 16 and 30 years (χ^2 = 16.8, p < 0.001). Most vascular risk factors, that is, hypertension, diabetes, hyperlipidemia, and cigarette smoking, but not family history of stroke, were more frequent in patients aged 31–45 years; however, the initial stroke severity (NIHSS) was similar between the 2 age groups (Table 2).

3.3. Risk factors and family history of stroke

Hypertension is the top risk factor for both ICH and infarction. Hyperlipidemia, diabetes, and cigarette smoking were significantly more common in patients with cerebral infarction than in patients with ICH. A family history of stroke was also more frequent in patients with cerebral infarction than patients with SAH (Table 1). Comparing patients with and without a family history of stroke (n =104 vs 566, Table 3), familial stroke patients were younger (37.0 ± 7.4 vs 38.7 ± 7.0 years old), had a higher incidence of ischemic infarction, lower incidence of SAH, and a higher prevalence of diabetes and hypertension, but similar 1-year stroke recurrence and outcomes, suggesting gene-environment interactions in young stroke patients.

3.4. Outcomes

A total of 660 patients completed the 1-year follow-up (98.5%, only 4 infarction, 5 ICH and 1 SAH lost to follow-up). Notably, 76.4% of patients with cerebral infarction had favorable outcomes (mRS 0–2) at 1 year, whereas fewer patients with ICH (61.0%) had favorable outcomes at 1 year (χ^2 = 15.6, p < 0.001). From initial stroke severity to their condition at 1 year after stroke, patients with ICH showed worse functional outcomes than those with infarction (Table 1). The 1-year survival probability was 94.2% for cerebral infarction, 82.2% for ICH, and 79.4% for SAH (Fig. 3). Using multivariate Cox regression analysis, ICH and SAH showed higher hazard ratios of 2.21 (95% CI, 1.19%-4.12%, p = 0.012) and 2.48 (95% CI, 1.19%-4.12%,

Table 1

Basic demographics and outcomes of the young stroke population

	Total (n = 670)	Infarction (n = 292)	ICH (n = 259)	SAH (n=107)	CVT (n=12)	p
Age	37.5 ± 7.0	38.5 ± 6.5	36.4 ± 7.4[a]	38.2 ± 6.3[b]	30.2 ± 9.7[a,b,c]	<0.001
Male gender (%)	436 (65.1%)	194 (66.4%)	183 (70.7%)	55 (51.4%)[a,b]	4 (33.3%)[b]	<0.001
Risk factors						
Hypertension	259 (38.7%)	116 (39.7%)	113 (43.6%)	26 (24.3%)[a,b]	4 (33.3%)	0.006
Diabetes	83 (12.4%)	55 (18.8%)	24 (9.3%)[a]	2 (1.9%)[a]	1 (8.3%)	<0.001
Hyperlipidemia	139 (20.7%)	112 (38.4%)	24 (9.1%)[a]	2 (1.9%)[a]	1 (8.3%)	<0.001
Previous stroke	40 (6.0%)	24 (8.2%)	10 (3.9%)	4 (3.7%)	2 (16.7%)	0.044
Family history of stroke	104 (15.5%)	57 (19.5%)	38 (14.7%)	7 (6.5%)[a]	2 (16.7%)	0.016
Smoking	254 (37.9%)	123 (42.1%)	84 (32.4%)[a]	45 (42.1%)	2 (16.7%)	0.035
Alcohol	170 (25.4%)	66 (22.6%)	66 (25.5%)	37 (34.6%)	1 (8.3%)	0.152
Severity and Outcome						
Initial NIHSS	8.2 ± 10.7	6.1 ± 7.2	9.9 ± 12.3[a]	8.9 ± 13.0[a]	13.1 ± 14.3[a]	<0.001
mRS at 3 months	2.3 ± 2.1	1.8 ± 1.8	2.8 ± 2.1[a]	2.2 ± 2.4[b]	2.9 ± 2.6	<0.001
mRS at 1 y	2.0 ± 2.1	1.3 ± 1.8	2.3 ± 2.3[a]	1.9 ± 2.5[a]	2.4 ± 2.8	<0.001
1-y recurrence	15 (2.3%)	9 (3.1%)	4 (1.6%)	2 (1.9%)	0 (0%)	0.604
1-y mortality	90 (13.6%)	17 (5.9%)	46 (18.1%)[a]	22 (22.8%)[a]	4 (33.3%)[a]	<0.001

[a]p < 0.05, vs infarction, post hoc analysis.

[b]p < 0.05, vs ICH, post hoc analysis.

[c]p < 0.05, vs SAH, post hoc analysis.

CVT = cerebral venous thrombosis; ICH = intracerebral hemorrhage; LAA = large artery atherosclerosis; NIHSS = National Institute of Health Stroke; SAH = subarachnoid hemorrhage.

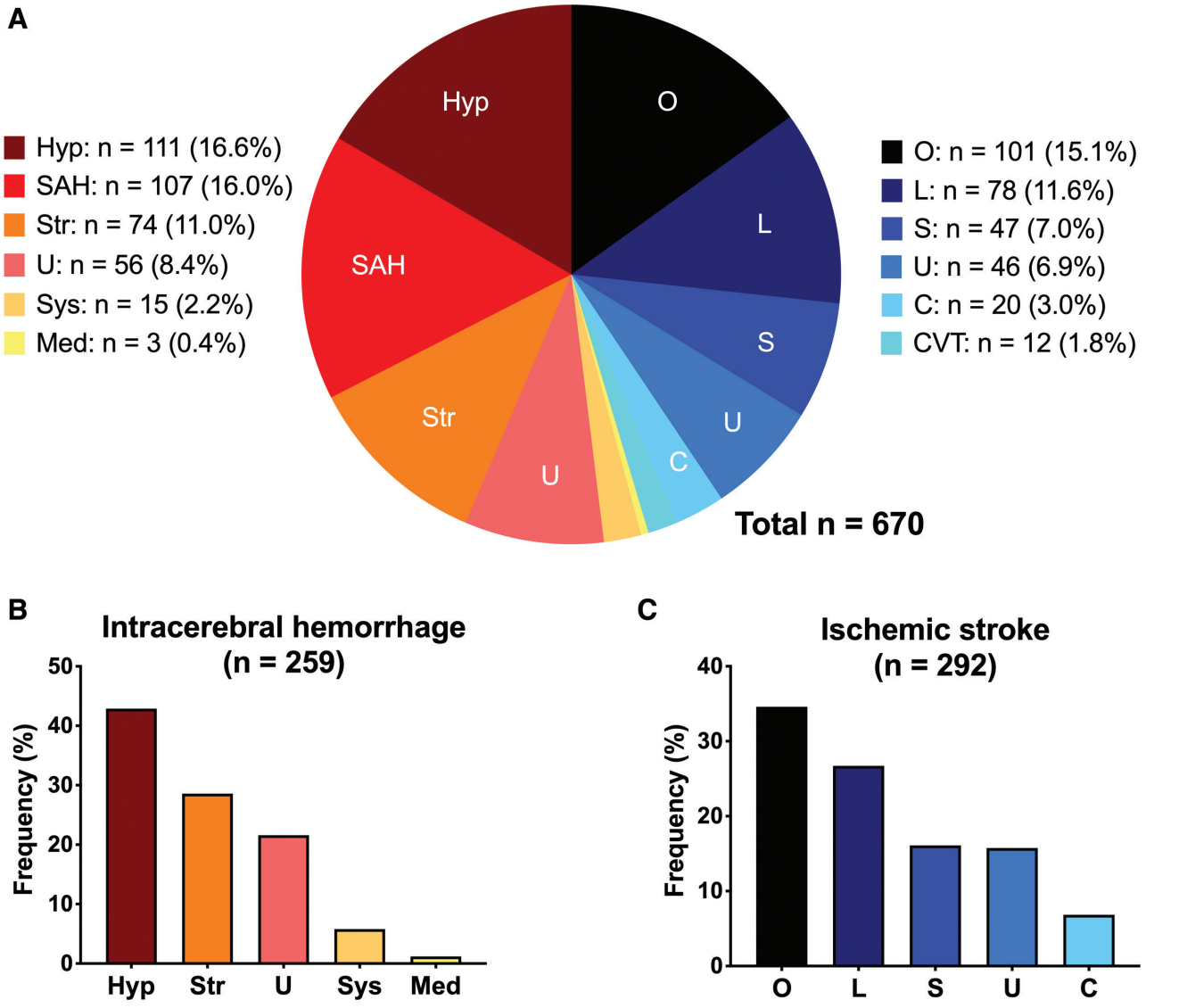

Fig. 2 Distribution of stroke subtypes in young patients. A, Pie chart for all etiologies of ischemic and hemorrhagic stroke. B, Frequency of etiologic subtypes of intracerebral hemorrhage. C, Frequency of etiologic subtypes of ischemic stroke. C, cardioembolism; CVT = cerebral venous thrombosis; Hyp = hypertension; L = large artery atherosclerosis; Med = medication-related; O = other determined; S = small artery occlusion; SAH = subarachnoid hemorrhage; Str = structural vasculopathy; Sys = systemic disease; U = undetermined (cryptogenic).

p = 0.016), respectively, than cerebral infarction for 1-year mortality. The hazard ratio for SAH relative to ICH was 1.12 (95% CI, 0.67%-1.90%, p = 0.664).

For overall ICH and infarction, the independent predictors from acute stage for favorable outcome at 3 months were a lower initial NIHSS score and infarction type on admission (Table 4). For either ICH or infarction, the only significant predictor for favorable outcomes at 3 months was lower initial NIHSS score. Of the 12 youn patients with recurrent stroke by 1 year after onset, 9 had cerebral infarction, and 4 had ICH. Of those 9 patients with an initial cerebral infarction, 7 had recurrent cerebral infarction, and 1 had recurrent hypertensive ICH. We did not identify any significant predictor for 1-year stroke recurrence.

4. DISCUSSION

We reported other determined diseases as the most common causal subtype of ischemic stroke (33.2%) in young Taiwanese, which was higher than most previous Asian studies ranging from 3.2% to 26.8%,[17–19] except for a Japanese report of 37%.[20] Among those infarctions due to other determined causes, our study showed that arterial dissection accounted for 54.5%, which is higher than in most other Asian cohorts (40.7% in another Taiwanese cohort[17] but 70% in a Japanese cohort).[20] Arterial dissection occurs mostly between 30 and 50 years of age.[21,22] The etiology of dissection remains largely unclear and there may be a link with trauma, connective tissue diseases and infection.[23] Intracranial arteriopathy with ischemic stroke is particularly prevalent and important in Asian populations.[20,24] These findings highlight the importance of high-resolution vessel wall imaging in young Asian patients and the necessity of cooperating with experienced neuroradiologists.[24]

More importantly, we found a higher proportion of hemorrhagic stroke (54.6%, including ICH and SAH) than previously reported studies of young Asian populations, ranging from 20 to 40%,[13] which was similar to the proportion reported in young Africans (52.5%).[25] Specifically, our study revealed that

Table 2

Characteristic comparison between patients aged 16–30 years and 31–45 years

	16–30 (n = 105)	31–45 (n = 565)	*p*
Age	24.5 ± 4.2	39.9 ± 4.2	
Male gender (%)	54 (51.4%)	382 (67.6%)	0.001
ICH	51 (48.6%)	208 (36.8%)	<0.001
Structural	32 (62.7%)	42 (20.2%)	<0.001
Undetermined	11 (21.6%)	45 (21.6%)	0.992
Hypertensive	6 (11.8%)	105 (50.5%)	<0.001
Systemic disease	2 (3.9%)	13 (6.3%)	0.524
Medication	0 (0%)	3 (1.4%)	0.744
SAH	16 (15.2%)	91 (16.1%)	0.824
Infarction	31 (29.5%)	261 (46.2%)	<0.001
Other	15 (48.4%)	86 (33%)	0.387
LAA	7 (22.6%)	71 (27.2%)	
Undetermined	5 (16.1%)	41 (15.7%)	
Cardioembolism	2 (6.5%)	18 (6.9%)	
Small vessel occlusion	2 (6.5%)	45 (17.2%)	
CVT	7 (6.7%)	5 (0.9%)	<0.001
Hypertension	11 (10.5%)	248 (43.9%)	<0.001
Diabetes	1 (1.0%)	82 (14.5%)	<0.001
Hyperlipidemia	3 (2.9%)	136 (24.1%)	<0.001
Smoking	19 (18.1%)	235 (41.6%)	<0.001
Alcohol	12 (11.4%)	158 (28.0%)	0.001
Family history of stroke	11 (10.5%)	93 (16.5%)	0.120
Initial NIHSS	8.4 ± 12.2	8.1 ± 10.4	0.830

ICH = intracerebral hemorrhage; SAH = subarachnoid hemorrhage; LAA = large artery atherosclerosis; CVT = cerebral venous thrombosis; NIHSS = National Institute of Health Stroke.

Table 3

Characteristics of young stroke with familial aggregation (first- or second-degree relatives had stroke by age 80)

		Family history (n = 104)	No family history (n = 566)	*p*
Age		37.3 ± 7.1	38.9 ± 6.4	0.025
Male gender (%)		72 (69.2%)	364 (64.3%)	0.333
Stroke types	ICH	38 (36.5%)	221 (39.0%)	0.629
	SAH	7 (6.7%)	100 (17.7%)	0.005
	Infarction	57 (54.8%)	235 (41.5%)	0.012
	CVT	2 (1.9%)	10 (1.8%)	0.912
Monogenic diseases		1 (1.0%)	6 (1.1%)	0.928
Hypertension		50 (48.1%)	209 (36.9%)	0.032
Diabetes		21 (20.2%)	62 (11.0%)	0.009
Hyperlipidemia		21 (20.2%)	118 (20.8%)	0.880
1-y stroke recurrence		2 (2.0%)	13 (2.3%)	0.818
1-y outcomes in mRS		1.6 ± 2.0	1.9 ± 2.3	0.233

CVT = cerebral venous thrombosis; ICH = intracerebral hemorrhage; mRS = modified Rankin Scale; SAH = subarachnoid hemorrhage.

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.[26] In our patients aged between 31 and 45 years, hypertensive ICH was the most common subtype, which is concordant with previous Taiwanese reports.[27,28] This finding may be explained by the increase in the development of risk factors with advancing age. Both hypertension and structural

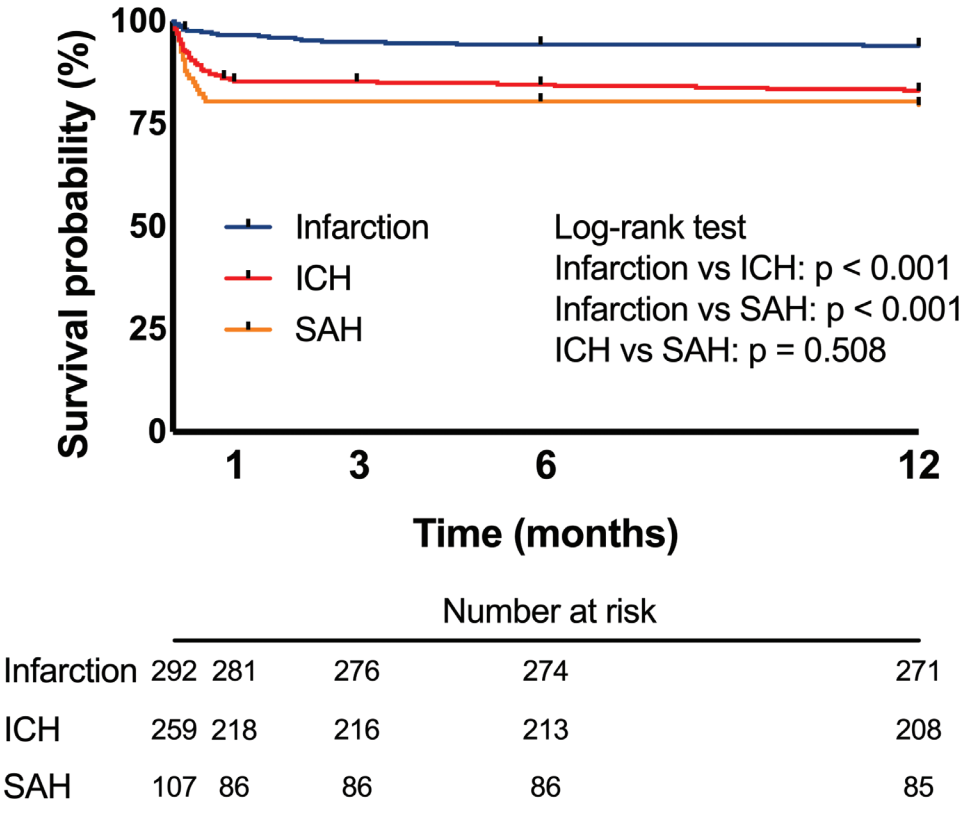

Fig. 3 Kaplan-Meier survival probability over 1 year in patients after stroke of cerebral infarction (in dark blue), ICH (in red) and SAH (in orange). ICH = intracerebral hemorrhage; SAH = subarachnoid hemorrhage.

Table 4

Logistic regression model for favorable outcome (modified Rankin scale 0–2) at 3 months after cerebral infarction and ICH

	ICH and infarction (n = 529)		Infarction (n = 282)		ICH (n = 247)	
	OR (95% CI)	*p*	OR (95% CI)	*P*	OR (95% CI)	*p*
Age	0.97 (0.94-1.01)	0.095	0.98 (0.92-1.04)	0.470	0.96 (0.92-1.00)	0.070
Male gender	1.00 (0.62-1.60)	0.992	1.63 (0.79-3.37)	0.186	0.62 (0.32-1.19)	0.111
Risk factor score[a]	1.02 (0.82-1.27)	0.878	0.95 (0.68-1.33)	0.777	1.02 (0.74-1.42)	0.898
Initial NIHSS	0.87 (0.84-0.90)	<0.001	0.79 (0.74-0.84)	<0.001	0.92 (0.89-0.94)	<0.001
Infarction type	2.47 (1.61-3.81)	<0.001				

[a]Risk factor scores were derived by summing the risk factors present in a stroke patient on admission, including hypertension, diabetes, hyperlipidemia and cigarette smoking (0–4).
CI = confidence interval; ICH = intracerebral hemorrhage; OR = odds ratio; NIHSS = National Institute of Health Stroke Scale.

vasculopathy are the leading causes of ICH in young individual in Western populations.[10] Different genetic and acquired risk factors may contribute to such differences and need further investigation.[12]

A family history of stroke has been identified as an independent risk factor for both ischemic and hemorrhagic strokes,[29–32] particular young stroke[33,34]; however, its association with stroke subtype is inconsistent.[32,35,36] Comparing familial and nonfamilial young stroke, we found that ischemic stroke in total, and not any subtype, was more common in patients with a family history of stroke; however, the high prevalence of conventional vascular risk factors (87.8%) in our familial young stroke group suggested complex gene-environment interactions. Familial aggregation of stroke and vascular risk factors has been observed worldwide.[37] In line with a previous study, ICH was not significantly associated with a family history of stroke.[38] Although CADASIL is the most frequently encountered monogenic stroke disease, it is less common in young stroke patients aged ≤45. Previous studies on Taiwanese CADASIL patients showed that the average age at onset was 54.1 ± 12.5 years[39] to 57.8 ± 10 years.[40] Only a few patients with homozygous NOTCH3 mutations had stroke onset by 45 years.[40,41] We identified only 2 patients with CADASIL out of 670 (0.3%) young stroke patients aged ≤45. The genetic diagnosis of rare monogenic diseases is likely underestimated because single gene analysis was only applied to candidate genes in phenotypically characteristic patients. Next-generation sequencing may help to disclose de novo mutations and more rare monogenic diseases in early-stage patients with a family history of stroke.

Regarding long-term outcomes in young stroke patients, few studies have been conducted on Asian populations. In ischemic stroke, the proportion of favorable functional outcomes was generally more than 80%.[42,43] In Western populations, initial stroke severity and diabetes were associated with poor outcomes at 3 months after onset.[44–46] A Chinese study reported that poor outcomes at discharge were associated with certain stroke subtypes of large artery atherosclerosis and cardioembolism.[47] In contrast, ICH usually led to poor long-term outcomes, which was suggested to be as high as 49% after a mean follow-up of 9.7 years in association with age, initial stroke severity, and intraventricular hemorrhage.[48] In our patients, the independent predictors for a 3-month favorable outcome were initial stroke severity (NIHSS scores) after cerebral infarction or ICH. Regarding stroke recurrence, an increasing number of vascular risk factors have been shown to be associated with long-term recurrence[8,16,49,50]; however, we did not find any independent predictor for stroke recurrence, possibly due to the limited duration of follow-ups.

There were several limitations in our study. First, this was a single-center retrospective analysis that might underestimate some specific etiologies, such as rare monogenetic diseases. Although we identified a few candidate monogenic stroke diseases, diagnosing rare hereditary diseases is challenging because genetic tests were only applied to highly selected patients with classic characteristics. Advanced genetic screening can be considered in prospective studies of young patients with family history of stroke. Second, there was a lack of validation of detailed family histories of stroke from affected family members in the retrospective setting. Third, cardiac assessment, including transthoracic or transesophageal echocardiography and cardiac rhythm monitoring, might be underinvestigated.

This study provides the characteristic subtypes of etiologies, risk factors, and outcomes of young adult stroke patients from a single medical center in Taiwan and suggests that high-resolution vascular imaging may be particularly valuable in young patients because other unusual causes of infarction and structural vasculopathy-induced ICH account for a significant proportion of young strokes.

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