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Research Article,

Etiology and Risk Factors of Ischemic Stroke in Young Adults: A Mongolian Two-Center Study

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Abstract:

Introduction: Young adults experiencing ischemic stroke often present with distinct risk factors and underlying causes that are less prevalent or different compared to older individuals. However, the existing classifications may not fully capture the unique risk and etiological factors specific to young adults. In this study, we utilized a modified risk factor categorization derived from the International Pediatric Stroke Study (IPSS) to analyze the risk factor profiles of Mongolian young patients diagnosed with ischemic stroke.

Methods: This study is a retrospective analysis conducted at two medical centers. We included patients between the ages of 18 and 49 years who were admitted to the First and Third Central Hospitals of Ulaanbaatar for their first-ever ischemic stroke during the period from 2018 to 2021. The study aimed to consecutively collect and analyze the risk factors of these patients, which were subsequently categorized into 10 groups based on the modified IPSS criteria. We also examined the potential differences in risk factor distribution based on both sex and age, thereby exploring any notable variations among these patient subgroups.

Results: The study included a total of 306 patients, with a median age of 42 years, and 60.5% of the participants were men. Among all patients, at least one IPSS risk factor category was identified in 91.5% of the cases. The most common IPSS subtype observed was atherosclerosis-related risk factors, accounting for 81% of the cases followed by cardiac disorders (16%), chronic systemic conditions (13.1%), arteriopathy (11.4%), and chronic head and neck disorders (6.2%). The prevalence of chronic systemic conditions was higher in patients aged below 35 years (16.7% vs. 11.4%) and in women (21.5% vs. 7.6%, $p < 0.05$). Atherosclerosis-related risk factors were more dominant in patients aged 35 years and older (87.1% vs. 67.7%, $p < 0.0001$) and in men (93.0% vs. 62.8%, $p < 0.0001$).

Conclusions: The IPSS classification has the potential to serve as an effective tool in identifying the risk factors associated with ischemic stroke in young adults.

Keywords: ischemic stroke in young adults, etiology, risk factors, stroke of undetermined etiology, IPSS category

Introduction:

Ischemic stroke in young people can be devastating in terms of loss in productive years and its impact on a young person's life, their families, and society in general. Although the incidence of ischaemic stroke increases with age, an estimated 10%-20% of these events occur in young adults aged 18 to 49 years [1]. In contrast to the incidence of stroke in the elderly, the incidence of ischemic stroke among young adults is increasing worldwide [2-4] and regardless of less vascular risk factors, young patients in low- and middle-income countries more often died within 3 months than those from high-income countries [5].

The etiologies of ischemic strokes in young adults are different and more diverse as compared to those observed in the elderly. Furthermore, etiological subtyping also varies according to nationality and geographical distribution [3,5,9]. It is important to define the etiological factors in young stroke patients in order to prevent recurrences. Unfortunately, approximately one-third of ischemic stroke cases occurring in young individuals remain of unknown etiology despite comprehensive clinical

investigation and the use of stroke classification systems such as the TOAST (Trial of ORG 10172 in Acute Stroke Treatment) classification [6,7,8] which is not conducive to rapid etiological identification and poses a challenge on the treatment and prevention of ischemic stroke in young adults.

Consequently, there is a growing focus on conducting more studies to investigate novel classifications of risk factors and the underlying mechanisms of stroke in young adults. In 2011, researchers introduced a novel classification system within the International Pediatric Stroke Study (IPSS) that categorized the presumed risk factors of childhood ischemic stroke into ten distinct categories [10]. The risk factor profiles for pediatric ischemic stroke have been found to differ significantly from those observed in older adults. In 2018, the Follow-Up of Transient Ischemic Attack and Stroke Patients and Unelucidated Risk Factor Evaluation (FUTURE) study aimed to categorize the risk factors of ischemic stroke in young adults based on the criteria established by the International Pediatric Stroke Study (IPSS). The study revealed that at least one IPSS category could be identified in 94% of all participants and in 88% of patients classified as having a stroke of unknown etiology according to the Trial of Org 10172 in Acute Stroke Treatment (TOAST) criteria [11]. This suggests that the IPSS criteria are applicable and useful in identifying risk factors for ischemic stroke among young adults, as the risk factor spectrum partially overlaps with that of pediatric ischemic stroke. Moreover, in recent multicenter prospective study have found that only 0.8% of 1322 patients had a cryptogenic stroke without any potential risk factors when applying the IPSS classification [12].

This study aimed to determine the distribution of risk factors for ischemic stroke in young adults within a Mongolian cohort, using the classification system provided by the International Pediatric Stroke Study (IPSS). A secondary objective was to investigate potential variations in risk factor distribution among different genders and age groups. By examining these variations, the study sought to enhance the identification of underlying mechanisms, improve clinical management, and enhance preventive measures for ischemic stroke in young adults.

Material and Methods:

Study Participants

This study is a two-center retrospective study. We carried out a hospital-based review of patients aged 18–49 years with a first-ever ischemic stroke between January 2018 and December 2021, and were admitted to a tertiary referral hospital in Ulaanbaatar (First and Third Central Hospitals). Ischemic stroke was defined as a sudden focal neurologic deficit with imaging-confirmed cerebral infarction. We excluded cases of intracranial and subarachnoid hemorrhages.

Study Design

As a matter of protocol, all stroke patients admitted to the neurology wards underwent hematological and biochemistry tests (transaminases, creatinine, urea nitrogen, electrolytes, fasting glucose, hemoglobin A1c, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, triglycerides, C-reactive protein, and homocysteine), electrocardiography, chest X-rays, and brain imaging, including computed tomography (CT) and magnetic resonance imaging (MRI) at admission. A majority of patients underwent vascular imaging studies such as CT angiography or MR angiography. Transthoracic echocardiography and more specific diagnostic testing (such as cardiovascular profile) were performed in selected patients. Other examinations were carried out depending on the patient-specific conditions, such as screening for thrombophilia (protein C and S and antithrombin), antiphospholipid antibodies (anticardiolipin, anti-β2 glycoprotein 1 antibody, and lupus anticoagulant), and screening for autoimmune diseases (antinuclear antibody, anti-extractable nuclear antigen antibody, and antineutrophil cytoplasmic antibodies). Patients were examined by an investigator-neurologists and data regarding each patient's clinical presentation, risk factors, results of vascular imaging, biochemical analysis and other diagnostic tests at admission and during hospital treatment were recorded in special proforma for research purpose.

Stroke subtyping was based on the clinical and neuroimaging findings available at hospital and according to the modified TOAST criteria [13,14] into the following subtypes: Large artery atherosclerosis, likely large artery disease cardioembolism, small-vessel occlusion, stroke of other determined etiology, multiple causes and the stroke of undetermined etiology.

The study collected and categorized the presumed risk factors for stroke into nine different categories based on the definitions provided by the International Pediatric Stroke Study (IPSS):

(1) arteriopathy: any arterial abnormality on

vascular imaging other than isolated vessel occlusion; (2) cardiac disorders: either a history of chronic cardiac disorder or when detected on electrocardiograph or echocardiography during the analysis of stroke; (3) chronic systemic conditions: a condition or disease with known changes in coagulation or vascular structure, such as autoimmune disease (e.g., systemic lupus erythematosus, Sjogren's syndrome, and vasculitis), genetic disorder, hematological disease, inflammatory or immune system disorder, oncological disease, and use of oral contraceptives;(4) acute systemic conditions: any acute condition that leads to systemic disturbances, e.g., hypotension, shock, <72 h after surgery; (5) prothrombotic states: a known disease in coagulation or found on laboratory testing, such as hyperhomocysteinemia, antiphospholipid syndrome, protein C/S deficiency; (6) acute head and neck disorders: an acute disease, surgery or trauma localized in the head or neck region; (7) chronic head and neck disorders: a chronic disease localized in the head or neck region, e.g., tumor, aneurysm, or migraine; (8) infection; and (9) atherosclerosis-related risk factors: either a history of a risk factor (mentioned in the medical history or the use of medication) or detected during the analysis of the stroke, e.g., hypertension, diabetes mellitus, dyslipidemia, smoking, and alcoholism [10].

Diseases were identified based on their clinical symptoms and diagnostic investigation, following the criteria outlined in the guidelines. In addition, the FUTURE study [11] incorporated pregnancy as the tenth category of risk factors, recognizing that the period of pregnancy and postpartum (within 6 weeks) poses a distinct risk for ischemic stroke among young women. A patient could be divided into several categories which are not exclusive.

The distribution of each TOAST subtype and IPSS category was calculated both as a whole and separately, with stratification by sex and age. Given the notable increase in vascular risk factors observed among individuals aged 35 years and older [1], and considering that the age of 35 years has commonly been employed as a cut-off value in previous studies examining young ischemic stroke [8,11], we utilized this age threshold for conducting stratified analyses.

We also compared TOAST subtype distribution among different age-groups: 18–25, 26–30, 31–35, 36–40, 41–45, and 46–49 years. Moreover, we applied the IPSS categorization additionally in patients divided into the stroke of cryptogenic and noncryptogenic to explore its feasibility.

Statistical Analyses

Means or medians were used to show the average levels of quantitative data with or without a normal distribution, respectively. The t-test or rank-sum test was used to compare quantitative variables between groups for data with a normal or non-normal distribution. Chi-square or Fisher's exact test was used to compare categorical variables between different groups. Data were analyzed using SPSS Software version 26 (IBM) and the value of $p < 0.05$ was considered statistically significant

Results:

Baseline characteristics

In total, 306 patients were enrolled in this study. The detailed demographic data are summarized in **Table 1.** The median age was 42 years (interquartile range [IQR]: 18–49 years), and 60.5% were men. Women were younger than men at stroke onset (41 vs. 42, $p < 0.05$). Besides, the proportion of men was larger in patients ≥35 years than patients <35 years (65.2 vs. 50%, respectively, $p < 0.05$).

Table 1. Demographic data and TOAST classification

Characteristics	Total (n=306)	Sex group		*p* value	Age group		*p* value
		Male (n=185)	Female (n=121)		<35 years (n=96)	≥35 years (n=210)	
Age (years)	42 (18,49)	42 (18,49)	41 (19,49)	0.006*	-	-	-
Male, n (%)	185 (60.5)	-	-	-	48 (50)	137 (65.2)	0.0016*
TOAST classification, n (%)							
Large artery atherosclerosis	21 (6.9)	16 (8.6)	5 (4.1)	0.166	2 (2.1)	19 (9)	0.027*
Likely large artery disease	33 (10.8)	19 (10.3)	14 (11.6)	0.711	5 (5.2)	28 (13.3)	0.045*
Cardioembolism	47 (15.4)	25 (13.2)	22 (18.2)	0.331	13 (13.5)	34 (16.2)	0.611
Small-vessel	32 (10.5)	18 (9.7)	14 (11.6)	0.703	9 (9.4)	23 (11)	0.841

disease							
Other defined	61 (19.9)	33 (17.8)	28 (23.1)	0.306	31 (32.3)	30 (14.3)	0.001*
Multiple causes	18 (5.9)	13 (7)	5 (4.1)	0.332	2 (2.1)	16 (7.6)	0.067
Unknown cause	94 (30.7)	61 (33)	33 (27.3)	0.313	134 (35.4)	60 (28.6)	0.233

*TOAST, Trial of Org 10,172 in Acute Stroke Treatment. *p < 0.05.*

Classification according to modified TOAST criteria:

The distribution of etiologic subtypes classified by the TOAST criteria is shown in **Table 1.** The stroke of unknown cause was the most prevalent stroke subtype (30.7%) in our cohort, followed by other defined etiology (19.9%), cardioembolism (15.4%), likely large artery disease (10.8%), small-vessel occlusion (10.5%), large-artery atherosclerosis (6.9%), and multiple causes (5.9%).

The etiological classification was also analyzed by dividing the cohort into 2 groups according to age (<35 and ≥35 years). Large artery atherosclerosis (9.0 vs. 2.1%, p < 0.05) and likely large artery disease (13.3 vs 5.2%, p < 0.05) were more prevalent in patients aged ≥35 years than in patients aged <35 years. On the other hand, the stroke of other determined etiology (35.4 vs 28.6%, p < 0.05) was more common in patients aged <35 years than in patients aged ≥35 years.

Women were more likely to have cardioembolism, and men were more likely to have large-artery disease, and both sexes presented with other determined causes as shown in **Table 1.**

The cause of stroke according to the TOAST classification differed between age-groups **(Figure).** **Figure** illustrates the evolution of etiologic spectrum as a function of age in the patient population. The most striking change was a constant decrease of other determined etiology in the proportion of the group. In contrast, the percentages of small vessel disease and likely atherothrombotic stroke showed increasing trends.

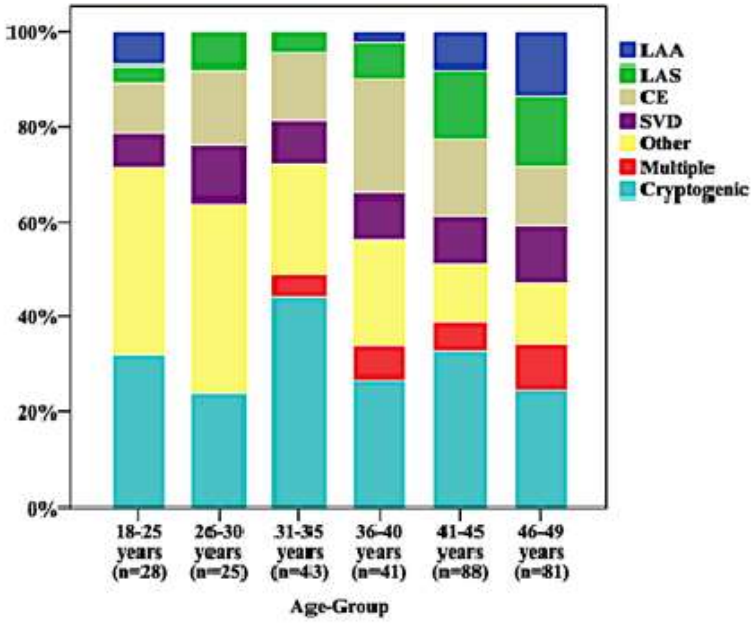

Figure1. TOAST causes distribution among different age-groups. CE, cardioembolic stroke; LAA, large artery atherosclerosis; LAS, likely atherothrombotic stroke; Other, other determined cause of stroke; and SVD, small vessel disease.

Classification of risk factors based on IPSS criteria

Table 2 displays the comprehensive IPSS classifications and illustrates the occurrence of risk factors organized based on IPSS criteria. Among 306 patients, 91.5% of them had at least one IPSS category. Besides atherosclerosis-related risk factors (81%), the most common IPSS subtype was cardiac disorders (16%), followed by chronic systemic conditions (13.1%), arteriopathy (11.4%), chronic head and neck disorder (6.2%) and the prevalence rates of other categories were all <5%.

There were significant differences in the IPSS category distribution between men and women. Men were more likely to be classified as arteriopathy than women. In this category,
vasculitis secondary to infections was more dominant in men (7.0 vs. 1.7%, $p < 0.05$) while reversible cerebral vasoconstriction syndrome (2.5 and 1.1%), primary angiitis of central nervous system was more common in women (2.5 and 0%) however these differences were nonsignificant. Chronic systemic conditions were more commonly present among female patients than male patients (21.5 vs. 7.6%, $p < 0.05$). In this category, hematological disorder (6.6 vs 1.1%, $p < 0.05$), hyperthyroidism (3.3 vs 0%, $p < 0.05$) were more prevalent in women. Chronic head and neck disorders were more reported in women (12.4 vs 2.2%, $p < 0.001$) while atherosclerosis-related risk factor were more predominant in men (93.0 vs. 62.8%, $p < 0.0001$).
Valvulopathy (7.4 vs 2.2%, $p < 0.05$) and migraine (9.9 vs 1.6%, $p < 0.05$) were more prevalent in women than men.

Table 2. Prevalence of risk factors in 306 young stroke patients categorized based on IPSS methods

IPSS risk factor category, n (%)	Total (n=306)	Sex group		*p* value	Age group		*p* value
		Male (n=185)	Female (n=121)		<35 years (n=96)	≥35 years (n=210)	
Arteriopathy	35 (11.4)	24 (13)	11 (9.1)	0.360	17 (17.7)	18 (8.6)	0.032*
Vasculitis secondary to infections	15 (4.9)	13 (7)	2 (1.7)	0.050*	6 (6.3)	9 (4.3)	0.569
Arterial dissection	10 (3.3)	8 (4.3)	2 (1.7)	0.321	6 (6.3)	4 (1.9)	0.077
Reversible cerebral vasoconstriction syndrome	5 (1.6)	2 (1.1)	3(2.5)	0.387	2 (2.1)	3 (1.4)	0.651
Primary angiitis of central nervous system	3 (1)	0 (0)	3 (2.5)	0.061	2 (2.1)	1 (0.5)	0.233
Moyamoya disease	2 (0.7)	1 (0.5)	1 (0.8)	1.000	1 (1)	1(0.5)	0.530
Cardiac disorders	49 (16)	25 (13.5)	24 (19.8)	0.153	13 (13.5)	36 (17.1)	0.503
Valvulopathy	13 (4.2)	4 (2.2)	9 (7.4)	0.039*	1 (1)	12 (5.7)	0.070
Atrial fibrillation	12 (3.9)	8 (4.3)	4 (3.3)	0.769	3 (3.1)	9 (4.3)	0.759
Myocardiopathy	8 (2.6)	5 (2.7)	3 (2.5)	1.000	3 (3.1)	5 (2.4)	0.709
Other[a]	9 (2.9)	4 (2.2)	5 (4.1)	0.326	3 (3.1)	6 (2.9)	1.000
Congenital heart disease	4 (1.3)	3 (1.6)	1 (0.8)	1.000	2 (2.1)	2 (1)	0.592
Patent foramen ovale	3 (1)	2 (1.1)	1 (0.8)	1.000	1 (1)	2 (1)	1.000
Endocarditis	1 (0.3)	0 (0)	1 (0.8)	0.395	0 (0)	1 (0.5)	1.000
Chronic systemic conditions	40 (13.1)	14 (7.6)	26 (21.5)	0.001*	16 (16.7)	24 (11.4)	0.207
Inflammatory disease	13 (4.2)	10 (5.4)	3 (2.5)	0.259	3 (3.1)	10 (4.8)	0.761
Hematological disorder	10 (3.3)	2 (1.1)	8 (6.6)	0.016*	3 (3.1)	7 (3.3)	1.000
Oncological disease	5 (1.6)	2 (1.1)	3 (2.5)	0.387	1 (1)	4 (1.9)	1.000
Hyperthyroidism	4 (1.3)	0 (0)	4 (3.3)	0.024*	1 (1)	3 (1.4)	1.000
Oral contraceptive pill	4 (1.3)	0 (0)	4 (3.3)	0.024*	4 (4.2)	0.(0)	0.009*
Autoimmune disease	2 (0.7)	0 (0)	2 (0.7)	0.156	2 (2.1)	0 (0)	0.098
Prothrombotic states	8 (2.6)	5 (2.7)	3 (2.5)	1.000	5 (5.2)	3 (1.4)	0.114
Hyperhomocysteinemia	3 (1)	1 (0.5)	2 (1.7)	0.567	1 (1)	2 (1)	1.000
Antiphosholipid syndrome	3 (1)	2 (1.1)	1 (0.8)	1.000	3 (3.1)	0 (0)	0.030*
Protein C or S deficiency	1 (0.3)	1 (0.5)	0.(0)	1.000	0 (0)	1 (0.5)	1.000
Thrombophilia	1 (0.3)	1 (0.5)	0 (0)	1.000	1 (1)	0 (0)	0.314
Acute systemic disorders	6 (2)	4 (2.2)	2 (1.7)	1.000	3 (3.1)	3 (1.4)	0.382
<72h after surgery	4 (1.3)	2 (1.1)	2 (1.7)	0.649	3 (3.1)	1 (0.5)	0.093
Shock	2 (0.7)	2 (1.1)	0 (0)	0.520	0 (0)	2 (1)	1.000
Chronic head and neck disorders	19 (6.2)	4 (2.2)	15 (12.4)	<0.001*	6 (6.3)	13 (6.2)	1.000
Aneurysm	2 (0.7)	0 (0)	2 (1.7)	0.156	1 (1)	1 (0.5)	0.530
Migraine	15 (4.9)	3 (1.6)	12 (9.9)	0.002*	4 (4.2)	11 (5.2)	0.783
Brain tumor	1 (0.3)	1 (0.5)	0 (0)	1.000	0 (0)	1 (0.5)	1.000

Intracranial AVM	1 (0.3)	0 (0)	1 (0.8)	0.395	1 (1)	0 (0)	0.314
Acute head and neck disorders	1 (0.3)	1 (0.5)	0 (0)	1.000	1 (1)	0 (0)	0.314
Head or neck surgery	1 (0.3)	1 (0.5)	0 (0)	1.000	1 (1)	0.(0)	0.314
Pregnancy related	7 (2.3)	0 (0)	7 (2.3)	-	5 (5.2)	2 (1)	0.033*
During pregnancy	6 (2)	0 (0)	6 (5)	-	5 (5.2)	1 (0.5)	0.013*
Postpartum	1 (0.3)	0 (0)	1 (0.8)	-	0 (0)	1 (0.5)	1.000
≥ 1 atherosclerosis related risk factor	248 (81)	172 (93)	76 (62.8)	<0.001*	65 (67.7)	183 (87.1)	<0..001*
≥ 2	90 (29.4)	73 (39.5)	17 (14)	<0.001*	21 (21.9)	69 (32.9)	0.058
≥ 3	42 (13.70	36 (19.5)	6 (5)	<0.001*	5 (5.2)	37 (17.6)	0.004*
≥ 4	15 (4.9)	13 (7)	2 (1.7)	0.054	1 (1)	14 (6.7)	0.043*
Hypertension	142 (46.4)	95 (51.4)	47 (38.8)	0.035*	23 (24)	119 (56.7)	<0.001*
Diabetes mellitus	32 (10.5)	23 (12.4)	9 (7.4)	0.185	2 (2.1)	30 (14.3)	0.001*
Dyslipidemia	63 (20.6)	35 (18.9)	28 (23.1)	0.388	21 (21.9)	42 (20)	0.761
Smoking	120 (39.2)	108 (58.4)	12 (9.9)	<0.001*	25 (26)	95 (45.2)	0.002*
Alcoholism	98 (32)	89 (48.1)	9 (7.4)	<0.001*	23 (24)	75 (35.7)	0.048*

*AVM indicates arteriovenous malformation; IPSS, International Pediatric Stroke Study. [a]Including chronic cardiac failure (n = 3), acute cardiac failure (n = 1), cardiac tumor (n = 1), cryptogenic mass in aortic root (n = 1), pulmonary arterial hypertension with cardiac failure (n = 1), myocardial infarction (n = 2), *p < 0.05.*

The distribution of IPSS category varied between different age groups. Patients <35 years of age were more likely to be classified as arteriopathy (17.7 vs. 8.6%, p < 0.05), while atherosclerosis-related risk factors were more dominant in patients ≥35 years (87.1 vs. 67.7%, p < 0.0001). Moreover, chronic systemic conditions (16.7 and 11.4%), pregnancy related (5.2 vs 1%, p <0.05) were more present in younger patients. In contrast, atherosclerosis related risk factors (87.1 vs 67.7%, p <0.001) was predominant in patients ≥35 years.

Atherosclerosis related risk factors

Table 2 summarizes the prevalence of classical cerebrovascular risk factors in our cohort. At least one modifiable cerebrovascular risk factor was found in 81.0% of all patients. We found hypertension in 146 of 306 patients (46.4%), smoking in 120 (39.2%), alcoholism in 98 (32%), dyslipidemia in 63 (20.6%) and diabetes mellitus in 32 (10.5%).

On average, men tended to have more modifiable cerebrovascular risk factors than women (39.5 vs. 14%, p < 0.0001). Hypertension (56.7 vs. 24%, p < 0.001), smoking (45.2 vs. 26.0%, p < 0.05), diabetes mellitus (14.3 vs 2.1, p < 0.05) and alcoholism (35.7 vs. 724%, p < 0.05) were found to be more significantly present in men than in women.

More modifiable cerebrovascular risk factors were found among patients aged 35 years or older than patients younger than 35 years (17.6 vs. 5.2, p < 0.05). Hypertension (57.6 vs. 26.7%, p < 0.0001), diabetes mellitus (27.1 vs. 10.5%, p < 0.0001), hyperlipidemia (30.5 vs. 18.8%, p < 0.05), smoking (36.9 vs. 22.5%, p < 0.05), and alcoholism (20.7 vs. 5.8%, p < 0.0001) were more prevalent in patients ≥35 years.

In 94 patient's classified as the stroke of undetermined etiology according to TOAST criteria, 75.5% were found to have at least one risk factor with IPSS approach. Besides atherosclerosis-related risk factors (86.2%), the most reported subtype was chronic systemic conditions (14.9%), followed by chronic head and neck disorders (9.6%) and pregnancy related (5.3%). The detailed information is demonstrated in **Table 3**.

In comparison with patients with a noncryptogenic stroke according to TOAST, patients with a cryptogenic stroke less often had arteriopathies (4.3% versus 14.6%, p <0.05)) and cardiac conditions (1.1% versus 22.6%, p <0.001), more often had pregnancy related (5.3% versus 0.9%, p <0.05) and more likely had chronic systemic condition (14.9 vs 12.3) and chronic head and heck disorders (9.6 vs 4.7 Table 3). Risk factors for early atherosclerosis were prevalent in both groups (86.2% vs 78.8%).

Table 3. Prevalence of risk factor categories based on IPSS in the group of patients classified as 'stroke of unknown etiology, cryptogenic' and noncryptogenic using TOAST criteria

IPSS Risk factor category n (%)	Cryptogenic stroke n =94	Noncryptogenic stroke n=212	P-value
Arteriopathy, n (%)	4 (4.3)	31 (14.6)	0,010*
Cardiac disorders, n (%)	1 (1.1)	48 (22.6)	<0.001*
Chronic Systemic conditions, n (%)	14 (14.9)	26 (12.3)	0.582
Prothrombotic states, n (%)	0 (0)	8 (3.8)	0.112
Acute systemic disorders, n (%)	4 (4.3)	2 (0.9)	0.074
Chronic Head and neck disorders, n (%)	9 (9.6)	10 (4.7)	0.124
Acute head and neck disorders, n (%)	1 (1.1)	2 (0.9)	0.307
Pregnancy related, n (%)	5 (5.3)	2 (0.9)	0.030*
Atherosclerosis related risk factors, n (%)	81 (86.2)	167 (78.8)	0.155

*IPSS, International Pediatric Stroke Study, *p < 0.05.*

Discussion:

This comprehensive cohort study in which we implemented a risk factor classification system, initially utilized in the IPSS, among Mongolian young patients with ischemic stroke. In our analysis, we found that a minimum of one IPSS category could be identified in 91.5% of all patients, with 75.5% of patients falling into the category of stroke with undetermined etiology as per the TOAST criteria. We observed noticeable variations in the distribution of IPSS risk factors among different genders and age groups. These findings indicate that the IPSS classification system has the potential to serve as a valuable tool in identifying risk factors associated with ischemic stroke in young adults.

The inclusion of the IPSS categorization can serve as a valuable addition to the conventional pathogenesis classifications used for ischemic stroke. Traditional classification systems like the TOAST criteria primarily cater to older adults. By incorporating the IPSS categorization, we can enhance the effectiveness of stroke classification in younger individuals and provide a more comprehensive understanding of the underlying mechanisms involved.

Numerous studies have reported that a significant percentage of young patients with ischemic stroke, ranging from 15% to 50% [6,8,9], would fall into the category of stroke with undetermined etiology when classified using the TOAST criteria. These figures, however, may vary depending on geographical regions and local medical resources available for accurate diagnosis and classification. These findings suggest that the existing categorizations for ischemic stroke may not be suitable for effectively classifying young patients who have experienced a stroke. Consequently, this poses challenges for studying the underlying pathogenesis and making accurate etiologic diagnoses in this specific population. There is a crucial need to delve into the potential risk factors and mechanisms associated with ischemic stroke in young adults. Establishing a specific classification approach for this population is vital as it can expedite the identification of etiological factors and the development of effective prevention strategies. By focusing on the unique characteristics of young adults with ischemic stroke, we can enhance the understanding of this condition and implement targeted measures to mitigate its occurrence and impact. Our study revealed that 91.5% of all patients exhibited at least one IPSS category, while 75.5% of patients fell under the category of stroke with undetermined etiology. These findings indicate the potential viability and effectiveness of this novel risk factors categorization approach. The results highlight the applicability and feasibility of using the IPSS classification system to better understand and classify ischemic stroke cases, particularly those with uncertain etiology.

It is important to emphasize that while rare causes and undetermined etiology contribute significantly to strokes in young adults, there is a growing prevalence of atherosclerosis and modifiable vascular risk factors among this population [15,16]. This indicates a shifting trend where traditional risk factors associated with older individuals are becoming more prominent in the occurrence of stroke among young patients. Understanding and addressing these modifiable risk factors are crucial in developing effective preventive measures and tailored treatment strategies for this specific demographic.

Within our study, large-artery atherosclerosis and likely atherothrombotic stroke were frequently

observed TOAST subtype (6.9% and 10.8%), with atherosclerosis-related risk factors identified in over 80% of all patients, particularly among men and patients aged 35 years and older. These findings underscore the critical importance of implementing stringent management protocols for traditional cerebrovascular risk factors among young individuals who have experienced ischemic stroke, irrespective of the presence of other potential causes. By prioritizing the strict control and monitoring of these risk factors, we can potentially mitigate the occurrence and impact of stroke in this population.

In addition to atherosclerosis-related risk factors, our cohort exhibited dominant IPSS subtypes, namely chronic systemic conditions, arteriopathy, and cardiac disorders, each accounting for over 10% of cases. Notably, prothrombotic states were found to be less prevalent in our cohort compared to the previous studies [11,12]. This difference can be attributed to the relatively high cost of diagnostic tests required to identify prothrombotic conditions in our study, which may have limited their detection. The higher costs associated with these specialized diagnostic tests could have resulted in fewer patients being evaluated for prothrombotic states in our cohort. This limitation underscores the need to consider the availability and affordability of diagnostic procedures when assessing the prevalence of specific subtypes in different study populations.

Significant differences were observed in the distribution of IPSS categories between male and female patients in our study. Among young women, chronic systemic conditions and chronic head and neck disorderswere more prevalent. Conversely, atherosclerosis-related risk factors were found to be more common among men. These gender-based variations highlight the importance of considering sex-specific risk profiles and potential underlying mechanisms when studying ischemic stroke in young adults. Such insights can aid in developing tailored prevention strategies and treatment approaches for both male and female patients. Migraine, hematological disorder, valvulopathy and hyperthyroidism were more common among women, while the prevalence of vasculitis secondary to infection in men was significantly higher. Some of those disparities, such as the variations are consistent with previous studies [17,18,19]. The underlying mechanism may include the cytoprotective properties of estrogen and and sex differences in immune response [20, 21]. The observed differences in the IPSS profile between male and female patients provide valuable insights into potential underlying etiological factors.

Recognizing the distinct risk profiles and etiological clues associated with each gender can enhance the accuracy of diagnoses and facilitate targeted treatment and preventive measures. Tailoring diagnostic and management approaches based on sex-specific considerations can ultimately lead to improved outcomes for young adults affected by ischemic stroke.

Furthermore, we observed significant variations in the distribution of IPSS categories based on age. Among patients below 35 years of age, non-atherosclerotic arteriopathy, and chronic systemic conditions were more commonly identified, while atherosclerosis-related risk factors were less frequently observed compared to relatively older patients. These age-related differences in the IPSS spectrum emphasize the importance of tailoring diagnostic work-ups and implementing targeted prevention projects for ischemic stroke in young adults based on age-specific considerations. By recognizing these age-related variations, healthcare professionals can optimize diagnostic approaches and design effective prevention strategies that cater to the specific needs of different age groups affected by ischemic stroke.

Conclusion:

In summary, our study provided a comprehensive description of the risk factor profile for ischemic stroke among young Mongolian adults using a modified categorization originally designed for pediatric stroke. Moreover, we identified notable differences in risk factor distribution between different age groups and genders, highlighting the need for age- and sex-specific approaches in the diagnosis and prevention of ischemic stroke among young adults. These findings contribute to a better understanding of the disease and can guide the development of targeted interventions to improve outcomes in this population. Our findings indicate the potential feasibility of implementing the IPSS categorization in clinical practice. We hope that our study serves as a foundation for future research conducted in diverse regional sites and ethnic populations. Ultimately, the aim is to develop a specialized etiological classification for young stroke patients, which can enhance our understanding of the underlying pathogenesis and facilitate the development of more individualized treatment strategies. By pursuing this line of

investigation, we can strive towards improved pathogenetic understanding and personalized care for young adults affected by stroke.

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