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# Hospital Based Study in Assessment of Risk Factors of Stroke in Young Adults

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## ABSTRACT

**Background:** Stroke is frequently thought of as an old age disease, yet 10% of stroke victims are thought to be under the age of 45. Although the causes of this increase are unknown, there is evidence that the incidence of ischemic stroke in young adults is growing. A different strategy to inquiry and care is needed for stroke in the young compared to stroke in the old. Patients undergoing carotid revascularization operations benefit from the diagnostic and post-interventional evaluation of carotid artery disease provided by neurosonology.

**Objective:** This study aimed at studying the risk factors and most common etiologies of stroke in young adults**.**

**Patients and Methods:** We recruited patients with acute ischemic stroke or transient ischemic attack with age older than 18 and younger than 40 years old, who were admitted in the Stroke Unit –Neurology department, Kasr-Alainy Hospital within the first week of acute event.

**Results:** Analysis was done for 70 ischemic stroke patients from urban and rural areas. In Males, cardio-embolic, drug-induced and undetermined causes were the most common etiologies for stroke representing together 63.3% (21 patients). While among females, about half of the cases (48.6%) were due to cardio-embolic etiology. Age was significantly lower in stroke of other determined etiology ($p<0.01$) and significantly higher in stroke of undetermined etiology ($p=0.01$).

**Conclusion:** Vascular risk factors, stroke type and presentation tend to differ in Egypt. Stroke in young adult patients still has more specific causes, which are less common in the older age group. So, diagnosis needs a more oriented approach to reach the proper stroke etiology for further secondary prevention in those patients.

**Keywords:** Stroke, Young adults, Carotid duplex, Transcranial Doppler.

## INTRODUCTION

Stroke is the second leading cause of mortality and the third leading cause of disability worldwide. Stroke occurs in neonates, babies, children, and young adults as well as more often in older individuals with severe morbidity and death [(1)].

Ischemic strokes make up around 80% of all strokes, and 10% of these so-called "young strokes" affect people under the age of 45 [(2)]. Cerebral infarction continues to be the most prevalent kind of stroke, with subarachnoid haemorrhage and intracranial haemorrhage accounting for 40–55% and 15–20%, respectively, of young adult strokes [(3)].

The prevalence of cardioembolic stroke is higher in younger patients. Vasculopathy (such as arterial dissection), heart abnormalities, recent pregnancy, other hypercoagulable states, smoking, illegal drug use, early atherosclerosis, hypertension, and probably migraine are other disorders linked to ischemic stroke. Patients report of having numerous neurological impairments that impact their sphincteric, sensory, motor, or coordination systems. Additionally, patients with a life expectancy of decades have a different post-stroke prognosis than older patients [(4)].

Investigating the causes of young-onset ischemic stroke frequently present difficulties. Contrary to stroke in older patients, stroke in young patients has a wide variety of, frequently uncommon causes and risk factors, such as use of illegal drugs, pregnancy, arterial dissections, and patent foramen ovale (PFO), which calls for particular extra research and treatment [(5)].

Neurosonology helps in diagnosis and peri-interventional assessment of Carotid Artery disease in patients who undergo carotid revascularization procedures. It is safe, low cost, bed side, noninvasive but operator dependent [(6)]. Trans cranial Doppler or transcranial colour coded duplex sonography helps in detection of occlusion or stenosis, confirmation of vascular origin of the presenting symptoms, mapping of the collateral circulation, detection of microemboli and right to left shunt [(7)].

## PATIENTS AND METHODS

Patients who were admitted at the Stroke Unit - Neurology Department, Kasr Alainy hospital within the first week of the acute event were included in the study, with age older than 18 and younger than 40 years old of both sexes. Diagnosis of acute arterial cerebral ischemic event or transient ischemic attack was based on both clinical assessment and cerebral imaging (a brain CT scan or MRI). According to the most recent definition of stroke for clinical trials. It had required either focal neurological deficit lasting > 24 hours or imaging of an acute clinically relevant brain lesion in patients with rapidly vanishing symptoms.

**Exclusion criteria:** Patients presented with cerebral hemorrhage, subarachnoid & venous sinus thrombosis, and focal brain lesion or demyelinating lesion were excluded.

## METHODS

**A-** Clinical Assessment:

- Full history had been obtained focusing on risk factors, neurological examination and assessment of stroke severity using National Institute of Health system score (NIHSS).



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- Electrocardiogram (ECG) to assess any cardiac rhythm abnormality or abnormal wave morphology.

**B-** Routine laboratory assessment for all patients and vasculitic profile and work up for high coagulable state was done for some patients.

**C-** Imaging Assessment:

1- Brain computed tomography (Brain CT) was carried out on admission for all studied patients . Some patients had done brain MRI if the diagnosis was not clear.
2- Cardiovascular imaging: Carotid and vertebrobasilar duplex and Doppler studies were performed using Phillips HDI 5000 ultrasound equipment (Phillips Corporation, Netherland, 2009) to assess the common carotid artery, internal carotid artery, vertebral and basilar arteries (Extracranial assessment), middle cerebral artery, anterior cerebral artery, posterior cerebral artery, distal internal carotid artery, vertebral and basilar arteries (Transcranial assessment). Evaluation of intima media thickness (IMT), the presence of atherosclerosis or arterial dissection, peak systolic velocity, end diastolic velocity and resistive index.
3- Transthoracic echocardiography was performed.

**Etiology of stroke:**

We used the classic Trial of Org 10172 in Acute Stroke Treatment (TOAST) classification to describe the stroke etiology [8, 9, 10].

The original TOAST classification includes five categories [large vessel disease (LVD), small vessel disease (SVD), cardioembolic (CE), undetermined etiology, and other determined (rare causes)] [11]. The sub group undetermined etiology includes three scenarios, either incomplete evaluation, negative evaluation or more than one etiology was detected [11].

Also, we considered embolic stroke of unknown source (ESUS) as a separate group to describe the undetermined etiology of stroke in patients who had non lacunar infarctions with otherwise normal routine evaluation [12].

**Ethical consent: The study was authorised by Minia University's Ethical Institutional Review Board. All study participants provided written informed consents after being informed of our research's goals. The Declaration of Helsinki for human beings, which is the international medical association's code of ethics, was followed during the conduction of this study.**

***Statistical analysis***

Statistical Package for Social Sciences (SPSS) version 22 for Windows was used to code, process, and analyse the obtained data (IBM SPSS Inc, Chicago, IL, USA). Using the Shapiro Walk test, the distribution of the data was examined for normality. Frequencies and relative percentages were used to depict qualitative data. To determine differences between two or more sets of qualitative variables, use the chi square test (2). Quantitative information was presented as mean±SD (Standard deviation). Two independent groups of normally distributed variables were compared using the independent samples t-test (parametric data). P value less than 0.05 was regarded as significant.

**RESULTS**

70 patients with a newly diagnosed stroke were included in the study. 69 patients had stroke while one patient was presented with TIA. More than half of the patients, 55.7% had right hemiplegia. The age of the patients ranged from 18 to 40 years with a mean age of 35.6 ± 5.8 years. Most patients (84.3%) were in the age group >30 to 40 years, while 15.7% were in the age group 18 to 30 years. Females (52.9%) were more than males (47.1%). 45 patients (64.3%) were from rural areas. Moreover, about one third of the patients (35.7%) had a positive family history of stroke at any age [two patients had family history of stroke at young age, while 11.4% had a positive family history of acute coronary syndrome (ACS)] (Table 1).

**Table (1):** Demographic data and non-modifiable risk factors

| Variable | Frequency | % |
|---|---|---|
| **Age:** | | |
| 18-30 years | 11 | 15.7 |
| 30-40 years | 59 | 84.3 |
| **Sex:** | | |
| Male | 33 | 47.1 |
| Female | 37 | 52.9 |
| **Residence:** | | |
| Rural | 45 | 64.3 |
| Urban | 25 | 35.7 |
| **Occupation:** | | |
| Unemployed | 18 | 25.7 |
| Housewife | 33 | 47.1 |
| Manual worker | 5 | 7.1 |
| Employee | 14 | 20 |
| **Handedness:** | | |
| Right handed | 70 | 100 |

The most prevalent risk factor was cigarette smoking in 45.7%, followed by cardiac risk factors in 36% of patients, dyslipidemia in 27.5% of patients and substance abuse came forth in 27.1% (mainly cannabis). Then, less commonly hypertension in 21.4%, obesity in17.1% and diabetes mellitus (DM) in15.7% of patients. Smoking and drug abuse were significantly higher among males (P<0.001), while RHD and AF were more common in females (P=0.011 and 0.028 respectively). More females were found migraineures (P=0.109) (Table 2 & table 3).

**Table (2):** Frequency of the modifiable risk factors in the studied patients

| Risk factors | | Number (Percent) |
|---|---|---|
| **Smoking** | | 32 (45.7%) |
| **Cardiac Risk Factors** | All Cardiac Risk Factors | 26 (36%) |
| | Rheumatic heart disease (RHD) | 13 (18.6%) |
| | Atrial fibrillation (AF ) | 5 (7.1%) |
| | Ischaemic Cardiomyopathy | 5 (7.1%) |
| | Other Cardiac disorders | 3 (4.3%) |
| **Dyslipidemia** | | 19 (27.5%) |
| **History of drug (substance) abuse** | | 19 (27.1%) |
| **Hypertension (HTN )** | | 15 (21.4%) |
| **History of previous stroke or transient ischemic attack (TIA)** | | 13 (18.6%) |
| **Obesity** | | 12 (17.1%) |
| **Diabetes mellitus (DM)** | | 11 (15.7%) |
| **History of migraine** | | 9 (12.9%) |
| **History of deep venous thrombosis (DVT )** | | 3 (4.3%) |
| **History of rheumatological affection (as arthritis, rash...)** | | 2 (2.9%) |
| **History of hepatic disease** | | 1 (1.4%) |
| **Female related risk factors** | History of contraception(n=37) | 16 (43.2%) |
| | History of abortion(n=37) | 6 (16.2%) |
| | Pregnancy (n=37) | 5 (13.5%) |

**Table (3):** Gender difference in some risk factors

| Risk factors | Male (n=33) | Female (n=39) | P value |
|---|---|---|---|
| **History of smoking** | 29 (87.9%) | 3 (8.1%) | <0.001** |
| **History of DM** | 8 (24.2%) | 3 (8.1%) | 0.064 |
| **History of HTN** | 8 (24.2%) | 7 (18.9%) | 0.588 |
| **History of RHD** | 2 (6.1%) | 11 (29.7%) | 0.011* |
| **History of AF** | 0 | 5 (13.5%) | 0.028* |
| **History of drug abuse** | 19 (57.6%) | 0 | <0.001** |

DM: diabetes mellitus; HTN: hypertension; A.F: atrial fibrillation; RHD: rheumatic heart disease.

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Regarding TOAST etiological classification of stroke: Cardio-embolism was the most frequent etiology for stroke, followed by other determined etiology 37.1% & 21% respectively. Undetermined etiology came third, followed by LVD, embolic stroke of unknown source (ESUS), then finally SVD (37.1%, 12.9%, 8.6% and 5.7% respectively) (Figure 1).

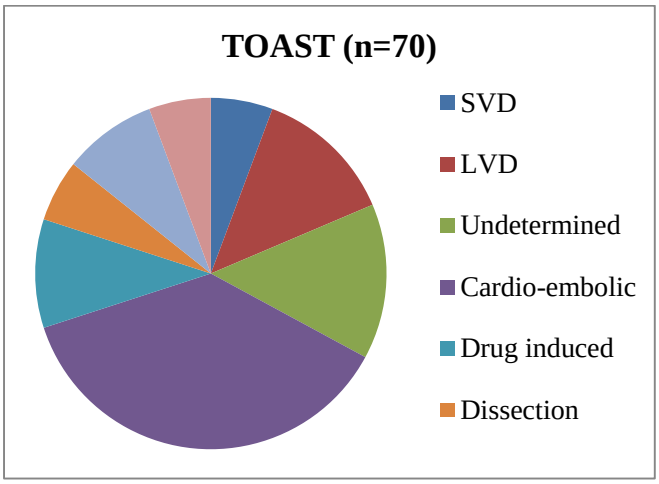


**Figure (1):** Showing the etiological classification of stroke.

Coagulopathy screening was positive in three patients (one with protein S and protein C deficiency), while the other two patients were diagnosed as antiphospholipid syndrome among 47 patients, while vasculitic profile was negative (Table 4).

**Table (4):** Drug screening, coagulation & vasculitic profiles in some patients of the studied group:

| | Number of patients who did the tests | Results | |
|---|---|---|---|
| **Coagulation profile** | **47** | **Negative** | **44 (93.6 %)** |
| | | **Positive** | **3 (6.4%)** |
| **Vasculitic profile** | **47** | **Negative** | **47 (100%)** |
| | | **Positive** | **0 (0%)** |
| **Drug screening:** | **10** | **Negative** | **90 (9%)** |
| | | **Positive** | **10 (1%)** |

All patients of the study had a brain imaging but the image of one patient was missed. 82.9% of patients had territorial infarction while 7 patients (11.4%) had lacunar strokes. Anterior circulation strokes were superior to posterior circulation strokes (74.3% and18.6%) respectively (Table 5).

As regards vascular imaging, it included carotid & vertebro-basilar duplex & transcranial duplex and or CT angiography and or MRA. 71% of the patients had normal vascular imaging while 10 patients had atherosclerotic vasculopathy 4 of them had extracranial atherosclerosis varying from carotid plaque causing stenosis to complete occlusion and similar number had intracranial atherosclerosis and the other two patients had combined both intra and extracranial atherosclerotic disease. The remaining ten patients had non atherosclerotic vasculopathy (Table 5).

**Table (5):** Brain and cardiovascular imaging

| | Frequency | % |
|---|---|---|
| Brain imaging (69) | | |
| Free | 4 | 5.7 |
| Territorial | 58 | 82.9 |
| Lacunar | 7 | 11.4 |
| Brain circulation: | | |
| (65) | 52 | 74.3 |
| Anterior | 13 | 18.6 |
| Posterior | | |
| Vascular imaging: | | |
| (extra cranial | 4 | 5.7 |
| atherosclerosis) | 3 | 4.3 |
| Plaque | 1 | 1.4 |
| Complete | | |
| occlusion | | |
| Vascular imaging: | | |
| (intra cranial | 4 | 5.7 |
| atherosclerosis) | 2 | 2.8 |
| Stenosis | 2 | 2.8 |
| Complete | | |
| occlusion | | |
| Vascular imaging: | | |
| (combined | 2 | 2.8 |
| extracranial and | | |
| intra cranial | | |
| atherosclerosis) | | |
| Vascular imaging: (nc | 10 | 14.4 |
| atherosclerotic) | 2 | 2.8 |
| Thrombosis | 4 | 5.7 |
| Dissection | 4 | 5.7 |
| Other causes | | |
| ECHO: (69) | | |
| Normal | 32 | 45.7 |
| LVH | 14 | 20 |
| Ischemic | 4 | 5.7 |
| cardiomyopathy | 17 | 24.3 |
| Valve lesion | 2 | 2.9 |
| Mitral valve | | |
| prolapse | | |
| TEE: (15) | | |
| Normal | 6 | 40 |
| PFO | 6 | 40 |
| MVP | 1 | 7 |
| Intra-cardiac | 2 | 13 |
| thrombus | | |

*Other determined etiology includes dissection, drug induced and others

* SVD= small vessel disease, LVD= large vessel disease, ESUS= embolic stroke of unknown source

## DISCUSSION

Young ischemic stroke appears to be on the rise, despite the fact that total stroke incidence has been dropping [13]. We discovered that women outnumbered males in the present study [(52.9% vs. 47.15%)]. The female preponderance was consistent with studies by **Barinagarrementeria *et al.*** [14] **and Yesilot *et al.*** [15], which revealed that women had a greater stroke incidence than males did in the age range of 18 to 34, with the trend reversing in the age range of 35 to 49. **El Tellawy *et al.*** [16] described female predominance among this age group (20 to <40 years of age) in their study about stroke epidemiology in Upper Egypt. **Li *et al.*** [17] explained more ischemic stroke in rural Chinese areas than urban regions by the poor control of traditional risk factors including DM and HTN among the rural populations.

In this study, we found smoking, cardiac risk factors, family history of stroke, dyslipidemia, drug abuse and hypertension were the most prevalent risk factors by 45.7%, 36%, 35.7%, 27.5%, 27% and 21.4% of patients respectively. In agreement to our study, **Putaala *et al.*** [18] in a retrospective study for analysis of the risk factors and etiology of ischemic stroke in 1008 patients aged between 15 and 49 years admitted to Helsinki University in Finland between 1994 and 2007. **Von Sarnowski *et al.*** [19] in Sifap study in 15 European countries, **Kefi *et al.*** [9] in Tunisia, **Gökçal *et al.*** [20] in Turkey and **Li *et al.*** [17] in China found that smoking was the most prevalent risk factor by nearly 44%, 55%, 56%, 45 %and 47 % of their samples respectively. Moreover, **Yoon *et al.*** [21] in South Korea also found that smoking was the most prevalent risk factor among their study populations by 57% of patients.

More than one quarter of the patients (27.5%) in our study were dyslipidemic as the third most prevalent risk factor. This is smaller than what **Magwood *et al.*** [22]**, Gökçal *et al.*** [20] and **Schneider *et al.*** [23] reported where dyslipidemia was the third most prevalent risk factor in their studies by nearly 35 % of patients. The lower percentage of dyslipidemia in our sample than most of other studies may be explained by the younger age of our patients.

The higher frequency of drug abuse among our study group (27%) is in agreement with **La Rosa *et al.*** [24] who reported marked increase in drug abuse among young adult stroke patients nowadays more than previously by comparing drug abuse and smoking among young adults with stoke over three periods of time (1993,1994,2005) in the united states.

The percentage of hypertension was 21% in this study, which was similar to **Montanaro *et al.*** [25] in Brazil who found about 20% of patients were hypertensive but lower than most of the other studies such as **Chraa *et al.*** [10] in Morocco, **Fahmi *et al.*** [26] in Egypt, **Schneider *et al.*** [23] in Estonia, **Magwood *et al.*** [22] in US, and **Kissela *et al.*** [8] where the percentage of hypertensive patients ranged from 36% to 56% of their patients.

15% of the studied patients were diabetic which is nearly similar to **Chraa *et al.*** [10]**, Gökçal *et al.*** [20]**, Magwood *et al.*** [22] and **Schneider *el al.*** [23] who found that DM was present in 13.2%, 15.9%, 13% and 12.6% of their patients respectively. In contrast, the frequency of DM was higher in the studies done by **Fahmi *et al.*** [26] and **Kissela *et al.*** [8] who found higher percentage of diabetics (40% and 35% of their patients respectively).

The low incidence of hypertension and diabetes mellitus in our study compared to other studies may be explained by the younger upper age limit in our studied group of patients.

About 13% of the sample was migraineurs with female predominance. This is in agreement with **Schneider *el al.*** [23] and **Van Alebeek *et al.*** [27] who found 12% and 16% of patients respectively were migraineurs. On the other hand, **Li *et al.*** [17] and **Kissela *et al.*** [8] found 1.3% and 1.2% only of patients were migraineurs.

Also 13% of the females were pregnant in their second or third trimester. This is almost identical to what **Miller *et al.*** [28] found, where they said that about 18% of strokes in women under the age of 35 are caused by pregnancy in young women.

As regards the stroke severity, it was classified according to **Denier *et al.*** [29]**.** Most patients of our study had mild (45.7%) to moderate (35.7%) strokes as measured by NIHSS at time of presentation. This is in agreement with **Lutski *et al.*** [30] and **Li *et al.*** [17] in Israel and china respectively who found that most strokes in young adults were mild.

In our study, two patients with antiphospholipid syndrome were diagnosed, which is nearly similar to the results reported by **Chraa *et al.*** [10] who found one patient with antiphospholipid syndrome among 128 young stroke patients in Morocco. Unlike, **Kefi *et al.*** [9] who found 14 patients, among 102 young patients with stroke in Tunisia, with antiphospholipid syndrome. This may be explained by the recruitment of patients with stroke that were admitted at the internal medicine department not at the neurology department.

Regarding parenchymal imaging, most of the studied patients (74%) had infarctions in the anterior circulation which was nearly similar to 71% and 80 % of patients found by **Lutski *et al.*** [30] and **Montanaro *et al.*** [25] respectively to have anterior circulation strokes. As regards vascular imaging, 70% of the studied patients had normal vascular imaging, about 15% had atherosclerotic vasculopathy [5.7% had extracranial atherosclerosis, 5.6% had intracranial atherosclerosis and 2.8% had combined intracranial and extracranial atherosclerosis] and 15% had non atherosclerotic vasculopathy.

Cervical artery dissection was the most prevalent non atherosclerotic vasculopathy representing nearly half (5.7 %) of these patients. This finding is in agreement with **Lutski *et al.*** [30] who found that dissection was the most common non-atherosclerotic vasculopathy among their young patients. Unlike, **Kissela *et al.*** [8] who found that sickle cell disease was the most prevalent non atherosclerotic vasculopathy among their patients in Saudi Arabia. Although cervicocerebral artery dissection accounted for 1-2.5% of all ischemic strokes, **Debette *et al.*** [31] reported that artery dissection accounts for 5-25% of ischemic stroke in patients under the age of 45. This reflects the fact that young people' cervicocephalic artery dissection is a significant cause of stroke.

According to the classic Trial of Org 10172 in Acute Stroke Treatment (TOAST) classification, our study revealed that cardioembolic (CE) etiology was the most prevalent etiology by nearly 37% mainly due to valvular heart disease. This is in agreement with **Chraa *et al.*** [10] who found that CE was the most predominant etiology by 35.5% mainly due to valvular heart disease and **Nacu *et al.*** [32] who found CE as the most prevalent determined etiology by 28.5%. Also, in agreement with **Fromm *et al.*** [33] who found that cardioembolic etiology is the most predominant in their study. On the other hand, **Schneider *et al.*** [23] found that cardioembolism represented 17% of their study. **Gökçal *et al.*** [20] found 19% of the sample had CE while **Montanaro *et al.*** [25] and **Lutski *et al.*** [30] found only 15.7% and 8% had CE etiology respectively.

The second most prevalent etiology in our study was other determined etiology by about 21 % (drug-induced strokes representing about 50% of them followed by dissection and others such as coagulopathy). This is nearly in agreement with **Nacu *et al.*** [32] who found about 19% of patients with other determined etiology mainly dissection and **Kissela *et al.*** [8] who found other determined etiology in 17.6% of patients with sickle cell disease was the most prevalent by 33% followed by dissection 20%**.**

The third most frequent etiology in the studied patients was undetermined etiology (UDE) by 14.3% of the patients mainly due to incomplete evaluation. This is in agreement with **Kissela *et al.*** [8] who found stroke with undetermined etiology in about 15% of patients according to TOAST classification. The relatively small percentage of patients with stroke of undetermined etiology in our study may be due to the more detailed evaluation of patients in the stroke center being a tertiary hospital including cardiac evaluation up to trans-esophageal ECHO (TEE) and extensive evaluation of neck and brain vasculature including carotid and transcranial duplex and /or CTA and/ or MRA and work up for hypercoagulability or vasculitis and drug screening if needed according to the clinical circumstances.

The fourth most frequent etiology was large vessel disease (LVD), it was found in 13% of patients in our study, which is in accordance to the study performed by **Gökçal *et al.*** [20] and **Schneider *et al.*** [23] that found LVD in 13.2% and 14.3% of patients respectively. On the other hand, **Kissela *et al.*** [8] found 16.5% of patients with LVD, which is higher than our study results.

Embolic stroke of unknown source in the studied patients came later by nearly 8.6% smaller than what **Putaala *et al.*** [18] in the Helsinki Young Stroke Registry where they found 20.9% of patients had ESUS and were more younger, females, with milder symptoms and fewer vascular risk factors than patients with SVD and LVD. The lower percentage of ESUS in our studied patients could be explained by low risk cardiac sources such as PFO were considered as a cardioembolic etiology for stroke, while **Majander *et al.*** [12] considered the low risk cardiac sources (such as PFO) as ESUS not among cardioembolic stroke.

The least prevalent etiology in our study was small vessel disease (SVD) by about 5.7%. This is nearly similar to **Schneider *et al.*** [23] who found 6% of patients with SVD but smaller than **Kissela *et al.*** [8] who found SVD as the most prevalent etiology by 30.6% and **Lutski *et al.*** [30] who reported that 17.6% of patients had SVD as the second most prevalent etiology in their study.

## CONCLUSION

Young ischemic stroke often poses a real diagnostic challenge to physicians. Though the traditional risk factors play a significant role in young patients with stroke, the presence of a wide variety of different etiologies makes diagnostic evaluation in young patients more challenging. Cervicocephalic arterial dissection and coagulopathy are less common stroke etiology but should be kept in mind in evaluation of a young adult patient with stroke.

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