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Recognition and management of stroke in young adults and adolescents

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ABSTRACT

Approximately 15% of all ischemic strokes (IS) occur in young adults and adolescents. To date, only limited prior public health and research efforts have specifically addressed stroke in the young. Early diagnosis remains challenging because of the lack of awareness and the relative infrequency of stroke compared with stroke mimics. Moreover, the causes of IS in the young are heterogeneous and can be relatively uncommon, resulting in uncertainties about diagnostic evaluation and cause-specific management. Emerging data have raised public health concerns about the increasing prevalence of traditional vascular risk factors in young individuals, and their potential role in increasing the risk of IS, stroke recurrence, and poststroke mortality. These issues make it important to formulate and enact strategies to increase both awareness and access to resources for young stroke patients, their caregivers and families, and health care professionals. The American Academy of Neurology recently convened an expert panel to develop a consensus document concerning the recognition, evaluation, and management of IS in young adults and adolescents. The report of the consensus panel is presented herein. ***Neurology*® 2013;81:1089–1097**

GLOSSARY

CI = confidence interval; **ICH** = intracerebral hemorrhage; **IS** = ischemic stroke; **PFO** = patent foramen ovale.

Approximately 15% of all ischemic strokes (IS) occur in young adults and adolescents.[1–8] Compared with stroke in older adults, stroke in the young has a disproportionately large economic impact by leaving victims disabled before their most productive years. To date, only limited prior public health and research efforts have specifically addressed stroke in the young. Early diagnosis remains challenging because of the lack of awareness and the relative infrequency of stroke compared with stroke mimics. Moreover, the causes of IS in the young are heterogeneous and relatively uncommon,[3,8,9] resulting in uncertainties about diagnostic evaluation and cause-specific management. Emerging data have raised public health concerns about the increasing prevalence of traditional vascular risk factors in young individuals, and their potential role in increasing the risk of IS, stroke recurrence, and poststroke mortality.[5–8,10,11] These issues make it important to formulate and enact strategies to increase both awareness and access to resources for young stroke patients, their caregivers, and health care professionals. The American Academy of Neurology convened an expert panel to develop a consensus document concerning IS in young adults and adolescents. Given the relative lack of high-level scientific evidence concerning stroke in young individuals, an evidence-based management guideline was considered unfeasible. The report of the consensus panel is presented herein.

EPIDEMIOLOGY As young adults approach middle age, stroke prevalence increases[5,7] (table 1). Based on self-report, 532,000[12] to 852,000[13] persons aged 18 to 44 years in the United States have had a stroke. For comparison, among adults aged 17 to 44 years, the self-reported prevalence of stroke is more than twice that of

Supplemental data at www.neurology.org

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Table 1 Prevalence of stroke by age and sex, NHANES 1998–2002

Age, y	Men, %	Women, %
20–34	0.4	0.3
35–44	1.1	0.8
45–54	1.2	2.1

Abbreviation: NHANES = National Health and Nutrition Examination Survey.
National Heart, Lung, and Blood Institute data.

multiple sclerosis.[14] Of all strokes among persons 15 to 44 years of age, approximately 50% are IS, 20% are intracerebral hemorrhage (ICH), and 30% are subarachnoid hemorrhage.[4] Incidence rates for IS in this age range are approximately 10 per 100,000 person-years for US populations of predominantly European ancestry,[15,16] with similar rates for men and women. Compared with persons of European ancestry, African Americans have incidence rates 2-fold higher for IS.[15] It should be acknowledged that the available epidemiologic data are mostly based on national surveys and population-based studies, the upper age cutoff has varied from 44 years to 55 years, and stroke remains underrecognized in this population. These issues limit our understanding of the causes of stroke in the young and its true incidence and prevalence.

There are conflicting data on trends in incidence rates over time. Data from Sweden for first discharge for stroke among persons aged 20 to 44 years show no trend over time.[16] In contrast, analyses of all discharges for stroke among persons aged 15 to 44 years from the US Nationwide Inpatient Sample from 1995–1996 through 2008–2008 show a 23% to 53% increase for IS, depending on the age-sex group.[5] There was a concurrent trend for an increasing prevalence of stroke risk factors in this age range, specifically hypertension, diabetes mellitus, obesity, lipid disorders, congenital heart disease, and smoking. Similar increasing trends were recently reported in a population-based study.[7] Other studies[1,8,11] have shown that young stroke patients have a high incidence of modifiable vascular risk factors, which contribute a nearly 12% risk of recurrent cardiovascular events and increased 5-year mortality.[6,10] A prospective cohort study showed that the observed 20-year mortality rates (24.8% for TIAs and 26.8% for IS) were significantly higher than expected mortality rates.[17] These data emphasize the importance of implementing primary and secondary vascular preventive strategies in young individuals.

RECOGNITION AND DIFFERENTIAL DIAGNOSIS

Younger patients are less likely to utilize 911 and prehospital systems for stroke-like symptoms because they do not appreciate they are at risk of stroke. Even after arrival to the emergency department, the diagnosis is often delayed or missed[18] because stroke is still considered a disease of the elderly, and because young individuals may not have vascular risk factors to raise suspicion for stroke.

Few studies have addressed the reasons for underdiagnosis of stroke in the young. In a single-center analysis of 57 IS patients aged 16 to 50 years, 8 were initially misdiagnosed, including 7 who were initially discharged.[18] Predictors of a missed diagnosis were age younger than 35 years and posterior-circulation stroke. Early (<48-hour) MRI may reduce the rate of misdiagnosis. There is more literature regarding stroke overdiagnosis (false-positives), an important concern given the potential risks of thrombolytic complications in stroke mimics. Approximately 20% to 50% of adults and children with acute stroke-like symptoms will prove to have an alternative diagnosis.[19–21] The most frequent mimics of IS in young adults and adolescents are seizures, acute vestibular syndrome, migraine, infections, brain tumors, toxic-metabolic encephalopathy (particularly hypoglycemia), hypertensive encephalopathy, gastroenteritis, and conversion disorder. Less frequent sources of misdiagnosis are cardiac events, herpes-simplex virus encephalitis, demyelinating disease, and myasthenia gravis. Among patients treated with IV thrombolysis, the proportion of mimics is lower, between 3% and 13%.[22] Reassuringly, among young patients with stroke (including mimics) treated with IV thrombolysis, there does not seem to be an increased risk of symptomatic ICH.[8,22,23]

The symptoms of IS in young adults and adolescents are often similar to those in older patients. The diagnosis is straightforward when presented with typical stroke symptoms such as an acute hemiparesis. However, the diagnosis becomes challenging with atypical symptoms (table 2).[24] A few salient points are worth highlighting. Right-hemispheric strokes are often misdiagnosed initially because language is preserved. Nonlocalizing syndromes, including neuropsychiatric symptoms, acute confusional states, and diminished level of alertness, may sometimes be the presenting features. Even small infarcts in the midbrain and thalamus may cause diminished levels of alertness. While strokes usually cause negative symptoms such as weakness, positive symptoms can develop, including unilateral limb-shaking, hemiballismus, or chorea. In patients presenting with dizziness, it is particularly difficult to distinguish stroke from vestibular neuronitis or Ménière disease. There is evidence that the presence of a negative head-impulse test, skew deviation, or direction-changing nystagmus in eccentric gaze has a sensitivity of 100% and specificity of 96% for stroke.[25] Patients

Table 2 Atypical stroke presentations
Nonlocalizing symptoms
Neuropsychiatric symptoms
Acute confusional state/delirium
Depressed level of consciousness
Abnormal movements
Chorea
Hemiballismus
Dystonia
Unilateral asterixis
Hemifacial spasm
Alien hand syndrome/deafferentation
Limb-shaking TIAs
Seizures secondary to stroke
Cranial neuropathies
Acute vestibular syndrome
Acute hearing loss
Ischemic optic neuropathy
Horner syndrome
Third nerve palsy
Seventh nerve palsy
Other cranial neuropathies
Isolated symptoms
Isolated dysarthria
Isolated dysphagia/stridor
Isolated facial paresis
Monoparesis of arm or leg or a part of limb or distal extremity
Isolated sensory symptoms
Isolated visual loss
Isolated headache
Headache

Adapted from *The Lancet Neurology*, 10, Edlow JA, Selim MH. Atypical presentations of acute cerebrovascular syndromes, 550–560, Copyright 2011, with permission from Elsevier.

should not be dismissed unless they can walk without imbalance. Patients with severe nausea and vomiting due to missed cerebellar infarction may later experience fatal brainstem compression due to swelling, a condition ironically labeled "fatal gastroenteritis." Patients presenting with isolated symptoms (e.g., cranial neuropathies, visual symptoms, pure sensory loss, monoparesis) may also be misdiagnosed because these are relatively uncommon.

Several studies have shown an increased risk of stroke in patients with migraine with aura, especially women younger than 45 years, cigarette smokers, and those using hormonal contraception.[26] In migraineurs who present with prolonged focal neurologic symptoms, particularly visual or language disturbance, it can be challenging to distinguish migraine from stroke. Migraine-induced stroke is extremely rare, should always be the diagnosis of exclusion, and the criteria of the International Headache Society's *International Classification of Headache Disorders*, 2nd edition[27] should be fulfilled in order to make this diagnosis. The absence of a history of migraine with aura, or a change in the quality of headache, should make one question the diagnosis of migraine. Moreover, sensory changes in migraine usually have a migrating quality, moving over 20 to 30 minutes across parts of the body, whereas stroke-related sensory changes usually occur abruptly. Adolescents and children usually have a headache or a seizure at the time of stroke onset and the presence of either can falsely reassure providers that a child with new focal deficits has a complicated migraine or postictal Todd paralysis.

STROKE ETIOLOGY The causes of IS in young adults and adolescents are diverse (table 3)[28] and vary by age and geographic region.[1–5,8,15,29] Contemporary stroke etiologic classification schemes have attempted to grade causality according to the level of evidence and the presence of multiple potential causes.[8,30,31] Because the incidence of IS strongly correlates with increasing age, the causes listed in table 2 are, in the aggregate, considered uncommon. Arteriopathies, including mainly nonatherosclerotic arteriopathies such as dissection as well as premature atherosclerosis, are collectively the most common cause of IS in young individuals.[29,32] Relative to adults older than 55 years, young individuals infrequently develop stroke from atherosclerosis; however, the older end of the young-adult age range still has a higher incidence of atherosclerotic stroke due to the concurrence of multiple modifiable risk factors such as hypertension, cigarette smoking, and hyperlipidemia.

CLUES FOR SPECIFIC ETIOLOGIES Certain historical features, symptoms, and signs may serve as clues toward specific stroke etiologies.[9] Recent minor trauma or sudden neck movements, including chiropractic neck manipulation or vigorous exercise, are associated with arterial dissection.[33] Patients with cervical artery dissection will frequently complain of headache or neck pain. A painful Horner syndrome, or coexisting cranial neuropathies, should always raise suspicious for dissection; all cranial nerves except the olfactory nerve may be affected by dissection.

Clinical clues to the presence of an underlying arteriopathy include headache (particularly recurrent "thunderclap" headache), recurring stereotyped TIAs, psychiatric disturbances, skin rash, exposure to vasoconstrictive agents, pregnancy, hormonal contraceptive

Table 3 Selected causes and risk factors for ischemic stroke in young adults and adolescents

A. Frequency of stroke etiology[a]
Large-vessel atherosclerosis (2%–11%)
Small-vessel disease (7%–14%)
Cardiac embolism (20%–47%)
Other determined etiology (20%–34%)
Multiple etiologies (2%–3%)
B. Arterial
1. Cerebral artery dissection
2. Reversible cerebral vasoconstriction syndromes
3. Moyamoya disease
4. Sickle cell disease
5. Transient cerebral arteriopathy of childhood
6. Premature atherosclerosis, lipohyalinosis
7. Radiation-induced arteriopathy
8. Migraine-induced stroke
9. Illicit drug abuse (e.g., cocaine, amphetamines, ecstasy)
10. Infectious arteriopathy (e.g., post-varicella; tuberculous, fungal, or bacterial meningitis; syphilis, HIV)
11. Inflammatory arteriopathy (e.g., Takayasu arteritis, giant cell arteritis, primary angiitis of the CNS, polyarteritis nodosa, Behçet disease, Churg-Strauss syndrome, Kohlmeier-Degos disease)
12. Genetic or inherited arteriopathy (e.g., Fabry disease, fibromuscular dysplasia, dolichoectasia, Susac syndrome, cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy, *TREX1* mutation disorders, mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes (MELAS), hyperhomocysteinemia, neurofibromatosis type 1)
C. Cardiac
1. Patent foramen ovale
2. Congenital heart disease
3. Infectious and nonbacterial thrombotic endocarditis
4. Rheumatic valvular heart disease
5. Post-cardiac surgery or catheter intervention
6. Arrhythmia (e.g., atrial fibrillation, sick sinus syndrome)
7. Cardiac tumors (e.g., atrial myxoma, papillary fibroelastoma)
8. Recent myocardial infarction
9. Dilative cardiomyopathy
D. Hematologic
1. Heparin-induced thrombocytopenia
2. Hypercoagulable state due to deficiencies of protein S, protein C, or antithrombin; factor V Leiden mutation, prothrombin gene G20210A mutation
3. Acquired hypercoagulable state (e.g., cancer, pregnancy, hormonal contraceptive use, exposure to hormonal treatments such as anabolic steroids and erythropoietin, nephrotic syndrome, antiphospholipid antibody syndrome)
4. Primary hematologic disorders (e.g., polycythemia vera, essential thrombocythemia, paroxysmal nocturnal hemoglobinuria, thrombotic thrombocytopenic purpura, leukemia, lymphoma, multiple myeloma)

[a] Classified according to the Trial of Org 10172 in Acute Stroke Treatment schema.
From *New England Journal of Medicine*, Yager PH, Singhal AB, Nogueira RG, Case records of the Massachusetts General Hospital. Case 31-2012. An 18-year-old man with blurred vision, dysarthria, and ataxia, 367, 1450–1460. Copyright © 2012 Massachusetts Medical Society. Reprinted with permission.

use, head trauma, and HIV infection.[9,32] Transient cerebral arteriopathy is the most common cause of stroke in children, but typically has no clinical clues.[34] Genetic disorders are suggested by abnormal eye and skin examination findings such as retinal arteriolar irregularities, ectopia lentis (Marfan syndrome), iris hamartomas and optic nerve tumors (neurofibromatosis), cataracts, corneal opacities, angiokeratomas (Fabry disease), hyperelastic skin (Ehlers-Danlos type IV), and neurofibromas or café-au-lait spots (neurofibromatosis). On brain imaging, it is important to consider stroke lesion topography; e.g., a unilateral "string-of-pearls" appearance may indicate middle- or internal-cerebral artery stenosis.

A history of recent prolonged immobility, such as after recent surgery, should raise suspicion for paradoxical embolism through a patent foramen ovale (PFO). Fevers, back pain, and joint pain should raise concern for endocarditis. Clues for a hypercoagulable state include a history of deep venous thrombosis or multiple miscarriages. Skin examination may reveal underlying coagulation problems, vasculitis, endocarditis, or stigmata of IV drug abuse.

LABORATORY TESTS Given the broad spectrum of etiologies (table 3), the fear of litigation from missing ominous or rare causes, and the absence of evidence-based diagnostic algorithms, young stroke patients are invariably subjected to a wide array of diagnostic tests, often ordered simultaneously at the time of presentation. This includes the usual test panel performed for any stroke patient, and specialized tests[9] for causes relatively more frequent in young patients (table 4). The clinical clues outlined above should be considered to tailor the diagnostic work-up, and an organized, stepwise evaluation should follow.

The yield of several diagnostic tests was investigated in a small retrospective study (figure).[8] The yield was relatively low for Holter monitoring (1%) and toxicology screening (5%), and relatively high for cardiac ultrasound (51%) and cerebral angiography (64%). Others have shown a similar high yield for cerebral angiography.[1,2] Because younger patients are at higher risk of developing leukemia and brain tumors from CT scans, exposure to radiation should be limited when possible.[35] The clinical significance and treatment implications of findings such as a positive hypercoagulable panel test result, or a PFO on cardiac ultrasound, remain controversial.[36–39] Nevertheless, in view of the variable yield and high cost of specialized tests, it seems justified to routinely perform high-yield tests such as cardiac ultrasound and vascular imaging in young stroke patients. More research is warranted to determine the cost-effectiveness of diagnostic tests and design appropriate strategies to evaluate stroke in the young.

Table 4 Laboratory evaluation

Common tests
Complete blood count with differential cell counts
Erythrocyte sedimentation rate
Urinalysis
Prothrombin time (PT with INR), activated partial thromboplastin time
Serum electrolytes, liver and renal function tests
Blood glucose, hemoglobin A1C level
Lipid panel, lipoprotein (a) level, C-reactive protein level
Pregnancy test
Head CT, brain MRI
Cerebral arterial imaging: CT, MR, or digital subtraction angiography of the head and neck, carotid artery Duplex ultrasound, transcranial Doppler ultrasound
Brain perfusion imaging, e.g., CT-perfusion or MR-perfusion (*optional*)
Transthoracic and/or transesophageal echocardiography
Holter monitoring
Selected tests for specific stroke etiologies
Serum and urine toxicology screen
Lower extremity ultrasound, pelvic CT or MR venography (in patients with PFO)
Advanced brain imaging: axial fat-suppressed T1-weighted MRI, high-resolution (3T) contrast-enhanced T1-weighted MRI, PET scan, MR spectroscopy, transcranial Doppler ultrasound studies for cerebrovascular "reserve"
CSF examination: opening and closing pressure, cell counts, protein and glucose level, oligoclonal bands, cytology, immunoglobulin gene rearrangement analysis, and special tests for viral, fungal, bacterial, and parasitic infections, mitochondrial disease, and rheumatologic diseases
Rheumatologic panel blood tests: antinuclear antibody, antibody to double-stranded DNA, rheumatoid factor, anticardiolipin antibodies, complement levels, cryoglobulin level, neutrophil cytoplasm antibody (cANCA and pANCA), Scl-70 antibody, anti-centromere antibody, anti-Ro (SSA) and anti-La (SSB) cytoplasmic antibodies, serum angiotensin-converting enzyme, anti-proteinase 3
Infectious disease panel tests: varicella-zoster virus, herpes simplex virus, Epstein-Barr virus, HIV, hepatitis B and C viruses, tuberculosis, syphilis, Lyme, and others
Hypercoagulable panel tests: protein C, protein S, and antithrombin levels, prothrombin gene mutation, factor V Leiden mutation, and others
Hematologic panel tests: serum protein electrophoresis, homocysteine level, serum viscosity, Coombs test, bone marrow aspiration biopsy, and others
Ophthalmologic evaluation: fluorescein retinal angiography, Schirmer test
Biopsy: brain/leptomeningeal, skin, temporal artery, sural nerve, muscle, etc.
Genetic tests: for conditions such as CADASIL, RVCL, MTHFR 677C-T pleomorphism, and others

Abbreviations: CADASIL = cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy; cANCA = cytoplasmic antineutrophil cytoplasmic antibodies; INR = international normalized ratio; MR = magnetic resonance; MTHFR = methylenetetrahydrofolate reductase; pANCA = perinuclear antineutrophil cytoplasmic antibodies; PFO = patent foramen ovale; PT = prothrombin time; RVCL = retinal vasculopathy with cerebral leukodystrophy.

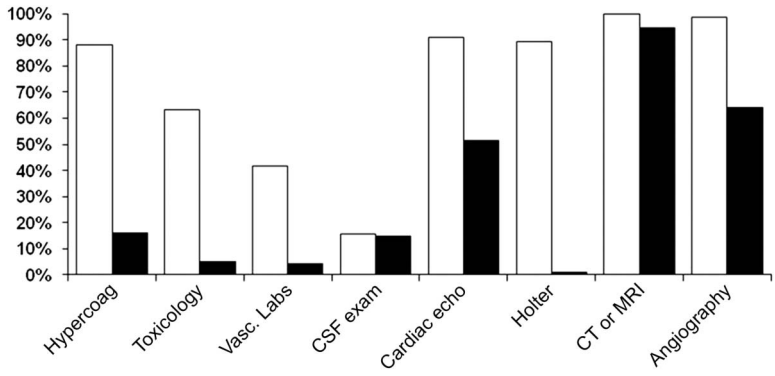
ACUTE MANAGEMENT Emergent treatment of younger stroke patients is similar to older patients.[40] Recommendations for physiologic management, e.g., blood pressure, temperature, glucose, and oxygenation, as well as thrombolysis, are the same as for older stroke patients. Younger patients benefit from access to stroke expertise and ideally should be admitted to comprehensive stroke centers with neurocritical care units.[41] Those with large strokes, especially malignant middle-cerebral artery infarction, require aggressive neurocritical care monitoring, intracranial pressure management, and early assessment for decompressive hemicraniectomy, which not only lowers mortality but also improves long-term neurologic and functional outcomes.[42] Several studies have shown that reperfusion strategies are efficacious and appear to be safe in young adults.[8,23,43–45] For example, in one study, young patients (18–50 years) had significantly better functional outcome and lower rates of symptomatic brain hemorrhage and 3-month mortality compared with older patients (51–80 years).[43] At present, thrombolysis is approved only for those aged 18 years and older; the ongoing NIH-funded Thrombolysis in Pediatric Stroke trial will provide safety and dosing data for thrombolysis in children and adolescents.[46]

STROKE PREVENTION As stated, young stroke survivors have substantial rates of modifiable vascular risk factors, which contribute significantly to stroke recurrence and mortality. Young adults with or without stroke warrant multimodal efforts to adopt healthy lifestyles, treat vascular risk factors aggressively, and abstain from recreational drug use including marijuana.[47,48] In one cohort, a disappointingly low 22% of young adults with IS gave up smoking.[49]

Although young adults are underrepresented in randomized controlled trials of secondary stroke prevention, we can extrapolate from the results of some of these trials. The Perindopril Protection Against Recurrent Stroke Study trial included younger individuals and found that the specific combination of angiotensin-converting enzyme inhibitor and thiazide diuretic reduced recurrent stroke in stroke survivors with or without hypertension defined as blood pressure >160/90 mm Hg. The benefit was greater in stroke survivors younger than 65 years compared with those 65 years and older[50] and observed in those with isolated diastolic hypertension or systolic-diastolic hypertension (hypertension types more common in younger adults).[51] The Stroke Prevention by Aggressive Reduction in Cholesterol Levels trial of adults aged 18 years and older with recent IS or ICH showed that 80 mg of atorvastatin, a high-potency statin, reduced recurrent stroke compared with placebo.[52] Although statin therapy was associated with fewer recurrent vascular events in young patients with cryptogenic stroke,[53] it remains controversial whether all young stroke patients with predominantly nonatherosclerotic stroke etiologies should receive statins.

A detailed review of the prevention of stroke from specific etiologies is outside the scope of this article. Published guidelines of stroke prevention in infants and children address many of these entities.[54] However, a few common conditions will be highlighted. In

Figure **Diagnostic tests in young adults with ischemic stroke**



White bars show the percentage of patients who underwent the test, and black bars show the percentage of tests showing a "positive" result relative to stroke etiology (i.e., diagnostic yield). See Methods for individual tests included under each panel. Hypercoag = hypercoagulation panel; toxicology = serum/urine toxicology screening panel; vasc. labs = vasculitis panel. From Ji R, Schwamm LH, Pervez MA, Singhal AB. Ischemic stroke and transient ischemic attack in young adults: risk factors, diagnostic yield, neuroimaging, and thrombolysis. JAMA Neurol 2013;70:51–57. Reprinted with permission of the American Medical Association.

patients with cryptogenic stroke, device closure of a PFO did not offer greater benefit than medical therapy alone for preventing recurrent stroke.[37–39] Evidence-based guidelines do not recommend anticoagulation over antiplatelet therapy for arterial dissection. In patients with migraine with aura, smoking cessation and aggressive treatment of vascular risk factors is important; women should consider birth control with methods other than estrogen-containing hormonal contraception. In patients with migraine who develop IS, the above measures become even more relevant and therapy with triptans and ergots is contraindicated. Whether prophylactic migraine treatment affects future stroke occurrence remains unclear. Hormonal contraception is used by 15% to 35% of young women at the time of the stroke.[1,49] Clinical guidelines recommend against using combined estrogen-progesterone contraception in women with stroke.[55] Progestin-only contraceptives (pills or implants) can be initiated after stroke but should be discontinued if the woman was taking it when stroke occurred.[55] Although pregnancy is not contraindicated after stroke, young women with stroke merit multidisciplinary discussions regarding the risks of pregnancy. The teratogenicity of drugs such as statins and angiotensin-converting enzyme inhibitors should be noted.

PROGNOSIS Prognosis is an important issue in premature stroke because of the longer expected survival compared with older people with stroke. In addition, those affected by stroke in young adulthood often have significant stress, and primary responsibility for generating income for the family or providing child care. Prognosis will be discussed in relationship to mortality, stroke recurrence, and other vascular events, poststroke epilepsy, functional outcome, poststroke depression and quality of life, return to work, and other social consequences.

Mortality rates in a large study of first IS in patients aged 15 to 49 years in Finland[56] were 2.7% (95% confidence interval [CI] 1.5%–3.9%) at 1 month, 4.7% (95% CI 3.1%–6.3%) at 1 year, and 10.7% (95% CI 9.9%–11.5%) at 5 years, consistent with prior smaller studies.[49,57,58] Five-year mortality was higher for those aged 45 and older (14.7%) vs those younger than 45 (7%), and higher for large-artery atherosclerosis (approximately 30%) and cardioembolism (approximately 20%) vs other determined or undetermined etiology or small-vessel disease (approximately 5%–7%). The 5-year rate for stroke recurrence and other vascular events, both nonfatal and fatal, was 11.5% (95% CI 9.2%–13.7%); independent predictors of higher rates were type-1 diabetes, heart failure, large-artery atherosclerosis, prior TIA, and increasing age.[6] The 5-year rate for poststroke epilepsy among patients with first IS ages 15 to 49 in Norway[58] was 10.5% overall, but 34% among patients with severe neurologic deficits from index stroke.

Functional independence (no or slight disability and able to look after own affairs without assistance; modified Rankin Scale score ≤2) ranged from 78%[58] to 85%[59] to 94%.[49] Diabetes and severe neurologic deficits at admission were predictors of poor functional outcome.[58] Although most patients regained functional independence, there was a high rate of poststroke depression ranging from 28%[60] to 46%[57]; fatigue, reported in 54%[60]; and impaired quality of life, particularly in the SF-36 dimensions of physical functioning, role limitations due to physical health, and social functioning. Estimates of the percent returning to work after stroke vary, but have been reported at 42%[57] to 53%[49] with 23% of those returning to work requiring adjustments in their occupation. Other social consequences of stroke have not been well studied in large representative samples of young stroke patients. Young adults with stroke frequently are parents of young children. While quantitative estimates are lacking, this role may be impaired in some stroke patients. Limited data are available on changes in family structure; a French study reported a 7% divorce rate after a mean follow-up of 3 years.[49]

SUGGESTIONS FOR RAISING AWARENESS There has been a relative explosion in the number of Web sites addressing young stroke (table 5). Many discuss the need for greater awareness and provide links to other sites as well as an opportunity for young stroke victims and caregivers to tell their stories and interact with others while also getting needed

Table 5	Web sites concerning stroke in young adults (source: www.google.com)
Young Adult Stroke Survivor Group/Stroke Awareness Foundation: http://www.strokeinfo.org/about/events.html	
Young stroke support group: MY SInS (Facebook/Twitter/YouTube)	
Stroke Awareness and Support Association (SASA): http://strokeawarenessandsupport.com	
Generation S Young Stroke Survivors: http://www.orgsites.com/pa/generation-s/	
Children's Hemiplegia and Stroke Association (CHASA): http://www.chasa.org/	
YoungStroke, Inc.: http://www.youngstroke.org/	
Blog, Neurotalk communities: http://neurotalk.psychcentral.com/thread27811.html	
http://www.fightingstrokes.org/	
http://www.differentstrokes.co.uk/	
http://www.ukstrokeforum.org/about_us/	
http://www.scyss.org/	
Brendon's Smile, raising awareness for childhood stroke: http://brendonssmile.org/	
http://www.pediatricstrokenetwork.com/ (the first support group for pediatric stroke that registered with the American Heart Association)	
The Hazel K. Goddess Fund for Stroke Research in Women: http://www.thegoddessfund.org/	
Youth Stroke Foundation: http://www.youthstroke.org/	
Childhood Stroke and Hemiplegia Connections of Illinois: http://www.cshconnections.org/advocacy.htm	
Canadian Paediatric Stroke Support Association: http://www.cpssa.org/	

information. While coping with the shock of having a stroke, younger survivors may be dealing with relationships, careers, and raising children—issues that require additional awareness and resources (appendix e-1 on the *Neurology*® Web site at www.neurology.org).

Web sites allow people to donate money (online charities) for young stroke, and offer research, message boards, survivor stories, networking, and other opportunities to connect. For example, The Stroke Awareness and Support Association is a 501(c)3 nonprofit organization with a mission to raise awareness on the prevalence of strokes at young ages occurring each year in the United States, and to provide support directly to younger stroke victims and their families. Sickle Cell and Young Stroke Survivors is a registered charity that was formerly set up as a support group for parents/carers whose children have had a stroke. For more than 2 years, the Stroke Awareness Foundation in California has been working with the California Department of Public Health to develop a plan of stroke prevention that will serve everyone in California. They promote a Young Adult Stroke Survivor Group (Stroke Awareness) that can be modeled in other communities and countries. The Children's Hemiplegia and Stroke Association Web site provides information and support to families of pediatric stroke survivors. There is information on therapy, dressing, school, and general support information needed by parents who face the daily challenges of raising a child with poststroke hemiplegia. The mission of YoungStroke, Inc. is to advocate the needs of those who experienced their first stroke between ages 20 and 65. It provides information on research and education initiatives.

Social media networking can provide additional avenues for raising awareness and linking individuals and families. Awareness can also be raised through World Stroke Day Runs, Walks, and Family Events that raise both money and awareness, support groups, national stroke agencies (American Stroke Association, National Stroke Association), local and national media, and legislative and congressional initiatives (e.g., the US Senate approved a resolution declaring May 6, 2006 as Childhood Stroke Awareness Day). Workplace information about stroke risk, warning signs, and what to do if one witnesses someone with a stroke can help educate the public.

FUTURE DIRECTIONS While physicians, patients, and caregivers grapple with the shifting landscape of health care and its reform, it is crucial to include a voice for young stroke victims and their caregivers in setting national health priorities as the costs and burden of disability from young stroke continue to increase. As information is increasingly spread rapidly via electronic media, there is a great opportunity to connect people and resources. We need greater emphasis on teaching about young stroke and its risk factors and warning signs in school, at the workplace, in primary care physician's offices, and media. As an example of developing momentum, the YoungStroke project (http://www.youngstroke.org/) is a 5-year research initiative to document the experience of young stroke survivors and to measure their satisfaction with community services within the 28 coastal counties of South Carolina. The resulting media report will serve as a resource for policy-makers and health care providers. It will likely validate the experience of an underserved patient population, which could help increase resources and access to care for young stroke survivors.

Given the increasing physical, emotional, and financial burden young stroke causes, there will need to be greater research into reducing this burden. The formation of multicenter collaborative research groups could help facilitate meaningful and practical aims. A national young stroke registry could improve our understanding of risk factors, identify research priorities, and facilitate clinical trials of treatments and rehabilitative strategies of stroke in the young.

AUTHOR CONTRIBUTIONS

Study concept and design: Drs. Singhal, Biller, Elkind, Fullerton, Jauch, Kittner, D. Levine, and S. Levine. Acquisition of data: Drs. Singhal, Biller, Elkind, Fullerton, Jauch, Kittner, D. Levine, and S. Levine. Analysis and interpretation: Drs. Singhal, Biller, Elkind, Fullerton, Jauch, Kittner, D. Levine, and S. Levine. Critical revision of the manuscript for important intellectual content: Drs. Singhal, Biller, Elkind, Fullerton, Jauch, Kittner, D. Levine, and S. Levine. Study supervision: Dr. Singhal.

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DISCLOSURE

A. Singhal receives research support from NIH; serves as site investigator in clinical trials sponsored by Pfizer, Inc. and Photothera, Inc.; is a consultant for Biogen-Idec, Inc., serves on event adjudication committees for the TIMI Study Group; has served as a medical expert witness in individual cases concerning stroke in young adults; is Associate Editor for the journal *Medical Gas Research*; and his wife is an employee of Biogen-Idec, Inc. and holds stock in Biogen-Idec, Inc. and Vertex Pharmaceuticals, Inc. J. Biller serves as Editor of the *Journal of Stroke and Cerebrovascular Diseases* and Chief Editor of *Frontiers in Neurology*. M. Elkind receives research support from diaDexus Inc., Bristol-Myers Squibb/Sanofi Pharmaceuticals Partnership, and the NIH; serves on an event adjudication committee for Jarvik Heart; has received compensation for consulting from Biogen-Idec, Inc. and BMS-Pfizer Partnership, and for participation in litigation on behalf of Novartis, Organon, and GlaxoSmithKline; and receives compensation from the American Academy of Neurology for service as Resident and Fellow Section Editor for the journal *Neurology®*. H. Fullerton receives research support from the NIH and American Heart Association. E. Jauch reports research support from the National Institute of Neurological Disorders and Stroke (NINDS), Novo Nordisk, and Genentech, and serves as a consultant to Genentech. S. Kittner was supported by the Office of Research and Development, Medical Research Service, and the Baltimore Geriatrics Research, Education, and Clinical Center of the Department of Veterans Affairs, and by a grant from NINDS (U01 NS069208-01). D. Levine was supported by grant P30DK092926 from the National Institute of Diabetes and Digestive and Kidney Diseases (investigator) and by grant K23AG040278 (D. Levine PI) from the National Institute of Aging, and serves as a consultant (cardiovascular event adjudicator) on the Platelet-Oriented Inhibition in New TIA and Minor Ischemic Stroke (POINT) Trial (NINDS 1U01S062835; Johnston SC/Easton JD, multiple PIs). S. Levine has previously served on the advisory board of Genentech, Inc. (honorarium donated to stroke research), is Associate Editor of MEDLINK, receives research funding from the NIH, PCORI, and Genentech, and has served as an expert witness in stroke cases including stroke in the young. Go to Neurology.org for full disclosures.

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