Stroke in the Young

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Disclosures

- published studies and registries most commonly define young adults as those **less than 50 or 55 years of age**
- Stroke in young adults comprises approx. **10-12% of total stroke patients**

research study of stroke and

stroke risk factors among the

multi-ethnic community of

Northern Manhattan, New York.

Northern Manhattan study showed greater incidence of stroke in young African Americans and Hispanics

GCNKSS

Greater Cincinnati / North Kentucky epidemiology of stroke study reported a **relative risk of 5 for all strokes** reported in African Americans within 35-44 year age group and RR of 2.2 in the < 34 year age group.

J Neurol Neurosurg Psychiatry 2005;76: 191–195.

Stroke, 2002;33: 2789–2793.

Neurology 2012;79:1781–1787.

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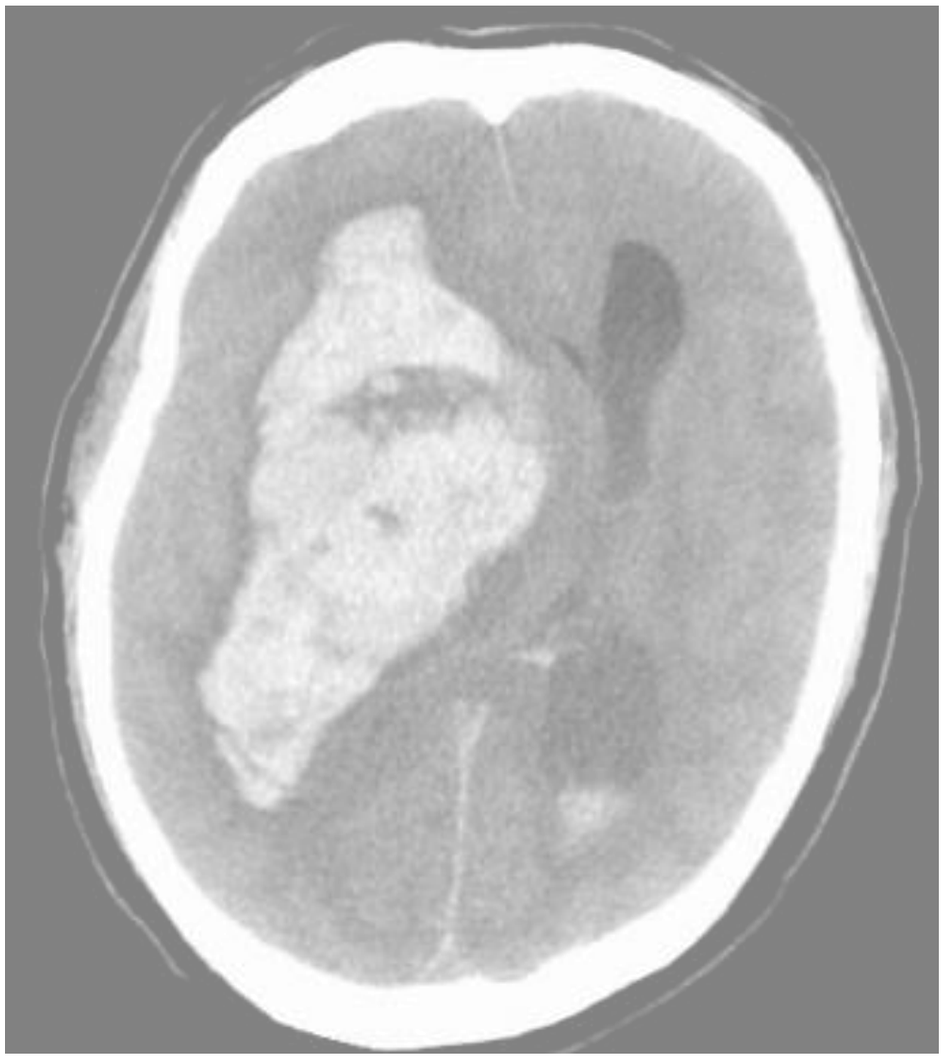
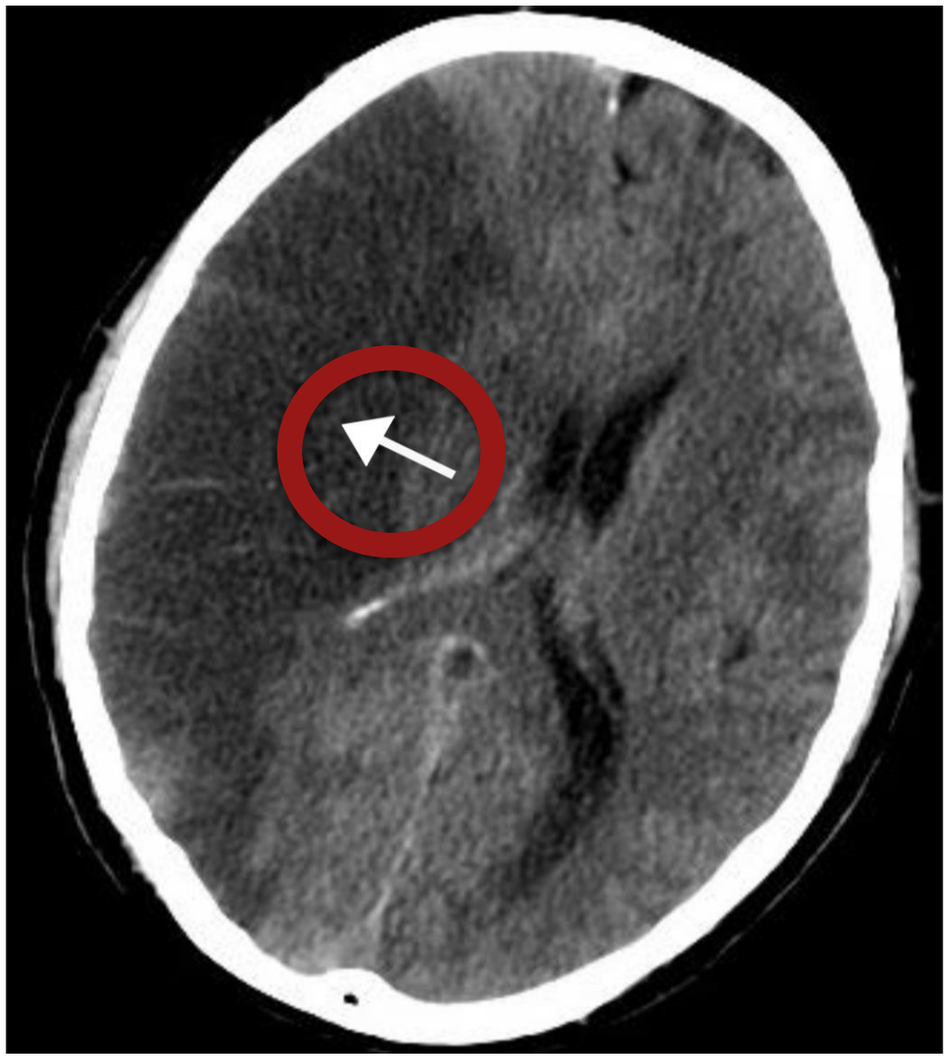
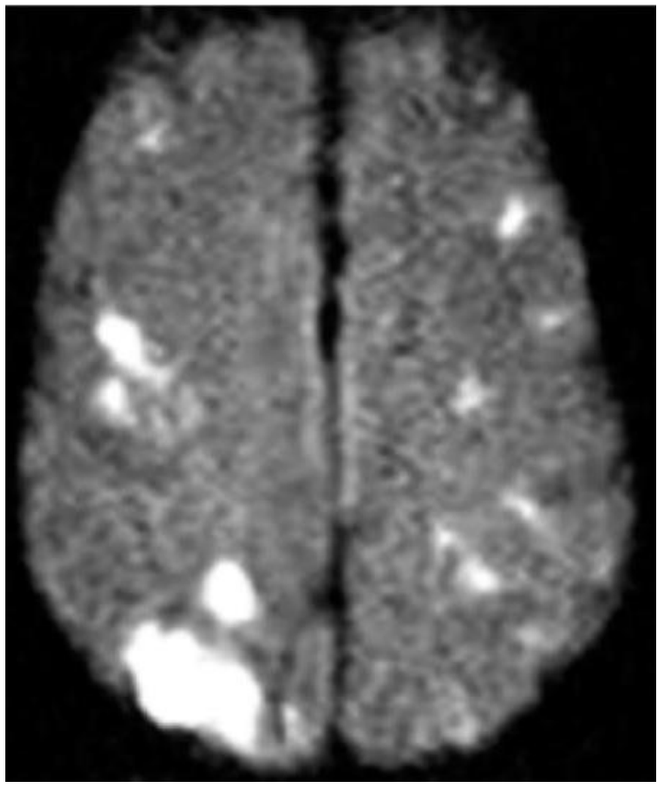
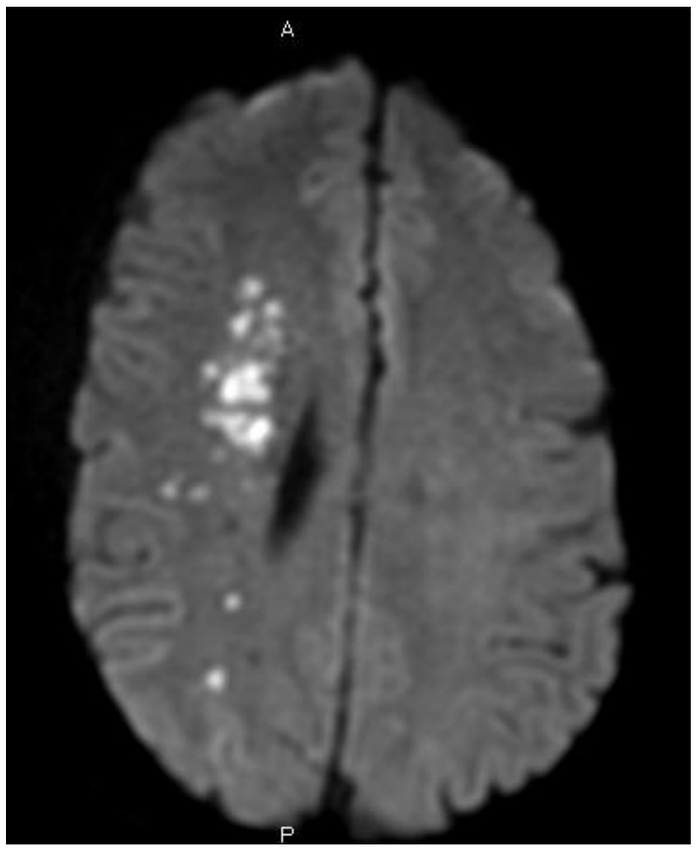


Hemorrhagic



Ischemic

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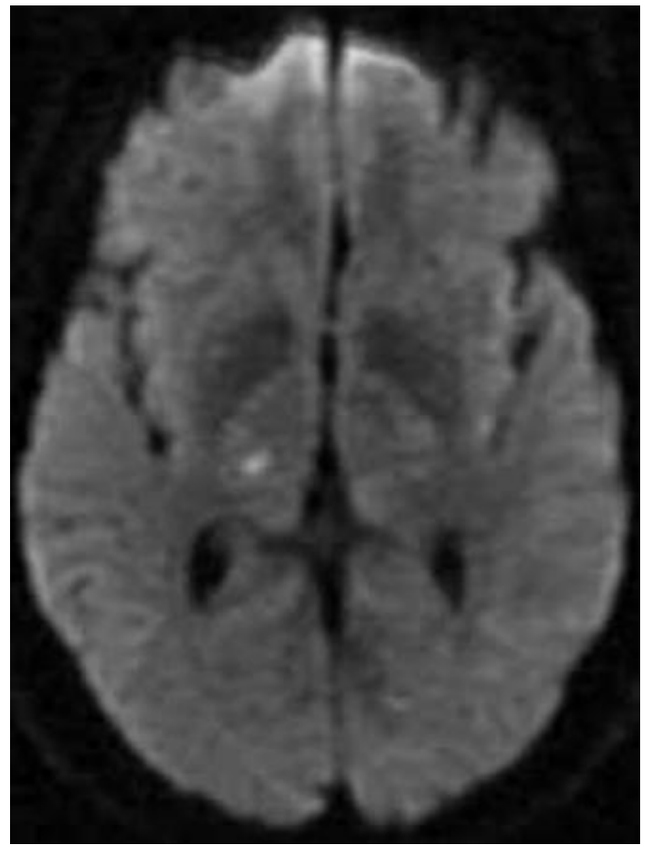
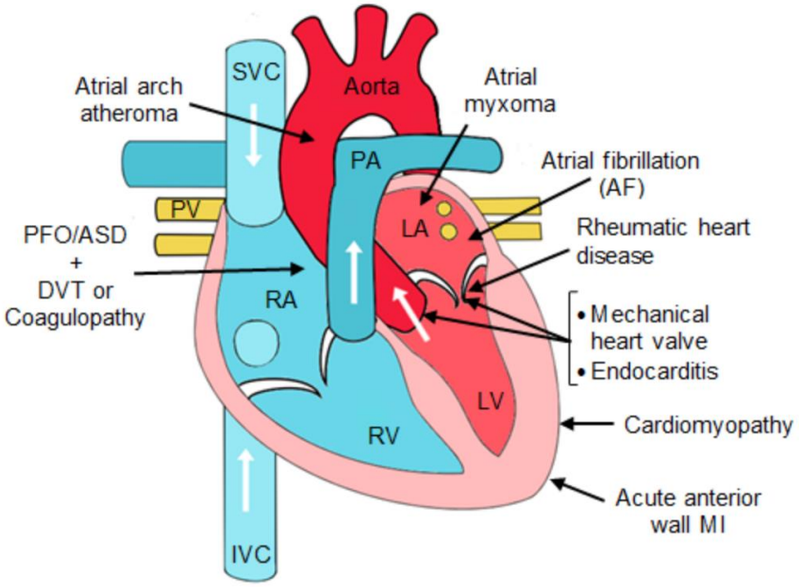
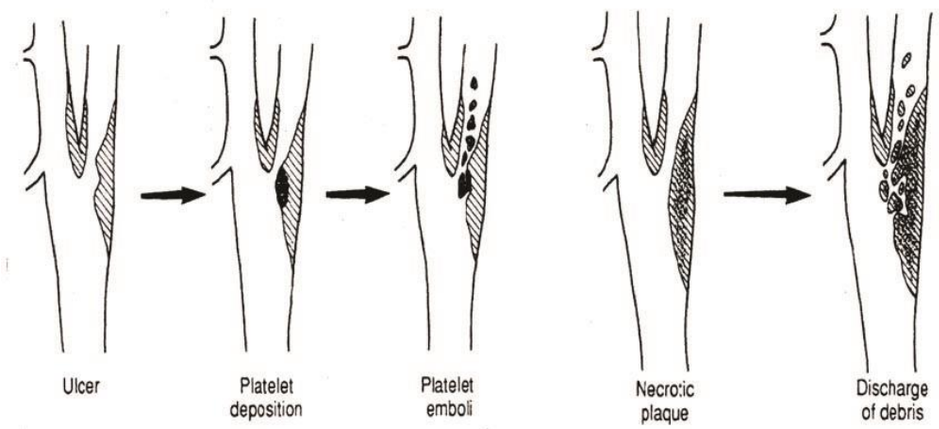
P

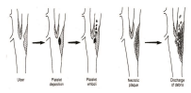



Atrial arch atheroma
SVC
Aorta
Atrial myxoma
PA
Atrial fibrillation (AF)
PV
LA
PFO/ASD + DVT or Coagulopathy
Rheumatic heart disease
RA
• Mechanical heart valve
• Endocarditis
LV
RV
Cardiomyopathy
Acute anterior wall MI
IVC

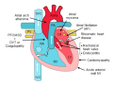

Ulcer
Platelet deposition
Platelet emboli
Necrotic plaque
Discharge of debris


Humulin 70/30

TABLE 1. TOAST Classification of Subtypes of Acute Ischemic Stroke



Large-artery atherosclerosis (embolus/thrombosis)*



Cardioembolism (high-risk/medium-risk)*

Small-vessel occlusion (lacune)*

Stroke of other determined etiology*

Stroke of undetermined etiology

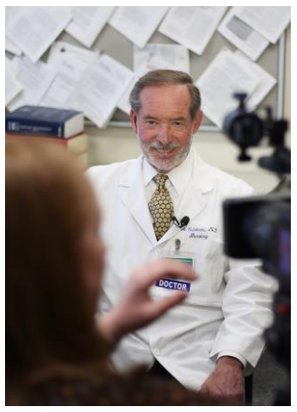
a. Two or more causes identified

b. Negative evaluation

c. Incomplete evaluation

TOAST, Trial of Org 10172 in Acute Stroke Treatment.
*Possible or probable depending on results of ancillary studies.

Dr. Culebras
Upstate Professor
of Neurology

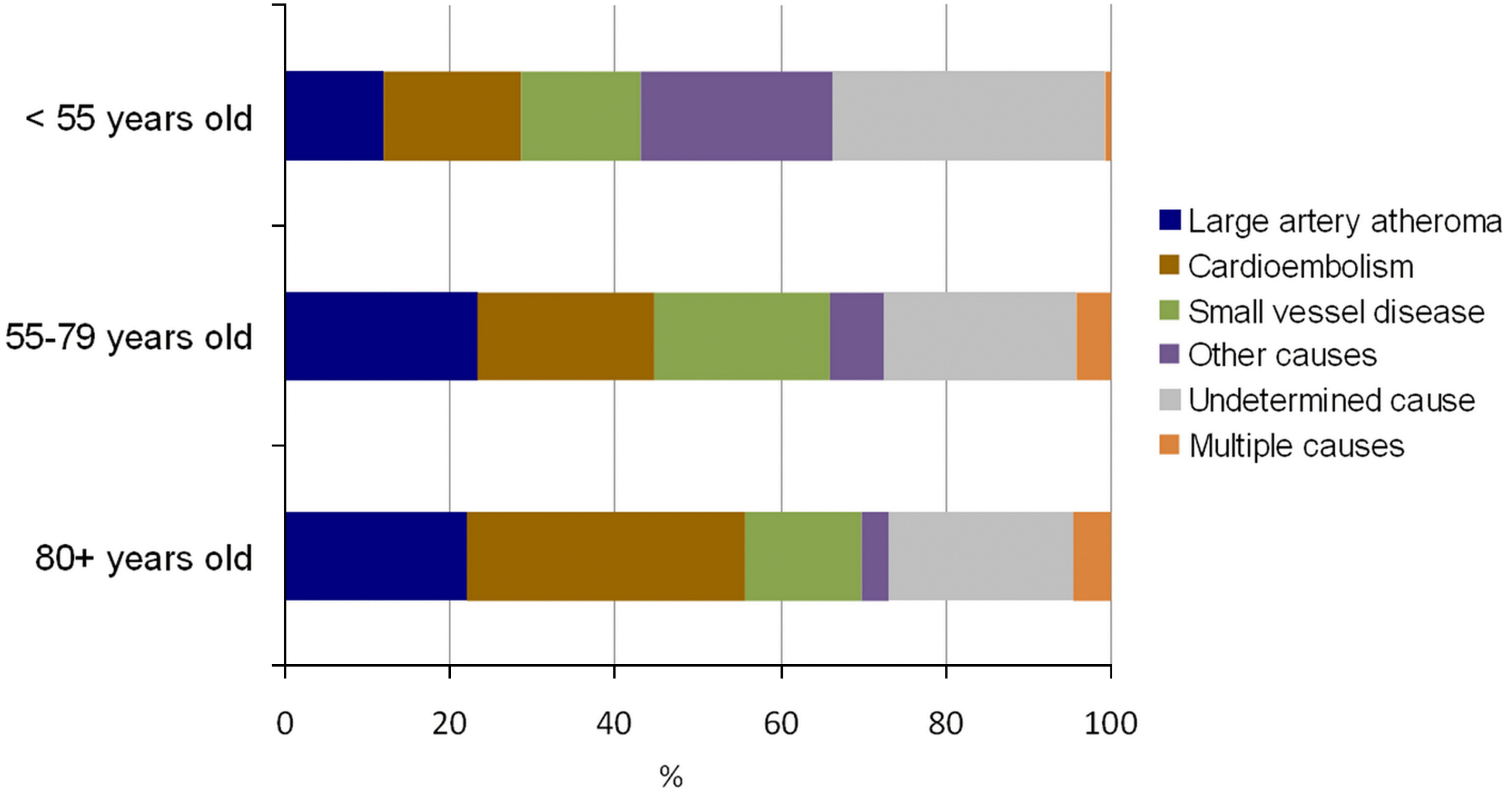


Appendix

TOAST Research Group
TOAST Participating Clinical Centers

SUNY Health Sciences Center, Syracuse, N.Y. Antonio Culebras, MD (PI); Guy Carey, MD, and Nidsa I. Martir, MD (Co-I); Carole Ficarra (SC).

Figure 1. Distribution of etiological subtypes of ischemic stroke according to the TOAST classification by age group. Data from the Dijon Stroke Registry. TOAST indicates Trial of ORG 10172 in Acute Stroke Treatment.



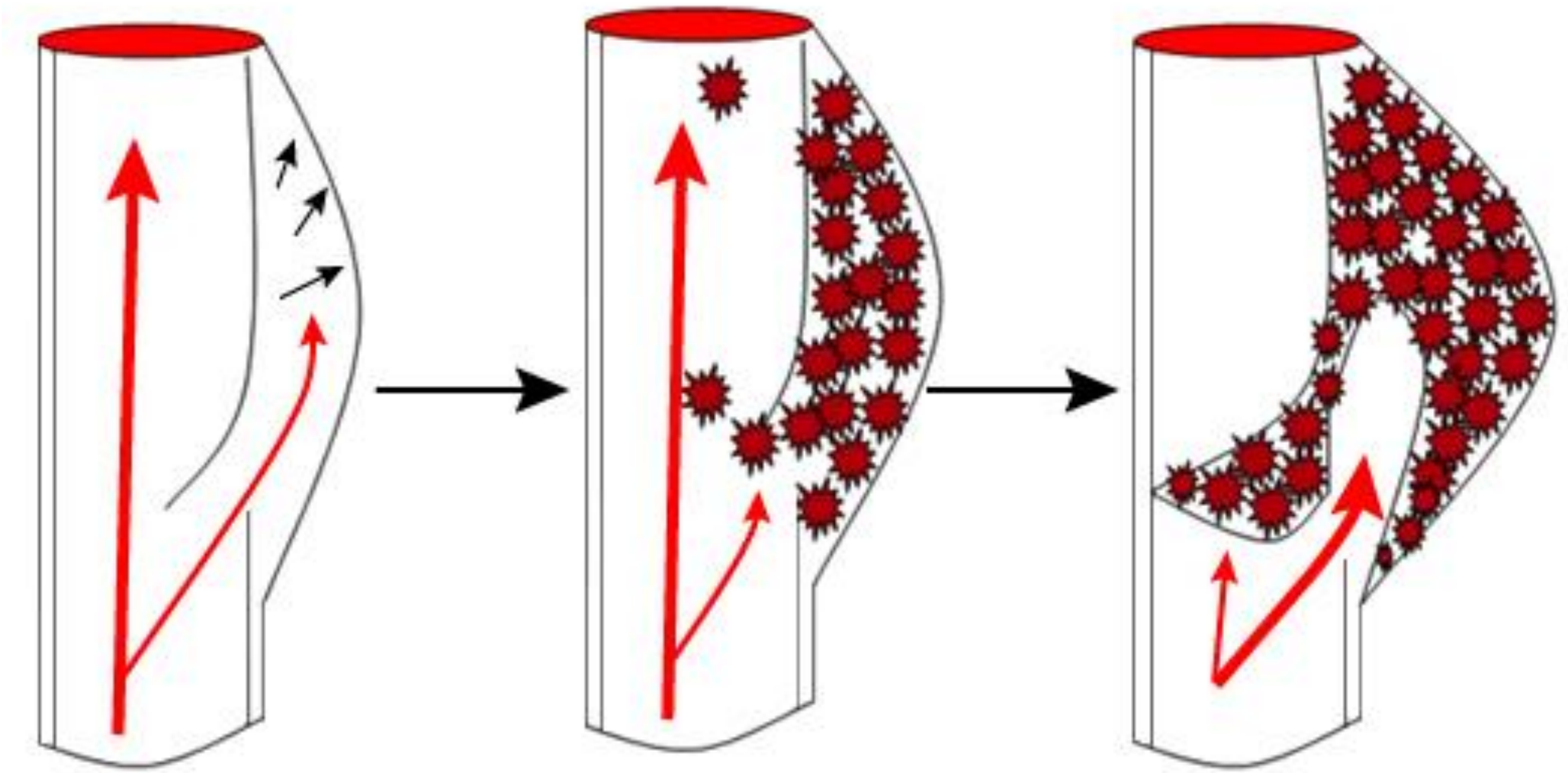
Rising Stroke Incidence in Young Adults: More Epidemiological Evidence, More Questions to Be Answered, Volume: 5, Issue: 5, DOI: (10.1161/JAHA.116.003661)

Table 2 Uncommon causes of stroke in young adults

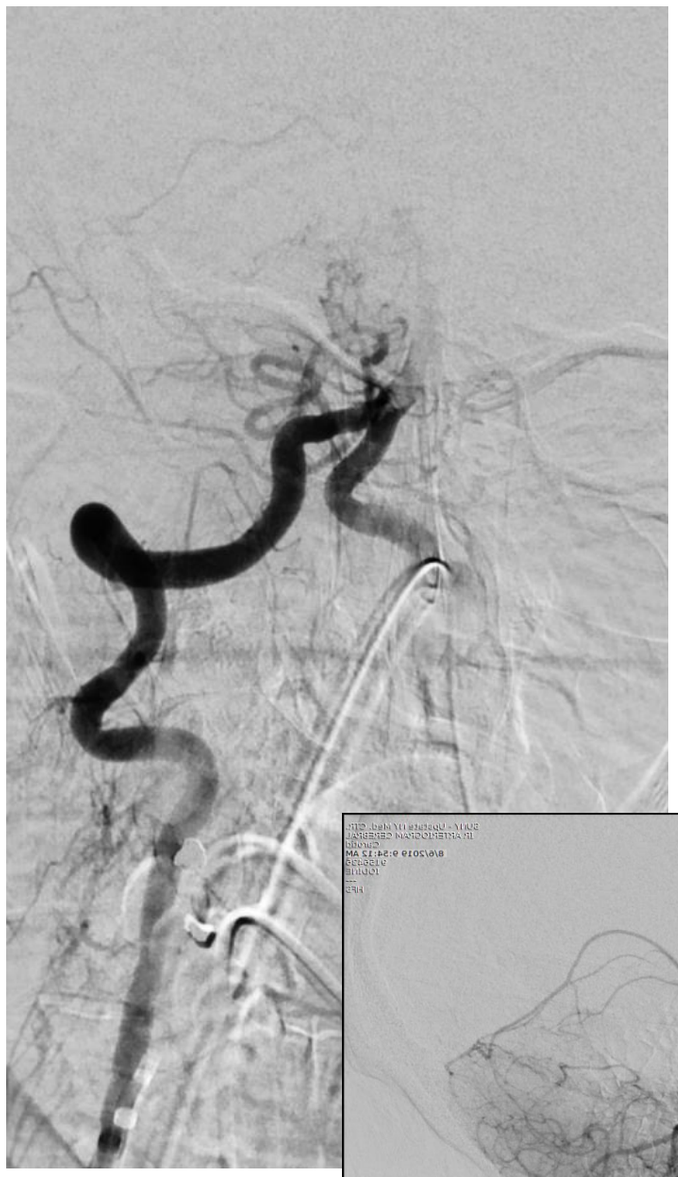
Nonatherosclerotic angiopathies	Cervicocephalic arterial dissection
	Cerebral amyloid angiopathy
	Moyamoya disease
	Fibromuscular dysplasia
	Reversible cerebral vasoconstriction syndrome
	Susac's syndrome
	Sneddon's syndrome
	Migraine-induced stroke
Hematologic conditions	Hypercoagulable state due to deficiencies of protein S, protein C, or antithrombin; factor V Leiden mutation, prothrombin gene G20210A mutation
	Acquired hypercoagulable state (eg, cancer, pregnancy, hormonal contraceptive use, exposure to hormonal treatments such as anabolic steroids and erythropoietin, nephrotic syndrome)
	Antiphospholipid syndrome
	Hyperhomocysteinemia
	Sickle cell disease
	Myeloproliferative disorders (eg, leukemia, lymphoma)
Genetic	Fabry disease
	CADASIL
	MELAS
	Marfan syndrome
	Neurofibromatosis
	Sturge-Weber disease
Inflammatory and infectious	Vasculitis (primary angiitis of the CNS, Sjögren syndrome, Wegener's granulomatosis)
	Temporal arteritis
	Takayasu disease
	Behçet's syndrome
	Neurosarcoidosis
	Neurocysticercosis
	HIV
	Varicella zoster virus
	Neurosyphilis
	Tuberculous meningitis

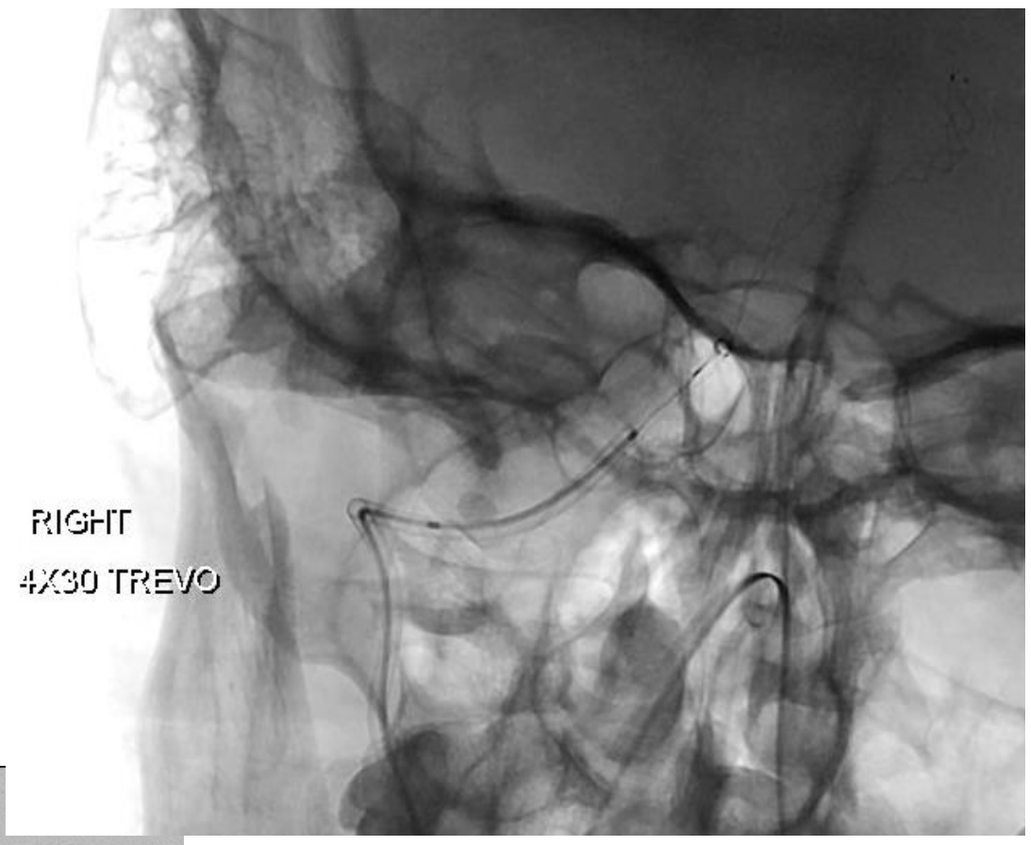
Abbreviations: CADASIL, cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy; CNS, central nervous system; HIV, human immunodeficiency virus; MELAS, mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes.

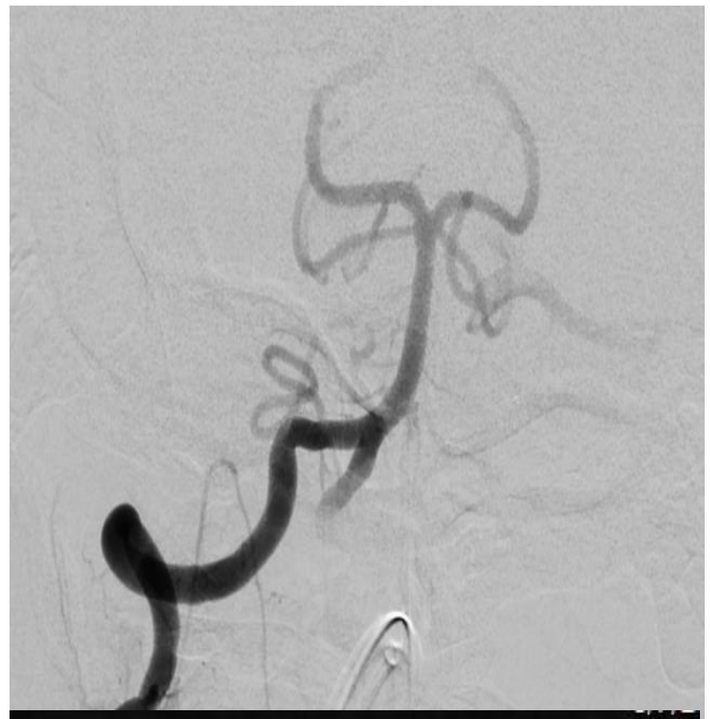
- **Cervico-cephalic arterial dissection** is the 2nd most common lesion of cervical arteries (after atherosclerosis) and accounts for up to **25% of all causes of stroke in young adults.** Stroke Res Treat. 2013;2013:715380. 24
  Eur J Neurol. 2013;20:1431–1439

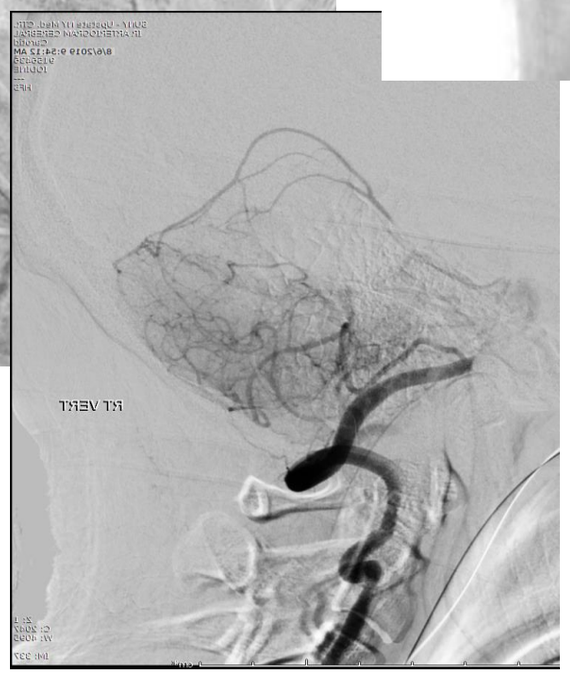


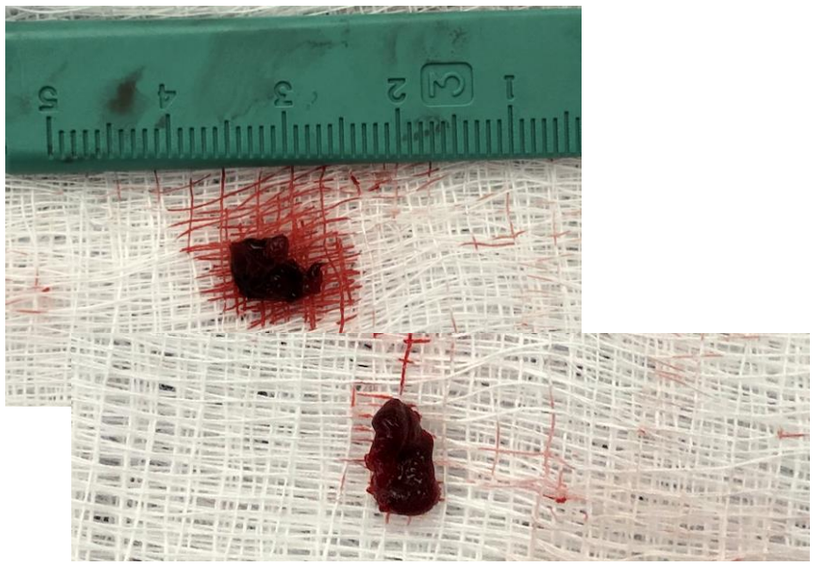
Presents to ED found down, vomiting and left sided weakness. Level of consciousness declin

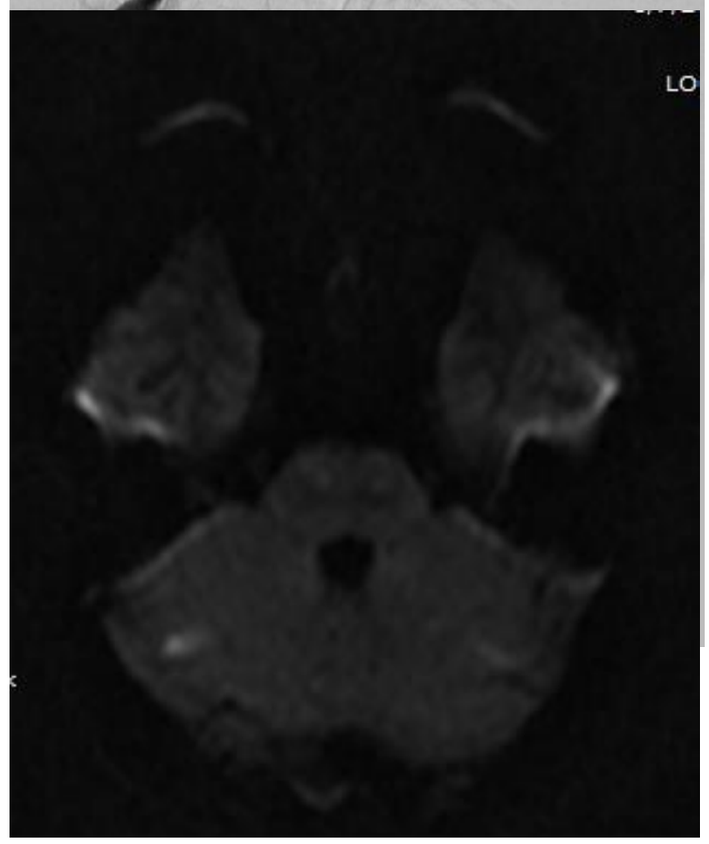












Genetic causes of stroke

although several monogenic factors that increase the risk of stroke in the young have been identified, **screening for these conditions on a routine basis has been found to be low yield**

American Heart Association | American Stroke Association

Guidelines for the Primary Prevention of Stroke

Genetic Factors: Recommendations

1. **Obtaining a family history can be useful in identifying people who may have increased stroke risk (*Class IIa; Level of Evidence A*).**
2. **Referral for genetic counseling may be considered for patients with rare genetic causes of stroke (*Class IIb; Level of Evidence C*).**

10. **Genetic screening of the general population for the prevention of a first stroke is not recommended (*Class III; Level of Evidence C*).**

Stroke. 2014;45:3754–3832

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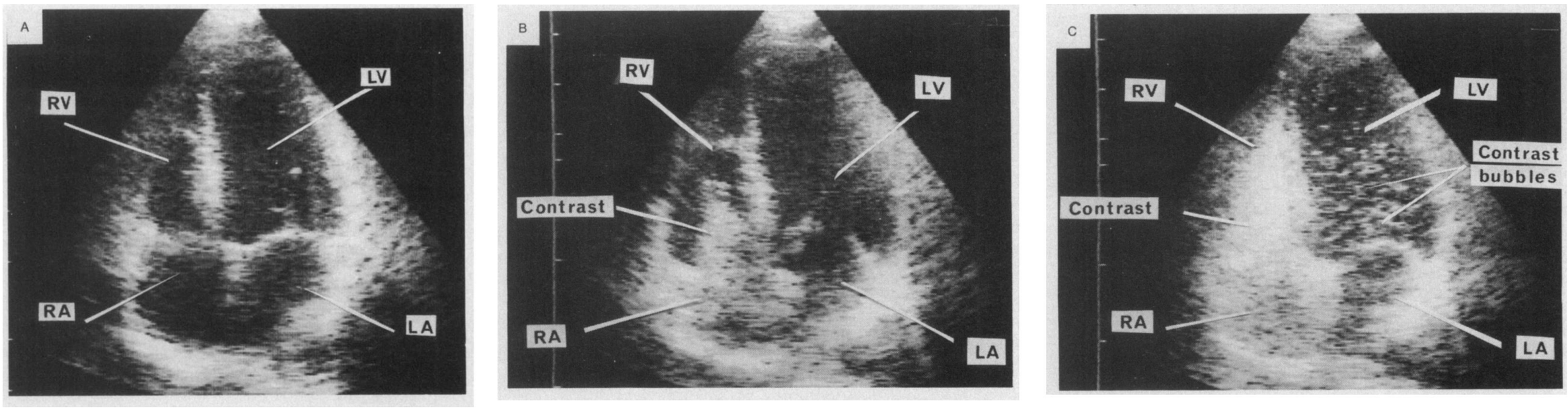
PREVALENCE OF PATENT FORAMEN OVALE IN PATIENTS WITH STROKE

PH. LECHAT, M.D., PH.D., J.L. MAS, M.D., G. LASCAULT, M.D., PH. LORON, M.D., M. THEARD, M.D., M. KLIMCZAC, M.D., G. DROBINSKI, M.D., D. THOMAS, M.D., AND Y. GROSGOGEAT, M.D.

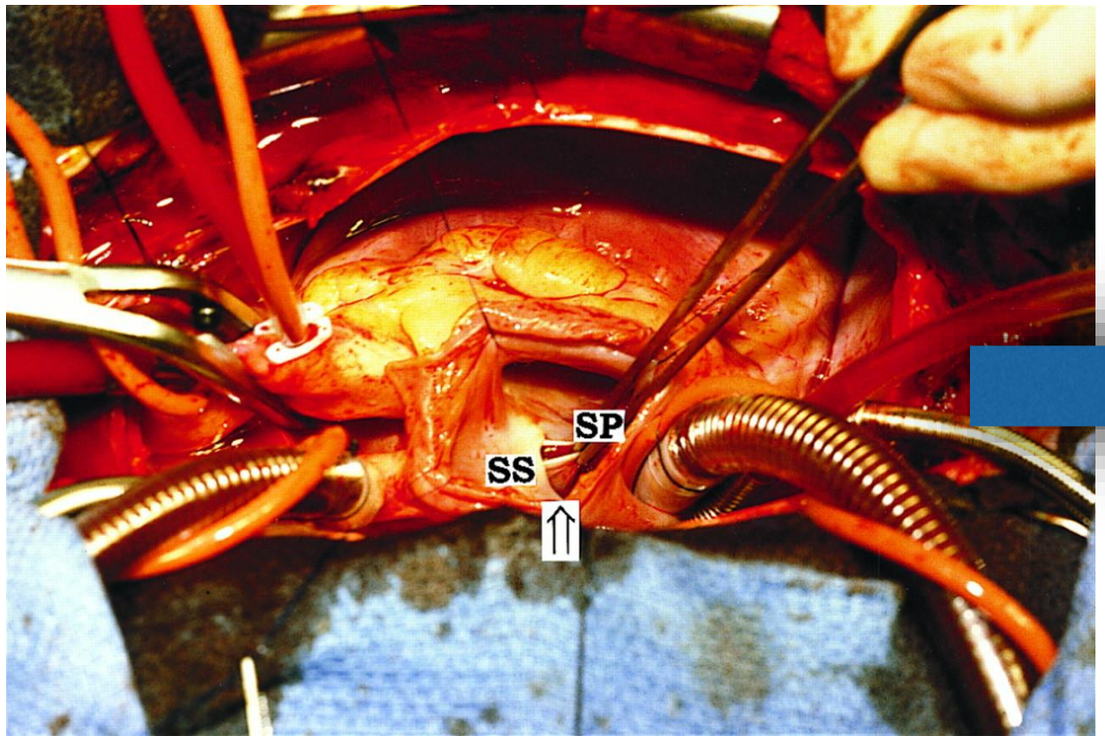
Abstract The cause of ischemic stroke in younger adults is undefined in as many as 35 percent of patients. We studied the prevalence of patent foramen ovale as detected by contrast echocardiography in a population of 60 adults under 55 years old with ischemic stroke and a normal cardiac examination. We compared the results with those in a control group of 100 patients.

The prevalence of patent foramen ovale was significantly higher in the patients with stroke (40 percent) than in the control group (10 percent, $P<0.001$). Among the patients with stroke, the prevalence of patent foramen ovale was 21 percent in 19 patients with an identifiable cause of their stroke, 40 percent in 15 patients with no identifiable cause but a risk factor for stroke, such as mitral-valve prolapse, migraine, or use of contraceptive agents, and 54 percent in 26 patients with no identifiable cause ($P<0.10$).

These results suggest that because of the high prevalence of clinically latent venous thrombosis, paradoxical embolism through a patent foramen ovale may be responsible for stroke more often than is usually suspected.
(N Engl J Med 1988; 318:1148-52.)



PFO Closure



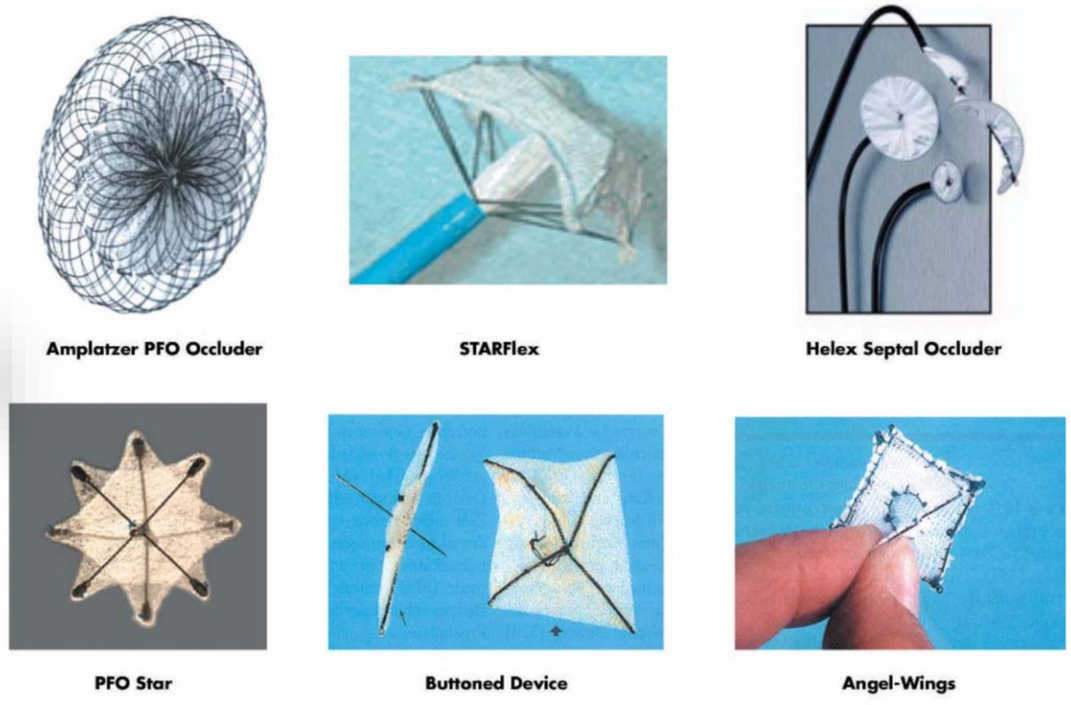


Figure 1 Various devices used for percutaneous catheter based patent foramen ovale (PFO) closure.

Stroke. 1997;28:2376–2381

Heart 2005;91:444–448.

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Table 1. Six Trials of Patent Foramen Ovale Closure for Stroke with Results Published in the *Journal*.*

Trial Name (Year of Publication)	No. of Patients	Mean or Median No. of Years of Follow-up	Comparator	Primary Outcome	Hazard Ratio†	P Value†
Trials with negative findings						
CLOSURE I (2012)[2]	909	2	Antiplatelet therapy, warfarin, or both	Composite of stroke or transient ischemic attack at 2 years, death from any cause during the first 30 days, or death from neurologic causes between 31 days and 2 years after randomization	0.78	0.37
PC (2013)[3]	414	4.1 (PFO closure group), 4.0 (medical-therapy group)	Antiplatelet therapy or anticoagulation‡	Composite of death, stroke, transient ischemic attack, or peripheral embolism	0.63	0.34
RESPECT (2013)[4]	980	2.1	Antiplatelet therapy or warfarin	Composite of recurrent nonfatal ischemic stroke, fatal ischemic stroke, or early death after randomization	0.49	0.08
Trials with positive findings						
Gore REDUCE (2017)[5]	664	3.2	Antiplatelet therapy	Ischemic stroke and new brain infarction on imaging	0.23	0.002
CLOSE (2017)[6]	663	5.3	Antiplatelet therapy or anticoagulation‡	Stroke	0.03	<0.001
RESPECT extended follow-up (2017)[7]	980	5.9	Antiplatelet therapy or warfarin	Composite of recurrent nonfatal ischemic stroke, fatal ischemic stroke, or early death after randomization	0.55	0.046

Table 2 Key features of recently published randomized controlled trials on management of cryptogenic stroke due to a PFO

	Close—PFO	Reduce	Respect
Inclusion criteria	a. Age 16–60 y	a. Age 18–59 y	a. Age 18–60 y
	b. Cryptogenic stroke within 6 mo with specific characteristics as below	b. Cryptogenic stroke within 6 mo	b. Cryptogenic stroke within 270 d
Identification of cryptogenic stroke	Standard stroke workup including a negative 24-h Holter monitoring	Standard stroke workup, 24-h Holter monitoring not required.	Standard stroke workup, 24-h Holter monitoring not required.
Morphologic characteristics of PFO	One of the following criteria should be met:	Shunt size characterized as follows:	Shunt size characterized as follows:
	a. Presence of a large shunt (>30 microbubbles)	a. Small: 1–5 microbubbles	a. Grade 1: 1–9 microbubbles
	b. Presence of an ASA	b. Moderate: 6–25 microbubbles	b. Grade 2: 10–20 microbubbles
		c. Large: >25 microbubbles	c. Grade 3: >20 microbubbles
Mean RoPE score	>7 across all groups	Not available	Not available
Presence of a large shunt in closure group	66%	42.8%	49.5%
Presence of an ASA in the closure group	33%	20%	36%
Follow-up	Mean 5.3 ± 2 y	Median 3.2 y	Median 5.9 y
Primary outcome	Recurrent ischemic stroke	a. Freedom from recurrent ischemic stroke through at least 24 mo	Composite end point of the following:
		b. Presence of a new ischemic stroke including silent brain infarctions.	a. Recurrent ischemic stroke
			b. Early death

Table 2 Key features of recently published randomized controlled trials on management of cryptogenic stroke due to a PFO

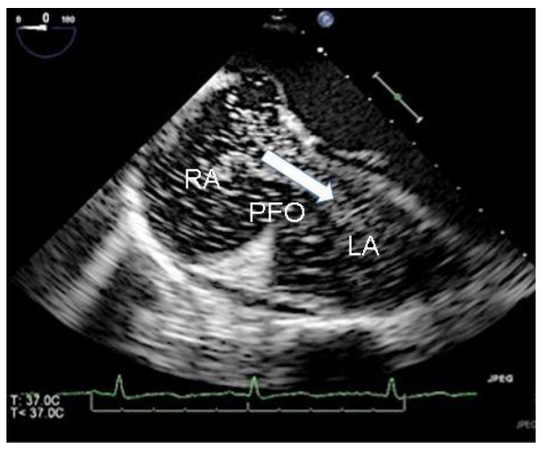
	Close—PFO	Reduce	Respect
Type of device used	Several devices used, more than half were Amplatzer device	Helex Septal Occluder or Cardioform Septal Occluder	Only Amplatzer septal occluder used
Main results	20 patients need to be treated to prevent 1 stroke over 5 y	28 patients need to be treated to prevent 1 stroke over 2 y	42 patients need to be treated to prevent 1 stroke over 5 y
Rate of atrial fibrillation in the treatment group	4.6%	6.6%	0.2%

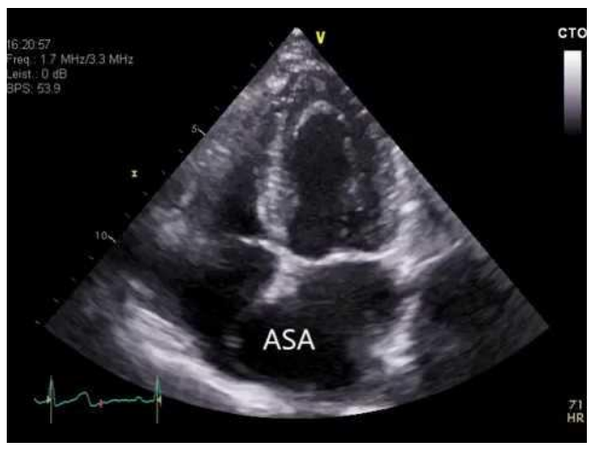
Abbreviations: ASA = Atrial septal aneurysm; PFO = patent foramen ovale; RoPE = Risk of Paradoxical Embolism.

Rate of recurrent cryptogenic stroke from PFO is as low as 1% per year

Trials limited by lack of long term heart monitoring to exclude pAF

Risk moderately reduced in patients with PFO aggressive features; **large size** and/or presence of **atrial septal aneurysm** (ASA)





RoPE Score

An index to identify stroke-related vs incidental patent foramen ovale in cryptogenic stroke

David M. Kent, MD, CM, MSc
Robin Ruthazer, MPH
Christian Weimar, MD
Jean-Louis Mas, MD
Joaquín Serena, MD, PhD
Shunichi Homma, MD
Emanuele Di Angelantonio, MD, MSc
Marco R. Di Tullio, MD
Jennifer S. Lutz, MS
Mitchell S.V. Elkind, MD, MS
John Griffith, PhD
Cheryl Jaigobin, MD, MSc
Heinrich P. Mattle, MD
Patrik Michel, MD
Marie-Louise Mono, MD
Krassen Nedeltchev, MD
Federica Papetti, MD
David E. Thaler, MD, PhD

ABSTRACT

Objective: We aimed to create an index to stratify cryptogenic stroke (CS) patients with patent foramen ovale (PFO) by their likelihood that the stroke was related to their PFO.

Methods: Using data from 12 component studies, we used generalized linear mixed models to predict the presence of PFO among patients with CS, and derive a simple index to stratify patients with CS. We estimated the stratum-specific PFO-attributable fraction and stratum-specific stroke/TIA recurrence rates.

Results: Variables associated with a PFO in CS patients included younger age, the presence of a cortical stroke on neuroimaging, and the absence of these factors: diabetes, hypertension, smoking, and prior stroke or TIA. The 10-point Risk of Paradoxical Embolism score is calculated from these variables so that the youngest patients with superficial strokes and without vascular risk factors have the highest score. PFO prevalence increased from 23% (95% confidence interval [CI]: 19%–26%) in those with 0 to 3 points to 73% (95% CI: 66%–79%) in those with 9 or 10 points, corresponding to attributable fraction estimates of approximately 0% to 90%. Kaplan-Meier estimated stroke/TIA 2-year recurrence rates decreased from 20% (95% CI: 12%–28%) in the lowest Risk of Paradoxical Embolism score stratum to 2% (95% CI: 0%–4%) in the highest.

Conclusion: Clinical characteristics identify CS patients who vary markedly in PFO prevalence, reflecting clinically important variation in the probability that a discovered PFO is likely to be stroke-related vs incidental. Patients in strata more likely to have stroke-related PFOs have lower recurrence risk. *Neurology*® 2013;81:619–625

GLOSSARY

auROC = area under the receiver operating characteristic curve; **CS** = cryptogenic stroke; **PFO** = patent foramen ovale; **RoPE** = Risk of Paradoxical Embolism.

Neurology 2013;81:619–625

Table 4 RoPE score calculator

Characteristic	Points	RoPE score
No history of hypertension	1	
No history of diabetes	1	
No history of stroke or TIA	1	
Nonsmoker	1	
Cortical infarct on imaging	1	
Age, y		
18-29	5	
30-39	4	
40-49	3	
50-59	2	
60-69	1	
≥70	0	
Total score (sum of individual points)		
Maximum score (a patient <30 y with no hypertension, no diabetes, no history of stroke or TIA, nonsmoker, and cortical infarct)		10
Minimum score (a patient ≥70 y with hypertension, diabetes, prior stroke, current smoker, and no cortical infarct)		0

Abbreviation: RoPE = Risk of Paradoxical Embolism.

SPECIAL ARTICLE LEVEL OF RECOMMENDATION

Practice advisory update summary: Patent foramen ovale and secondary stroke prevention

Report of the Guideline Subcommittee of the American Academy of Neurology

Steven R. Messé, MD, Gary S. Gronseth, MD, David M. Kent, MD, MSc, Jorge R. Kizer, MD, MSc, Shunichi Homma, MD, Lee Rosterman, DO, John D. Carroll, MD, Koto Ishida, MD, Navdeep Sangha, MD, and Scott E. Kasner, MD, MSCE

Correspondence
American Academy of Neurology
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Neurology® 2020;94:876-885. doi:10.1212/WNL.0000000000009443

Abstract

Objective

To update the 2016 American Academy of Neurology (AAN) practice advisory for patients with stroke and patent foramen ovale (PFO).

Methods

The guideline panel followed the AAN 2017 guideline development process to systematically review studies published through December 2017 and formulate recommendations.

MORE ONLINE

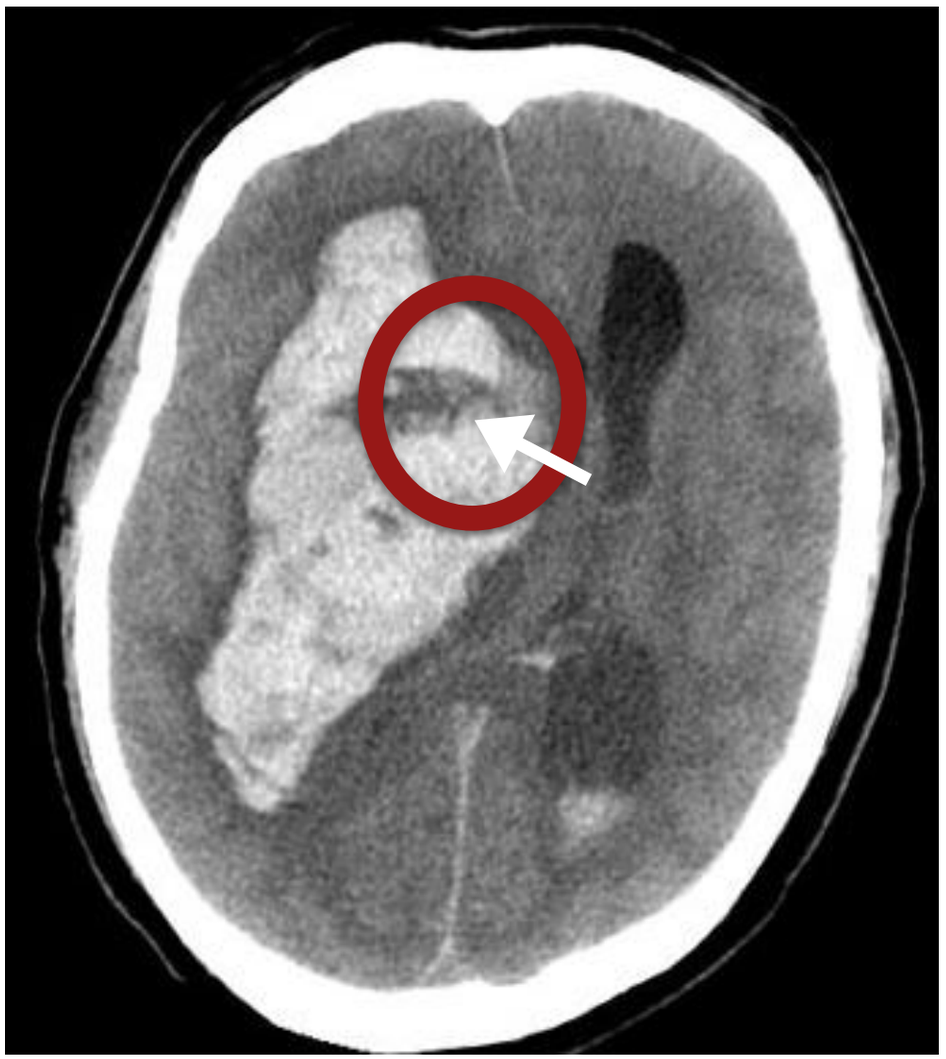
Podcast

Dr. Andrew Southerland talks with Dr. Steven Messé about his practice advisory update paper on patent foramen ovale and secondary stroke prevention.

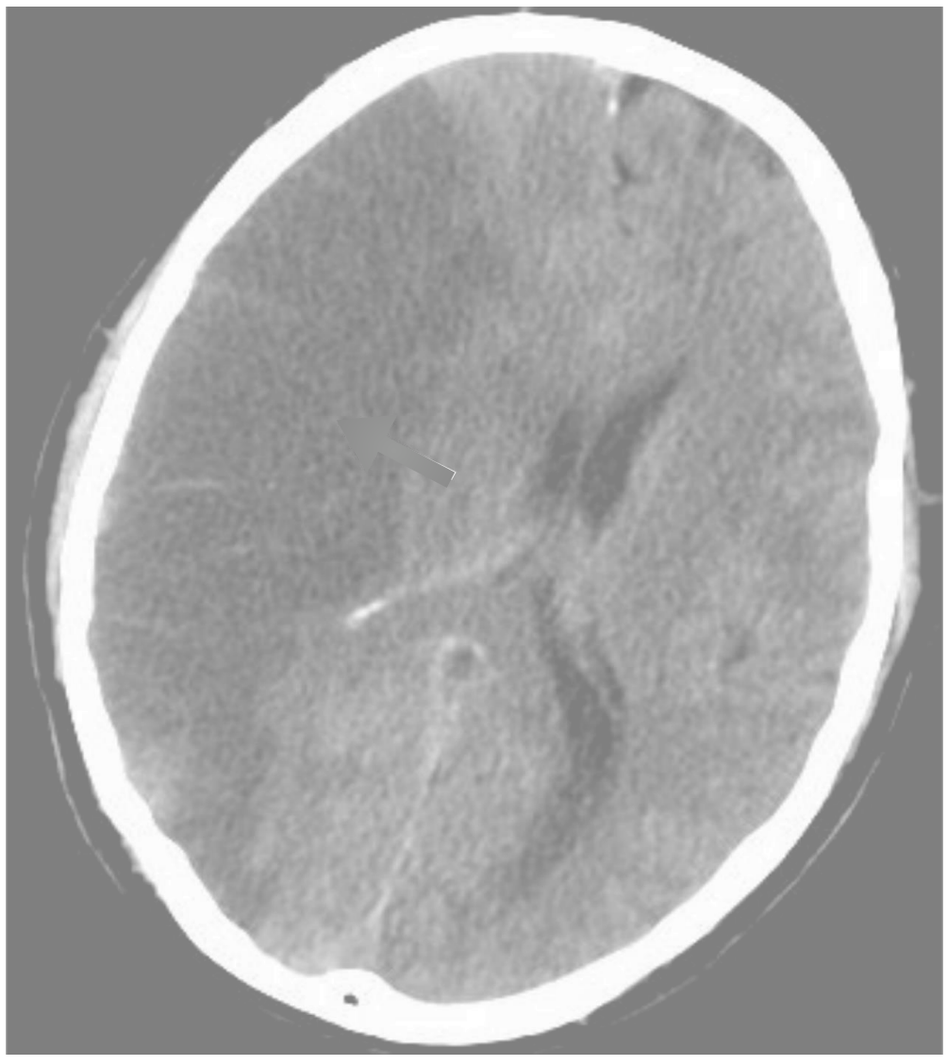
In patients **< 60 years with a PFO and embolic-appearing infarct and no other mechanism of stroke identified**…

may recommend PFO closure following a discussion of potential benefits (**3.4% ARR at 5 years**) and risks (3.9% peri-procedural complication rate and increased absolute rate of non-periprocedural atrial fibrillation of 0.33% per year) (*Level C*).

In patients who opt to receive medical therapy alone without PFO closure, clinicians may recommend an antiplatelet medication such as **aspirin or anticoagulation** (*Level C*).



Hemorrhagic



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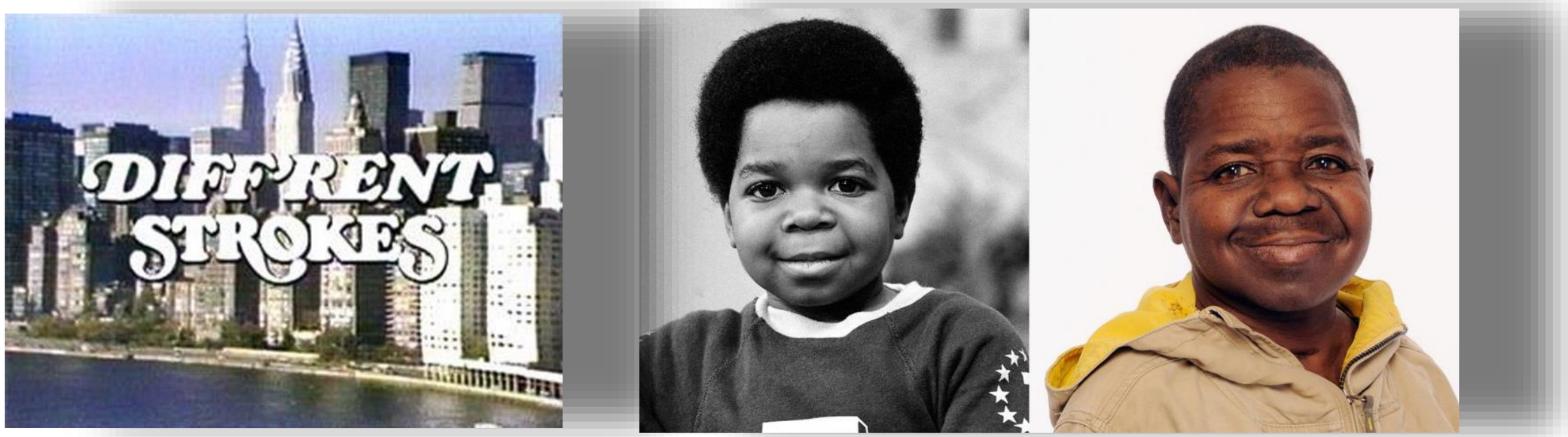

Gary Coleman 1968-2010

- hemorrhagic stroke (subarachnoid and intra-cerebral bleeds) accounts for **up to 50% of all strokes that occur under the age of 45** years

Generally causes are similar in young and older patients

High blood pressure a frequent cause

Illicit drugs implicated more often in younger patients

Increasing Incidence of Hospitalization for Stroke and Transient Ischemic Attack in Young Adults: A Registry-Based Study

Maiken Tibæk, MD; Christian Dehlendorff, PhD, MS; Henrik S. Jørgensen, DMSc, MD; Hysse B. Forchhammer, PhD, NP; Søren P. Johnsen, PhD, MD; Lars P. Kammersgaard, DMSc, MD

***Background*—**Studies have reported increasing incidence of ischemic stroke in adults younger than 50 to 55 years. Information on temporal trends of other stroke subtypes and transient ischemic attack (TIA) is sparse. The aim of this study was to investigate temporal trends of the incidence of hospitalizations for TIA and stroke including sex- and subtype-specific trends in young adults aged 15 to 30 years.

***Methods and Results*—**From the Danish National Patient Register, we identified all cases of first-ever stroke and TIA (age 15–30 years) in Denmark, who were hospitalized during the study period of 1994 to 2012. Incidence rates and estimated annual percentage changes (EAPCs) were estimated by using Poisson regression. During the study period, 4156 cases of first-ever hospitalization for stroke/TIA were identified. The age-standardized incidence rates of hospitalizations for stroke increased significantly (EAPC 1.83% [95% CI 1.11–2.55%]) from 11.97/100 000 person-years (PY) in 1994 to 16.77/100 000 PY in 2012. TIA hospitalizations increased from 1.93/100 000 PY in 1994 to 5.81/100 000 PY in 2012 and after 2006 more markedly in men than in women (EAPC 16.61% [95% CI 10.45–23.12%]). The incidence of hospitalizations for ischemic stroke was markedly lower among men, but increased significantly from 2006 (EAPC 14.60% [95% CI 6.22–23.63%]). The incidences of hospitalizations for intracerebral hemorrhage and subarachnoid hemorrhage remained stable during the study period.

***Conclusions*—**The incidence rates of first-time hospitalizations for ischemic stroke and TIA in young Danish adults have increased substantially since the mid 1990s. The increase was particularly prominent in the most recent years. **(*J Am Heart Assoc*. 2016;5: e003158 doi: 10.1161/JAHA.115.003158)**

ARTICLE

Stroke incidence in young adults according to age, subtype, sex, and time trends

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Objective

To investigate incidence of stroke and its subtypes in young adults, according to sex and age, and to study trends over time.

Methods

We established a nationwide cohort through linkage of national registries (hospital discharge, cause of death, and population register) with patients aged 18–50 years and those ≥50 years with first-ever ischemic stroke, intracerebral hemorrhage, or unspecified stroke, using ICD-9/ICD-10 codes between 1998 and 2010 in the Netherlands. Outcomes were yearly incidence of stroke stratified by age, sex, and stroke subtype, its changes over time, and comparison of incidence in patients 18–50 years to patients ≥50 years.

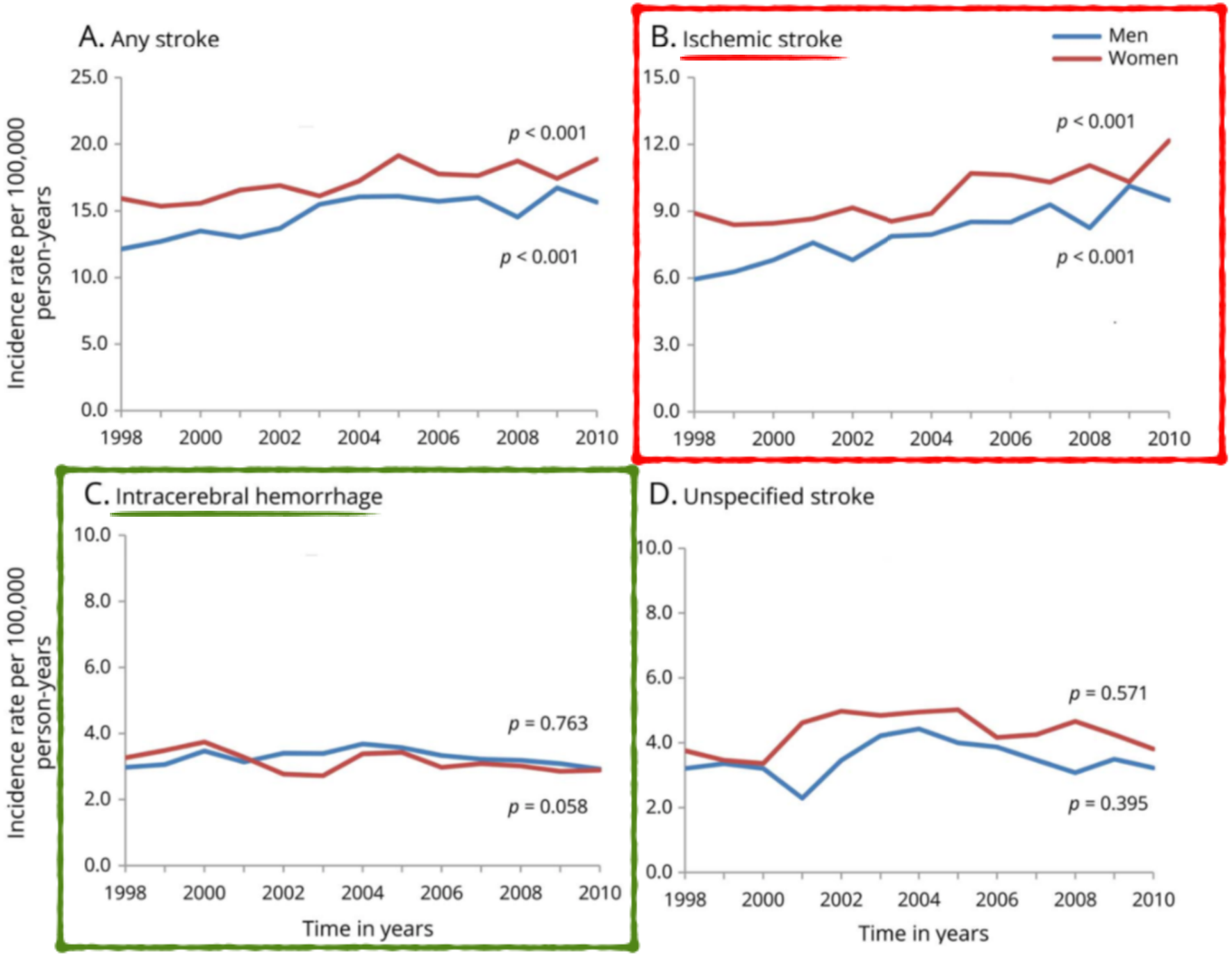
Results

We identified 15,257 patients (53% women; mean age 41.8 years). Incidence increased exponentially with age ($R^2 = 0.99$) and was higher for women than men, most prominently in the youngest patients (18–44 years). The relative proportion of ischemic stroke increased with age (18–24 years: 38.3%; 44–49 years: 56.5%), whereas the relative proportion of intracerebral hemorrhage decreased (18–24 years: 34.0%; 44–49 years: 18.3%). Incidence of any stroke in young adults increased (1998: 14.0/100,000 person-years: 2010: 17.2; +23%; $p < 0.001$), driven by an increase in those aged over 35 years and ischemic stroke incidence (46%), whereas incidence decreased in those ≥50 years (329.1%–292.2%; −11%; $p = 0.009$).

Conclusions

Incidence of any stroke in the young increases with age in patients over 35, is higher in women than men aged 18–44 years, and has increased by 23% in one decade, through an increase in ischemic stroke. Incidence of intracerebral hemorrhage is comparable for women and men and remained stable over time.

Figure 2 Time trends in incidence of stroke and stroke subtypes in young adults from 1998 to 2010



Incidence per 100,000 person-years calculated with Dutch population estimates.[18] *p* Values calculated by linear regression. (A) Any stroke. (B) Ischemic stroke. (C) Intracerebral hemorrhage. (D) Unspecified stroke.

Are More Young People Having Strokes?— A Simple Question With an Uncertain Answer

James F. Burke, MD, MS; Lesli E. Skolarus, MD, MS

Confounders:

- Increase in size of the 18-54 year old US population
- Changes in the measurement system; definitions based on imaging rather than previous time-based
- More accurate coding practices over time
- Hospitals incentivized to select stroke diagnosis over TIA, may explain increasing stroke care cost

JAMA Neurology, 74(6): 639-641.

Research

JAMA Neurology | Original Investigation

Prevalence of Cardiovascular Risk Factors and Strokes in Younger Adults

Mary G. George, MD, MSPH; Xin Tong, MPH; Barbara A. Bowman, PhD

DESIGN, SETTING, AND PARTICIPANTS Hospitalization data from the National Inpatient Sample from 1995 through 2012 were used to analyze acute stroke hospitalization rates among adults aged 18 to 64 years. Hospitalization data from 2003 to 2012 were used to identify the prevalence of associated risk factors for acute stroke. Acute stroke hospitalizations were identified by the principal *International Classification of Diseases, Ninth Revision, Clinical Modification* code and associated risk factors were identified by secondary *International Classification of Diseases, Ninth Revision, Clinical Modification* codes for each hospitalization.

RESULTS The 2003-2004 set included 362 339 hospitalizations and the 2011-2012 set included 421 815 hospitalizations. The major findings in this study are as follows: first, acute ischemic stroke hospitalization rates increased significantly for both men and women and for certain race/ethnic groups among younger adults aged 18 to 54 years; they have almost doubled for men aged 18 to 34 and 35 to 44 years since 1995-1996, with a 41.5% increase among men aged 35 to 44 years from 2003-2004 to 2011-2012. Second, the prevalence of stroke risk factors among those hospitalized for acute ischemic stroke continued to increase from 2003-2004 through 2011-2012 for both men and women aged 18 to 64 years (range of absolute increase: hypertension, 4%-11%; lipid disorders, 12%-21%; diabetes, 4%-7%; tobacco use, 5%-16%; and obesity, 4%-9%). Third, the prevalence of having 3 to 5 risk factors increased from 2003-2004 through 2011-2012 (men: from 9% to 16% at 18-34 years, 19% to 35% at 35-44 years, 24% to 44% at 45-54 years, and 26% to 46% at 55-64 years; women: 6% to 13% at 18-34 years, 15% to 32% at 35-44 years, 25% to 44% at 45-54 years, and 27% to 48% at 55-65 years; *P* for trend < .001). Finally, hospitalization rates for intracerebral hemorrhage and subarachnoid hemorrhage remained stable, with the exception of declines among men and non-Hispanic black patients aged 45 to 54 with subarachnoid hemorrhage (13.2/10 000 to 10.3/10 000 hospitalizations and 15.8/10 000 to 11.5/10 000 hospitalizations, respectively).

CONCLUSIONS AND RELEVANCE The identification of increasing hospitalization rates for acute ischemic stroke in young adults coexistent with increasing prevalence of traditional stroke risk factors confirms the importance of focusing on prevention in younger adults.

Key Points

From National (Nationwide) Inpatient Sample (NIS)

Questions Are stroke hospitalization rates for younger adults continuing to increase, and is the prevalence of associated risk factors increasing among those hospitalized for acute stroke?

Findings This analysis found that stroke hospitalization rates from 2003 to 2012 significantly increased for acute ischemic stroke hospitalization rates among men (41.5%) and women (30%) aged 35 to 44 years, with a near doubling of the prevalence of 3 or more of 5 common stroke risk factors among both men and women aged 18 to 64 years hospitalized for acute ischemic stroke.

Meaning Hospitalization rates for acute ischemic stroke in younger adults continued to increase since 1995-1996, coexistent with increasing prevalence of stroke risk factors.

Contribution of Established Stroke Risk Factors to the Burden of Stroke in Young Adults

Annette Aigner, MA, MSc*; Ulrike Grittner, PhD*; Arndt Rolfs, MD; Bo Norrving, MD; Bob Siegerink, PhD; Markus A. Busch, MD

Background and Purpose—As stroke in young adults is assumed to have different etiologies and risk factors than in older populations, the aim of this study was to examine the contribution of established potentially modifiable cardiovascular risk factors to the burden of stroke in young adults.

Methods—A German nationwide case–control study based on patients enrolled in the SIFAP1 study (Stroke In Young Fabry Patients) 2007 to 2010 and controls from the population-based GEDA study (German Health Update) 2009 to 2010 was performed. Cases were 2125 consecutive patients aged 18 to 55 years with acute first-ever stroke from 26 clinical stroke centers; controls (age- and sex-matched, n=8500, without previous stroke) were from a nationwide community sample. Adjusted population-attributable risks of 8 risk factors (hypertension, hyperlipidemia, diabetes mellitus, coronary heart disease, smoking, heavy episodic alcohol consumption, low physical activity, and obesity) and their combinations for all stroke, ischemic stroke, and primary intracerebral hemorrhage were calculated.

Results—Low physical activity and hypertension were the most important risk factors, accounting for 59.7% (95% confidence interval, 56.3–63.2) and 27.1% (95% confidence interval, 23.6–30.6) of all strokes, respectively. All 8 risk factors combined explained 78.9% (95% confidence interval, 76.3–81.4) of all strokes. Population-attributable risks of all risk factors were similar for all ischemic stroke subtypes. Population-attributable risks of most risk factors were higher in older age groups and in men.

Conclusions—Modifiable risk factors previously established in older populations also account for a large part of stroke in younger adults, with 4 risk factors explaining almost 80% of stroke risk.

Clinical Trial Registration—URL: http://www.clinicaltrials.gov. Unique identifier: NCT00414583.

(*Stroke*. 2017;48:1744-1751. DOI: 10.1161/STROKEAHA.117.016599.)

Table 1 Rates of prevalence of vascular risk factors, (%)

Demographic	Age 18–34 y 2003–2004 → 2011–2012		Age 35–44 y 2003–2004 → 2011–2012		Age 45–54 y 2003–2004 → 2011–2012	
Male						
HTN	34	↑ 41.3	54.5	↑ 65.9	69.7	↑ 76.3
HLD	14.6	↑ 29.1	29	↑ 47.8	34.6	↑ 54.7
Tobacco use	23.1	↑ 35.7	31.3	↑ 41.7	32.5	↑ 47.3
Obesity	6.8	↑ 13.3	7.7	↑ 15.2	6.1	↑ 11.7
Female						
HTN	26.1	↑ 30.7	50.1	↑ 57.3	69.8	↑ 73.7
HLD	9.6	↑ 21.7	20.8	↑ 37.8	32.4	↑ 50.9
Tobacco use	21.1	↑ 26.5	26.9	↑ 35.8	27.4	↑ 43.5
Obesity	9.1	↑ 15.7	10.9	↑ 21	9.9	↑ 17

Abbreviations: HLD = hyperlipidemia; HTN = hypertension.

Prevalence of 3 or more traditional risk factors nearly doubled among young

Registry data 2009-2015

> 1 million patients

~ 2000 hospitals

2.3% aged ≤ 40

American Heart Association | American Stroke Association

GET WITH THE GUIDELINES. STROKE

Table 1 Baseline characteristics of young and old patients with ischemic stroke

Baseline characteristics	Age 18–40 y (n = 30,448)	Age >40 y (n = 1,290,517)	Absolute standardized difference[a]
Patient characteristics			
Medical history, n (%)			
Prosthetic heart valve	482 (1.6)	15,922 (1.24)	3.0
Previous stroke/TIA	5,619 (18.6)	410,136 (32)	31.1
CAD/prior MI	1,626 (5.4)	327,816 (25.6)	58.1
Diabetes	5,331 (17.7)	434,175 (33.9)	37.7
Peripheral vascular disease	258 (0.9)	61,870 (4.8)	24.1
Hypertension	11,834 (39.3)	993,110 (77.5)	84.2
Smoking	9,735 (32.3)	221,879 (17.3)	35.2
Heart failure	1,136 (3.8)	117,468 (9.2)	22.1
Atrial fibrillation/flutter	571 (1.9)	240,660 (18.8)	57.7
Dyslipidemia	4,631 (15.4)	575,808 (44.9)	68.1
Carotid stenosis	206 (0.7)	49,397 (3.9)	21.4

Neurology 2019;92:e2784-e2792.

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Obesity Increases Risk of Ischemic Stroke in Young Adults

Andrew B. Mitchell; John W. Cole, MD, MS; Patrick. F. McArdle, PhD;
Yu-Ching Cheng, PhD; Kathleen A. Ryan, MPH; Mary J. Sparks, RN, BSN;
Braxton D. Mitchell, PhD; Steven J. Kittner, MD, MPH

Background and Purpose—Body mass index has been associated with ischemic stroke in older populations, but its association with stroke in younger populations is not known. In light of the current obesity epidemic in the United States, the potential impact of obesity on stroke risk in young adults deserves attention.

Methods—A population-based case–control study design with 1201 cases and 1154 controls was used to investigate the relationship of obesity and young onset ischemic stroke. Stroke cases were between the ages of 15 and 49 years. Logistic regression analysis was used to evaluate the association between body mass index and ischemic stroke with and without adjustment for comorbid conditions associated with stroke.

Results—In analyses adjusted for age, sex, and ethnicity, obesity (body mass index >30 kg/m^2) was associated with an increased stroke risk (odds ratio, 1.57; 95% confidence interval, 1.28–1.94) although this increased risk was highly attenuated and not statistically significant after adjustment for smoking, hypertension, and diabetes mellitus.

Conclusions—These results indicate that obesity is a risk factor for young onset ischemic stroke and suggest that this association may be partially mediated through hypertension, diabetes mellitus, or other variables associated with these conditions. **(*Stroke*. 2015;46:1690-1692. DOI: 10.1161/STROKEAHA.115.008940.)**

Trends in Substance Abuse Preceding Stroke Among Young Adults

A Population-Based Study

Background and Purpose—Approximately 5% of strokes occur in adults aged 18 to 44 years. Substance abuse is a prevalent risk factor for stroke in young adults. We sought to identify trends in substance abuse detection among stroke patients.

Methods—Using a population-based design, we sought to identify all patients aged 18 to 54 years experiencing a stroke (ischemic or hemorrhagic) in the Greater Cincinnati and Northern Kentucky Study region during 1993 to 1994, 1999, and 2005. Demographic and clinical characteristics and substance use data were obtained retrospectively from chart review and adjudicated by physicians.

Results—The number of young patients identified with a stroke increased from 1993 to 1994 (297) to 2005 (501). Blacks (61% vs 51%; $P<0.02$) and men (61% vs 47%; $P<0.002$) reported substance abuse (current smoking, alcohol, or illegal drug use) more frequently than did whites and women. Overall use of substances increased across study periods, 45% in 1993 versus 62% in 2005 ($P=0.003$). The trend was significant for illegal drug use (3.8% in 1993 vs 19.8% in 2005) and ever smoking (49% in 1993 vs 66% in 2005). Documentation of both cocaine and marijuana use increased over time. In 2005, half of young adults with a stroke were current smokers, and 1 in 5 abused illegal drugs.

Conclusions—Substance abuse is common in young adults experiencing a stroke. The observed increase in substance abuse is contributing to the increased incidence of stroke in young adults. Patients aged younger than 55 years who experience a stroke should be routinely screened and counseled regarding substance abuse. **(*Stroke*. 2012;43:3179–3183.)**

Table 3. Substance Use by Age in Stroke Patients Across Study Periods

	Current Smoker			Illicit Drug Abuse		
Age	1993–1994	1999	2005	1993–1994	1999	2005
18–35 y	15 (38%)	17 (44%)	17 (36%)	5 (12%)	6 (15%)	13 (28%)
35–44 y	26 (41%)	45 (48%)	66 (55%)	2 (3%)	15 (16%)	24 (20%)*
45–54 y	88 (43%)	125 (47%)	162 (53%)	6 (2%)	18 (7%)	59 (19%)†

Data presented as raw n (weighted %).

*Change from 1993–1994 to 2005, $P<0.01$.

†Change from 1993 to 1994 and 1999 to 2005, $P<0.01$.

Cocaine Use and Risk of Ischemic Stroke in Young Adults

Yu-Ching Cheng, PhD; Kathleen A. Ryan, MPH; Saad A. Qadwai, MD; Jay Shah, MD; Mary J. Sparks, RN, BSN; Marcella A. Wozniak, MD, PhD; Barney J. Stern, MD; Michael S. Phipps, MD, MHS; Carolyn A. Cronin, MD, PhD; Laurence S. Magder, MPH, PhD; John W. Cole, MD, MS; Steven J. Kittner, MD, MPH

Background and Purpose—Although case reports have long identified a temporal association between cocaine use and ischemic stroke (IS), few epidemiological studies have examined the association of cocaine use with IS in young adults, by timing, route, and frequency of use.

Methods—A population-based case–control study design with 1090 cases and 1154 controls was used to investigate the relationship of cocaine use and young-onset IS. Stroke cases were between the ages of 15 and 49 years. Logistic regression analysis was used to evaluate the association between cocaine use and IS with and without adjustment for potential confounders.

Results—Ever use of cocaine was not associated with stroke with 28% of cases and 26% of controls reporting ever use. In contrast, acute cocaine use in the previous 24 hours was strongly associated with increased risk of stroke (age–sex–race adjusted odds ratio, 6.4; 95% confidence interval, 2.2–18.6). Among acute users, the smoking route had an adjusted odds ratio of 7.9 (95% confidence interval, 1.8–35.0), whereas the inhalation route had an adjusted odds ratio of 3.5 (95% confidence interval, 0.7–16.9). After additional adjustment for current alcohol, smoking use, and hypertension, the odds ratio for acute cocaine use by any route was 5.7 (95% confidence interval, 1.7–19.7). Of the 26 patients with cocaine use within 24 hours of their stroke, 14 reported use within 6 hours of their event.

Conclusions—Our data are consistent with a causal association between acute cocaine use and risk of early-onset IS.
(*Stroke*. 2016;47:918-922. DOI: 10.1161/STROKEAHA.115.011417.)

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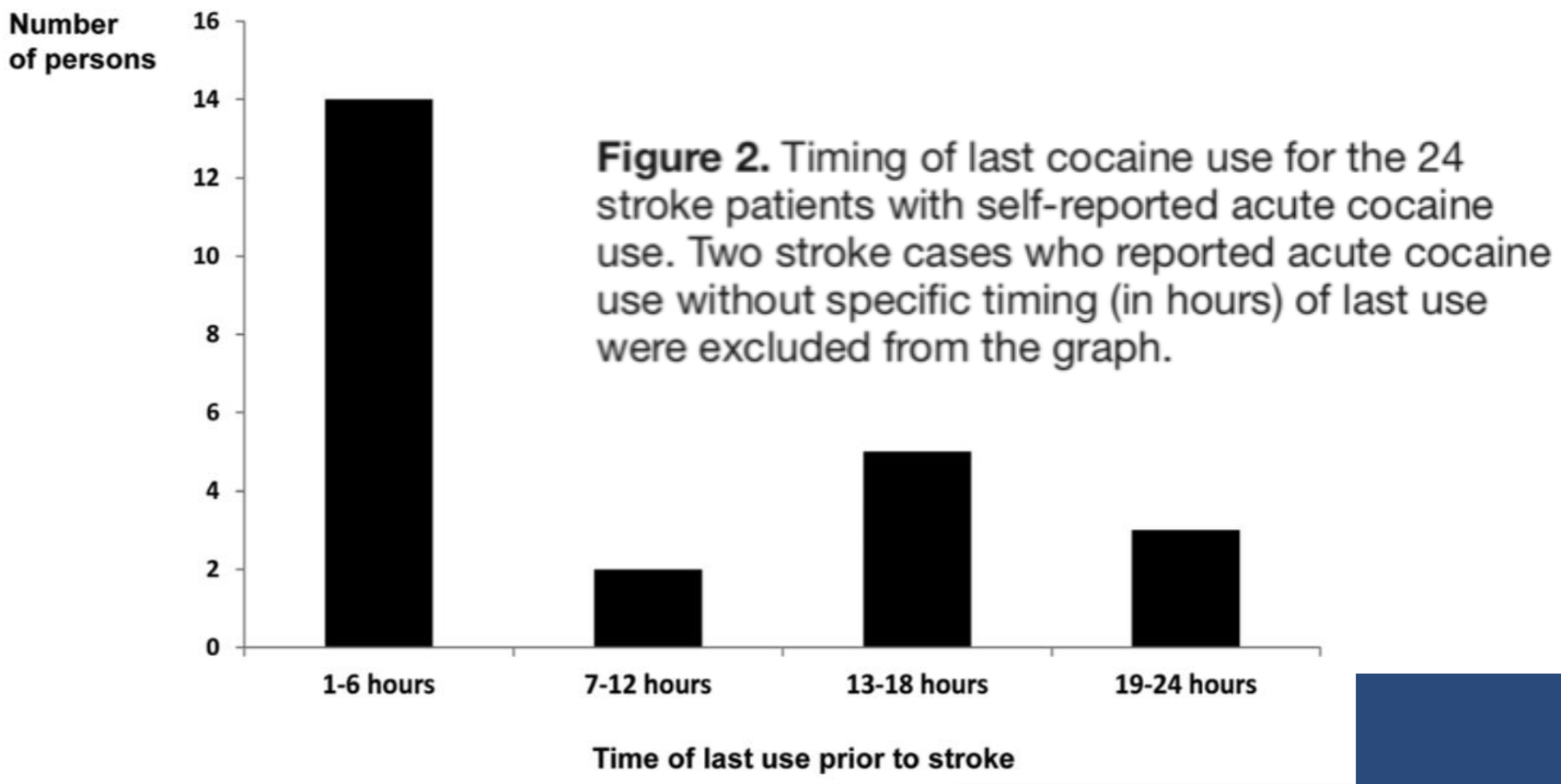

Figure 2. Timing of last cocaine use for the 24 stroke patients with self-reported acute cocaine use. Two stroke cases who reported acute cocaine use without specific timing (in hours) of last use were excluded from the graph.

Thrombolysis in young adults with stroke

Findings from Get With The Guidelines–Stroke

Abstract

Objective

To determine whether young adults (≤40 years old) with acute ischemic stroke are less likely to receive IV tissue plasminogen activator (tPA) and more likely to have longer times to brain imaging and treatment.

Methods

We analyzed data from the Get With The Guidelines–Stroke registry for patients with acute ischemic stroke hospitalized between January 2009 and September 2015. We used multivariable models with generalized estimating equations to evaluate tPA treatment and outcomes between younger (age 18–40 years) and older (age >40 years) patients with acute ischemic stroke.

Results

Of 1,320,965 patients with acute ischemic stroke admitted to 1,983 hospitals, 2.3% (30,448) were 18 to 40 years of age. Among these patients, 12.5% received tPA vs 8.8% of those >40 years of age (adjusted odds ratio [aOR] 1.63, 95% confidence interval [CI] 1.56–1.71). However, younger patients were less likely to receive brain imaging within 25 minutes (62.5% vs 71.5%, aOR 0.78, 95% CI 0.73–0.84) and to be treated with tPA within 60 minutes of hospital arrival (37.0% vs 42.8%, aOR 0.74, 95% CI 0.68–0.79). Compared to older patients, younger patients treated with tPA had a lower symptomatic intracranial hemorrhage rate (1.7% vs 4.5%, aOR 0.55, 95% CI 0.42–0.72) and lower in-hospital mortality (2.0% vs 4.3%, aOR 0.65, 95% CI 0.52–0.81).

Conclusions

In contrast to our hypothesis, younger patients with acute ischemic stroke were more likely to be treated with tPA than older patients, but they were more likely to experience delay in evaluation and treatment. Compared with older patients, younger patients had better outcomes, including fewer intracranial hemorrhages.

Neurology 2019;92:e2784-e2792.

Table 2 Treatment and evaluation times in young and old patients with ischemic stroke treated with tPA

Measures	Age 18–40 y	Age >40 y	Adjusted difference (95% CI), min
Door-to-imaging time, median (IQR), min	20 (12–33)	18 (11–27)	2.53 (1.89–3.17)
Door-to-imaging time ≤25 min, n (%)	2,212/3,537 (62.5)	75,825/106,026 (71.5)	0.78 (0.73–0.84)
Door-to-needle time, median (IQR), min	72 (52–101)	66 (50–90)	7.34 (6.12–8.56)
Door-to-needle time ≤60 min, n (%)	1,395/3,767 (37.0)	48,225/112,599 (42.8)	0.74 (0.68–0.79)

Abbreviations: CI = confidence interval; tPA = tissue plasminogen activator.

National STROKE Association™

F **FACE:** Ask the person to smile. Does one side of the face droop?

A **ARMS**: Ask the person to raise both arms. Does one arm drift downward?

S **SPEECH**: Ask the person to repeat a simple phrase. Is their speech slurred or strange?

T **TIME**: If you observe any of these signs, call 9-1-1 immediately.

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