ESC Heart & Brain Workshop

Atherosclerosis and stroke

Prof. Natan M. Bornstein M.D.
Director of Brain Division,
Shaare Zedek Medical Center, Jerusalem
Chairman of the Israeli Neurological Association
Vice President of the WSO
natanb@szmc.org.il

Supported by Bayer, Bristol-Myers Squibb and Pfizer Alliance, Boehringer Ingelheim, Daiichi Sankyo Europe GmbH and Medtronic in the form of educational grants. The scientific programme has not been influenced in any way by its sponsors.

ESC Council Stroke

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Declaration of Interest:

none

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ESC Council Stroke

BAYER

Boehringer Ingelheim

Daiichi-Sankyo

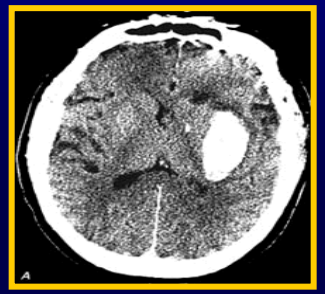
Bristol-Myers Squibb

Pfizer

Medtronic
Further, Together

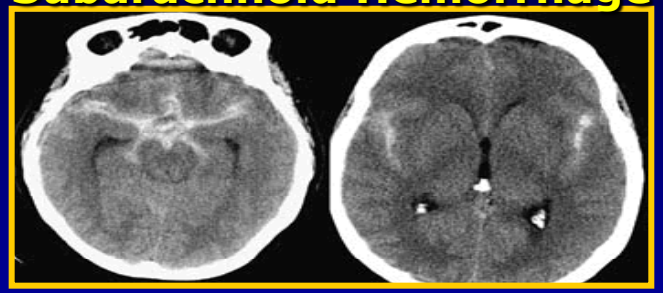
Cerebrovascular Disease: Stroke Subtype

Hemorrhagic Stroke (15%)



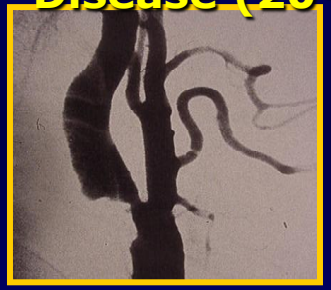
Intracerebral Hemorrhage (59%)

Subarachnoid Hemorrhage (41%)



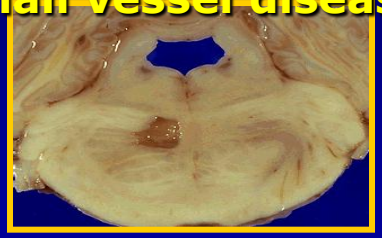
Ischemic Stroke (85%)

Atherothrombotic Cerebrovascular Disease (20%)

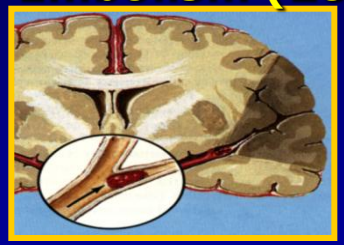


Cryptogenic (30%)

Lacunar (25%) Small vessel disease



Embolism (20%)

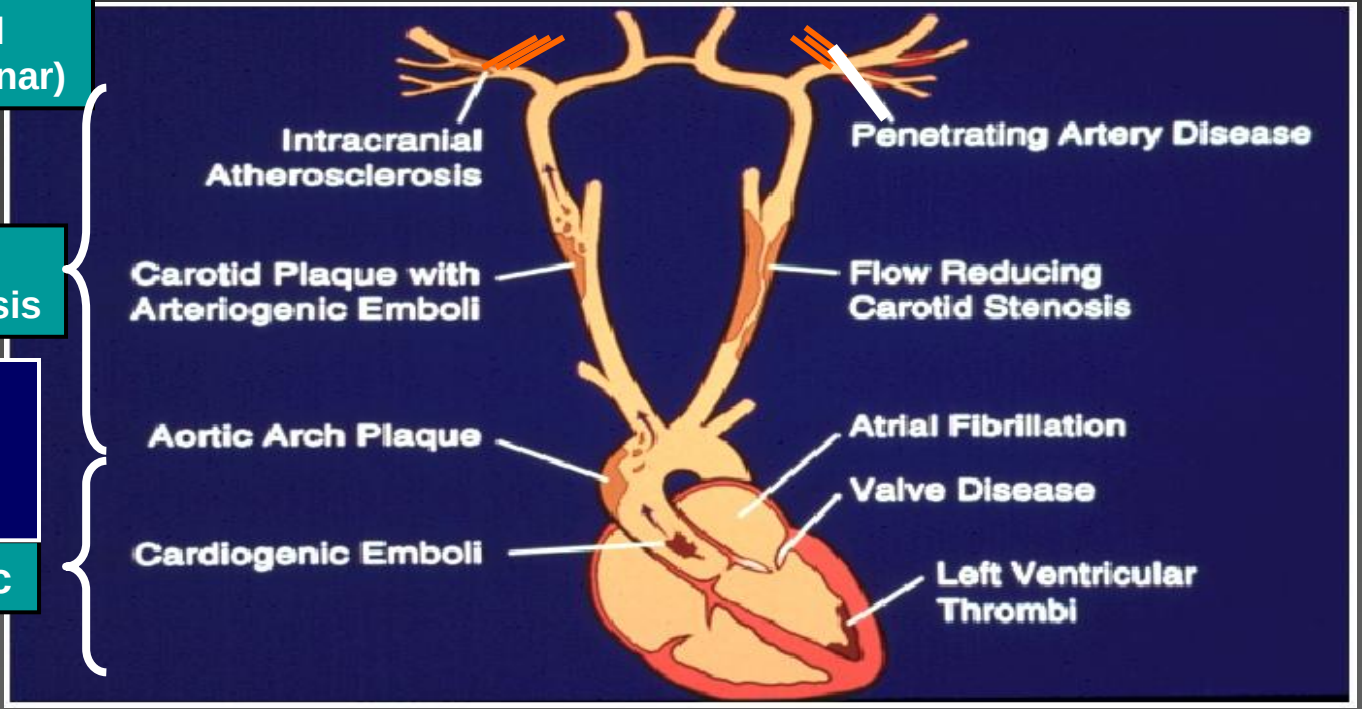


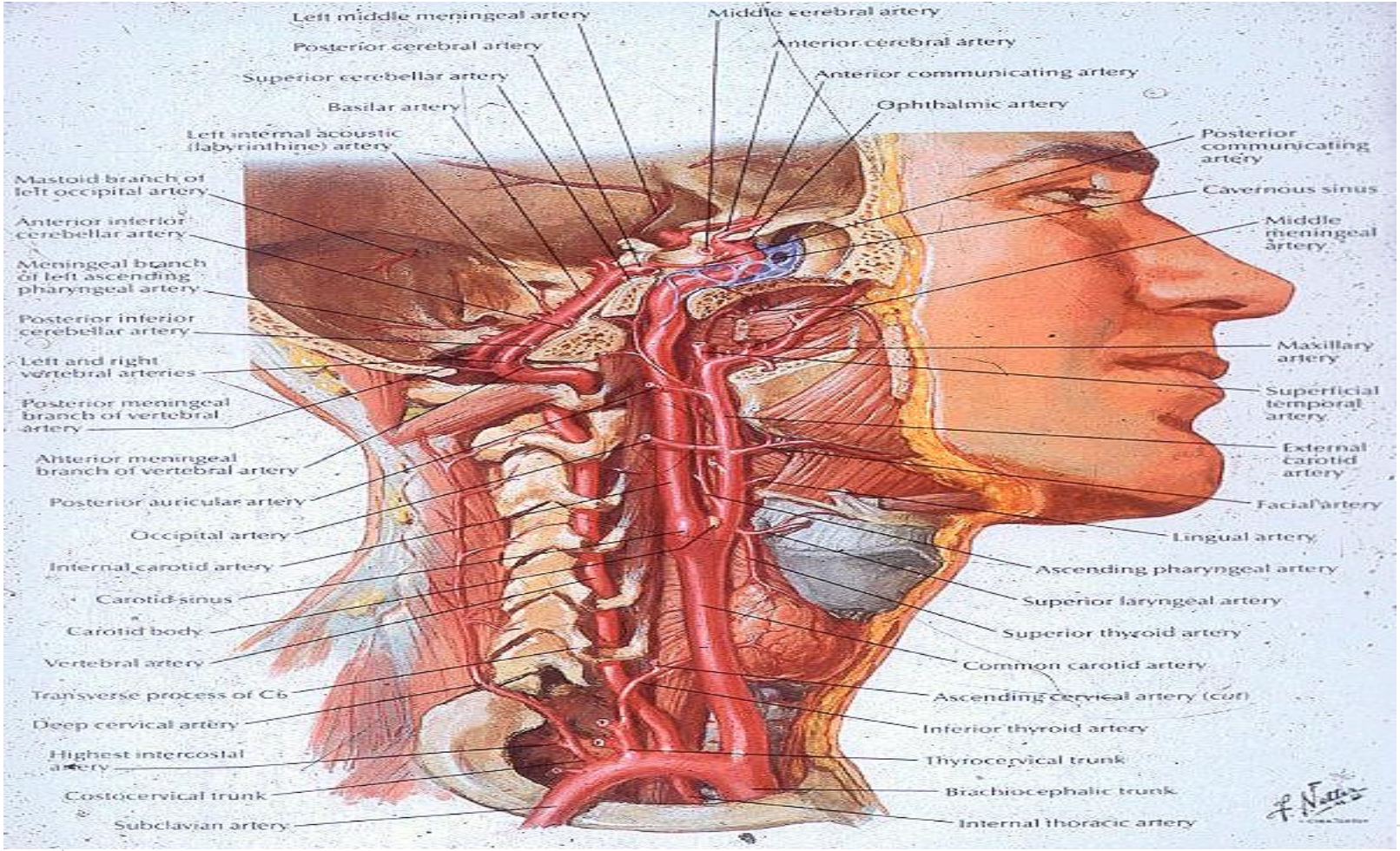
Albers GW, et al. *Chest*. 1998;114:683S-698S.
Rosamond WD, et al. *Stroke*. 1999;30:736-743.

STROKE

ICH

- Small vessel Occlusive (lacunar)
- Large vessel Atherothrombosis
- Other determined
- Undetermined
- Cardioembolic





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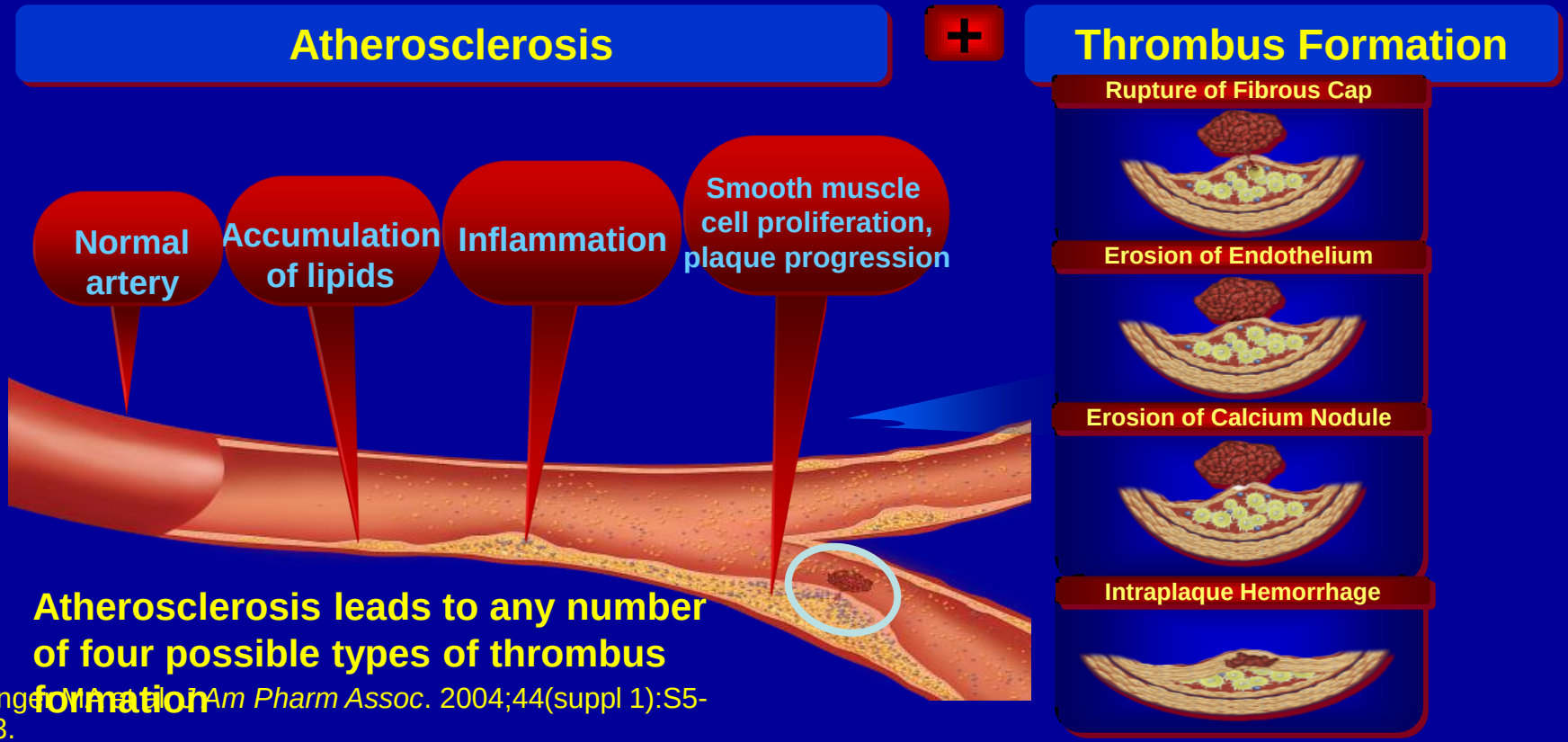
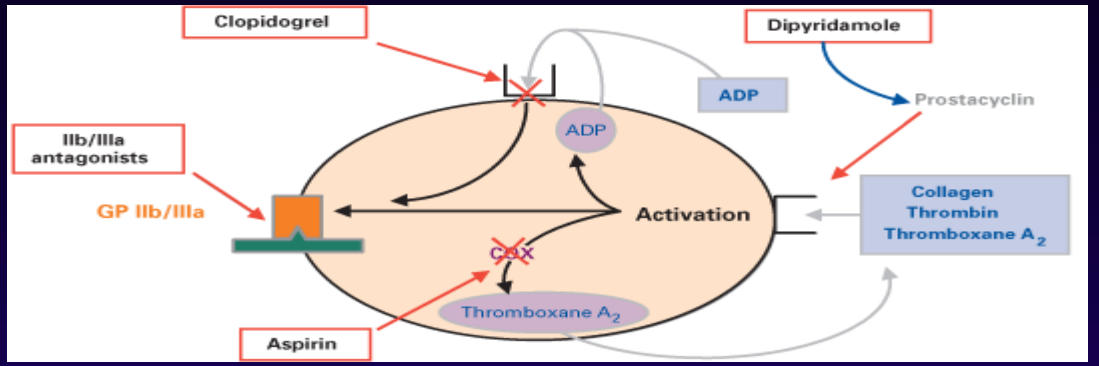
Pathophysiology of Atherothrombosis



1. Mungen M et al. *J Am Pharm Assoc*. 2004;44(suppl 1):S5-S13.
2. Libby P et al. *Circulation*. 2005;111:3481-3488.

Antiplatelets



Clopidogrel

Block ADP receptors

Aspirin

Inhibits cyclooxygenase and thromboxane A_2

Dipyridamole

Increases plasma adenosine

Inhibits platelet phosphodiesterase

Inhibition of platelet activation and aggregation

ESO recomendation - 2008

- **Patients are recommended to take antithrombotic therapy (Class I, Level A) .**

- **Those not requiring anticoagulation are recommended to take antiplatelet therapy (Class I, Level A). Where possible, combined aspirin and dipyridamole, or clopidogrel alone, should be taken. Alternatively, aspirin alone, or triflusal alone, may be used (Class I, Level A)**

- **The combination of aspirin and clopidogrel is not recommended in patients with recent ischemic stroke except in patients with specific indications, e.g. unstable angina or non-Q-wave MI during the last 12**

AHA/ASA Guideline

Guidelines for the Prevention of Stroke in Patients With Stroke and Transient Ischemic Attack

A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association

The American Academy of Neurology affirms the value of this guideline as an educational tool for neurologists.

Endorsed by the American Association of Neurological Surgeons and Congress of Neurological Surgeons

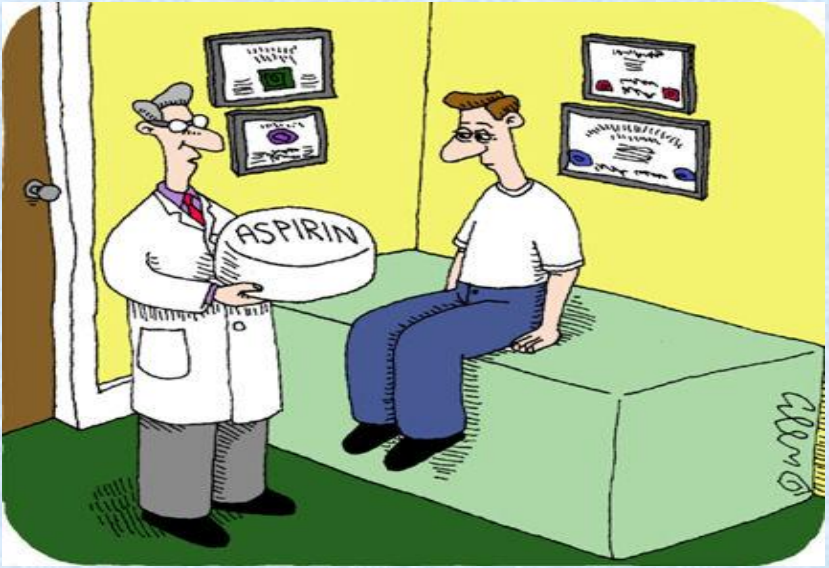
Walter N. Kernan, MD, Chair; Bruce Ovbiagele, MD, MSc, MAS, Vice Chair; Henry R. Black, MD; Dawn M. Bravata, MD; Marc I. Chimowitz, MBChB, FAHA; Michael D. Ezekowitz, MBChB, PhD; Margaret C. Fang, MD, MPH; Marc Fisher, MD, FAHA; Karen L. Furie, MD, MPH, FAHA; Donald V. Heck, MD; S. Claiborne (Clay) Johnston, MD, PhD; Scott E. Kasner, MD, FAHA; Steven J. Kittner, MD, MPH, FAHA; Pamela H. Mitchell, PhD, RN, FAHA; Michael W. Rich, MD; DeJuran Richardson, PhD; Lee H. Schwamm, MD, FAHA; John A. Wilson, MD; on behalf of the American Heart Association Stroke Council, Council on Cardiovascular and Stroke Nursing, Council on Clinical Cardiology, and Council on Peripheral Vascular Disease

Abstract—The aim of this updated guideline is to provide comprehensive and timely evidence-based recommendations on the prevention of future stroke among survivors of ischemic stroke or transient ischemic attack. The guideline is addressed to all clinicians who manage secondary prevention for these patients. Evidence-based recommendations are provided for control of risk factors, intervention for vascular obstruction, antithrombotic therapy for cardioembolism, and antiplatelet therapy for noncardioembolic stroke. Recommendations are also provided for the prevention of recurrent stroke in a variety of specific circumstances, including aortic arch atherosclerosis, arterial dissection, patent foramen ovale, hyperhomocysteinemia, hypercoagulable states, antiphospholipid antibody syndrome, sickle cell disease, cerebral venous sinus thrombosis, and pregnancy. Special sections address use of antithrombotic and anticoagulation therapy after an intracranial hemorrhage and implementation of guidelines. (***Stroke***. 2014;45:2160-2236.)

Key Words: AHA Scientific Statements ■ atrial fibrillation ■ carotid stenosis ■ hypertension ■ ischemia ■ ischemic attack, transient ■ prevention ■ stroke

ESC Council Stroke

Antiplatelets



- Aspirin offers **15%** relative risk reduction for stroke after TIA or stroke
- Most widely studied dosages of aspirin are 50-150mg
- Aspirin, ASA+Dipyridamole, Clopidogrel are all acceptable initial therapy.

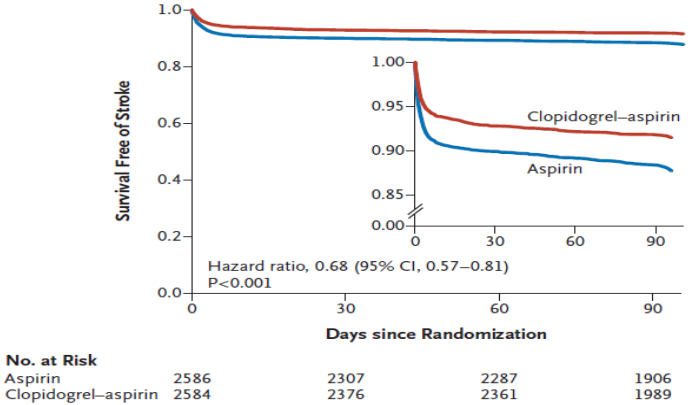
Long term Clopidogrel + Aspirin

Short-term DAPT after high-risk TIA/minor stroke?

ORIGINAL ARTICLE

Clopidogrel with Aspirin in Acute Minor Stroke or Transient Ischemic Attacl

CHANCE



No. at Risk

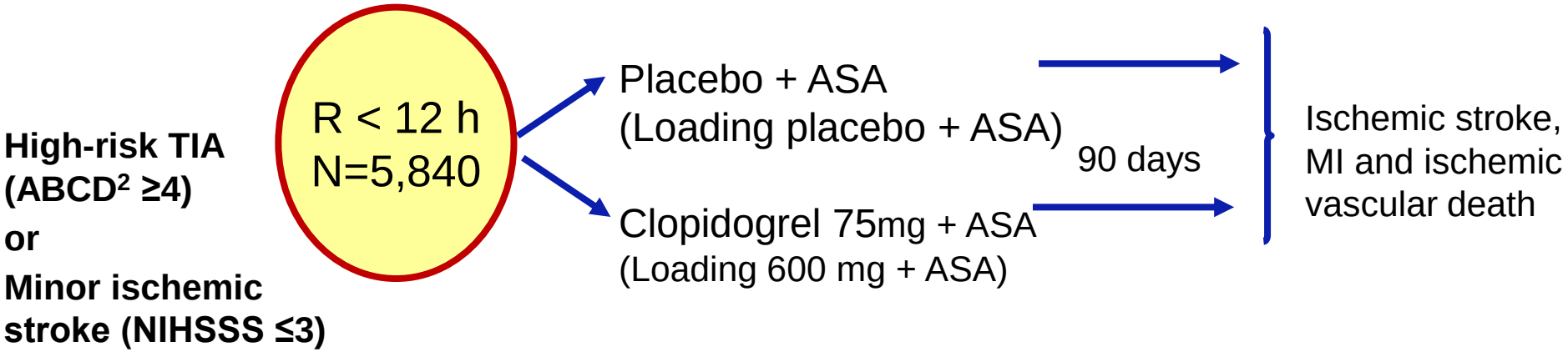
Aspirin	2586	2307	2287	1906
Clopidogrel–aspirin	2584	2376	2361	1989

Hazard ratio, 0.68 (95% CI, 0.57–0.81)
P<0.001

Clopidogrel 300 mg loading followed by 75 mg daily for 90 days + aspirin at a dose of 75 mg daily for the first 21 days **vs.** aspirin only in a Chinese population

N Engl J Med 2013;369:11-19.

Platelet-Oriented Inhibition in New TIA and minor ischemic stroke



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The NEW ENGLAND JOURNAL of MEDICINE

EDITORIALS

Ticagrelor — Is There Need for a New Player in the Antiplatelet-Therapy Field?

Albert Schömig, M.D.

N Engl J Med 361:1108, September 10, 2009 *Editorial*

ESC Council Stroke

SOCRATES

Acute Stroke Or Transient IsChaemic Attack TReated With Aspirin or Ticagrelor and Patient OutcomES

Sponsor
AstraZeneca

R < 24 h
N=13,600

High-risk TIA (ABCD² ≥4)
or
Minor ischemic stroke (NIHSSS ≤5)

Aspirin 100mg
(Loading 300 mg)

Ticagrelor 90 mg bid
(Loading 180 mg)

A P2Y12 inhibitor

90 days

Composite of stroke, MI and death

The NEW ENGLAND JOURNAL of MEDICINE

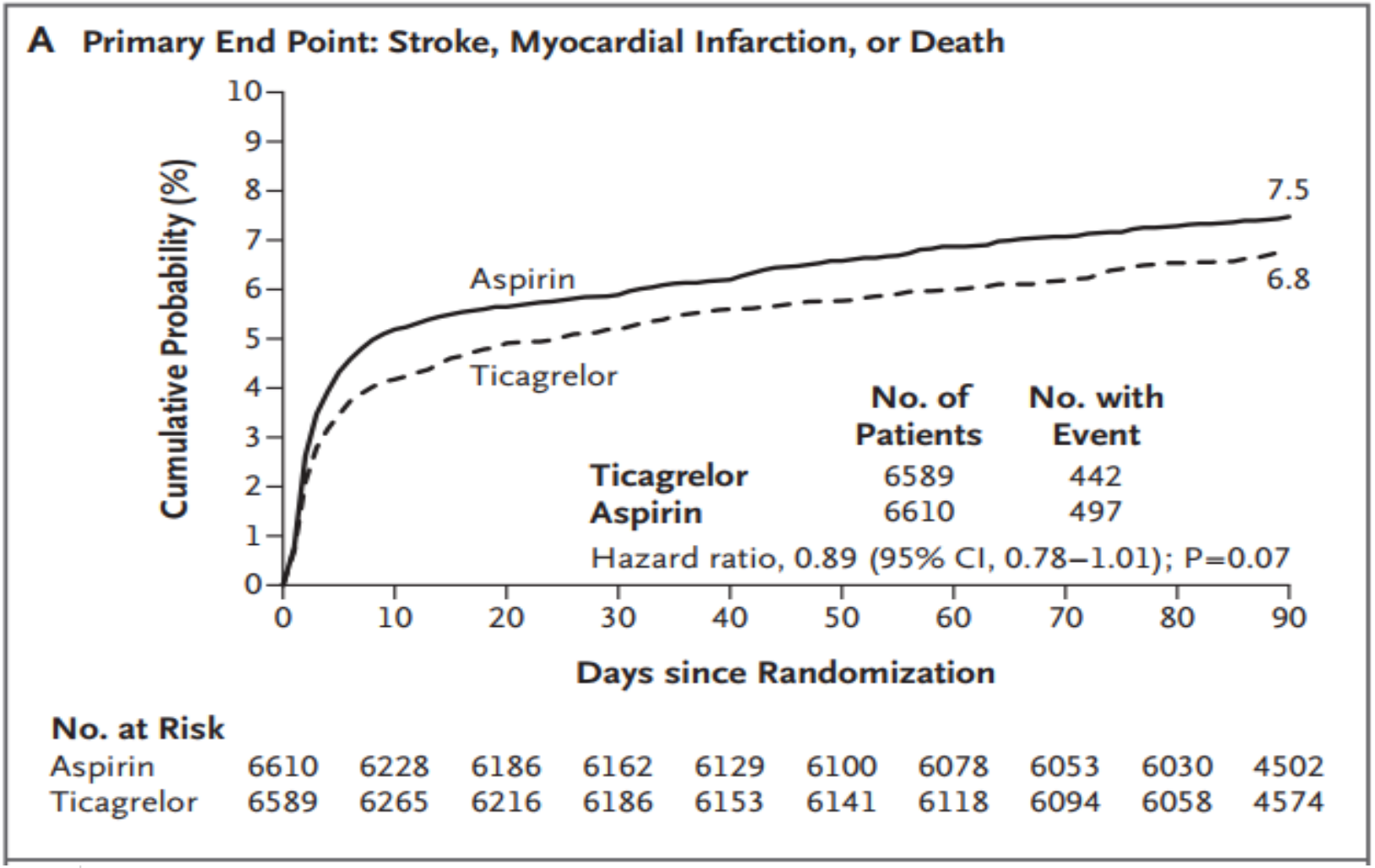
ORIGINAL ARTICLE

Ticagrelor versus Aspirin in Acute Stroke or Transient Ischemic Attack

S. Claiborne Johnston, M.D., Ph.D., Pierre Amarenco, M.D., Gregory W. Albers, M.D., Hans Denison, M.D., Ph.D., J. Donald Easton, M.D., Scott R. Evans, Ph.D., Peter Held, M.D., Ph.D., Jenny Jonasson, Ph.D., Kazuo Minematsu, M.D., Ph.D., Carlos A. Molina, M.D., Yongjun Wang, M.D., and K.S. Lawrence Wong, M.D., for the SOCRATES Steering Committee and Investigators*

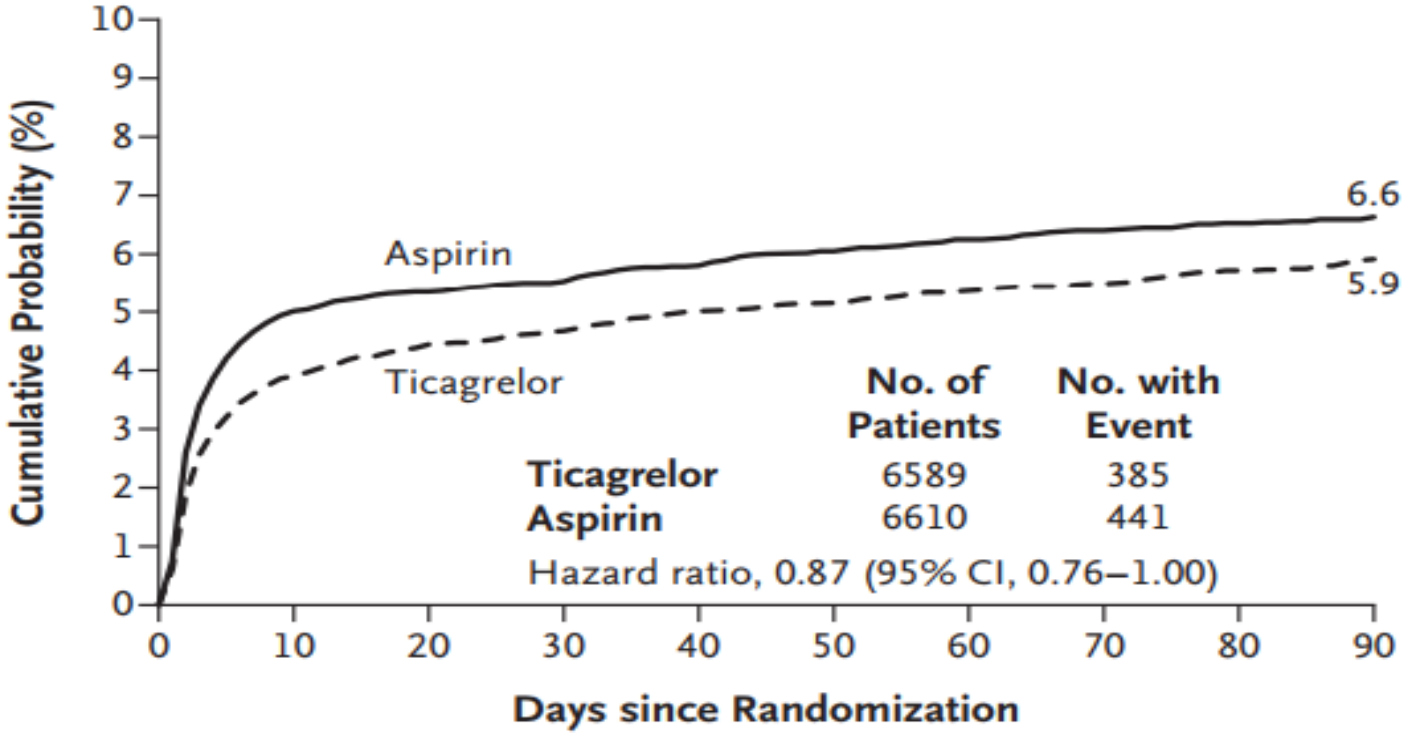
N Engl J Med 2016;375:35-43.

ESC Council Stroke



ESC Council Stroke

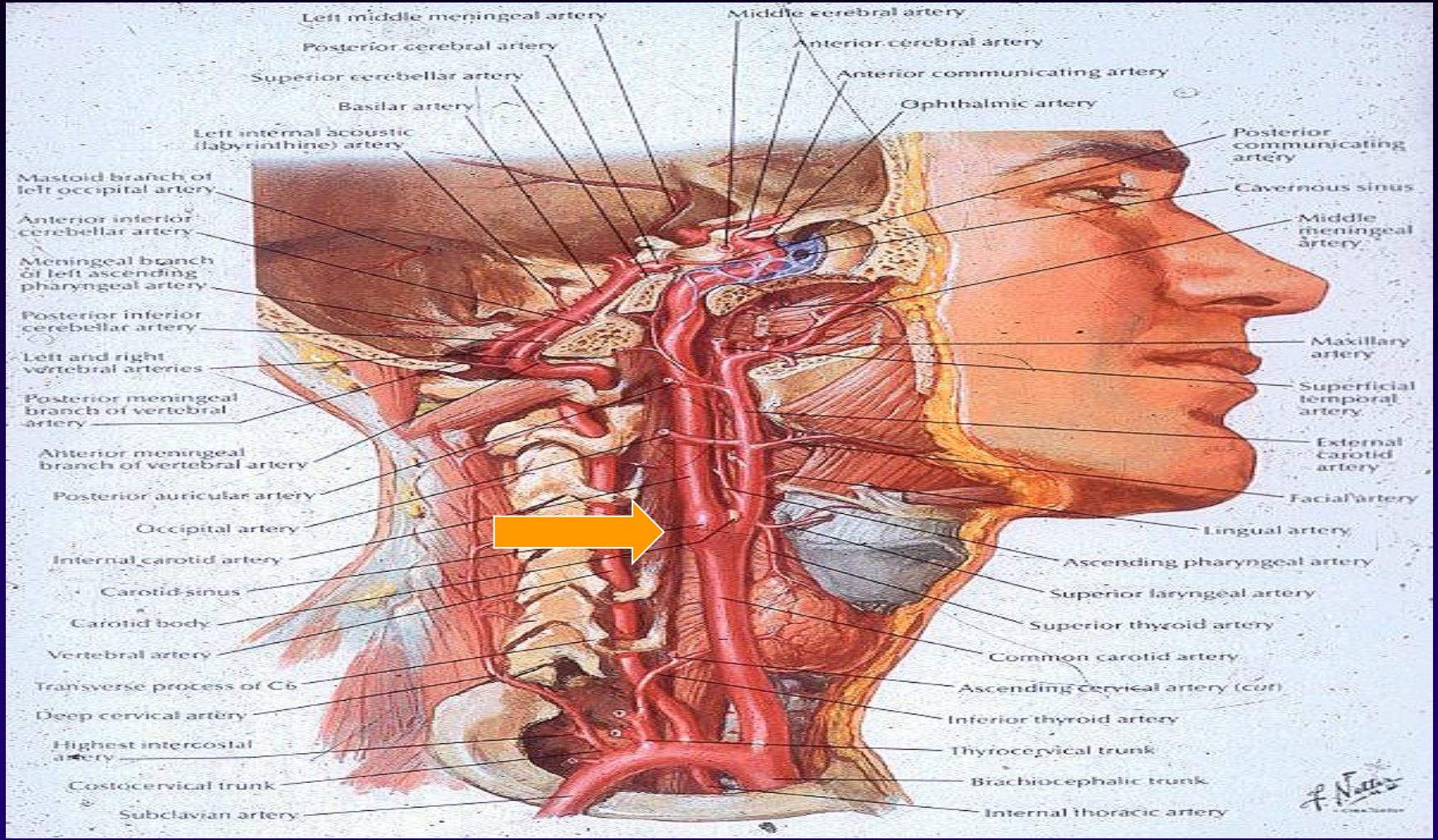
B **Ischemic Stroke**



No. at Risk

Aspirin	6610	6230	6193	6169	6134	6112	6092	6065	6046	4518
Ticagrelor	6589	6272	6230	6204	6169	6157	6133	6102	6073	4587

ESC Council Stroke


Left middle meningeal artery
Middle cerebral artery
Posterior cerebral artery
Anterior cerebral artery
Superior cerebellar artery
Anterior communicating artery
Basilar artery
Ophthalmic artery
Left internal acoustic (labyrinthine) artery
Posterior communicating artery
Mastoid branch of left occipital artery
Cavernous sinus
Anterior inferior cerebellar artery
Middle meningeal artery
Meningeal branch of left ascending pharyngeal artery
Posterior inferior cerebellar artery
Maxillary artery
Left and right vertebral arteries
Superficial temporal artery
Posterior meningeal branch of vertebral artery
External carotid artery
Anterior meningeal branch of vertebral artery
Facial artery
Posterior auricular artery
Occipital artery
Lingual artery
Internal carotid artery
Ascending pharyngeal artery
Carotid sinus
Superior laryngeal artery
Carotid body
Superior thyroid artery
Vertebral artery
Common carotid artery
Transverse process of C6
Ascending cervical artery (cut)
Deep cervical artery
Inferior thyroid artery
Highest intercostal artery
Thyrocervical trunk
Costocervical trunk
Brachiocephalic trunk
Subclavian artery
Internal thoracic artery

Efficacy and safety of ticagrelor versus aspirin in acute stroke or transient ischaemic attack of atherosclerotic origin: a subgroup analysis of SOCRATES, a randomised, double-blind, controlled trial

Pierre Amarenco, Gregory W Albers, Hans Denison, J Donald Easton, Scott R Evans, Peter Held, Michael D Hill, Jenny Jonasson, Scott E Kasner, Per Ladenvall, Kazuo Minematsu, Carlos A Molina, Yongjun Wang, K S Lawrence Wong, S Claiborne Johnston, for the SOCRATES Steering Committee and Investigators

Lancet Neurol 2017

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Department of Neurology and Stroke Center, Bichat University Hospital and Paris-Diderot, Sorbonne University, Paris, France (Prof P Amarenco MD); Stanford University Medical Center, Stanford Stroke Center, Palo Alto, CA, USA (Prof G W Albers MD); AstraZeneca, Gothenburg, Sweden (H Dennison MD, P Held MD, J Jonasson PhD, P Ladenvall MD); Department of Neurology, University of California, San Francisco, San Francisco, CA, USA (Prof J D Easton MD); Department of Biostatistics, Harvard T.H. Chan School of Public Health, Boston, MA, USA (Prof S R Evans PhD); Department of Clinical Neurosciences, Hotchkiss Brain Institute, University of Calgary, Calgary, AB, Canada (Prof M D Hill MD); Department of Neurology, Perelman School of Medicine, University of Pennsylvania Health System, Philadelphia, PA, USA (Prof S E Kasner MD); National Cerebral and Cardiovascular

Summary

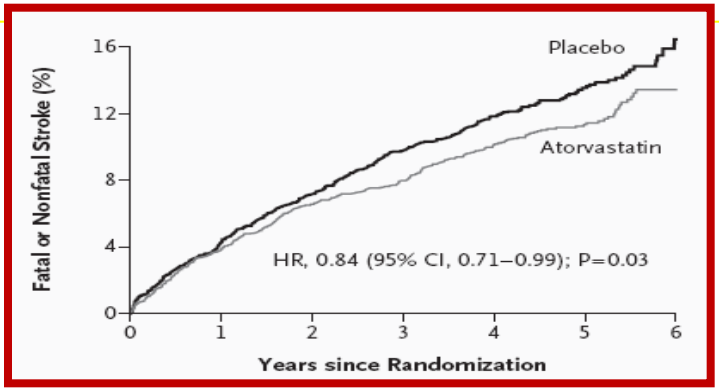
Background Ticagrelor is an effective antiplatelet therapy for patients with coronary atherosclerotic disease and might be more effective than aspirin in preventing recurrent stroke and cardiovascular events in patients with acute cerebral ischaemia of atherosclerotic origin. Our aim was to test for a treatment-by-ipsilateral atherosclerotic stenosis interaction in a subgroup analysis of patients in the Acute Stroke or Transient Ischaemic Attack Treated with Aspirin or Ticagrelor and Patient Outcomes (SOCRATES) trial.

Methods SOCRATES was a randomised, double-blind, controlled trial of ticagrelor versus aspirin in patients aged 40 years or older with a non-cardioembolic, non-severe acute ischaemic stroke, or high-risk transient ischaemic attack from 674 hospitals in 33 countries. We randomly allocated patients (1:1) to ticagrelor (180 mg loading dose on day 1 followed by 90 mg twice daily for days 2–90, given orally) or aspirin (300 mg on day 1 followed by 100 mg daily for days 2–90, given orally) within 24 h of symptom onset. Investigators classified all patients into atherosclerotic and non-atherosclerotic groups for the prespecified, exploratory analysis reported in this study. The primary endpoint was the time to occurrence of stroke, myocardial infarction, or death within 90 days. Efficacy analysis was by intention to treat. The SOCRATES trial is registered with ClinicalTrials.gov, number NCT01994720.

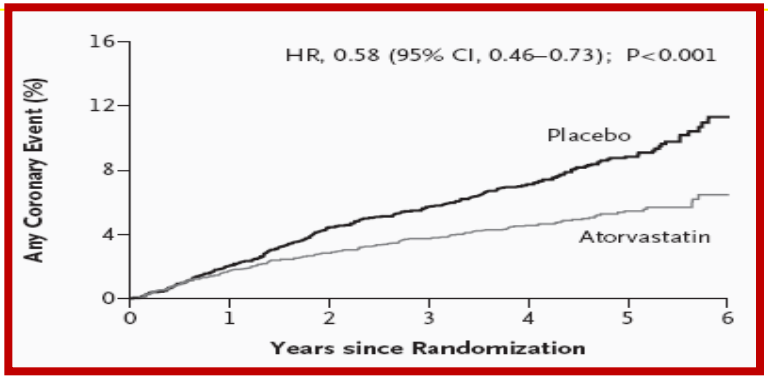
Findings Between Jan 7, 2014, and Oct 29, 2015, we randomly allocated 13 199 patients (6589 [50%] to ticagrelor and 6610 [50%] to aspirin). Potentially symptomatic ipsilateral atherosclerotic stenosis was reported in 3081 (23%) of 13 199 patients. We found a treatment-by-atherosclerotic stenosis interaction (p=0·017). 103 (6·7%) of 1542 patients with ipsilateral stenosis in the ticagrelor group and 147 (9·6%) of 1539 patients with ipsilateral stenosis in the aspirin group had an occurrence of stroke, myocardial infarction, or death within 90 days (hazard ratio 0·68 [95% CI 0·53–0·88]; p=0·003). In 10 118 patients with no ipsilateral stenosis, 339 (6·7%) of 5047 patients in the ticagrelor group had an occurrence of stroke, myocardial infarction, or death within 90 days compared with 350 (6·9%) of 5071 in the aspirin group (0·97 [0·84–1·13]; p=0·72). There were no significant differences in the proportion of life-threatening bleeding or major or minor bleeding events in patients with ipsilateral stenosis in the ticagrelor group compared with the aspirin group.

Interpretation In this prespecified exploratory analysis, ticagrelor was superior to aspirin at preventing stroke, myocardial infarction, or death at 90 days in patients with acute ischaemic stroke or transient ischaemic attack when associated with ipsilateral atherosclerotic stenosis. An understanding of stroke mechanisms and causes is important to deliver safe and efficacious treatments for early stroke prevention.

Statins After Stroke



Fatal or nonfatal stroke



Any coronary event

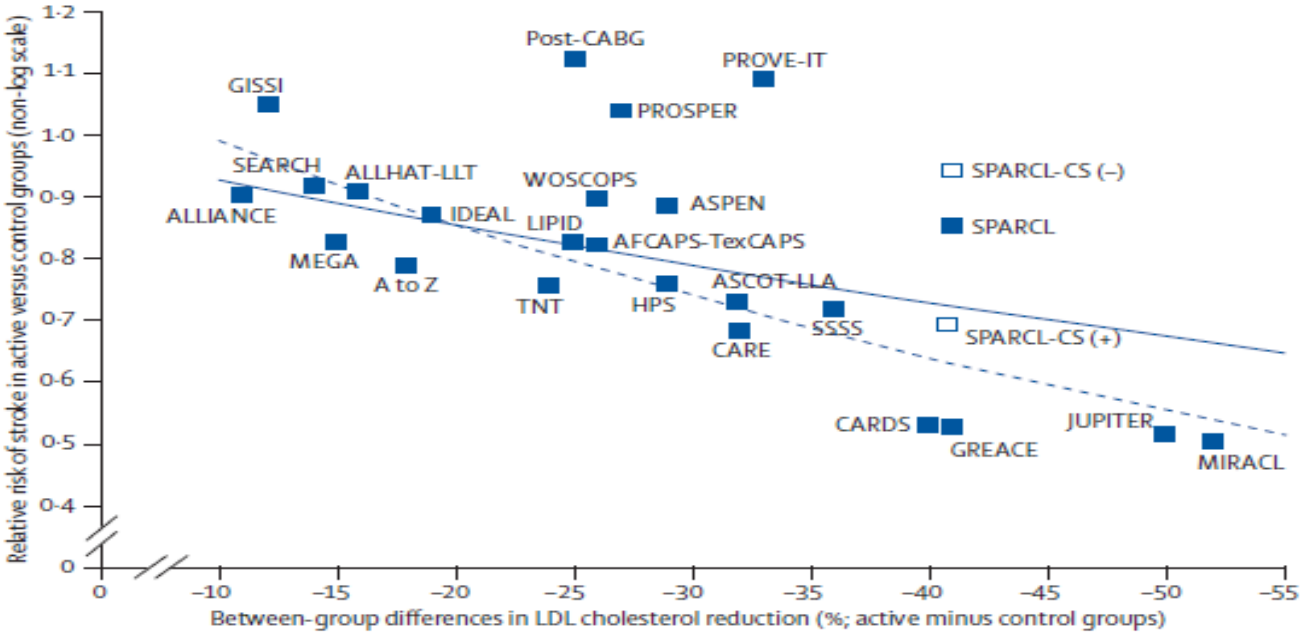
Atrovastatin 80mg vs. placebo after stroke/TIA, LDL-C 100-190mg/dL and no known CHD

AHA/ASA Secondary prevention guidelines

Statin therapy with intensive lipid-lowering effects is recommended to reduce risk of stroke and CV events among patients with ischemic stroke or TIA presumed to be of atherosclerotic origin and an LDL-C level ≥100 mg/dL (*Class I; Level of Evidence B*)

2006

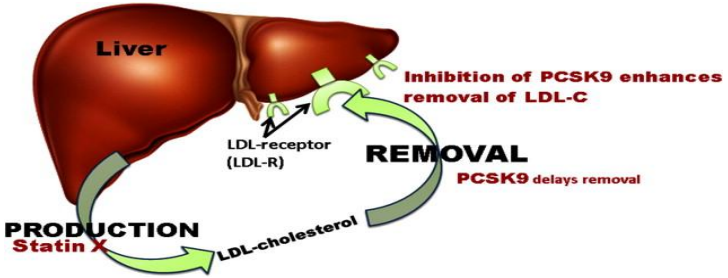
Reduction of LDL cholesterol and stroke incidence



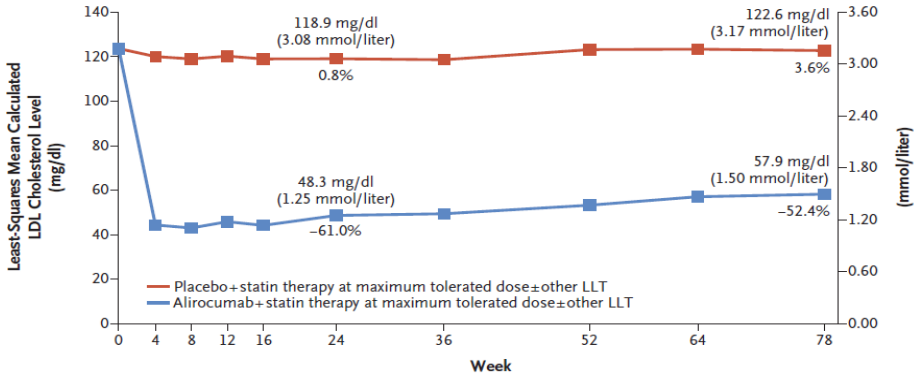
Estimates of relative risk reduction

- 10% LDL reduction: relative risk reduction 7·5% (2·3–12·5) overall
  relative risk reduction 13·5% (7·7–18·8) for primary prevention of stroke
- 1 mmol/L (39 mg/dL) LDL reduction: relative risk reduction 21·1% (6·3–33·5) overall
  relative risk reduction 35·9% (21·7–47·6) for primary prevention of stroke

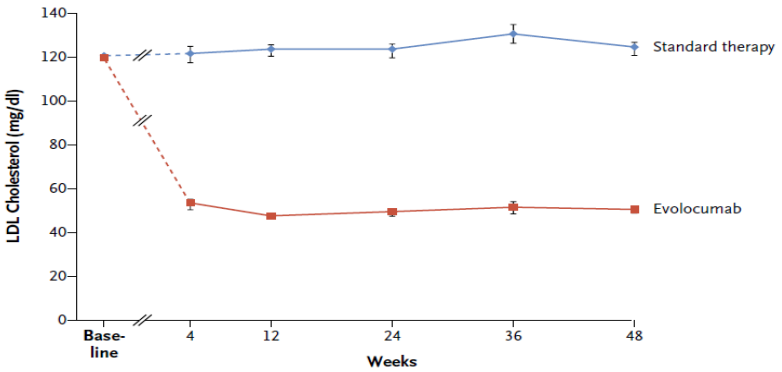
Lancet Neurol 2009; 8: 453–63



PCSK-9 Inhibitors



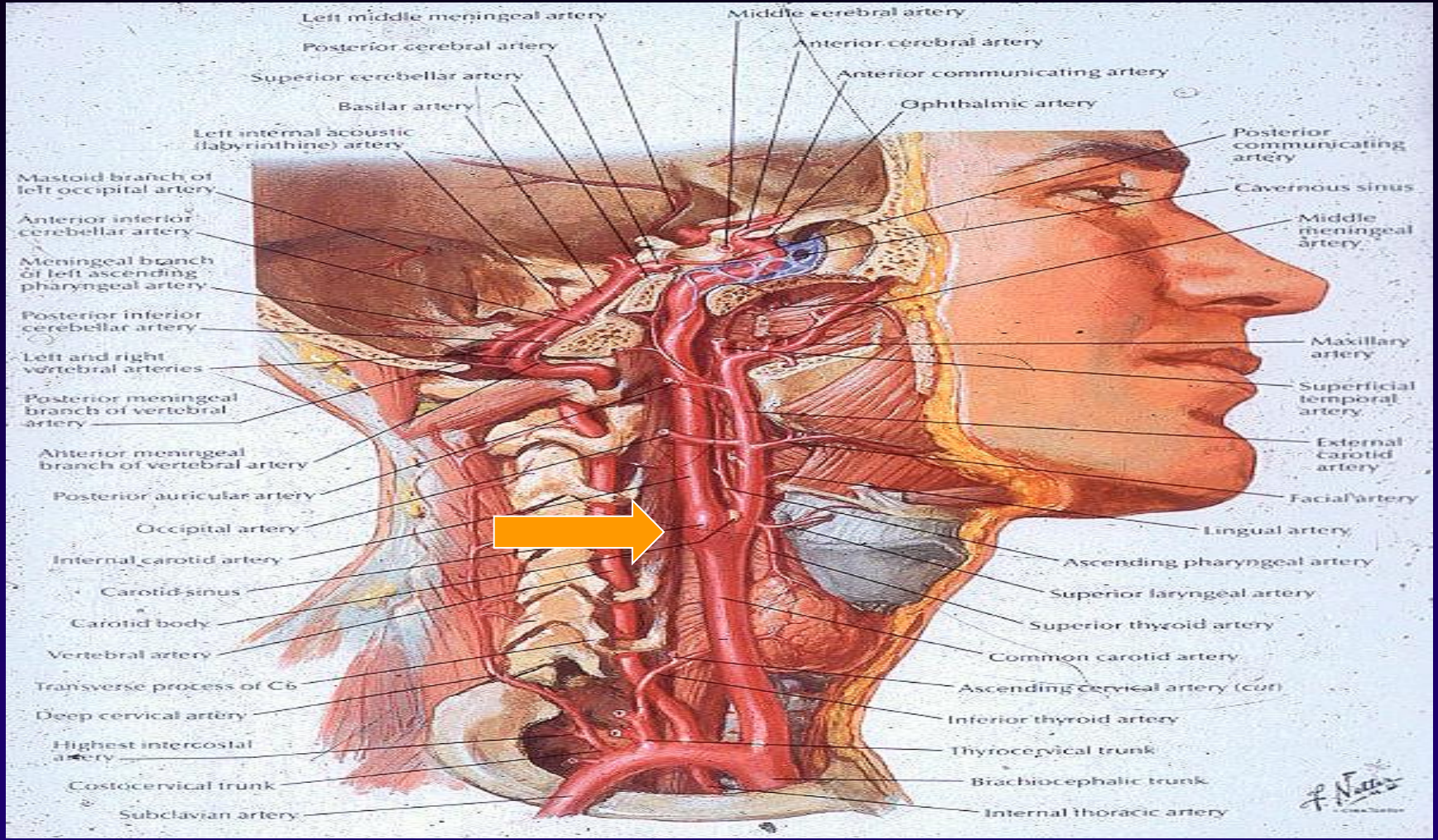
ODYSSEY LONG-TERM



OSLER

Monoclonal antibodies targeting PCSK9 result in large reductions in plasma LDL cholesterol

This article was published on March 15, 2015, at NEJM.org.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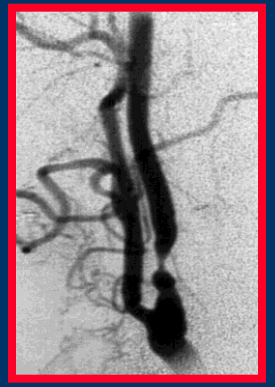
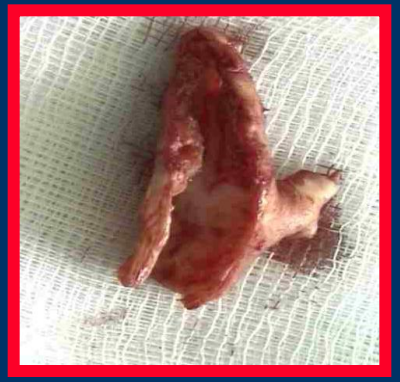
Mastoid branch of left occipital artery
Cavernous sinus
Anterior inferior cerebellar artery
Middle meningeal artery
Meningeal branch of left ascending pharyngeal artery
Posterior inferior cerebellar artery
Maxillary artery
Left and right vertebral arteries
Superficial temporal artery
Posterior meningeal branch of vertebral artery
External carotid artery
Anterior meningeal branch of vertebral artery
Facial artery
Posterior auricular artery
Occipital artery
Lingual artery
Internal carotid artery
Ascending pharyngeal artery
Carotid sinus
Superior laryngeal artery
Carotid body
Superior thyroid artery
Vertebral artery
Common carotid artery
Transverse process of C6
Ascending cervical artery (cut)
Deep cervical artery
Inferior thyroid artery
Highest intercostal artery
Thyrocervical trunk
Costocervical trunk
Brachiocephalic trunk
Subclavian artery
Internal thoracic artery

Surgery vs Stenting for Symptomatic Carotid Stenosis

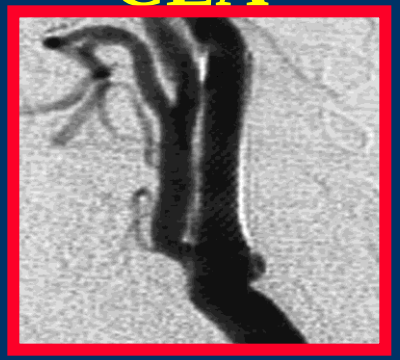
Treatment optionsfor symptomatic carotid stenosis:



revascularization



CEA



CAS

Medical treatment

Risk factor management

CETC

ECST, NASCET & VA studies combined and
reanalysed after standardisation to NASCET
angiographic measurement method (n>6000)

any stroke at 5 years including operative risk

stenosis		CEA	BMT	AR	NNT	strokes prev /1000 CEAs
<30%	n=1746	18.36%	15.71%	-2.6		
30-49%	n=1054	22.80%	25.50%	2.6%	38	26
50-69%	n=2312	20.00%	27.70%	7.8%	13	78
70-99%	n=1344	17.13%	32.70%	15.6%	6	156
nr occln	n= 262	16.82%	15.15%	-1.7%	n/k	n/k

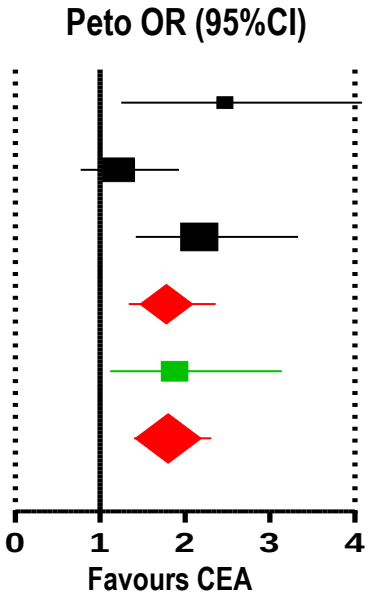
Lancet 2004;363:915-924
Lancet 2003;361:107-116
Stroke 2004;35:2855-2861

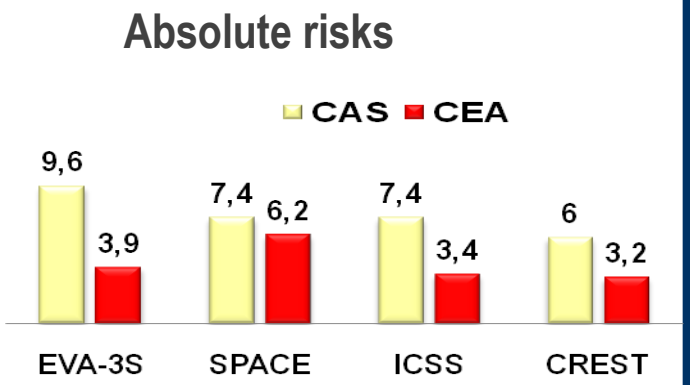
Symptomatic carotid stenosis

Is CAS as safe as CEA?

Stroke or death within 30 days of treatment (per protocol analysis)

Study	CAS	CEA
EVA-3S	25/260	10/257
SPACE	44/591	35/567
ICSS	61/828	28/821
Subtotal *	130/1679	73/1645
CREST	40/668	21/653
Total	170/2347	94/2298





OR (Fixed) = 1.80 (1.40 – 2.31), p = 0.000

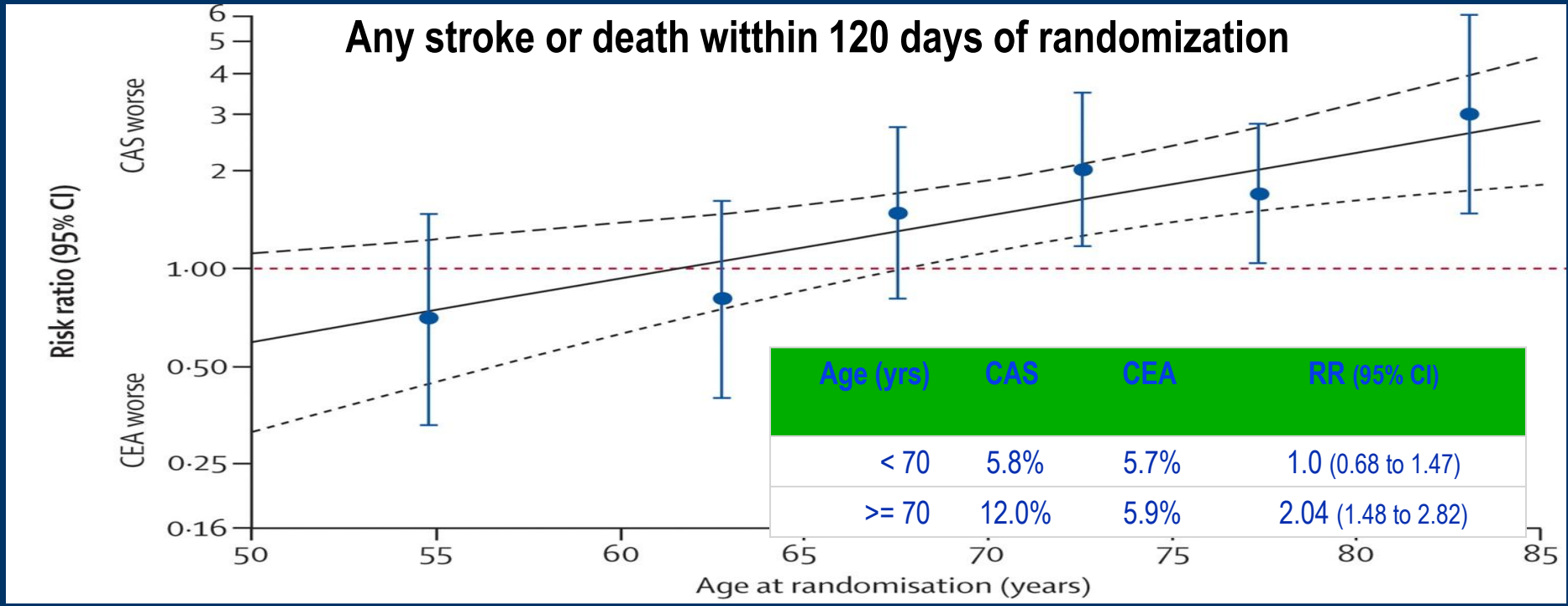
Heterogeneity p = 0.23

P. Amarenco, Lancet 2010

Symptomatic carotid stenosis

CAS vs. CEA : effect of age

Carotid Stenting Trialists' Collaboration, Lancet 2010



Age (yrs)	CAS	CEA	RR (95% CI)
< 70	5.8%	5.7%	1.0 (0.68 to 1.47)
>= 70	12.0%	5.9%	2.04 (1.48 to 2.82)

AHA/ASA Guideline

Guidelines for the Prevention of Stroke in Patients With Stroke and Transient Ischemic Attack

A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association

The American Academy of Neurology affirms the value of this guideline as an educational tool for neurologists.

Endorsed by the American Association of Neurological Surgeons and Congress of Neurological Surgeons

Walter N. Kernan, MD, Chair; Bruce Ovbiagele, MD, MSc, MAS, Vice Chair; Henry R. Black, MD; Dawn M. Bravata, MD; Marc I. Chimowitz, MBChB, FAHA; Michael D. Ezekowitz, MBChB, PhD; Margaret C. Fang, MD, MPH; Marc Fisher, MD, FAHA; Karen L. Furie, MD, MPH, FAHA; Donald V. Heck, MD; S. Claiborne (Clay) Johnston, MD, PhD; Scott E. Kasner, MD, FAHA; Steven J. Kittner, MD, MPH, FAHA; Pamela H. Mitchell, PhD, RN, FAHA; Michael W. Rich, MD; DeJuran Richardson, PhD; Lee H. Schwamm, MD, FAHA; John A. Wilson, MD; on behalf of the American Heart Association Stroke Council, Council on Cardiovascular and Stroke Nursing, Council on Clinical Cardiology, and Council on Peripheral Vascular Disease

Abstract—The aim of this updated guideline is to provide comprehensive and timely evidence-based recommendations on the prevention of future stroke among survivors of ischemic stroke or transient ischemic attack. The guideline is addressed to all clinicians who manage secondary prevention for these patients. Evidence-based recommendations are provided for control of risk factors, intervention for vascular obstruction, antithrombotic therapy for cardioembolism, and antiplatelet therapy for noncardioembolic stroke. Recommendations are also provided for the prevention of recurrent stroke in a variety of specific circumstances, including aortic arch atherosclerosis, arterial dissection, patent foramen ovale, hyperhomocysteinemia, hypercoagulable states, antiphospholipid antibody syndrome, sickle cell disease, cerebral venous sinus thrombosis, and pregnancy. Special sections address use of antithrombotic and anticoagulation therapy after an intracranial hemorrhage and implementation of guidelines. (***Stroke*****. 2014;45:2160-2236.)**

Key Words: AHA Scientific Statements ■ atrial fibrillation ■ carotid stenosis ■ hypertension ■ ischemia ■ ischemic attack, transient ■ prevention ■ stroke

ESC Council Stroke

Extracranial Carotid Disease Recommendations

For patients with a TIA or ischemic stroke within the past 6 months and ipsilateral severe (70%–99%) carotid artery stenosis as documented by noninvasive imaging, CEA is recommended if the perioperative morbidity and mortality risk is estimated to be <6% (*Class I; Level of Evidence A*).

For patients with recent TIA or ischemic stroke and ipsilateral moderate (50%–69%) carotid stenosis as documented by catheter-based imaging or noninvasive imaging with corroboration (eg, magnetic resonance angiogram or computed tomography angiogram), CEA is recommended depending on patient-specific factors, such as age, sex, and comorbidities, if the perioperative morbidity and mortality risk is estimated to be <6% *(Class I;*

ESC Council Stroke

Extracranial Carotid Disease Recommendations

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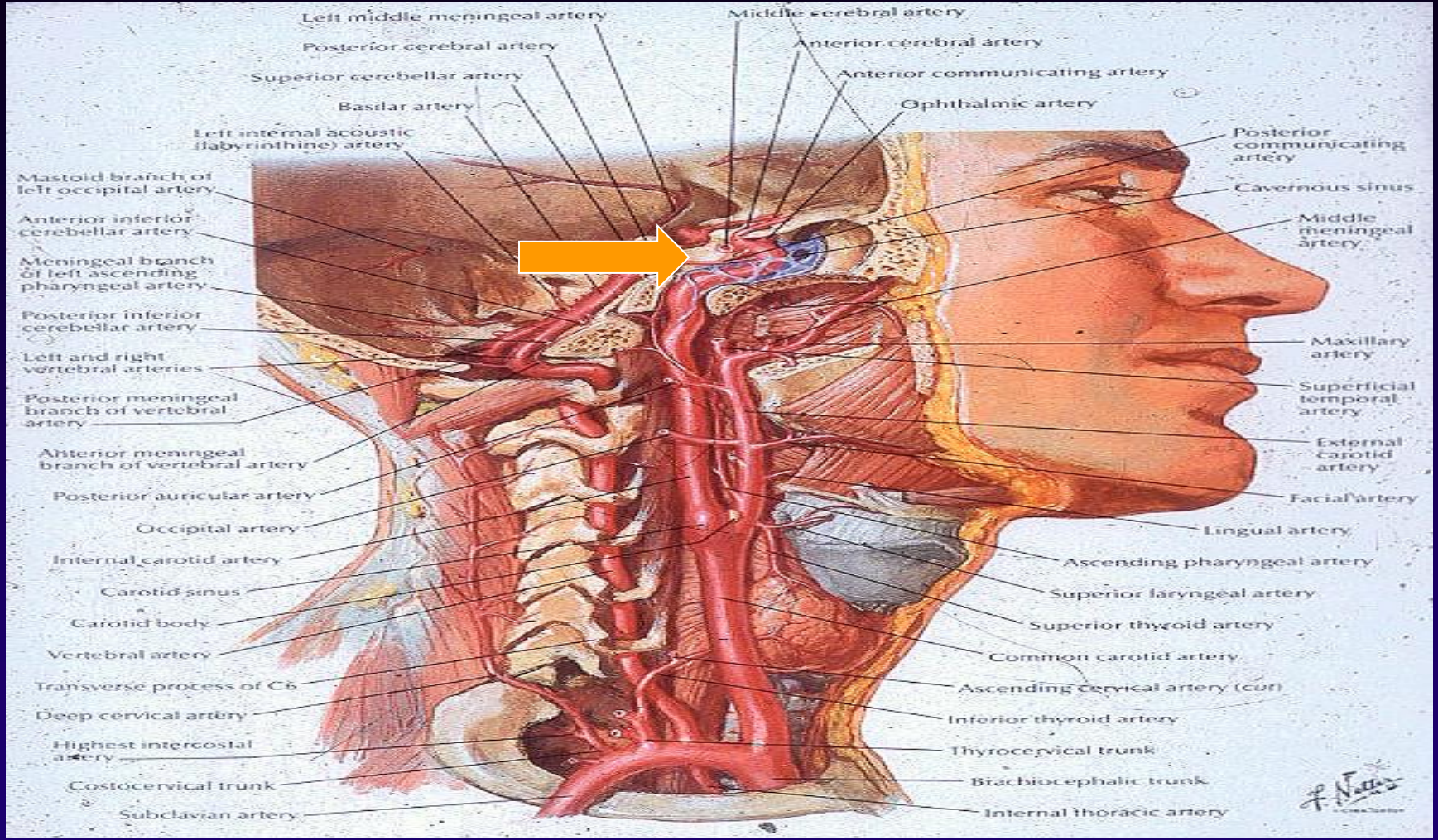
- When the degree of stenosis is <50%, CEA and CAS are not recommended *(Class III; Level of Evidence A*).

- When revascularization is indicated for patients with TIA or minor, nondisabling stroke, it is reasonable to perform the procedure within 2 weeks of the index event rather than delay surgery if there are no contraindications to early revascularization *(Class IIa; Level of Evidence B*).

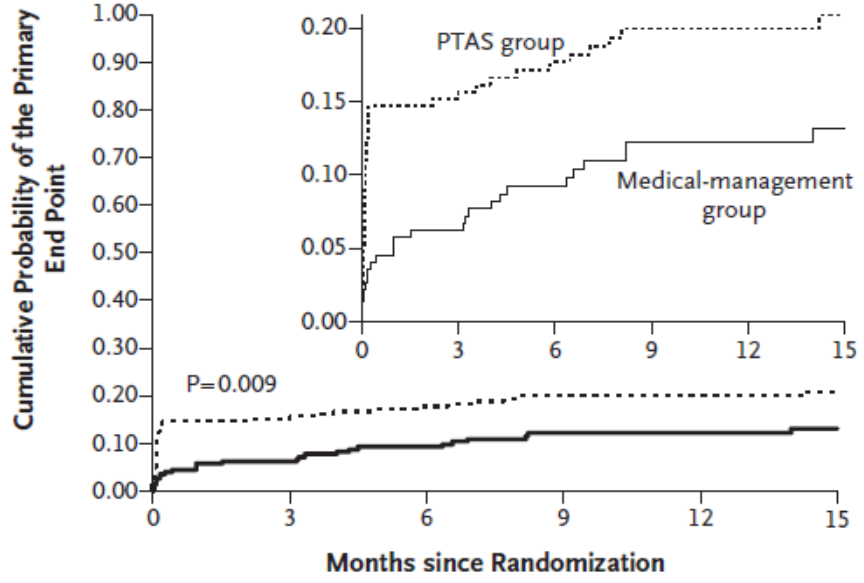
- CAS is indicated as an alternative to CEA for symptomatic patients at average or low risk of complications associated with endovascular intervention when the diameter of the lumen of the ICA is reduced by >70% by noninvasive imaging or >50% by catheter-based imaging or noninvasive imaging with corroboration and the anticipated rate of periprocedural stroke or death is <6% *(Class IIa; Level of Evidence B*). (Revised recommendation)

- It is reasonable to consider patient age in choosing between CAS and CEA. For older patients (ie, older than ≈70 years), CEA may be associated with

ESC Council Stroke


Left middle meningeal artery
Middle cerebral artery
Posterior cerebral artery
Anterior cerebral artery
Superior cerebellar artery
Anterior communicating artery
Basilar artery
Ophthalmic artery
Left internal acoustic (labyrinthine) artery
Posterior communicating artery
Mastoid branch of left occipital artery
Cavernous sinus
Anterior inferior cerebellar artery
Middle meningeal artery
Meningeal branch of left ascending pharyngeal artery
Posterior inferior cerebellar artery
Maxillary artery
Left and right vertebral arteries
Superficial temporal artery
Posterior meningeal branch of vertebral artery
External carotid artery
Anterior meningeal branch of vertebral artery
Facial artery
Posterior auricular artery
Occipital artery
Lingual artery
Internal carotid artery
Ascending pharyngeal artery
Carotid sinus
Superior laryngeal artery
Carotid body
Superior thyroid artery
Vertebral artery
Common carotid artery
Transverse process of C6
Ascending cervical artery (cut)
Deep cervical artery
Inferior thyroid artery
Highest intercostal artery
Thyrocervical trunk
Costocervical trunk
Brachiocephalic trunk
Subclavian artery
Internal thoracic artery

Intracranial Atherosclerosis SAMMPRIS Trial

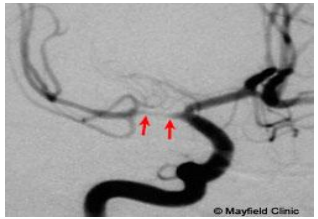


No. at Risk						
Medical management group	227	196	164	132	115	92
PTAS group	224	182	153	125	98	83

Figure 1. Kaplan–Meier Curves for the Cumulative Probability of the Primary End Point, According to Treatment Assignment.

Medical Management:
Aspirin 325mg per day
+ Clopidogrel 75mg per day for 90 days

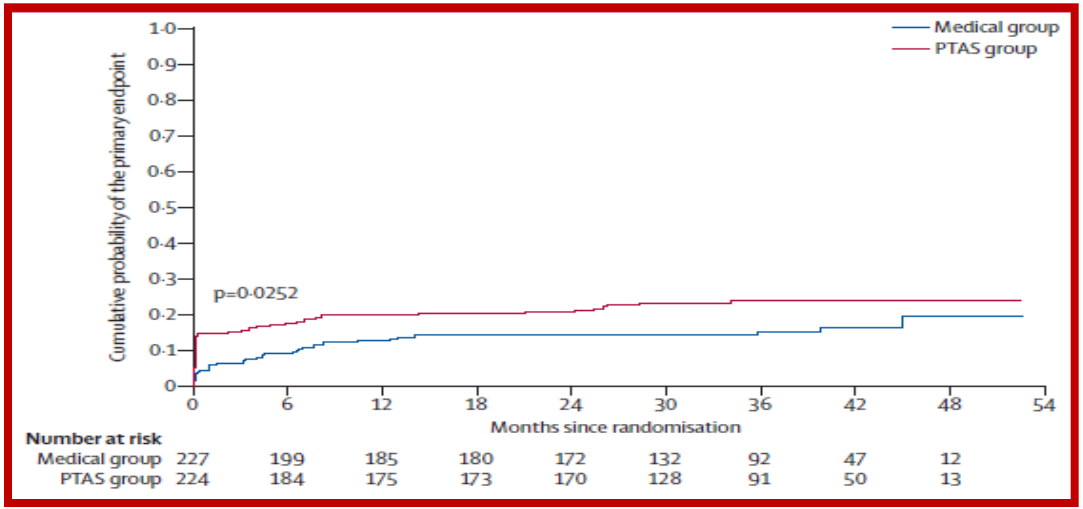
N Engl J Med 2011;365:993-1003.



Symptomatic intracranial artery stenosis:

Aggressive medical treatment ± stenting

SAMMPRIS Trial



AHA/ASA secondary prevention guidelines 2014

For patients with recent stroke or TIA (within 30 days) attributable to severe stenosis (70%–99%) of a major intracranial artery, the addition of clopidogrel 75 mg/d to aspirin for 90 days might be reasonable *(Class IIb; Level of Evidence B)*.

Lancet 2014;383:333-41

N Engl J Med 2011;365:993-1003.

Original Investigation

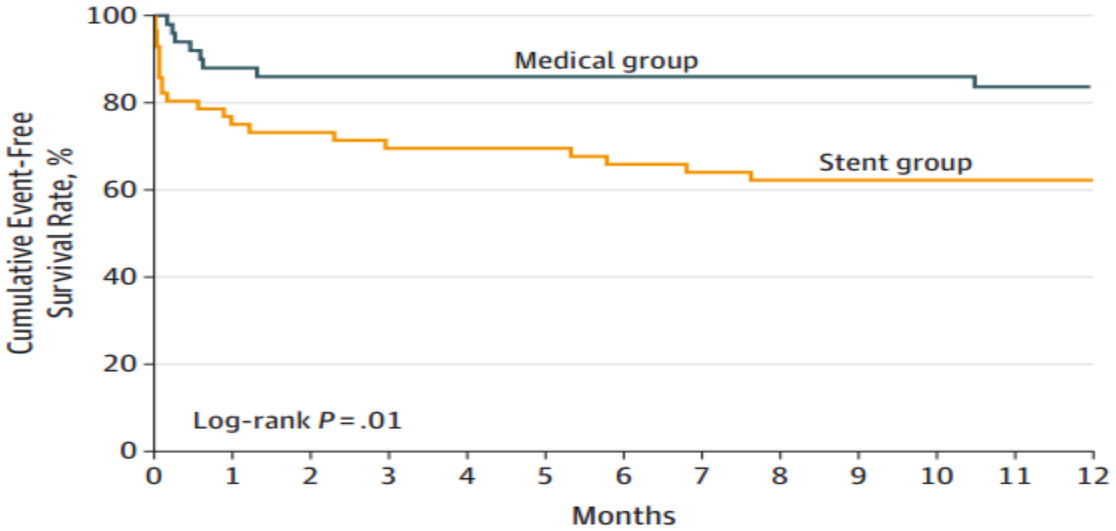
Effect of a Balloon-Expandable Intracranial Stent vs Medical Therapy on Risk of Stroke in Patients With Symptomatic Intracranial Stenosis

The VISSIT Randomized Clinical Trial

Osama O. Zaidat, MD, MS; Brian-Fred Fitzsimmons, MD; Britton Keith Woodward, MD; Zhigang Wang, MD; Monika Killer-Oberpfalzer, MD; Ajay Wakhloo, MD, PhD; Rishi Gupta, MD, MBA; Howard Kirshner, MD; J. Thomas Megerian, MD, PhD; James Lesko, PhD; Pamela Pitzer; Jandira Ramos, MPH; Alicia C. Castonguay, PhD; Stanley Barnwell, MD; Wade S. Smith, MD; Daryl R. Gress, MD; for the VISSIT Trial Investigators

JAMA. 2015;313(12):1240-1248. doi:10.1001/jama.2015.1693

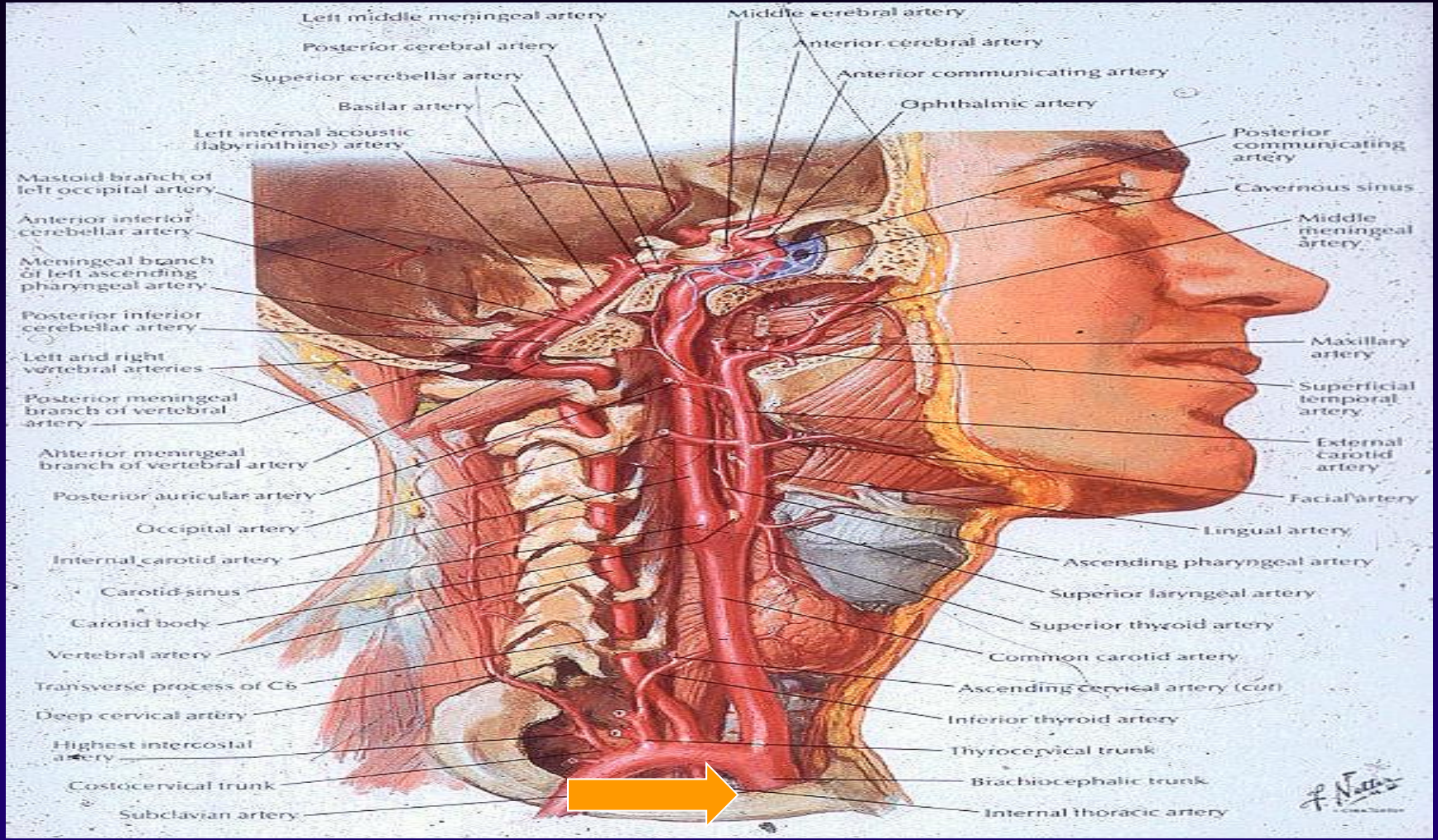
Figure 2. Kaplan-Meier Estimate of Event-Free Survival Rates in Treatment Groups Intent-to-Treat Population



No. at risk

Medical group	53	44	43	43	41	40	39	38	38	38	38	33	20
Stent group	57	42	40	38	38	38	36	35	34	33	33	31	21

Log-rank test was used to test the hypothesis that event-free survival rates (primary end point) between groups were the same.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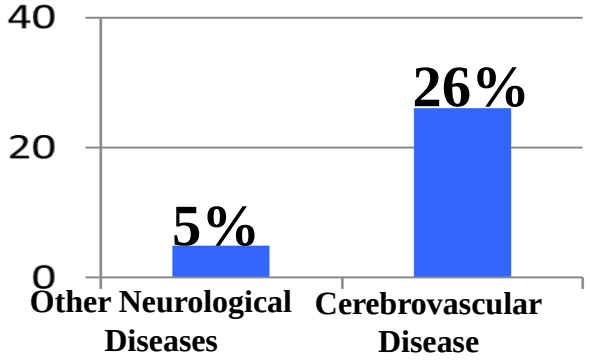
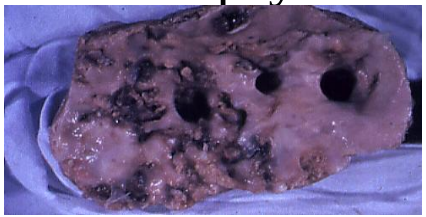
Meningeal branch of left ascending pharyngeal artery
Posterior inferior cerebellar artery
Maxillary artery
Left and right vertebral arteries
Superficial temporal artery
Posterior meningeal branch of vertebral artery
External carotid artery
Anterior meningeal branch of vertebral artery
Facial artery
Posterior auricular artery
Lingual artery
Occipital artery
Ascending pharyngeal artery
Internal carotid artery
Superior laryngeal artery
Carotid sinus
Superior thyroid artery
Carotid body
Common carotid artery
Vertebral artery
Ascending cervical artery (cut)
Transverse process of C6
Inferior thyroid artery
Deep cervical artery
Thyrocervical trunk
Highest intercostal artery
Brachiocephalic trunk
Costocervical trunk
Internal thoracic artery
Subclavian artery

Management of patients with Aortic arch atheroma

Ulcerated Plaques in the Aortic Arch and Brain Infarction : Autopsy



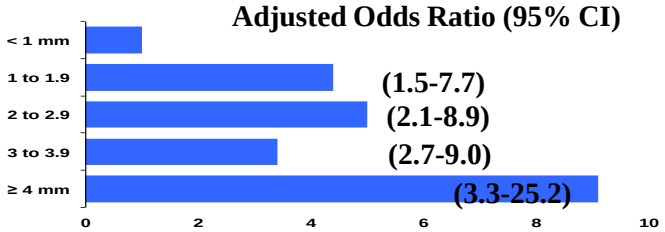
500 Autopsy Cases *

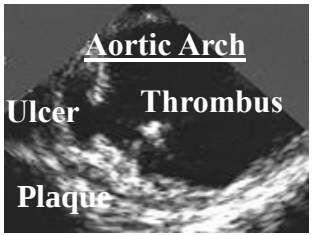


Adjusted OR
4.0 [95%CI, 2.1-7.8]

* Amarenco et al. N Engl J Med 1992;326:221

Aortic Arch Plaque and Brain Infarction :TEE*



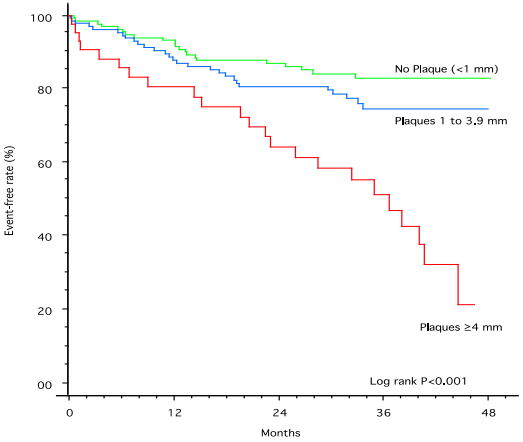


* Amarenco P et al. N Engl J Med 1994;331:1474

Event Rates

Risk of Recurrent BI 12%/yr *

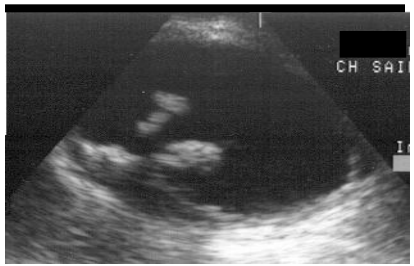
Risk of Vasc Event 26%/yr *

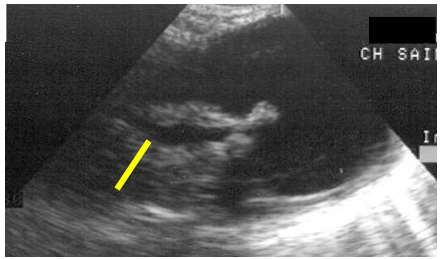


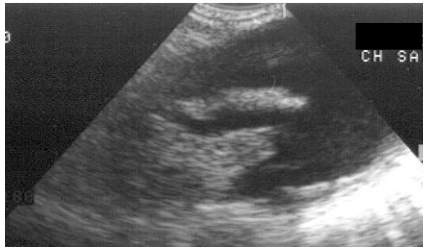
* Amarenco et al. FAPS Study
N Engl J Med 1996;334:1216

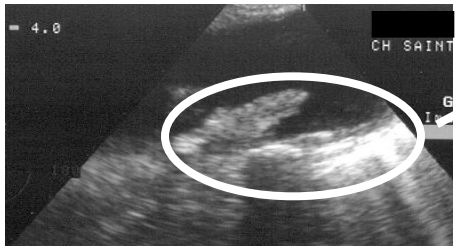
Transesophageal echocardiography

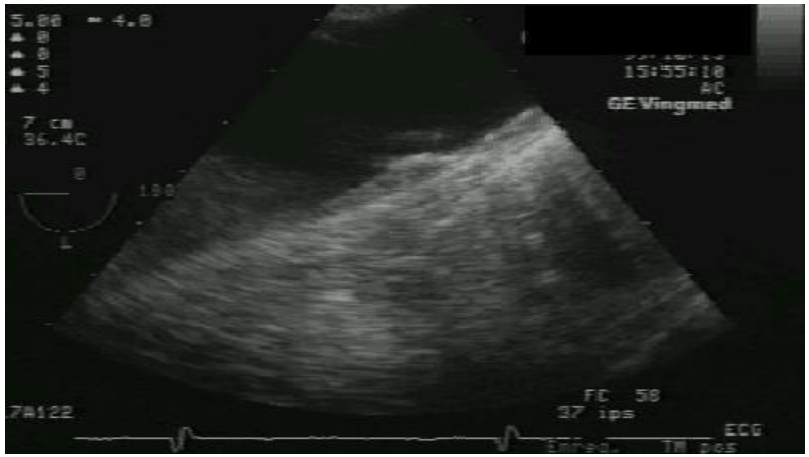
« Complex plaques »

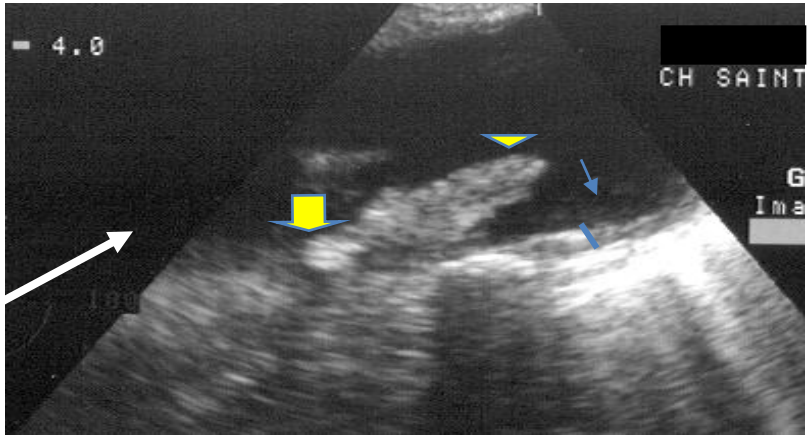












Pr. Ariel Cohen's collection

THE A.R.C.H. TRIAL

Aortic arch Related Cerebral Hazard

An academic driven trial

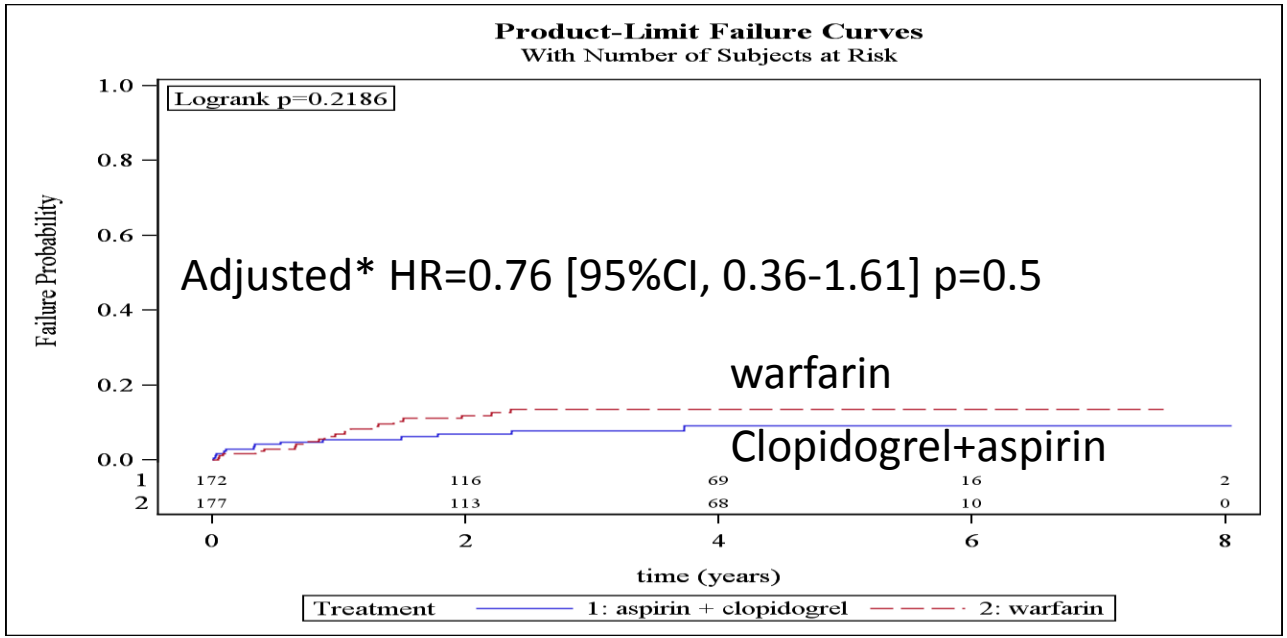
Non disabling Brain Infarct, TIA or Peripheral Embolism
& Aortic Arch Plaque ≥4 mm

- Warfarin
  INR 2 to 3
- Aspirin 75 mg/d
  +
  Clopidogrel 75 mg/d

Source of Funding:
French governement through PHRC (1 M€)
Australian MRC (0.5 M€)

Drug supply: Sanofi and Bristol Myers-Squibb

Time to Primary End-point



*Age, sex, country, history of MI , on-treatment BP (time-dependent covariate)

Conclusions

- We found no significant difference on the incidence of stroke, MI, or vascular death in patients treated with C+A compared to those treated with warfarin

- No significant difference in major and in intracranial hemorrhages, although we found 2 ICH in C+A vs 1 in W
- TTR analysis suggests that « super » INR group trended to do better than C+A strategy, which opens the door for testing new drugs with much stable full anticoagulation (e.g., NOACs) over C+A or C

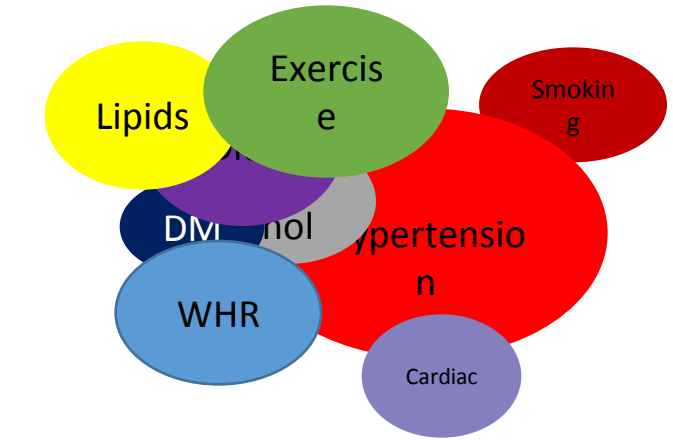
Global and regional effects of potentially modifiable risk factors associated with acute stroke in 32 countries (INTERSTROKE): a case-control study

	Overall (n=13 447)	Western Europe, North America, Australia (n=1917)	Eastern and central Europe, Middle East (n=1394)	South America (n=1471)	China (n=3987)	South Asia (n=2850)	Southeast Asia (n=855)	Africa (n=973)
Age, years	62·2 (13·6)	66·7 (13·4)	63·9 (13·4)	65·8 (14·3)	61·9 (12·5)	59·6 (12·9)	56·6 (13·0)	58·7 (15·2)
Age ≤45 years	1582 (11·8%)	141 (7·4%)	143 (10·3%)	123 (8·4%)	364 (9·1%)	451 (15·8%)	156 (18·3%)	204 (21·0%)
Women	5434 (40·4%)	781 (40·7%)	556 (39·9%)	652 (44·3%)	1606 (40·3%)	1017 (35·7%)	352 (41·2%)	470 (48·3%)
Intracerebral haemorrhage	3059 (22·7%)	128 (6·7%)	117 (8·4%)	348 (23·7%)	1102 (27·6%)	785 (27·5%)	285 (33·3%)	294 (30·2%)
Ischaemic stroke	10 388 (77·3%)	1789 (93·3%)	1277 (91·6%)	1123 (76·3%)	2885 (72·4%)	2065 (72·5%)	570 (66·7%)	679 (69·7%)

Case-Control Study: 13.477 cases

*Martin J O'Donnell, Siu Lim Chin, Sumathy Rangarajan, Denis Xavier, Lisheng Liu, Hongye Zhang, Purnima Rao-Melacini, Xiaohe Zhang, Prem Pais, Steven Agapay, Patricio Lopez-Jaramillo, Albertino Damasceno, Peter Langhorne, Matthew J McQueen, Annika Rosengren, Mahshid Dehghan, Graeme J Hankey, Antonio L Dans, Ahmed Elsayed, Alvaro Avezum, Charles Mondo, Hans-Christoph Diener, Danuta Ryglewicz, Anna Czlonkowska, Nana Pogosova, Christian Weimar, Romaina Iqbal, Rafael Diaz, Khalid Yusoff, Afzalhussein Yusufali, Aytekin Oguz, Xingyu Wang, Ernesto Penaherrera, Fernando Lanas, Okechukwu S Ogah, Adesola Ogunniyi, Helle K Iversen, German Malaga, Zvonko Rumboldt, Shahram Oveisgharan, Fawaz Al Hussain, Daliwonga Magazi, Yongchai Nilanont, John Ferguson, Guillaume Pare, Salim Yusuf; on behalf of the INTERSTROKE investigators**

INTERSTROKE: POPULATION ATTRIBUTABLE RISK



Collective PAR (99%CI)	
All Stroke	**90.7% (88.7-92.4)**
Ischemic Stroke	**91.5% (89.4-93.2)**
ICH	**87.1% (82.2-90.8)**

HTN Cardiac Exercise Smoking Lipids Diet WHR Alcohol DM

Summary

- Stroke is largely a preventable disease.
- Aggressive risk factor management is important.
- All antiplatelets have almost similar efficacy with marginal benefit of clopidogrel or ASA+DP over aspirin
- Warfarin is indicated for cardioembolic strokes. Newer OAC agents are also effective without any major benefit over warfarin.
- CEA/CAS is beneficial in >50% symptomatic stenosis. CAS is more appropriate in e selected cases.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June 28-30, 2018
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EXPLORE THE INTER-RELATIONSHIP BETWEEN
CARDIOVASCULAR HEALTH AND STROKE
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