Stroke Prevention: Primary and Secondary

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Introduction

- In the US there are 750,000 new strokes each year
- Stroke is the third leading cause of death and the leading cause of disability in the US
- There are racial differences in stroke manifestations
  - African Americans have significantly increased rates of mortality compared to Whites
  - Little information is available on stroke in Asian and Pacific Islanders (API) in the US

Introduction

- Impact of Risk Reduction
  - Cost effective
  - Reduced mortality form stroke and other causes of vascular death
  - Reduced cost of disability
    - Lost productivity
    - Cost of long term nursing care

Introduction

- Primary Prevention
  - Nonmodifiable risk factors
  - Modifiable risk factors
  - Medical prevention
  - Surgical prevention
  - Public health strategies

Risk Factors

Nonmodifiable

- Age
- Sex
- Family History
- Race

Modifiable

- Diet: Fat and Cholesterol
- Diabetes
- Hypertension
- Atrial fibrillation
- Tobacco
- Exercise

Race as a Risk Factor for Stroke

- ~ 6 million strokes each conservative estimates in Mainland China
  - ~ 2 million deaths each year making stroke the second leading cause of death
- Age adjusted mortality for stroke in the Chinese is 2-3 times that for heart attack
- Chinese have a higher incidence of intracranial atherosclerosis than Whites
  - Chinese have much lower rates of extracranial carotid artery disease than Whites
- Chinese have higher rates of ICH

Modifiable Risk Factors: Hypertension

- Stroke risk increases as systolic blood pressure rises above 120 mm Hg.
- Stroke rates in hypertensive patients in China doubled between 1960 and 1980
- Poorly controlled blood pressure is felt to be a major problem among Chinese living in North America
  - The true incidence of hypertension among Chinese living in North America is unknown

Hypertension

- Risk reduction with treatment approaches 45%
  - STOP Trail: Stroke reduction of 50% in patients over 70
  - Treatment of hypertension alone has been shown to dramatically reduce stroke incidence in Chinese living in Mainland China

Hypertension

- Use of ACE inhibitors
  - HOPE
    - Ramipril vs Placebo: reduced stroke incidence even after control for blood pressure changes
  - PROGRESS
    - Perendiprel +/- Indapamide vs. Placebo: Reduced incidence of stroke even after accounting for control of hypertension
      - 40% of patients enrolled were Chinese

Hypertension

- Control of hypertension reduces stroke incidence
- Use of ACE inhibitors may augment this effect
- Combined use of ACE and diuretics may reduce risk even more than ACE alone?
- Are their race specific considerations to keep in mind when selecting agents to control hypertension?

Hypertension

- What is the incidence of (untreated) hypertension in Chinese living in North America?
  - What is its significance as a stroke risk factor?
  - How should hypertension be managed?
    - Are there racial differences in treatment responses?
  - Strategies for developing community awareness of the dangers of untreated hypertension

Lipid Lowering

- Elevated cholesterol increases risk of extracranial carotid disease
  - increases risk of intracranial atherosclerosis in Chinese?
- Protective effect of HDL
- Increased risk of dementia and stroke in patients with elevated LDL

Lipid Lowering

- Early studies of lipid lowering agents failed to show benefit
- More recent studies using HMG-CoA inhibitors (Statins) associated with reduced risk (SSS, CARE, LIPID, WOSCOPS)
  - Risk reduction is between 20% to close to 40% depending on the study

Diabetes

- Associated with increased risk of stroke and heart attack
  - End-organ damage via microcirculatory damage
- Treatment Goals:
  - Average preprandial glucose <120 mg/dL
  - Average bedtime glucose 100 to 140 mg/dL
  - HbA_{1c} <7%
  - Blood pressure (BP) <130/85 mm Hg

Diet and Stroke

- What is the incidence of elevated Cholesterol and diabetes in the Chinese community?
- What is the role of lipid levels and risk of ischemic vs. ICH in the Asian population?
- What is the true incidence of diabetes?
  - What health implications does untreated diabetes carry in the Chinese community?

Cigarette Smoking

- Recognized as a significant risk factor in stroke
  - Strokes in Chinese (Taiwan) <40
  - Is this true among Chinese as well?
- Associated with aneurysmal rupture in women
- In the U.S. it is estimated that stopping cigarette smoking would prevent at least 90,000 strokes annually
- Tobacco use and Alcohol
  - Increased risk of ICH?

Antiplatelet/Antithrombotic Agents

- Aspirin has clearly been shown to reduce stroke risk
  - Clopidogrel superior to aspirin?
  - Aspirin/Dipyrimadole associated with reduced stroke rates in patients who have failed aspirin
  - Aspirin/Dipyrimadole superior to clopidogrel?
- WARSS
  - No difference between warfarin and aspirin
    - No difference in complication rate
- HAEST
  - No difference between LMWH and aspirin

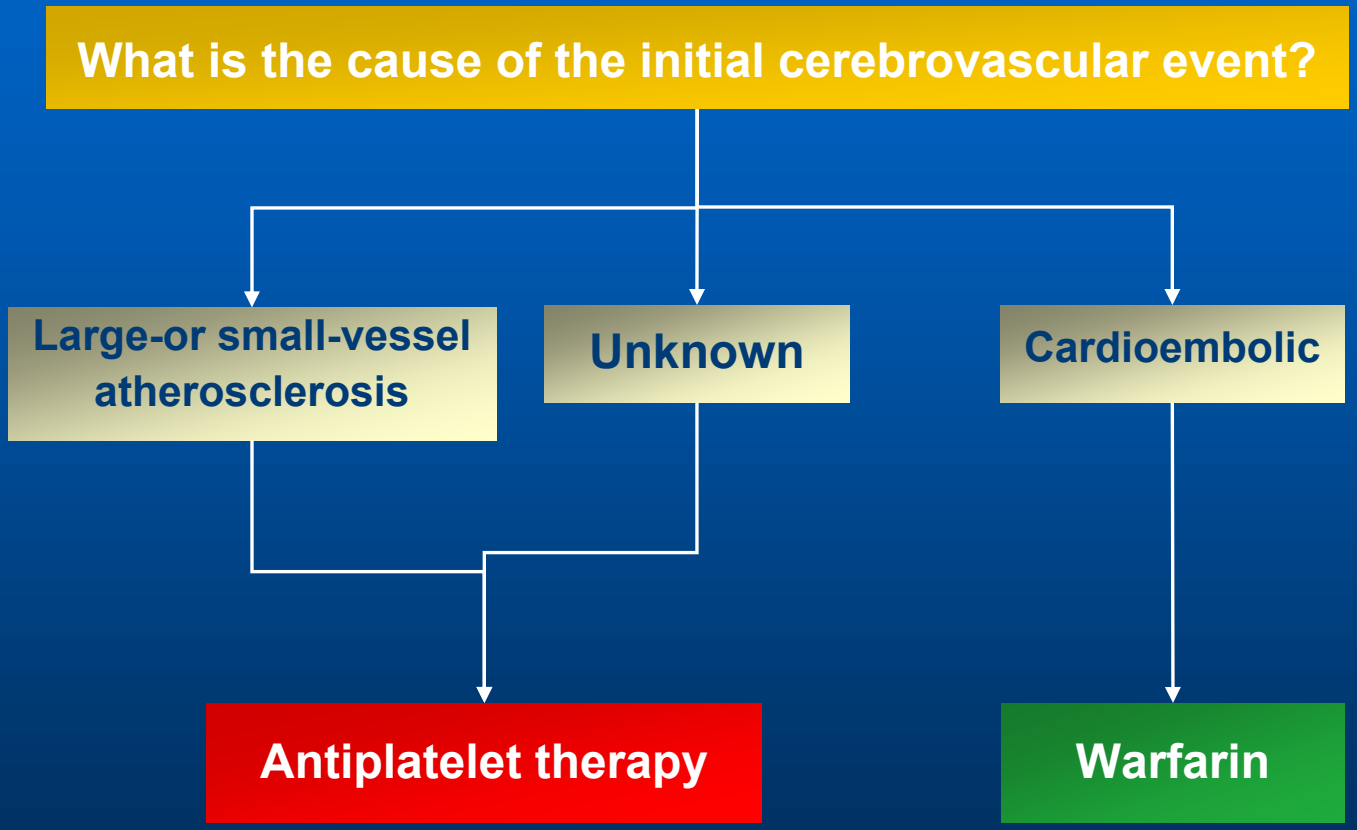
Antiplatelet/Antithrombotic

- WASID
  - Warfarin vs aspirin in large vessel intracranial stenosis
    - A small decrease in stroke incidence in patients being treated with warfarin; but with higher hemorrhage rates.
    - Effect of small vessel (lacunar stroke) in patients with large vessel intracranial disease
    - Is there a higher hemorrhage rate in Chinese patients on warfarin?
  - Atrial fibrillation
    - Warfarin with INR 2-3 clearly beneficial
    - Risk of hemorrhage in Chinese patients on warfarin?

Secondary Prevention

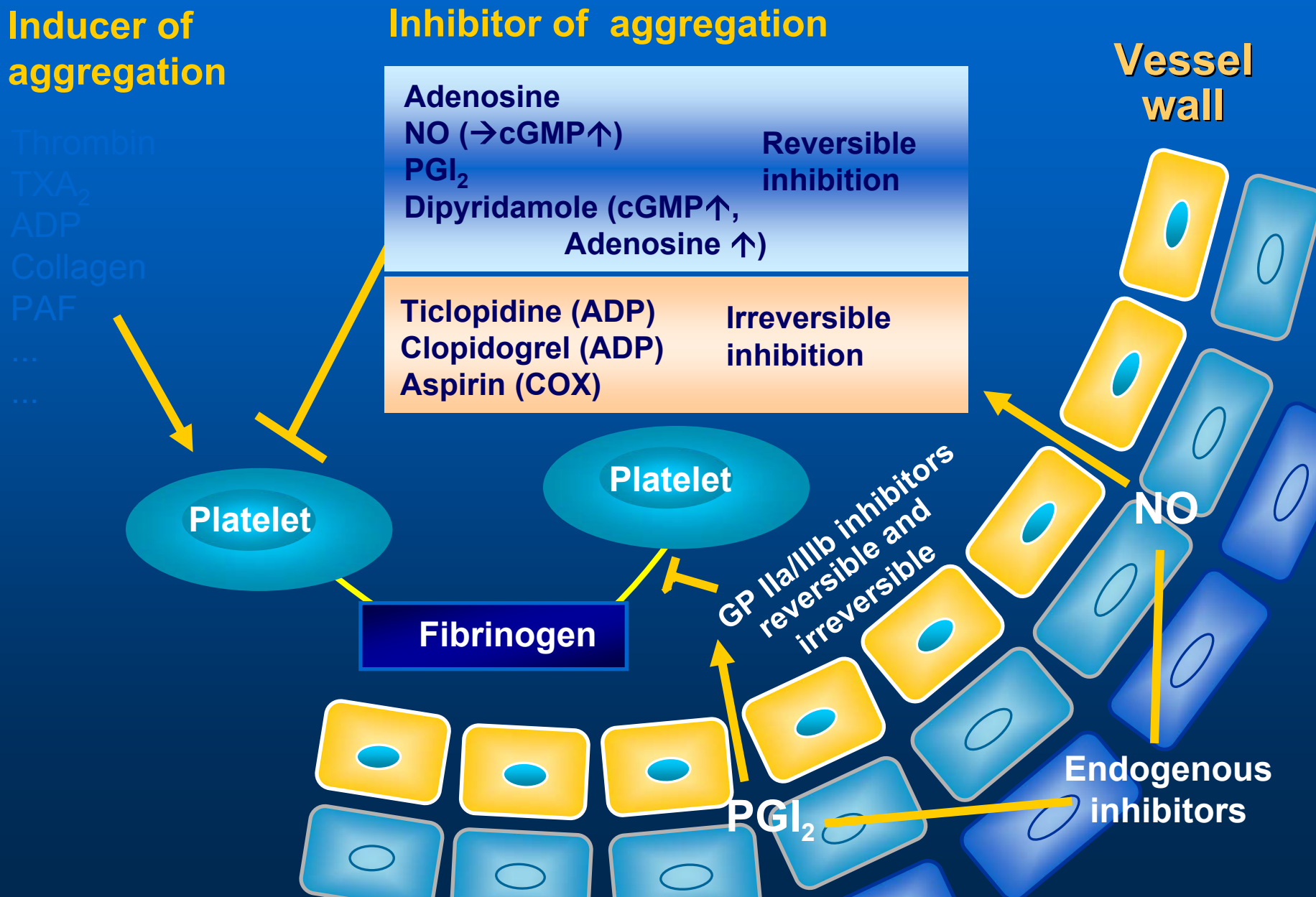
- Prevention of further stroke in patients who have suffered stroke already
- Prevention of stroke in patients who have suffered TIA

Secondary Stroke Prevention of Ischemic Stroke



Albers GW, et al. *Chest* 1998;114:683S-698S.
Barnett HJ, et al. *N Engl J Med* 1998;339:1415-1425.

Mode of Action of Antiplatelets



Indirect Comparison of Stroke Prevention Therapy

Endpoint = Stroke

Therapy (vs ASA)	NNT	Mean follow-up time years
ASA/ER-DP	33	2
Clopidogrel	121	1.91
Ticlopidine	40	3

Gorelick P.*Stroke* 2002;33:862-875

Secondary Prevention and Antiplatelet Agents

- Presence or absence of underlying coronary artery disease
- Large or small vessel intracranial atheroseclerosis
- Candidate for stent placement
- Dual antiplatelet effect of Clopidogrel and Aspirin

TIA and Stroke Risk

- Little is known about TIA in Chinese living in China or in North America
  - What is the short term stroke risk after a transient ischemic attack (TIA)?
  - What are the markers for high short-term risk of stroke after TIA?
- What environmental and genetic factors can be modified to reduce short-term risk after TIA?

The ED TIA Study*

- Cohort study
  - All Kaiser enrollees given a diagnosis of TIA in the emergency department
  - March 1997 – February 1998
  - Follow-up from record review for 3 months after presentation.
    - Risk of stroke after TIA
  - 1707 patients total

*Johnston et al 2000

Prognosis

- **3-month risk of stroke: 10.5%**
  - **1-week risk of stroke 6%**

- Cardiovascular hospitalization 2.7%
- Recurrent TIA 13.2%
- Death 2.6%
- Any of these events 26.2%

Stroke Risk Factors

Independent Risk Factors in Multivariable Models

	OR	95% CI	p value
Age >60 yrs	1.8	1.1-2.7	0.01
Diabetes	2.0	1.4-2.9	<0.001
Duration >10 min	2.3	1.3-4.1	0.006
Any Weakness	1.9	1.4-2.6	<0.001
Speech Difficulty	1.5	1.1-2.1	0.01

Possible Scoring System

Possible Prognostic model, scoring one point for each risk factor:

- Age >60 yrs
- Diabetes
- Duration >10 min
- Any Weakness

Final Score 0-4

Possible Scoring System

Possible Prognostic model

Points	Prevalence	Stroke Risk
0	2%	0%
1	15%	3%
2	41%	8%
3	34%	14%
4	8%	26%

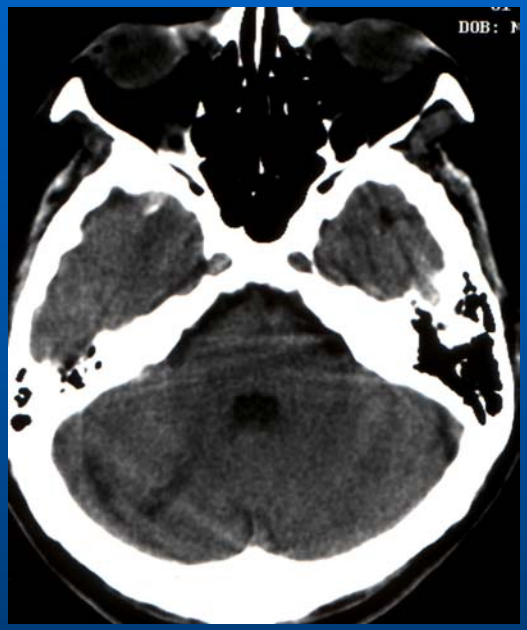
Surgical Prevention

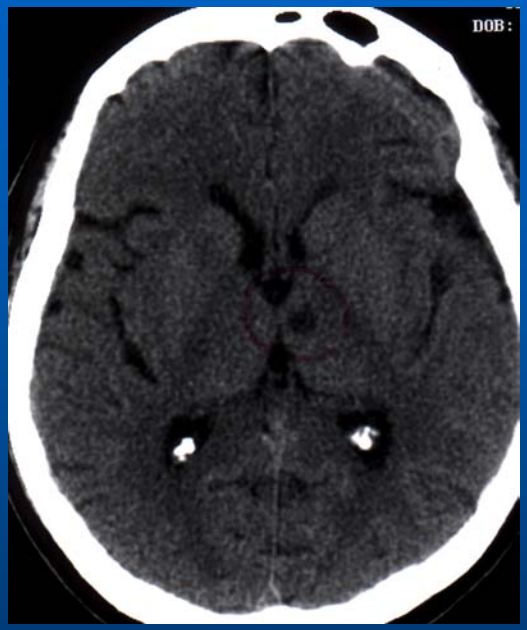
- Clear benefit of carotid endarterectomy in patients with extracranial carotid artery disease with >70% stenosis
  - No conclusive data from extracranial carotid stenting trial
  - Ongoing trials currently: no results available
- Intracranial stenosis
  - No randomized trials available
    - Anecdotal reports suggests better success with posterior circulation (vertebrobasilar) stenting

Endovascular Techniques

- 50 year old Chinese woman with history of poorly controlled hypertension, and previous stroke presents with 4 hours of dizziness and numbness on the left side.
  - PMH: Previous Posterior circulation stroke and hypertension
  - Meds: ASA, Enalapril, Atenolol

Case I

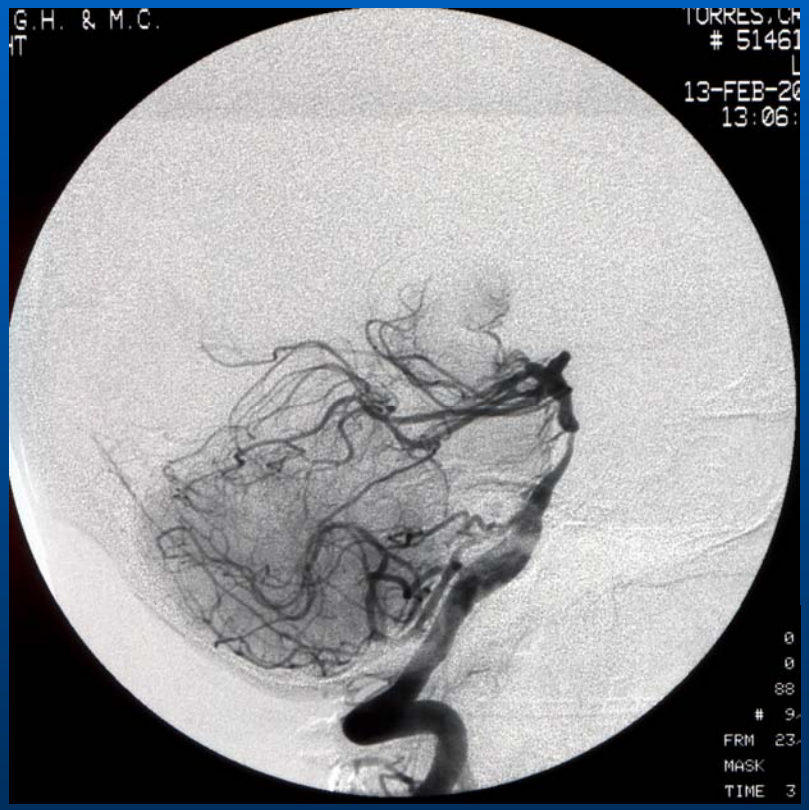


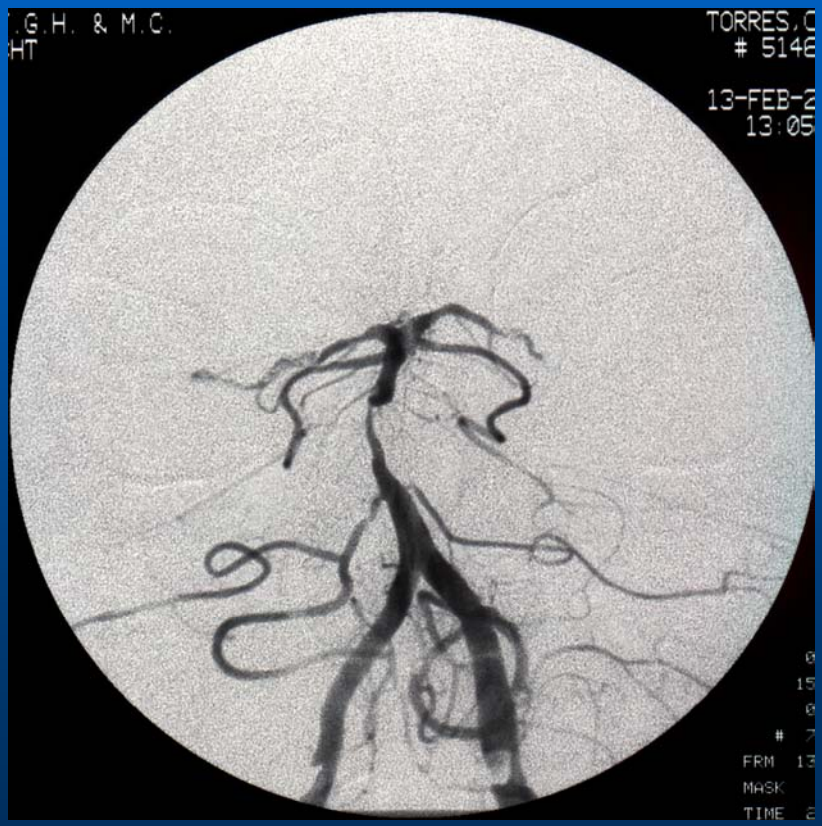


Endovascular Techniques

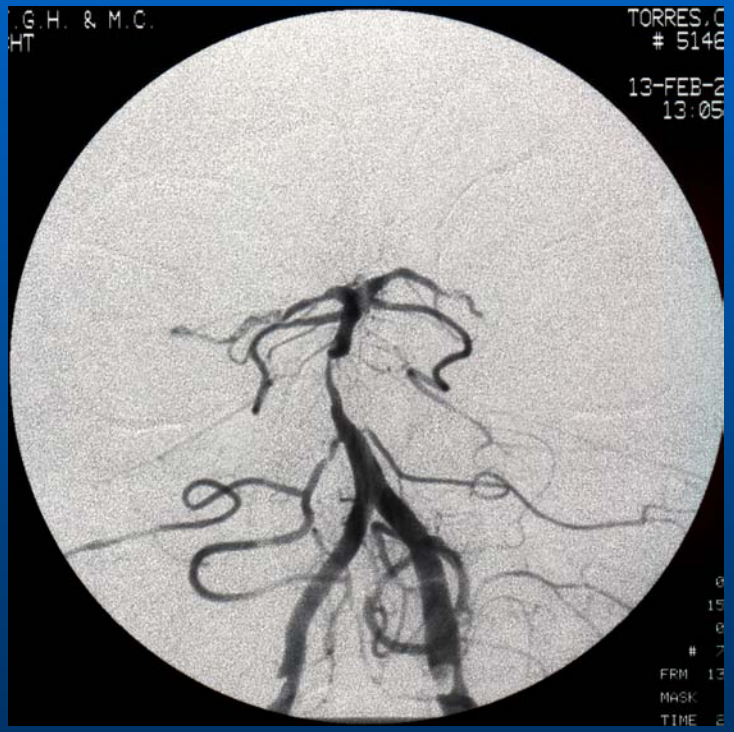
- The patient continued to have recurrent symptoms on aspirin, clopidogrel; aspirin and clopidogrel in combination and on heparin as an inpatient
  - Recurrent symptoms whenever she would sit-up or try to stand
- An Angiogram was performed

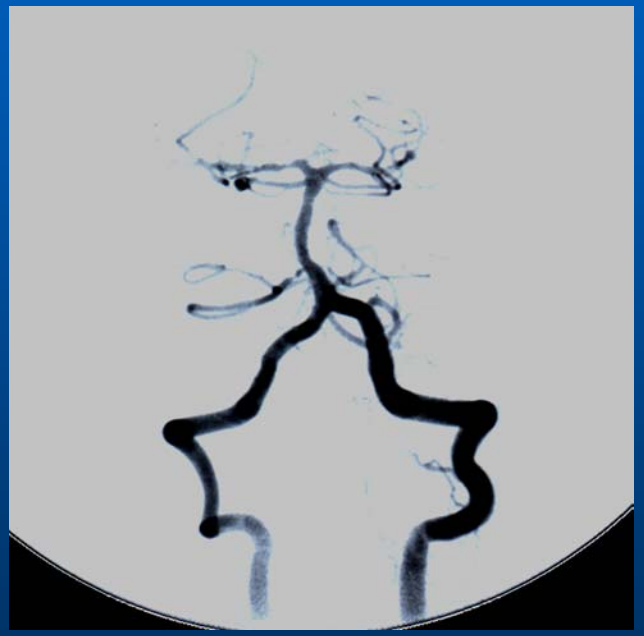
Endovascular Techniques





Endovascular Techniques





Conclusions

- Stroke prevention strategies are the most cost effective way of treating cerebrovascular disease
- Recognizing and treating risk factors is important in primary prevention
  - Currently little is known regarding risk factors for stroke in the Chinese population

Conclusions

- Understanding stroke subtype is important in developing strategies for secondary prevention
- Understanding the differences in the pathophysiology of stroke in the Chinese population vs other racial groups is important in developing strategies of stroke prevention and treatment