

# **Primary Stroke Prevention**

**Yousef Mohammad MD., MSc.  
Assistant Professor of Neurology  
and Director of the Stroke Fellowship Program  
Rush University**

# The High Socioeconomic Cost of Stroke

## Morbidity and Mortality

- A leading cause of serious, long-term disability
- Approximately 700,000 new or recurrent strokes occur annually in the US
- A leading cause of death, behind heart disease and cancer
- Approximately every 45 seconds someone in the US experiences a stroke

## Economic Impact

- Total direct and indirect costs are \$56.8 billion annually
- In the US, the mean lifetime cost of ischemic stroke is estimated at \$140,048

## Stroke Epidemiology

- Around 4 Million are living with neurologic deficits due to stroke
- In China, 1.5 million people die each year because of stroke
- Leading cause of serious long-term disability

## Stroke Epidemiology

- Stroke risk and mortality increase with age
- Stroke incidence is more in men than woman
- Stroke risk differs among races and ethnic population

## Stroke Epidemiology

- Risk is higher in the southeastern U.S., than elsewhere (mortality is 30% higher)
- The increase in life expectancy will increase the incidence of recurrent stroke

# Stroke Impact

- The economic, social, and psychological costs of stroke are enormous.
- Many important leaders in science, medicine, and politics had their productivity end prematurely short by stroke:
  - Marcello Malpighi
  - Louis Pasteur (at age 46)
  - Vladimir Lenin
  - Woodrow Wilson
  - Dwight Eisenhower
  - Richard Nixon



# Primary Stroke Prevention

- Currently, only <1% of acute stroke patients receive thrombolysis in U.S.  
(Mohammad et al. International Stroke Conference. February 2006).
- Despite the advent of treatment of selected patients with acute ischemic stroke with t-PA and mechanical thrombolysis, the best approach to reducing the burden of stroke remains prevention.
- High risk or stroke prone individuals can be identified and targeted for specific intervention

# Primary Stroke Prevention

## Nonmodifiable Risk Factors

- Age
- Race
- Sex
- Family History
- Birth Weight

# Primary Stroke Prevention

## Well-Documented Modifiable Risk Factors

- Hypertension
- Smoking
- Diabetes
- Asymptomatic Carotid Stenosis
- Sickle Cell Disease
- Hyperlipidemia
- Atrial Fibrillation

# Primary Stroke Prevention

## Potentially Modifiable Risk Factors

- Obesity
- Physical Inactivity
- Alcohol Abuse
- Hyperhomocystenemia
- Drug Abuse
- Hypercoagulability
- Hormone Replacement Therapy
- Oral Contraceptive Use
- Inflammatory Processes

# Primary Stroke Prevention

## Nonmodifiable Risk Factors

- **Age:** The risk of stroke doubles in each successive decade after 55 years of age
- **Sex:** Men have higher age-specific stroke incidence rates than women, except in 35-44 year olds and in those over 85 years of age. Stroke related case-fatality rates are higher in women than men.

# Primary Stroke Prevention

## Nonmodifiable Risk Factors

- **Race:** Blacks and some Hispanic Americans, have high stroke incidence and mortality rates compared with whites (Blacks have 38% greater incidence of stroke than whites.
- **Family History:** Both paternal and maternal history of stroke may be associated with increased stroke risk (RR paternal history: 2.4 and RR maternal history: 1.4.
- **Birth weight:** Birth weight is inversely associated with incident of stroke.

# Primary Stroke Prevention

## Well-Documented Modifiable Risk Factors

### Hypertension:

- It is a major risk factor for stroke.
- Both systolic and diastolic hypertension are important risk factors for stroke
- Isolated systolic hypertension is an important risk factor for stroke in the elderly
- There is compelling evidence for more than 30 years that the control of high blood pressure contributes to the prevention of stroke.

# Primary Stroke Prevention

## Well-Documented Modifiable Risk Factors

### Hypertension:

- Unfortunately, a significant proportion of the population has undiagnosed or inadequately treated hypertension, especially in high-risk race/ethnic groups.
- Regular screening for hypertension (at least every 2 years in adults). Management should include both life style modification and antihypertensive medications.

# Primary Stroke Prevention

## Well-Documented Modifiable Risk Factors

### Smoking:

- 25% of adults are active smokers
- A prospective estimate of a 1.8 fold increase in stroke risk associated with smoking from the Framingham Heart Study.
- Former smoking also place individuals at increased risk for stroke (RR 1.34).
- Exposure to environmental tobacco also increase the risk of stroke.
- Patient and family should be encouraged to stop smoking (counseling, nicotine replacement etc..)

# Primary Stroke Prevention

## Well-Documented Modifiable Risk Factors

### Diabetes:

- It is an independent risk for stroke (RR 1.8 to 6).
- Syndrome X is relatively common in type 2 diabetics.
- High BP is common in patients with type 2 diabetes, with a prevalence of 40 to 0% in adults.
- Tight BP control resulted in a convincing 44% relative risk reduction.
- Glycemic control is recommended to reduce microvascular complications.

# Primary Stroke Prevention

## Well-Documented Modifiable Risk Factors

### Asymptomatic Carotid Stenosis:

- 7% of women and 9% of men aged 66 to 93 years have carotid stenosis >50% (Framingham Study)
- The rate of stroke ipsilateral to the asymptomatic carotid stenosis is 1-2% annually
- ACAS Study: randomized asymptomatic carotid stenosis (>60%) to CEA vs. medical therapy

# Primary Stroke Prevention

## Well-Documented Modifiable Risk Factors

### Asymptomatic Carotid Stenosis:

- ACAS Results: 2.3% aggregate perioperative stroke risk
- The aggregate rate of ipsilateral stroke, any perioperative stroke, or death in the surgically treated patients was 5% over 5 years compared to 11% in the medically treated group
- This correspond to an annual event of 1% in the surgical group compared to 2% in the medically treated group (50% RR reduction)

# Primary Stroke Prevention

## Well-Documented Modifiable Risk Factors

### Asymptomatic Carotid Stenosis:

- ACAS Results: Women did not benefit
- CEA may be considered in patients with high grade asymptomatic carotid stenosis performed by a surgeon with <3% morbidity/mortality rate
- Careful patient selection, guided by comorbid conditions, life expectancy, patient preference, as well as other individual factors, including sex

# Primary Stroke Prevention

## Well-Documented Modifiable Risk Factors

### Atrial Fibrillation:

- The annual risk for stroke in unselected patients with nonvalvular atrial fibrillation is 3-5% and there is a dramatic increase in stroke risk associated with Afib. With advancing age
- Predictors of high stroke risk include advancing age, prior TIA or stroke, hypertension, impaired LVF, and DM.

# Primary Stroke Prevention

## Well-Documented Modifiable Risk Factors

### Atrial Fibrillation:

- Based on combined analysis of 5 major trials, the RR of thromboembolic strokes for patients treated with Warfarin was reduced by 68%.
- Antithrombotic medications (Warfarin or Aspirin) should be considered for patients with Afib based on an assessment of their risk for embolism and risk of bleeding complications

# Primary Stroke Prevention

## Well-Documented Modifiable Risk Factors

### Sickle Cell Disease:

- The prevalence of stroke in homozygous SS disease by age 20 is 11%
- The risk of stroke during childhood is 1% but patients with TCD evidence of stenosis have stroke rates in excess of 10% per year

# Primary Stroke Prevention

## Well-Documented Modifiable Risk Factors

### Sickle Cell Disease:

- STOP trial compared periodic transfusions with standard care: The risk of stroke was reduced from 10% per year to <1 % in the transfusion arm
- There are no systematic data on prevention of stroke in adults with SCD
- Children with SCD should be screened with TCD at 6 months interval to determine their level of stroke risk. Those at elevated risk should be considered for transfusion therapy

# Primary Stroke Prevention

## Well-Documented Modifiable Risk Factors

### Hyperlipidemia:

- There is an association between serum cholesterol and an increasing risk of stroke (1.8 to 2.6)
- An inverse relationship between HDL and stroke was demonstrated
- SPARCL Trial: 80 mg of Atrovastatin per day reduced the overall incidence of strokes and cardiovascular events, despite a small increase in the incidence of hemorrhagic stroke

# Primary Stroke Prevention

## Well-Documented Modifiable Risk Factors

### Hyperlipidemia:

- No CHD and <2 CHD risk factors: LDL goal < 160 with diet modifications for 6 months then drug therapy if LDL remains > 160 mg.dL
- No CHD but >2 CHD risk factors: LDL goal < 130 with diet modifications then drug therapy if LDL remains > 130 mg/dL
- Definite CHD: LDL goal of <100 with 6-12 week trial of diet modifications followed by drug therapy if LDL remains > 100 mg/dL

# Primary Stroke Prevention

## Potentially Modifiable Risk Factors

### Obesity:

- ABMI  $>30$  kg/m<sup>2</sup> predisposes to cardiovascular disease in general and stroke in particular
- Recent evidence support abdominal obesity in men and obesity in women as independent risk factors for stroke
- Weight reduction in overweight persons is recommended on the basis of the associated increase in comorbid conditions. Reduction in stroke risk with weight loss has not been established

# Primary Stroke Prevention

## Potentially Modifiable Risk Factors

### Physical Inactivity:

- Framingham Study and the Nurses Health Study demonstrated an inverse association between level of physical activity and stroke incidence
- NHANES and the Northern Manhattan Study showed protective effects of leisure-time physical activity in Blacks and Hispanics
- Americans should exercise moderately for at least 30 minutes on most, and preferably all days of the week. For stroke, the benefits are apparent even for light to moderate activities such as walking

# Primary Stroke Prevention

## Potentially Modifiable Risk Factors

### Poor Diet/Nutrition:

- There is no evidence that the use of dietary vitamin E or C supplements reduces the risk of stroke
- Based on the nurses Health Study, there may be a protective relationship between stroke and consumption of fruits and vegetables, especially green leafy vegetables and citrus fruit and juice
- A healthy diet containing at least 5 daily servings of fruits and vegetables may decrease the risk of stroke

# Primary Stroke Prevention

## Potentially Modifiable Risk Factors

### Alcohol Abuse:

- For hemorrhagic stroke, cohort studies have shown that alcohol consumption has a direct dose-dependent effect
- There is a J-shaped dose-response curve between alcohol intake and ischemic stroke risk with protection for those drinking up to 2 drinks per day and an increased risk for those drinking >5 drinks per day compared to Nondrinkers
- The US Preventive Services Task Forces recommended no more than 2 drinks per day for men and 1 drink per day for nonpregnant women

# Primary Stroke Prevention

## Potentially Modifiable Risk Factors

### Hyperhomocysteinemia:

- Meta-analysis, NHANES, Framingham studies have shown an association between hyperhomocysteinemia and stroke (OR: 1.5, 2.25, and 1.8)
- Folic Acid, together with vitamin B6 and b12, has been shown to be effective in reducing elevated plasma Homocysteine level
- VISP Trial: Reduction of Homocysteine level with Folic Acid, Vitamin B 6 and 12 was not effective in reducing the incidence of recurrent stroke events.
- Current recommendations include daily amounts of Folate (400 microg/d, Vitamin B6(1.7mg/d) and Vitamin b12 92.4 microg/d)

# Primary Stroke Prevention

## Potentially Modifiable Risk Factors

### Drug Abuse:

- Amphetamines, cocaine and Heroin increase the risk of both ischemic and hemorrhagic stroke (7 fold increase in stroke risk among drug users)
- History of illicit drug abuse should be sought during medical evaluation and the patient referred for appropriate and counseling

# Primary Stroke Prevention

## Potentially Modifiable Risk Factors

### Hypercoagulability:

- The presence of antiphospholipid antibodies has been shown in several case-control studies and one prospective study to be associated with ischemic stroke
- Other coagulation abnormalities (Factor V Leiden and Prothrombin mutation, Protein C and S and anti-Thrombin III deficiency) are not important risk factors for ischemic stroke

# Primary Stroke Prevention

## Potentially Modifiable Risk Factors

### Hormone Replacement Therapy:

- Framingham Heart Study: 2.6 fold increase in the relative risk of stroke among women receiving hormone replacement therapy compared with non-users
- Women Health Initiative Study: Increased risk of stroke , CHD, and pulmonary embolism in the arm receiving HRT

# Primary Stroke Prevention

## Potentially Modifiable Risk Factors

### Oral Contraceptive Use:

- A meta-analysis concluded that the risk of ischemic stroke is increased in oral contraceptive users but that the absolute increase in risk is small
- Women who are cigarette smokers, are hypertensive, or have diabetes, migraine, or prior thromboembolic events may be at increased stroke risk if they use oral contraceptives
- Oral contraceptives should be avoided in women with additional risk factors (cigarette smoking, or prior thromboembolic events)