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Specific secondary stroke risk factors in women after stroke

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Disclosure

- Nothing to disclose

There are 2 main strategies to reduce the global burden of stroke

- 1) to effectively treat patients with acute stroke to minimize death and disability
- 2) to prevent first-ever stroke and recurrent stroke

Conventional risk factors

- INTERSTROKE study identified modifiable risk factors that explain 90% of the population-attributable risk (PAR) of stroke in both sexes

- ✓ Hypertension
- ✓ Current smoking
- ✓ Waist-to-hip ratio
- ✓ Diet
- ✓ Physical activity
- ✓ Diabetes
- ✓ Alcohol consumption
- ✓ Cardiac causes (atrial fibrillation/flutter, previous myocardial infarction, rheumatic valve disease, prosthetic heart valve)
- ✓ Psychosocial factors
- ✓ Apolipoprotein B to A1 ratio

Stroke risk factors in women

Women specific

- Pregnancy
- Preeclampsia
- Gestational diabetes
- Oral contraceptive use
- Postmenopausal hormonal use

Stronger or more prevalent in women

- Migraine with aura
- Atrial fibrillation
- Diabetes mellitus
- Hypertension

Similar prevalence in men, unknown impact

- Physical inactivity
- Age
- Prior CV disease
- Diet
- Smoking
- Obesity
- Metabolic syndrome

Conventional stroke risk factors

Risk Factor	Prevalence	Association with IS	Treatment Disparity
Hypertension	Lower in women (vs. men) in younger age groups, higher in older age groups	Similar in women (vs. men) in younger age groups, higher in older age groups	In younger age groups, women more likely to have BP controlled; in older age groups, women less likely to have BP controlled
Dyslipidemia	Data conflict; either similar between sexes or lower in women	Lower in women	Women less likely to be on statins and have LDL controlled
Atrial Fibrillation	Higher in women	Higher in women	Women less likely to be prescribed oral anticoagulants, less likely to have cardiac ablation, and receive lower doses of NOACs

Conventional stroke risk factors

Risk Factor	Prevalence	Association with IS	Treatment Disparity
Migraine	Higher in women	Higher in women	Unknown if migraine treatment reduces stroke risk
Diabetes	Similar women vs. men	Higher in women	Data conflict regarding sex differences in meeting HbA1c goal
Cognitive Impairment	Higher in women	Unknown whether there is a sex difference	Women less likely to be treated with anti-dementia drugs

Unique risk factors for women

- **Parenthood** likely increases the risk for CVD
- Linear association between the **number of children** and stroke (each additional child increases stroke in women and men)
- **Stillbirth**: increased risk of any type stroke later in life
- **Gestational hypertension** : over five times risk of hemorrhagic stroke
- **Hysterectomy**: protective in women
- Women who **breastfed** for ≥ 24 months had a 17% lower risk of stroke compared with women who had never breastfed

Stroke: large negative impact on society

➤ Women are disproportionately affected



➤ 5th leading cause of death for men & 3rd leading cause for women

➤ By 2030, there will be 72 million people >65 years old (19% of the population), and women will increasingly outnumber men

Increase of the stroke burden in women

- Half of stroke survivors have residual deficits (weakness or cognitive dysfunction) 6 months after stroke, which means **200 000 more disabled women** with stroke than men

Women live longer than men

- Lifetime risk of stroke in people aged 55-75 years is higher in women (20%) than men (17%)
- Women are more likely to be
 - ❖ living alone and widowed before stroke
 - ❖ more often institutionalized after stroke
 - ❖ have poorer recovery from stroke than men
- Women are more adversely affected by stroke than men

Due to biological characteristics and female-specific risk factors

- females have a higher risk of stroke
- higher chance of experiencing recurrence
- higher severity of stroke symptoms than that of males

Secondary stroke prevention after TIA or ischemic stroke

- **After ischemic stroke and TIA, the risk of recurrent stroke without treatment is:**
 - 10% at 1 week,
 - 15% at 1 month,
 - 18% at 3 months
- **The longer-term risk of recurrent stroke is**
 - 10% at 1 year,
 - 25% at 5 years
 - 40% at 10 years

Immediate evaluation of patients with stroke or TIA is necessary

- Initiation of secondary prevention treatment depending on the underlying cause will **reduce the risk** of recurrent stroke by **up to 80%**



HYPERTENSION



- Antihypertensive therapy reduces the risk of ischemic and hemorrhagic stroke
- All antihypertensive drugs are equally effective in secondary stroke prevention
- Beta-blockers may be least preferred due to an increased blood pressure variability
- Optimal blood pressure target for secondary stroke prevention is $< 130/80$ mmHg and might be 120- to 128- mm Hg systolic and 65- to 70- mm Hg diastolic after lacunar stroke

Hypertension in pregnancy



- Women with chronic hypertension/ history of pregnancy-related hypertension should take **low-dose aspirin** from **12th week** of gestation until **delivery** (Class I Level A)
- Control hypertension: methyldopa, labetalol, nifedipine (Class I Level A)

– Atenolol, ACEI, ARBS are contraindicated



Pregnancy after stroke?

- Once a woman has had a stroke during a first pregnancy, the risk of recurrent stroke during subsequent pregnancies is slightly increased, mainly in the post-partum period, but does not represent a contraindication to subsequent pregnancies
- Risk increased with further risk factors (i.e. antiphospholipid syndrome) and higher age of the mother (>35 years)



LIPID DISORDERS



- Lowering LDL cholesterol by 1 mmol/l with statins reduces the risk of recurrent stroke by at 12%
- Guidelines recommend target LDL cholesterol of 1.4mmol/l for high vascular risk patients
- For secondary prevention in very high-risk patients, LDL cholesterol reduction of $\geq 50\%$ from baseline and LDL cholesterol goal of **$< 1.4\text{mmol/l}$ ($<55\text{mg/dl}$)** is recommended



LIPID DISORDERS



- For patients with atherosclerotic CV disease who experience **second vascular event within 2 years** (not necessarily of the same type as the first event) while taking maximally tolerated statin therapy, **LDL cholesterol goal of <1.0 mmol/l (<40mg/dl)** may be considered

HORMONE REPLACEMENT THERAPY AFTER MENOPAUSE

- A randomized, placebo-controlled study in women who experienced stroke and received hormone replacement therapy after menopause showed an increase in stroke mortality and a poorer prognosis in nonfatal strokes
- Hormone replacement after menopause is **not effective** in the secondary stroke prevention in women and may **increase mortality** after stroke

ANTIPLATELET THERAPY

- TIA / ischemic stroke: aspirin, clopidogrel, aspirin plus extended-release dipyridamole, ticagrelor, cilostazol
- Short-term use of dual antiplatelet therapy for up to 21 days may be considered in acute minor stroke or TIA and high risk of recurrence

ANTICOAGULATION THERAPY

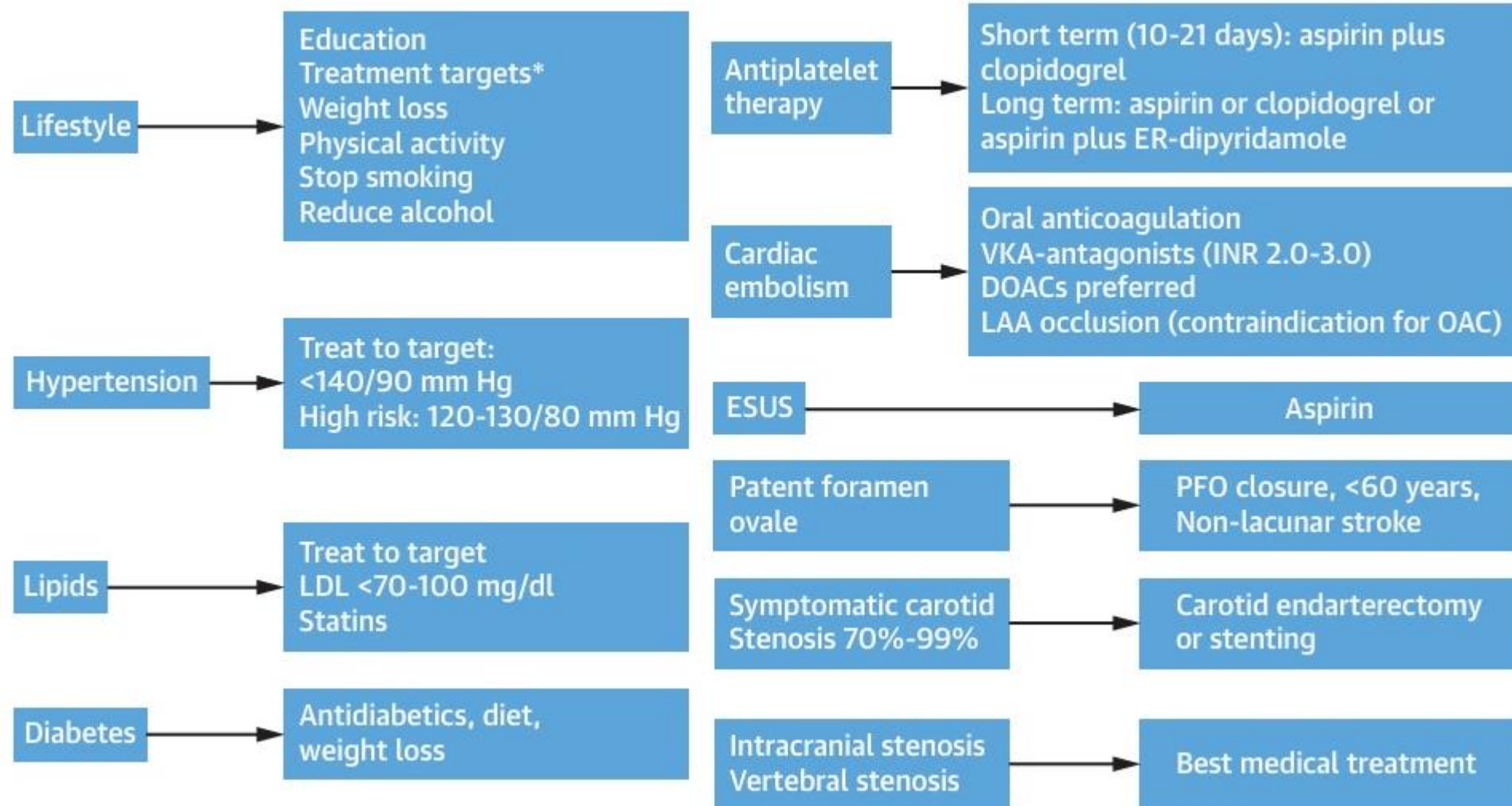
- Oral anticoagulation for patients with minor ischemic stroke or TIA reduces the risk of recurrent stroke by about 66% compared with placebo
- Patients with cardiac embolism, in particular with AF, should be treated with oral anticoagulation
- Dose-adjusted warfarin (INR 2.0 - 3.0) or DOACs apixaban, dabigatran, edoxaban, and rivaroxaban
- DOACs are contraindicated in patients with moderate-to-severe mitral stenosis, rheumatic heart disease, or mechanical heart valves

Anticoagulation: challenges in women

- Some data demonstrate that women are less likely to be treated with anticoagulation and that women have a higher risk for stroke despite anticoagulation with warfarin
- Difference between men and women was not seen in women treated with novel anticoagulants

Secondary stroke prevention

Patients with TIA or Ischemic Stroke



Conclusion

- Optimal stroke prevention requires
 - harmonious, integrated approach to educating about stroke risk and healthy lifestyle behaviors
 - simple screening
 - management of individuals for a history and presence of modifiable and treatable causal risk factors
 - improving social and environmental factors

THANK YOU FOR YOUR KIND ATTENTION

