Penn State College of Medicine
Continuing Education

Neurology for the Non-Neurologist

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Any names or ages used on the upcoming slides are fictitious and not referring to an actual patient.

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1

Updates in Primary and Secondary Ischemic Stroke Prevention

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2

Disclosures

No relevant financial disclosures.

3

Objectives

- Define primary and secondary stroke prevention and understand the differences in approaches for each.
- Review current evidence-based strategies for primary and secondary prevention of ischemic stroke, including lifestyle modification and medical interventions.
- Examine the role of medications including anti-thrombotic, lipid-lowering therapy, and diabetes medications in both primary and secondary stroke prevention.
- Develop skills for assessing stroke risk and creating individualized prevention plans for patients in primary care settings.

4

Importance

≈ 795K people experience stroke each year
- 690K ischemic
- 610K first attacks, 185K recurrent strokes
- 240K TIA

Someone dies of stroke every **3 minutes 11 seconds**
- Stroke deaths increased by **28.7%** from 2012-2022

Aspirin + statin + antihypertensive + diet + exercise
- = **80%** cumulative risk reduction

Primary and secondary prevention

Primary prevention

- Screening patients for increased risk of stroke and cardiovascular disease
- Modifying risk factors
- Population-based and high-risk individual approaches

Secondary prevention

- Guided by stroke etiology and mechanism with aggressive modification of risk factors
- Individual approach

Primary Prevention: Screening

- For patients aged 40-79 years, CVD risk estimations every 1-5 years beneficial to guide decisions on treatments and lifestyle recommendations (class 1)
- CHA2DS2-VASc score recommended to guide oral anticoagulation decisions in patients with AF (1)
- Periodic screening for modifiable behaviors and medical conditions that increase stroke risk recommended (1)
- Periodic screening for SDoH beneficial to identify additional factors which contribute to stroke risk (1)

7

Secondary Prevention: Diagnostic Evaluation

- ECG to screen for AF/atrial flutter and assess for other concomitant cardiac conditions (1)
- Diagnostic evaluation completed/underway within 48 hours of onset (1)
- CT or MRI to confirm diagnosis (1)
- Laboratory tests: CBC, PT, PTT, glucose, HbA1c, creatinine, fasting/non-fasting lipid profile (1)

8

Secondary Prevention: Diagnostic Evaluation

- Non-invasive cervical carotid imaging (US, CTA, or MRA) for anterior circulation stroke/TIA (1) and intracranial arterial imaging (2a)
- Non-invasive intracranial and extracranial imaging of vertebrobasilar arterial system in posterior circulation stroke/TIA (2a)
- Echo to evaluate for possible cardiac sources or transcardiac pathways for cerebral embolism (2a)
- Long-term rhythm monitoring with MCOT, ILR, or other approach for patients with cryptogenic stroke and no contraindication to anticoagulation (2a)

9

Secondary Prevention: Diagnostic Evaluation

- If initial CT/MRI negative in suspected stroke, follow-up CT/MRI reasonable (2a)
- If initial CT/MRI negative in suspected stroke/TIA, follow-up MRI reasonable (2a)
- For cryptogenic stroke, tests for inherited/acquired hypercoagulable state, bloodstream or CSF infections, infections that cause CNS vasculitis (eg, HIV, syphilis), drug use (eg, cocaine, amphetamines), markers of systemic inflammation, and genetic tests for inherited diseases associated with stroke reasonable (2a)

10

Secondary Prevention: Diagnostic Evaluation

- If stroke treatment plan includes anticoagulation, CT or MRI before therapy is started may be considered to assess for hemorrhagic transformation and final size of infarction (2b)
- In embolic stroke of undetermined source (ESUS), TEE, cardiac CT, or cardiac MRI reasonable to identify possible cardioaortic sources or transcardiac pathways for embolism (2b)
- If PFO closure would be contemplated, transcranial doppler with embolus detection reasonable to screen for right-to-left shunt

11

Modifiable risk factors

12

Diet: Eat Better

(AHA)

Primary prevention

- Mediterranean diet for adults with intermediate-high CVD risk (1)
- Salt substitution reasonable for adults 60+ with uncontrolled BP (2a)

Secondary prevention

- Mediterranean diet preferred over low-fat diet (2a)
- Reduce sodium intake by at least 1g/d in those with hypertension (2a)

Physical Activity: Be More Active

(AHA)

Primary prevention

- Screen adults for physical activity (1)
- Counsel to get ≥ 150 min moderate intensity or 75 min vigorous intensity physical activity/week (1)
- Counsel to avoid excessive time spent in sedentary behavior (1)

Secondary prevention

- If capable, moderate activity ≥ 10 min 4x/wk or vigorous 20 min 2x/wk (1)
- If able to increase, exercise class that includes counseling (2a)
- If impaired ability, supervision by health care professional and routine rehabilitation (2a)
- At least 3 min standing for every 30 min sedentary (2b)

Diabetes: Manage Blood Sugar

(AHA)

Primary prevention

- Screen adults with overweight, obesity, or ASCVD for diabetes (1)
- GLP-1 for patients with diabetes and high CV risk or CVD (1)
- Intensive glycemic control in T1D or T2D not beneficial (3)

Secondary prevention

- Individualized goal (1), HbA1c ≤ 7% for most (1)
- Agents with proven cardiovascular benefit (1), multidimensional care (1)
- Lifestyle optimization for pre-diabetes (2a), add metformin if pre-diabetes with BMI ≥ 35 kg/m^2, age <60, or GDM hx (2b)
- Screen with HbA1c (2a)

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15

Weight and Obesity: Manage Weight

(AHA)

Primary prevention

- Screen for overweight and obesity (1)
- Consider bariatric surgical procedures for Obesity Class II and above (2b)

Secondary prevention

- Weight loss if overweight or obese (1)
- Referral to intensive, multicomponent, behavioral lifestyle-modification program if obese (1)
- Calculate BMI at time of event and annually thereafter (1)

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16

Lipids: Control Cholesterol

(AHA)

Primary prevention

- Statin treatment per AHA guidelines (1)
- Benefit of PCSK9 inhibitors not proven for those without CVD (2b)
- Bempedoic acid not proven for statin intolerance with increased CV risk (2b)
- Omega-3 fatty acids not recommended (3)

Secondary prevention

- If no CAD or atherosclerotic source & LDL-C >100 mg/dL, atorvastatin 80 mg daily (1)
- Statin ± ezetimibe for goal LDL-C <70 mg/dL if atherosclerosis (1)
- Fasting lipids, 4-12 wks after initiation/adjustment, then 3-12 months (1)
- PCSK9 inhibitor if LDL-C >70 mg/dL (2a)

17

Blood Pressure: Manage Blood Pressure

(AHA)

Primary prevention

- screen for HTN (1)
- Stage 1-2: lifestyle modification & drug treatment, goal <130/80 (1)
- Thiazide or thiazide-like diuretics, CCB, ACEI, & ARBs recommended initial therapies (1)
- One or more medications indicated (1)

Secondary prevention

- Treatment with thiazide-diuretic, ACEI, or ARB (1)
- Office BP goal <130/80 mmHg for most (1)
- Individualized drug regimens (1)
- If average office BP ≥130/80 mmHg, drug treatment beneficial (2a)

18

Tobacco Use: Quit Tobacco

(AHA)

Primary prevention

- Cessation medication & behavioral counseling (1)
- Assistance with cessation recommended (1)
- Cessation medications & behavioral counseling reasonable in a hospital setting (2a)
- Long-term health benefits of using e-cigarettes not established (2)

Secondary prevention

- Counseling ± drug therapy (nicotine replacement, bupropion, varenicline) (1)
- Avoid environmental (passive) exposure (1)

19

Obstructive Sleep Apnea: Get Healthy Sleep

(AHA)

Primary prevention

- Effectiveness of screening for OSA unclear (2b)
- In patients with OSA, CPAP might be reasonable (2b)

Secondary prevention

- Treatment of OSA with PAP can be beneficial (2a)
- Evaluation for OSA may be considered (2b)

20

Antithrombotic therapy

21

Primary prevention

- Benefit of antiplatelet therapy in adults with silent cerebral infarcts uncertain (2b)
- Anticoagulation not indicated for left ventricular systolic function without AF or left ventricular thrombus (3)
- In patients with stable CAD and low bleeding risk, ticagrelor + aspirin beyond 12 months up to 3 years may be beneficial (2b)
- In patients without CAD…
  - With diabetes or other common vascular risk factors, use of aspirin not well established (2b)
  - ≥ 70 years with at least one additional cardiovascular risk factor, aspirin not beneficial (3)
  - With CKD, aspirin not effective (3)

22

Secondary prevention: noncardioembolic stroke/TIA

- Antiplatelet preferred over anticoagulation (1)
- Aspirin 50-325 mg daily, clopidogrel 75 mg, or combination aspirin 25 mg and extended-release dipyridamole 200 mg twice daily (1)
- Recent minor stroke (NIHSS ≤3) or high-risk TIA ($ABCD^2$ score ≥ 4), DAPT (aspirin + clopidogrel) initiated early (ideally 12-24 hours, at least 7 days of onset), continued for 21-90 days, followed by SAPT (1)
- Recent (< 24 hours) minor-moderate stroke (NIHSS ≤5) or high-risk TIA ($ABCD^2$ score ≥ 6), or symptomatic intracranial or extracranial ≥30% stenosis, DAPT (aspirin + ticagrelor) for 30 days but may increase risk of serious bleeding, including ICH (2b)
- Already taking aspirin, effectiveness of increasing dose or changing antiplatelet medication not well established (2b)
- Continuous use of DAPT >90 days or triple antiplatelet therapy has excess risk of hemorrhage (3)

Secondary prevention: intracranial large artery atherosclerosis

- If stroke/TIA caused by 50-99% stenosis of major intracranial artery…
  - Aspirin 325 mg/d recommended over warfarin (1)
  - Consider addition of cilostazol 200 mg/day or clopidogrel (2b)
  - Clopidogrel alone, aspirin-dipyridamole, ticagrelor alone, or cilostazol alone not well established (2b)
- If stroke/TIA within 30 days caused by 70-99% stenosis of major intracranial artery, addition of clopidogrel 75 mg/d for up to 90 days reasonable (2a)
- If minor stroke/high-risk TIA within 24 hours and concomitant ipsilateral >30% stenosis of major intracranial artery, consider addition of ticagrelor 90 mg BID for up to 30 days (2b)

Secondary prevention: extracranial atherosclerosis

- Carotid or extracranial vertebral artery stenosis: intensive medical therapy with antiplatelet, lipid-lowering therapy, and hypertension treatment (1)
- Aortic arch atheroma: antiplatelet therapy (1) in addition to intensive lipid management with LDL-C goal <70 mg/dL (1)

Secondary prevention: small vessel disease

- Benefit of cilostazol uncertain (2b)

25

Secondary prevention: atrial fibrillation

- Nonvalvular AF: OAC recommended (1); apixaban, dabigatran, edoxaban, or rivaroxaban preferred over warfarin (1), including if unable to maintain therapeutic INR level with warfarin (1)
- OAC regardless of AF pattern (eg paroxysmal, persistent, or permanent) (1); atrial flutter similar (1)
- Reasonable to initiate immediately after index TIA (2a), 2-14 days after stroke with low risk of hemorrhagic conversion (2b), or delay beyond 14 days if stroke with high risk of hemorrhagic conversion (2a)
- If lifelong anticoagulation contraindicated but can tolerate 45 days, consider percutaneous left atrial appendage closure (2b)
- If ESRD or dialysis, warfarin or apixaban (dose adjusted) (2b)

26

Secondary prevention: valvular heart disease

- Valvular AF: warfarin (1)
- Mechanical mitral valve and stroke/TIA before valve replacement: aspirin (75-100 mg/d) in addition to warfarin with INR range 2.5-3.5 (1)
- Native aortic or nonrheumatic mitral valve disease without AF: antiplatelet (1)
- Bioprosthetic aortic or mitral valve and stroke before valve replacement: long-term aspirin preferred to anticoagulation (1)
- Mechanical aortic valve: higher-intensity warfarin (range 2.5-3.5) or addition of aspirin (75-100 mg/day) (2a)
- Mechanical valves: dabigatran harmful (3)

27

Secondary prevention: LV thrombus and cardiomyopathy

- LV thrombus: warfarin for at least 3 months (1); safety of DOAC uncertain (2b)
- Acute MI
  - Advanced cardiac imaging to assess for LV thrombus (2a)
  - Reduced EF (<50%): consider empirical anticoagulation for at least 3 months (2b)
- LA or LV thrombus with cardiomyopathy: warfarin for at least 3 months (1)
- Mechanical assist device: warfarin and aspirin (2a)
  - LVAD: dabigatran harmful (3)
- LV noncompaction: warfarin (2a)
- Reduced EF: anticoagulation versus antiplatelet uncertain (2b)

28

Secondary prevention: embolic stroke of undetermined source

- DOAC not recommended (3)
- Ticagrelor not recommended (3)

29

Wrap-up

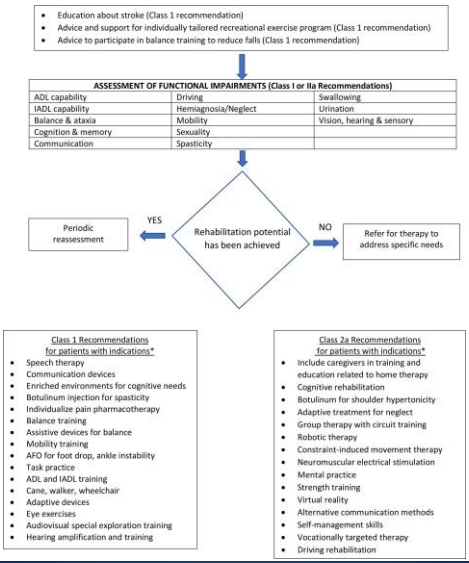
30

Post-stroke primary care

- Goals: patient-centered care, prevent recurrent brain injury, maximize function, prevent late complications, optimize quality of life
- First visit should occur within 1-3 weeks from discharge
- Assess for consequences of stroke and update medical and social history at every visit
- Screen for complications and unmet needs
- Consider referral to PT, OT, SLT even in chronic phase
- Determine cause of stroke and ensure adequate secondary stroke prevention
- Assess function and refer for rehab services
- Encourage physical activity

31

Post-stroke primary care



(Stroke, 2021)

32

Summary

Stroke is a preventable disease with high morbidity and mortality

Primary prevention to minimize stroke risk factors
Life's Essential 8 as a guiding framework

Secondary prevention tailored to identified risk factors by etiology

Look to AHA/ASA guidelines and scientific statements

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Thank you

Questions?

35