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512 Stroke

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Stroke

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Foreword

More than 795,000 individuals in the United States experience a stroke each year, and approximately 75% of those are first strokes.[1] In 2009, 34% of patients hospitalized with stroke were younger than 65 years. Up to 50% of patients older than 65 years who have a stroke experience a loss in mobility,[1] and one study reported 20% to 25% were unable to walk poststroke.[2] Others recover without sequelae.

As clinicians, we know there are many risk factors associated with stroke, but patients often perceive themselves to be in good health until the moment the stroke occurs. Because strokes feel random and severe, patients are afraid of the consequences. Patients who experienced a stroke recently viewed the common consequences of stroke, such as incontinence or speech difficulty, as "worse than death."[3]

This edition of *FP Essentials*™ covers the evaluation and management of acute ischemic stroke, which accounts for 87% of all strokes.[1] *Section One* addresses primary prevention of stroke and details the common cardiovascular risk factors and less common risk factors (eg, migraine, COVID-19 infection). *Section Two* describes the initial diagnostic evaluation of patients with a presumed acute ischemic stroke, including evaluation settings (eg, prehospital, emergency department), assessment of severity, etiologies, and patent foramen ovale. *Section Three* discusses acute management, including evaluation for thrombolysis or thrombectomy; poststroke care in the inpatient setting; and management of blood pressure, blood glucose, and edema. *Section Four* covers poststroke care of patients, including rehabilitation care, secondary prevention, and ambulatory care.

The care of patients with stroke is a routine part of the practice of family medicine, whether preventive or follow-up care. I hope you find this edition useful in your practice.

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1. Centers for Disease Control and Prevention. Stroke facts. 2021. https://www.cdc.gov/stroke/facts.htm
2. Dobkin BD. Rehabilitation after stroke. *N Engl J Med*. 2005; 352(16): 1677–1684.
3. Everett EA, Everett W, Brier MR, White P. Appraisal of health states worse than death in patients with acute stroke. *Neurol Clin Pract.* 2021;11(1):43-48.

Learning Objectives

1. Summarize common risk factors for ischemic stroke.
2. Describe the rationale behind the U.S. Preventive Services Task Force (USPSTF) recommendation against screening asymptomatic patients for carotid artery stenosis.
3. Diagnose acute ischemic stroke.
4. Assess the severity of acute ischemic stroke.
5. Determine which patients with acute ischemic stroke are eligible for thrombolysis or thrombectomy.
6. Summarize the medical management of hospitalized patients after an acute ischemic stroke.
7. Differentiate among the appropriate discharge options for patients after an acute ischemic stroke.
8. Summarize the short- and long-term management of patients after acute ischemic stroke.

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Editorial Mission and Policies

FP Essentials is an editorially independent, peer-reviewed publication of the American Academy of Family Physicians (AAFP). It, and its derivative product *FP Comprehensive*™, are produced to assist family physicians and other learners in meeting their continuing medical education (CME), practice, and board certification goals.

Editorial Mission

The mission of *FP Essentials* is to provide practicing family physicians, family medicine residents, and other clinicians and trainees with high-quality, cost-effective educational content that emphasizes new advances in clinical practice.

Objectives

1. To provide learners with information on advances in clinical practice to aid them in providing up-to-date care for their patients.
2. To assist learners in preparing for the American Board of Family Medicine (ABFM) certification and recertification examinations. Each monthly edition of *FP Essentials* is part of a 9-year curriculum that presents topics with areas of emphasis similar to those on the ABFM examinations.
3. To provide learners with content that meets their CME needs and requirements.
4. To present the content of *FP Essentials* in both print and online formats, thus enabling learners to have access to information anywhere, anytime.

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Manuscripts are solicited from family physicians and subspecialists. For information about writing or peer reviewing, contact Medical Editor Barry D. Weiss, MD, FAAFP, at bdweiss@u.arizona.edu.

Pretest Questions

1. Which one of the following best describes the choice of treatment for stroke prevention in patients with atrial fibrillation (AF)?

- ❑ A. Anticoagulation is preferred for all patients with AF.
- ❑ B. Direct oral anticoagulants are preferred for patients with nonvalvular AF.
- ❑ C. Surgical options, such as left atrial appendage closure, are indicated for secondary prevention only.
- ❑ D. Warfarin is no longer indicated for AF.

2. Which one of the following is true of stroke screening and treatment in patients with sickle cell disease (SCD)?

- ❑ A. Adults with SCD should undergo screening with carotid ultrasonography and head computed tomography (CT) scan.
- ❑ B. Adults with sickle cell trait should undergo screening with carotid ultrasonography and a head CT scan.
- ❑ C. Children between ages 2 to 16 years with SCD should undergo screening with transcranial doppler ultrasound.
- ❑ D. Positive screening results warrant referral for statin and antiplatelet therapy.

3. Which one of the following laboratory tests should be obtained as part of the initial emergency department evaluation of acute ischemic stroke?

- ❑ A. Blood glucose level.
- ❑ B. Complete blood cell count.
- ❑ C. Complete metabolic panel.
- ❑ D. International normalized ratio.

4. Which one of the following is true of computed tomography (CT) scan of the brain in acute ischemic stroke?

- ❑ A. CT angiography, if indicated, should not be performed concurrently with the initial noncontrast CT scan.
- ❑ B. Results of a noncontrast head CT scan performed within 6 hours of ischemic stroke onset may appear normal.
- ❑ C. Visible changes on CT scan will be present within 3 hours of acute ischemic stroke in most patients.
- ❑ D. Urgent head CT scan is performed to evaluate the extent of injury.

5. In which one of the following cases would thrombectomy possibly be contraindicated?

- ❑ A. Age older than 80 years.
- ❑ B. Baseline functional impairment (modified Rankin Scale [mRS] greater than 2).
- ❑ C. Large vessel occlusion.
- ❑ D. Last seen normal time 8 hours ago.
- ❑ E. Previous thrombolysis.

6. Which one of the following is true of hypertension treatment in patients after acute ischemic stroke?

- ❑ A. For neurologically stable patients, resuming usual antihypertensive drugs is associated with improved blood pressure (BP) control.
- ❑ B. For patients who have received thrombolysis, target BP during hospitalization is less than 140/90 mm Hg.
- ❑ C. For patients who have not received thrombolysis, target BP is 180/105 mm Hg in the first 24 hours.
- ❑ D. For patients with BP greater than 220/120 mm Hg, rapid reduction to less than 160/90 mm Hg is associated with improved outcomes.

7. Which one of the following is the most prevalent risk factor for stroke?

- ❑ A. Hypercoagulable state.
- ❑ B. Hyperglycemia.
- ❑ C. Hyperlipidemia.
- ❑ D. Hypertension.

8. Which one of the following drugs should be recommended for use in stroke patients with diabetes to reduce the risk of future cardiovascular events?

- ❑ A. Analog insulin.
- ❑ B. Human insulin.
- ❑ C. Sodium-dependent glucose cotransporter 2 inhibitor.
- ❑ D. Sulfonylureas.

Pretest Answers

Question 1: The correct answer is B.
The more recent 2019 American Heart Association/American College of Cardiology/Hearth Rhythm Society (AHA/ACC/HRS) guidelines for atrial fibrillation (AF) management suggest that use of direct-acting oral anticoagulants is preferable in patients with nonvalvular AF. *See page 13.*

Question 2: The correct answer is C.
Children with sickle cell disease should be screened for stroke with transcranial Doppler ultrasound from ages 2 to 16 years. *See page 15.*

Question 3: The correct answer is A.
The emergency department evaluation of stroke should include assessment of vital signs, measurement of the blood glucose level, calculation of the National Institutes of Health Stroke Scale (NIHSS) (*Table 7*) or initial neurologic assessment with focal deficits identified, review of any use of antithrombotics, and the time that the patient was last reported to have been seen well. *See page 19.*

Question 4: The correct answer is B.
Results of a noncontrast computed tomography scan performed less than 6 hours after ischemic stroke onset may appear normal. *See page 19.*

Question 5: The correct answer is B.
It is unknown if thrombectomy is beneficial for patients with a functional disability (modified Rankin [mRS] of 2 or higher) at baseline. *See page 26.*

Question 6: The correct answer is A.
Typically, it is safe for neurologically stable patients to resume taking their usual antihypertensive drugs during the hospital stay. This approach has been shown to improve blood pressure control but is not associated with changes in patient-oriented outcomes, such as functional outcomes or mortality. *See page 29.*

Question 7: The correct answer is D.
Hypertension is the most prevalent risk factor for stroke. *See page 33.*

Question 8: The correct answer is C.
Diabetes management in patients with stroke should include blood glucose-lowering drugs shown to reduce the rate of cardiovascular events, such as a glucagon-like peptide 1 receptor agonist, sodium-dependent glucose cotransporter 2 inhibitor, or thiazolidinediones. *See page 33.*

Key Practice Recommendations

1. For primary prevention of stroke, patients with hypertension should be treated with antihypertensive drugs to achieve a goal blood pressure level less than 140/90 mm Hg.
2. In patients with suspected acute ischemic stroke, obtain brain imaging on first arrival to a hospital using noncontrast computed tomography scan and/or magnetic resonance imaging study to help identify candidates for thrombolysis or thrombectomy.
3. After an acute ischemic stroke, screen patients for dysphagia before the patient resumes oral intake of foods, fluids, or drugs to identify patients at increased risk of aspiration.
4. After an acute ischemic stroke, administer aspirin within the first 24 to 48 hours in patients without contraindications.
5. Before discharge from the hospital, all patients who have had an acute ischemic stroke should undergo a formal assessment of rehabilitation needs.
6. For most patients with hypertension and a history of stroke, the goal blood pressure level should be less than 130/80 mm Hg.

Evidence Ratings and Sources

1. **Evidence rating: SORT A**
   Source: American Heart Association/American Stroke Association, reference 3
   Website: https://www.ahajournals.org/doi/10.1161/STR.0000000000000046
2. **Evidence rating: SORT A**
   Source: American Heart Association/American Stroke Association, reference 45
   Website: https://www.ahajournals.org/doi/full/10.1161/STR.0000000000000211
3. **Evidence rating: SORT A**
   Source: American Heart Association/American Stroke Association, reference 45
   Website: https://www.ahajournals.org/doi/full/10.1161/STR.0000000000000211
4. **Evidence rating: SORT A**
   Source: American Heart Association/American Stroke Association, reference 45
   Website: https://www.ahajournals.org/doi/full/10.1161/STR.0000000000000211
5. **Evidence rating: SORT A**
   Source: American Heart Association/American Stroke Association, reference 74
   Website: https://www.ahajournals.org/doi/10.1161/STR.0000000000000098
6. **Evidence rating: SORT A**
   Source: American Heart Association/American Stroke Association, reference 39
   Website: https://www.ahajournals.org/doi/full/10.1161/STR.0000000000000375

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Evidence Rating	Definition
A	▪ Recommendation based on consistent and good-quality patient-oriented evidence.[a]
B	▪ Recommendation based on inconsistent or limited-quality patient-oriented evidence.[a]
C	▪ Recommendation based on consensus, usual practice, opinion, disease-oriented evidence,[a] or case series for studies of diagnosis, treatment, prevention, or screening.

[a]*Patient-oriented evidence measures outcomes that matter to patients: morbidity, mortality, symptom improvement, cost reduction, and quality of life. Disease-oriented evidence measures intermediate, physiologic, or surrogate end points that may or may not reflect improvement in patient outcomes (eg, blood pressure, blood chemistry, physiologic function, pathologic findings).*

(From Ebell MH, Siwek J, Weiss BD, et al. Strength of recommendation taxonomy [SORT]: a patient-centered approach to grading evidence in the medical literature. Am Fam Physician. *2004;69:548-556.)*

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Section One
Primary Prevention

Stroke is a leading cause of long-term disability in adults and the fifth leading cause of mortality in the United States. One of the main tasks related to stroke in the family medicine setting is assessment and management of modifiable risk factors. The American Heart Association/American Stroke Association (AHA/ASA) guidelines on primary prevention of stroke recommend that cigarette smoking, physical inactivity, overweight and obesity, dyslipidemia, hypertension, and diabetes be addressed and/or managed to decrease the risk of stroke. Obstructive sleep apnea (OSA) is an independent risk factor for stroke. Screening for OSA in patients at risk of stroke can be considered. Atrial fibrillation (AF) contributes to more than 20% of acute ischemic strokes. Guidelines recommend that some patients with AF be treated with warfarin or direct-acting oral anticoagulants for stroke prevention, as the clinical situation warrants. Other risk factors for stroke include carotid artery disease, migraine with aura, sickle cell disease, alcohol or drug use, hypercoagulable states (including COVID-19), and previous stroke or transient ischemic attack. Recent meta-analyses have found that aspirin may not be beneficial for primary prevention of stroke. Aspirin currently is not recommended for primary stroke prevention in low-risk individuals.

Case 1. MB is a 72-year-old woman who comes to your office reporting occasional palpitations. She has hypertension and type 2 diabetes. She says she is worried about stroke risk and asks about prevention.

Stroke is a leading cause of long-term disability in adults[1] and the fifth leading cause of mortality in the United States.[2] Women tend to have fewer strokes than age-matched men until the eighth decade of life, at which time the incidences in men and women match. Black and Hispanic patients tend to be younger at the time of stroke and typically have worse outcomes than other patients. Although there are several kinds of stroke, this edition of *FP Essentials*™ focuses on arterial ischemic strokes.

Modifiable Risk Factors

Primary prevention guidelines from the American Heart Association/American Stroke Association (AHA/ASA) recommend that cigarette smoking, physical inactivity, overweight and obesity, dyslipidemia, hypertension, and diabetes be addressed and/or managed, as with other cardiovascular risk reduction for primary prevention.[3] Common lifestyle-related risk factors and suggested modifications are listed in *Table 1*.

Cigarette Smoking

Cigarette smoking and tobacco use are modifiable risk factors for ischemic and hemorrhagic stroke.[2,3] A combination of pharmacotherapy, cognitive and behavioral therapy, and skills training has been shown to be effective in achieving smoking cessation.[3]

Physical Inactivity

Physical inactivity has been associated with increased rates of all-cause mortality, cardiovascular mortality, and stroke. Physically active adults typically have a 25% to 30% lower risk of stroke or mortality than the least active adults.[3] Guidelines from the American College of Cardiology (ACC) and AHA recommend 150 min/week of accumulated moderate-intensity physical activity or 75 min/week of vigorous-intensity physical activity (or an equivalent combination of moderate and vigorous activity) to reduce the risk of cardiovascular events.[4]

Obesity and Overweight

Prospective studies have shown an association between an increase in body mass index (BMI) and an increase in the rate of stroke mortality.[3] Obesity in the setting of metabolic syndrome is associated with stroke and vascular death, but this appears to be linked to the additional vascular comorbidities that can develop and hypertension, and not an independent risk factor. Obesity also has been shown to be associated with hypertension. There is no compelling evidence that weight loss is associated directly with a reduced risk of

Table 1
Recommendations to Modify Lifestyle Risk Factors to Prevent Stroke

Lifestyle Risk Factor	Recommendation
Physical inactivity	Moderate to vigorous activity for at least 40 min/day 3-4 days/week
Cigarette smoking	Counseling with nicotine replacement therapy for cessation
Obesity	Weight loss
Alcohol consumption[a]	≤2 drinks/day for men; ≤1 drink/day for women
Substance use disorder	Referral to therapeutic program or other effective intervention
Diet	Mediterranean diet supplemented with nuts

[a]Heavy alcohol intake is defined as:
For men: >4 drinks/day or >14 drinks/week
For women: >3 drinks/day and >7 drinks/week

Information from Meschia JF, Bushnell C, Boden-Albala B, et al. Guidelines for primary prevention of stroke: statement for healthcare professionals from American Heart Association. Stroke. *2014;45(12):3754-3832.*

stroke.[5] Weight loss can reduce the effects of other risk factors for stroke.[3]

Dyslipidemia

Management of dyslipidemia also can reduce the risk of stroke.[3] The AHA/ACC guidelines on cholesterol management recommend that a risk assessment to review major risk factors and calculation of the atherosclerotic cardiovascular disease (ASCVD) risk score be performed before initiation of statin therapy in adults ages 40 to 75 years.[6] For these adults found to have intermediate ASCVD risk, statin therapy should be considered.

A meta-analysis of 134,537 patients evaluated statin therapy for low-density lipoprotein cholesterol reduction in the prevention of major cardiovascular events.[6] For every 39 mg/dL reduction in the low-density lipoprotein level, a 24% (95% CI = 5-39) reduction in stroke was shown.[3,7]

Hypertension

Hypertension has a strong direct correlation to ischemic stroke risk.[3] It is the primary attributable risk factor in primary ischemic stroke.[8] The AHA/ASA guidelines for primary prevention of stroke recommend treatment with antihypertensive drugs to achieve a target blood pressure level of less than 140/90 mm Hg.[3] No specific class of antihypertensive drug is preferable to another for prevention of stroke.

Other Risk Factors

Obstructive Sleep Apnea

Obstructive sleep apnea (OSA) is an independent risk factor for stroke.[3] Screening for OSA in patients at risk of stroke can be considered, but no trials of OSA screening specifically have evaluated stroke as an outcome.

Multiple screening tools have been developed. The STOP-Bang (snoring, tiredness during daytime, observed apnea, high blood pressure–BMI, age, neck

Table 2
STOP-BANG Score for Obstructive Sleep Apnea Assessment

Patient Self-Reported Questions	Score[a]
Do you snore loudly? (louder than talking or sufficiently loud to be heard through closed doors)	1
Do you often feel tired, fatigued, or sleepy during the daytime?	1
Has anyone observed you stop breathing during sleep?	1
Do you have (or are you being treated for) high blood pressure?	1
Clinical Information	**Score**
BMI >35 kg/m^2	1
Age >50 years	1
Neck circumference >40 cm	1
Gender (male)	1

[a]A score <3 indicates a low risk of obstructive sleep apnea.

BMI = body mass index; STOP-Bang = snoring, tiredness during daytime, observed apnea, high blood pressure–BMI, age, neck circumference, gender.

Adapted from Chung F, Yegneswaran B, Liao P, et al. STOP questionnaire: a tool to screen patients for obstructive sleep apnea. Anesthesiology. *2008;108(5):821. https://pubs.asahq.org/anesthesiology/article/108/5/812/8377/STOP-QuestionnaireA-Tool-to-Screen-Patients-for*

circumference, gender) scale[9] (*Table 2*) and the 4-variable screening tool[10] have been shown to be most effective for the stroke population.[11] The STOP-Bang scale includes patient-reported answers to four questions and four clinical observations.[9] The 4-variable screening tool includes three clinical observations (ie, sex, body mass index, blood pressure) and one self-reported response about snoring.[10]

Atrial Fibrillation

Atrial fibrillation (AF) contributes to more than 20% of acute ischemic strokes.[12] The CHA_2DS_2-VASc (congestive heart failure, hypertension, age 75 years or older [doubled], diabetes, prior stroke or transient ischemic attack or thromboembolism [doubled], vascular disease, age 65 to 74 years, sex category) score is used to calculate the risk of ischemic stroke in patients with AF (*Table 3* and *Table 4*).[3] For patients with nonvalvular AF, a CHA_2DS_2-VASc score of 2 or greater, and an acceptably low risk of bleeding, the AHA/ASA guidelines for primary prevention of stroke recommend oral anticoagulation with warfarin (with an international normalized ratio [INR] goal of 2.0 to 3.0) or another oral anticoagulant.

The more recent 2019 AHA/ACC/Hearth Rhythm Society (HRS) guidelines for AF management suggest that use of direct-acting oral anticoagulants (DOACs) is preferable in patients with nonvalvular AF.[13] For stroke prevention in these patients, recommended DOACs include apixaban (Eliquis) (5 mg 2 times/day), dabigatran (Pradaxa) (150 mg 2 times/day), and rivaroxaban (Xarelto) (20 mg once daily).[3]

Table 3
CHA_2DS_2-VASc Score to Estimate Stroke Risk in Patients With Atrial Fibrillation

Risk Factor (Score if Yes)	Number of Points
Congestive heart failure history	1
Hypertension history	1
Age ≥75 years	2
Diabetes history	1
Stroke/TIA/thromboembolism history	2
Vascular disease history (prior MI, PAD)	1
Age 65-74 years	1
Sex category (female)	1
Age <65 years	0

CHA_2DS_2-VASc = congestive heart failure, hypertension, age ≥75 years (doubled), diabetes, prior stroke or TIA or thromboembolism (doubled), vascular disease, age 65 to 74 years, sex category; MI = myocardial infarction; PAD = peripheral artery disease; TIA = transient ischemic attack.

Adapted from Chest, *137(2). Lip GY, Nieuwlaat R, Pisters R, Lane DA, Crijns HJ. Refining clinical risk stratification for predicting stroke and thromboembolism in atrial fibrillation using a novel risk factor-based approach: the euro heart survey on atrial fibrillation. Page 266. Copyright (2010), with permission from Elsevier.*

Table 4
CHA_2DS_2-VASc Score Interpretation

Score	Risk of Ischemic Stroke (Event/100 Years)[a]
0	0.2
1	0.6
2	2.2
3	3.2
4	4.8
5	7.2
6	9.7
7	11.2
8	10.8[a]
9	12.2

[a]Data from the Friberg validation study, but, in general, would assume the higher the score, the higher the risk of ischemic stroke.

CHA_2DS_2-VASc = congestive heart failure, hypertension, age ≥75 years (doubled), diabetes, prior stroke or TIA or thromboembolism (doubled), vascular disease, age 65 to 74 years, sex category.

Adapted from Friberg L, Rosenqvist M, Lip GY. Evaluation of risk stratification schemes for ischaemic stroke and bleeding in 182 678 patients with atrial fibrillation: the Swedish Atrial Fibrillation cohort study. Eur Heart J. *2012;33(12):1505 by permission of Oxford University Press.*

The criteria for modified dosages vary by drug. A reduced dosage of apixaban (2.5 mg 2 times/day) is recommended if two of three criteria are met: creatinine level of 1.5 mg/dL or greater, age 80 years or older, and body weight of 60 kg (132.3 lb) or greater.[3,13] A reduced dosage of dabigatran (75 mg 2 times/day) is recommended for patients with a creatinine clearance of 15 to 30 mL/minute. A reduced dosage of rivaroxaban (15 mg once daily) is recommended for patients with a creatinine clearance of 50 mL/min or less.

Shared decision-making is indicated when prescribing these drugs, with patient preference, cost, and adherence being considerations.[3,13,14] Patients taking warfarin require regular monitoring to achieve and maintain a therapeutic INR. Warfarin is associated with substantial drug-drug interactions, but its effects can be rapidly reversed.

The DOACs have simpler dosing than warfarin.[14] Dabigatran, rivaroxaban, and apixaban appear to have similar effectiveness, although apixaban may be associated with lower bleeding risk and rivaroxaban may be associated with higher bleeding risk.[15] Drugs to reverse the effects of DOACs now are available for emergency use.

For patients with AF who need anticoagulation and also hemodialysis, apixaban is the novel oral anticoagulant of choice. The recommended dosage is 5 mg 2 times/day, with a dosage reduction to 2.5 mg 2 times/day for patients 80 years and older and with a body weight of 60 kg (132.28 lb) or less.[3] Controversy exists as to whether any anticoagulant should be used in patients receiving dialysis given other risks of bleeding. Shared decision-making should be used in prescribing these drugs.[13] The AHA/ACC/HRS guidelines suggest that warfarin or apixaban can be used in patients with end-stage renal disease.

The HAS-BLED (hypertension, abnormal liver/renal function, stroke, bleeding tendency/predisposition, labile INR, elderly [older than 65 years], drug/alcohol concomitantly) score[16] can be used to calculate the risk of rebleeding in patients with a history of bleeding (*Table 5* and *Table 6*). It has been validated in patients taking warfarin but has not been studied in patients taking DOACs. If the annual risk of bleeding is higher than the annual risk of ischemic stroke, alternative stroke prophylaxis should be discussed with the patient and considered.[13,16]

Patients with AF who cannot undergo anticoagulation may be considered for placement of a left atrial appendage device, closure device, or surgical ligation of the left atrial appendage.[3,13] Use of a closure device has been found to be noninferior compared with a DOAC in preventing a composite of stroke, transient ischemic attack (TIA), embolism, mortality, and bleeding in patients with AF.[17]

Table 5
HAS-BLED Score to Estimate Bleeding Risk in Anticoagulated Patients With Atrial Fibrillation

Risk Factor	Number of Points
Hypertension (uncontrolled, >160 mm Hg systolic)	1
Renal disease (Cr level >2.26 mg/dL, dialysis or transplant)	1
Liver disease (cirrhosis or bilirubin >2x ULN with AST/ALT/AP >3x ULN)	1
Stroke history	1
Prior major bleeding or predisposition to bleeding	1
Labile INR (unstable INR, time in therapeutic range <60%)	1
Elderly (age >65 years)	1
Drugs (predisposing to bleeding [aspirin, clopidogrel, NSAIDs])	1
Alcohol (≥8 drinks/week)	1

ALT = alanine aminotransferase; AP = alkaline phosphatase; AST = aspartate aminotransferase; Cr = creatinine; HAS-BLED = hypertension, abnormal liver/renal function, stroke, bleeding tendency/predisposition, labile INR, elderly (>65 years), drug/alcohol concomitantly; INR = international normalized ratio; NSAID = nonsteroidal anti-inflammatory drug; ULN = upper limits of normal.

Adapted from Chest, *138(5). Pisters R, Lane DA, Nieuwlaat R, de Vos CB, Crijns HJ, Lip GY. A novel user-friendly score (HAS-BLED) to assess 1-year risk of major bleeding in patients with atrial fibrillation: the Euro Heart Survey. Pages 1093-1095. Copyright (2010), with permission from Elsevier.*

Carotid Artery Disease

The U.S. Preventive Services Task Force (USPSTF) recommends against screening for asymptomatic carotid artery stenosis in the general population.[18] Although screening ultrasonography has not been associated with a specific risk of harm, the follow-up interventions (eg, carotid endarterectomy, carotid stenting) have been associated with up to a 5% risk of stroke or mortality in the 30 days after intervention.

Aggressive medical management is recommended for patients with no history of stroke when carotid disease is found incidentally.[19] The additional decision to pursue medical management alone, carotid endarterectomy, or carotid stenting depends on the patient's risk of stroke, degree of stenosis, and perioperative morbidity.

In asymptomatic patients with greater than 70% stenosis of the artery, carotid endarterectomy can be considered if the perioperative risks of stroke, myocardial infarction, and mortality are acceptably low.[19] Stenting appears to be associated with an increased risk of nondisabling stroke compared with endarterectomy,[20] but may be an option for high-risk patients who are not good candidates for surgery. Chronic 100% carotid occlusions do not warrant surgical intervention as they rarely cause clinical events.[21,22]

Table 6
HAS-BLED Score Interpretation

Score	Annual Risk of Major Bleeding (%)	Recommendation
0	0.9	Anticoagulation can be considered
1	3.4	
2	4.1	
3	5.8	More frequent monitoring and review of risk factors. Alternative to anticoagulation can be considered
4	8.9	
5	9.1	
>5	>10[a]	

[a]*Data are limited, but a score >5 is thought to be associated with a high risk of bleeding.*

Adapted from J Am Coll Cardiol, *57(2). Lip GY, Frison L, Halperin JL, Lane DA. Comparative validation of a novel risk score for predicting bleeding risk in anticoagulated patients with atrial fibrillation: the HAS-BLED (Hypertension, Abnormal Renal/Liver Function, Stroke, Bleeding History or Predisposition, Labile INR, Elderly, Drugs/Alcohol Concomitantly) score. Page 177. Copyright (2011), with permission from Elsevier; Information from Lip GY. Implications of the CHA(2) DS(2)-VASc and HAS-BLED Scores for thromboprophylaxis in atrial fibrillation.* Am J Med. *2011;124(2):111-114; Lip GYH, Banerjee A, Boriani G, et al. Antithrombotic therapy for atrial fibrillation: CHEST guideline and expert panel report.* Chest. *2018;154(5):1121-1201.*

Migraine

Patients with migraine with aura have an increased risk of stroke, whereas patients with migraine without aura do not appear to have the same risk.[23] The risk of stroke in these patients can be compounded by use of tobacco or oral contraceptives.

There are no clear recommendations for the primary prevention of stroke in patients with migraine. Use of antiplatelets for this purpose is not routinely recommended.[3,24] Smoking cessation is strongly recommended in women with migraine headache with aura. The Centers for Disease Control and Prevention (CDC) recommends against the use of combined hormonal contraceptives (ie, estrogen-progesterone combinations) in women with migraine with aura, although progesterone-only methods are considered acceptable.[25]

Epidemiologic studies have identified a correlation among migraine, patent foramen ovale (PFO), and stroke.[26] They have shown that 79% of stroke patients with migraine also have a PFO, whereas stroke patients without migraine have a 59% likelihood of having a PFO. The prevalence of PFO in the general population is approximately 18%.

Sickle Cell Disease

Stroke related to sickle cell disease (SCD) can manifest as silent infarcts on imaging. Children with SCD should be screened with transcranial Doppler ultrasound from ages 2 to 16 years.[3,27] For stroke prevention, patients with abnormal screening results should receive periodic red blood cell transfusions with the goal of maintaining a hemoglobin S fraction of less than 30%.[28] This screening method has not been shown to improve outcomes and is not performed routinely in adults with SCD.[29]

Because no studies have examined primary prevention of stroke in adults with SCD, no primary prevention measures currently are recommended for adult patients with SCD.[3] For secondary prevention,

a goal hemoglobin S fraction of less than 30% of total hemoglobin and maintaining a hemoglobin level of more than 9 g/dL are recommended.[27] There does not appear to be a strong association between sickle cell trait and stroke.[29]

Cigarette Smoking, and Alcohol and Drug Use

Cigarette smoking, and alcohol and drug use are associated with an increased risk of stroke.[3] Tobacco use can potentiate the effects of other risk factors, such as hypertension and hormonal contraceptive use. Heavy alcohol use is associated with ischemic and hemorrhagic stroke. Heavy use is defined as more than 4 drinks/day or more than 14 drinks/week for men, and more than 3 drinks/day and more than 7 drinks/week for women.

Stimulant use (eg, cocaine, amphetamine) can be associated with acute vasospasm and acute hypertension. Marijuana use is associated with reversible vasoconstriction syndrome.[30] In a study of hospitalized patients, amphetamine use was associated with intracranial hemorrhage (adjusted odds ratio [OR] = 4.95; 95% CI = 3.24-7.55) but not with ischemic stroke.[31] Cocaine use was associated with hemorrhagic (OR = 2.33; 95% CI = 1.74-3.11) and ischemic stroke (OR = 2.03; 95% CI = 1.48-2.79).

COVID-19

It is known that COVID-19 infection, particularly severe COVID-19 infection, is associated with a hypercoagulable state, and hospitalized patients with COVID are at higher risk of stroke than patients with other infections. One case study in a large New York hospital system found that 32 out of 3,556 patients (0.9%) with COVID-19 had an imaging-proven acute ischemic stroke.[32] Compared with patients in a control sample, patients with COVID-19 more frequently had cryptogenic stroke (65% versus 30% in the control sample, P =.003) and higher National Institutes of Health Stroke Scale (NIHSS) scores and higher D-dimer levels. Patients with stroke and COVID-19 had higher mortality rates than patients with stroke and without COVID-19.

One global registry of patients with COVID-19 and stroke included 174 patients in 28 sites in 16 countries.[33] On analysis, it was found that patients with stroke and COVID-19 tended to have more severe strokes, and patients who survived had worse functional outcomes compared with patients with stroke and without COVID-19.

Recent meta-analyses have found that aspirin may not be beneficial for primary prevention of stroke or cardiovascular disease.

Previous Stroke or TIA

The greatest risk factor for a stroke is a previous stroke or TIA. Older studies from 1997-2003 have shown that the risk of stroke or coronary syndrome is between 12% and 20% in the first 3 months after TIA.[34,35] A more recent registry of 4,789 patients with TIA from 2009-2011 found that stroke rates at days 2, 7, 30, 90, and 365 after TIA were 1.5%, 2.1%, 2.8%, 3.7%, and 5.1%, respectively.[36] The overall downward trend in recurrent stroke risk may be reflective of more urgent implementation of secondary prevention measures.

The commonly used ABCD^2 (age, blood pressure, clinical features, duration, diabetes) score is used to estimate the risk of stroke in the setting of suspected TIA.[37] Factors are assigned point values that are added to generate a score: age 60 years or older (1 point); blood pressure level 140/90 mm Hg or greater (1); clinical features of TIA consisting of unilateral weakness (2) or speech impairment without weakness (1); duration of symptoms 60 min or longer (2) or 10 to 59 min (1); and a history of diabetes (1).

In a meta-analysis of 29 studies that included 13,766 patients with TIA, an ABCD^2 score of 4 or greater was shown to be sensitive (86.7%; 95% CI = 81.4%-90.7%) but not specific (35.4%; 95% CI = 33.3%-37.6%) in predicting recurrent stroke within 7 days.[38] Twenty percent of patients with an ABCD^2 score of less than 4 had greater than 50% carotid stenosis or atrial fibrillation. Approximately 35% to 41% of patients with conditions mimicking TIA and 66% of patients with TIA had an ABCD^2 score of 4 or greater. Thus, it is advised to evaluate patients for large vessel stenosis regardless of the ABCD^2 score.[39]

Reducing Stroke Risk

Recent meta-analyses have found that aspirin may not be beneficial for primary prevention of stroke or cardiovascular disease. Older studies were more likely

to find a benefit of aspirin, whereas studies conducted more recently, in an era of statin therapy and more effective antihypertensive management, have not shown a benefit.[40] Aspirin is not recommended for primary stroke prevention in low-risk individuals.[3]

Patients with peripheral artery disease or coronary artery disease may benefit from the addition of a low-dose factor Xa inhibitor to low-dose aspirin.[41] In a peripheral artery disease analysis of the Cardiovascular Outcomes for People Using Anticoagulation Strategies (COMPASS) trial, the combination of 2.5 mg 2 times/day rivaroxaban (Xarelto) plus aspirin was compared with aspirin alone in these patients. The combination treatment was shown to reduce the composite end point of cardiovascular death, myocardial infarction, or stroke. (This is an off-label use of combination therapy of rivaroxaban and aspirin.)

For stroke risk reduction specifically, in the aspirin alone group, there was a 2% risk of stroke.[41] In the combination group, there was a 1% risk of stroke (hazard ratio 0.54; 95% CI = 0.33-0.87). There was an increase in the rate of bleeding requiring hospitalization, but no increases in rates of fatal bleeding, intracranial bleeding, or bleeding of critical organs. The trial excluded patients who required anticoagulation, had a stroke within the previous month, had previous lacunar stroke, or had an intracerebral hemorrhage.

Case 1, cont'd. Because MB reports occasional palpitations, you obtain a 12-lead electrocardiogram, which does not show any evidence of atrial fibrillation. Because of a history of diabetes and hypertension, you prescribe daily atorvastatin for primary cardiovascular prevention. She will continue to walk for 30 min/day to maintain physical activity.

Section Two
Diagnostic Evaluation

Ischemic stroke is an episode of neurologic dysfunction caused by focal cerebral, spinal, or retinal infarction. In patients with stroke symptoms, an urgent evaluation is advised. In the prehospital setting, early recognition of stroke signs allows appropriate triage of patients to hospitals that specialize in stroke management for thrombolysis or thrombectomy. In the hospital setting, evaluation of patients with suspected stroke includes clinical assessment, using the National Institutes of Health Stroke Scale (NIHSS), imaging of the head and blood vessels of the neck, and assessing for the cause of stroke. Evaluation for the etiology may include laboratory tests, cardiac imaging, and cardiac rhythm monitoring. Early measures for secondary stroke prevention can be initiated.

Case 1, cont'd. MB suddenly develops left-sided numbness and weakness after having a morning cup of coffee. She calls your office because the symptoms have lasted 30 minutes. You instruct her to call 911 for transport to the emergency department for evaluation for a possible stroke.

Definitions

The American Heart Association/American Stroke Association (AHA/ASA) define ischemic stroke as an episode of neurologic dysfunction caused by focal cerebral, spinal, or retinal infarction.[42] Infarcts are areas of tissue death in the brain, spinal cord, or retina that are identified based on imaging or other objective findings of ischemic injury or clinical evidence of injury based on symptoms. Ischemic stroke manifests as focal neurologic symptoms with a corresponding infarct on imaging.

The AHA and ASA define transient ischemic attack (TIA) as a transient episode of neurologic dysfunction caused by focal brain ischemia without evidence of acute infarction on brain imaging.[42]

If a patient has transient focal neurologic symptoms that resolve, but magnetic resonance imaging (MRI) study of the brain shows an acute infarct that corresponds with those neurologic symptoms, the patient should be diagnosed with ischemic stroke.[42] With the advent of use of brain imaging, the term *reversible ischemic neurologic deficit* (RIND) is no longer used.

Common Signs and Symptoms

Stroke symptoms depend on the part of the central nervous system that is affected. Common signs and symptoms include difficulty speaking, facial droop, unilateral limb paralysis, or difficulty walking (ie, ataxia).[43] Singularly or in combination, facial weakness, arm weakness, and speech difficulty symptoms are present in 88% of all patients with stroke or TIA.[44] Such symptoms warrant immediate evaluation.

Patients with a decreased level of consciousness with associated cranial nerve symptoms or posturing may have a basilar artery syndrome.[45] Cortical deficits, such as aphasia or neglect, may indicate carotid or middle cerebral artery syndrome. These signs are indicative of large vessel syndrome and may help clinicians identify patients who need access to a thrombectomy center.

Prehospital Setting

The goals of prehospital management of a suspected acute ischemic stroke are rapid assessment and activation of stroke protocols, which allow for triage of patients to undergo early thrombolysis if eligible.[45] Various prehospital stroke scales are used to assist with triage, including the Cincinnati Prehospital Stroke Scale (CPSS) and the Los Angeles Prehospital Stroke Screen (LAPSS). Evidence is mixed regarding which prehospital tools most accurately identify patients experiencing stroke, and the 2019 AHA/ASA guidelines on early management of acute ischemic stroke do not recommend use of a specific tool.

Emergency Department Evaluation

The goals of initial evaluation in the emergency department setting are identification of the severity of stroke, indications for and contraindications to thrombolysis, and assessment for possible other causes of neurologic symptoms, such as hypoglycemia.[45] The

evaluation should include assessment of vital signs, measurement of the blood glucose level, calculation of the National Institutes of Health Stroke Scale (NIHSS) (*Table 7*) or initial neurologic assessment with focal deficits identified, review of any use of antithrombotics, and the time that the patient was last reported to have been seen well. These initial data points will help guide decision-making regarding the need for acute thrombolysis.

Inpatient Evaluation

Imaging

Brain imaging should be performed on first arrival at the hospital to rule out hemorrhagic stroke, a contraindication to thrombolysis. Noncontrast computed tomography (CT) scan and MRI study are effective for this.[45]

CT scan. Results of a noncontrast CT scan performed less than 6 hours after ischemic stroke onset may appear normal. In one study of 1,329 patients with stroke, 30% had early ischemic changes noted on CT scan performed within 3 hours of symptom onset.[46]

Early visible signs of acute ischemic stroke on noncontrast CT scan include a hyperdense vessel sign (often the middle cerebral artery). Another early change may be loss of gray and white matter differentiation. The cortex may become ill-defined, with the deep gray nuclei appearing more obscured. These changes are quantified in the Alberta Stroke Program Early CT Score (ASPECTS).[47]

For patients who may be candidates for thrombectomy, noninvasive vessel imaging, such as CT angiography (CTA) of the head and neck, should be obtained (*Figure 1*).[45] This typically is done at the same time as the noncontrast CT scan. Identification of thrombectomy candidates is discussed in more detail in *Section Three*.

Table 7
NIHSS Score for Stroke Severity Assessment

Item	Title	Response and Scoring
1A	Level of consciousness	0 = Alert 1 = Drowsy 2 = Obtunded 3 = Coma/unresponsive
1B	Orientation questions (2) ("How old are you?" "What month is it?")	0 = Answers both correctly 1 = Answers 1 correctly 2 = Answers neither correctly
1C	Response to commands (2) ("Open and close your eyes." "Open and close your hand.")	0 = Performs both correctly 1 = Performs 1 correctly 2 = Performs neither correctly
2	Gaze	0 = Normal horizontal eye movements 1 = Partial gaze palsy 2 = Forced deviation, or total gaze paresis
3	Visual fields	0 = No visual field defect 1 = Partial hemianopia 2 = Complete hemianopia 3 = Bilateral hemianopia
4	Facial movement	0 = Normal 1 = Minor facial weakness 2 = Partial facial weakness (lower half) 3 = Complete facial weakness (including forehead)
5	Motor function (arm) a. Left b. Right	0 = No downward drift 1 = Drift before 10 sec 2 = Falls before 10 sec 3 = No effort against gravity 4 = No movement
6	Motor function (leg) a. Left b. Right	0 = No downward drift 1 = Drift before 5 sec 2 = Falls before 5 sec 3 = No effort against gravity 4 = No movement
7	Limb ataxia	0 = No ataxia 1 = Ataxia in 1 limb 2 = Ataxia in 2 limbs

continues

NIHSS = National Institutes of Health Stroke Scale.

Table 7 *(continued)*
NIHSS Score for Stroke Severity Assessment

Item	Title	Response and Scoring
8	Sensory	0 = No sensory loss 1 = Mild sensory loss 2 = Severe sensory loss
9	Language	0 = Normal 1 = Mild aphasia 2 = Severe aphasia 3 = Mute or global aphasia
10	Articulation	0 = Normal 1 = Mild dysarthria 2 = Severe dysarthria
11	Extinction or inattention (test for visual and sensory extinction)	0 = Absent 1 = Mild loss (in 1 sensory modality) 2 = Severe loss (in more than 1 sensory modality)

NIHSS = National Institutes of Health Stroke Scale.

Adapted from National Institutes of Health. NIH Stroke Scale. 2003. https://www.stroke.nih.gov/documents/NIH_Stroke_Scale_508C.pdf

Magnetic resonance imaging study. An MRI study of the brain will reveal the extent of injury and evidence of previous brain injury and clarify the potential etiology of stroke.[45] It is useful in cases in which tissue injury is not visualized on CT scan. Although MRI study (*Figure 2a*) is more sensitive in acute ischemic stroke than noncontrast CT scan,[48] it may be more difficult to access in the emergency setting and is used less commonly in decision-making about thrombolysis.[45] An MRI study often is obtained after a patient is admitted to the hospital.

For patients with a contraindication to MRI study, a repeat CT scan of the head after 24 to 48 hours to evaluate the extent of acute brain injury may be useful.[39] Infarcts appear as hypodense areas (*Figure 3*).

An MRI study can reveal evidence of previous strokes (*Figure 2b*) as well as areas of acute or chronic hemorrhage. Determining the brain regions involved in acute or chronic stroke, the size of the infarct, and the vascular territory of the infarct can help in identifying the etiology of stroke. Identification of areas of hemorrhage also may be useful in making decisions about antithrombotic therapy or identifying a different etiology of stroke, such as amyloid angiopathy.[44]

Imaging of blood vessels. Noninvasive imaging of the blood vessels typically is obtained, which may include the large vessels in the neck and the intracranial vessels of the brain. However, there is only high-quality evidence to support this in patients with nondisabling stroke.[44,45] Imaging modalities include carotid ultrasonography, CTA of the head and neck, or magnetic resonance angiography (MRA) of the head and neck. The modality chosen may be based on resource accessibility or patient factors.

The technical quality of carotid ultrasonography can vary based on patient body habitus and technician proficiency, but it often is the least expensive type of vessel imaging and is readily accessible. Thus, this modality often is used for first-line screening in initial evaluation of patients with suspected stroke. CTA includes contrast, so it may not be the best choice for a patient with kidney injury or a dye allergy. CTA also is limited by calcification artifacts and associated with radiation

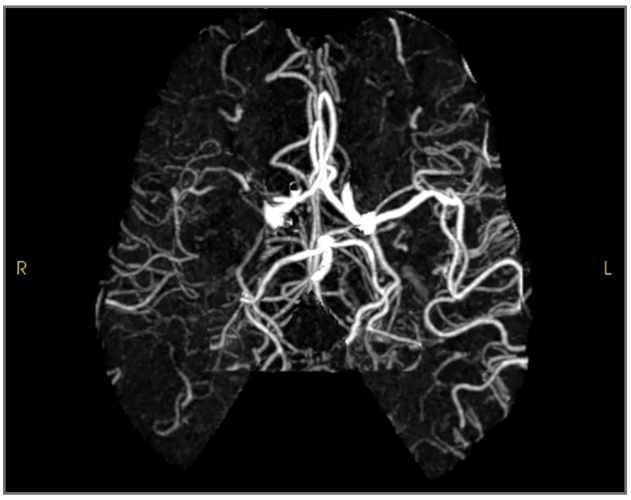

Figure 1. CT Angiogram Showing Right Middle Cerebral Artery Occlusion

CT = computed tomography.

Image courtesy of Waimei Amy Tai, MD.

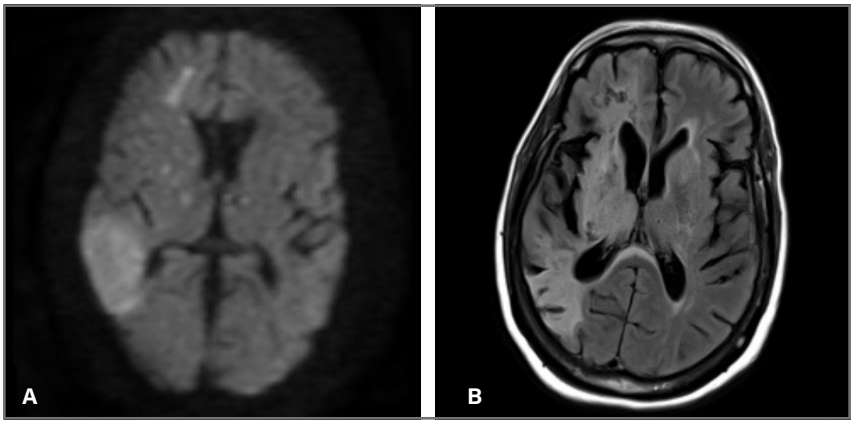

Figure 2. MRI Study of Right Middle Cerebral Artery Territory Stroke

A. This image shows DWI on MRI study of an acute right middle cerebral artery stroke. The region of infarct is hyperintense.

B. This image shows an MRI FLAIR of a right middle cerebral artery stroke. The region of infarct is hyperintense. Note the gliosis; this area of damaged brain has atrophied.

FLAIR = fluid attenuated inversion recovery; DWI = diffusion-weighted [magnetic resonance] imaging; MRI = magnetic resonance imaging.

Images courtesy of Waimei Amy Tai, MD.

exposure. However, it is the most specific modality in terms of estimating the degree of carotid stenosis.[49]

Magnetic resonance angiography also is sensitive but is not as specific as CTA in estimating carotid stenosis. MRA often is obtained for convenience because it can be acquired at the same time as MRI study of the brain. When obtained without contrast, MRA can overestimate the degree of vessel stenosis. It also is limited by motion artifacts because of the longer acquisition time (compared with CTA) and calcification or metallic artifacts.[49]

Bedside ultrasonography (ie, transcranial Doppler) is not used in routine evaluation for acute ischemic stroke. Transcranial Doppler can be used for microemboli detection and screening in a subset of patients, such as in evaluation for patent foramen ovale or other acute embolic phenomena.[39]

Stroke Severity Assessment

In the hospital, use of the NIHSS is recommended to assess the severity of a stroke (*Table 7*).[45] This score is calculated initially during assessment for thrombolysis and acute treatment. Subsequent serial scores are calculated if thrombolysis or thrombectomy is used to assess for adverse effects. It may be used to monitor improvement as well, although it may not detect subtle clinical changes.[50]

There are limitations to clinical use of the NIHSS outside of clinical trials. Accurate use requires users to complete training to become certified in assessment and ensure reproducibility of scoring.[39,51]

The NIHSS is a 42-point scale, with higher scores indicating more severe stroke. Typically, a score of 1 to 4 is classified as minor stroke; 5 to 15 is considered moderate; 16 to 20 is classified as moderate to severe; and 21 to 42 is considered a severe stroke.[52] The score corresponds with functional deficits but may not correspond with the amount of cerebral tissue with infarct.

The baseline NIHSS score strongly correlates with functional outcomes. One additional point on the NIHSS is associated with a decrease in the likelihood of excellent outcomes at 7 days by 24% and at 3 months by 17%. After 3 months, excellent outcomes were seen

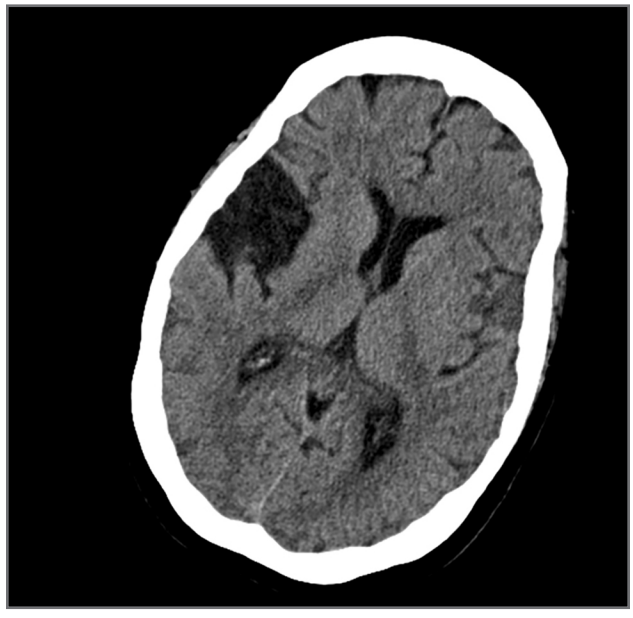

Figure 3. CT Scan of the Head Showing Chronic Right Middle Cerebral Artery Territory Stroke

The area of hypodensity on the right is the area of completed infarct.

CT = computed tomography.

Images courtesy of Waimei Amy Tai, MD.

in 46% of patients with NIHSS scores of 7 to 10, whereas only 23% of patients with scores of 11 to 15 achieved excellent outcomes.[53]

The NIHSS is weighted heavily to assess the left hemisphere of the brain and is less focused on the posterior circulation. Thus, posterior circulation strokes may not be detected with use of this scale alone. Patients may report symptoms of a brainstem stroke, such as dizziness, nausea, vomiting, and double vision, but none of these items are assigned points on the NIHSS.[54] Caution should be taken to avoid over-reliance on a single scale for decision-making in the diagnosis or management of stroke.

Determining Etiology

A major goal of acute hospitalization is to determine the etiology of stroke. Based on the results of the initial neuroimaging studies and laboratory tests, stroke can be classified into the following diagnostic categories: large vessel occlusion; small vessel stroke; potential cardioembolic; other; or undetermined.[55]

Large vessel occlusion. Large vessel occlusion is one manifestation of acute ischemic stroke and refers to blockages of the intracranial internal carotid; posterior, middle, and anterior cerebral arteries; and the basilar and vertebral arteries.[56] Patients with large vessel atherosclerotic strokes have clinical and brain imaging findings of significant (ie, greater than 50%) stenosis or occlusion of a major artery or branch cortical artery, presumably due to atherosclerosis proximal to the area of stroke.[55] Typical locations of a large vessel stroke include cortical or cerebellar lesions and subcortical lesions greater than 1.5 cm in diameter. Aortic arch atherosclerotic disease also is categorized as a large vessel etiology.

Less common causes of large and medium vessel arteriopathy leading to stroke include infection (eg, varicella zoster encephalitis, neurosyphilis), inflammatory disease (eg, vasculitis), accelerated atherosclerotic disease (seen in HIV), or reversible vasculopathy (seen in preeclampsia and reversible cerebral vasoconstriction syndrome).[39]

The emergency department evaluation focuses on the diagnosis of ischemic stroke and assessment of the safety of thrombolysis. The only laboratory test required before thrombolysis decision-making is a blood glucose level.

Small vessel stroke. A small vessel (lacunar type) stroke typically is less than 1.5 cm (0.6 in) in diameter, in a subcortical region, such as the thalamus, basal ganglia, internal capsule, or brain stem. Cortical symptoms and locations of stroke should be excluded. The presence of vascular risk factors, such as hypertension and diabetes, supports this diagnosis.[55]

Cardioembolic stroke. Cardioembolic stroke occurs when emboli from the heart lodge in the brain.[55] High-risk cardiac sources include infective endocarditis, valvular atrial fibrillation, and mechanical valves. Moderate-risk cardiac sources include patent foramen ovale and atrial fibrillation without underlying structural heart disease. On imaging, the infarcts often appear in a distribution similar to that in large vessel stroke.

Stroke of other determined pathology or unknown origin. Stroke of other determined pathology includes arterial dissections and hypercoagulable states.[55] However, in one population-based study, approximately 35% of patients with first ischemic stroke were found to have a stroke of undetermined cause despite appropriate acute testing.[57] Stroke of unknown origin after initial diagnostic studies but that has an embolic appearance on imaging is classified as embolic stroke of unknown source.

Embolic stroke of undetermined source. Stroke with no known attributable large or small vessel lesion and without a known cardiac source is called *embolic stroke of unknown source*. For these strokes, additional assessment for a cardioembolic source should be performed, which is discussed in the following sections.[55]

Laboratory Tests

The emergency department evaluation focuses on the diagnosis of ischemic stroke and assessment of the safety of thrombolysis. The only laboratory test required before thrombolysis decision-making is a blood glucose level.[45] If a patient is taking an anticoagulant or has a medical history concerning for coagulopathy, then additional testing, such as complete blood cell count and international normalized ratio, may be required to guide thrombolysis decision-making.

Additional laboratory tests include those to assess for comorbidities or conditions that mimic stroke, with a troponin level, complete blood cell count, and basic

metabolic panel.[45] Although various serum biomarkers (eg, C-reactive protein, lipoprotein A) have been studied to assess their utility in stroke diagnosis, no biomarkers have been validated sufficiently for use in clinical practice.[44,45]

Cardiac Tests and Monitoring

For patients with acute ischemic stroke, evaluation for occult atrial fibrillation is important. This should include electrocardiographic monitoring in the hospital for at least 24 hours.[44,45]

For patients with a cryptogenic stroke who do not have a contraindication to anticoagulation, further testing with outpatient remote monitoring should be considered to evaluate for occult atrial fibrillation.[39] Remote monitoring options include outpatient telemetry or an implantable loop recorder.

A 2016 randomized controlled trial showed atrial fibrillation in 30% of 221 patients with implantable cardiac monitors and in 3% of 220 control patients after 36 months of follow-up (hazard ratio = 8.8; 95% CI = 3.5-22.2; $P < .0001$).[39,58] It is unknown whether this monitoring with subsequent initiation of oral anticoagulants in affected patients will lower the rate of subsequent stroke.

The AHA/ASA guidelines for stroke prevention in patients with previous stroke do not recommend an echocardiogram for all patients.[39] However, they do recommend that an echocardiogram be obtained for patients with cryptogenic strokes of unknown source to evaluate for structural heart pathology.

Transesophageal echocardiography (TEE) may be more effective in evaluating for other structural heart lesions or occult cardiac causes of strokes, but it is unclear how often the test results will change management. In one retrospective study of 370 patients with stroke, 19 patients out of 307 (6.2%) had a change in management after transthoracic echocardiography (TTE), and 7 patients out of 63 (11.1%) after TEE.[59] The study found male sex, abnormal electrocardiogram results on admission, and an embolic pattern of stroke were predictors of abnormal findings on TTE or TEE.

Patent Foramen Ovale

Patent foramen ovale (PFO) is found in up to 25% of adults in the general population,[60] but is considered a less common cause of ischemic stroke. Evaluation for PFO should be considered in patients younger than 60 years who do not have other traditional vascular risk factors.[39,45]

Transthoracic echocardiography with intravenous saline injection (ie, bubble contrast) is used to evaluate for a PFO.[60] For patients with an embolic stroke of unknown source and a PFO, closure of the PFO reduces the risk of stroke recurrence by 3.4% at 5 years. For patients who do not undergo PFO closure, aspirin or anticoagulation are equally effective in reducing subsequent stroke risk.

The Risk of Paradoxical Embolism (RoPE) score (available online at https://www.mdcalc.com/risk-paradoxical-embolism-rope-score) is helpful in identifying patients with embolic stroke of unknown source who are likely to have a PFO that is pathogenic rather than incidental.[61] This score uses the risk factors of hypertension, diabetes, TIA/stroke history, tobacco use, cortical infarct appearance on imaging, and age at time of stroke (younger age being higher likelihood that PFO is attributable) to determine the likelihood that PFO was attributable cause of stroke. The higher the score, the more likely the PFO was the attributable cause of stroke. Use of the RoPE score may be useful in discussing the likelihood of PFO as a risk factor for stroke and in shared decision-making with patients when considering PFO closure.

Case 1 cont'd. MB calls 911 and the prehospital evaluation suggests an acute ischemic stroke. She is evaluated in the emergency department and has a National Institutes of Health Stroke Scale (NIHSS) score of 12 (for left-sided facial droop, left-sided hemiparesis, neglect, and hemianopia). A computed tomography (CT) scan of the head shows no acute hemorrhage but does show a hyperdense middle cerebral artery sign on the right middle cerebral artery. A CT angiogram shows right middle cerebral artery occlusion.

Section Three
Hospital Management

Urgent evaluation of patients with acute ischemic stroke allows for a comprehensive assessment of management options. These include thrombolysis and thrombectomy, depending on symptom onset and severity, the presumed location of the occlusion, and patient comorbidities and potential for improvement. For patients who present within 4.5 hours of onset of disabling symptoms consistent with acute ischemic stroke and with no contraindications, intravenous thrombolysis is indicated. Acute mechanical thrombectomy may be indicated for patients who present within 24 hours of symptom onset and have symptoms consistent with a large vessel occlusion. After reperfusion therapy, patients require close neurologic monitoring. Patients who receive reperfusion therapy tend to have better functional outcomes than patients who do not. Secondary prevention includes use of antithrombotics and glycemic control. Common issues in the acute setting include cerebral edema, hemorrhagic transformation, and symptomatic carotid disease.

Case 1, cont'd. After the evaluation in the emergency department, MB is admitted to the hospital and evaluated for thrombolytic therapy as well as thrombectomy.

Thrombolysis

Thrombolysis is the standard of care for eligible patients with disabling symptoms of acute ischemic stroke.[45] As with acute ST-segment myocardial infarction, in which lower door-to-balloon times are associated with improved outcomes, lower door-to-thrombolysis times are associated with improved disability-free survival times in acute ischemic stroke.[62] Time to treatment is defined as the time from when the patient was last reported to have been seen well (ie, last known normal time) to the time treatment is initiated (ie, thrombolysis or thrombectomy). For patients who have symptoms upon awakening from sleep, the last known normal time is the time they went to sleep.

Alteplase

Alteplase, a tissue plasminogen activator (tPA), is the only thrombolytic drug approved by the Food and Drug Administration (FDA) for thrombolysis in acute ischemic stroke.[63] Its mechanism of action is transformation of native plasminogen into active plasmin that promotes breakdown of occlusive thrombus by degrading fibrin.

According to the 2019 American Heart Association/American Stroke Association (AHA/ASA) guidelines on early management of acute ischemic stroke, the criteria for thrombolysis eligibility are age 18 years or older, clinical diagnosis of acute ischemic stroke causing neurologic symptoms, and a last known normal time within 4.5 hours of treatment (*Table 8*).[44,45] The FDA has approved use of alteplase in the 0- to 3-hour time window, but based on results of the European Cooperative Acute Stroke Study III (ECASS III) and AHA guidelines, alteplase is used up to the 4.5-hour time window worldwide.[45,64]

At 3 to 6 months of follow-up from stroke onset, alteplase is associated with an absolute increase in disability-free survival time of 10% for patients treated in less than 3 hours and approximately 5% for patients treated in 3 to 4.5 hours.[65]

Contraindications to alteplase include an international normalized ratio greater than 1.7, blood pressure (BP) level greater than 185/105 mm Hg (if not controlled), recent trauma or surgery, myocardial infarction within 3 months, or use of another anticoagulant within 48 hours.[45]

For appropriate candidates, 0.9 mg/kg of alteplase (up to 90 mg) is administered for 1 hour for intravenous thrombolysis.[45] Ten percent of the dose is administered with a 1-minute bolus, with the rest administered over the remaining 59 minutes.

For patients with minor stroke (ie, National Institutes of Health Stroke Scale [NIHSS] score 1-4) with nondisabling symptoms, there is no known benefit of alteplase.[66] Nondisabling symptoms are defined as those that would not interfere with activities or delay or prevent a return to work. For example, a musician

with mild sensory loss in the fingers may benefit from alteplase, whereas a patient with advanced dementia with chronic sensory neuropathy may not benefit. In such cases, shared decision-making with the patient or caregiver is warranted to help determine optimal use of alteplase.[45]

Tenecteplase

Tenecteplase is an alternative thrombolytic drug. It is a genetically modified tPA with greater fibrin specificity, a slower clearance rate, and higher resistance to plasminogen activator inhibitor.[67]

Tenecteplase is approved by the FDA for the management of acute myocardial infarction and coronary artery thrombosis, and is being studied in acute ischemic stroke. The 2019 AHA/ASA guidelines recommend consideration of tenecteplase use in patients undergoing thrombectomy.[45] As a precursor to thrombectomy, tenecteplase has been shown to be neither less nor more effective than alteplase. One study that compared tenecteplase and alteplase in patients undergoing thrombectomy showed improved recanalization rates with use of tenecteplase, which resulted in better 90-day functional outcomes for patients.[68]

Postthrombolysis Care

After intravenous thrombolysis, close monitoring, including frequent neurologic and vital sign evaluation, typically in the intensive care unit or step-down unit, is required for the first 24 hours (*Table 9*).[45] For some emergency departments that do not have access to intensive care units, patients can be treated with thrombolysis and then transferred to another facility to prevent delays in treatment.

Thrombectomy

Thrombectomy is the mechanical removal of a stroke-causing clot using direct aspiration thrombectomy and/or stent retriever devices.[45] Criteria for thrombectomy eligibility are listed in *Table 10*. Patients are eligible for thrombectomy if they have an anterior circulation large vessel occlusion and a last known normal time up to 16 hours from symptom onset or on awakening from sleep with stroke symptoms.[69]

In addition to large vessel occlusion, thrombectomy candidates should have a moderate or high NIHSS

Table 8
Patient Eligibility Criteria for Thrombolysis

Eligibility Criteria to Receive tPA
Age ≥18 years
Clinical diagnosis of acute ischemic stroke causing neurologic symptoms
Time of onset ≤4.5 hours
Absolute Contraindications
Intracranial hemorrhage on CT scan of the head
Clinical presentation suggests subarachnoid hemorrhage
Neurosurgery, head trauma, or ischemic stroke in past 3 months
Uncontrolled hypertension (≥185/110 mm Hg)
History of intracranial hemorrhage
Known intracranial arterial venous malformation, neoplasm, or aneurysm
Active internal bleeding
Known bleeding diathesis (current use of warfarin with INR >1.7 or current use of oral anticoagulant, platelet count <100,000/mm^3, patient received heparin within 48 hours and has aPTT > upper limits of normal)
Abnormal blood glucose level that is uncorrected (≤50 mg/dL)
Relative Contraindications
Rapidly improving or very mild nondisabling neurologic symptoms
Major or serious nonhead trauma in the previous 14 days
History of gastrointestinal or urinary tract hemorrhage in the past 21 days
Seizure at stroke onset
Recent arterial puncture at noncompressible site or recent surgery
Postmyocardial infarction pericarditis
Pregnancy
Intracranial neoplasm

aPTT = activated partial thromboplastin time; CT = computed tomography; INR = international normalized ratio; tPA = tissue plasminogen activator.

Information from Powers WJ, Rabinstein AA, Ackerson T, et al. Guidelines for the early management of patients with acute ischemic stroke: 2019 update to the 2018 guidelines for the early management of acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. *2019;50:344-418.*

Table 9
Treatment of AIS: IV Administration of Alteplase

Infuse 0.9 mg/kg (maximum dose 90 mg) over 60 min, with 10% of dose administered as a bolus over 1 min
Admit the patient to intensive care or stroke unit for monitoring
If the patient develops severe headache, acute hypertension, nausea, or vomiting or has worsening neurological examination, discontinue the infusion (if IV alteplase is being administered) and obtain emergency head CT scan
Measure BP and perform neurologic assessments every 15 min during and after IV alteplase infusion for 2 h, then every 30 min for 6 h, then hourly until 24 h after IV alteplase treatment
Increase the frequency of BP measurements if SBP is >180 mm Hg or if DBP is >105 mm Hg; administer antihypertensive medications to maintain BP at or below these levels
Delay placement of nasogastric tubes, indwelling bladder catheters, or intra-arterial pressure catheters if the patient can be safely managed without them
Obtain a follow-up CT or MRI scan at 24 h after IV alteplase before starting anticoagulants or antiplatelet agents

Reprinted from Powers WJ, Rabinstein AA, Ackerson T, et al. Guidelines for the early management of patients with acute ischemic stroke: 2019 update to the 2018 guidelines for the early management of acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke*. 2019;50:e370. Erratum in* Stroke*. 2019;50(12):e440-e441. Reprinted with permission Stroke.2019;50:e344-e418 ©2013 American Heart Association, Inc. https://www.ahajournals.org/doi/10.1161/STR.0000000000000211*

Table 10
Patient Eligibility Criteria for Thrombectomy

Modified Rankin Score (mRS) 0-1
Causative occlusion in the internal carotid artery or middle cerebral artery (also considered for posterior cerebral artery, basilar artery, vertebral arteries, and M2-M3 segments)
Age ≥18 years
NIHSS score ≥6
ASPECTS ≥6
Treatment can occur within 6 h of symptom onset
Patients in the 6-24 h time window after stroke may be eligible based on additional criteria; perfusion data is useful

ASPECTS = Alberta Stroke Program Early CT Score; CT = computed tomography; NIHSS = National Institutes of Health Stroke Scale.

Information from Powers WJ, Rabinstein AA, Ackerson T, et al. Guidelines for the early management of patients with acute ischemic stroke: 2019 update to the 2018 guidelines for the early management of acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke*. 2019;50:344-418.*

score (ie, 6 or greater) and evidence on computed tomography perfusion of a large area of tissue at risk (ie, penumbra) compared with ischemic core (tissue already infarcted) (*Figure 4*).[45,69] Affected arteries should include the internal carotid artery (including intracranial, cervical segments, or tandem occlusion) or proximal segments of the middle cerebral artery.[69]

Age older than 80 years is not a contraindication for thrombectomy.[69] One pooled meta-analysis of five trials that reviewed individual patient data showed that mechanical thrombectomy was associated with a reduction in disability compared with standard care in patients 80 years or older (odds ratio = 3.68; 95% CI =1.95-6.92).[70] It is unknown if thrombectomy is beneficial for patients with a functional disability (modified Rankin [mRS] of 2 or higher) at baseline.[45]

Thrombectomy should not be delayed for patients who are eligible for the procedure, and thrombolysis should not be delayed during assessment for thrombectomy in patients who are candidates for both.[45] The thrombectomy eligibility window may be expanded to 24 hours in some patients based on imaging criteria, which should be considered in consultation with neurology and neurointerventional radiology subspecialists.[69,71,72]

Poststroke Inpatient Care

The main goals of hospitalization are to restore blood flow, if possible; evaluate for etiology of stroke; manage any acute complications; initiate secondary preventive measures; and assess the need for

rehabilitation. *Table 11* summarizes the general medical care of these patients.

Dysphagia

The AHA/ASA guidelines on early management of acute ischemic stroke recommend screening for dysphagia in patients who have had a stroke before patients resume oral intake of foods, fluids, or drugs to identify patients at increased risk of aspiration.[45] Dysphagia is associated with increased risks of aspiration pneumonia, dependency, and mortality. One study found that patients with positive dysphagia screening results had a higher rate of multiple comorbidities, were older, and were more likely to come from long-term care facilities than patients with negative results.

Randomized controlled trials have not yet shown that dysphagia screening reduces rates of aspiration pneumonia, morbidity, or mortality.[45,73] The AHA/ASA guidelines note that insufficient evidence does not mean that dysphagia screening is ineffective.[45] Patients with negative results of dysphagia screening should undergo evaluation by a speech-language pathologist or other health provider.[74]

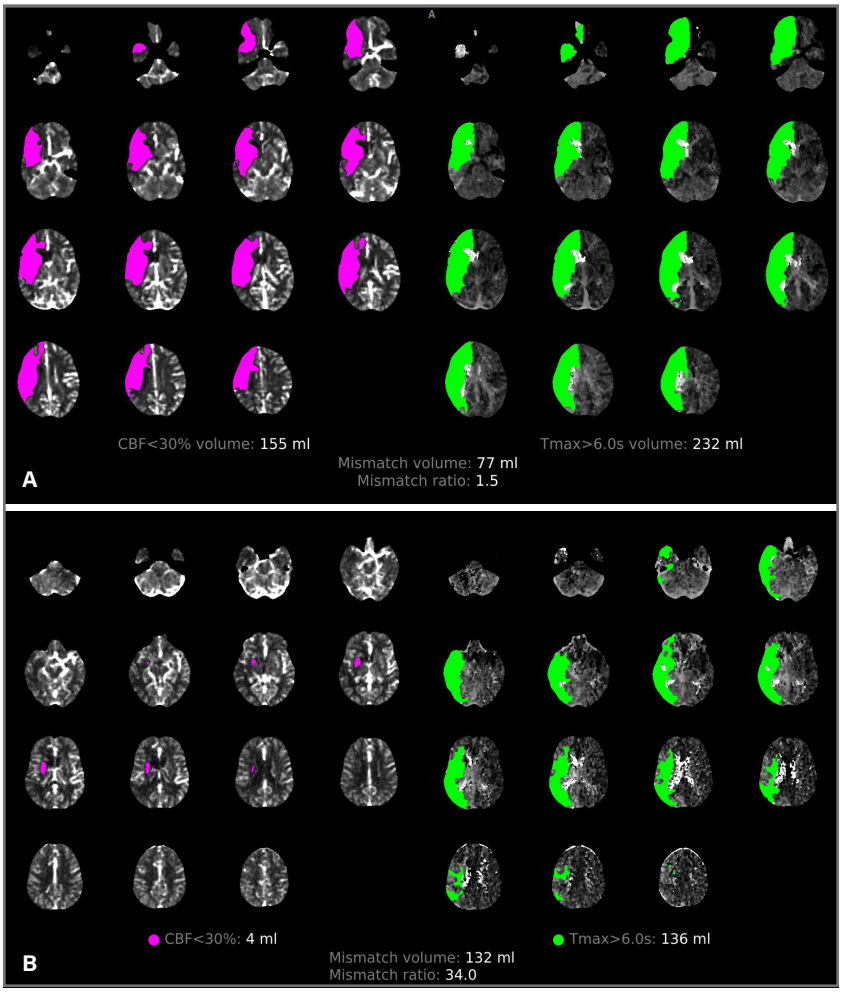

Figure 4. CT Perfusion Map

A. Shows area of estimated ischemic core (images at left) versus a larger territory of at risk tissue/penumbra (images at right). This penumbra to ischemic core ratio of 1.5 would make the patient a poor candidate for reperfusion therapy.

B. Shows a much smaller estimated ischemic core (images at left) versus a larger area of territory at risk (images at right) with a penumbra to ischemic core ratio of greater than 1.6, which makes the patient a good candidate for reperfusion therapy.

CT = computed tomography.

Images courtesy of Waimei Amy Tai, MD.

Seizure

Acute stroke may provoke seizures as a result of acute brain injury. The presence of seizures warrants evaluation with an electroencephalogram and repeat imaging of the head to assess for stroke expansion or secondary hemorrhage. Seizures should be managed as other focal epilepsy seizures, with pharmacotherapy individualized to the patient.[45]

Seizures are more common after intracranial hemorrhage than after ischemic stroke.[75] They also are more common if the site of injury is in the cortex, and less common if the stroke is in the subcortical white matter or brainstem.

Seizures often develop after initial hospitalization as the brain is undergoing long-term remodeling. Poststroke seizures occur in approximately 7% of patients, and poststroke epilepsy in approximately 5% of patients.[75] In the absence of seizures, there is no role for routine seizure prophylaxis in patients with acute ischemic stroke.[45]

Depression

The AHA/ASA guidelines recommend screening for depression

because of the high prevalence of poststroke depression, although the optimal timing is unclear.[45] Common depression questionnaires, such as the Patient Health Questionnaire 2 (PHQ-2) or Patient Health Questionnaire 9 (PHQ-9), typically are used. *Section 4* discusses poststroke depression in depth.

Table 11
Inpatient Management of Patients With Acute Ischemic Stroke

Medical Factor	Management Recommendation
Airway protection	Recommended for patients with decreased level of consciousness or bulbar dysfunction that can compromise the airway
Blood glucose control	Goal blood glucose level is 140-180 mg/dL Avoid hypoglycemia and treat if level is <60 mg/dL
BP	Early treatment to manage associated acute conditions (eg, acute coronary event, heart failure) is appropriate Lowering BP level by 15% probably is safe
BP for patients who did not receive alteplase or undergo thrombectomy	Benefit of antihypertensives in the first 48-72 hours is unknown Lowering BP level by 15% probably is safe
Fluid status	Goal is normovolemia Avoid use of dextrose-only solutions (eg, 5% dextrose in water [D5W]) as they may cause osmotic shifts and cerebral edema in strokes of large size
Head positioning	Benefit of positioning the head flat is uncertain
Oxygen	Administer supplemental oxygen to maintain oxygen saturation >94% Administration not recommended in nonhypoxic patients
Pain	Avoid use of sedating analgesics, if possible
Prophylactic antibiotics	Not recommended
Rehabilitation initiation	Early rehabilitation is recommended High-dose, very early mobilization <24 hours of stroke should not be performed, as it can cause harm
Seizures	Prophylaxis is not recommended Manage seizures if they occur
Temperature	Maintenance of normothermia is recommended Manage fevers and assess for underlying cause
Venous thromboembolism prophylaxis	For immobile patients without contraindications, intermittent pneumatic compression is recommended Prophylaxis with heparin or enoxaparin is of less certain benefit but may be appropriate if patients have other risk factors

BP = blood pressure.

Information from Powers WJ, Rabinstein AA, Ackerson T, et al. Guidelines for the early management of patients with acute ischemic stroke: 2019 update to the 2018 guidelines for the early management of acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. 2019;50:344-418; Wijdicks EF, Sheth KN, Carter BS, et al. Recommendations for the management of cerebral and cerebellar infarction with swelling: a statement for healthcare professionals from the American Heart Association/American Stroke Association. Stroke*. 2014;45(4):1222-1238.*

Infection Prophylaxis

There is no role of antibiotics for infection prophylaxis in the routine inpatient care of patients with acute ischemic stroke.[45] Some studies have shown a decrease in infections (mostly urinary tract infections); other studies have not shown any long-term mortality or morbidity benefits.[45,76]

Blood Pressure

According to the AHA/ASA guidelines, for patients who have received thrombolysis with alteplase, the BP level should be maintained at less than 180/105 mm Hg in the 24 hours afterward to prevent hemorrhagic transformation.[45]

For patients who have not received thrombolysis, the optimum BP range is unclear. It also is uncertain whether patients with a high BP level who have not undergone thrombolysis should have the BP level reduced, by how much, or how quickly.[45] Typically, patients are allowed permissive hypertension for the first 24 hours after stroke to allow perfusion of collateral blood vessels.

For patients with severe hypertension (ie, 220/120 mm Hg or greater), excessive management in the acute setting may extend the size of infarct, worsen cerebral edema, or result in other systemic sequelae (eg, impaired kidney function).[45] The AHA/ASA guidelines state that for such patients, it might be reasonable to lower the BP level by no more than 15% during the first 24 hours after stroke onset.

Typically, it is safe for neurologically stable patients to resume taking their usual antihypertensive drugs during the hospital stay.[45] This approach has been shown to improve BP control but is not associated with changes in patient-oriented outcomes, such as functional outcomes or mortality. The AHA/ASA guidelines do not make specific recommendations for selection of antihypertensives.

Cerebral Edema

Patients with large ischemic strokes may experience poststroke cerebral edema. Maximum swelling typically manifests 3 to 5 days after stroke onset. Signs and symptoms include impairment of consciousness, ipsilateral pupil dilation, and worsening motor response.[77] Hourly neurologic monitoring is advised.

An infarct larger than one-third of the middle cerebral artery territory seen on diffusion imaging within 6 hours of stroke is a risk factor for cerebral edema.[77] A large cerebellar infarct also is a risk factor. In patients with cerebral edema, isotonic fluids should be used and fluids with dextrose avoided. A neurosurgical subspecialist should be consulted early if patient condition deteriorates. When comprehensive care and timely neurosurgical intervention are not available locally, patients at risk should be transferred to a facility that can provide a higher level of care.

Blood Glucose

The goal blood glucose level after acute ischemic stroke is 140 to 180 mg/dL.[45] Severe hyperglycemia in the first 24 hours has been associated with worse disability outcomes. However, tight glycemic control has been shown to be associated with poor outcomes; a target glucose level of less than 110 mg/dL may increase the size of the infarct.[78] Depending on the severity of hyperglycemia, intravenous or subcutaneous insulin may be used to manage the blood glucose level.

Hemorrhagic Transformation of Acute Ischemic Stroke

A systematic review and meta-analysis of 55 studies found that older age, greater stroke severity, cardiac and renal comorbidities, and baseline antiplatelet use were associated with an increased risk of symptomatic intracranial hemorrhage after acute ischemic stroke.[79] Current smoking was associated with a reduced risk. The prognosis for patients with a large symptomatic hemorrhagic transformation (ie, space-occupying hematoma of more than 30% of the infarct) is poor, with a mortality rate of nearly 50% and significant morbidity for survivors.[80]

If a hemorrhage is noted, a significant risk of expansion is present in 30% to 40% of patients. If symptomatic intracranial bleeding occurs after alteplase therapy in the past 24 hours, a reversal drug should be initiated.[45] If alteplase is still being infused, it should be discontinued. A complete blood cell

For patients who have received thrombolysis with alteplase, the blood pressure level should be maintained at less than 180/105 mm Hg in the 24 hours afterward to prevent hemorrhagic transformation.

count, international normalized ratio, activated partial thromboplastin time, fibrinogen level, and blood type and crossmatch should be obtained. An emergent noncontrast CT scan of the head should be obtained. Cryoprecipitate 10 U should be infused over 10 to 30 minutes. An additional dose should be administered to patients with a fibrinogen level less than 150 mg/dL. Other drug choices for reversal include platelets, fresh frozen plasma, prothrombin complex concentrate, and recombinant factor VIIa.

Cervical Carotid Disease

The AHA/ASA guidelines on stroke prevention recommend that patients with a nondisabling ischemic stroke in the past 6 months be considered for vascular intervention if stenosis of 70% or greater is present.[39] Carotid endarterectomy and carotid artery stenting are options.[39,45,81] These procedures should be performed by a surgeon with established periprocedural stroke and mortality rates of less than 6% to reduce the risk of adverse effects.[39] In patients with nondisabling stroke, it is reasonable to perform these procedures within 2 weeks of the event.

Transcarotid artery revascularization has been associated with a periprocedural stroke rate of 1.4%.[82] It is uncertain as to whether this procedure results in a long-term reduction in recurrent stroke risk when performed in patients with a stroke in the past 6 months.[39]

Cervical Arterial Dissection

Dissections are intimal tears of the arteries. They are thought to cause up to 25% of strokes in patients younger than 45 years.[83] Patients may present with focal neurologic deficits and associated neck pain. They may have had an antecedent neck maneuver, (eg, chiropractic maneuvers) or other torsional neck maneuvers (eg, hyperextension).[84] Arterial dissections can occur in the extradural carotid artery, extradural vertebral artery, or less commonly in the intracranial blood vessels.

Clinical trials have shown that recurrent strokes occur in 1% to 2% of patients with dissection, and aspirin and warfarin appear to be equivalent in preventing recurrence.[83] However, another study found an increased risk of stroke recurrence in an aspirin-only treatment group.[85] None of these studies included direct-acting oral anticoagulants. (This is an off-label use of the direct-acting oral anticoagulants.) The AHA/ASA guidelines recommend a 3- to 6-month course of an antiplatelet or anticoagulant for these patients.[39,45]

Antiplatelets

Aspirin (50 to 325 mg/day) should be administered within the first 24 to 48 hours after acute ischemic stroke.[39,45] If the patient has an allergy to aspirin, clopidogrel is a reasonable option.[39] (Ischemic stroke is an off-label use of aspirin and clopidogrel.)

Early use of antithrombotics also is recommended, assuming no contraindications, such as use of alteplase in the past 24 hours, hemorrhagic transformation of ischemic stroke, or other acute bleeding.[45] For patients with a noncardioembolic ischemic stroke, antiplatelets are preferred.[39] For patients with a minor stroke (ie, NIHSS score of 3 or less), dual antiplatelet therapy with aspirin and clopidogrel should be started within 12 to 24 hours of the stroke. It should be continued for at least 21 days and up to 90 days after the initial event to reduce the risk of recurrence.[39,86,87]

For patients who were taking an antiplatelet and experienced a recurrent noncardioembolic ischemic stroke, the benefit of switching to an alternative antiplatelet is unclear.[39] In addition, switching to oral anticoagulation is not advised.[45] Triple antiplatelet therapy (ie, with aspirin, clopidogrel, and dipyridamole) can cause additional risk of hemorrhage without added ischemic stroke benefit and, thus, is not recommended.[39,88]

Case 1, cont'd. MB undergoes thrombectomy of the right middle cerebral artery with a stent retriever device that results in adequate reperfusion. She has negative results on a dysphagia evaluation. She still has mild residual weakness on the left side of the face and body. Inpatient rehabilitation is recommended for further strengthening.

Several days later, she is discharged from the hospital to an inpatient rehabilitation facility with a prescription for aspirin 81 mg/day. Because she had an emoblic stroke of undetermined source, further cardiac monitoring is needed to evaluate for occult atrial fibrillation.

Section Four
Long-Term Poststroke Management

It is estimated that after stroke patients live 33% fewer remaining years compared with age- and sex-matched controls. Functional recovery after stroke depends on many factors, including age, functional status before stroke, stroke severity, and comorbidities. The purpose of rehabilitation services is to improve functional status. All patients with stroke should undergo a formal assessment of rehabilitation needs before hospital discharge. Types of rehabilitation include inpatient, subacute, and home health care. Primary care of patients after stroke focuses on secondary stroke prevention, including antiplatelet therapy, hypertension and hyperlipidemia management, diet, and glycemic control. In patients with ischemic stroke and no contraindications, dual antiplatelet therapy with aspirin and clopidogrel is recommended for 21 to 90 days after stroke, but not longer. A blood pressure goal of less than 130/80 mm Hg is recommended for most patients. For most patients with diabetes, a goal A1c level of 7% or less is reasonable. Diabetes management should include a glucagon-like peptide 1 receptor agonist or sodium-dependent glucose cotransporter 2 inhibitor. Various tests, drugs, and screenings are indicated for patients with specific hypercoagulable states (eg, coagulopathies, antiphospholipid syndrome, occult malignancy, hormone therapy). Poststroke follow-up should address sequelae, such as fatigue, depression, contracture and spasticity, hemiplegic shoulder pain, and central poststroke pain.

Case 1, cont'd. After hospital discharge, MB had a short stay in an inpatient rehabilitation facility and was later discharged home. On a follow-up visit in your office, she wants to discuss how she can prevent future strokes, as well as deal with the effects of the stroke she had.

Prognosis

Life expectancy after a stroke varies by degree of infarct. Using data from 1999-2009, it has been estimated that patients with stroke live 33% fewer remaining years (95% CI =30.9%-34.7%), with a 31.6% greater proportion of remaining life with disability, compared with age- and sex-matched controls.[89] Calculations on estimated life expectancy using a functional scale, such as the modified Rankin Scale (mRS), age, and sex, can help predict rehabilitation outcomes.[90]

Clinicians are poor at judging the degree to which a specific patient is likely to recover.[1] Functional recovery after stroke depends on many factors, including age, functional status before the stroke, stroke severity, and comorbidities.

Rehabilitation

The purpose of rehabilitation services is to improve functional status in patients with stroke. The American Heart Association/American Stroke Association (AHA/ASA) guidelines on adult stroke rehabilitation and recovery recommend that all patients undergo a formal assessment of rehabilitation needs before hospital discharge.[74] This assessment often is performed by an interdisciplinary team that includes an occupational therapist, physical therapist, and speech-language pathologist, among others. Their assessments, along with such factors as family support, help determine the appropriate level of care after discharge. This may include home without further services, home with home rehabilitation services, inpatient rehabilitation, or subacute rehabilitation.

Inpatient Rehabilitation

Inpatient rehabilitation has been shown to improve disability in terms of physical, occupational therapy, speech, and swallowing outcomes.[74] Physical medicine and rehabilitation physicians visit patients at least 3 times/week and oversee the rehabilitation team.[74,91] In addition to this team, social workers may help with coordination of home health services, drug copayments, or social benefits. Counseling and psychological assessment may be offered.[92]

To qualify for inpatient rehabilitation under Medicare, patients must have a diagnosis that meets

admission criteria, as well as a deficiency with rehabilitation potential in at least two modalities of therapy. They must be able to tolerate 3 hours/day of rehabilitation services for 5 days/week. In addition, they must have the potential to improve sufficiently to return to a community setting.[74,91]

Inpatient rehabilitation is associated with an improvement in functional outcomes compared with subacute rehabilitation. However, this may be due in part to the baseline functional ability of patients in each setting. Patients who are discharged to inpatient rehabilitation typically are younger, have fewer comorbidities, and have lower prestroke disability levels than patients who are discharged to skilled nursing facilities. Disparities in discharge location by socioeconomic status, age, and race have been found.[74]

Subacute Rehabilitation

Patients who do not qualify for or do not want inpatient rehabilitation may be discharged to a skilled nursing facility (ie, subacute rehabilitation). It is the common discharge location for patients with lower levels of prestroke function who require skilled nursing care to maintain safe care, or for patients who are not expected to make a full or substantial functional recovery. Subacute rehabilitation at a skilled nursing facility accounts for the largest percentage of discharge locations for Medicare patients who have had an acute ischemic stroke (ie, 32% of all patients).[74]

Home Health Care

Eligible patients can receive physical, occupational, and speech therapy at home. Medicare home health eligibility regulations require that a physician certify that the patient is homebound. Most services are approved initially for 60 days, which can be extended if clinically warranted. Approximately 15% of patients who experience an acute ischemic stroke use home health rehabilitation services during recovery.[74]

Secondary Prevention

Major considerations in secondary prevention of ischemic stroke include antiplatelet therapy, management of hypertension and hyperlipidemia, diet, and glycemic control.

Antiplatelet Therapy

Traditionally, aspirin 81 mg/day is used for secondary stroke prevention.[39] Newer evidence suggests that for short-term use, dual antiplatelet therapy has an additional benefit in preventing recurrent ischemic stroke.

The Clopidogrel in High-Risk Patients with Acute Nondisabling Cerebrovascular Events (CHANCE) trial showed that dual antiplatelet therapy (ie, clopidogrel 75 mg/day plus aspirin for 21 days, followed by clopidogrel alone) was associated with an 8.2% risk of recurrent stroke versus aspirin alone (11.7%).[86] Dual antiplatelet therapy for longer than 1 year is not recommended because of concerns about increased risk of hemorrhage without added benefit in ischemic stroke prevention.[93] Dual antiplatelet therapy is recommended for 21 to 90 days after acute ischemic stroke, but not longer.[39,45]

The Acute Stroke or Transient Ischaemic Attack Treated with Ticagrelor and ASA [acetylsalicylic acid] for Prevention of Stroke and Death (THALES) trial examined antiplatelet pharmacotherapies in patients with a mild to moderate acute noncardioembolic ischemic stroke (ie, National Institutes of Health Stroke Scale [NIHSS] score of 5 or less) or transient ischemic attack who were not undergoing intravenous or endovascular thrombolysis. It showed that the risk of the composite outcome of stroke or death within 30 days was lower with ticagrelor and aspirin than with aspirin alone, but the incidence of disability did not differ significantly between the two treatment groups.[94] Severe bleeding occurred more frequently with ticagrelor.

For patients with symptomatic large vessel atherosclerotic disease, the author recommends longer-term dual antiplatelet therapy with clopidogrel 75 mg/day and aspirin 81 mg/day for 3 months. Alternatively, clopidogrel 75 mg/day or aspirin 81 mg/day plus cilostazol 200 mg/day can be considered.[39] (Prevention is an off-label use of cilostazol.)

The medical management arm of the Stenting and Aggressive Medical Management for Preventing Recurrent Stroke in Intracranial Stenosis (SAMMPRIS) trial included patients at high risk of stroke who received aspirin 325 mg/day and clopidogrel 75 mg/day for 90 days.[95] Patients in the medical management arm also underwent aggressive blood pressure control and a tobacco cessation intervention. Patients in this group had better outcomes than patients in the intracranial stenting arm. This difference primarily was due to higher rates of perioperative complications in patients in the intracranial stenting arm.

For patients with an embolic stroke of undetermined source, direct oral anticoagulant use is not recommended.[39]

Hypertension Management

Hypertension is the most prevalent risk factor for stroke.[96] A blood pressure goal of less than 130/80 mm Hg is recommended for most patients in the outpatient setting.[39] The choice of drug is less important than achieving the goal blood pressure level. Patient comorbidities (eg, diabetes, coronary disease) may guide the choice of drug.[39,45]

Hyperlipidemia Management

High-intensity statin therapy is recommended after an ischemic stroke in patients with atherosclerotic disease to achieve a low-density lipoprotein goal of less than 70 mg/dL.[6,39] Atorvastatin 80 mg/day is recommended for patients with stroke with no previous hyperlipidemia with a low-density lipoprotein level greater than 100 mg/dL.[39] Routine monitoring of liver test results no longer is recommended.[97] For patients who cannot tolerate statins or patients in whom statins do not decrease the low-density lipoprotein level to less than 70 mg/dL, ezetimibe can be added.[39] (Stroke prophylaxis and atherosclerosis are off-label uses of some statins.)

The addition of a proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor to a statin for secondary prevention has been shown to reduce rates of major vascular end points, including stroke, although absolute numbers were small.[98] PCSK9 inhibitors are expensive, with an estimated cost-effectiveness of $141,700 to $450,000 per quality-adjusted life year added.[6]

The purified omega-3 fatty acid icosapent ethyl has been shown to reduce the risk of cardiovascular death, myocardial infarction, and nonfatal stroke in patients with known cardiovascular disease or at high risk (ie, older than 50 years with diabetes).[99] The number needed to treat with icosapent ethyl is 21 over approximately 5 years to prevent 1 outcome. The AHA/ASA guidelines for secondary prevention of stroke recommend consideration of icosapent ethyl use in patients with elevated triglyceride levels despite statin therapy.[39]

Diet

Dietary recommendations for secondary stroke prevention mostly are extrapolated from the effects of diet on cardiovascular disease risk factors, including hyperlipidemia and hypertension. There is modest evidence to support consumption of a Mediterranean-type diet focused on monounsaturated fat, plant-based foods, and fish consumption, and supplemented with extra virgin olive oil or nuts to reduce the risk of secondary stroke.[39]

The Dietary Approaches to Stop Hypertension (DASH) diet is another recommended option, with a focus on reducing dietary salt intake to 2.5 g/day in patients who have not already done so.[39] The DASH diet is thought to reduce stroke risk through blood pressure reduction.

Glycemic Control

For patients with diabetes, a goal A1c level of 7% or less is reasonable, unless the patient is older than 65 years or has other life-limiting conditions.[39] Diabetes management should include blood glucose-lowering drugs shown to reduce the rate of cardiovascular events, such as a glucagon-like peptide 1 receptor agonist, sodium-dependent glucose cotransporter 2 inhibitor, or thiazolidinediones. Other drugs, such as insulins and sulfonylureas, among others, may reduce blood glucose levels, but they have not been shown to reduce the rate of cardiovascular events.

Hypercoagulable States

Hypercoagulable states may increase the risk of stroke via various mechanisms. Conditions that result in hypercoagulable states include congenital or autoimmune coagulopathies, antiphospholipid syndrome, and occult malignancies. Iatrogenic causes (eg, contraceptive use, hormone therapy) also may result in such states.

Coagulopathies

Genetic coagulopathies, such as prothrombin 20210A gene mutation, factor V Leiden, *MTHFR* mutation, and protein C and S deficiencies, are associated with venous events (eg, cerebral venous sinus thrombosis) and typically not an increased risk of first

Hypertension is the most prevalent risk factor for stroke. A blood pressure goal of less than 130/80 mm Hg is recommended for most patients in the outpatient setting.

stroke.[3,39] In patients who have had a stroke, it is not clear whether these are associated with an increased risk of second stroke. The decision to test for thrombophilia in a patient with an embolic stroke of unknown source or a patient with a stroke and acute deep venous thrombosis should be guided by whether the test result would change management.[39]

Antiphospholipid Syndrome

Many neurology subspecialists will obtain tests for antiphospholipid syndrome in patients younger than 50 years without traditional vascular risk factors who experience an arterial stroke. Serum studies for antiphospholipid antibodies include the dilute Russell viper venom test. This test is extremely sensitive, and results should be interpreted in conjunction with the results of other tests. Anticardiolipin antibody immunoglobulin (Ig) G, anticardiolipin antibody IgM, anti-beta$_2$ glycoprotein IgG, and anti-beta$_2$ glycoprotein IgM should be assessed.[3,39,100]

The Antiphospholipid Antibodies and Stroke Study (APASS), a prospective cohort study within the Warfarin vs Aspirin Recurrent Stroke Study (WARSS), compared warfarin (international normalized ratio of 1.4-2.8) with aspirin 325 mg for prevention of recurrent stroke or mortality in patients with stroke with one set of positive anticardiolipin antibodies.[100] The results showed no difference in the 2-year rate of recurrent thrombo-occlusive events.

For patients with stroke who have positive test results for antibodies but do not meet the criteria for antiphospholipid syndrome, an antiplatelet is recommended.[101] Patients who meet the criteria for antiphospholipid syndrome (ie, positive antibody test result twice over 12 weeks plus recurrent venous thromboembolism event, pregnancy morbidity, or single arterial event) require anticoagulation.[39,101]

Occult Malignancy

Consideration of screening for occult malignancy in patients with cryptogenic stroke and without other traditional risk factors may be warranted.[102] Age-appropriate cancer screening may be offered to these patients.

Patients with stroke have been shown to have a higher incidence of cancer compared with patients without stroke.[102] In one meta-analysis, studies of patients with cryptogenic stroke found that in 62 of 1,000 patients with strokes, cancer was detected within 1 year of the stroke. Many cases were detected soon after the stroke event. Predictors of cancer included older age, smoking, involvement of multiple vascular territories, and elevated C-reactive protein levels and D-dimer assay results.

Contraceptive Use and Hormone Therapy

In two meta-analyses, combination oral contraceptives were found to be associated with stroke by a factor of 1.4 to 2 times.[103,104] Progestin-only contraceptives have not been shown to increase stroke risk.[24] Additional risk factors (eg, tobacco use) or prior thromboembolic events have been shown to compound the thrombotic risk related to oral contraceptive use. Postmenopausal hormone therapy does not reduce the risk of stroke; it is unclear if it increases the risk of stroke.

A recent review found insufficient evidence to determine the risk of stroke associated with exogenous hormone therapy for sex affirmation.[105] Routine screening for dyslipidemia, diabetes, and hypertension are recommended for patients taking hormones for sex affirmation. There are insufficient data to determine the risk of cardiovascular outcomes related to the exogenous use of testosterone in transgender men.[106] As with the use of testosterone replacement therapy in hypogonadal men, there is no clear evidence of an increased number of strokes.

Poststroke Symptoms

Fatigue

Up to 40% of patients experience fatigue after stroke.[107] The etiology is unclear and effective therapies are limited. A systematic review that examined the associations among poststroke fatigue, physical fitness, and physical activity found no statistically significant relationship. However, one study found that patients with higher levels of fatigue were more likely to have lower self-efficacy expectations for exercise.[107,108] Limited data suggest that exercise and physical fitness can improve fatigue.[74]

Physical deconditioning after stroke is common and can trigger fatigue.[109] There may be a feedback mechanism in which patients who wish to reduce fatigue choose to decrease voluntary motor activity and avoid physical activity, thus worsening their physical conditioning.[110] Stroke survivors typically are less active than survivors of other cardiovascular events.[109]

The AHA/ASA guidelines on physical activity and exercise for stroke survivors recommend customization of an exercise program to promote physical activity

for improving aerobic fitness, strength training, and reduction of sedentary behavior.[109] For patients with stroke who can tolerate it, moderate-intensity aerobic activity for a minimum of 10 min 4 times/week or vigorous-intensity aerobic activity for a minimum of 20 min 2 times/week is recommended to decrease the risk of recurrent stroke and the composite cardiovascular end point of recurrent stroke, myocardial infarction, or vascular death.[39,109]

Depression

Up to one-third of patients experience depression after stroke.[74] There are no clear patterns based on age or sex, but a history of depression is a risk factor.[111] Patients with more severe strokes are more likely to develop depression. Routine screening for depression is recommended in the outpatient follow-up of patients after stroke.[74]

Management with selective serotonin reuptake inhibitors (SSRIs) has been shown to reduce poststroke depression and improve survival times.[74] (This is an off-label use of some SSRIs.) There is evidence that some of these drugs may improve motor outcomes for patients with stroke and motor disability.[112]

Contracture and Spasticity

After hemiparetic stroke, joint contracture will form on the affected side in 60% of patients in less than 1 year.[74] Wrist contractures are common in patients with hand weakness.

Many clinicians recommend daily stretching of the affected limbs to prevent contracture.[74] Patients and caregivers should be instructed in appropriate techniques to prevent injury and maximize the effectiveness of passive stretching exercises. Patients and caregivers also should be educated about prevention of skin breakdown.

Hemiplegic Shoulder Pain

Hemiplegic shoulder pain is common after stroke; the cause often is multifactorial.[74] Pain is associated with tissue injury, abnormal joint mechanics, and central nociceptive hypersensitivity. Patients with hemiplegia have altered movement patterns in specific stages of stroke recovery. In the acute phase, shoulder subluxation is associated with pain. In the chronic phase, there is capsular stiffness and altered resting position of the scapula in lateral rotation.

In cases of shoulder pain and for shoulder care poststroke, education for patients and caregivers is recommended, particularly before hospital discharge or transitions in care.[74] This should include information on maintenance of range of motion and appropriate body positioning, botulinum toxin injection can be used to reduce severe hypertonicity in hemiplegic shoulder muscles.

Central Poststroke Pain

Up to 11% of patients will develop central poststroke pain (CPSP), a neuropathic syndrome that results from injury to the thalamus or somatosensory area.[113] One meta-analysis that included more than 20,000 patients showed an 11% pooled prevalence (95% CI of 7% to 18%) of CPSP in patients with stroke at any location.[113] For patients with medullary or thalamic strokes, the prevalence was more than 50%.

In patients with CPSP, 26% developed it at stroke onset, 31% within 1 month of stroke, and 41% between the first month and the first year after stroke.[113] Late-onset CPSP, which develops more than 1 year after stroke, occurs in 5% of patients.

Evidence is limited, but pharmacotherapy options may include amitriptyline, gabapentin, pregabalin, duloxetine, or lamotrigine.[74,113] Therapeutic exercise and psychosocial support also may be reasonable. (This is an off-label use of gabapentin, pregabalin, duloxetine, and lamotrigine.)

Case 1, cont'd. MB continues to follow-up visits for poststroke prevention. In addition to addressing other concerns, at each visit you assess for depression with the Patient Health Questionnaire 2 (PHQ-2) and encourage MB to pursue a modified exercise regimen to maintain physical activity and improve poststroke fatigue.

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Posttest Questions

1. Which one of the following is true of the association among obesity and weight loss, and cerebrovascular disease risk?

- ❑ A. Increased body mass index is associated with increased stroke mortality.
- ❑ B. Obesity is an independent risk factor for stroke.
- ❑ C. Obesity is not associated with vascular death.
- ❑ D. Weight loss is associated with a reduced risk of stroke.

2. Which one of the following best describes the choice of treatment for stroke prevention in patients with atrial fibrillation (AF)?

- ❑ A. Anticoagulation is preferred for all patients with AF.
- ❑ B. Direct oral anticoagulants are preferred for patients with nonvalvular AF.
- ❑ C. Surgical options, such as left atrial appendage closure, are indicated for secondary prevention only.
- ❑ D. Warfarin is no longer indicated for AF.

3. Which one of the following is true of screening and management of asymptomatic carotid artery stenosis?

- ❑ A. Carotid endarterectomy is associated with up to a 5% risk of stroke or death in the 30 days after intervention.
- ❑ B. Chronic, complete occlusions of the carotid artery should be considered for carotid endarterectomy.
- ❑ C. Screening ultrasonography is recommended by the U.S. Preventive Services Task Force (USPSTF) in the presence of vascular risk factors for carotid disease.
- ❑ D. Stenting and carotid endarterectomy have equivalent risk profiles in patients without a history of transient ischemic attack or stroke.

4. Which one of the following is true of stroke screening and treatment in patients with sickle cell disease (SCD)?

- ❑ A. Adults with SCD should undergo screening with carotid ultrasonography and head computed tomography (CT) scan.
- ❑ B. Adults with sickle cell trait should undergo screening with carotid ultrasonography and a head CT scan.
- ❑ C. Children between ages 2 to 16 years with SCD should undergo screening with transcranial doppler ultrasound.
- ❑ D. Positive screening results warrant referral for statin and antiplatelet therapy.

5. Which one of the following is true of stroke and COVID-19 infection?

- ❑ A. COVID-19 infection is associated with an increased risk of stroke.
- ❑ B. Mild COVID-19 infection is more likely to be associated with stroke than severe COVID-19 infection.
- ❑ C. Patients with stroke without COVID-19 had a higher mortality rate than patients with stroke and COVID-19.
- ❑ D. Patients with stroke without COVID-19 had worse functional outcomes than patients with stroke and COVID-19.

6. Which one of the following symptoms may be present in a patient with stroke and basilar artery syndrome?

- ❑ A. Aphasia.
- ❑ B. Decreased level of consciousness with associated cranial nerve symptoms.
- ❑ C. Unilateral neglect or hemineglect.

7. Which one of the following laboratory tests should be obtained as part of the initial emergency department evaluation of acute ischemic stroke?

- ❑ A. Blood glucose level.
- ❑ B. Complete blood cell count.
- ❑ C. Complete metabolic panel.
- ❑ D. International normalized ratio.

8. Which one of the following is true of computed tomography (CT) scan of the brain in acute ischemic stroke?

- ❑ A. CT angiography, if indicated, should not be performed concurrently with the initial noncontrast CT scan.
- ❑ B. Results of a noncontrast head CT scan performed within 6 hours of ischemic stroke onset may appear normal.
- ❑ C. Visible changes on CT scan will be present within 3 hours of acute ischemic stroke in most patients.
- ❑ D. Urgent head CT scan is performed to evaluate the extent of injury.

9. Which one of the following describes a clinical scenario with stroke of other determined pathology?

- ❑ A. Arterial dissection.
- ❑ B. Foramen ovale.
- ❑ C. Infective endocarditis.
- ❑ D. Mechanical heart valve.

10. Patients with which one of the following types of stroke has an indication for testing for occult atrial fibrillation with remote outpatient monitoring?

- ❑ A. Cardioembolic.
- ❑ B. Cryptogenic stroke.
- ❑ C. Lacunar.

11. Thrombolysis is the standard of care for emergency treatment of eligible patients with disabling symptoms of acute ischemic stroke.

- ❑ A. True.
- ❑ B. False.

12. Which one of the following is an absolute or relative contraindication to thrombolysis?

- ❑ A. Disabling stroke symptoms.
- ❑ B. Last known normal time normal time of 3 to 4.5 hours.
- ❑ C. National Institutes of Health Stroke Scale (NIHSS) score of 6.
- ❑ D. Seizure at stroke onset.

13. In which one of the following cases would thrombectomy possibly be contraindicated?

- ❑ A. Age older than 80 years.
- ❑ B. Baseline functional impairment (modified Rankin Scale [mRS] greater than 2).
- ❑ C. Large vessel occlusion.
- ❑ D. Last seen normal time 8 hours ago.
- ❑ E. Previous thrombolysis.

14. Which one of the following is true of hypertension treatment in patients after acute ischemic stroke?

- ❑ A. For neurologically stable patients, resuming usual antihypertensive drugs is associated with improved blood pressure (BP) control.
- ❑ B. For patients who have received thrombolysis, target BP during hospitalization is less than 140/90 mm Hg.
- ❑ C. For patients who have not received thrombolysis, target BP is 180/105 mm Hg in the first 24 hours.
- ❑ D. For patients with BP greater than 220/120 mm Hg, rapid reduction to less than 160/90 mm Hg is associated with improved outcomes.

15. Which one of the following describes a current recommendation for antiplatelet therapy after acute ischemic stroke?

- ❑ A. Consider anticoagulation with warfarin or a dual oral anticoagulant for patients with aspirin allergy.
- ❑ B. Consider dual antiplatelet therapy for up to 1 year for minor stroke.
- ❑ C. Consider triple antiplatelet therapy with aspirin, clopidogrel, and dipyridamole for patients at very high risk of recurrent stroke.
- ❑ D. Initiate aspirin within 24 to 48 hours.

16. Which one of the following is true of inpatient and/or subacute rehabilitation facilities, the discharge criteria for them, or patients with stroke who use them?

- ❑ A. Discharge rates to inpatient and subacute rehabilitation facilities are equivalent across socioeconomic strata.
- ❑ B. More Medicare patients are discharged to inpatient rehabilitation facilities than to subacute rehabilitation facilities.
- ❑ C. Outcomes are better in patients in subacute rehabilitation facilities compared with inpatient rehabilitation facilities.
- ❑ D. Patients discharged to inpatient rehabilitation facilities tend to be younger and have lower prestroke disability.

17. Which one of the following is the most prevalent risk factor for stroke?

- ❑ A. Hypercoagulable state.
- ❑ B. Hyperglycemia.
- ❑ C. Hyperlipidemia.
- ❑ D. Hypertension.

18. The American Heart Association/American Stroke Association (AHA/ASA) guidelines for secondary prevention of stroke recommend consideration of which one of the following treatments in patients with elevated triglyceride levels despite statin therapy?

- ❑ A. Dietary Approaches to Stop Hypertension (DASH) diet.
- ❑ B. Ezetimibe.
- ❑ C. Icosapent ethyl.
- ❑ D. Proprotein convertase subtilisin/kexin type 9 inhibitors.

19. Which one of the following drugs should be recommended for use in stroke patients with diabetes to reduce the risk of future cardiovascular events?

- ❑ A. Analog insulin.
- ❑ B. Human insulin.
- ❑ C. Sodium-dependent glucose cotransporter 2 inhibitor.
- ❑ D. Sulfonylureas.

20. Which one of the following hormone therapies is associated with an increased risk of stroke?

- ❑ A. Combination oral contraceptives.
- ❑ B. Postmenopausal hormone therapy.
- ❑ C. Progesterone-only contraceptives.
- ❑ D. Testosterone replacement in hypogonadal men.

Posttest Answers

Question 1: The correct answer is A.
Prospective studies have shown an association between an increase in body mass index (BMI) and an increase in the rate of stroke mortality. *See page 11.*

Question 2: The correct answer is B.
The more recent 2019 American Heart Association/American College of Cardiology/Hearth Rhythm Society (AHA/ACC/HRS) guidelines for atrial fibrillation (AF) management suggest that use of direct-acting oral anticoagulants is preferable in patients with nonvalvular AF. *See page 13.*

Question 3: The correct answer is A.
The U.S. Preventive Services Task Force (USPSTF) recommends against screening for asymptomatic carotid artery stenosis in the general population. Although screening ultrasonography has not been associated with a specific risk of harm, the follow-up interventions (eg, carotid endarterectomy, carotid stenting) have been associated with up to a 5% risk of stroke or mortality in the 30 days after intervention. *See page 15.*

Question 4: The correct answer is C.
Children with sickle cell disease should be screened for stroke with transcranial Doppler ultrasound from ages 2 to 16 years. *See page 15.*

Question 5: The correct answer is A.
It is known that COVID-19 infection, particularly severe COVID-19, is associated with a hypercoagulable state, and hospitalized patients with COVID are at higher risk of stroke than patients with other infections. *See page 16.*

Question 6: The correct answer is B.
Patients with stroke with a decreased level of consciousness with associated cranial nerve symptoms or posturing may have a basilar artery syndrome. *See page 18.*

Question 7: The correct answer is A.
The emergency department evaluation of stroke should include assessment of vital signs, measurement of the blood glucose level, calculation of the National Institutes of Health Stroke Scale (NIHSS) (*Table 7*) or initial neurologic assessment with focal deficits identified, review of any use of antithrombotics, and the time that the patient was last reported to have been seen well. *See page 19.*

Question 8: The correct answer is B.
Results of a noncontrast computed tomography scan performed less than 6 hours after ischemic stroke onset may appear normal. *See page 19.*

Question 9: The correct answer is A.
Stroke of other determined pathology includes arterial dissections and hypercoagulable states. *See page 22.*

Question 10: The correct answer is B.
For patients with a cryptogenic stroke who do not have a contraindication to anticoagulation, further testing with outpatient remote monitoring should be considered to evaluate for occult atrial fibrillation. *See page 23.*

Question 11: The correct answer is A.
Thrombolysis is the standard of care for eligible patients with disabling symptoms of acute ischemic stroke. *See page 24.*

Question 12: The correct answer is D.
Seizure at stroke onset is a relative contraindication to thrombolysis. *See Table 8.*

Question 13: The correct answer is B.
It is unknown if thrombectomy is beneficial for patients with a functional disability (modified Rankin [mRS] of 2 or higher) at baseline. *See page 26.*

Question 14: The correct answer is A.
Typically, it is safe for neurologically stable patients to resume taking their usual antihypertensive drugs during the hospital stay. This approach has been shown to improve blood pressure control but is not associated with changes in patient-oriented outcomes, such as functional outcomes or mortality. *See page 29.*

Question 15: The correct answer is D.
Aspirin 50 to 325 mg/day should be administered within the first 24 to 48 hours after acute ischemic stroke. *See page 30.*

Question 16: The correct answer is D.
Patients who are discharged to inpatient rehabilitation typically are younger, have fewer comorbidities, and have lower prestroke disability levels than patients who are discharged to skilled nursing facilities. *See page 32.*

Question 17: The correct answer is D.
Hypertension is the most prevalent risk factor for stroke. *See page 33.*

Question 18: The correct answer is C.
The American Heart Association/American Stroke Association (AHA/ASA) guidelines for secondary prevention of stroke recommend consideration of icosapent ethyl use in patients with elevated triglyceride levels despite statin therapy. *See page 33.*

Question 19: The correct answer is C.
Diabetes management in patients with stroke should include blood glucose-lowering drugs shown to reduce the rate of cardiovascular events, such as a glucagon-like peptide 1 receptor agonist, sodium-dependent glucose cotransporter 2 inhibitor, or thiazolidinediones. *See page 33.*

Question 20: The correct answer is A.
In two meta-analyses, combination oral contraceptives were found to be associated with stroke by a factor of 1.4 to 2 times. *See page 34.*

Notes

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Notes

The next edition of AAFP FP Essentials™ *will be:*

Childhood Respiratory Conditions


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