Secondary prevention of stroke (2021 guideline)

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Table 3. Applying Class of Recommendation and Level of Evidence to Clinical Strategies, Interventions, Treatments, or Diagnostic Testing in Patient Care (Updated May 2019)*

CLASS (STRENGTH) OF RECOMMENDATION	LEVEL (QUALITY) OF EVIDENCE‡
CLASS 1 (STRONG) — **Benefit >>> Risk** **Suggested phrases for writing recommendations:** • Is recommended • Is indicated/useful/effective/beneficial • Should be performed/administered/other • Comparative-Effectiveness Phrases†: — Treatment/strategy A is recommended/indicated in preference to treatment B — Treatment A should be chosen over treatment B	**LEVEL A** • High-quality evidence‡ from more than 1 RCT • Meta-analyses of high-quality RCTs • One or more RCTs corroborated by high-quality registry studies
CLASS 2a (MODERATE) — **Benefit >> Risk** **Suggested phrases for writing recommendations:** • Is reasonable • Can be useful/effective/beneficial • Comparative-Effectiveness Phrases†: — Treatment/strategy A is probably recommended/indicated in preference to treatment B — It is reasonable to choose treatment A over treatment B	**LEVEL B-R** — **(Randomized)** • Moderate-quality evidence‡ from 1 or more RCTs • Meta-analyses of moderate-quality RCTs
CLASS 2b (WEAK) — **Benefit ≥ Risk** **Suggested phrases for writing recommendations:** • May/might be reasonable • May/might be considered • Usefulness/effectiveness is unknown/unclear/uncertain or not well-established	**LEVEL B-NR** — **(Nonrandomized)** • Moderate-quality evidence‡ from 1 or more well-designed, well-executed nonrandomized studies, observational studies, or registry studies • Meta-analyses of such studies
CLASS 3: No Benefit (MODERATE) (Generally, LOE A or B use only) — **Benefit = Risk** **Suggested phrases for writing recommendations:** • Is not recommended • Is not indicated/useful/effective/beneficial • Should not be performed/administered/other	**LEVEL C-LD** — **(Limited Data)** • Randomized or nonrandomized observational or registry studies with limitations of design or execution • Meta-analyses of such studies • Physiological or mechanistic studies in human subjects
Class 3: Harm (STRONG) — **Risk > Benefit** **Suggested phrases for writing recommendations:** • Potentially harmful • Causes harm • Associated with excess morbidity/mortality • Should not be performed/administered/other	**LEVEL C-EO** — **(Expert Opinion)** • Consensus of expert opinion based on clinical experience

COR and LOE are determined independently (any COR may be paired with any LOE).

A recommendation with LOE C does not imply that the recommendation is weak. Many important clinical questions addressed in guidelines do not lend themselves to clinical trials. Although RCTs are unavailable, there may be a very clear clinical consensus that a particular test or therapy is useful or effective.

* The outcome or result of the intervention should be specified (an improved clinical outcome or increased diagnostic accuracy or incremental prognostic information).

† For comparative-effectiveness recommendations (COR 1 and 2a; LOE A and B only), studies that support the use of comparator verbs should involve direct comparisons of the treatments or strategies being evaluated.

‡ The method of assessing quality is evolving, including the application of standardized, widely-used, and preferably validated evidence grading tools; and for systematic reviews, the incorporation of an Evidence Review Committee.

COR indicates Class of Recommendation; EO, expert opinion; LD, limited data; LOE, Level of Evidence; NR, nonrandomized; R, randomized; and RCT, randomized controlled trial.

DIAGNOSTIC EVALUATION FOR SECONDARY STROKE PREVENTION

1.Diagnostic evaluation is recommended for gaining

insights into the etiology of and planning optimal strategies for preventing recurrent stroke,

with testing completed or underway **within 48** hours of onset of stroke symptoms

2.Blood tests, including CBC,PT, PTT, glucose, HbA1c, creatinine, and fasting or non-fasting lipid profile are recommended

3.ECG is recommended to screen for atrial fibrillation (AF) and atrial flutter and assess for other

concomitant cardiac conditions

4. In patients with **symptomatic anterior circulation cerebral infarction or TIA** who are candidates for revascularization, **noninvasive carotid imaging** with carotid ultrasonography, CTA or MRA to screen for stenosis

For patients at high risk of carotid artery stenosis who can undergo surgery without delay, immediate CTA is the most cost-effective strategy

5. **Noninvasive imaging of the intracranial large arteries and imaging of the extracranial vertebrobasilar arterial system** with MRA or CTA can be effective to identify atherosclerotic disease, dissection, moyamoya, or other etiologically relevant vasculopathies

6.In patients with **cryptogenic stroke, echocardiography with or without contrast** is reasonable to evaluate for possible cardiac sources or transcardiac pathways for cerebral embolism

TTE is preferred over TEE for the detection of left ventricular (LV) thrombus, but TEE is superior to TTE in detecting left arterial thrombus, aortic atheroma, prosthetic valve abnormalities, nativevalve abnormalities, atrial septal abnormalities, and cardiac tumors

7.In patients with **cryptogenic stroke** who do not have a contraindication to anticoagulation, **long-term rhythm monitoring** with mobile cardiac outpatient telemetry, implantable loop recorder, or other approach is reasonable to detect intermittent AF

8.In patients with **cryptogenic stroke**, **tests for inherited or acquired hypercoagulable state**, bloodstream or cerebral spinal fluid **infections**, infections that can cause central nervous system **(CNS) vasculitis** (eg, HIV and syphilis), **drug use** (eg, cocaine and amphetamines), and **markers of systemic inflammation** and **genetic tests** for inherited diseases associated with stroke are reasonable to perform if clinically indicated to identify contributors for stroke

9.**In patients with ESUS, TEE, cardiac CT, or cardiac MRI** might be reasonable to identify possible cardio-aortic sources or transcardiac pathways for cerebral embolism to or relevant risk factors

10.In patients with ischemic stroke or TIA in whom **patent foramen ovale (PFO) closure would be contemplated, TCD** with embolus detection might be reasonable to screen for right-to-left shun

11. In patients suspected of having ischemic **stroke, if CT or MRI does not demonstrate symptomatic cerebral infarct, follow-up CT or MRI** of the brain is reasonable to confirm diagnosis

For posterior circulation strokes in particular, a follow-up MRI may be appropriate to confirm a diagnosis even when the initial MRI is negative

12. In patients suspected of having ischemic **TIA, if CT or MRI does not demonstrate symptomatic cerebral infarct, follow-up MRI** of the brain is reasonable to confirm diagnosis

DIAGNOSTIC EVALUATION FOR SECONDARY STROKE PREVENTION

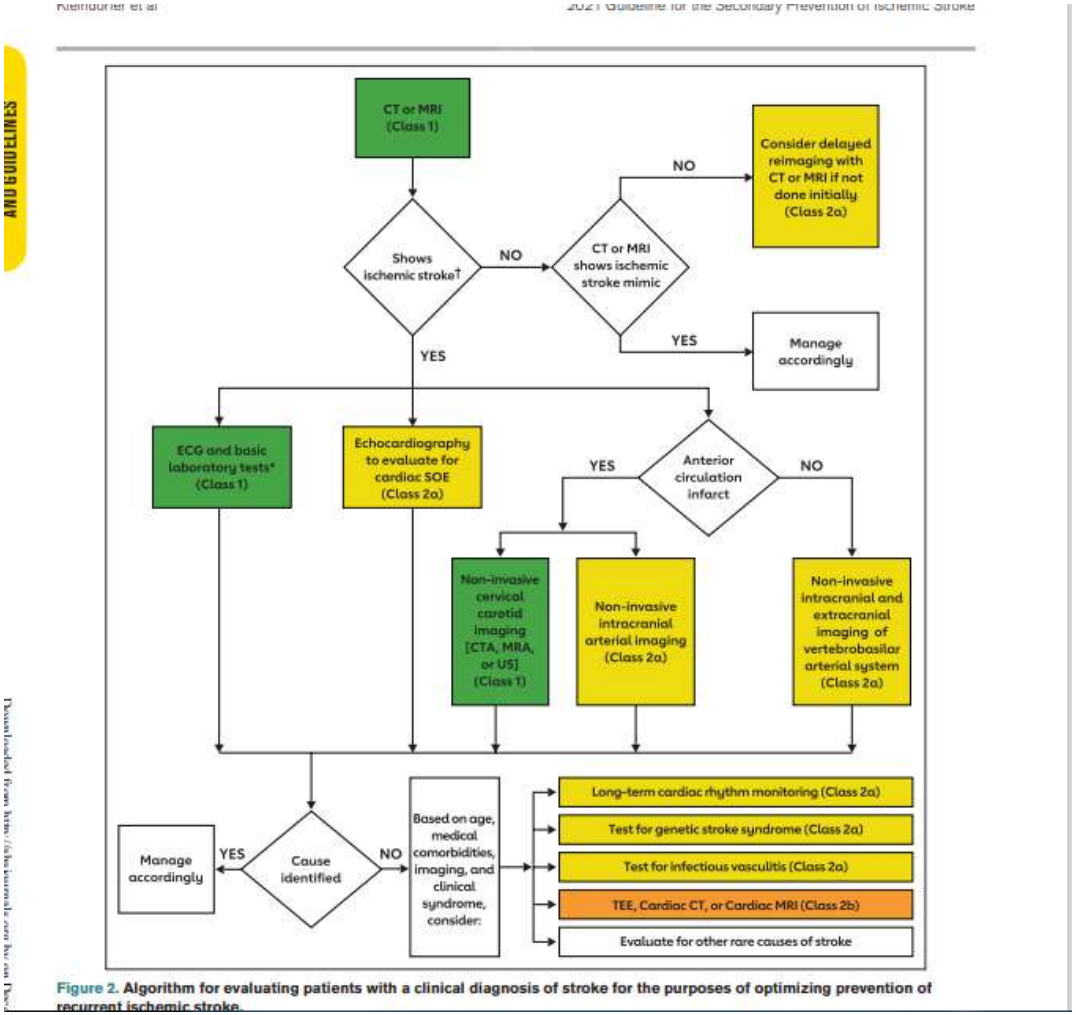


Figure 2. Algorithm for evaluating patients with a clinical diagnosis of stroke for the purposes of optimizing prevention of recurrent ischemic stroke.

Risk factor management

Hypertension

1. In patients with hypertension who experience

a stroke or TIA, treatment with a **thiazide diuretic**, **angiotensin-converting enzyme inhibitor**, or **angiotensin II receptor blockers** is useful for lowering BP and reducing recurrent

2.In patients with hypertension who experience

a stroke or TIA, an office **BP goal of <130/80** mmHg is recommended for most patients to reduce the risk of recurrent stroke and vascular events

3.Individualized drug regimens that take into account patient comorbidities, agent pharmacological class, and patient preference are recommended to maximize drug efficacy

Risk factor management

Hyperlipidemia

1. In patients with ischemic stroke with **no known coronary heart disease, no major cardiac sources of embolism, and LDL cholesterol (LDL-C) >100 mg/dL,** **atorvastatin 80 mg daily** is indicated to reduce risk of stroke recurrence

2.In patients with ischemic stroke or TIA **and atherosclerotic disease (intracranial, carotid, aortic, or coronary**), lipid-lowering therapy with **a statin and also ezetimibe**, if needed, to a **goal LDL-C of <70 mg/dL** is recommended to reduce the risk of major cardiovascular events

3.In patients with ischemic stroke who are **very high risk** (defined as stroke plus another major ASCVD or stroke plus multiple high-risk conditions), **are taking maximally tolerated statin and ezetimibe therapy and still have an LDL-C >70 mg/dL**, it is reasonable to treat with **PCSK9** (proprotein convertase subtilisin/kexin type 9) inhibitor therapy to prevent ASCVD event

4. In patients with stroke or TIA and hyperlipidemia, patients' adherence to changes in lifestyle and the effects of LDL-C–lowering medication should be assessed by measurement of fasting lipids and appropriate safety indicators 4 to 12 weeks after statin initiation or dose adjustment and every 3 to 12 months thereafter, based on need to assess adherence or safety

Risk factor management

Diabetes

1.In patients with an ischemic stroke or TIA who also have diabetes, the **goal for glycemic control should be individualized** based on the risk for adverse events, patient characteristics and preferences, and, **for most patients, especially those <65 years of age and without life-limiting comorbid illness, achieving a goal of HbA1c ≤7%** is recommended to reduce risk for microvascular complications

2.In patients with an ischemic stroke or TIA who also have diabetes, **treatment of diabetes should include glucose-lowering agents with proven cardiovascular** benefit to reduce the risk for future major adverse cardiovascular events (ie, stroke, MI, cardiovascular death)

In patients with established ASCVD, including ischemic stroke when prevention of further vascular events is the priority, GLP-1 receptor agonist therapy should be added to metformin independently of baseline HbA1c. When concern for heart failure or chronic kidney disease predominates, addition of a sodium glucose cotransporter 2 inhibitor to metformin is recommended

Management by ethiology

Intracranial Large Artery Atherosclerosis

1. In patients with a stroke or TIA caused by **50%**

to 99% stenosis of a major intracranial artery, aspirin 325 mg/d is recommended in preference to warfarin to reduce the risk of recurrent ischemic stroke and vascular death

2. In patients with **recent stroke or TIA** (within

30 days) attributable to severe stenosis

(70%–99%) of a major intracranial artery, the

addition of clopidogrel 75 mg/d to aspirin for up to 90 days is reasonable to further reduce recurrent stroke risk

In patients with **recent (within 24 hours**) minor stroke or high-risk TIA and **concomitant ipsilateral >30% stenosis** of a major intracranial artery, the addition of **ticagrelor 90 mg twice a day to aspirin for up to 30 days** might be considered to further reduce recurrent stroke risk

Management by ethiology

3.In patients with stroke or TIA attributable to

50% to 99% stenosis of a major intracranial artery, the **addition of cilostazol 200 mg/day to aspirin or clopidogrel** might be considered to reduce recurrent stroke risk

4. In patients with stroke or TIA attributable to 50% to 99% stenosis of a major intracranial artery, the usefulness of clopidogrel alone, the combination of aspirin and dipyridamole, ticagrelor alone, or cilostazol alone for secondary stroke prevention is not well established

5.In patients with a stroke or TIA attributable to

50% to 99% stenosis of a major intracranial artery, **maintenance of SBP below 140 mmHg, high-intensity statin therapy, and at least moderate physical activity** are recommended to prevent recurrent stroke and vascular events

Management by ethiology

6.In patients with **severe stenosis (70%-99%)** of a major intracranial artery and actively **progressing** symptoms or recurrent TIA or stroke

after institution of aspirin and clopidogrel

therapy, achievement of SBP <140 mmHg,

and high- intensity statin therapy (so-called

medical failures), the **usefulness of angioplasty alone or stent placement** to prevent ischemic stroke in the territory of the stenotic artery is unknown

7.In patients with stroke or TIA attributable to **severe stenosis (70%–99%)** of a major intracranial artery, **angioplasty and stenting**

should not be performed as an initial treatment, even for patients who were taking an antithrombotic agent at the time of the stroke or TIA

8. In patients with a stroke or TIA attributable to **moderate stenosis (50%–69%)** of a major intracranial artery, **angioplasty or stenting is**

associated with excess morbidity and mortality compared with medical management alone

. In patients with stroke or TIA attributable to **50% to 99% stenosis or occlusion** of a

major intracranial artery, extracranial-intracranial bypass surgery is not recommended

Management by ethiology

Extracranial Carotid Stenosis

1. In patients with a **TIA or nondisabling ischemic stroke within the past 6 months and ipsilateral severe (70%–99%) carotid artery stenosis, carotid endarterectomy (CEA)** is recommended to reduce the risk of future stroke, provided that perioperative morbidity and mortality risk is estimated to be <6%(**A**)

2.In patients with ischemic stroke or TIA and

symptomatic extracranial carotid stenosis who are scheduled for carotid artery stenting (CAS) or CEA, procedures should be

performed by operators with established periprocedural stroke and mortality rates of <6% to reduce the risk of surgical adverse

events(**A**)

3.In patients with carotid artery stenosis and a TIA or stroke**, intensive medical therapy**, with antiplatelet therapy, lipid-lowering therapy,

and treatment of hypertension, is recommended to reduce stroke risk(**A**)

Management by ethiology

4.In patients with recent TIA or ischemic stroke and

ipsilateral **moderate (50%–69%) carotid stenosis** as documented by catheter-based imaging or noninvasive imaging, **CEA** is recommended to reduce the risk of future stroke, depending on patient-specific factors such as age, sex, and comorbidities, if the perioperative morbidity and

mortality risk is estimated to be <6%(**B-R**)

5. In **patients ≥70 years** of age with stroke or TIA in whom carotid **CEA**)revascularization is being considered**, it is reasonable to select over CAS** to reduce the periprocedural stroke rate(**B-R)**

6.In patients in whom r**evascularization is planned within 1 week** of the index stroke, it is reasonable to choose CEA over CAS to

reduce the periprocedural stroke rate(**B-R**)

Management by ethiology

7.In patients with TIA or nondisabling stroke, when **revascularization** is indicated, it is reasonable to perform the procedure **within 2 weeks** of the index event rather than delay surgery to increase the likelihood of stroke free outcome(**C-LD)**

8.In patients with symptomatic severe stenosis (≥70%) in whom anatomic or medical conditions are present that increase the risk for surgery (such as radiation-induced stenosis or restenosis after CEA) it is reasonable to **choose CAS** to reduce the periprocedural complication rate **(C-LD)**

9.In symptomatic patients at average or low risk of complications associated with endovascular intervention, when the ICA stenosis is ≥70% by noninvasive imaging or >50% by catheter-based imaging and the anticipated rate of periprocedural stroke or death is <6%, **CAS** may be considered as an alternative to CEA for stroke prevention, particularly in patients with significant cardiovascular comorbidities predisposing to cardiovascular complications with endarterectomy(**A**)

Management by ethiology

10.In patients with a recent stroke or TIA (past 6 months), **the usefulness of transcarotid artery revascularization (TCAR)** for prevention of recurrent stroke and TIA is uncertain(**B-NR**)

11.In patients with **recent** TIA or ischemic stroke and when the degree of **stenosis is <50%,** revascularization with CEA or CAS to reduce the risk of future stroke is not recommended (**A)**

12. In patients with a **recent** (within 120 days) TIA or ischemic stroke ipsilateral to atherosclerotic stenosis or occlusion of the middle cerebral or carotid artery, **extracranial-intracranial bypass surgery is not recommended** (**A**)

Management by ethiology

Extracranial Vertebral Artery Stenosis

1.In patients with recently symptomatic extracranial vertebral artery stenosis, **intensive medical therapy (antiplatelet therapy, lipid lowering, BP control)** is recommended to reduce stroke risk(**A**)

2.In patients with ischemic stroke or TIA and extracranial vertebral artery stenosis who are **having symptoms despite optimal medical** , **B-the usefulness of stenting is not well established** (**R**)

3.In patients with ischemic stroke or TIA and extracranial vertebral artery stenosis who are **having symptoms despite optimal medical treatment, the usefulness of open surgical procedures**, including vertebral endarterectomy and vertebral artery transposition, **is not well established**(**CE-O)**

Management by ethiology

Aortic Arch Atherosclerosis

1.In patients with a stroke or TIA and evidence of an aortic archatheroma, **intensive lipid management to an LDL cholesterol target <70 mg/dL is recommended to prevent recurrent**

2.In patients with a stroke or TIA and evidence of an aortic arch atheroma, antiplatelet therapy is recommended to prevent recurrent stroke

Management by ethiology

Moyamoya Disease

1.In patients with moyamoya disease and a history of ischemic stroke or TIA, **surgical revascularization** with direct or indirect extracranial-intracranial bypass can be beneficial for the prevention of ischemic stroke

or TIA(**C-LD**)

2.In patients with moyamoya disease and a history of ischemic stroke or TIA, the use of **antiplatelet**

therapy, typically aspirin monotherapy for the prevention of ischemic stroke or TIA may be reasonable**(C-LD**)

Ischemic Stroke Caused by Small Vessel Disease

In patients with ischemic stroke related

to small vessel disease, the usefulness of **cilostazol** for secondary stroke prevention is uncertain

Management by ethiology

Cardio embolism

In patients with nonvalvular AF and stroke or

TIA,

1.oral anticoagulation (eg, apixaban, dabigatran, edoxaban, rivaroxaban, or warfarin) is recommended to reduce the risk of recurrent Stroke(**A**)

2.Oral anticoagulation is indicated to reduce the risk of recurrent stroke regardless of whether the AF pattern is paroxysmal, persistent, or permanent

3.In patients with stroke or TIA and AF who do not have moderate to severe mitral stenosis or a mechanical heart valve, **apixaban, dabigatran, edoxaban, or rivaroxaban is recommended in preference to warfarin** to reduce the risk of recurrent stroke

Management by ethiology

4.In patients with **atrial flutter** and stroke or TIA, anticoagulant therapy similar to that in AF is indicated to reduce the risk of recurrent Stroke(**B-NR**)

5.In patients with AF and stroke or TIA, without moderate to severe mitral stenosis or a mechanical heart valve, who are unable to maintain a therapeutic INR level with warfarin, use of dabigatran, rivaroxaban, apixaban or edoxaban is recommended to reduce the risk of recurrent Stroke(**C-EO**)

6.In patients with stroke at high risk of hemorrhagic conversion in the setting of AF, it is reasonable **to delay initiation of oral anticoagulation beyond 14 days** to reduce the risk of ICH(**B-NR**)

Management by ethiology

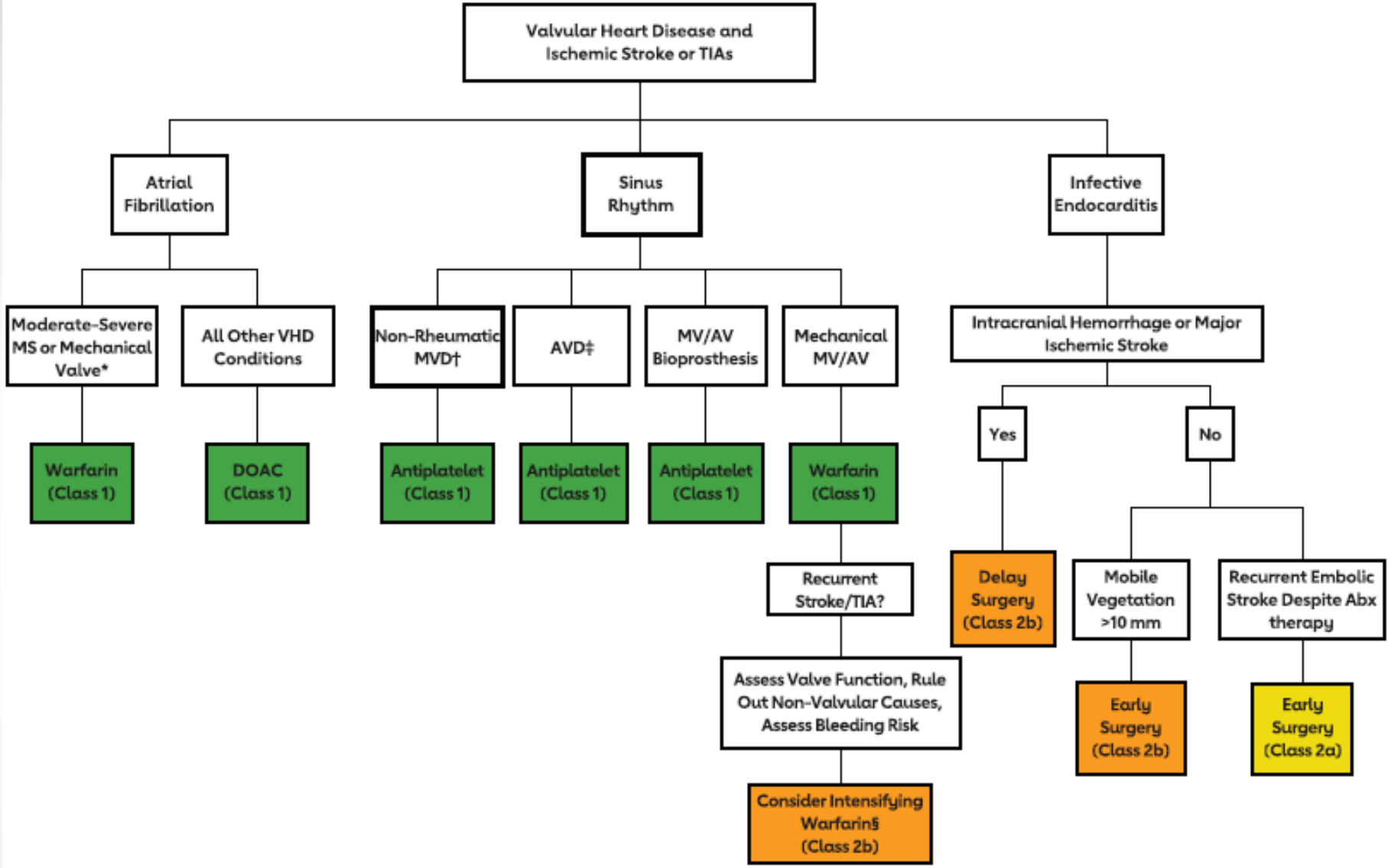
7.In patients with TIA in the setting of nonvalvular AF, It is reasonable to **initiate anticoagulation immediately after the index event** to reduce the risk of recurrent stroke(**C-EO**)

8. In patients with TIA in the setting of non-valvular AF who have contraindications for lifelong anticoagulation but can tolerate at least 45 days, it may be reasonable to **consider percutaneous closure of the left atrial appendage with the Watchman device** to reduce the chance of recurrent stroke and bleeding (**B-R**)

Management by ethiology

9.In patients with stroke at low risk for hemorrhagic conversion in the setting of AF, it may be reasonable to **initiate anticoagulation 2 to 14 days after the index event** to reduce the risk of recurrent stroke(**B-NR**)

10.In patients with AF and stroke or TIA who have end-stage renal disease or are on dialysis, it may be reasonable to use **warfarin or apixaban (dose adjusted if indicated**) for anticoagulation to reduce the chance of recurrent stroke (**B-NR**)



igure 3. Recommended antithrombotic regimen in patients with history of ischemic stroke or transient ischemic attack (TIA) nd different valvular heart disease conditions.

olors correspond to Class of Recommendation in Table 3. Abx indicates antibiotics; AF, atrial fibrillation; AV, aortic valve; AVD, aortic valve sease; DOAC, direct oral anticoagulant; MAC, mitral annular calcification; MS, mitral stenosis; MV, mitral valve; MVD, mitral valve disease; MVP, itral valve prolapse; and VHD, valvular heart disease. *Definition of valvular AF. †Includes MAC and MVP. ‡Rheumatic and nonrheumatic AVD. ncrease the target international normalized ratio by 0.5, depending on bleeding risk.

Management by ethiology

Valvular Disease

1.In patients with ischemic stroke or TIA and valvular AF (moderate to severe mitral stenosis or any mechanical heart valve), **warfarin** is recommended to reduce the risk of recurrent stroke or TIA (**B-R**)

2.In patients with a mechanical mitral valve and a history of ischemic stroke or TIA before valve replacement, **aspirin (75–100 mg/d) is recommended in addition to warfarin with an INR target of 3.0 (range, 2.5–3.5**) to reduce the risk of thrombosis and recurrent stroke or TIA (**C-LD**)

3.In patients with ischemic stroke or TIA and mechanical heart valves, **treatment with dabigatran causes harm(B-R)**

Management by ethiology

4.In patients with ischemic stroke or TIA and native aortic or nonrheumatic mitral valve disease (eg, mitral annular calcification or mitral valve prolapse) who do not have AF or another indication for anticoagulation, **antiplatelet therapy** is recommended to reduce the risk of recurrent stroke or TIA(**C-EO**)

5.In patients with a bioprosthetic aortic or mitral valve, a history of ischemic stroke or TIA before valve replacement and no other indication for anticoagulation therapy **beyond 3 to 6 months from the valve placement, long-term therapy with aspirin is recommended in preference to long-term anticoagulation** to reduce the risk of recurrent stroke or TIA(**C-EO**)

Management by ethiology

6.In patients with history of ischemic stroke or TIA and a mechanical aortic valve, anticoagulation with higher-intensity warfarin to achieve an INR of 3.0 (range, 2.5–3.5) or the addition of aspirin (75–100 mg/d) can be beneficial to reduce the risk of thromboembolic events(**C-EO**)

7.In patients with ischemic stroke or TIA and IE who present with recurrent emboli and persistent vegetations despite appropriate antibiotic therapy, early surgery (during initial hospitalization before completion of a full therapeutic course of antibiotics) is reasonable to reduce the risk of recurrent embolism if there is no evidence of intracranial hemorrhage or extensive neurological damage(**B-NR**)

Management by ethiology

8.In patients with ischemic stroke or TIA and native left-sided valve endocarditis who exhibit mobile vegetations >10 mm in length, **early surgery** (during initial hospitalization before completion of a full therapeutic course of antibiotics) may be considered to reduce the risk of recurrent embolism if there is no evidence of intracranial hemorrhage or extensive neurological damage(**B-NR**)

9.In patients with ischemic stroke or TIA and IE, **early valve surgery** (during initial hospitalization before completion of a full therapeutic course of antibiotics) may be considered in patients with an indication for surgery who have no evidence of intracranial hemorrhage or extensive neurological damage (**B-NR**)

Management by ethiology

10.In patients with IE and major ischemic stroke, **delaying valve surgery for at least 4 weeks** may be considered for patients with IE and major ischemic stroke or intracranial hemorrhage if the patient is hemodynamically stable

Management by ethiology

LV thrombus

1.In patients with stroke or TIA and LV thrombus, **anticoagulation with therapeutic warfarin for at least 3 months** is recommended to reduce the risk of recurrent stroke(**B-NR**)

2.In patients with stroke or TIA in the setting of acute MI, it is reasonable to **perform advanced cardiac imaging** (eg, contrasted echocardiogram or cardiac MRI) to assess for the presence of LV thrombus(**C-EO**)

Management by ethiology

3.In patients with stroke or TIA and new LV thrombus (<3 months), the **safety of anticoagulation with a direct oral anticoagulant** to reduce risk of recurrent stroke is uncertain(**C-LD**)

4.In patients with stroke or TIA in the setting of acute anterior MI with reduced ejection fraction (EF; <50%) but no evidence of LV thrombus, **empirical anticoagulation for at least 3 months** might be considered to reduce the risk of recurrent cardio-embolic stroke(**C-EO**)

Management by ethiology

Cardiomyopathy

1.In patients with ischemic stroke or TIA and left atrial or left atrial appendage thrombus in the setting of ischemic, nonischemic, or restrictive cardiomyopathy and LV dysfunction, **anticoagulant therapy with warfarin** is recommended for at **least 3 months** to reduce the risk of recurrent stroke or TIA (**C-EO**)

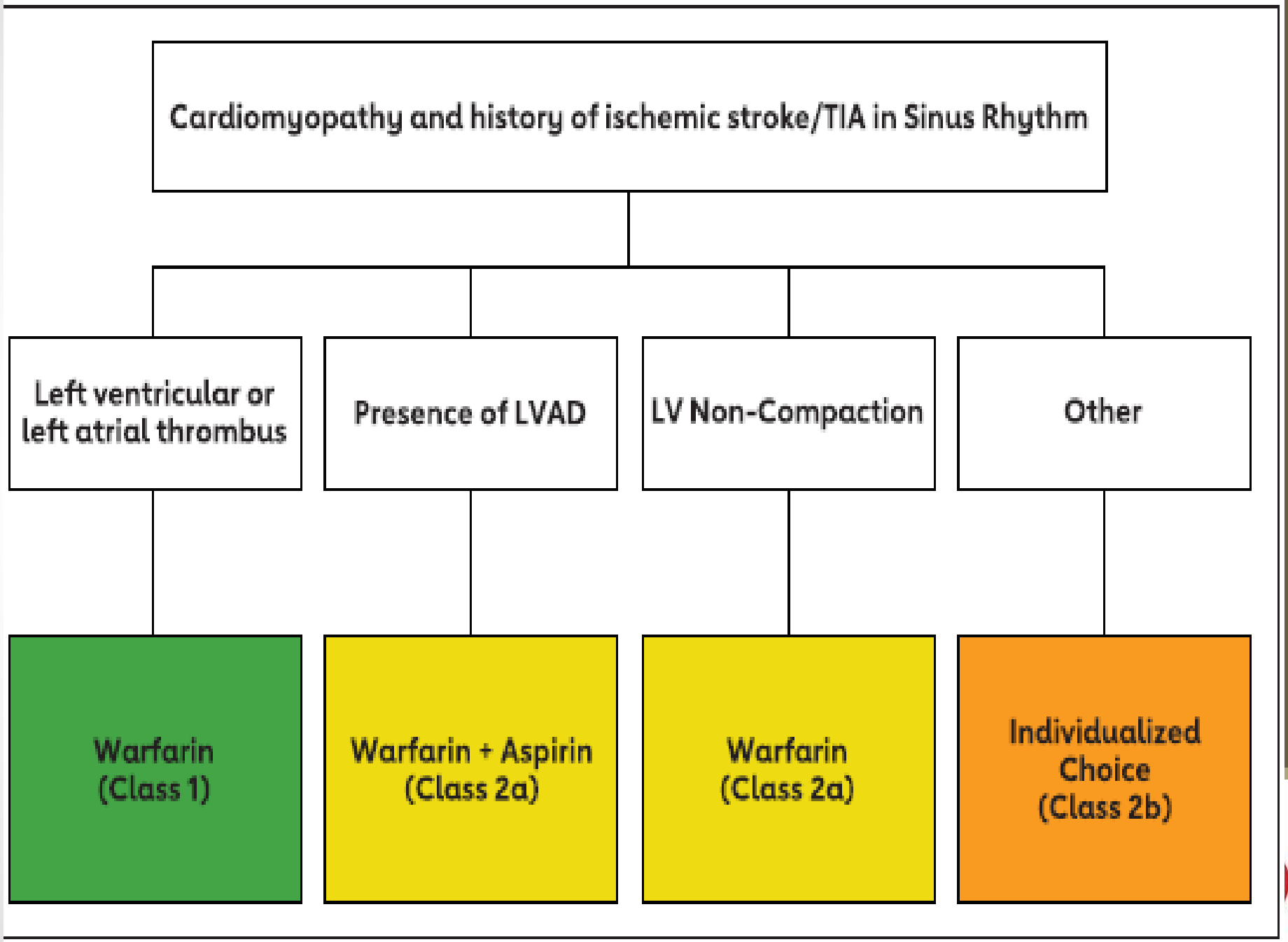
2.In patients with ischemic stroke or TIA in the setting of a mechanical assist device, **treatment with warfarin and aspirin** can be beneficial to reduce the risk of recurrent stroke or TIA (**C-LD**)

Management by ethiology

3.In patients with ischemic stroke or TIA in the setting of LV noncompaction, **treatment with warfarin** can be beneficial to reduce the risk of recurrent stroke or TIA (**C-EO**)

4.In patients with ischemic stroke or TIA in sinus rhythm with ischemic or nonischemic cardiomyopathy and reduced EF without evidence of left atrial or LV thrombus, **the effectiveness of anticoagulation compared with antiplatelet therapy is uncertain** and the choice should be individualizedV(**B-R**)

5.In patients with stroke or TIA and LV assist devices (LVADs), **treatment with dabigatran instead of warfarin for the primary or secondary prevention of ischemic stroke or TIA causes harm (B-R)**


Cardiomyopathy and history of ischemic stroke/TIA in Sinus Rhythm
Left ventricular or left atrial thrombus
Presence of LVAD
LV Non-Compaction
Other
Warfarin (Class 1)
Warfarin + Aspirin (Class 2a)
Warfarin (Class 2a)
Individualized Choice (Class 2b)

Management by ethiology

Patent Foramen Ovale (PFO)

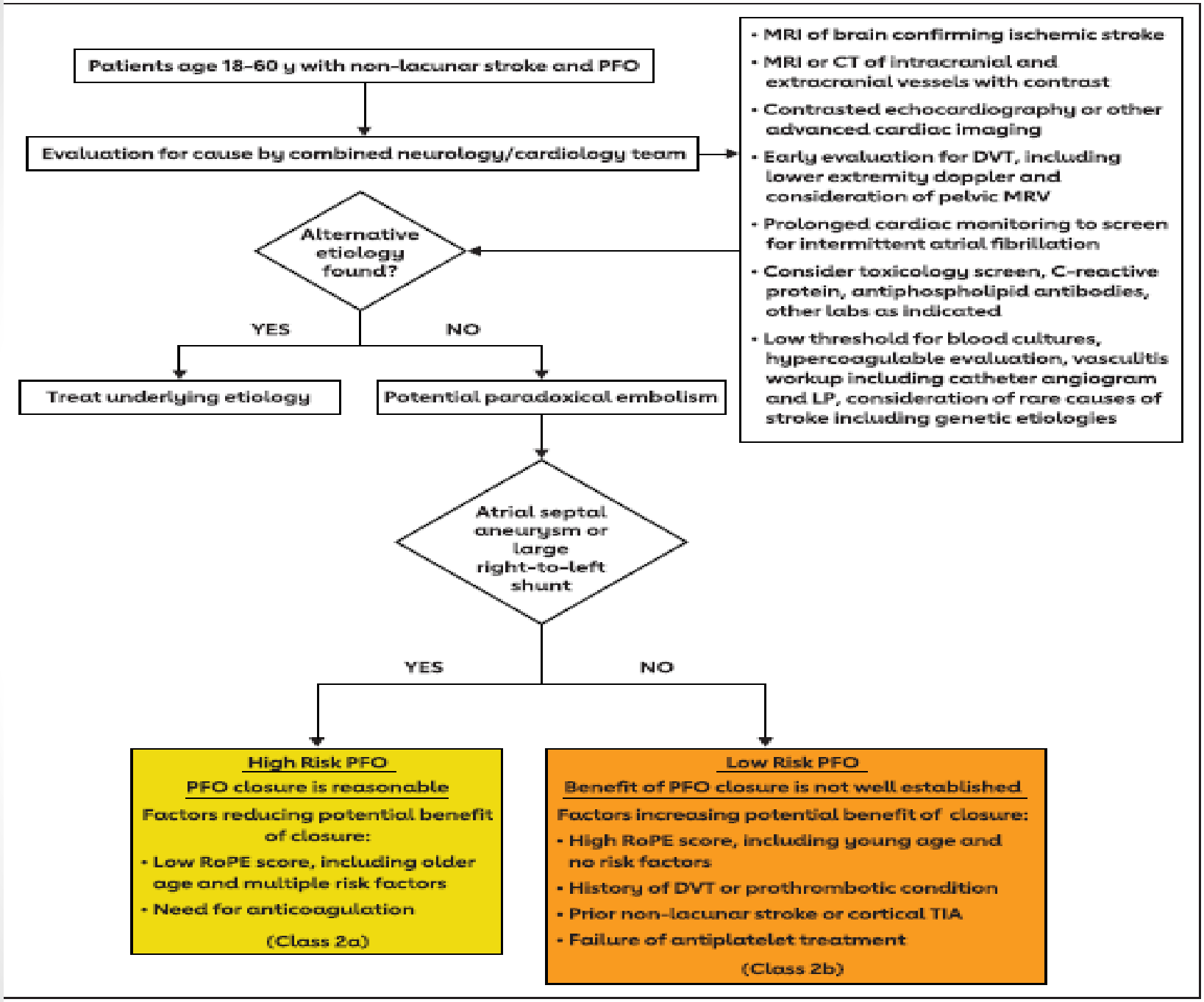
1. In patients with a nonlacunar ischemic stroke of undetermined cause and a PFO, recommendations for PFO closure versus medical management should be made jointly by the patient, a cardiologist, and a neurologist, taking into account the probability of a causal role for the PFO(**C-EO**)

2.In patients 18 to 60 years of age with a nonlacunar ischemic stroke of undetermined cause despite a thorough evaluation and a PFO with high-risk anatomic features, it is reasonable to choose **closure with a transcatheter device and long-term antiplatelet therapy over antiplatelet therapy alone** for preventing recurrent stroke(**B-R**)

Management by ethiology

3.In patients 18 to 60 years of age with a nonlacunar ischemic stroke of undetermined cause despite a thorough evaluation and a PFO without high-risk anatomic features,* the benefit of closure with a transcatheter device and long-term antiplatelet therapy over antiplatelet therapy alone for preventing recurrent stroke is not well established(**C-LD**)

4.In patients 18 to 60 years of age with a nonlacunar ischemic stroke of undetermined cause despite a thorough evaluation and a PFO, the comparative benefit of closure with a transcatheter device versus warfarin is unknown(**C-LD**)



5. Patent foramen ovale (PFO) and ischemic stroke management guide.

TAKE-HOME MESSAGES FOR THE SECONDARY STROKE PREVENTION

1.Specific recommendations for prevention strategies

often depend on the ischemic stroke/TIA subtype

2.Management of vascular risk factors remains

extremely important in secondary stroke prevention,

including (but not limited to) diabetes, smoking cessation, lipids, and especially hypertension

3.Lifestyle factors, including healthy diet and physical

activity, are important for preventing a second

stroke. Low-salt and Mediterranean diets are recommended for stroke risk reduction

TAKE-HOME MESSAGES FOR THE SECONDARY STROKE PREVENTION

4.Antithrombotic therapy, including antiplatelet or anticoagulant agents, is recommended for nearly all patients without contraindications

5.With very few exceptions, the combination of antiplatelets and anticoagulation is typically not indicated for secondary stroke prevention

6.Dual antiplatelet therapy is not recommended long term, and short term, it is recommended only in very specific patients, including those with early arriving minor stroke and high-risk TIA or severe symptomatic intracranial stenosis

7.Atrial fibrillation remains a common and high risk condition for second ischemic stroke. Anticoagulation is usually recommended if the patient has no contraindications. Heart rhythm monitoring for occult atrial fibrillation is usually recommended if no other cause of stroke is discovered

TAKE-HOME MESSAGES FOR THE SECONDARY STROKE PREVENTION

8.Extracranial carotid artery disease is an important and treatable cause of stroke. Patients with severe stenosis ipsilateral to a nondisabling stroke or TIA who are candidates for intervention should have the stenosis fixed, likely relatively early after their ischemic stroke

The choice between carotid endarterectomy and carotid artery stenting should be driven by specific patient comorbidities and features of their vascular anatomy

9.Patients with **severe intracranial stenosis** in the vascular territory of ischemic stroke or TIA should not receive angioplasty and stenting as a first-line therapy for preventing recurrence

Aggressive medical management of risk factors and short-term dual antiplatelet therapy are preferred

TAKE-HOME MESSAGES FOR THE SECONDARY STROKE PREVENTION

10. It is now considered reasonable **to percutaneously close PFO** in patients who meet each of the following criteria: age 18–60 years, nonlacunar stroke, no other identified cause, and high risk patent foramen ovale features

11. Patients with **embolic stroke of uncertain source** should not be treated empirically with anticoagulants or ticagrelor because it was found to be of no benefit

Time Is Brain In Stroke