6 Cardiac Evaluation and Management After Ischemic Cerebral Stroke

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Large proportion of ischemic stroke is attributable to cardioembolic source. Cardiovascular diseases such as atherosclerotic coronary artery disease, atrial fibrillation, valvular heart disease, or heart failure are closely related to increased risk of ischemic strokes. Furthermore, recent investigations are revealing that substantial portion of cryptogenic strokes arises from cardioembolic source. These cardioembolic strokes often recur early and repeatedly in a long lifetime, even after all the efforts preventing recurrent stroke. Thus, prevention and management after cardioembolic stroke are particularly important issues in practical fields. Evidence-based strategies have been established in prevention and management of some spectrum of cardioembolism, such as atrial fibrillation. Meanwhile, there is little, we know, in some other cardioembolic sources in terms of pathophysiology and prevention of strokes. We focus on currently available methods and practical evaluations to identify cardioembolic stroke and stroke preventions related to diverse cardiac conditions such as atrial fibrillations, valvular heart disease, myocardial infarctions, heart failure, and intracardiac and extracardiac shunt in this chapter.

6.1 Background

Embolism of cardiac origin accounts for 15–30 % of ischemic strokes [1–3]. Cardioembolic stroke has higher in-hospital morality and more frequent fatal recurrence than other causes of stroke [4–6]. Identification of embolic source is often challenging in some patients. However, discovering cardioembolic source is an important issue in stroke patients when deciding treatment and prevention strategy. Patients with atrial fibrillation, heart failure, valvular heart disease, prosthetic heart valve, and symptom and sign of endocarditis are obviously candidates for the cardiac evaluation. In patients with multiple ischemic lesion or concomitant systemic emboli, cardioembolism should be strongly considered, either. Table 6.1 is demonstrating potential cardioembolic sources of ischemic stroke. This chapter will discuss about cardiac evaluation and management after acute ischemic stroke.

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Table 6.1 Common cardioembolic sources in ischemic stroke

Major source	Minor source
Atrial fibrillation	Patent foramen ovale
Rheumatic valve disease (mitral stenosis)	Atrial septal defect
Prosthetic valve	Ventricular septal defect
Infective endocarditis	Calcified aortic stenosis
Marantic endocarditis	Mitral annular calcification
Atrial myxoma	Fibroelastoma
Acute myocardial infarction	Lambl's excrescence
Heart failure	Mitral valve prolapse

6.2 Cardiac Evaluation

6.2.1 Electrocardiogram (ECG)

Standard 12-lead ECG is mandatory in all patients with acute stroke. ECG abnormalities are observed in 60–90 % of the patients with acute stroke [7, 8]. Not only heart rhythm disorder like atrial fibrillation (AF) but also diverse ECG changes following acute stroke can be detected on ECG. Myocardial ischemia-like ECG changes, such as ST-segment deviation, T wave abnormalities, and QTc prolongations are most frequent secondary ECG changes after acute stroke, which can mimic acute myocardial ischemia.

AF detection rate in acute stroke patients varies from 7 to 25 % [9–11]. Absence of AF in standard ECG test cannot exclude AF as a cause of the stroke event. Dedicated effort to detect paroxysmal AF possibly affect the AF detection rate. One study demonstrated that serial ECG follow-up during 72 h from stroke event can increase the chance of AF detection by 2.6-fold [12]. Continuous cardiac monitoring for at least 24 h is reasonable to detect AF and other serious arrhythmias [13, 14].

Arrhythmias other than AF also can be associated with acute phase of stroke. Serious arrhythmias, such as ventricular tachycardia, supraventricular tachycardia, various degrees of atrioventricular block, as well as AF, can be seen in approximately 25 % of the patients with acute stroke in first 3 days [15]. Arrhythmic events are especially frequent in the first 24 h and decline with time.

6.2.2 Holter Monitor

There is no strong recommendation of patient selection, time, and duration of Holter monitoring in patients with acute stroke. Detection rate of paroxysmal AF on 24-h Holter monitoring after ischemic stroke is between 2 and 7 % [16–18]. Some limited studies expressed a doubt about the efficacy of routine Holter monitoring to detect AF and other serious arrhythmias after acute stroke, because of the low detect rate and poor cost-effectiveness [16, 17, 19]. However, such findings might result from unselected patients, varying time and duration of monitoring. The Holter monitor can be especially effective in detecting cardiac rhythm disorder in patients with embolic infarction pattern, old age, and concomitant coronary artery disease [20]. Stroke patients with large deficits or right hemispheric stoke are at risk of various cardiac pathologic conditions, such as AF, myocardial ischemia, congestive heart failure, and other serious cardiac arrhythmias, and may need close cardiac monitoring and Holter monitoring [21]. One study suggested that routine Holter monitoring for over 24 h can identify new AF/atrial flutter in 1 out of 20 patients [18].

6.2.3 Event Recorder

The longer duration of ECG monitor definitely increases the detection rate of AF and other cardiac arrhythmia. Table 6.2 demonstrated monitoring type and detection of paroxysmal AF [22]. Seven days of ECG monitoring using external event recorder revealed 16–25 % patients with paroxysmal AF among the patients who did not show AF in 24-h Holter monitoring [23, 24]. More prolonged monitoring may be considered up to a year or more using implantable loop recorder in patients with cryptogenic stroke or highly suspected heart rhythm disorder like AF. One study including patients with cryptogenic stroke revealed that

Table 6.2 Type of monitoring and detection of paroxysmal atrial fibrillation (AF)

Type of monitoring	Invasiveness	Duration	Rate of AF detection (%)
Admission ECG	Noninvasive	N/A	2.7
Inpatient continuous telemetry	Noninvasive	3–5 days	5.5–7.6
Holter monitoring	Noninvasive	24 h	3.2–4.8
		48 h	6.4
		7 days	12.5
Mobile continuous outpatient telemetry	Noninvasive	21–30 days	16–25
Implantable loop recorders	Invasive	6 months	9
		36 months	30

Adapted from Yaghi et al. [22]

16 % of the patients had an event of paroxysmal AF using an implantable loop recorder during over a year of follow-up [25].

6.2.4 Transthoracic Echocardiography (TTE)

Echocardiography can provide information about functional and structural abnormalities inside and even outside of the heart. We should focus on the size and functions of left atrium (LA) and left atrial appendage (LAA), right ventricular and left ventricular (LV) function and regional wall motion abnormality, valvular disease, prosthetic valve, intracardiac shunt, and atheromatous embolic sources of aorta. All ischemic stroke patients with embolic character or without other clear etiology may need to undergo TTE. Although, some data suggested that transesophageal echocardiography (TEE) presented higher diagnostic yields in detecting embolic source compared to TTE [26, 27], TTE still has strong clinical advantages, which is noninvasive test, relatively lower price, and easier to perform and repeat. Furthermore, TTE is often better to evaluate native or prosthetic valve function and usually better for the detection of LV thrombus compared to TEE.

TTE is presenting very high sensitivity and specificity for detecting LV thrombus (Fig. 6.1) [28]. It is also an essential part to identify the presence of regional or global wall motion abnormality of left ventricle related to LV thrombus. However, in some patients who have poor echocardiographic window or spontaneous echocontrast around the suspected area, it is quite challenging to define thrombus. Contrast echocardiography technique can help to visualize thrombus in such cases. Computed tomography and cardiac magnetic resonance imaging can be options otherwise.

In patients with AF, most common site of the thrombus formation is LAA. TTE has limitations on visualizing LAA thrombus in patients with AF compared with TEE. LAA emptying velocity, which can be measured by LAA contraction using TEE by pulsed Doppler, is a parameter of the LAA dysfunction, and low velocity (≤20 cm/s) is related to risk of thrombus formation [29]. Some data showed that new technique of second harmonic imaging allows TTE to evaluate LAA function with better sensitivity [30, 31].

One of the most serious conditions causing embolic event is infective endocarditis (IE). Clinically, diagnosis of IE is made on basis of clinical, echocardiographic, and biological findings. Modified Duke criteria have been widely used in diagnosis of IE (Table 6.3) [32]. Vegetation, abscess, valvular regurgitations, and prosthetic valve dehiscence are frequently observed in IE (Fig. 6.2). Echocardiographic findings play a key role in diagnosis of IE. In patients with IE, embolic risk can be estimated by echocardiographic findings, such as size and mobility of the vegetation. Vegetation size in response to antibiotic therapy is also associated with risk of embolic event [33–36]. Vegetation size >10 mm tends to be highly embolic [37].

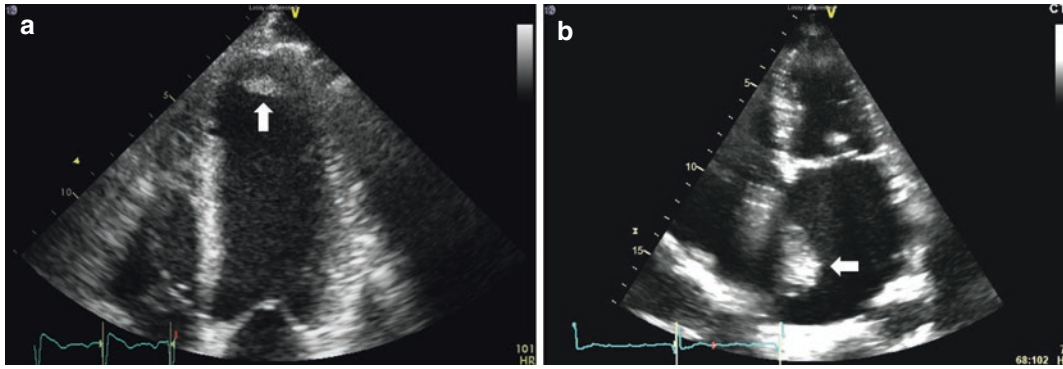

Fig. 6.1 (**a**) Patients with acute myocardial infarction and mural thrombus at left ventricular apex, (**b**) left atrial thrombus attached to interatrial septum in patients with rheumatic mitral valve disease and severe left atrial dilatation

Table 6.3 Modified Duke criteria of infective endocarditis (IE)

Major criteria	
Blood cultures positive for IE:	
Typical microorganisms consistent with IE from two separate blood cultures:	
Viridans streptococci, *Streptococcus bovis*, HACEK group, *Staphylococcus aureus*, or community-acquired enterococci, in the absence of primary focus	
or	
Microorganisms consistent with IE from persistently positive blood cultures:	
At least two positive blood cultures if blood sample drawn > 12 h apart or all of three or a majority of ≥ 4 separate cultures of blood (with first and last sample drawn at least 1 h apart)	
or	
Single positive blood culture for *Coxiella burnetii* or phase I IgG antibody titer > 1:800	
Evidence of endocardial involvement	
Echocardiography positive for IE	
Vegetation – abscess – new partial dehiscence of prosthetic valve	
New valvular regurgitation	
Minor criteria	
Predisposition: predisposing heart condition, infection drug use	
Fever: temperature > 38 °C	
Vascular phenomena: major arterial emboli, septic pulmonary infarcts, mycotic aneurysm, intracranial hemorrhages, conjunctival hemorrhage, Janeway lesions	
Immunologic phenomena: glomerulonephritis, Osler's nodes, Roth's spots, rheumatoid factor	
Microbiological evidence: positive blood culture but does not meet a major criterion or serological evidence of active infection with organism consistent with IE	
Definite IE	**Possible IE**
2 major criteria	1 major and 1 minor criteria
1 major and 3 minor criteria	3 minor criteria
5 minor criteria	

Adapted from Li et al. [32]
※HACEK: *Haemophilus*, *Aggregatibacter* (previously *Actinobacillus*), *Cardiobacterium*, *Eikenella*, *Kingella*

Paradoxical embolism is originated from venous side and cross to the systemic circulation through a shunt. Intracardiac shunt could be detected by echocardiography. TTE usually detect secundum- or primum-type atrial septal defect (ASD). Chamber size and pulmonary artery pressure also should be evaluated for further management. TEE is often needed in case of

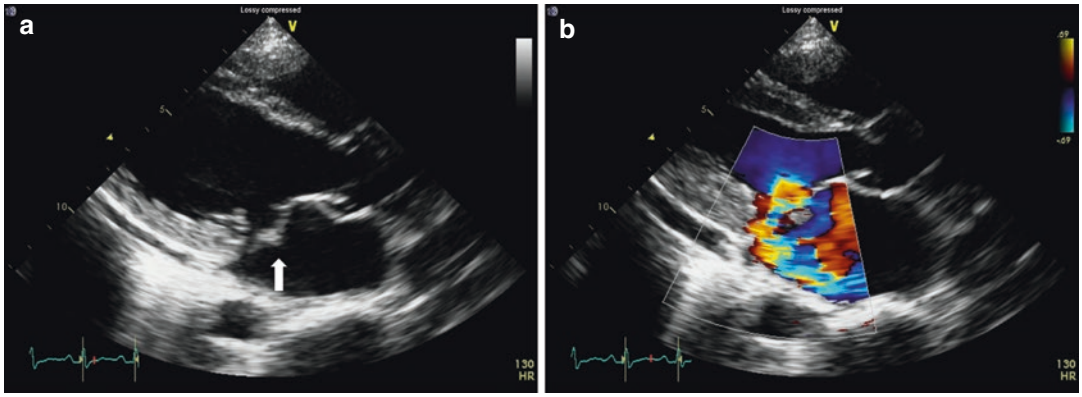

Fig. 6.2 Apical two-chamber view revealing mitral leaflet prolapse (**a**, *white arrow*) and severe mitral regurgitation (**b**) in patient with infective endocarditis

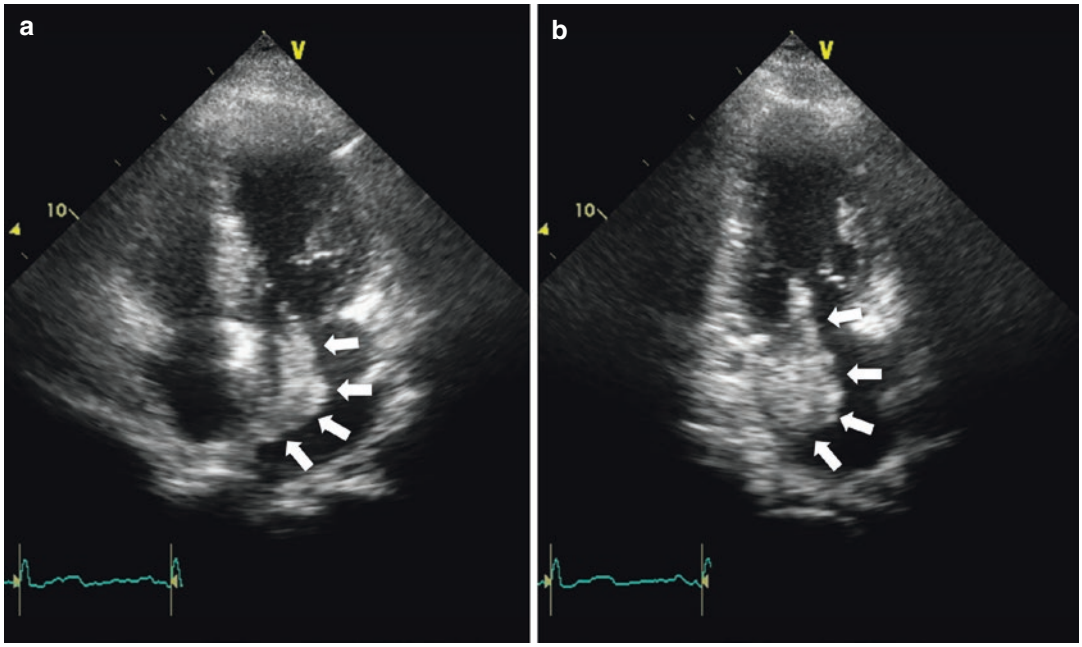

Fig. 6.3 Apical two chamber (**a**) and two-chamber view (**b**) of cardiac myxoma (*white arrows*) in the left atrium, which caused ischemic stroke and systemic embolism in a 40-year-old male

sinus venosus defect. Patent foramen ovale (PFO) also can cause paradoxical embolisms. Traditionally, TEE with Valsalva maneuver after agitated saline injection is the gold standard test for detecting PFO. However, with recent advance in techniques, TTE may be sufficient for the agitated saline test by using second harmonic imaging [38, 39].

Cardiac tumor frequently causes embolic event [40]. TTE provides not only anatomical information but also functional significance in those cardiac tumors. Cardiac myxoma is the most common primary tumor in the heart. Approximately 90% of cardiac myxoma occurred in LA [41], which can be highly associated with cardioembolic stroke (Fig. 6.3). Most common valve-associated tumor, fibroelastoma, is also related to embolic risk [42, 43]. Differential diagnosis between fibroelastoma and Lambl's excrescences or infective endocarditis is often challenging.

6.2.5 Transesophageal Echocardiography (TEE)

Although TEE is an invasive, more expensive procedure which needs experienced physician, complication rate is less than 0.02 % [44], and diagnostic sensitivity can be superior than that of TTE especially for detection of thromboembolic source [26]. TEE can provide better spatial resolution of intracardiac structure even in patients with poor transthoracic window. Because TTE and TEE have their own pros and cons, respectively, the physician should make proper decision based on clinical circumstances as well as the cost-effectiveness.

TEE can sensitively detect LAA thrombus directly and highly thrombogenic conditions like spontaneous echocontrast in patients with AF. Doppler measurement in LAA is also a useful tool for evaluating thrombogenic risk in atrial fibrillation. LAA is not an immobile structure but is believed to have contraction and dynamic flow changes inside of it. LAA contraction forced blood out, and LAA emptying velocity is considered as a parameter of LAA function. The velocity below 20 cm/s is associated with risk of thrombus formation in LAA [45]. LAA emptying velocity also can be a parameter for successful cardioversion in patients with AF.

Regarding paradoxical embolism, sinus venosus-type or coronary sinus-type ASDs are often difficult to be found in TTE. TEE provides higher resolution around the inferior and superior vena cava area and even in the coronary sinus area. TEE also is a gold standard for PFO diagnosis. In differential diagnosis between PFO and pulmonary arteriovenous malformation as a source of paradoxical emboli, TEE test can be more accurate.

Presence of prosthetic valve is a highly thrombogenic condition. Although TTE has an important role in evaluating prosthetic valve function, TEE is required in many cases. In circumstances when prosthetic valve malfunction is present, differential diagnosis between pannus formation and thrombus formation is a crucial part in therapeutic strategy. High-resolution TEE image can provide important additional information in differential diagnosis [46].

Approximately 60 % of the patients 60 years or older who had stroke have aortic arch atherosclerosis (Fig. 6.4) [47]. Complex atheroma with ulceration and high mobility is closely related to the embolic stroke. TTE can approach aortic arch in suprasternal window, but imaging quality and information are often limited. TEE provides high-resolution images of ascending, descending aorta, and aortic arch. Thickness of atheroma and ulceration and presence of highly mobile portions can be assessed to estimate the embolic risk [45].

6.3 Management and Prevention of Cardioembolic Stroke

6.3.1 Atrial Fibrillation (AF)

Dilatation and contractile dysfunction of the left atrium (LA) and left atrial appendage (LAA) in AF are significantly associated with blood stasis and thrombus formation. Ischemic stroke patient with AF can present worse short-term and long-term survival than those without, as well as higher recurrence rate of stroke [9]. There is a large body of evidence that anticoagulation is recommended in patients with AF according to their risk factors. Risk stratification using CHA2DS2-VASc score has been widely used to determine anticoagulation (Tables 6.4 and 6.5) [48]. Many studies showed that benefit of anticoagulation overweighs the risk in patients with AF and elevated risk of embolization. Thus, all patients with stroke/TIA who have AF got at least 2 points and should be anticoagulated unless there is contraindication for anticoagulation.

Traditionally, anticoagulation using vitamin K antagonist, warfarin, had been widely used in stroke prevention of AF patients. Recently, new anticoagulation agent blocking a specific target of coagulation cascade became popular, as an alternative to warfarin. Dabigatran, rivaroxaban, apixaban, and edoxaban are non-vitamin K antagonist oral anticoagulant, abbreviated as NOAC. NOACs demonstrated non-inferior efficacy in prevention of ischemic stroke compared to warfarin and secured their safety profiles in patient with non-valvular AF

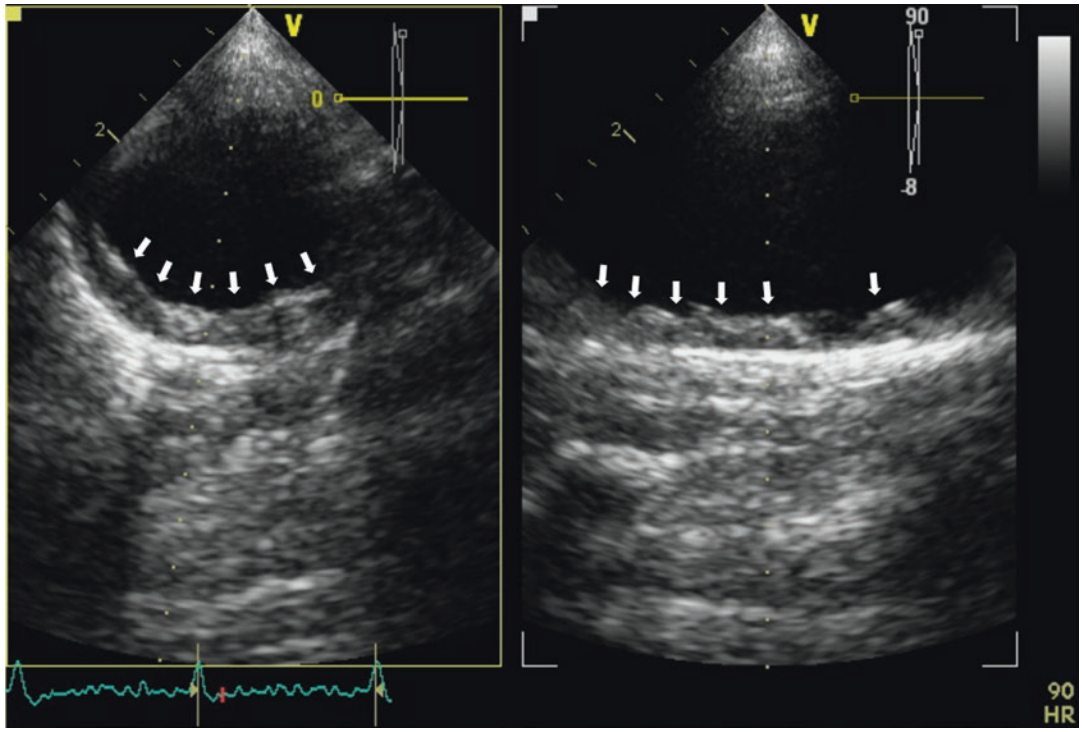

Fig. 6.4 Diffuse atherosclerotic plaque of approximately 10 mm thickness (white arrows) in aortic arch of 60-year-old male who presented with acute ischemic stroke

Table 6.4 CHA2DS2-VASc score

CHA2DS2-VASc acronym	Score
Congestive heart failure	1
Hypertension	1
Age ≥ 75 years	2
Diabetes mellitus	1
Stroke/TIA/TE	2
Vascular disease (prior MI, pad, or aortic plaque)	1
Age 65–74 years	1
Sex category (female sex)	1
Maximum score	9

Adapted from Friberg et al. [48]
TIA transient ischemic attack, *TE* thromboembolic event, *MI* myocardial infarction, *PAD* peripheral artery disease

Table 6.5 Stroke risk with CHA2DS2-VASc score

Score	Unadjusted ischemic stroke rate (%)
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
9	12.2

Adapted from Friberg et al. [48]

[49–52]. Because NOACs have their own pharmacokinetics, different renal excretion, side effect, and drug interaction, selection of the agent should be based on patients' condition, risk factors, economic status, tolerability, and preference.

For patients who are not indicated for or cannot tolerate anticoagulation, antiplatelet treatment may be considered. Options can be aspirin monotherapy or dual antiplatelet therapy in combination with clopidogrel. However, evidences are not supporting the efficacy of aspirin preventing stroke in patients with AF [53]. Dual antiplatelet therapy in combination of aspirin and clopidogrel may be superior to aspirin monotherapy

in preventing stroke but at the cost of increased bleeding [49].

6.3.2 Left Ventricular Thrombus

Incidence of LV thrombus within 3 months after acute myocardial infarction (MI) vary from 3 to 16 % [54–57]. Recently, more aggressive antiplatelet therapy in acute stage may reduce the incidence of thrombus formation after MI. More than 10 % of the patients with LV thrombus are at risk of embolic event unless they are treated with anticoagulation [58, 59]. Available data is supporting the use of warfarin to reduce embolic risk at the presence of LV thrombus after MI. One meta-analysis data demonstrated 86 % reduction of embolic risk with warfarin in patients with LV thrombus after anterior MI [59]. It is reasonable to start unfractionated heparin or a low molecular weight heparin as soon as possible before warfarin effect gets to the therapeutic rage of international normalized ratio (INR) 2–3. There is limited data on the duration of anticoagulation therapy. Decision may need physician's discretion based on the degrees of LV dysfunction, LV reverse remodeling during follow-up, and recurrence of thrombi. There is also limited data available about NOAC reducing the embolic risk of patients with LV thrombus.

6.3.3 Mitral Stenosis (MS)

Patients with mitral stenosis (MS) who suffered from ischemic stroke are recommended to receive warfarin therapy regardless of accompanying AF. In mitral stenosis patients with sinus rhythm who had ischemic stroke, paroxysmal AF or complicated infective endocarditis should be considered as an aggravating factor for stroke. Limited data suggested that adding aspirin to warfarin can reduce major adverse event compared to warfarin alone [60]. Regarding NOAC in patients with mitral stenosis, most of the NOAC studies excluded patients with highly thrombogenic conditions such as mitral stenosis and presence of prosthetic valve. Thus, there is little evidence of using NOAC in patients with MS to date.

6.3.4 Prosthetic Heart Valve

Presence of mechanical prosthesis is also one of the highly thrombogenic conditions. Warfarin is routinely recommended for all patients with mechanical prosthesis to prevent thromboembolic event [61, 62]. Intensity of the treatment is different according to the site of the prosthesis. Therapeutic rage or INR 2.5–3.5 and 2.0–3.0 is recommended for mitral and aortic mechanical prosthesis, respectively [63–66]. Low-dose aspirin (75–100 mg) may have additional benefit on top of warfarin monotherapy in patients with mechanical prosthesis [67, 68].

Bioprosthesis is usually less thrombogenic than mechanical prosthesis with exception of the first 3 months after surgery. Anticoagulation may be reasonable for the first 3 months after bioprosthetic valve replacement, but supporting data is lacking [61, 62]. After 3 months from bioprosthetic valve replacement, antiplatelet therapy with aspirin is generally recommended for stroke prevention unless there is other indication for anticoagulation. One study investigating the effect of dabigatran in patients with mechanical prosthesis demonstrated unfavorable results of increased thromboembolic event and higher bleeding risk compared to warfarin [69]. There is no evidence of NOAC in patients with prosthetic valve to prevent thromboembolic events.

When ischemic stroke occurs in spite of adequate anticoagulation in patients with mechanical prosthesis, low-dose aspirin should be added in patients not taking aspirin. If the patient is taking aspirin already, target INR can be increased with care, taking into account the individual bleeding risk [62]. In patients with bioprosthetic valve thrombus who are taking aspirin monotherapy, anticoagulation should be considered when ischemic stroke occurs.

6.3.5 Atrial Septal Abnormality

Paradoxical embolism is a phenomenon that thromboembolism originated from venous vasculature cross to arterial circulation resulting in arterial embolism in the presence of intracardiac shunt or pulmonary shunt. Patients with atrial

septal defect (ASD) have increased risk of paradoxical embolism. Some data reported the risk of paradoxical embolism in patients with ASD is up to 14 % [70, 71]. ASD closure is usually decided on the basis of pathologic changes in the right heart. However, in the presence of paradoxical embolism, ASD closure is reasonable, whether surgically or percutaneously [72].

PFO is seen in 15–25 % of adults and recently considered as one possible cause of cryptogenic stroke. Some data is supporting evidence that younger patients have a higher PFO-attributable stroke fraction than the older patients in cryptogenic stroke [73]. For patients with isolated PFO, who experienced ischemic stroke, there is insufficient evidence for the superiority of anticoagulation over antiplatelet therapy [74, 75]. Thus, aspirin monotherapy is recommended for patients with PFO, who had ischemic stroke. Exceptions are stroke patients with PFO and concomitant deep vein thrombosis (DVT), pulmonary thromboembolism, or venous thrombosis. Anticoagulation is indicated in those patients. There is a controversy whether PFO and concomitant atrial septal aneurysm (ASA) increase the risk of ischemic stroke or not. One study suggested the increased risk of PFO plus ASA [76], whereas other data did not [77, 78]. Prevalence of ASA is very low (≤2 %) in general population. Scarce data is available for isolated ASA in terms of the risk of stroke and optimal treatment. There are three random trials which tested efficacy of PFO closure preventing recurrent stroke in patients who experienced stroke [79–81]. None of them presented significant benefit of PFO closure in intention-to-treat analysis, whereas procedure-related complications, like new-onset AF, were higher with PFO closure. Thus, PFO closure is not recommend in patients with PFO, who had ischemic stroke. One exception is in patients with PFO and concomitant DVT. PFO closure may be considered in those patients depending on the recurrence risk of DVT [82].

6.3.6 Infective Endocarditis (IE)

IE is a fatal infectious condition of high mortality and morbidity [83]. Approximately 15–35 % of the patients suffer from clinically evident systemic embolism, and silent ischemic events are supposedly much more frequent [62]. Prompt antibiotics can reduce the risk of embolization significantly [84]. Embolic events are most frequent during the first day following the initiation of antibiotics, and incidence decreases gradually until 2 weeks [37, 85, 86]. Early surgery may reduce the incidence of embolic event in patients with large vegetation size and severe valve disease [87]. Timing of surgery should be decided based on multidisciplinary approach taking into account the embolic risk, heart failure, severity of valvulopathy, duration of antibiotics therapy, and comorbidities. Because of the risk of hemorrhagic transformation of embolic infarction, temporary discontinuation of anticoagulation may be considered at the time of diagnosis [85].

6.3.7 Aortic Atheroma

Aortic atherosclerotic plaque can cause systemic embolization [47, 88, 89]. Complex aortic plaques, which defined thickness >4 mm, or ulceration, or mobile component, are at high risk of embolization. Optimal treatment for aortic atheroma in preventing ischemic stroke is not clear. Although limited data suggested the superiority of warfarin therapy over antiplatelet therapy [90, 91], they are observational study and included patients are limited in number. The benefit of warfarin therapy over antiplatelet therapy is still not clear. One random trial that compared efficacy of dual antiplatelet therapy (aspirin plus clopidogrel) to anticoagulation revealed that dual antiplatelet therapy significantly reduced major vascular events versus warfarin [92]. Available data demonstrated that there is no additional benefit of dual antiplatelet therapy over aspirin monotherapy. Single antiplatelet therapy seems a reasonable treatment in patients with aortic atheroma at present. Although available data is limited [93], statin therapy in patients with aortic atheroma may be reasonable to stabilize atherosclerotic plaque and prevent embolic event. There is no data available for NOAC preventing embolic event in patients with aortic atheroma to date.

There is also limited data on surgical atherectomy. One study demonstrated event higher stroke incidence in patients underwent atherectomy than patients without atherectomy [94].

6.4 Summary and Recommendations

Stroke from cardioembolic source is generally associated with high recurrence and poor prognosis. Diverse spectrum of cardiac disease can contribute to the ischemic stroke. Identification of underlying cardiac condition can be mandatory for proper management and prevention in those patients. There is considerable disagreement in proper methodology for cardiac evaluation, management, and prevention of stroke in different cardiac conditions. In spite of all the efforts to reveal the cause of ischemic stroke, approximately 30 % of the stroke patients remain cryptogenic stroke. Based on understanding of cardiac evaluation techniques, systemic approach will be needed to improve prognosis in patients with ischemic stroke.

References

1. Ferro JM. Cardioembolic stroke: an update. Lancet Neurol. 2003;2(3):177–88.
2. Goldstein LB, Adams R, Alberts MJ, et al. Primary prevention of ischemic stroke: a guideline from the american heart association/american stroke association stroke council: cosponsored by the atherosclerotic peripheral vascular disease interdisciplinary working group; cardiovascular nursing council; clinical cardiology council; nutrition, physical activity, and metabolism council; and the quality of care and outcomes research interdisciplinary working group: the american academy of neurology affirms the value of this guideline. Stroke. 2006;37(6):1583–633.
3. Adams Jr HP, Bendixen BH, Kappelle LJ, et al. Classification of subtype of acute ischemic stroke. Definitions for use in a multicenter clinical trial. TOAST. Trial of org 10172 in acute stroke treatment. Stroke. 1993;24(1):35–41.
4. Kolominsky-Rabas PL, Weber M, Gefeller O, et al. Epidemiology of ischemic stroke subtypes according to TOAST criteria: incidence, recurrence, and long-term survival in ischemic stroke subtypes: a population-based study. Stroke. 2001;32(12):2735–40.
5. Eriksson SE, Olsson JE. Survival and recurrent strokes in patients with different subtypes of stroke: a fourteen-year follow-up study. Cerebrovasc Dis. 2001;12(3):171–80.
6. Arboix A, Garcia-Eroles L, Massons J, et al. Predictive clinical factors of in-hospital mortality in 231 consecutive patients with cardioembolic cerebral infarction. Cerebrovasc Dis. 1998;8(1):8–13.
7. Khechinashvili G, Asplund K. Electrocardiographic changes in patients with acute stroke: a systematic review. Cerebrovasc Dis. 2002;14(2):67–76.
8. Bozluolcay M, Ince B, Celik Y, et al. Electrocardiographic findings and prognosis in ischemic stroke. Neurol India. 2003;51(4):500–2.
9. Marini C, De Santis F, Sacco S, et al. Contribution of atrial fibrillation to incidence and outcome of ischemic stroke: results from a population-based study. Stroke. 2005;36(6):1115–9.
10. CAST: randomised placebo-controlled trial of early aspirin use in 20,000 patients with acute ischaemic stroke. CAST (Chinese Acute Stroke Trial) Collaborative Group. Lancet. 1997, 349(9066):1641–9.
11. Tsang TS, Petty GW, Barnes ME, et al. The prevalence of atrial fibrillation in incident stroke cases and matched population controls in Rochester, Minnesota: changes over three decades. J Am Coll Cardiol. 2003;42(1):93–100.
12. Douen AG, Pageau N, Medic S. Serial electrocardiographic assessments significantly improve detection of atrial fibrillation 2.6-fold in patients with acute stroke. Stroke. 2008;39(2):480–2.
13. Sulter G, Elting JW, Langedijk M, et al. Admitting acute ischemic stroke patients to a stroke care monitoring unit versus a conventional stroke unit: a randomized pilot study. Stroke. 2003;34(1):101–4.
14. Cavallini A, Micieli G, Marcheselli S, et al. Role of monitoring in management of acute ischemic stroke patients. Stroke. 2003;34(11):2599–603.
15. Kallmunzer B, Breuer L, Kahl N, et al. Serious cardiac arrhythmias after stroke: incidence, time course, and predictors – a systematic, prospective analysis. Stroke. 2012;43(11):2892–7.
16. Schaer BA, Zellweger MJ, Cron TA, et al. Value of routine holter monitoring for the detection of paroxysmal atrial fibrillation in patients with cerebral ischemic events. Stroke. 2004;35(3):e68–70.
17. Koudstaal PJ, van Gijn J, Klootwijk AP, et al. Holter monitoring in patients with transient and focal ischemic attacks of the brain. Stroke. 1986;17(2):192–5.
18. Liao J, Khalid Z, Scallan C, et al. Noninvasive cardiac monitoring for detecting paroxysmal atrial fibrillation or flutter after acute ischemic stroke: a systematic review. Stroke. 2007;38(11):2935–40.
19. Schaer B, Sticherling C, Lyrer P, et al. Cardiological diagnostic work-up in stroke patients – a comprehensive study of test results and therapeutic implications. Eur J Neurol. 2009;16(2):268–73.
20. Lazzaro MA, Krishnan K, Prabhakaran S. Detection of atrial fibrillation with concurrent holter monitoring

and continuous cardiac telemetry following ischemic stroke and transient ischemic attack. J Stroke Cerebrovasc Dis. 2012;21(2):89–93.
21. Jauch EC, Saver JL, Adams Jr HP, et al. Guidelines for the early management of patients with acute ischemic stroke: a guideline for healthcare professionals from the american heart association/american stroke association. Stroke. 2013;44(3):870–947.
22. Yaghi S, Elkind MS. Cryptogenic stroke: a diagnostic challenge. Neurol Clin Pract. 2014;4(5):386–93.
23. Barthelemy JC, Feasson-Gerard S, Garnier P, et al. Automatic cardiac event recorders reveal paroxysmal atrial fibrillation after unexplained strokes or transient ischemic attacks. Ann Noninvasive Electrocardiol. 2003;8(3):194–9.
24. Jabaudon D, Sztajzel J, Sievert K, et al. Usefulness of ambulatory 7-day ECG monitoring for the detection of atrial fibrillation and flutter after acute stroke and transient ischemic attack. Stroke. 2004;35(7):1647–51.
25. Christensen LM, Krieger DW, Hojberg S, et al. Paroxysmal atrial fibrillation occurs often in cryptogenic ischaemic stroke. Final results from the SURPRISE study. Eur J Neurol. 2014;21(6):884–9.
26. de Bruijn SFTM, Agema WRP, Lammers GJ, et al. Transesophageal echocardiography is superior to transthoracic echocardiography in management of patients of any age with transient ischemic attack or stroke. Stroke. 2006;37(10):2531–4.
27. McNamara RL, Lima JA, Whelton PK, et al. Echocardiographic identification of cardiovascular sources of emboli to guide clinical management of stroke: a cost-effectiveness analysis. Ann Intern Med. 1997;127(9):775–87.
28. Stratton JR, Lighty Jr GW, Pearlman AS, et al. Detection of left ventricular thrombus by two-dimensional echocardiography: sensitivity, specificity, and causes of uncertainty. Circulation. 1982;66(1):156–66.
29. Handke M, Harloff A, Hetzel A, et al. Left atrial appendage flow velocity as a quantitative surrogate parameter for thromboembolic risk: determinants and relationship to spontaneous echocontrast and thrombus formation – a transesophageal echocardiographic study in 500 patients with cerebral ischemia. J Am Soc Echocardiogr. 2005;18(12):1366–72.
30. de Luca I, Colonna P, Sorino M, et al. New monodimensional transthoracic echocardiographic sign of left atrial appendage function. J Am Soc Echocardiogr. 2007;20(3):324–32.
31. Moreira FC, Miglioransa MH, Hartmann IB, et al. Left atrial appendage assessment by second harmonic transthoracic echocardiography after an acute ischemic neurologic event. J Am Soc Echocardiogr. 2005;18(3):206–12.
32. Li JS, Sexton DJ, Mick N, et al. Proposed modifications to the Duke criteria for the diagnosis of infective endocarditis. Clin Infect Dis. 2000;30(4):633–8.
33. Rohmann S, Erbel R, Darius H, et al. Prediction of rapid versus prolonged healing of infective endocarditis by monitoring vegetation size. J Am Soc Echocardiogr. 1991;4(5):465–74.
34. Erbel R, Liu F, Ge J, et al. Identification of high-risk subgroups in infective endocarditis and the role of echocardiography. Eur Heart J. 1995;16(5):588–602.
35. Sanfilippo AJ, Picard MH, Newell JB, et al. Echocardiographic assessment of patients with infectious endocarditis: prediction of risk for complications. J Am Coll Cardiol. 1991;18(5):1191–9.
36. Mugge A, Daniel WG, Frank G, et al. Echocardiography in infective endocarditis: reassessment of prognostic implications of vegetation size determined by the transthoracic and the transesophageal approach. J Am Coll Cardiol. 1989;14(3):631–8.
37. Thuny F, Di Salvo G, Belliard O, et al. Risk of embolism and death in infective endocarditis: prognostic value of echocardiography: a prospective multicenter study. Circulation. 2005;112(1):69–75.
38. Daniels C, Weytjens C, Cosyns B, et al. Second harmonic transthoracic echocardiography: the new reference screening method for the detection of patent foramen ovale. Eur J Echocardiogr. 2004;5(6):449–52.
39. Kuhl HP, Hoffmann R, Merx MW, et al. Transthoracic echocardiography using second harmonic imaging – diagnostic alternative to transesophageal echocardiography for the detection of atrial right to left shunt in patients with cerebral embolic events. J Am Coll Cardiol. 1999;34(6):1823–30.
40. Elbardissi AW, Dearani JA, Daly RC, et al. Embolic potential of cardiac tumors and outcome after resection: a case-control study. Stroke. 2009;40(1):156–62.
41. Knepper LE, Biller J, Adams Jr HP, et al. Neurologic manifestations of atrial myxoma. A 12-year experience and review. Stroke. 1988;19(11):1435–40.
42. Santos AF, Pinho J, Ramos V, et al. Stroke and cardiac papillary fibroelastoma: mechanical thrombectomy after thrombolytic therapy. J Stroke Cerebrovasc Dis. 2014;23(5):1262–4.
43. Abbasi AS, Da Costa M, Hennessy T et al: Cardiac papillary fibroelastoma presenting as acute stroke. BMJ Case Rep. 2013.
44. Peterson GE, Brickner ME, Reimold SC. Transesophageal echocardiography – clinical indications and applications. Circulation. 2003;107(19):2398–402.
45. Transesophageal echocardiographic correlates of thromboembolism in high-risk patients with nonvalvular atrial fibrillation. The Stroke Prevention in Atrial Fibrillation Investigators Committee on Echocardiography. Ann Intern Med 1998, 128(8):639–47.
46. Roudaut R, Serri K, Lafitte S. Thrombosis of prosthetic heart valves: diagnosis and therapeutic considerations. Heart. 2007;93(1):137–42.
47. Amarenco P, Cohen A, Tzourio C, et al. Atherosclerotic disease of the aortic arch and the risk of ischemic stroke. N Engl J Med. 1994;331(22):1474–9.
48. 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):1500–10.
49. Connolly SJ, Ezekowitz MD, Yusuf S, et al. Dabigatran versus warfarin in patients with atrial fibrillation. N Engl J Med. 2009;361(12):1139–51.
50. Granger CB, Alexander JH, McMurray JJ, et al. Apixaban versus warfarin in patients with atrial fibrillation. N Engl J Med. 2011;365(11):981–92.
51. Patel MR, Mahaffey KW, Garg J, et al. Rivaroxaban versus warfarin in nonvalvular atrial fibrillation. N Engl J Med. 2011;365(10):883–91.
52. Giugliano RP, Ruff CT, Braunwald E, et al. Edoxaban versus warfarin in patients with atrial fibrillation. N Engl J Med. 2013;369(22):2093–104.
53. Hart RG, Pearce LA, Aguilar MI. Meta-analysis: antithrombotic therapy to prevent stroke in patients who have nonvalvular atrial fibrillation. Ann Intern Med. 2007;146(12):857–67.
54. Zielinska M, Kaczmarek K, Tylkowski M. Predictors of left ventricular thrombus formation in acute myocardial infarction treated with successful primary angioplasty with stenting. Am J Med Sci. 2008;335(3):171–6.
55. Osherov AB, Borovik-Raz M, Aronson D, et al. Incidence of early left ventricular thrombus after acute anterior wall myocardial infarction in the primary coronary intervention era. Am Heart J. 2009;157(6):1074–80.
56. Solheim S, Seljeflot I, Lunde K, et al. Frequency of left ventricular thrombus in patients with anterior wall acute myocardial infarction treated with percutaneous coronary intervention and dual antiplatelet therapy. Am J Cardiol. 2010;106(9):1197–200.
57. Gianstefani S, Douiri A, Delithanasis I, et al. Incidence and predictors of early left ventricular thrombus after ST-elevation myocardial infarction in the contemporary era of primary percutaneous coronary intervention. Am J Cardiol. 2014;113(7):1111–6.
58. Stratton JR, Resnick AD. Increased embolic risk in patients with left ventricular thrombi. Circulation. 1987;75(5):1004–11.
59. Vaitkus PT, Barnathan ES. Embolic potential, prevention and management of mural thrombus complicating anterior myocardial infarction: a meta-analysis. J Am Coll Cardiol. 1993;22(4):1004–9.
60. Perez-Gomez F, Salvador A, Zumalde J, et al. Effect of antithrombotic therapy in patients with mitral stenosis and atrial fibrillation: a sub-analysis of NASPEAF randomized trial. Eur Heart J. 2006;27(8):960–7.
61. Joint Task Force on the Management of Valvular Heart Disease of the European Society of C, European Association for Cardio-Thoracic S, Vahanian A, et al. Guidelines on the management of valvular heart disease (version 2012). Eur Heart J. 2012;33(19):2451–96.
62. Nishimura RA, Otto CM, Bonow RO, et al. 2014 AHA/ACC guideline for the management of patients with valvular heart disease: a report of the american college of cardiology/american heart association task torce on practice guidelines. J Am Coll Cardiol. 2014;63(22):e57–185.
63. Torella M, Torella D, Chiodini P, et al. LOWERing the INtensity of oral anticoaGulant therapy in patients with bileaflet mechanical aortic valve replacement: results from the "LOWERING-IT" Trial. Am Heart J. 2010;160(1):171–8.
64. Hering D, Piper C, Bergemann R, et al. Thromboembolic and bleeding complications following St. Jude Medical valve replacement: results of the german experience with low-intensity anticoagulation study. Chest. 2005;127(1):53–9.
65. Acar J, Iung B, Boissel JP, et al. AREVA: multicenter randomized comparison of low-dose versus standard-dose anticoagulation in patients with mechanical prosthetic heart valves. Circulation. 1996;94(9):2107–12.
66. Horstkotte D, Scharf RE, Schultheiss HP. Intracardiac thrombosis: patient-related and device-related factors. J Heart Valve Dis. 1995;4(2):114–20.
67. Meschengieser SS, Fondevila CG, Frontroth J, et al. Low-intensity oral anticoagulation plus low-dose aspirin versus high-intensity oral anticoagulation alone: a randomized trial in patients with mechanical prosthetic heart valves. J Thorac Cardiovasc Surg. 1997;113(5):910–6.
68. Turpie AG, Gent M, Laupacis A, et al. A comparison of aspirin with placebo in patients treated with warfarin after heart-valve replacement. N Engl J Med. 1993;329(8):524–9.
69. Eikelboom JW, Connolly SJ, Brueckmann M, et al. Dabigatran versus warfarin in patients with mechanical heart valves. N Engl J Med. 2013;369(13):1206–14.
70. Bannan A, Shen R, Silvestry FE, et al. Characteristics of adult patients with atrial septal defects presenting with paradoxical embolism. Catheter Cardiovasc Interv. 2009;74(7):1066–9.
71. Geva T, Martins JD, Wald RM. Atrial septal defects. Lancet. 2014;383(9932):1921–32.
72. Warnes CA, Williams RG, Bashore TM, et al. ACC/AHA 2008 guidelines for the management of adults with congenital heart disease: a report of the american college of cardiology/american heart association task force on practice guidelines (writing committee to develop guidelines on the management of adults with congenital heart disease). Developed in collaboration with the american society of echocardiography, heart rhythm society, international society for adult congenital heart disease, society for cardiovascular angiography and interventions, and society of thoracic surgeons. J Am Coll Cardiol. 2008;52(23):e143–263.
73. Kent DM, Ruthazer R, Weimar C, et al. An index to identify stroke-related vs incidental patent foramen ovale in cryptogenic stroke. Neurology. 2013;81(7):619–25.
74. Kent DM, Dahabreh IJ, Ruthazer R, et al. Anticoagulant vs. antiplatelet therapy in patients with cryptogenic stroke and patent foramen ovale: an individual participant data meta-analysis. Eur Heart J. 2015;36(35):2381–9.
75. Shariat A, Yaghoubi E, Farazdaghi M, et al. Comparison of medical treatments in cryptogenic

stroke patients with patent foramen ovale: a randomized clinical trial. J Res Med Sci. 2013;18(2):94–8.
76. Lamy C, Giannesini C, Zuber M, et al. Clinical and imaging findings in cryptogenic stroke patients with and without patent foramen ovale: the PFO-ASA study. Atrial Septal Aneurysm Stroke. 2002;33(3):706–11.
77. Serena J, Marti-Fabregas J, Santamarina E, et al. Recurrent stroke and massive right-to-left shunt: results from the prospective Spanish multicenter (CODICIA) study. Stroke. 2008;39(12):3131–6.
78. Homma S, Sacco RL, Di Tullio MR, et al. Effect of medical treatment in stroke patients with patent foramen ovale: patent foramen ovale in cryptogenic stroke study. Circulation. 2002;105(22):2625–31.
79. Furlan AJ, Reisman M, Massaro J, et al. Closure or medical therapy for cryptogenic stroke with patent foramen ovale. N Engl J Med. 2012;366(11):991–9.
80. Meier B, Kalesan B, Mattle HP, et al. Percutaneous closure of patent foramen ovale in cryptogenic embolism. N Engl J Med. 2013;368(12):1083–91.
81. Carroll JD, Saver JL, Thaler DE, et al. Closure of patent foramen ovale versus medical therapy after cryptogenic stroke. N Engl J Med. 2013;368(12):1092–100.
82. Kernan WN, Ovbiagele B, Black HR, et al. Guidelines for the prevention of stroke in patients with stroke and transient ischemic attack: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. 2014;45(7):2160–236.
83. Baddour LM, Wilson WR, Bayer AS, et al. Infective endocarditis: diagnosis, antimicrobial therapy, and management of complications: a statement for healthcare professionals from the Committee on Rheumatic Fever, Endocarditis, and Kawasaki Disease, Council on Cardiovascular Disease in the Young, and the Councils on Clinical Cardiology, Stroke, and Cardiovascular Surgery and Anesthesia, American Heart Association: endorsed by the Infectious Diseases Society of America. Circulation. 2005;111(23):e394–434.
84. Chu VH, Sexton DJ, Cabell CH, et al. Repeat infective endocarditis: differentiating relapse from reinfection. Clin Infect Dis. 2005;41(3):406–9.
85. Vilacosta I, Graupner C, San Roman JA, et al. Risk of embolization after institution of antibiotic therapy for infective endocarditis. J Am Coll Cardiol. 2002;39(9):1489–95.
86. Steckelberg JM, Murphy JG, Ballard D, et al. Emboli in infective endocarditis: the prognostic value of echocardiography. Ann Intern Med. 1991;114(8):635–40.
87. Kang DH, Kim YJ, Kim SH, et al. Early surgery versus conventional treatment for infective endocarditis. N Engl J Med. 2012;366(26):2466–73.
88. Tunick PA, Kronzon I. Atheromas of the thoracic aorta: clinical and therapeutic update. J Am Coll Cardiol. 2000;35(3):545–54.
89. Amarenco P, Duyckaerts C, Tzourio C, et al. The prevalence of ulcerated plaques in the aortic arch in patients with stroke. N Engl J Med. 1992;326(4):221–5.
90. Ferrari E, Vidal R, Chevallier T, et al. Atherosclerosis of the thoracic aorta and aortic debris as a marker of poor prognosis: benefit of oral anticoagulants. J Am Coll Cardiol. 1999;33(5):1317–22.
91. Dressler FA, Craig WR, Castello R, et al. Mobile aortic atheroma and systemic emboli: efficacy of anticoagulation and influence of plaque morphology on recurrent stroke. J Am Coll Cardiol. 1998;31(1):134–8.
92. Amarenco P, Davis S, Jones EF, et al. Clopidogrel plus aspirin versus warfarin in patients with stroke and aortic arch plaques. Stroke. 2014;45(5):1248–57.
93. Tunick PA, Nayar AC, Goodkin GM, et al. Effect of treatment on the incidence of stroke and other emboli in 519 patients with severe thoracic aortic plaque. Am J Cardiol. 2002;90(12):1320–5.
94. Stern A, Tunick PA, Culliford AT, et al. Protruding aortic arch atheromas: risk of stroke during heart surgery with and without aortic arch endarterectomy. Am Heart J. 1999;138(4 Pt 1):746–52.