New Advances in the Diagnosis and Management of Cardioembolic Stroke

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Cardioembolic stroke accounts for one-fifth of ischemic stroke and is severe and prone to early recurrence. Magnetic resonance imaging, transcranial Doppler, echocardiography, 24-hour electrocardiographic monitoring and electrophysiological study are tools for detecting cardioembolic sources. Non-valvular atrial fibrillation (AF) is the most common cause of cardioembolic stroke and long-term anticoagulation is proved to prevent stroke. Despite knowledge of guidelines, doctors recommend anticoagulant for less than half of patients with AF who have risk factors for cardioembolic stroke and no contraindication for its usage. Direct thrombin inhibitor offers the advantage of not needing prothrombin time controls and dose adjustments, but it needs large clinical trial for confirmation. Any type of anticoagulant by any route should not be used in acute cardioembolic stroke. Stroke after percutaneous coronary intervention (PCI), although rare, is associated with high mortality. Cardiologist must flush catheters thoroughly, minimize catheter manipulation and use minimal contrast medium during PCI.

Key Words: Stroke • Heart • Embolism • Percutaneous coronary intervention

INTRODUCTION

Cardioembolic stroke accounts for about 20% of ischemic strokes. Cardioembolic strokes are severe and prone to early recurrence. Cardiac emboli may cause massive, superficial, single large striatocapsular or multiple infarcts in the middle cerebral artery. Certain clinical syndromes such as Wernicke’s aphasia or global aphasia without hemiparesis are common in cardioembolic stroke. In the posterior circulation, cardioembolism can produce Wallenberg’s syndrome, cerebellar infarcts, basilar syndrome, multilevel infarcts, or posterior cerebral artery infarct. Hemiparesis and lacunar infarct, especially multiple lacunar infarcts, are not likely cardioembolism-related.

Cardioembolism can be reliably predicted clinically but is hard to document. The features suggestive of cardioembolic stroke are clinically decreased consciousness at onset, rapid regression of symptoms, sudden onset to maximal deficit < 5 min, and visual field defects, neglect, or aphasia. Simultaneous or sequential strokes in different arterial territories (combined anterior and posterior, or bilateral, or multilevel posterior circulation) and hemorrhagic transformation of an ischemic infarct found on computed tomography (CT) or magnetic resonance imaging (MRI) are all characteristic findings. Early recanalization of occluded intracranial vessel, occlusion of the carotid artery by mobile thrombus, and microembolism in both middle cerebral arteries noted on ultrasound or angiography indicate cardioembolic stroke. The clinical and imaging features suggestive of...
Cardioembolism are highly specific but less sensitive with a positive predictive value below 50%.\textsuperscript{1,6} Only a few papers regarding cardioembolic stroke in Taiwan have been published. The National Taiwan University Hospital Stroke Registry in 1995 described 676 patients with cerebral infarction, 20% of which were cardioembolic stroke.\textsuperscript{7} Lacunar stroke was the most common type (29%). The percentage and characteristic features of cardioembolic stroke in Taiwan were similar to those in western countries.\textsuperscript{1,6,7} Cardioembolic patients had a higher percentage of atrial fibrillation (AF) (69%), cardiomegaly, and ischemic heart disease than non-cardioembolic patients, which might account for a higher case-fatality rate than other cerebral infarction patients. Interestingly, only 3% of cardioembolic patients had carotid stenosis > 50%.

**HOW TO IDENTIFY A CARDIOEMBOLIC STROKE?**

**Brain**

MRI is more sensitive for the detection of cardioembolic stroke than CT.\textsuperscript{1,6} The sensitivity of MRI to hemorrhagic transformation is higher than that of CT.\textsuperscript{1,6} Hemorrhagic transformation develops in up to 70% of cardioembolic strokes.\textsuperscript{1,6} About 90% of hemorrhagic transformations are caused by cardiogenic brain embolism.\textsuperscript{1,6} There are two types of hemorrhagic transformation: multifocal, which is less symptomatic, and hematoma, which has mass effect and clinical deterioration. The mechanism of hemorrhagic transformation is reperfusion of ischemic zones, which occurs with spontaneous resolution of the emboli. Arterial wall trauma and dissection at the site of the thrombus are alternative explanations.\textsuperscript{9} Decreased conscious level, total circulation infarcts, severe strokes (National Institute of Health Stroke Scale score > 14), proximal occlusion, large hypodensity in more than 1/3 of the middle cerebral artery territory, and delayed recanalization > 6 hours after onset predict hemorrhagic transformation in acute cardioembolic stroke.\textsuperscript{1,6,9} Gradient-echo T2-weighted brain MRI-shown old microbleeds are predictors of hemorrhagic transformation.\textsuperscript{10}

**Between brain and heart**

A thrombus originating in the heart can occlude the internal carotid artery. Ultrasonography can detect such emboli as oscillating, homogeneous, elastic-mass echos.\textsuperscript{11} The suspicion of cardioembolism increases if angiography or transcranial Doppler shows that the artery in the territory of the infarct is patent, or if there is early recanalization of a previously occluded vessel. Transcranial Doppler is helpful for the diagnosis of right-to-left shunting by detecting bubble signals (“high-signal bubble sign”) passing the middle cerebral artery less than 20 seconds after agitated saline is injected in an antecubital vein.\textsuperscript{1} Transcranial Doppler can also detect microembolic signals (“high-intensity transient sign”) in the middle cerebral artery.\textsuperscript{1} However, high-intensity transient signs are rarer in cardiac embolism than in carotid embolism. They disappear a few days after the embolic event, and their relationship with the cardioembolic risk or with the type of antithrombotic treatment is controversial.\textsuperscript{12}

**Heart**

There are three high-risk cardiac origins\textsuperscript{1,6,13} for cardioembolic strokes: atrium, valve and ventricle. Atrial fibrillation (AF), atrial flutter, sick sinus syndrome, left atrial thrombus, left atrial appendage thrombus and left atrial myxoma are atrial origins. Mitral stenosis, prosthetic valve and endocarditis are valvular origins. Left ventricular thrombus, left ventricular myxoma, recent anterior myocardial infarct and dilated cardiomyopathy are ventricular origins. However, patent foramen ovale (PFO), atrial septal aneurysm (ASA), atrial spontaneous echo contrast, mitral annulus calcification, mitral valve prolapse, calcified aortic stenosis, akinetic/dyskinetic ventricular wall segment, hypertrophic obstructive cardiomyopathy and congestive heart failure are low or uncertain risks. In many patients such as those with AF, sick sinus syndrome, rheumatic valve and prosthetic valve disease, it is sufficient to make the diagnosis of a cardioembolic condition by history, physical examination, and electrocardiogram (ECG).\textsuperscript{1,6,13} Paroxysmal AF is an important cause of brain embolism that is difficult to document. It might be detected by 48-hour ECG monitoring immediately after stroke, by events recorder, or by electrophysiological studies.\textsuperscript{14} The ability of ambulatory ECG monitoring to detect embolicogenic arrhythmias such as AF or sick sinus syndrome in patients with stroke is low.\textsuperscript{1,6,13} Electrophysiological studies can measure atrial refractoriness and conduction time to define
a vulnerability index (latent atrial vulnerability). Pro-
grammed atrial stimulation assesses the inducibility of
sustained AF. In patients with cryptogenic stroke, there
is a significant association between atrial vulnerability
and atrial septal abnormalities, which raises the question
of atrial transient arrhythmias resulting in thrombus for-
mation. However, the prognostic significance of atrial
vulnerability is uncertain.

Transthoracic echocardiogram (TTE) can detect mitral
stenosis, dilated cardiomyopathy and other structural ven-
tricular diseases, ventricular thrombus, vegetations, or
tumors. This method also enables the measurement of left
atrial size and left ventricular systolic function. However,
TTE provides little information additional to history, physi-
cal examination, and ECG; thus, its cost-effectiveness is
doubtful. Transesophageal echocardiogram (TEE) is used
to study the aortic arch and ascending aorta, left atrium
and left atrial appendages, inter-atrial septum, pulmo-
rary veins, and valve vegetations. The common
potential findings of echocardiography in patients with
cardioembolic stroke and negative cardiac disease his-
tory and in sinus rhythm are left atrial or left atrial
appendage thrombus, atrial spontaneous echo contrast,
PFO, ASA, and aortic plaques. Left atrial thrombus and
left atrial appendage thrombus are conditions with a con-
sensual indication for anticoagulation. A Markov
decision analysis of benefit and cost concluded that doing
TEE in all stroke patients in sinus rhythm was more
cost-effective than either a sequential strategy (TTE fol-
lowed by TEE) or TEE alone in patients with negative
cardiac disease history. This study also found the preva-
ence of left atrial or left atrial appendage thrombus to be
8%. However, in another study, TEE detected atrial
thrombus in no more than 1% of patients in sinus rhythm,
leading the researchers to conclude that TEE is not
cost-effective if used routinely. A plausible implication
of such conflicting evidence is that TEE is more likely to
be helpful in young patients with stroke, all-age stroke of
unknown cause, and patients with non-lacunar stroke.

IMPORTANT CARDIOEMBOLIC SOURCES
AND CONDITIONS

Atheroma on aortic arch

Autopsy and TEE studies both showed that protrud-
ing aortic atheroma (> 4-5 mm) is 3-9 times more
common in stroke patients than in healthy controls. The
relative risk of recurrent stroke and other ischemic
events in stroke patients with atheroma in the aorta
thicker than 4 mm ranges from 1.5 to 4. Besides thick-
ness over 4 mm, ulcerated, non-calcified plaques and
those with mobile components are associated with an in-
creased risk of stroke recurrence. Thick or complex
aortic arch atheroma is more common in elderly patients
with stroke and is associated with carotid stenosis, coro-
nary artery disease, AF, hypertension, diabetes, and
smoking. Antiplatelet treatment, anticoagulants,
statins, and surgery have been advocated to reduce the
risk of stroke in patients with aortic atheroma. Unfortu-
nately, no large randomized trials have been completed
to prove the beneficial results in patients with aortic
atheroma receiving these treatments. Anticoagulant ther-
apy has a theoretical risk of cholesterol embolism.
Patients with aortic plaque who were treated with warfa-
rin had a low (1%) rate of cholesterol embolism. The
rate of embolism was significantly lower in patients
treated with conventional warfarin than in patients
treated with low-dose warfarin and aspirin. The
ongoing ARCH (Aortic arch-Related Cerebral Hazard)
trial, a randomized controlled trial, is comparing the ef-
effect of warfarin with target international normalized ratio
(INR) 2.0-3.0 and those of clopidogrel (75 mg/day) plus
aspirin (75-325 mg/day) in the secondary prevention of
stroke and other serious vascular events in patients with
prior ischemic stroke or peripheral embolism associated
with proximal aortic plaque with complex (≥ 4 mm thick-
ness and/or mobile) features. At the present time, a
reasonable strategy is to use antiplatelet drugs and statins
in all patients with symptomatic aortic atheroma greater
than 4 mm and to reserve anticoagulants for those with
mobile thrombus. Surgery is an option for patients with
recurrent embolism and permanent thrombus despite
anticoagulation.

Percutaneous Coronary Intervention (PCI)

Stroke after PCI, although rare, is associated with high
rates of mortality and morbidity. Recently, Dukkipati et al.
identified the incidence, predictors, and outcomes of stroke in patients undergoing PCI. Stroke occurred in hospital in 0.3% after PCI. On multivariate analysis, patients with stroke more fre-
quently had diabetes, hypertension, previous stroke and creatinine clearance ≤ 40 mL/min. Strokes also were noted more often when PCI were urgent or emergent and when intra-aortic balloons were used. Thrombolytics or heparin use before PCI was independently associated with periprocedural stroke. Stroke was independently associated with in-hospital death, renal failure, and the new need for hemodialysis. Also, the amount of contrast agent used in those with stroke was significantly higher and was independently associated with this complication. The editorial comment from Bittl and Caplan suggested it is self-evident and well known that thrombolytics and heparin increase the risk of hemorrhagic stroke, and commented these two agents might contribute directly or indirectly to the risk of brain embolism as the most common cause of ischemic stroke after PCI. Thrombolytics on occasion may break up intracavitary thrombi, and their use has been associated with the cholesterol embolization syndrome. Thus, primary PCI should be favored over thrombolytics to avoid stroke for acute myocardial infarction. The use of heparin has also been associated with an increased risk of the cholesterol embolization syndrome, providing one hypothetical connection between heparin use and adverse outcomes among patients with stroke. Heparin is not recommended for the treatment of cholesterol embolization syndrome. Dukkipati et al. and Bittl and Caplan also suggested coronary interventional procedures must be performed with meticulous attention to technical detail. Large-bore catheters or intra-aortic balloons may dislodge atheromatous material that embolizes to the cerebral circulation. They indicated back bleeding should be allowed whenever guide catheters are advanced around the aortic arch over a guide wire. If the catheter is connected to a Y-adapter during advancement, the valve should be left open. This should always be followed by strict double flushing, to discard any atherosclerotic debris that may be entrained by the guide catheter. Cholesterol embolization to the kidneys is probably responsible for the occurrence of renal failure and the new need for dialysis. They also suggested that use of minimal contrast medium is important and stroke may relate to the previously described thrombogenic potential of some types of contrast agents. Bittl and Caplan suggested more refined identification of risk factors for embolization might come from the preprocedural assessment of cardiac and aortic anatomy. Most plaques are located in the curvature of the arch from the distal ascending aorta to the proximal descending aorta, regions that can be shown by ultrasound. Although it may seem intuitive that a right brachial or radial approach may reduce cholesterol embolization by decreasing the linear contact between catheter and aorta, a recent prospective study showed an equal incidence of the cholesterol embolization syndrome for both the brachial and femoral approaches. Patients with protruding atheromas confined to the arch or descending aorta, however, may have a lower risk of catheter-induced embolization if a right forearm approach is used. Bittl and Caplan concluded that further efforts should be made to move beyond such traditional broad clinical categories as diabetes and hypertension to define the individual characteristics such as shaggy aortas that put patients at high risk of stroke from embolization.

**Mitral valve prolapse (MVP)**

MVP is found in about 3-6% of asymptomatic population; it is most common in young women. The early studies using M-mode echocardiographic criteria found up to 30% of patients under age 45 years with cerebral ischemia had MVP. The recurrent stroke event rate was reported to be as high as 15%. Subsequent investigations identified myxomatous degeneration, redundant valve, and supraventricular arrhythmias as risk factors for stroke in MVP. The recent cohort and case control studies have cast doubt on the role of uncomplicated MVP in stroke, even in youth.

**Endocarditis**

Two types of endocarditis, infective and non-infective, cause cardioembolic stroke. TEE can confirm valve vegetations more reliably than TTE, and should be the initial diagnostic procedure for all patients with moderate to high clinical suspicion of endocarditis. Non-infective endocarditis can complicate systemic cancer, lupus, and the antiphospholipid syndrome. Valvular lesions are common in patients with high anticardiolipin antibodies. Patients with stroke and non-infective endocarditis should receive heparin followed by oral anticoagulants.

Infective endocarditis complicated with stroke occurs in about 10% of cases. Most stroke in infective
endocarditis happens early in the course of the disease and before or during the first 2 weeks of antimicrobial therapy. Emboli can be multiple, especially in the case of infection of prosthetic valves and in infections due to aggressive organism, such as Staphylococcus aureus. Most emboli are fragments of vegetations, and therefore, the best antiembolic regimen is appropriate antibiotic treatment. The use of anticoagulants in native valve infective endocarditis is associated with increased mortality. In most patients with mechanical prosthetic valves who were given anticoagulants, treatment was maintained lifelong. Echocardiographic features that favor surgery to prevent embolism include persistent large vegetation > 10 mm, embolic event during the first 2 weeks of antimicrobial treatment, or more than one embolic event later in treatment. If urgent valve replacement is necessary, stroke is not necessarily a contraindication. Cardiac surgery may preferably be performed within 72 hours of stroke if CT/MRI excludes hemorrhagic transformation.

Mycotic aneurysms complicate 1-5% of infective endocarditis. Screening for mycotic aneurysms with contrast CT or MR angiography is only warranted in patients with neurological symptoms. Mycotic aneurysms can heal with medical therapy, but they may also enlarge and rupture, which is fatal in many cases. Decisions concerning medical versus surgical treatment of mycotic aneurysms must be individualized. Cardiac surgery may preferably be performed within 72 hours of stroke if CT/MRI excludes hemorrhagic transformation.

**PFO/ASA**

PFO is present in 1/3 of all patients with stroke and is found in up to 40% of patients with ischemic stroke who are younger than 55 years of age. PFO can cause stroke through paradoxical embolism, an event that is difficult to prove because it requires the thrombus to be shown at the PFO by echocardiography, particularly by TEE. Paradoxical embolism is a possible diagnosis if there is an arterial embolism without source found in the left cardiac cavities and valves, ascending aorta and aortic arch, pulmonary veins, cervical extracranial arteries, or in the large basal intracranial arteries. Paradoxical embolism may occur in case of right-to-left shunt coexisting with deep venous thrombosis or pulmonary embolism, or cough or Valsalva maneuver immediately preceding the onset of stroke. ASA is detected in 0.2-4.0% of patients examined with TEE. Criteria for the diagnosis of ASA by TEE are a minimum of 10 mm interatrial septal phasic movement and a diameter of the ASA of at least 15 mm. Paradoxical embolism, supraventricular arrhythmia, and thrombus from a coexistent ASA are the more likely causes of stroke in patients with PFO. A recently completed study recruited patients with an ischemic stroke of unknown origin to clarify the risks of recurrent stroke associated with PFO and/or ASA. All patients had undergone TEE and received aspirin (300 mg/day) and were followed up for 4 years. Patients with PFO were younger and less likely to have traditional risk factors for stroke. The risk of recurrent stroke was 15% among those with PFO and ASA, 2% among the patients with PFO alone, 0% among the patients with ASA alone, and 4% among those with neither of these cardiac abnormalities. Only the subgroup of patients with PFO and ASA had an increased risk ratio of 4 for recurrent stroke. Aspirin is an appropriate preventive medication for patients with ischemic stroke and ASA or PFO alone (regardless of its size). More aggressive preventive strategies other than aspirin should be considered for patients who have both PFO and ASA. In the PICSS (the Patent foramen ovale In the Cryptogenic Stroke Study), patients with PFO were randomly assigned to receive either aspirin or warfarin. There was no significant difference in recurrent stroke or death rate between the two treatment groups. The implication is that warfarin offers no advantage over aspirin for the secondary prevention of stroke in patients with PFO.

Surgical or interventional closures of the PFO are alternatives to aspirin. Device closure of PFO is safe and results in substantial hospital-related cost savings when compared with surgical closure. However, device closure must be assessed against antithrombotic regimen (aspirin, clopidogrel, or a combination of antiplatelet drugs) in randomized clinical trials, such as the ongoing PC (Patent foramen ovale and Cryptogenic embolism) trial.

**Non-valvular AF**

Non-valvular AF is the commonest cause of cardioembolic stroke. The disorder is associated with thyroid disorders, hypertension and heavy drinking. The risk of
stroke is at least six times higher in patients with AF than in healthy controls. AF is an increasingly important risk factor for stroke, both symptomatic and asymptomatic, in older people. The attributable risk of stroke due to AF rises from 1.5% at the age of 50 years to 25% at the age of 80. Loss of atrial contraction in AF leads to stasis that is most marked in the left atrial appendage. Stasis is associated with increased concentrations of fibrinogen, D-dimer, and von Willebrand factor, which are indicative of a prothrombotic state.

Treatment of AF aims to restore sinus rhythm, control of ventricular rate, and prevention of thromboembolism. A strategy for the control of rhythm is not inferior to a strategy for the restoration of sinus rhythm for the prevention of embolism and death. Restoration of sinus rhythm in AF can be achieved pharmacologically or by electrical cardioversion. Cardioversion is associated with an increased risk of stroke, which may occur if left atrial thrombi are dislodged when sinus rhythm is restored. The strategy used to decrease such risk is to keep the patient anticoagulated for 3 weeks before and 4 weeks after cardioversion. An alternative is established if cardioversion is urgent. Such an alternative requires TEE to detect atrial thrombi. If no thrombus is found, cardioversion is done immediately under heparin protection. If a thrombus is identified, the patient should be treated with warfarin for 3 weeks and repeat TEE thereafter. In some patients, maintenance of sinus rhythm is not possible with antiarrhythmic therapy. Such patients are candidates for atrial pacing, implantation of atrial defibrillator, or radiofrequency/surgical ablation of foci that cause AF. On the basis that in AF there are multiple re-entrant wavelets in both atria, the maze operation aims to restore sinus rhythm. In maze surgery, the atria are dissected into several segments and rejoined by suturing. However, this procedure does not improve atrial function. An alternative intervention that was recently introduced is the surgical or catheter radiofrequency isolation of the four pulmonary veins. This intervention is based on the finding that AF can originate in muscular sleeves that extend to the proximal pulmonary veins. The left atrial appendage, where thrombi are most commonly situated, can also be transcatheter-occluded.

Postoperative AF occurs in 30% of patients who undergo open heart surgery and is associated with a three-fold increase in the risk of stroke or transient ischemic attack. Oral amiodarone and beta-blockers significantly reduce the risk of postoperative stroke.

How to prevent stroke and recurrent stroke in patients with AF?

Risk factors for thromboembolism in AF include previous stroke (including previous transient ischemic attack or ischemic stroke or embolic stroke), age > 65 years, structural cardiac disease (particularly rheumatic or other significant valvular heart disease), prosthetic valve, hypertension, heart failure and significant left ventricular systolic dysfunction, diabetes, and coronary artery disease. Patients with AF associated with history of transient ischemic attack or stroke have indication for long-term anticoagulation with a target INR of between 2 and 4. Only those patients without risk factors or with contraindications to warfarin should be given aspirin. Aspirin has a modest protective effect in patients with AF and seems to primarily reduce non-cardioembolic strokes. The risk of stroke rises largely at INR below 2. The risk of intracranial bleeding rises at INR over 4. The INR should not exceed 3.0 in primary prevention of embolism in patients with AF (except those with prosthetic valves) and 4.0 in patients with previous stroke or transient ischemic attack. If the INR rises to over 6, low-dose oral vitamin K should be prescribed.

Despite the preventive potential of warfarin in patients with AF (70% reduction of the risk of ischemic stroke and 30% reduction of the risk of death), several studies done in western countries have shown that warfarin is underused. Despite knowledge of guidelines, doctors recommend anticoagulation for less than half of patients with AF who have risk factors and no contraindications for warfarin. In the ATRIA (AnTicoagulation and Risk factors In Atrial fibrillation) study, the strongest predictors of receiving warfarin were previous stroke and heart failure. However, an age of 85 years or older and previous intracranial or gastrointestinal hemorrhages were predictors of not receiving warfarin.

Alternative to warfarin in patients with AF

The SPAF (Stroke Prevention in Atrial Fibrillation) III study reported that adjusted-dose warfarin (target INR 2.0-3.0) is highly efficacious for prevention of stroke in patients with non-valvular AF at high risk for thromboembolism. However, low-intensity, fixed-dose
# Cardioembolic Stroke

**Table 1. Antithrombotic treatment for the prevention of stroke in different cardioembolic sources**

<table>
<thead>
<tr>
<th>Sources</th>
<th>Managements</th>
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<tbody>
<tr>
<td><strong>AF</strong></td>
<td></td>
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<tr>
<td>High risk: previous stroke/TIA, systemic embolus, valve disease, hypertension, LV dysfunction, age &gt; 75, ≥ 2 moderate risk factors</td>
<td>Warfarin (INR 2-3); If age &gt; 75: INR 1.5-2.0</td>
</tr>
<tr>
<td>Moderate risk: age 65-75, DM, CAD, thyrotoxicosis</td>
<td>Warfarin or aspirin</td>
</tr>
<tr>
<td>Low risk: no risk factor, age &lt; 65</td>
<td>Aspirin or none</td>
</tr>
<tr>
<td>Acute</td>
<td>Heparin then warfarin</td>
</tr>
<tr>
<td>Cardioversion</td>
<td>Warfarin for 3 wks before and 4 wks after, or if no thrombus on TEE, heparin before and warfarin 4 wks after</td>
</tr>
</tbody>
</table>

| AMI |             |
| Risk factor (-) | Aspirin and LMWH |
| Risk factors (+): anterior MI, CHF, AF, systemic/pulmonary embolism, mural thrombus, severe LV dysfunction | Heparin then warfarin |

| Previous MI |             |
| With CHF | Aspirin or warfarin |
| With ventricular aneurysm | Aspirin |
| With mobile or protuberant thrombus | Warfarin |
| None of above | Aspirin |
| Mechanical valve prosthesis | Warfarin +/- aspirin |

| Bio-prosthesis |             |
| < 3 ms after valve insertion | Warfarin |
| With AF, LA thrombus, systemic emboli | Warfarin |
| None of above | Aspirin |
| Rheumatic valve | Warfarin |
| Atrial flutter | Warfarin |

| Sick sinus syndrome | Warfarin |

| Heart failure + sinus rhythm, for primary prevention | None |
| DCM | Warfarin |

| Atrial thrombus | Warfarin |
| Ventricular Thrombus | Aspirin or warfarin |
| Mobile or protuberant | Warfarin |
| Calcified aortic stenosis | Aspirin |
| HOCM | Aspirin |

| MVP | Aspirin or none |
| Mitral annular calcification | Aspirin or warfarin |

| Infective endocarditis | Antibiotics |
| native valve | No anticoagulant |
| mechanical valve prosthesis | Continue anticoagulant |
| mechanical valve prosthesis + large stroke | Stop anticoagulant |

| Non-infective endocarditis | Heparin then warfarin |
| Myxoma | Surgery |
| ASA | Aspirin or none |

| Mitral echo contrast | Aspirin |

| Aortic atheroma |             |
| < 4 mm | None or aspirin |
| ≥ 4 mm | Aspirin + statin |
| ≥ 4 mm + mobile or protuberant thrombus | Warfarin |

**Abbreviations:** INR = international normalized ratio; AF = atrial fibrillation; TIA = transient ischemic attack; LV = left ventricle; DM = diabetes mellitus; CAD = coronary artery disease; TEE = transesophageal echocardiography; AMI = acute myocardial infarction; LMWH = low molecular weight heparin; CHF = congestive heart failure; LA = left atrium; DCM = dilated cardiomyopathy; vent = ventricular; HOCM = hypertrophic obstructive cardiomyopathy; MVP = mitral valve prolapse; ASA = atrial septal aneurysm; PFO = patent foramen ovale.
warfarin (INR 1.2-1.5 for initial dose adjustment) plus aspirin (325 mg/day) was insufficient for stroke prevention. The rates of major bleeding were similar in both treatment groups. In the AFASAK 2 (Second Copenhagen Atrial Fibrillation, Aspirin, and Anticoagulation) Study, minidose warfarin (1.25 mg/day) plus aspirin (300 mg/day) had no advantage over adjusted-dose warfarin (target INR 2.0-3.0) for stroke prevention in AF. Prevention of embolic events in patients with mechanical valve prosthesis and prevention of serious vascular events in acute myocardial infarction and probably in congestive heart failure are the evidence-based indications for the use of combined warfarin and aspirin. The SPORTIF (Stroke Prevention using an ORal Thrombin Inhibitor in patients with atrial Fibrillation) III and V trials, comparing a direct thrombin inhibitor (ximelagatran) with warfarin for prevention of thromboembolism in patients with non-valvular AF, are underway. Ximelagatran offers the advantage of not needing prothrombin time controls and dose adjustments.

ACUTE ANTITHROMBOTIC THERAPY

Several recent trials, reviews, and meta-analyses clearly showed that subcutaneous unfractionated heparin and low molecular weight heparin do not have any effect on stroke outcome or progression, and that their small benefit in reducing early recurrent stroke is outweighed by a small increase in intracranial hemorrhages. The effect of intravenous heparin in acute ischemic stroke will be elucidated in the ongoing RAPID (Rapid Anticoagulation Preventing Ischemic Damage) trial. Until this trial is completed, any type of heparin by any route should not be used in acute cardioembolic stroke. The time to start anticoagulation for secondary prevention is unclear. It seems reasonable to start anticoagulant immediately in transient ischemic attacks and minor strokes with a high-risk source of cardioembolism and non-hemorrhagic infarcts and to delay it for 5-15 days in disabling strokes and large or hemorrhagic infarcts.

Intravenous tissue plasminogen activator given within 3 hours seems to be beneficial for patients with AF and acute ischemic stroke based on limited evidence. Observational data suggested that thrombolysis might be more effective in patients with cardioembolic stroke than in those with atherothrombotic stroke. A recent study indicated that embolic occlusions due to cardiac thrombi had a lower likelihood of being resolved by intra-arterial thrombolysis.

Discontinuation of anticoagulant in patients with high thromboembolic risk cardiac disorders and a hemorrhagic stroke is a therapeutic dilemma. The data from Mayo Clinic, including half of the patients with prosthetic valve, showed that discontinuation of warfarin for a median of 10 days was associated with a 30-day low (3%) risk of embolic stroke.

CONCLUSIONS

During the past two decades, enormous progress has been made in the diagnosis of cardioembolic disorders and in establishing evidence-based recommendations for the primary and secondary prevention of cardioembolic stroke. Table 1 summarizes the updated antithrombotic treatment for the prevention of stroke in different cardioembolic sources and conditions. Because AF is by far the commonest cause of cardioembolic stroke, the mortality, disability, and costs related to cardioembolic stroke will mainly be decreased by advances in the treatment of AF. The future task is to develop more sensitive methods to identify paroxysmal AF, to achieve definitive treatment of this disorder by the least invasive methods and to introduce safer anticoagulants to obtain optimal control of anticoagulation. For low- or uncertain-risk cardioembolic disorders, the preventive therapeutic alternatives should be studied in large randomized controlled trials.

What is to be learned from the pathogenesis of stroke after PCI? Avoiding stroke continues to be good reason to choose primary PCI over thrombolitics for acute myocardial infarction. Cardiologists must flush catheters thoroughly, minimize catheter manipulation, and use minimal contrast medium during PCI.

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心因性腦中風在診斷及處置上之新進展

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缺血性中風有 1/5 是源自心臟的栓塞所造成。心因性腦中風通常病況嚴重且易早期復發。核磁共振、穿顱都卜勒、心臟超音波、24 小時心電圖及電氣生理學檢查可協助辨認心因性栓塞之來源。非瓣膜性心房顫動是心因性中風最常見的原因，而持續口服抗凝血劑已證實可預防中風之發生。然而臨床統計卻顯示：有心房顫動伴隨有發生中風的危險因子且無使用抗凝血劑之禁忌者，有一半以上並沒有持續使用口服抗凝血劑。新一世代抗凝血劑似乎具有較高的安全性及使用之方便性，但是仍待大規模的臨床試驗來證實。發生急性心因性中風時，目前並不建議立即常規使用抗凝血劑治療。冠狀動脈介入治療後之中風雖然罕見，但一旦併發中風時死亡率卻很高。導管操作中完全沖刷導管、最小限度的操作導管、及使用最少量的顯影劑可減少冠狀動脈介入治療後中風之發生。

關鍵詞：中風、心臟、栓塞、冠狀動脈介入術。