# Chinese expert consensus on the diagnosis of cardiogenic stroke (2019)

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Cardioembolic stroke (CES), also known as cardiogenic stroke, refers to a clinical syndrome caused by a cardiogenic embolus from the heart, leading to cerebral artery embolism through circulation, and it consequently results in corresponding brain dysfunction. CES is associated with greater severity, poor outcomes, and a relatively high recurrence rate, compared with other subtypes of ischemic stroke.[1]

To date, no universal diagnostic criteria for CES have been well established. In order to perform differential diagnosis of CES, we hereby presented the Chinese expert consensus on CES-based diagnostic criteria with respect to the latest development on clinical research, aiming to improve the accuracy of clinical diagnosis of CES, and facilitate the prevention and treatment of CES.

## Classification of CES Etiology

According to the potential causes of CES presented in A-S-C-O (phenotype) classification system[2] and its epidemiological characteristics, the etiology of CES was divided into nine categories as follows: atrial fibrillation (AF), heart failure, acute coronary syndrome, patent foramen ovale (PFO), rheumatic heart disease, artificial heart valve, infective endocarditis, dilated cardiomyopathy, and cardiac myxoma [Supplemental Table S1, http://links.lww.com/CM9/A380 and S5, http://links.lww.com/CM9/A380].

## Clinical Features

CES occurs in patients of all ages, and the majority of them have a history of heart disease. It is generally characterized by abrupt onset of severe neurological symptoms corresponding to the cerebral cortex damage, such as aphasia or visual field defect.[3,4] These symptoms rapidly peak at the onset of disease, accompanied by other signs of systemic thromboembolism, including edge-shaped infarction of kidney or spleen, Osler split, and blue toe syndrome.[3]

## Auxilary Examination

### Neuroimaging profile

Cranial computed tomography/magnetic resonance imaging can demonstrate single or multiple infarcts distributed in the cerebral cortex and subcortical region, as well as cerebellum and brainstem.[5] The infarcts often exceed a region of single vascular supply, exist with lesions at different stages,[3] and are prone to hemorrhagic transformation. T2*-weighted gradient-echo images revealed the presence of two-layered susceptibility vessel sign and a high overestimation ratio.[6]

### Vascular & cardiac assessment

The purpose is to find out an evidence supporting high-risk cardiogenic embolism, and to exclude the shedding of large artery plaques. At present, it remains controversial concerning the detailed examination scheme to clarify the potential etiology of CES.

(1) Echocardiography: Transthoracic echocardiography or/and transesophageal echocardiography (TEE) detect high-risk cardiogenic embolism [Supplemental Table S2, http://links.lww.com/CM9/A380 and S4,

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**Table 1: Diagnostic criteria for cardiogenic stroke.**

| A | B | C |
|---|---|---|
| Typical clinical manifestations | Cardiogenic embolus on echocardiography[*] | Exclusion of other diseases |
| Characteristic neuroimaging (brain CT/MRI) findings | Arrhythmia on electrocardiogram, especially atrial fibrillation | |
| | Characteristic vascular neuroimaging/ cerebral angiography findings[†] | |

[*]Intracardiac thrombus, intracardiac vegetation, intracardiac tumor and right-to-left intracardiac shunt. [†]An abrupt cut-off of the main trunk or branch of an intracranial large-vessel, in the absence of significant atherosclerotic plaques which cause narrowing of the upstream vessels (eg, internal carotid artery). CT: Computed tomography; MRI: Magnetic resonance imaging.

http://links.lww.com/CM9/A380].[4] Contrast TEE, contrast transthoracic echocardiography, and contrast-enhanced transcranial Doppler ultrasound (cTCD) detect right-to-left shunt in the cardiac cavity. TCD monitoring for microemboli may discover microembolic signal. Repetitive TCD/cTCD evaluation shows rapid recanalization of occluded major brain artery.[3] Carotid ultrasound reveals no atherosclerotic stenosis at carotid or vertebral artery.

(2) Electrocardiogram (ECG) examination: Standard 12-lead ECG displays abnormalities (eg, AF or recent myocardial infarction), or remote ECG monitoring, 24-h Holter ECG monitoring and long-term ECG monitoring (>24 h) identifies arrhythmias, especially paroxysmal AF.

(3) Vascular neuroimaging/cerebral angiography: computed tomography angiography (CTA) often shows multisegmental clot, that is, two or more than two segmental stenosis in the same large intracranial vessel, including middle cerebral artery (MCA).[7] CTA/magnetic resonance angiography (MRA) or digital subtraction angiography often demonstrates multiple stenosis or an abrupt vessel cut-off of the main trunk or branch of an intracranial large-vessel, in the absence of significant atherosclerotic narrowing of the upstream vessels, such as internal carotid artery. CTA/MRA or high-resolution intracranial vessel wall imaging typically reveals no atherosclerotic plaque of intracranial artery.

### Blood biochemistry

Measurement of the levels of B-type natriuretic peptide and N-terminal pro-B-type natriuretic peptide is significant in the differential diagnosis of non-cardiogenic stroke.[8]

### Clinical scale

CHA2DS2-VASc (congestive heart failure, hypertension, age ≥75 years [doubled], diabetes mellitus, prior stroke/transient ischemic attack [doubled], vascular disease, age 65-74 years, sex category [female]) score is generally used to evaluate the risk of stroke in non-valvular AF, and the risk of paradoxical embolism score can be used to assess the correlation between stroke and PFO.

### Pathology

Autopsy analysis may assist in the definite diagnosis via indicating mural thrombus, valvular vegetation or tumor fragments (eg, myxoma) from MCA and/or vertebrobasilar arterial system.

## Diagnosis and Risk Stratification

### Diagnostic criteria

Based on clinical and neuroimaging features, together with other key points including vascular and cardiac assessment [Table 1], the Chinese expert consensus recommends that CES is categorized into the definite CES, probable CES, and possible CES as follows: Definite CES = 2 of (A) + at least 1 of (B) + C; Probable CES = 2 of (A); or at least 1 of (A) + at least 1 of (B); Possible CES = at least 1 of (A).

### Risk stratification

Risk stratification is highly significant to guide the treatment of CES and reduce recurrence and death. When the cause of CES remains elusive after the diagnosis of CES, the risk of embolism should be evaluated immediately [Supplemental Figure 1, http://links.lww.com/CM9/A379]. Given the lack of reliable data for risk stratification, this consensus utilized a standard recommended by the Journal of the American Society of Echocardiography.[9] The risk factors related to high and low embolic potential are presented in Supplemental Table S3, http://links.lww.com/CM9/A380.

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### Conflicts of interest

None.

### References

1. Bjerkreim AT, Khanevski AN, Thomassen L, Thomassen L, Selvik HA, Waje-Andreassen U, et al. Five-year readmission and mortality differ by ischemic stroke subtype. J Neurol Sci 2019;403:31–37. doi: 10.1016/j.jns.2019.06.007.
2. Amarenco P, Bogousslavsky J, Caplan LR, Donnan GA, Wolf ME, Hennerici MG. New approach to stroke sub-typing: the A-S-C-O (phenotypic) classification of stroke. Cerebrovasc Dis 2009;27:502–508. doi: 10.1159/000210433.
3. Pepi M, Evangelista A, Nihoyannopoulos P, Flachskampf FA, Athanassopoulos G, Colonna P. European Association of Echocardiography. Recommendations for echocardiography use in the diagnosis and management of cardiac sources of embolism: European Association of Echocardiography (EAE) (a registered branch of the ESC). Eur J Echocardiogr 2010;11:461–476. doi: 10.1093/ejechocard/jeq045.
4. Adams HP Jr, 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;24:35–41. doi: 10.1161/01.str.24.1.35.
5. Frid P, Drake M, Giese AK, Wasselius J, Schirmer MD, Donahue KL, et al. Stroke Genetics Network (SiGN), the International Stroke Genetics Consortium (ISGC), and the MRI-Genetics Interface Exploration (MRI-GENIE) Study. Detailed phenotyping of posterior vs. anterior circulation ischemic stroke: a multi-center MRI study. J Neurol 2020;267:649–658. doi: 10.1007/s00415-019-09613-5.
6. Bourcier R, Derraz I, Bracard S, Oppenheim C, Naggara O. Two-layered susceptibility vessel sign and high overestimation ratio on MRI are predictive of cardioembolic stroke. AJNR Am J Neuroradiol 2019;40:65–67. doi: 10.3174/ajnr.A5865.
7. Chen Z, Shi F, Zhang M, Gong X, Lin L, Lou M. Prediction of the multisegment clot sign on dynamic CT angiography of cardioembolic stroke. AJNR Am J Neuroradiol 2018;39:663–668. doi: 10.3174/ajnr.A5549.
8. Bai J, Sun H, Xie L, Zhu Y, Feng Y. Detection of cardioembolic stroke with B-type natriuretic peptide or N-terminal pro-BNP: a comparative diagnostic meta-analysis. Int J Neurosci 2018;128:1100–1108. doi: 10.1080/00207454.2017.1408612.
9. Saric M, Armour AC, Arnaout MS, Chaudhry FA, Grimm RA, Kronzon I, et al. Guidelines for the use of echocardiography in the evaluation of a cardiac source of embolism. J Am Soc Echocardiogr 2016;29:1–42. doi: 10.1016/j.echo.2015.09.011.