Perspectives in Medicine (2012) 1, 214—217

Bartels E, Bartels S, Poppert H (Editors):
New Trends in Neurosonology and Cerebral Hemodynamics — an Update.
Perspectives in Medicine (2012) 1, 214—217

journal homepage: www.elsevier.com/locate/permed

The contribution of microembolic signals (MES) detection in cardioembolic stroke

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KEYWORDS
Microembolic signals;
Atrial fibrillation;
Left ventricular assist devices;
Cardioembolic stroke

Summary
Background: Cardioembolic stroke accounts for about one third of all strokes. Microembolic signals (MES) are frequently found in patients with acute stroke. The role of MES in cardioembolic stroke is less well investigated.
Methods: Medline based literature review of clinical trials linking MES and stroke with cardiac sources of various risks.
Results: MES are a rare finding in patients with cardioembolic stroke as well as in sources of potential cardiac embolism (e.g. myocardial infarction, atrial fibrillation, left ventricular thrombus). The low number of patients with MES and the low number of MES during the investigation times leads to a limited statistical power of positive and negative findings. MES in patients with artificial heart valves and the DeBakey left ventricular assist device (LVAD) are predominantly gaseous and do not correlate with stroke risk. In patients with the Novacor LVAD, MES strongly correlate with stroke risk.
Conclusion: Currently, the role of MES in cardioembolic stroke is only limited due to both, the low prevalence of MES and the number of MES per investigation. Larger studies would be needed to strengthen this role.

Background

Cardioembolic stroke accounts for about one third of all strokes. In some registries, percentages even reach 40%. The diagnosis of cardioembolic stroke requires that alternative stroke etiologies have been ruled out comprehensively. Diagnosis of cardiac embolism thus usually requires the presence of a structural abnormality of the heart or the diagnosis of rhythm disturbances with high embolic risk such as atrial fibrillation (AF) [1].

According to general consensus, cardiac lesions can be divided into ''high risk'' and ''low or uncertain risk'' of subsequent embolism [2]. The differentiation is of considerable importance, as the therapeutic regimen to prevent future embolism varies between different embolic risks. Table 1 gives an overview of ''high'' and ''low'' risk lesions.

Even without proving a cardiac source, some features of an acute stroke give clues to a cardiac source of stroke. For example, patients with cardioembolic stroke frequently have clinically more severe stroke than others, frequently decreased level of consciousness, and severe cortical symptoms such as neglect or aphasia [2]. On cerebral imaging especially multiple lesions in different arterial territories

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2211-968X
doi:10.1016/j.permed.2012.02.031

Table 1 High and low risk lesions for cardiac embolism [2].

High risk	Low risk
Atrial	Atrial
Atrial fibrillation	Patent foramen ovale
Atrial flutter	Atrial aneurysm
Sick sinus syndrome	Spontaneous echo contrast
Left atrial thrombus	
Left atrial myxoma	
Ventricular	Ventricular
Left ventricular thrombus	Dyskinetic wall segments
Left ventricular myxoma	Hypertrophic cardiomyopathy
Recent myocardial infarction	Congestive heart failure
Dilated cardiomyopathy	
Valvular	Valvular
Mitral stenosis	Lambl's excrescences
Prosthetic valves	Fibroelastoma
Infective/non-infective endocarditis	Mitral-valve prolapse

strongly favours a cardiac source of embolism. Furthermore, microembolic signals (MES) detected in both middle cerebral arteries make a proximal source of embolism, mainly the heart, very likely [2].

Microembolic signals (MES) are frequently found in patients with acute stroke and especially in those with symptomatic carotid stenosis [3]. The role of MES in cardioembolic stroke is less well investigated. The following overview will highlight the current role of MES detection in the diagnosis and therapy of various sources of cardiac embolism.

Methods

Medline listed studies were identified by the following search terms: ''MES'' OR ''ES'' OR ''HITS'' AND ''Cardia*'' OR ''heart'' OR ''atri*'' OR ''ventri*''. Studies were selected upon relevance to the subtitles of the following overview. If appropriate, data from different studies were grouped in tables and commented in context.

Prevalence of MES in patients with cardioembolic stroke

There are a number of studies investigating the prevalence of MES in unselected stroke cohorts. An overview on the studies comparing the prevalence of MES in detailed stroke etiologies according to TOAST criteria is given in Table 2.

In a recent study, Idicula found quite a high prevalence of MES in patients with cardiac embolism that even topped the prevalence found in patients with symptomatic carotid stenosis [4]. However, in this study, only 40 patients had been included in total and MES were found in four of eleven patients with cardiac embolism. In the larger studies the prevalence of MES was generally low. The lowest percentage was found in the largest study of Poppert and colleagues, finding MES in only five of 143 (3.5%) patients with cardiac embolism [5]. The overall prevalence of MES in patients with cardio-embolic stroke is about 5%. No study found MES to be predictive of recurrent cardioembolic stroke, which could also be the effect of the low case numbers with MES and the restricted observation times.

Table 2 Prevalence of MES in various stroke etiologies.

Author, year	Large artery embolism *n/N*, %	Cardioembolic stroke *n/N* %	Small vessel disease *n/N* %
Idicula, 2010 [4]	4/13, 30%	4/7, 36%	0/2, 0%
Poppert, 2006 [5]	20/103, 20%	5/143, 3.5%	0/147, 0%
Serena, 2000 [6]	8/39, 20%	6/35, 17%	0/64, 0%
Kaposzta, 1999 [7]	10/20, 50%	1/22, 4%	0/20, 0%
Daffertshofer, 1996 [8]	18/105, 17.1%	4/65, 6.2%	3/67, 4.5%
Sum	60/280, 21%	20/272, 5%	3/300, 1%

Ferro commented in his paper that cardioembolic stroke should be assumed in case MES are found bilaterally [2]. However although this assumption is quite plausible, its clinical relevance is very low. First, as mentioned above, only a minority of patients with cardioembolic stroke will have MES at all. Second, the number of MES per investigation is very low (about 1 or 2 MES per hour). Finding larger numbers of MES is rare. However, bilateralism cannot be assumed in case of only one MES per session and even with two signals during the session there is still a 50% chance that these two signals occur on the same side of the brain.

Furthermore, bilateral MES can also be found in cases with artery to artery embolism. Poppert et al. found in his study bilateral MES in 3 of 20 patients with this stroke etiology [5]. In one patient, contralateral carotid occlusion may have accounted for this finding, but no obvious reason was depicted in two cases. In summary, MES are an infrequent finding in cardioembolic stroke, MES detection does thus not contribute to the work-up of unselected stroke patients to determine stroke etiology.

MES in cardiac disease with a risk of stroke

This paragraph will look at cardiac embolism from the other side of the medal. What does MES detection contribute to the patients' work-up in case there are known cardiac lesions and the investigator wants to address the risk of future stroke.

MES after myocardial infarction

Stroke is a possible complication of acute myocardial infarction and affects 2–3% of patients with acute coronary syndromes (ACS) [9]. The risk to suffer stroke within the