

Available online at [www.sciencedirect.com](http://www.sciencedirect.com)**ScienceDirect**journal homepage: <http://www.elsevier.com/locate/crvasa>**Original research article****The findings of the oesophageal echocardiography in patients with acute cerebral ischaemia****Marketa Peskova<sup>\*</sup>, Jan Lhotsky, Richard Rokyta***Department of Cardiology, Complex Cardiovascular Center, University Hospital in Pilsen, Faculty of Medicine in Pilsen, Charles University in Prague, Alej Svobody 80, 30460 Pilsen, Czech Republic***ARTICLE INFO****Article history:**

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**ABSTRACT**

**Introduction:** The cerebrovascular accident ranks among the main causes of mortality and morbidity worldwide. In the Czech Republic, the cerebrovascular disease was the direct cause of death in 10% of the cases in the year 2012 (Healthcare Annual CZ 2012).

**Aim:** The aim of our study was to evaluate the transoesophageal echocardiogram findings (TOE) in patients with suspicion for cardioembolic stroke or TIA who were indicated to this examination in our echocardiography laboratory.

**Methodology:** During the period from July 2009 to March 2013 (45 months), 108 TOE had been realized in our echocardiographic laboratory that was indicated for ischaemic stroke or TIA. We monitored the occurrence of pathological findings that have the cardioembolic potential according to the literature.

**Results:** The examination was performed for a suspect of an infective endocarditis 10 times, this was proven in 3 cases. 5 patients were holders of a mechanical valvular prosthesis, and its dysfunction was discovered in neither case. The most frequent diagnosis was foramen ovale patens in the other patients (30 patients, i.e. 37%); in 3 cases it occurred simultaneously with an atrial septal aneurysm. We found a haemodynamic little significant atrial septal defect in 3 patients and a presence of an endocardial thrombus in 2 patients. A left atrial dilation and a systolic dysfunction of a left atrium auricle can relate with an occurrence of an atrial fibrillation. A left atrium volume was determined in 86 cases; only 35 patients (i.e. 40.7%) have the normal left atrium volume. A pathology, which can be connected with a cerebral ischaemia that took place, was found in 56% of the patients.

**Conclusion:** Transoesophageal echocardiography is an independent method in examination of potential sources of cardioembolism. In our sample, a pathology in more than half of the patients was diagnosed that could refer to a suffered ischaemic stroke and the diagnosis led to a change in a treatment strategy in 17 cases of the total number of 95 patients (i.e. at 18%).

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<sup>\*</sup> Corresponding author. Tel.: +420 723207514/377103342.

E-mail addresses: [peskovam@fnplzen.cz](mailto:peskovam@fnplzen.cz), [zahomolkou10@gmail.com](mailto:zahomolkou10@gmail.com) (M. Peskova).<http://dx.doi.org/10.1016/j.crvasa.2014.07.001>

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## Introduction

The cerebrovascular accident ranks among the main causes of the mortality and morbidity worldwide. In the Czech Republic, the cerebrovascular disease was the direct cause of death in 10% cases in the year 2012 (Healthcare Annual CZ 2012). It is predictable that the increasing life expectancy and the growing incidence of stroke risk factors in population will bring even higher incidence and prevalence [1].

The therapy of patients with the ischaemic form of stroke or the transient ischaemic attack (TIA) – which is considered an equivalent clinical unit – includes not only the acute treatment but, in addition to that, the earliest possible assessment of the aetiology for the purpose of secondary prevention.

Cardioembolism is one of the possible causes of the stroke. It is responsible for about 15–30% of ischaemic attacks [2–4]. The prognosis of patients with cardioembolic type of stroke is significantly adverse – 50% of the patients die within 3 years and unidentified origin of the embolization increases the incidence of the next attack two to three times [2,5]. Recognition of aetiology is the basic principle here, as an accurate diagnosis often initiates a change of the therapy strategy.

Cardioembolic aetiology is suspected if the neurological deficit develops rapidly. The neurological deficit is the largest at the beginning and it is mostly severe. The ischaemia most often affects the cortex or it causes subcortical lenticulostriate infarctions. The infarctions may be multilobar and of different time of origin. More systemic thromboembolic symptoms can be present (affecting e.g. kidneys or spleen) [2,5].

The most common origin of cardioembolism is the atrial fibrillation – be it paroxysmal, persistent, or the chronic one (it is supposed to be responsible for 50% stroke of cardioembolic origin) [2]. Other diseases like acute myocardial infarction, ischaemic cardiomyopathy (mostly with aneurysm formed in the left ventricle), dilated cardiomyopathy, pathological intracardial mass presence (intracardial thrombus or tumour), vegetation in infective endocarditis, rheumatic heart disease (especially mitral stenosis) and the presence of a mechanical valve prosthesis significantly increase the cardioembolic disease incidence. Other possible factors with lower risk include the patent foramen ovale, presence of an atrial septum aneurysm, aortic valve calcification, mitral annular calcification, mitral valve prolapse or giant Lambl's excrescences [2,4,6,7].

In many cases, the presence of a heart disease that is behind the cardioembolic stroke is evident as soon as the patient's history has been taken and the initial examinations routinely done at every patient have been done (ECG – 12-lead graphic record and continual heart rhythm monitoring after the patient's admission) [1]. A transthoracic echocardiographic examination is performed if need be. If these examinations do not reveal an embolic origin, the transoesophageal probe examination is indicated. Generally it is indicated in younger patients with ischaemic stroke of unknown origin, patients with valve prosthesis, and patients with suspected infective

endocarditis [3,5] and in the case of a difficult interpretable transthoracic diagnosis.

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## Aim

In the present literature only limited information is available about findings in transoesophageal echocardiographic examinations in patients with ischaemic stroke or TIA. Available papers dealing with this issue come from the nineties, their conclusions may therefore be difficult to interpret in retrospect because of an advance in a technical quality of echocardiographic apparatus and transoesophageal probes (nowadays multiplanar are used as a standard) and development of view of a cardioembolic potential of the individual heart diseases [6,8]. The aim of our study was to evaluate the actual transoesophageal echocardiographic findings (TOE) in patients with suspicion for cardioembolic stroke or TIA who were indicated to this examination in our echocardiography laboratory.

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## Methodology

During the period from July 2009 to March 2013 (45 months), 1207 TOE had been realized in our echocardiography laboratory. 95 patients from this group were put into our group. These are patients who suffered an ischaemic stroke or TIA. Everybody was examined by a neurologist on admission. He indicated a graphic examination of the brain and the afferent cerebral arteries, according to a clinical situation and he expressed a suspicion of cardioembolic aetiology of the ischaemic stroke/TIA. It was thought of the cardioembolic aetiology of an ictus in the case of a typical clinical picture and an anamnesis, a diagnosis compatible with a cerebral ischaemia on the graphic examinations and simultaneously an absence of a significant stenosis of an ipsilateral carotid artery (i.e. stenosis  $\geq 50\%$ ) or a vertebral artery. In the case of the patients with TIA an exclusion of the significant stenosis of the ipsilateral carotid artery or the vertebral artery and the typical clinical picture was enough. The age of the patients was not a deciding factor in indicating TOE. There were 75 patients with the ischaemic stroke in total and 20 patients with TIA in a carotid and vertebrobasilar basin. The patients with lacunar infarcts were not included in the group.

Chart 1 presents a representation of the individual graphic examinations used for diagnostics of the cerebral ischaemia and an imaging of the afferent cerebral arteries.

In order to get the basic characteristics of the patients (present risk factors of stroke, comorbidity, antithrombotic therapy at the beginning of the stroke), we used the patients' medical records.

Echocardiographic examination with transoesophageal probe itself always followed after transthoracic examination. An examining echocardiographer decided on the indication of TOE definitively. A patient was equipped with peripheral vein catheter for application of premedication. Subsequently it was used for application of the echo contrast not passing through pulmonary microcirculation; in our case, the agitated physiological solution was used.

Brain imaging		
Method	Number of patients	%
Noncontrast CT scan	87	91.6
Contrast CT scan	74	77.9
Magnetic resonance	31	32.6
Large vessels imaging		
Method	Number of patients	%
Duplex Ultrasonography	20	21.1
CT angiography	75	78.9
MR angiography	3	3.2
Digital subtraction angiography	4	4.2

**Chart 1 – Brain and large vessels imaging.**

We monitored the occurrence of pathological findings that have the cardioembolic potential according to the literature.

A thrombus is defined as echo dense mass distinguishable from endocardium, formed in left atrium or left ventricle. It is observable in at least two views and it is distinguishable from the pectinate muscles and trabeculae. It typically occurs in the left atrium auricle, or in its apex. Most often it adheres to the side in the left ventricle which is hypokinetic or akinetic, and is obvious both during systole and diastole [5].

A tumour is another intracardial solid formation with cardioembolic potential. The most common primary tumour we can find in the heart is the myxoma. It is a movable polypoid formation attached to the endocardial tissue by a stem, most frequently found in the left atrium in the area of fossa ovalis; less common is the myxoma in the right atrium or the left ventricle. The papillary fibroelastoma is the most common tumour of the valves and it is morphologically hard to distinguish from vegetation [9].

Vegetation is the mass adhering to the valve and usually it is distinguishable by its echogenicity and its active movement independent on the valve. In fewer cases the vegetation can adhere to papillary muscles, to the suspension apparatus of the cuspid valves or the endocardium of cardiac cavities [5].

The presence of a patent foramen ovale (PFO) was identified by the means of agitated physiological solution (i.e. echo contrast not passing through pulmonary microcirculation) applied into the peripheral vein. The presence of microbubbles in the left atrium during 3 cycles following the opacification of the right atrium (either spontaneous, or using the Valsalva manoeuvre) was considered the diagnosis of a PFO presence [10]. The size of a shunt could not be determined from the documentation unambiguously and so in all cases, we gave in the evaluation of this parameter.

An atrial septal aneurysm was defined as a permanent prolapse at the area of fossa ovalis with the base diameter 10 mm at least, either a prolapse protruding at least 10 mm in one direction, or an intermittent prolapse into the left/right atrium with the excursion of at least 10 mm [5,11]. Its occurrence usually coincides with PFO.

An aortic valve calcification was defined as a hyperechogenicity of the tip connected with its lower mobility, and the mitral valve calcification as a hyperechogenicity of a lumpy shape of 3 mm in the diameter at least [3].

A mitral valve prolapse was defined as a systolic displacement of a leaflet or leaflets at least 1 mm relative to the line connecting annular hinge points in parasternal long axis projection.

Stages IV and V (complex sclerotic plates at least 4 mm wide, occasionally with a mobile component – thrombus), were considered a significant atherosclerotic involvement of the thoracic aorta [5].

The left atrium volume was examined in relation to the risk of paroxysmal atrial fibrillation as a cause of ischaemic stroke. The size was divided into categories according to the volume, covering normal volume ( $22 \pm 6$  ml/m<sup>2</sup>), mild dilatation (29–33 ml/m<sup>2</sup>), moderate dilatation (34–39 ml/m<sup>2</sup>) and severe left atrium dilatation ( $\geq 40$  ml/m<sup>2</sup>) [12]. In some of the patients, the ejection speed of the left atrium auricle was determined.

## Results

Our set of patients consisted of 95 people. Their basic demographic data, atherosclerotic risk factors and other associated diseases are presented in Chart 2. In 88 cases it was possible to identify what antithrombotic therapy the patient was given before the onset of ischaemic stroke/TIA (see Chart 3).

In average, the transoesophageal echocardiography was performed 19 days following the ischaemic stroke/TIA (SD 34, the absolute time span between the stroke and the examination was 0–169 days). For the findings see Chart 4.

Knowledge of the clinical situation, in which the examination was indicated, is necessary for the precise interpretation of the diagnoses of the transoesophageal echocardiography. As mentioned above, there are several indications for the transoesophageal probe examination – the suspect of the infective endocarditis, the presence of the mechanical valve prosthesis, the ictus in the patients, which origination could not be explained by an atherosclerotic affection of the afferent cerebral arteries, and the patients with the difficult interpretable transthoracic diagnosis.

The suspect of the infective endocarditis (i.e. a febrile condition and elevation of inflammatory parameters at the time of the ictus origination) was in our group of indications for execution of the transoesophageal echocardiography in

	Number of patients	%
Gender - male	54	56.8
- female	41	43.2
Arterial hypertension	47	49
Diabetes mellitus	8	8.4
Nicotine addiction	37	38.9
Dyslipidemia	57	60
Chronic lower limb ischemia	54	4.2
Ischemic heart disease	4	4.2
COPD	3	3.2
Obesity	20	21
Atrial fibrillation	9	9.5
Age	Average 52 years (19–83 years)	

**Chart 2 – Basic demographical data, cardiovascular diseases and risk factors.**

Therapy	Number of patients	%
Effective warfarinisation	6	6.4
Ineffective warfarinisation	0	0
Acetylsalicylic acid	8	8.4
Clopidogrel	1	1.1
Dual antiplatelet therapy	3	3.1
LMWH	1	1.1
No treatment	69	72.6
Unknown treatment	7	7.3

**Chart 3 – Antithrombotic therapy before onset of ischaemic stroke/TIA.**

10 patients. This diagnosis was confirmed in 3 of them. In other cases, 2 patients had a respiratory infection, in 1 patient the source of the infection was a carious dentition, and in other one it was a wound on a lower arm after a dog bite. The source of the infection could not be identified 2 times. In the last patient was the non-infectious inflammation, it was an autoimmune vasculitis. In this group of patients the diagnostics focused from the beginning on the presence of vegetation, or paravalvular spread of the inflammation. From the point of view of the suffered ictus the patients were treated after exclusion of the infective endocarditis by the standard

anti-aggregation treatment or the anticoagulant treatment, if they had the atrial fibrillation.

Another group of the patients indicated for the transoesophageal probe examination were 5 patients with valvular prosthesis. Its dysfunction, the presence of the thrombus or the vegetation was not established in a single one.

After exclusion of the patients with the suspect of the infective endocarditis and with the valvular prosthesis, the group of the patients with the ictus remains, which could not be explained by the atherosclerotic affection of the cerebral arteries. These are 81 patients. Their average age was 48 years,

	Number of patients	%
Foramen ovale patens	30	31.6
Atrial septal aneurysm	3	3.2
Atrial septal defect	3	3.2
Thoracic aortic atherosclerosis	8	8.4
Aortic valve calcification	7	7.4
Mitral valve calcification	3	3.2
Mitral valve prolapse	3	3.2
Infective endocarditis	3	3.2
Intracardiac thrombus	2	2.1
Left ventricle systolic dysfunction	4	4.2
Negative finding	41	43

**Chart 4 – Oesophageal echocardiography findings in whole group of patients.**

	Number of patients	%
Foramen ovale patens	30	37
Atrial septal aneurysm	3	3.7
Atrial septal defect	3	3.7
Thoracic aortic atherosclerosis	6	7.4
Aortic valve calcification	5	6.2
Mitral valve calcification	1	1.2
Mitral valve prolapse	1	1.2
Intracardiac thrombus	2	2.1
Left ventricle systolic dysfunction	2	2.5
Negative finding	37	45.7

**Chart 5 – Oesophageal echocardiography findings in patients with ischaemic stroke/TIA of unknown origin.**

which ranged from 19 years to 77 years. The transoesophageal echocardiography diagnoses of this subgroup of the patients are stated in the [Chart 5](#) in the summary.

The most frequent diagnosis here was the foramen ovale patens, it was discovered in 37% of the patients. In 3 cases it was connected with the presence of the atrial septal aneurysm. Another possible basis for a paradoxical embolization is the atrial septal defect, which was discovered in 3 patients in this subgroup. All of the atrial septal defects were insignificant in terms of haemodynamics.

A thrombus was found only in 2 patients; in one of the cases it adhered to the mitral valve (the thrombus was confirmed by a histological examination after the surgical removal), the other was located in the left atrium auricle.

In the subgroup of the ischaemic stroke/TIA of the unknown origin was quite negative diagnosis present in 46% of the patients. In the whole group (i.e. including the patients examined for the suspect of the infective endocarditis and the patients with the valvular prosthesis) the negative diagnosis was present in 43% of the patients.

The atrial fibrillation was present altogether in 9 patients from the whole group. It is by itself the indication for the anticoagulant treatment. Reasons for why was the examining programme in these patients extended by TEE as were following – the suspect of the infective endocarditis (in 2 patients), the presence of the valvular prosthesis (in 2 patients), effective warfarinization at the time of origin of the cerebral ischaemia (3 patients), and the unclear transthoracic diagnosis with the suspect of a waving structure on a mitral valve (1 patient). The paroxysmal atrial fibrillation was discovered in the last patient only after the transoesophageal echocardiography.

The left atrium volume was determined in 86 cases (see [Chart 6](#) for the results). Only 35 patients (40.7%) had a normal

left atrium volume. The ejection speed of the left atrium auricle was determined in 27 cases. Low speed (less than 0.5 m/s) was registered in 4 patients. It was always connected with severe left atrium dilatation and in one case with atrial fibrillation.

## Discussion

The echocardiographic examination with oesophageal probe should either confirm or eliminate the presence of diseases that need a change in the therapy strategy in patients with ischaemic stroke or TIA. This examination is generally indicated in patients with suspected cardioembolic aetiology of ischaemic stroke/TIA that was not proven by non-invasive tests including transthoracic echocardiography, in patients with suspected infective endocarditis, and in patients with mechanical valve prosthesis.

An ischaemic stroke connected with permanent atrial fibrillation is a clear indication for permanent anticoagulation therapy. Sometimes it is difficult to diagnose paroxysmal atrial fibrillation in a patient with stroke of unknown origin if the arrhythmia has not been detected during the admission of the patient to the stroke unit or during the subsequent monitoring [5,13]. In such a case the oesophageal echocardiography can help with evaluation of the left atrium volume, the left atrium auricle function and, although rather rarely, it may display the thrombus itself. The heavily dilated left atrium and the low ejection speed of the auricle is the sign of the dysfunction of the left atrium. It is by itself suspected of the possible occurrence of the atrial fibrillation. A rhythm monitoring extension with Holter ECG or reveal loop monitoring after the discharge seems to be a reasonable decision [14].

Size		Number	%
Normal size	16–28 ml/m <sup>2</sup>	35	40.7
Mild dilatation	29–33 ml/m <sup>2</sup>	22	25.6
Moderate dilatation	34–39 ml/m <sup>2</sup>	10	11.6
Sever dilatation	≥40 ml/m <sup>2</sup>	19	22.1

**Chart 6 – Left atrium size.**



The presence of a thrombus in the left ventricle in relation to an ischaemic stroke is an indication for permanent anticoagulation treatment as well. This therapy is inevitable especially in the case of big movable thrombi protruding to the left ventricle cavity or in the case of thrombi detected in relation to an acute heart attack. Sessile thrombi attached to the wall constitute lower cardioembolic risk. A transthoracic echocardiographic examination for thrombus detection in the left ventricle is usually sufficient [5], which is possibly the reason why there was no occurrence of an intraventricular thrombus in our sample. However, it is necessary to understand thromboembolism as a dynamic process. It is possible for a thrombus to form in the heart and to embolize subsequently, leaving no obvious residues detectable by echocardiography until a new thrombus is formed. In a cardioembolic incident, any pathology i.e. the dilatation and the heavy systolic dysfunction of the left ventricle or the presence of the post-infarct aneurysm that has a disposition for the formation of intracardial thrombi should be a sufficient reason for an anticoagulation therapy [2].

A change in treatment strategies in patients with a stroke is unavoidable if vegetation has been found and, therefore, infectious endocarditis diagnosed. The diagnosis of such a case is the domain of oesophageal echocardiography.

The most common heart tumours are metastatic or malignant tumours growing through the heart tissue. In such cases, the basic disease has been usually diagnosed earlier and the disease is in an advanced stage already. Echocardiography can bring significant benefits in the diagnosis of primary benign tumours [9]. These, however, are very rare and no case of brain ischaemia had an origin in a heart tumour in our sample.

The oesophageal echocardiography is an excellent modality for presenting minor cardiac shunts that create the pathophysiological basis for paradoxical embolism. Patent foramen ovale is the most common of them and its incidence in population is between 25% and 30% [4,16]. In our sample, 37% of patients with ischaemic stroke/TIA of unknown origin have been identified to have PFO. The systemic embolism risk increases with the occurrence of an atrial septal aneurysm and with the size of the shunt. A shunt is considered large if over 20 microbubbles get to the left atrium during Valsalva manoeuvre [5,17]. Patients with suspected paradoxical embolism through PFO causing ischaemic stroke may be treated, apart from antithrombotic therapy, with a shunt closure by the means of an occluder. The recent RESPECT and PC Trial studies' results are available [10,7], which allow for a conclusion that the transcatheter closure in correctly indicated patients is no inferior option compared to antithrombotic therapy. In our sample, the closure was indicated and implemented in 11 cases of 30 PFO detected. These patients were then treated by the dual antiplatelet therapy (acetylsalicylic acid + clopidogrel) for 6 months, then by the monotherapy with the acetylsalicylic acid permanently. It was proceeded conservatively in the other 19 patients on account of their preference, eventually on the basis of the indication for the anticoagulant treatment on account of the present coagulation disorder.

The significance of the mitral valve prolapse is questionable. Historically, it was considered a classical cardioembolic source. At present, this mitral valve inflection is regarded as

generally benign and its possible connection with cardioembolism as unproven [2,18]. Its occurrence was low also in our sample.

The role of calcifications in the mitral annulus in the cardioembolic formation is similarly controversial. Patients with this kind of inflection have higher incidence of cardiovascular disease and death but it is attributed mostly to the atherosclerotic inflection of cardiovascular apparatus (either obvious or subclinical) rather than cardioembolism. Further treatment should be derived from the associated diseases (such as IHD, atrial fibrillation, etc.) [2,19].

An isolated degenerative aortic valve inflection is not considered a disease with clinically significant embolic potential either.

An aortic atherosclerotic involvement can be diagnosed by TOE. It can be the cause of embolism to CNS. This is not a cardioembolic stroke but the embolism coming from the great blood vessels (the subtype I according to TOAST criteria). The treatment in this case should be aimed at massive reduction of LDL cholesterol. Both antiaggregation therapies using acetylsalicylic acid and anticoagulation warfarin therapy can be considered. The new ARCH study will, hopefully, help us decide which antithrombotic therapy is preferable in this case.

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## Conclusion

Determination of the correct aetiology of the cerebrovascular accident or the transitory ischaemic attack is essential for the decision for the long-term treatment to reduce the risk of the ictus recurrence. If the patient suffers the cerebral ischaemia and the significant carotid stenosis was not discovered, he will be treated by the antiplatelet therapy standardly. This need not be sufficient in the case of the cardioembolic aetiology of the ictus.

Transoesophageal echocardiography is an independent method in examination of potential sources of cardioembolism. In our sample, a pathology in more than half of the patients was diagnosed that could refer to a suffered ischaemic stroke and in 17 cases (i.e. at 18%) it led to the change of the treatment strategy – the infective endocarditis was treated in 3 cases, the patient was indicated for the anticoagulant treatment for the diagnosis of the thrombus in the left atrium auricle in 1 case, the structure from the mitral valve was removed cardiosurgically at 1 time (it was diagnosed also as the thrombus on the basis of the histological analysis consequently), the patient underwent the catheterization closure of the atrial septal defect in 1 case and FOA was occluded 11 times.

However, not every heart inflection has the same cardioembolic potential and many heart diseases coexist with atherosclerosis in other locations including CNS.

An echocardiographer who examines the patient with ischaemic stroke should be aware of these issues. He/she should perform the examination concerning all clinical units of embolic potential relevant for the decision on the subsequent treatment. The finding is to be always interpreted within the context of the results of other examinations and patient's comorbidity.

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## Conflict of interest

The authors rule out any potential or real conflict of interests concerning their study.

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## Ethical statement

The patient was treated in accordance with ethical standards, *lege artis*.

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## Informed consent

An informed agreement with the treatment was not necessary in this case.

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