

Transoesophageal echocardiography in selecting patients for anticoagulation after ischaemic stroke or transient ischaemic attack

M Strandberg, R J Marttila, H Helenius, J Hartiala

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See end of article for authors' affiliations

Correspondence to:
Dr M Strandberg, Turku University Hospital, Department of Clinical Physiology, Kiinamyyllynkatu 4-8, 20520 Turku, Finland; marjatta.strandberg@phks.fi or marjatta.strandberg@tyks.fi

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Objectives: To investigate prospectively the role of transoesophageal echocardiography (TEE) in selecting patients for anticoagulation in an unselected stroke population.

Methods: Transthoracic echocardiography (TTE) and TEE were done in all clinically suitable hospitalised patients (n = 457) with transient ischaemic attack or ischaemic stroke in the acute phase during a two year period in Turku University Hospital. 441 patients were successfully evaluated for cardiac sources of embolism using TEE within 31 days of the event.

Results: A major risk factor for a cardiac source of embolism excluding atrial fibrillation, acute myocardial infarction, and prosthetic valve was detected in 10% of patients and a minor risk factor for a cardiac source of embolism in 46%. When a major risk factor of a cardiac source of embolism was detected using TTE or TEE and no contraindications were present, the patient was given anticoagulation drugs. If a minor risk factor for a cardiac source of embolism was detected, anticoagulation treatment was started after clinical assessment, if no contraindications were present. In 62 (14%) cases, the patient was given oral anticoagulation drugs or the necessity of ongoing anticoagulation treatment was confirmed on the basis of TEE. When these anticoagulation treated patients were evaluated using logistic regression analysis, they were found to have significantly more atrial fibrillation and histories of myocardial infarctions. Moreover, the patients were mainly men. When patients in sinus rhythm and without any history of cardiac disease were analysed, 8% of patients were found to have been given anticoagulation drugs on the basis of TEE data.

Conclusion: This study suggests that TEE should be used in patients with stroke even without any clinical evidence of cardiac disease when the patients are candidates for anticoagulation.

Transient ischaemic attacks (TIA) or ischaemic strokes are caused by cardiac embolism in 15–40% of cases.^{1–8} Transoesophageal echocardiography (TEE) has proved more sensitive than transthoracic echocardiography (TTE) in diagnosing intracardiac sources of embolism.^{9–16} With the use of TEE, a potential cardiac source of embolism has been found in 41–57% of patients with ischaemic stroke or TIA.^{9–12}

Patients with cardiac disorders diagnosed using TEE may benefit from anticoagulation drug treatment for secondary prevention of recurrent cerebral embolism.³ However, the place of echocardiography in selecting patients for anticoagulation remains to be determined. When 19 studies (n = 3524) on the effect of TTE in patients with suspected systemic arterial embolism were evaluated, a new therapeutic concept emerged from TTE in 4% of the examinations.¹⁷ Although TEE has improved the visualisation of the left atrium, the mitral and aortic valves, and the aorta, only a few authors have studied the effect of TEE on the decision to use anticoagulation for stroke and TIA.^{12–18–19} In one study,¹² TEE changed management in only 5% of cases, but the authors did not discuss cases where TEE was used to confirm the necessity of ongoing anticoagulation. In another study,¹⁸ TEE had influenced the management of 10% of patients. That study included patients with atrial fibrillation; anticoagulation may thus have been indicated regardless of TEE results. In a third study,¹⁹ all patients were in sinus rhythm, had non-diagnostic TTE, and had no carotid artery stenosis. TEE changed the management of 10% of patients. It is noteworthy that study groups in all these previous studies were small, ranging from 30 to 63 patients. As the effect of routine TEE on the decision to start anticoagulation treatment in unselected stroke populations is controversial, we decided to readdress the question

in a larger patient population. Moreover, we wanted to determine what kind of patients benefit most from this examination.

PATIENTS AND METHODS

During a two year period from 1 January 1997 through 31 December 1998, 457 consecutive patients with TIA or ischaemic stroke in the acute phase were routinely admitted to undergo a TEE examination in the Department of Clinical Physiology at Turku University Hospital.

Only 16 of the patients were excluded from the study because of severe swallowing problems on TEE. The remaining 441 patients were successfully evaluated for cardiac sources of embolism using TEE, most of them (85%) within a week and all within 31 days (mean 5.5 days, median 4.6 days) of the event. The patients' medical records including laboratory and imaging studies were reviewed retrospectively. The findings from TEE, the patients' medical records, and the results of other examinations were collected for statistical analysis.

The basic study population (n = 441) was unselected, and the age of the patients ranged from 21 to 86 years (mean 63, median 65). In this population, 259 (59%) were men and 182 (41%) were women. The Ethics Committee of the University of Turku and University Central Hospital of Turku approved the study.

Abbreviations: CI, confidence interval; OR, odds ratio; TEE, transoesophageal echocardiography; TIA, transient ischaemic attack; TTE, transthoracic echocardiography

Table 1 Modification of Hart's classification of echocardiographic findings

Major risk factors	Minor risk factors
Left atrial cavity thrombus	Mitral valve prolapse
Left atrial appendage thrombus	Mitral annular calcification
Left ventricular thrombus	Calcified aortic stenosis
Aortic thrombus	Patent foramen ovale
Atrial myxoma	Slow flow (spontaneous echo contrast)
Vegetation	Atrial septal aneurysm
Infective endocarditis	Left ventricular aneurysm
Marantic endocarditis	Aortic aneurysm
Dilated cardiomyopathy	False tendon
Mitral valve stenosis	Aortic arch plaques

Abnormalities on transoesophageal echocardiography (TEE) that are potential cardiac sources of embolism are listed as major or minor risk factors. Atrial fibrillation, acute myocardial infarction, and prosthetic valve are also major risk factors but not listed here because they can be identified without TEE.

The echocardiographic examinations were done using the Acuson 128 XP (Acuson Corp, Mountain View, California, USA) echocardiographic system and a 2.5–3.5 MHz scanning frequency linear array transducer for TTE, as well as a 5.0 MHz biplane and a 5.0 MHz multiplane transducer for TEE. TTE was done before TEE in all patients. The TEE study was done in awake patients using lidocaine gel for local pharyngeal anaesthesia; no other medication was needed. Standard imaging TTE and TEE planes (basal short axis, two chamber, four chamber, transgastric short axis and thoracic aorta) were viewed in all patients.²⁰ Dimensions were measured from the TTE parasternal long axis view, and an injection of intravenous sterile isotonic saline and Valsalva manoeuvre were routinely given to every patient. The echocardiograms were stored on videotape.

The echocardiographic findings were categorised according to a modification of Hart's classification.^{21–23} Consequently, echocardiographic abnormalities were considered major or minor risk factors for cardiac sources of embolism (table 1). When a major risk factor for a cardiac source of embolus was detected in TEE and no contraindications were present, the patient was given anticoagulation drugs. Atrial fibrillation, acute myocardial infarction, and prosthetic valve were not included in the major risk factors in this study because they are identified before TEE. If a minor risk factor for a cardiac source of embolism was detected, anticoagulation treatment was started after clinical consideration of the probability of cardiac embolism and treatment hazards.

Statistical analysis

The statistical analyses were done using SAS statistical software (version 8.00 for Windows, SAS Institute, Cary,

North Carolina, USA). The results are expressed as means (SD) and percentages where appropriate. Two by two tables were constructed to analyse associations between the groups. Significance was tested using the χ^2 test and Fisher's exact test. The level of significance for testing all null hypotheses was a two tailed $p < 0.05$. Odds ratios (ORs) and confidence intervals (95% CIs) were calculated for the risk factors. A logistic regression analysis was used to model the profile of the person to be in that group where TEE findings changed or confirmed the necessity of management. The two sample t test was used to compare the mean age of patients receiving anticoagulation drugs with the mean age of the other examined patients.

RESULTS

Of all 441 studied patients, 73% had an ischaemic stroke and 27% had a TIA. Table 2 shows a more specific division by subtype. Coronary artery disease was present in 24% of the patients and 50% of them also had a history of myocardial infarction, and three patients had an acute myocardial infarction when hospitalised. Of these patients, 23% had undergone coronary artery bypass or percutaneous transluminal coronary angioplasty. Of all examined patients, 7% had had manifestations of congestive heart failure, 2% had a history of valve disease, and only 2% had been given anticoagulation drugs previously. Fourteen per cent of the patients had a history of chronic (2%) or paroxysmal (12%) atrial fibrillation.

We identified a major or a minor risk factor for a cardiac source of embolism (table 1) in 49% of patients examined, and when the plaques in the descending aorta were included, in 57%. A major risk factor was identified in 10% of patients and a minor risk factor in 46% in the study population. Of those with stroke or TIA, 62 (14%) were being given anticoagulation drugs or their ongoing anticoagulation treatment was justified on the basis of TEE. In 17 of the 62 patients, the suspected source of embolism had already been detected on TTE, but even in these cases TEE often gave useful additional information (eight thrombi, two slow flows, and four aortic plaques). Only in five cases did TEE not give additional information.

Patients with atrial fibrillation had significantly more major ($p < 0.001$, OR 6.8, 95% CI 3.5 to 13.3) and minor ($p = 0.01$, OR 2.1, 95% CI 1.2 to 3.6) risk factors for cardiac sources of embolism than those in sinus rhythm. If patients with atrial fibrillation were excluded, 36 of 381 (9%) were still receiving anticoagulation drugs on the basis of TEE data: 23 of 36 because of a major and 13 of 36 because of a minor risk factor for a cardiac source.

In the anticoagulation treated group ($n = 62$), 41 thrombi were found on TEE (table 3). Of these, 21 were in the left atrial appendage, eight in the descending aorta, seven in the aortic

Table 2 Classification of ischaemic stroke and transient ischaemic strokes (TIA) by subtypes

	No (%)	Male (%)	Mean (SD) age (years)
Transient ischemic attack			
Carotid TIA	68 (16)	59	59 (11)
Vertebrobasilar TIA	50 (11)	64	64 (9)
Infarction			
Anterior cerebral artery	9 (2)	56	65 (3)
Middle cerebral artery	186 (42)	58	64 (11)
Posterior cerebral artery	32 (7)	53	61 (12)
Brainstem	51 (12)	59	63 (11)
Cerebellum	24 (5)	63	59 (12)
Lacunar infarction	21 (5)	57	65 (8)
Total	441 (100)		

The patients were divided into subgroups by a neurologist on the basis of computed tomography or magnetic resonance imaging findings, or of clinical manifestations.

Table 3 Cardiac risk factors for embolism detected using transthoracic echocardiography (TTE) and TEE in 441 unselected patients with stroke or TIA

Cardiac risk factors for embolism	Detected by TTE No (%)	Detected by TEE No (%)
Major risk factors		
Left atrial cavity thrombus	2 (0.5)	*
Left atrial appendage thrombus	0	21 (4.8)
Left ventricular thrombus	2 (0.5)	*
Aortic thrombus	0	16 (3.6)
Dilated cardiomyopathy with ejection fraction <35%	7 (1.6)	*
Mitral valve stenosis	1 (0.2)	*
Minor risk factors		
Mitral valve prolapse	21 (4.8)	*
Mitral annular calcification	8 (1.8)	*
Calcified aortic stenosis	6 (1.4)	*
Patent foramen ovale	0	67 (15.2)
Slow flow (spontaneous echo contrast)	0	20 (4.5)
Atrial septal aneurysm	20 (4.5)	*
Left ventricular aneurysm	10 (2.3)	*
Aortic aneurysm	0	1 (0.2)
False tendon	7 (1.6)	*
Aortic plaques	0	73 (16.6)

*Similar number was detected by TEE as by TTE.

arch, one in the left ventricle, one in a left ventricular aneurysm, one in an aortic arch aneurysm, one in an atrial septal aneurysm, and one attached to a prosthetic mitral valve. Of the patients receiving anticoagulation drugs, 15 of 62 (24%) had a patent foramen ovale. Twelve of these 15 patients were receiving anticoagulation drugs on the basis of the patent foramen ovale, and in all these cases pronounced right to left shunting was seen on Valsalva manoeuvre. In 12 of 62 (19%) cases, the left ventricle was dilated, but in only two was it in the patient's recorded history. Slow flow (spontaneous echo contrast) was detected in 16 of 62 (26%) patients, and in five anticoagulation treatment was started mainly for this reason. Two of the patients were treated mainly for left ventricular wall motion abnormality and two for left ventricular aneurysm. Thirteen cardiac aneurysms were found in the anticoagulation treated group, and none of these cardiac aneurysms had been identified before the examination.

We analysed more closely the group of 62 patients in whom TEE changed or confirmed the necessity of management. The age of the patients ranged from 21 to 86 years (mean 63, median 65), and the difference in age was not significant ($p = 0.27$) between them and the rest of the patients ($n = 379$) examined, here considered to be the non-anticoagulation treated group on the basis of TEE. No significant dominance of any subtype of infarction or TIA was seen. Of patients receiving anticoagulation drugs, 49 of 62 (79%) were men, significantly ($p < 0.001$) more than women (table 4), and 26 (42%) had atrial fibrillation, which was naturally

significantly more ($p < 0.001$) than the rate for the non-anticoagulation treated group. Significantly more had coronary artery disease ($p = 0.006$). These patients significantly more often had histories of myocardial infarction ($p = 0.003$) than patients in the non-anticoagulation treated group on the basis of TEE. Significantly more had histories of valve disease ($p = 0.016$) and congestive heart failure ($p = 0.002$). Only 7 of 62 (11%) patients received anticoagulation drugs when they experienced their ischaemic attacks. Two of the patients had a prosthetic mitral valve, and in five of seven patients anticoagulation treatment was inadequate.

In this study, 26 of 62 patients could already have been given anticoagulation drugs on the basis of atrial fibrillation. There were still 36 patients in sinus rhythm who were treated on the basis of their TEE findings. When these 36 patients were analysed more closely, significantly more men ($p < 0.001$, OR 5.1, 95% CI 1.9 to 13.5) were seen in this group with a significantly higher prevalence of coronary artery disease ($p = 0.02$, OR 2.4, 95% CI 1.2 to 5.0) and previous myocardial infarctions ($p = 0.02$, OR 3.0, 95% CI 1.3 to 6.8) than were seen in other patients in sinus rhythm.

When the patients in sinus rhythm and with no history of cardiac disease were evaluated as an independent group, in 22 of 286 (8%) patients anticoagulation treatment appeared to be based on TEE data. In this group, a major risk factor for a cardiac source of embolism was found in 5% of patients and a minor risk factor for a cardiac source of embolism in 39%.

On logistic regression analysis ($n = 441$), adjusted by the other variables, the strongest predictor of the effect of TEE on

Table 4 Cerebrovascular risk factors and their prevalences in patients who received anticoagulation drugs on the basis of TEE findings and the other patients examined

	Anticoagulation (n=62) No (%)	No anticoagulation (n=379) No (%)	p Value	OR	95% CI
Men	49 (79)	210 (55)	<0.001	3.0	1.6 to 5.8
Atrial fibrillation	26 (42)	34 (9.0)	<0.001	7.3	4.0 to 13.6
Coronary artery disease	24 (39)	81 (21)	0.006	2.3	1.3 to 4.1
Previous myocardial infarction	15 (24)	37 (9.8)	0.003	3.0	1.5 to 5.8
Valve disease	4 (6.5)	4 (1.0)	0.016	6.5	1.6 to 26.6
Congestive heart failure	11 (18)	21 (5.5)	0.002	3.7	1.7 to 8.1
Hypertension (medication)	20 (33)	148 (39)	NS	0.7	0.4 to 1.3
Hypercholesterolaemia (medication)	8 (13)	28 (7.4)	NS	1.9	0.8 to 4.3
Diabetes	16 (26)	84 (22)	NS	1.2	0.7 to 2.3

CI, confidence interval; OR, odds ratio.

the decision to give the patient anticoagulation drugs was, as expected, atrial fibrillation ($p < 0.001$, OR 7.7, 95%CI 4.0 to 14.7). The other significant predictors were male sex ($p < 0.003$, OR 2.8, 95%CI 1.4 to 5.6) and previous myocardial infarction ($p = 0.005$, OR 2.9, 95%CI 1.4 to 6.1).

DISCUSSION

TEE is a useful tool for detecting potential intracardiac or aortic sources of embolism. It has proved to be superior to TTE in the identification of structural changes related to possible cardiac embolism, especially in the absence of any clinical evidence of cardiac disease.^{11–23} Such cardiac changes include thrombi, patent foramen ovale, atrial septal aneurysm, slow left atrial flow, and myxomatous degeneration of the mitral valve associated with mitral valve prolapse.¹⁰ However, it remains to be determined whether all patients should undergo TEE. Previous studies with TEE have shown a high frequency of cardiac changes in patients with stroke, not only in those with but also in those without heart disease.^{10–11, 13–24, 25} No established guidelines for patient selection are available yet.

Our study was done to determine the usefulness of TEE as a routine examination in unselected patients with stroke. TEE was done in 441 patients with ischaemic stroke or TIA very soon after the onset of symptoms (mean 5.5 days), and in 62 (14%) cases it led to anticoagulation treatment. In some cases, TEE was done rather late and something important may therefore have been overlooked. When all patients with atrial fibrillation were excluded from the analysis, it was found that TEE caused a change in or confirmed the appropriateness of management of 36 of 381 (9%) patients.

The presence of a major risk factor for a cardiac source of embolism (table 1) or some of the minor risk factors detected by TEE may predict future thromboembolic events, indicating the need for long term anticoagulation treatment. Cardiac evaluation may be indicated in patients even when a coexistent explanation for the event exists, for example, when a cerebral ischaemic event can be clinically associated with atherosclerotic disease of the carotid artery. Reportedly, 13 to 48% of patients with a potential cardiac source of embolism have significant cerebrovascular atherosclerosis.³ For example, when patients with critical carotid stenosis on carotid ultrasound in our study were analysed as a group, 8 of 47 (17%) were found to have been given anticoagulation drugs on the basis of TEE findings, although a coexistent explanation was also available.

Some clinical factors have been independently associated with stroke in previous analyses. These include increasing age, previous TIA or stroke, history of diabetes, history of heart failure, or history of hypertension.^{26–27} We found in our analysis that patients with an identified cardiac source of embolism were significantly more often men and more often had coronary artery disease, previous myocardial infarction, known valve disease, myocardial insufficiency, or atrial fibrillation.

The decision to do TEE after stroke or TIA should be based on the likelihood of the findings contributing to the patient's management. Consequently, TEE should not be considered if the patient is not a candidate for anticoagulation treatment. An algorithm has already been proposed for the use of TEE in evaluating patients with stroke or TIA.²⁸ Considering that most patients with atrial fibrillation are candidates for empirical anticoagulation treatment, the use of this algorithm would limit the use of TEE to patients with clinical evidence of heart disease but without atrial fibrillation and to those with TTE findings suggestive of a severe abnormality. This would decrease the number of TEEs by at least two thirds. However, in our study, where TEE was done in an unselected stroke population, there were reasonably many patients in sinus rhythm with no history of cardiac disease with an obvious cardiac source of embolism (22 of 286). Of these patients, 5% had a major risk factor for a cardiac source of embolism and

39% had a minor risk factor and, consequently, 8% of these patients were given anticoagulation drugs solely on the basis of TEE findings. In conclusion, the effect of TEE on the decision to give anticoagulation drugs was found to be higher than previously reported. Therefore, TEE should be used more often in patients with stroke or TIA who are candidates for receiving anticoagulation drugs and in sinus rhythm.

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Authors' affiliations

M Strandberg, J Hartiala, Department of Clinical Physiology, Turku University Hospital, Turku, Finland

R J Marttila, Department of Neurology, Turku University Hospital, Turku, Finland

H Helenius, Department of Biostatistics, University of Turku, Turku, Finland.

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