RESEARCH ARTICLE

Is transesophageal echocardiography needed for evaluating tissue-based transient ischemic attack?

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Abstract

Transient ischemic attack (TIA) is a warning signal for stroke. A comprehensive evaluation of TIA may reduce the risk for subsequent stroke. Data on the findings of cardiac evaluation with transesophageal echocardiography (TEE) in patients with TIA are sparse. Our aims were to determine the frequency of TEE performance and to investigate the findings of TEE in patients with TIA based on the new definition of TIA (*i.e.*, transient neurological symptoms without evidence of infarction). During a 4-year period (2011–2014), 1071 patients (mean age, 70 ± 13 years; female, 49.7%) with TIA were included in a prospective study and evaluated. Of 1071 consecutive patients suffering from TIA, 288 patients (27%) underwent TEE. The median time between admission and TEE was 6 days. Patients with TIA who were evaluated by TEE were younger (67 *vs.* 71 years, $P < 0.001$) than those who were not evaluated by TEE. They had a higher rate of sensibility disturbance as a TIA symptom (39% *vs.* 31%, $P = 0.012$) but a lower rate of previous stroke (15% *vs.* 25%, $P = 0.001$) and atrial fibrillation (2% *vs.* 21%, $P < 0.001$) than those who did not. Foramen ovale was detected in 71 patients (25.7%), atrial septal aneurysm in 13 patients (4.6%), and severe atherosclerotic plaques (grade 4 and 5) in the aortic arch in 25 patients (8.7%). One patient (0.3%) had a fibroma detected by TEE. In 17 of the 288 patients (6%) who underwent TEE, the indication for anticoagulation therapy was based on the TEE results, and 1 patient with fibroma underwent heart surgery. During hospitalization, 7 patients experienced a subsequent stroke, and 27 patients had a recurrent TIA. At 3 months following discharge, the rates of readmission, stroke, recurrent TIA, and death were 19%, 2.7%, 4.2%, and 1.6%, respectively. The rates of mortality (0.9% *vs.* 1.8%, $P = 0.7$), stroke risk (1.9% *vs.* 3.0%, $P = 0.8$), and recurrent TIA (5.0% *vs.* 3.9%, $P = 0.8$) were similar in patients who underwent TEE and in those who did not. Performing TEE in patients with tissue-based TIA is helpful in detecting cardiac sources for embolism and may indicate for anticoagulation.

Key Words: *transesophageal echocardiography; transient ischemic stroke; anticoagulation; management; therapy change*

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doi: *10.4103/1673-5374.235058*

Accepted: *2018-05-25*

Introduction

Transient ischemic attack (TIA) was first clinically defined in 1964 as any transient neurological deficit lasting less than 24 hours caused by focal cerebral or retinal ischemia (Marshall, 1964; 1988). Generally, TIA is considered an unstable condition and is associated with an increased risk of stroke in the following time after fist event. Previous research has shown that up to 20% of patients with TIA experienced a stroke in the following 3 months, with the most critical time being the first 48 hours after the initial event (Giles and Rothwell, 2007). New revised definitions of TIA, based on the findings of diffusion weighted imaging-magnetic resonance imaging, have been proposed (Albers et al., 2002; Easton et al., 2009). Study has also shown that tissue-based TIA is linked with a high risk of stroke (Al-Khaled and Eggers, 2013). In tissue-based TIA, a higher risk of stroke is associated with evidence of acute infarction than without (Redgrave et al., 2007; Giles et al., 2011; Amarenco et al., 2016). In addition, studies have revealed that an immediate comprehensive evaluation of TIA sources and initiation of treatment of pathological findings, for example, cardioembolic sources such as atrial fibrillation or large-artery arteriosclerosis such symptomatic carotid stenosis, as well as the immediate implementation of secondary prophylaxis, reduced the risk of stroke remarkably (Rothwell and Warlow, 2005; Lavallee et al., 2007; Al-Khaled and Eggers, 2014; Amarenco et al., 2016).

According to the recommendations of the German Stroke Society and the European guidelines of the European Stroke Organization, the evaluation of TIA sources should include cardiac evaluation by transesophageal echocardiography (TEE) to detect cardioembolic sources of TIA to prevent subsequent stroke (European Stroke Organisation Executive and Committee, 2008; Ringleb et al., 2008; Laufs et al., 2010). Data on the frequency and findings of TEE performed in patients with TIA are rare, particularly in patients with TIA who were diagnosed in accordance with the tissue-based definition of TIA. The few studies investigating TEE used data from unselected patients with TIA or stroke (Strandberg et al., 2002; Morris et al., 2009; Jauch et al., 2013; Pallesen et al., 2016). Only one study determined the pathological findings among 59 patients suffering from time-based TIA (Dawn et al., 2006). TEE is the most sensitive ultrasound investigation of the heart's structure and function and to detect cardioembolic sources causing TIA and stroke. Even the procedure is easy to perform and take short time, it has several limitations, particularly the need of expert knowledge and prior planning, *e.g.*, fasting patient, sedative or general anesthesia.

Our primary aims were to determine the frequency of TEE and to evaluate the performance of TEE in patients with TIA

Table 1 A comparison of baseline characteristics between patients undergoing TEE *vs.* those who not

	TEE		
	Yes (n = 288)	No (n = 783)	P-value
Male	148(51.5)	390(49.8)	0.7
Age (year, mean±SD)	66.8(12.4)	71.3(13.4)	< 0.001
TIA-symptoms			
Amaurosisfugax	14(4.9)	42(5.4)	0.8
Fazialisparesis	49(17.0)	139(17.8)	0.8
Dysarthria	56(19.4)	142(18.2)	0.6
Aphasia	64(22.2)	176(22.5)	0.9
Weakness	105(36.5)	269(34.4)	0.5
Sensory disturbance	111(39.1)	240(30.9)	0.012
Vertigo	70(24.7)	156(19.9)	0.1
Medical history			
Hypertension	211(73.3)	586(75.0)	0.6
Hypercholesterolemia	94(32.6)	251(32.2)	0.9
Myocardinfarction	20(7.0)	53(6.8)	0.9
Diabetes mellitus	63(21.7)	178(22.8)	0.8
Atrial fibrillation	5(1.7)	163(20.8)	< 0.001
Previous stroke	43(15.1)	199(25.5)	< 0.001
Diagnostic procedures			
cCT	284(98.6)	766(97.8)	0.4
cMRI	134(46.5)	222(28.4)	< 0.001
Brain and neck duplexsonography	286(99.3)	741(94.7)	0.1
Secondary prophylaxis before TIA			
AT	91(32.3)	309(40.6)	0.015
Oral anticoagulation	4(1.4)	130(16.7)	< 0.001
Hospitalization (day, mean±SD)	8.3±2.3	6.0±1.5	< 0.001
Stroke-Unit treatment	248(86.1)	577(73.9)	< 0.001
Stroke-Unit stay (day, mean±SD)	1.7±1.3	1.9±1.5	0.2

Data are n (%) unless otherwise indicated. TEE: Transoesophageal echocardiography; cCT: cranial computer tomography; cMRI: cranial magnet resonance imaging; TIA: transient ischemic attack; AT: antiplatelet treatment.

in accordance with the tissue-based definition of TIA.

Subjects and Methods

Study design

This prospective cohort study included consecutive patients with TIA who underwent treatment in the Department of Neurology at the University hospital of Schleswig-Holstein, Campus Lübeck between 2011 and 2014.

A TIA diagnosis was defined in this study as any sudden focal neurological deficit lasting less than 24 hours and showed no evidence of infarction on brain imaging (Easton et al., 2009). Patients with TIA were treated by neurologists. The diagnosis of TIA was made by at least one vascular neurologist upon completion of the TIA evaluation and during the patients' hospital stay. Patients with neurological symptoms who were admitted to hospital were evaluated during their hospital stay. According to the abovementioned guidelines (Laufs et al., 2010); patients with TIA are generally hospitalized so as to undergo an evaluation of TIA causes and monitoring of vital parameters.

Baseline characteristics (**Table 1**) – age, gender, TIA symptoms, medical history, diagnostic and therapeutic procedures, and secondary prevention strategies – were recorded. Patients who were admitted with TIA symptoms but were diagnosed with an epileptic seizure, migraine, or functional disorders during hospitalization and subsequent diagnostic procedures were not included in the study. In addition, patients who presented with TIA to the Department of Neurology but were rejected hospital admission were not included in the study.

The study was approved by the Ethics Committee of the University of Lübeck (AZ: 4-147). All patients or caregiver provided written informed consent for their inclusion and evaluation in the present study.

TEE

As part of the TIA evaluations, TEE investigations were performed at the Department of Cardiology of the University Hospital of Schleswig-Holstein, Campus Lübeck by cardiologists who were not involved in the present study. The TEE findings were retrieved from the TEE reports.

Statistical analysis

SPSS 22.0 (IBM SPSS Statistics, Armonk, NY, USA) was used to analyze the data. The data were described with mean and standard deviation (SD) values for continuous variables, median and interquartile range (IQR) values for scores, and absolute numbers and percentages for nominal and categorical variables. We performed a chi-square test or Student's t-test to determine the difference between categorical or continuous variables, and a Mann-Whitney U test was used for the difference between scores. Adjusted logistic regression was carried out to estimate the odds ratio (OR). All variables with a P-value < 0.1 were entered into the logistic regression model. A P-value < 0.05 was considered significant.

Results

Patients with and without TEE

A total of 1071 patients with TIA were included in the study. The mean age of the patients was 70 years (SD, 13), and the sex distribution was approximately equal (female patients, 49.7%). The median time between symptom onset and hospital admission was 6 hours.

TEE and associated factors

Of 1071 patients, 288 patients (27%) underwent TEE as part of the TIA evaluations. The median time between hospital admission and TEE investigation was 6 days. The mean time between TEE and discharge from hospital was 1.3 days (SD, 1.7), with a median value of 1 day. Patients who underwent TEE stayed in hospital 2 days longer and more frequently received treatment in a stroke unit than those who did not undergo TEE (**Table 1**). A comparison between patients who underwent TEE and those who did not undergo TEE is shown in **Table 1**.

Table 2 Pathological findings detected by transesophageal echocardiography in 288 patients

Item	*n* (%)
Pathological findings detected by the TEE	133(47.8)
Thrombogenic arch	36(13)
Grade 1	2(0.7)
Grade 2	1(0.3)
Grade 3	8(2.7)
Grade 4	8(2.7)
Grade 5	17(6)
Patent foramen ovale	71(25)
Atrial septal aneurysm	13(4.6)
Aortic insufficiency	41(15)
Grade 1	32(11)
Grade 2	5(2)
Unknown	4(1.7)
Aortic valve stenosis	5(2)
Grade 1	2(0.7)
Grade 2	2(0.7)
Unknown	1(0.3)
Cardiomyopathy	0
Fibroma	1(0.3)

Findings of TEE

The TEE investigation showed that of the 288 patients who underwent TEE, 133 patients (48%) had abnormal findings. Based on the TEE findings, 17 patients (6%) received oral anticoagulation. In 1 patient (0.3%), an atrial fibroma was found, which led to heart surgery (**Table 2**). A change of therapeutic procedures was carried out in 18 patients (6.3%). During hospitalization, 7 patients (2.4 %) experienced a subsequent stroke, and 27 patients (9.4%) had a recurrent TIA (Re-TIA). The rates of stroke, Re-TIA, and death were 2.7%, 4.2%, and 1.6%, respectively, at 3 months after patients' discharge from hospital. The rates of mortality (0.9% *vs*. 1.8%, $P = 0.7$), stroke (1.9% *vs*. 3.0%, $P = 0.8$), and Re-TIA (5.0% *vs*. 3.9%, $P = 0.8$) were similar in patients who underwent TEE and in those who did not.

Discussion

Our study showed that the performance of TEE was associated with age, TIA symptoms, and previous medical history. We also found that the performance of the TEE investigation seemed to lead to a prolonged hospital stay. Approximately half of the cohort that underwent TEE showed pathological findings. A change of therapeutic procedures was carried out in 18 patients (6.3%) and comparable with the findings of other studies investigating the diagnostic impact of TEE on unselected patients with an acute cerebral ischemia (Censori et al., 1998; Pallesen et al., 2016). Previous studies have revealed the presence of a patent foramen ovale (PFO) to be the most common pathological finding detected by echocardiography after stroke and TIA (Bogousslavsky et al., 1986; Hausmann et al., 1992; Censori et al., 1998; Pallesen et al., 2016). Whereas the performance of TEE is superior to the transthoracal echocardiography (de Bruijn et al., 2006).

In addition, research has shown that a PFO with an atrial septal aneurysm leads to an exponentially higher risk of stroke (Mas et al., 2001). Recent research has also found that an occlusion of the PFO could be associated with a reduced risk of a subsequent stroke (Carroll et al., 2013). Therefore, the TEE investigation is now considered an important aspect of the evaluation of a cerebral ischemic event. However, the rate of the performance of TEE in our cohort of patients with TIA was low. This finding may be attributable to the fact that our study design only used the tissue-based definition of TIA. Furthermore, following the identification of the cause of TIA with the use of electrocardiography, long-term electrocardiography, or duplex sonography of the brain-supplying arteries, the diagnostic impact of TEE investigation may be less. In accordance with the tissue-based definition of TIA, we included only patients with negative brain imaging. Previous research has shown embolic causes of cerebral ischemic events in about 23% of patients with TIAs; however, the etiology of TIA remains undetermined in 33% of patients(Al-Khaled and Eggers, 2013). We found that during hospitalization and at 3 months of follow-up, the risk of stroke and the risk of death were lower in patients who underwent TEE than in those who did not, but this finding was not statistically significant, which may be attributable to the small size of the groups who experienced stroke or died. Furthermore, the patient group who experienced a change in medical management after TEE was too small (only 17 patients) for multivariate analysis to detect associated factors. Our findings are comparable with that of other studies detecting the cardioembolic sources by TEE and cardiac MRI in patients suffering from stroke or time-based TIA (Wehrum et al., 2018).

Our study has several limitations. One is that not all TIA patients underwent TEE, older patients may be under represented in the study. The lack of long-term follow-up represents another limitation. The fact that complications of the TEE investigation were not recorded is also a limitation.

In summary, we found that 47.8% of patients with TIA who underwent TEE showed abnormal findings and 6.3% of patients experienced a change of treatment owing to TEE findings in patients with tissue-based TIA. Patients with tissue-based TIA of an undetermined etiology or a suspected cardioembolic cause may benefit from the implementation of TEE.

Author contributions: *MAK designed the study, conducted the statistics, interpreted the data results and wrote the manuscript. BS collected the data and reviewed the manuscript. TB searched the literature and reviewed the manuscript. All authors approved the final version of the paper.*
Conflicts of interest: *The authors reported that they have no any conflicts of interest.*
Financial support: *None.*
Institutional review board statement: *Approval for the study was obtained from the Ethics Committee of the University of Lübeck (AZ: 4-147).*
Declaration of patient consent: *The authors certify that they have obtained all appropriate patient consent forms. In the form the patients have given their consent for their clinical information to be reported in the journal. The patients understand that their names and initials will not be published.*
Reporting statement: *This study follows the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement.*

Data sharing statement: *The study was part of the department own bench marking project, the data used in this study can not be shared.*
Plagiarism check: *Checked twice by iThenticate.*
Peer review: *Externally peer reviewed.*

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