Transesophageal Echocardiography Is Superior to Transthoracic Echocardiography in Management of Patients of Any Age With Transient Ischemic Attack or Stroke

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Background and Purpose—The merits of transthoracic echocardiography (TTE) and transesophageal echocardiography (TEE) in the management of transient ischemic attack (TIA) and stroke patients remains matter of debate.

Methods—Two hundred and thirty-one consecutive patients with a recent TIA or stroke, for which no definite cause and indication for anticoagulation was assessed after standardized work-up underwent TTE and TEE. Echocardiographic findings were categorized into minor and major risk factors.

Results—A potential cardiac source of embolism was detected in 55% (127/231) of the patients by echocardiography, in 39% (90/231) only identified on TEE. Major risk factors, with an absolute indication for oral anticoagulation, were detected in 20% (46/231) of the patients, in 16% (38/231) of all patients identified on TEE only. A thrombus in the left atrial appendage was the most common major risk factor (38 patients, 16%). The presence of major risk factors was independent of age (χ²=1.48; P=0.224). The difference in proportions of cardiac sources detected in favor of TEE was highly significant in both patients ≤45 years of age (10/39, P=0.002) and in those >45 years of age (80/192; P<0.004).

Conclusions—TEE proved superior to TTE for identification of a cardiac embolic source in patients with TIA or stroke without pre-existing indication or contraindication for anticoagulation. In patients with normal TTE, a cardiac source of embolism was detected by TEE in ≈40% of patients, independent of age. More than 1 of 8 patients of any age with normal TTE revealed a major cardiac risk factor on TEE, in whom anticoagulation is warranted. (Stroke. 2006;37:2531-2534.)

Key Words: anticoagulation ■ echocardiography ■ stroke ■ TIA

It has been estimated that cardiogenic emboli are a source of transient ischemic attack (TIA) or stroke in 20% to 40% of all cases. Recently, transesophageal echocardiography (TEE) has been proven superior to transthoracic echocardiography (TTE) for the detection of potential sources of cardiac embolism in patients with previous stroke. The diagnostic yield of TEE for the detection of a cardiac source of embolism is estimated between 40% and 60%. However, the precise relative merits of TEE and TTE in the management of TIA and stroke patients remain a matter of debate. In clinical practice, TTE is still the first choice technique in patients with normal TTE, particularly in patients over 45 years of age, in whom TEE is still far from routine procedure, was evaluated. In addition, emphasis was placed on therapeutic consequences, ie, the indication for anticoagulation, based on the results of TTE and TEE in patients with TIA or stroke of all ages.

Methods
From January 2002 to March 2004, 231 consecutive patients, both from the clinics and the outpatient clinic, were prospectively enrolled. Eligible patients had a recent TIA or stroke, for which no definite cause and indication for anticoagulation was assessed after standardized diagnostic work-up (12-lead ECG, carotid ultrasound if applicable, routine blood tests with hematology included). We included strokes of all subtypes, both from the anterior and the posterior circulation. Patients with a pre-existing indication or contraindication to anticoagulation were excluded.

All patients underwent TTE, directly followed by TEE, which were performed by experienced sonographers (W.R.P.A., E.R.H., J.J.B.) according to a predefined protocol. For TTE, patients were imaged in the left lateral decubitus position using a commercially available system.

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TABLE 1. Potential Cardiac Sources of Embolism in 231 TIA or Stroke Patients Assessed by TTE or TEE

<table>
<thead>
<tr>
<th>Potential Cardiac Source</th>
<th>TTE</th>
<th>TEE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major risk factor</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LA cavity thrombus</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>LA appendage thrombus</td>
<td>1</td>
<td>38</td>
</tr>
<tr>
<td>LV thrombus</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Aortic thrombus</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Dilated cardiomyopathy (LVEF&lt;35%)</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Mitral valve prolapse</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Minor risk factors</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mitral valve prolapse</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Mitral annular calcification</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Calcified aortic stenosis</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>Patent foramen ovale</td>
<td>3</td>
<td>12</td>
</tr>
<tr>
<td>Spontaneous echo contrast</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>Atrial septal aneurysm</td>
<td>5</td>
<td>8</td>
</tr>
<tr>
<td>LV aneurysm</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Aortic aneurysm</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>False tendon</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Aortic plaques</td>
<td>1</td>
<td>69</td>
</tr>
<tr>
<td>Other</td>
<td>2</td>
<td></td>
</tr>
</tbody>
</table>

LA indicates left atrium; LV, left ventricular; LVEF, left ventricular ejection fraction.
Percentages below 0.5% are rounded off upwards to 1%.
*Identical values.

(Vingmed system FiVe/Seven, General Electric-Vingmed). Images were obtained using a 3.5-MHz transducer, at a depth of 16 cm in the parasternal (standard long- and short-axis images) and apical views (standard long-axis, 2- and 4-chamber images). Standard 2-dimensional and color Doppler data, triggered to the QRS complex, were saved in cine loop format. Pulsed and continuous wave Doppler data were also stored digitally. Data were analyzed using commercial software (Echopac 6.1, General Electric-Vingmed).

TEE was performed using a 5.0-MHz multiplane transducer. The procedure was performed without sedation in awake patients; lidocaine spray was used for local pharyngeal anesthesia. TEE was performed according to a standardized protocol including adequate visualization of all cardiac structures with emphasis on both atria, left atrial appendage, interatrial septum, mitral valve apparatus, and thoracic aorta. Administration of intravenous sterile isotonic saline was used to assess atrial septal defects. Echo contrast with air (ratio 9:1) and a subsequent Valsalva maneuver was used to evaluate the presence of a patent foramen ovale. All patients were instructed to perform a Valsalva maneuver just before the injection of the contrast, and to release on command after arrival of contrast in the right atrium. The Valsalva maneuver was considered successful if the interatrial septum in the fossa ovalis region showed a leftward deviation. A moderate-severe shunt secondary to patent foramen ovale was defined as passage of a cloud of bubbles, or intense opacification of the left atrium.7 Echocardiographic findings were categorized into minor and major risk factors (Table 1).9,10

We assessed the intermethod agreement with Cohen κ (0.21 to 0.40 fair; 0.41 to 0.60 moderate; 0.61 to 0.80 substantial; 0.81 to 1.00 almost perfect agreement).11 Differences in the correlated proportions of detection successes were analyzed with the test of McNemar.12 All statistical analyses were performed in SPSS version 12.0.1

Results

All results are summarized in Tables 1 and 2. A potential cardiac source of embolism was detected in 55% (127/231) of the patients by echocardiography. In 39% (90/231) a potential cardiac source was only identified on TEE.

Major risk factors, with an absolute indication for oral anticoagulation, were detected in 20% of the patients (46/231), and 16% (38/231) of them were only identified on TEE. A thrombus in the left atrial appendage was the most commonly observed major cardiac risk factor, occurring in 16% (38/231). Of note, left atrial appendage thrombi were virtually never adequately detected on TEE.

The presence of major and minor risk factors was independent of age (Table 2; major risk factors, χ²=1.48; P=0.224). Eighty-three percent (192/231) of the patients were ≥45 years old. In these patients echocardiography (TTE or TEE) revealed a potential cardiac source of embolism in 59% (114/192) of the patients. TTE identified a cardiac source in 18% (34/192) of the patients, with 4% (8/192) having a major risk factor and an indication for anticoagulation therapy. TEE confirmed the potential cardiac source in these 34 patients, but also detected a potential source in 80 additional patients (80/192, 35%). In these 114 patients, a major risk factor was present in 36% (41/114), 21% (41/192) of all patients above 45 years of age, with an indication for anticoagulation therapy. In 80% (33/41) of these patients, the indication for anticoagulation therapy was based on the TEE results only.

A total of 39 (17%) patients were ≤45 years of age. In this patient category echocardiography (TTE or TEE) detected a potential cardiac source of embolism in 33% (13/39) of these patients. TTE identified a potential cardiac source in 8% (3/39), with none of them having a major risk factor. A

TABLE 2. Presence of Potential Cardiac Source of Embolism Detected With TTE vs TEE

<table>
<thead>
<tr>
<th></th>
<th>TTE(+) &amp; TEE(+)</th>
<th>TTE(+) &amp; TEE(−)</th>
<th>TTE(−) &amp; TEE(+)</th>
<th>TTE(−) &amp; TEE(−)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All 231 patients</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiac source</td>
<td>16% (37/231)</td>
<td>0</td>
<td>39% (90/231)</td>
<td>45% (104/231)</td>
</tr>
<tr>
<td>Major risk factor</td>
<td>3% (8/231)</td>
<td>0</td>
<td>16% (38/231)</td>
<td>80% (185/231)</td>
</tr>
<tr>
<td>192 patients ≥45 years</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiac source</td>
<td>18% (34/192)</td>
<td>0</td>
<td>42% (80/192)</td>
<td>41% (78/192)</td>
</tr>
<tr>
<td>Major risk factor</td>
<td>4% (8/192)</td>
<td>0</td>
<td>17% (33/192)</td>
<td>79% (151/192)</td>
</tr>
<tr>
<td>39 patients ≤45 years</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiac source</td>
<td>8% (3/39)</td>
<td>0</td>
<td>26% (10/39)</td>
<td>67% (26/39)</td>
</tr>
<tr>
<td>Major risk factor</td>
<td>0</td>
<td>0</td>
<td>13% (5/39)</td>
<td>87% (34/39)</td>
</tr>
</tbody>
</table>
potential cardiac source on TEE was observed in 13 of 39 (33%) patients, confirming the 3 patients already identified on TTE. In these 13 patients, a major risk factor was present in 38% (5/13). In all of these 5 patients the indication for anticoagulation therapy was based on the TEE results only.

The analysis of agreement between the 2 methods in detecting a cardiac source resulted in a $\kappa$ of 0.286 for patients $\leq 45$ years of age, thus showing fair agreement and a $\kappa$ of 0.450 in those $>45$ years which is considered moderate.10

The difference in proportions of cardiac sources detected in favor of TEE was highly significant in patients $\leq 45$ years of age, as well as in those over 45 years of age (10/39; $P=0.002$ and 80/192; $P<0.004$ respectively, McNemar test). The relative merit of TEE in the detection of major risk factors was comparable between younger ($\leq 45$ years, 13% major risk factors on TEE) and older ($>45$ years, 17% major risk factors on TEE; $\chi^2=0.45$; $P=0.45$) patients.

**Discussion**

The findings in the current study can be summarized as follows. TEE proved superior to TTE for the identification of a cardiac source of embolism in this unselected series of patients with TIA or stroke without pre-existent indication or contraindication for anticoagulation. In TIA or stroke patients with a normal TTE, a cardiac source of embolism was yet detected by TEE in $\approx 40\%$ of patients, independent of age. More than 1 of 8 patients of any age with a normal TTE revealed a major cardiac risk factor on TEE, for whom anticoagulation therapy is recommended.

Identification of a cardiac source of embolism in patients with previous TIA/stroke is important because it influences future therapeutic management. Indeed, as outlined above, TEE was superior in detecting “major cardiac risk factors”, in particular the detection of a thrombus in the left atrial appendage. This is important because these findings have therapeutic implications (ie, anticoagulation therapy). In patients with major cardiac risk factors (thrombi in the left atrium, left atrial appendage and left ventricle, dilated cardiomyopathy) anticoagulation therapy is generally recommended.2,13,14 Anticoagulation is probably even more warranted after a thromboembolic event like a TIA or stroke, although there is no evidence at this time from randomized-controlled trials. Recruitment for these trials would probably also be difficult because large numbers of stroke patients are needed. In addition, many neurologists are likely to be reluctant to put patients with a major cardiac source, like a left atrial thrombus, after a TIA or stroke on aspirin (instead of anticoagulants).

In an earlier study TEE did not find any patient with left atrial thrombus in all 236 patients with stroke and other suspected embolic events with a normal TTE.15 Therefore, TTE was considered sufficient as a screening tool in stroke patients, especially in the older population. Clearly, in our study TEE showed superiority over TTE in detection of left atrial thrombus in stroke patients of all ages. The reason for this discrepancy is unknown, but based on the present results we do not consider TTE alone a valid screening tool to rule out a potential cardiac source, left atrial thrombus included.

Other studies have also demonstrated that TEE is superior to TTE for the assessment of possible sources of cardiac embolism, including intracardiac thrombi, patent foramen ovale, atrial septal aneurysm and slow left atrial flow.3,16

The diagnostic superiority of TEE was also demonstrated in an unselected series of 457 patients with previous TIA or stroke.3 In that series, TEE or TTE detected a potential cardiac source in 57% of patients. TEE appeared superior in the detection of some major risk factors (including left atrial appendage thrombus and aortic thrombus), and was reported to “change or confirm appropriateness of management” in 9% of all 457 patients. The current findings are in line with these results because a potential cardiac source of embolism was detected by echocardiography in 55% of patients. However, TEE changed therapy in a slightly higher percentage of patients in the current study. This difference may be related to differences in study populations.

The issue of age is an important one in the discussion on whether TTE or TEE should be used in patients with previous TIA or stroke. Sorescu et al demonstrated that older age ($>60$ years) was one of the strongest, independent risk factors for the presence of thrombus in the left atrial appendage and spontaneous echo contrast on echocardiography.6 In the current study, it was demonstrated that relative merit of TEE in the detection of major risk factors was comparable between younger and older patients.

In particular, in the present series, 96% of the TTEs in patients $>45$ years of age failed to identify a major risk factor, whereas TEE demonstrated a major risk factor in 17% (n=32 patients). These patients would have been incorrectly denied anticoagulation therapy if only TTE was used. Thus, the current observations support the additional value of TEE in both younger and older patients.

For many cardiac risk factors, referred to as “minor risk factors”, the optimal choice of therapy is not clear. At present, there is not enough evidence in the literature to recommend anticoagulation therapy over aspirin in patients with minor risk factors, and therefore TEE does not provide therapeutic gain in terms of medical treatment.

In patients with a pre-existing indication or contraindication to anticoagulation therapy, screening for cardiac sources of emboli is generally not considered useful, in terms of therapeutic consequences.2 These patients were, however, excluded in the present study. Still, it could be argued that detection of any cardiac source of embolism is helpful in understanding the underlying pathophysiological mechanism of stroke in an individual patient. Some cardiac abnormalities detected may also influence clinical decisions beyond medical therapy (eg, patent foramen ovale, which could be considered for device closure therapy).17

In conclusion, the current results demonstrate the relative merit of TEE over TTE in patients with previous TIA or stroke. The findings support the routine use of TEE in all patients with TIA or stroke of unknown origin.

**Disclosures**

None.
References

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