TRANSESOPHAGEAL ECHOCARDIOGRAPHY DISCLOSES UNEXPECTED CARDIAC SOURCES OF EMBOLUS IN STROKE PATIENTS AGED MORE THAN 45 YEARS

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ABSTRACT - Cerebral embolism from cardiac source is an important cause of stroke, specially in patients younger than 45 years old. Objective: To describe the transesophageal echocardiography (TEE) findings in young and non-young stroke patients without any prior evidence of cardiac source for cerebral embolism. Method: Transversal study: 523 patients (267 men and 256 women) with ischemic stroke, without any evidence of cardiac abnormality, underwent to TEE. Results: Ten percent were aged 45 years; or less. Left ventricular hypertrophy, left atrial enlargement, spontaneous contrast in aorta, interatrial septum aneurysm, mitral and aortic valve calcification, aortic valve regurgitation, and atherosclerotic plaques in aorta were significantly more frequent in patients aged more than 45 years; 2.8% of non-young patients had thrombus in left heart. Conclusion: TEE is widely used to diagnose cardiac source of cerebral embolism in young patients, but it seems to be as useful for older ones, in whom cerebral embolism risk is underestimated; atherogenic and cardioembolic causes may actually coexist, and both should be treated.

KEY WORDS: stroke, cardiac embolism, transesophageal echocardiogram.

Ecocardiograma transesofágico revela fonte cardíaca de embolia cerebral em pacientes com AVC e mais que 45 anos

RESUMO - Embolia cerebral de fonte cardíaca é frequentemente relacionada a acidente vascular cerebral (AVC) em jovem. Objetivo: Descrever achados ecocardiográficos em jovens e não jovens com AVC isquêmico, sem suspeita de fonte cardíaca. Método: Estudo transversal; 523 pacientes (267 homens e 256 mulheres) com AVC isquêmico sem evidência de fonte cardíaca submeteram-se ao ecocardiograma transesofágico (ECOTE). Resultados: 10% dos pacientes tinha 45 anos; ou menos. Hipertrofia do ventrículo esquerdo, aumento do átrio esquerdo, contraste espontâneo na aorta, aneurisma do septo interatrial, calcificação da válvula mitral e aórtica, insuficiência aórtica e placas de ateroma na aorta foram significativamente mais frequentes nos pacientes com mais que 45 anos; 2.8% dos não-jovens apresentaram trombos nas câmaras esquerdas. Conclusão: ECOTE é amplamente sugerido na investigação de embolia em pacientes jovens, porém parece ser tão importante também no grupo de pacientes mais velhos, nos quais o risco de embolia cerebral é subestimado; etiologia cardioembólica e aterosclerótica coexistem, e ambas devem ser identificadas e tratadas para melhor prognóstico.

PALAVRAS-CHAVE: acidente vascular cerebral, embolia cardíaca, ecocardiograma transesofágico.

Cerebral embolism from cardiac source (CECS) is considered the cause of 15 to 45% of all strokes, and many studies suggest that it is more prevalent in patients younger than 45 years old¹⁴. The absence of qualitatively valid criteria for the clinical diagnosis of CECS, and the frequent coexistence of a potential cardiac source of emboli and cerebral atherosclerosis, make the diagnosis presumptive in

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many situations. There is neither consensus nor guidelines for diagnosis of CECS. About one third of all stroke patients have some clinical evidence of potential cardiac source of embolism by physical examination, chest roentgenogram or electrocardiogram. The classical cardiac conditions associated with CECS are nonvalvular atrial fibrillation, acute myocardial infarction, ventricular aneurysm, rheumatic heart disease, and prostatic valves, and some studies have correlated specific entities to less common potential cardiac source of cerebral embolism: mitral valve prolapse, mitral annulus calcification, nonbacterial thrombotic endocarditis, calcified aortic valve stenosis, myxoma, paradoxical embolism and congenital heart disease, nonischemic dilated cardiomyopathy, and infective endocarditis. Aging produces major cardiovascular changes, including decreased elasticity and compliance of the aorta and other arteries, that leads to higher systolic arterial pressure and increased impedance to left ventricle ejection, and subsequent left ventricle hypertrophy. Heart valves thicken and calcification results at the basis of aortic valve and mitral annulus causing valve dysfunction. Aortic valve calcification is associated with atherosclerotic disease, specially coronary artery disease. Various types of arrhythmia are associated with cell degeneration, and occur preferentially in the elderly.

The transesophageal echocardiography (TEE) was first used in 1971, and has been very useful in the diagnosis of many cardiac abnormalities, some of them associated to unsuspected ethiology for stroke, as follows: patent foramen ovale, atrial communication, atrial septal aneurysm, aortic atheromatous plaques, echocardiographic spontaneous contrast, mitral valve strands, intracardiac thrombus specially in left appendagë. The TEE has been more widely used since the eighties when technical improvements mostly regarding transducers, and topic anesthetic procedures were achieved. It is well known the superiority of TEE compared to transthoracic echocardiography to detect the above mentioned abnormalities, but even so, it is not widely used in the stroke investigation.

Some algorithms for cardiac evaluation, until last decade, included TEE for young stroke patients, and for older only if there was some evidence of cardiac disease. A recent guideline recommend echocardiography for young stroke patients and for older patients (typically more than 45 years) only with neurological events without evidence of cerebrovascular disease or other obvious cause.

The objective of this study was to describe the TEE findings in young and non-young stroke patients without any prior evidence of cardiac source for cerebral embolism. Our hypothesis is that we are underestimating cerebral embolism risk in an older population and therefore it would be useful to submit every patient with acute stroke to TEE in order to diagnose unsuspected sources of embolism.

METHOD

Patients and design – Transversal study with consecutive inclusion of 523 adult patients between November 1998 and March 2004. Patients were admitted to the Division of Neurological Emergencies of São Paulo Hospital at Federal University of São Paulo, and were enrolled if they fulfilled the entry criteria, and signed the consent form. The diagnosis of ischemic stroke were performed by neurologists following a standard protocol including clinical examination and brain CT scan. The selected patients underwent TEE up to 15 days after stroke.

Exclusion criteria – Patients bearing any clinical suspicion of cardioembolism like atrial fibrillation, recent myocardial infarction (in the last 6 months), prosthetic cardiac valves, severe impairment of cardiac function, formal contraindication for TEE, critical care required or those hospitalized for more than 14 days were excluded from the study.

Group assignment – Based on current criteria patients aged 45 or less were considered young, and those aged more than 45 years were considered non-young. To analyze clinical data we split our sample into male and female groups because known epidemiological differences among them.

TEE – Multiplane transesophageal echocardiography with a 5MHz transesophageal probe (Vingmed echocardiography System V) were performed to the selected patients. Images were recorded on videotape for later review by two observers. TEE examinations were performed after administration of topical anesthesia with an aerosolized 10% solution of lidocaine and intravenous sedation with midazolan (1.5mg/ml) and meperidine (50mg/ml). Contrast studies were performed through rapid injection of microbubble solution (6ml of isotonic saline 0.9%, 4ml of glucose 50%, and 1ml of air) in the peripheral vein at rest, during coughing, and Valsalva maneuver. A comprehensive TEE examination was performed standardized scan planes. The following abnormalities were evaluated: left atrium enlargement, presence of masses, thrombi, or spontaneous contrast either inside the atrium or at the atrial appendage or left ventricle, interatrial septum aneurysm; patent foramen ovale, or any interatrial septal communication; fibrosis, mitral valve strands, calcifications, myxomatous
degeneration, significant stenosis, or regurgitation of
the mitral or aortic valve; enlargement, hypertrophy,
left ventricle segmental or global dysfunction; and also
atherosclerotic plaques or thrombi in the thoracic aor-
ta. Patent foramen ovale was diagnosed if more than
three microbubbles were detected in the left atrium wi-
thin 5 cardiac cycles, following the opacification in
the right atrium. Intratrial septal aneurysm was diagnosed
when excessive expansion was observed. Spontaneous
echo contrast was characterized by smooth echoes with
circular or spiral movement inside cardiac chambers. Mi-
tral valve strands were defined as a thin mobile filamen-
tous projections attached to the atrial surface of mitral
leaflets or subvalvar apparatus. The left atrium was con-
sidered enlarged when it was >40mm. The left ventri-
cle was considered enlarged when diastolic diameter
was >50mm and hypertrophic when diastolic thickness
was ≥12mm; atherosclerotic plaques in the ascending
aorta, aortic arch, and descending aorta had their max-
imum thickness measured and were classified into 2
groups: those ≤4mm and those ≥4mm.

Statistical analysis – Proportions and 95% confidence
interval were computed for echocardiographic findings.
Qui-square tests were performed to compare the propor-
tions of each group. A p value < 0.05 was considered
significant. Calculations were performed with SPSS 12
(SPSS Inc., U.S.A.) statistical package.

The sponsor played no role in elaboration and con-
duction of this study.

RESULTS
There were 523 patients included in the study
(267 men and 256 women); the ages ranged from
26 to 92 years (mean = 62.8; SD=12.47). Fifty-four
patients (10.3%) were aged 45 years or less (23 man
and 31 women) and 469 patients (89.7%) were aged
more than 45 years (244 men and 225 women).

No complications occurred during the echocardi-
ography exam. One patient could not be submit-
ted to TEE because of esophagitis diagnosed dur-
ing the procedure.

The women of non-young group presented a
higher proportion of hypertension and diabetes,
and lower proportion of cigarette smoking. The men
of non-young group had lower proportion of
cigarette smoking (Table 1).

Left ventricle hypertrophy, left atrial enlarge-
ment, spontaneous contrast in aorta, intratrial
septum aneurysm, mitral valve calcification, aortic
valve calcification, aortic valve regurgitation, and
atherosclerotic plaques in aorta were more fre-
quent in patients aged more than 45 years. Echocar-
diographic findings are presented in Table 2. Neither
mass in left atrium or ventricle nor strands in
mitral valve were found.

Four patients had intermittent atrial fibrilla-
tion not present during emergency management,
all of them were aged more than 45 years old. Four
patients presented aortic aneurysms with signs of
dissection (43 years old woman, 46 years old wo-
man, 59 years old woman, and 58 years old man).
In 1 patient of young group, who had aortic aneu-
rysm dissection and also thrombus, and in 17 pa-
tients of non-young group (atrial fibrillation, aor-
tic aneurysm dissection, mitral stenosis, aortic ste-
nosis, or thrombus) the treatment change was man-
datory and was performed immediately after TEE.
Six TEE were considered normal (14.3%) in the
group of young patients, and 5 (1.4%) amongst
older patients (p<0.0001).

DISCUSSION
The proportion of young patients with stroke in
the present study (10.8%) was similar to that pre-
viously reported in Brazil (10.6% of cerebral in-
farct)20, and in other countries21, showing that stro-
ke is not rare in young people. Considering that car-
dioembolism is an important ethiology of stroke
in young people (12 to 35% of the cases)2,19,22,23
and that patients with any suspected cardiac sour-
ce of embolism were excluded from our study, the

<table>
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<tr>
<th>Table 1. Atherosclerotic risk factors of male and female stroke patients distributed by ages.</th>
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<tbody>
<tr>
<td><strong>Women (n=256)</strong></td>
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<tr>
<td>-------------------</td>
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<tr>
<td>≤ 45 years</td>
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<tr>
<td>(n=31)</td>
</tr>
<tr>
<td>Hypertension</td>
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<tr>
<td>Diabetes mellitus</td>
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<td>Previous stroke</td>
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<td>Coronary disease</td>
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<td>Cigarette smoking</td>
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Qui-square test.
actual proportion is likely to be even greater. Because of the low prevalence of atherosclerosis in the young, the cardiac conditions are more frequently related to the ethiology of stroke\textsuperscript{2,21,24}.

Left ventricular hypertrophy, left atrial enlargement, left ventricle enlargement, spontaneous contrast in aorta, mitral valve calcification, aortic valve calcification, aortic valve regurgitation, and atherosclerotic plaques in aorta are related to aging, and were more prevalent in the older group as expected. PFO occurred in the older group in same proportion as younger group. PFO and atrial septal aneurysm are typically related to cryptogenic stroke\textsuperscript{25}.

Atrial fibrillation and myocardial infarction are more prevalent in older patients, and are considered main sources of emboli\textsuperscript{1}. However, in this study patients with some cardiac source of embolism were previously excluded, so the TEE findings were unexpected. Cabral et al. studied a similar population, without cardiac source of embolism, and found also more abnormalities in older group\textsuperscript{26}. We have previously reported that 16\% of patients had their treatments changed after TEE, leading to significant clinical impact\textsuperscript{27}.

In current guideline for clinical application of echocardiography, it is recommended for younger patients, typically less than 45 years, with cerebrovascular events and for older patients, typically more than 45 years, with neurological events without evidence of cerebrovascular disease or other obvious cause. As aging is frequently related to obvious cause of ischemic stroke, considered athe-
rothrombotic event, other etiologies are not systematically investigated. Last Brazilian echocardiography guideline also states as class I recommendations echocardiography for young patients (<45 years) with acute stroke, for patients older than 45 years without evidence of cerebrovascular disease, and for stroke with preexisting cerebrovascular disease with suspicion of embolus; also makes class II recommendations for echocardiography after acute neurological symptoms in patients with preexisting cerebrovascular disease, and for patients with stroke in whom echocardiography would not interfere in diagnosis or management.

Clinical or review studies recommend echocardiography with the same restrictions of current guidelines, i.e., only for patients with stroke and atrial fibrillation, coronary artery disease, and other cardiac diseases. Few studies recommend echocardiography for patients without clinical suspicion of cardiac source of embolism.

In our study we found in the group of non-young patients, 13 individuals (2.8%) with some thrombus, 6 (1.3%) with mitral or aortic valve stenosis, 4 (0.9%) with thoracic aorta dissection, 4 (0.9%) with intermittent atrial fibrillation. Those patients demanded proper management, as well as some patients with other TEE abnormalities needed specific care. In the group of young patients 54 TEE were performed and we found one case of thrombus, while in the non-young group a change in management was mandatory at each 21 TEE.

TEE is widely used to diagnose cardiac source of cerebral embolism in young patients, but it seems to be as useful for older ones, in whom rheumatic and cardioembolic causes may actually coexist. In these patients the ethiological diagnosis of stroke is even more difficult, and it might be multifactorial. Each cause should be promptly identified and treated, reducing recurrence.

REFERENCES