Diagnostic yield and therapeutic impact of transthoracic echocardiography in patients with potential cardiac sources of cerebral embolism

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ABSTRACT

الأهداف: لقياس دقة الأشعة الفوق الصوتية القلبية السطحية (TTE) في تشخيص الإنصمام الصادر من القلب وأثر هذه الوسيلة التشخيصية على العلاج فيما بعد.

الطريقة: في هذه الدراسة الإسترجاعية تمت مراجعة تقارير الأشعة الفوق صوتية القلبية (TTE) للمرضى الذين أصيبوا بحادثة وعائية دماغية، والذين حولوا لمعمل الأشعة الفوق الصوتية القلبية في مستشفى الملك خالد الجامعي – الرياض – المملكة العربية السعودية خلال الفترة ما بين يناير 2006م إلى ديسمبر 2008م، لمعرفة ما إذا كان لديهم إحتمال لإنصمام صادر من القلب (CSE). تم البحث عن 15 مؤشرا والتي قد تدل على صدور الإنصمام الوعائي الدماغي من القلب. تمت مراجعة ملفات المرضى الطبية لمعرفة أثر نتائج الأشعة الفوق الصوتية القلبية (TTE) على العملية العلاجية.

النتائج: بعد مراجعة 10563 تقرير أشعة صوتية قلبية، قمنا بدراسة 240 تقرير، كان معدل العمر للمرضى 14±58.5. تم تشخيص مريض واحد فقط بإنصمام صادر من القلب بشكل مؤكد، بينما كان محتملا في 35 مريض (14.6%). كانت الأسباب الأكثر شيوعا للإنصمام الصادر من القلب المحتمل، الضعف الإنقباضي للبطين الأيسر (31.4%)، واضطرابات الحركة لأي من جدران البطين الأيسر (25.7%). كانت الدلالات المستقلة على تشخيص الإنصمام الوعائي الدماغي الذي يحتمل صدوره من القلب، هي الإصابة السابقة بأمراض القلب الوعائية (OR 6.2, 95%CI:2.6-14.8, p=0.0001)، وجنسية المريض (OR 0.16, 95% CI 0.3-0.7 p=0.019). أدت الأشعة الفوق الصوتية القلبية السطحية إلى تغيير علاج 3 (1.2%) مرضى فقط.

خاتمة: الأشعة الفوق الصوتية القلبية السطحية التي تجرى لمعرفة ما إذا كانت الحادثة الوعائية الدماغية بسبب إنصمام صادر من القلب ذات قدرة تشخيصية منخفضة، وأثر النتائج على علاج المرضى محدود.

Objectives: To explore the diagnostic yield of transthoracic echocardiography (TTE), and assess the effect of echocardiographic findings on subsequent therapy.

Methods: In this retrospective study, we reviewed TTE reports and hospital records of patients diagnosed with a stroke or transient ischemic attack (TIA), screening for potential cardiac sources of embolism (CSE) from January 2006 to December 2008 at King Khalid University Hospital, Riyadh, Kingdom of Saudi Arabia by considering at least 15 predefined TTE criteria. The therapeutic interventions employed as a consequence of the TTE findings were sought.

Results: We analyzed 240 patients (mean patient age 58.5±14) out of 10563 TTEs. While only one patient exhibited a definite CSE on TTE, potential CSEs were found in 35 patients (14.6%), most commonly caused by left ventricular (LV) systolic dysfunction (31.4%), followed by LV regional wall motion abnormalities (25.7%). Multivariate analysis revealed 2 independent predictors for identifying a CSE on TTE: history of coronary artery disease (odds ratio [OR] 6.2, 95% confidence interval [CI]:2.6-14.8, p=0.0001), and nationality (OR 0.16, 95% CI: 0.3-0.7, p=0.019). The TTE findings affected therapy in only 3 patients (1.2%).

Conclusion: The TTE performed to exclude a CSE in patients with stroke or TIA resulted in low diagnostic yield, and had little impact on therapeutic decisions. Future refinement of clinical strategies to predict a CSE is needed to improve diagnosis, and possibly cost-effectiveness, of TTE.

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Cerebrovascular events are major sources of morbidity and mortality, with stroke the third leading cause of death and a major cause of disability worldwide.[1,2] In the United States, it has been estimated that out of every 700,000 patients, approximately 29% will experience recurrent strokes every year.[3] Furthermore, it is predicted that by 2020, cerebrovascular events will be the second leading cause of death, next to coronary artery disease (CAD), in the developing world.[4] Although the incidence of stroke in Saudi Arabia is relatively low when compared to the West (43.8/100,000 versus 150-250/100,000), affected patients are characteristically younger.[5] Cardioembolic strokes appear to be more likely in young patients, accounting for 15-20% of all strokes.[1,6] The diagnostic yield of echocardiography in detecting a cardiac source of embolism (CSE) is controversial,[1,7] yet many patients are referred for transthoracic echocardiography (TTE) to diagnose CSE. There is limited data from Saudi Arabia regarding the diagnostic yield of echocardiography in selected stroke patients. Accordingly, the objectives of the present study were to explore the diagnostic yield of TTE in detecting potential CSE, and to assess the impact of TTE findings on patient management.

Methods.

Patient population. Candidates for this study consisted of patients admitted to King Khalid University Hospital, Riyadh, Kingdom of Saudi Arabia, with the diagnosis of an ischemic stroke or a transient ischemic attack (TIA). Additionally, patients must have been referred to the adult echocardiography lab for a TTE to diagnose a CSE.

Study design. We manually screened the indication section of each echocardiography report from January 2006 to December 2008, identifying investigations of a CSE in patients admitted with a stroke or TIA. All TTEs were interpreted and reported by an experienced echocardiographer. Each report was systematically screened for predefined criteria indicating potential CSE. These criteria included: mitral stenosis, mitral valve prolapse, valve vegetation, left ventricular (LV) systolic dysfunction with an ejection fraction (EF) ≤35%, LV wall motion abnormalities (WMA), LV aneurysms, LV thrombus, left atrial (LA) thrombus, atrial septal defects, atrial septal aneurysm, patent foramen ovale (PFO), evidence of right to left intra-cardiac shunting following intravenous injection of agitated saline, aortic atheroma, cardiac masses, and mechanical valve thrombosis. Findings from TEE were documented. All exams were performed using an HP Sonos 5500 imaging system (Hewlett-Packard Co., Andover, MA, USA), equipped with a 3-4 MHz transducer, for 2-dimensional, M mode, and Doppler exams. We reviewed patient medical records, collecting the following data: baseline demographics, risk factors for atherosclerosis, heart rhythm, stroke, or TIA development, the presence of vascular disease such as CAD, carotid disease, peripheral arterial disease (PAD), or any past coronary revascularization procedures such as percutaneous coronary interventions (PCI), or coronary artery bypass surgery (CABG). In addition, we also reviewed hospital management, specifically to assess whether the findings of the TTE changed patient intervention. The interventions and time line relationship to the index TTE were documented. These interventions included anticoagulation, valve replacement, or surgical removal of a cardiac mass. Ethics approval was obtained from the hospital institutional review board.

Study endpoints. The yield of TTE in diagnosing a CSE, and its effect on patient management, were the primary endpoints of the current study.

Statistical analysis. Categorical values are presented as percentages. Continuous variables are summarized as mean ± standard deviation (SD). Fisher's exact test or chi-square test was used for categorical variables, and Student t test for continuous variables to assess group differences. Significant univariate variables (<0.05) were included in a multivariate logistic regression model by forced simultaneous entry rather than automated stepwise selection. We also reported odds ratios (OR) along with 95% confidence intervals (95% CI). For all comparisons, we regarded *p*-values less than 0.05 as significant, and all tests were two-sided. All analyses were performed using the Statistical Package for Social Sciences (SPSS Inc, Chicago, IL, USA), version 7.

Results.

A total of 10563 TTEs were performed during the study period; of those, 274 (2.6%) patients were referred to the adult echocardiography lab for a TTE to exclude a CSE. Thirty-four patients (12.4%) were subsequently excluded from our study due to 1) misdiagnosis of ischemic stroke or TIA (21 patients, 7.7%), and 2) incomplete medical records or TTE reports (14 patients, 5.1%). Therefore, 240 patients, representing 2.3% of the TTEs performed during the study period, were eventually analyzed in the current investigation. **Table 1** depicts the baseline characteristics of the study cohort. Referred patients were relatively young, mostly of Saudi nationality, and predominantly male. One hundred and eighty-four patients (76.7%) suffered from a stroke, while 56 (23.3%) experienced a TIA. Almost all patients were in sinus rhythm (95%) as documented on their hospital records or their echocardiography reports. The TTE was completely normal in 117 patients (48.8%), while 88 patients (36.7%) showed abnormalities that were not relevant to the indication. A finding classified as a potential CSE was identified in 35 patients (14.6%). The TTE findings are

Table 1 - Demographic and clinical characteristics of the 240 study patients.

Variable	Total (N=240)	Patients with CSE by TTE (n=35)	Patients with no CSE by TTE (n=205)	*P*-value
		n (%)		
Age (years, mean±SD)	58.5 ± 14	55.3 ± 13.7	59 ± 14.3	0.8
Saudi	231 (96.3)	31 (88.6)	200 (97.6)	0.03
Male	133 (55.4)	23 (65.7)	110 (53.7)	0.13
Diabetes	137 (57.1)	16 (45.7)	121 (59.0)	0.1
Hypertension	167 (69.6)	25 (71.4)	142 (69.3)	0.5
Smoking	17 (7.1)	2 (5.7)	15 (7.3)	0.5
Dyslipidemia	58 (24.2)	10 (28.6)	48 (23.4)	0.3
CAD	47 (19.6)	19 (54.3)	28 (13.7)	0.0001
Pre-existing stroke	13 (5.4)	1 (2.9)	12 (5.9)	0.4
PAD	16 (6.7)	4 (11.4)	12 (5.9)	0.2
PCI	4 (1.7)	2 (5.7)	2 (1.0)	0.1
CABG	9 (3.8)	6 (17.1)	3 (1.5)	0.0001
Carotid disease	17 (7.1)	3 (8.6)	14 (6.8)	0.5
Atrial fibrillation	12 (5.0)	2 (5.7)	10 (4.9)	0.5

CAD - coronary artery disease, PAD - peripheral arterial disease, CSE - cardiac sources of embolism, PCI - percutaneous coronary intervention, CABG - coronary artery bypass surgery, TTE - transthoracic echocardiography

summarized in **Table 2**. The average age of patients with a potential CSE was 55.3±13.7 years (range 29-76 years), and these patients were predominantly male. Patients with a potential CSE were less likely to be Saudi nationals (31 [88.6%] versus 200 [97.6%], p=0.03), more likely to have CAD (19 [54.3%] versus 28 [13.7%], p=0.0001), and more likely to have had CABG (6 [17.1%] versus 3 [1.5%], p=0.0001). Univariate analysis confirmed the preceding 3 characteristics as predictors for finding a potential CSE by TTE. Using multivariate logistic regression, however, only CAD (OR 6.2, 95% CI 2.6-14.8, p=0.0001), and being a non-Saudi national (OR 0.16, 95% CI 0.3-0.7, p=0.019), remained independent predictors for finding a potential CSE on TTE. The most common cause for a potential CSE was LV systolic dysfunction with an EF ≤35%, followed by LV WMA (**Table 2**). Intravenous agitated saline contrast study was performed in 51 patients (21.2%), and was positive in 5 patients (9.8%). Two patients were found to have more than one abnormality suggestive of CSE; one patient possessed a LV WMA and an LV thrombus, and the other patient displayed a PFO and evidence of right to left shunting by contrast saline study. The TTE findings that are highly probable for causing cardioembolic cerebral events were found in one patient with a definite LV thrombus, making the TTE yield for finding a highly probable CSE in this study cohort only 0.4%. A TEE was performed in 11 patients (4.6%), and this technique added a new finding suggestive of a CSE in 3 patients (one valve vegetation, and 2 PFOs). Regarding patient management, no patient underwent a valve replacement or surgical removal of a cardiac mass as a result of the findings from TTE. Anticoagulation was

Table 2 - The TTE results from 35 patients with potential CSE.

TTE findings	n	(%)
Mitral stenosis	2	(5.7)
Mitral valve prolapse	0	
Valve vegetation	0	
LV systolic dysfunction (EF ≤ 35%)	11	(31.4)
LV RWMA	9	(25.7)
LV aneurysm	0	
LV thrombus	1	(2.9)
LA thrombus	0	
ASD	0	
ASA	2	(5.7)
PFO	2	(5.7)
Positive contrast saline	4	(11.4)
Aortic atheroma	4	(11.4)
Cardiac masses	0	
Mechanical valve thrombosis	0	

LV - left ventricular, EF - ejection fraction, RWMA - regional wall motion abnormalities, LA - left atrial, ASD - atrial septal defect, ASA - atrial septal aneurysm, PFO - patent foramen ovale, TTE - transthoracic echocardiography, CSE - cardiac sources of embolism

Table 3 - Impact of TTE findings on patient management.

Management	Patients	
	n	(%)
Did not change management	237	(98.8)
Changed management	3	(1.3)
Anticoagulation		
Pre-event anticoagulation		
Atrial fibrillation	6	(2.5)
Mechanical valve	1	(0.4)
Other indications	3	(1.3)
Newly instituted anticoagulation		
Atrial fibrillation	5	(2.1)
Based on TTE	3	(1.3)
Other indication	2	(0.8)
Valve replacement	0	
Surgical mass removal	0	

TTE - transthoracic echocardiography

started in only 3 patients (2.1%) as a direct consequence of the TTE findings (**Table 3**).

Discussion. This study assessed the role of TTE in detecting a CSE in patients suffering from cerebrovascular events. Our study primarily reveals that the diagnostic yield of these TTEs is very low. These findings are important because a clinical diagnosis of a CSE has been estimated to be 60% (44% potential CSE, and 16% as a diagnosis of exclusion) in a study conducted in the eastern province of Saudi Arabia,[5] which would likely be translated into more referrals for echocardiography. Our findings confirm previous reports examining the diagnostic yield of TTE performed to diagnose a CSE. Sansoy et al[7] reviewed TTE reports in more than 1000 US patients with either an ischemic stroke or TIA, and found a highly probable source of CSE to be <3%, and a possible source to be 5%. On the other hand, a more recent study revealed that an echocardiographic diagnosis of a potential CSE was found in 18% of patients studied; however, most of the potential CSE in that study were driven by the diagnosis of atrial fibrillation, and presence of a PFO.[8]

Variability in reporting the diagnostic yield of TTE occurs partly as a result of the variability in the classification of what would be considered a high probability or low probability CSE. Additionally, diagnostic yield is heavily influenced by the age of the population tested,[1,8,9] and the prevalence of underlying cardiovascular disease.[10] The population of our study cohort is distinct in several aspects compared to previous studies addressing the same clinical question. Patients included in the present study were significantly younger than their Western counterparts (on average 10 years younger), and have significantly more risk factors for vascular disease, as well as established vascular disease. Young age of presentation in patients with cerebrovascular events has been reported in Saudi Arabia;[5] however, our study cohort is even younger, possibly reflecting patient selection for undergoing echocardiography. In addition, we found that patients with a potential CSE on TTE were 6 times more likely to have a history of CAD. Previous reports have demonstrated that the presence of cardiac disease increases TTE diagnostic yield.[2] The fact that more non-Saudis were found to have a CSE on TTE may partly reflect the younger age of expatriates who work in Saudi Arabia, resulting in a relatively higher TTE diagnostic yield in that population.

An effective screening test should address patient prognosis or change patient management. Therefore, we examined the therapeutic implications of the echocardiographic findings, and discovered that they were minimal. Our results are in contrast to other studies investigating therapeutic implications of echocardiographic findings. De Abreu et al[1] found that TTE results led to an indication for anticoagulation in 37% of patients. However, this indication was based on the diagnosis of dilated cardiomyopathy and LV EF <35%, which comprised almost 23% of what was considered an indication for anticoagulation. Anticoagulation for dilated cardiomyopathy and significant LV systolic dysfunction is controversial, and has been graded as class IIb (level of evidence C) in the most recent stroke prevention guidelines.[3] In another study[11] that examined the role of echocardiography in deciding anticoagulation, TEE uncovered a high risk CSE mandating anticoagulation in 8% of patients. However, most patient identifications of high risk CSE were based on diagnosis of an aortic thrombus and spontaneous echocardiographic contrast in the LA. These indications for anticoagulation are still controversial and are not yet supported by firm evidence.[3,10]

Our study suffers from several limitations. We employed a retrospective analysis, and thus selection bias could not be excluded. Moreover, no documentation exists for the number of echocardiograms requests that were rejected by the echocardiographers due to an inadequate indication for performing the exam. In our institution almost all patients with a stroke or a TIA are referred for a screening TTE. Assuming that a select population underwent the TTE, it is conceivable that more patients with a high clinical risk for cardioembolic events are referred, resulting in a higher diagnostic yield, a finding that is not demonstrated in this study. No control group was used for comparison, although the diagnostic yield of TTE in our study would remain very low even if a control group showed a statistically lower diagnostic yield. In addition, very few patients underwent a TEE; therefore, negative TTE exams could not be verified. Our objective, however, was to document the diagnostic yield of TTE in diagnosing CSE in patients with cerebrovascular events.

In conclusion, our study showed a low diagnostic yield of TTE in diagnosing a CSE in patients with either stroke or TIA. Our study also revealed a minimal impact of TTE results on therapeutic decisions. Patients with vascular disease in Saudi Arabia are unique in that they are younger and possess more cardiovascular risk factors than their Western, more often-studied, counterparts. Therefore, future studies should prospectively confirm the above findings, compared to a control group.

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