Routine echocardiography in the management of stroke and transient ischaemic attack: a systematic review and economic evaluation

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Scientific summary

Management of stroke and TIA
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Background

Stroke is a major cause of mortality in the UK. As a single cause of death, stroke is second only to coronary heart disease and it can cause a range of disabilities including speech problems, limb paralysis and dementia. Approximately half of all those affected by stroke are dependent on others for help with daily activities. A transient ischaemic attack (TIA) produces symptoms similar to those of a stroke but these symptoms resolve within 24 hours and usually within a few hours. One-fifth of patients who have experienced a TIA will later develop a stroke. Identification of the underlying cause of stroke and TIA is important so that preventative therapy can be used to reduce the risk of recurrence. The causes of stroke vary although it is thought that about 20% of ischaemic strokes are cardioembolic. Transthoracic echocardiography (TTE) is a diagnostic tool used to identify cardiac sources of stroke by using sound waves to produce images of the heart, facilitating the detection of blood clots, valvular disorders and structural defects associated with stroke. TTE can be performed in fundamental imaging mode (TTEf), which uses the reflected echoes from the same spectral band as that of the emitted pulse, or in second harmonic imaging mode (TTEh), which employs the second harmonic of the emitted frequency band to construct images. Transoesophageal echocardiography (TOE) uses similar sound wave technology to produce images of the heart; however, with TOE the ultrasound transducer, positioned on an endoscope, is guided down the patient's throat into the oesophagus. TOE is therefore more invasive than TTE but provides images without interference from the ribs or lungs.

Objectives

The overall aim was to use secondary research methods to determine the most appropriate echocardiography diagnostic management strategy for first-episode diagnosed stroke and TIA patients. More specifically, the objectives were to:

- undertake systematic reviews to determine (a) the prevalence of potential cardiac sources of stroke and TIA and (b) the diagnostic accuracy of echocardiography
- undertake a survey to describe current practice in the NHS in terms of guidelines and management strategies used by stroke centres
- evaluate the cost-effectiveness of the addition of TTE to the routine assessment of patients who have had a first-episode diagnosed stroke or TIA in the UK.

Methods

A systematic review was undertaken to identify the prevalence rates of cardiac sources of stroke and TIA in patients with first-episode ischaemic stroke or TIA. Major databases including EMBASE, MEDLINE and the Cumulative Index to Nursing and Allied Health Literature (CINAHL) were searched from inception to December 2010 and prevalence ranges were reported. In addition, diagnostic accuracy studies of sources of stroke that are not clinically apparent on routine examination were sought in MEDLINE, EMBASE, CINAHL, PsycINFO, Web of Science, The Cochrane Library (including the Cochrane Central Register of Controlled Trials and the Database of Abstracts of Reviews of Effects), the NHS Economic Evaluation Database and the Health Technology Assessment database (from inception to September 2011). Study quality was assessed using the Quality Assessment of Diagnostic Accuracy Studies (QUADAS) checklist. Included studies were meta-analysed using WinBUGS, using a bivariate normal model to calculate the logit sensitivities and specificities in each study to account for correlation within studies.

For the economic analysis a discrete event decision-analytic model was developed to estimate the costs and quality-adjusted life-years (QALYs) accrued by each potential echocardiography strategy in the management of stroke and TIA. The model took a lifetime horizon and the perspective of the NHS. Costs and health benefits were discounted at an annual rate of 3.5% as recommended by the National Institute for Health and Care Excellence. Utility values were identified by a literature review. Univariate and probabilistic sensitivity analyses were conducted. The only pathology for which evidence was found to enable modelling was left atrial thrombus. The cost-effectiveness of echocardiography is therefore based on all stroke patients being tested (apart from those contraindicated echocardiography) but only those with a left atrial thrombus receiving the benefits and harms of treatment. The benefits of early detection of left atrial thrombi were modelled using literature reviews to estimate the diagnostic accuracy of TTEh and TOE, the benefits and harms of treatment and the risks of stroke in treated and untreated patients with and without left atrial thrombi. Hospital and long-term care costs were estimated for each strategy and each stroke outcome. The analysis was conducted for patients aged 45, 55 and 65 years and the costs and QALYs accrued for each cohort were estimated for each diagnostic strategy.

To describe current NHS stroke management practice we provided a questionnaire survey to the lead clinician of all stroke units in the UK.

Results

The searches identified 17,278 citations for the systematic review of the prevalence of potential cardiac sources of stroke and TIA, of which 65 studies were included. From the studies retrieved, TOE (45 studies) was the most frequently reported diagnostic tool used to assess cardiac pathologies followed by TTE (38 studies of TTEh and TTEf). The prevalence rates of the identified pathologies in the selected study populations were wide-ranging. From the studies identified, patent foramen ovale (PFO) was the most frequently reported pathology (39 studies) with a prevalence ranging from 0.25% to 73%, followed by atrial septal aneurysm (28 studies) with a prevalence ranging from 0.4% to 28% and mitral valve prolapse (17 studies) with a prevalence ranging from 0% to 31.6%.

The searches identified 16,504 citations for the systematic review of the diagnostic accuracy of echocardiography, of which 51 studies were included. The pooled sensitivity to detect left atrial thrombus in three studies using TTEf was 0.34 [95% credible interval (CrI) 0.07 to 0.71] with a specificity of 1.00 (95% CrI 0.97 to 1.00) compared with TOE. The pooled sensitivity to detect left atrial thrombus in three studies using TTEh was 0.79 (95% CrI 0.47 to 0.94) with a specificity of 1.00 (95% CrI 0.99 to 1.00) compared with TOE. The pooled sensitivity to detect PFO in 13 studies using TTEf was 0.34 (95% CrI 0.21 to 0.47) with a specificity of 1.00 (95% CrI 0.99 to 1.00) compared with TOE. The pooled sensitivity to detect PFO in 11 studies using TTEh was 0.89 (95% CrI 0.80 to 0.95) with a specificity of 0.99 (95% CrI 0.97 to 1.00) compared with TOE. The pooled sensitivity to detect spontaneous echo contrast (SEC) in the left atrium in four studies using TTEf was 0.00 (95% CrI 0.00 to 0.02) with a specificity of 1.00 (95% CrI 0.99 to 1.00) compared with TOE. Superior diagnostic accuracy was found using TTEh to detect left atrial SEC, with a sensitivity of 0.88 (95% CrI 0.78 to 0.94) and a specificity of 1.00 (95% CrI 0.03 to 1.00) compared with TOE, although this was based on a single study. Differences in the diagnostic accuracy of TTE and TOE occurred mostly in their sensitivity to detect cardiac sources of stroke; in most studies the specificity of TTE and TOE was similar. No adverse events data were reported.

Our principal economic finding is that TTEh is a cost-effective use of NHS resources compared with TOE in those cases where clinicians deem it the most appropriate form of testing. Because of data limitations we have not evaluated the cost-effectiveness of TOE in those cases in which clinicians regard it the most appropriate test.

The survey of UK stroke units showed that the decision-making process in the management of stroke and TIA is very complex and varies considerably by site. It is clear that to accurately describe current management practice a very sophisticated questionnaire would be required, which may result in poor response rates and thus yield little useful information.

Discussion

There was considerable variation in the prevalence of cardiac causes of stroke, reflecting the heterogeneity of the included studies and the uncertainty surrounding the clinical importance of these cardiac pathologies in ischaemic stroke. Data were derived from risk factor findings on routine examination rather than established aetiology, and the relative importance of each of the cardiac pathologies in ischaemic stroke is uncertain.

Across a range of cardiac pathologies (PFO, atrial thrombus, atrial septal defect, atrial septal aneurysm, left atrial appendage thrombus, SEC) the diagnostic accuracy of TTEh was superior to that of TTEf, although the consequence of the improved sensitivity of TTEh was a decrease in specificity. The diagnostic accuracy of TOE was superior to that of TTEh across most cardiac pathologies, although TOE also demonstrated imperfect accuracy for the detection of PFO.

The deterministic and probabilistic economic analyses both show that in those cases in which clinicians consider TTEh to be the most appropriate test it is a cost-effective use of NHS resources. It should be noted that the evidence base for the analysis for some of the main parameters in the model was poor and thus the conclusions reached should be treated with a certain amount of caution.

This analysis has highlighted the need for further evaluation of current echocardiography technologies, the causal associations between potential risk factors and stroke and whether or not anticoagulation therapies prevent recurrent stroke. In the presence of multiple risk factors, establishing the cause of cardioembolic stroke is complex and unlikely to provide an unequivocal answer. Studies attempting to establish the prevalence of cardiac sources of stroke should perform a thorough clinical evaluation to identify all potential risk factors, rule out those that are not relevant and, when possible, grade the findings according to risk. Research is needed to reduce the uncertainty around the estimates of the sensitivity and specificity of TTEh and TOE, singly and in combination, in detecting treatable cardiac abnormalities compared with the ‘gold standard’ in each pathology. Answering these research questions would improve the accuracy of the results produced by the economic model.

Conclusion

The economic analysis indicates that, in those cases in which TTEh is deemed the most appropriate test for the management of stroke and TIA, it is a cost-effective use of NHS resources. Because of data limitations it was not possible to evaluate the cost-effectiveness of TTEh compared with TOE in subsets of cases in which TOE is considered most appropriate.

However, this analysis has highlighted the need for more research in several areas and until this is carried out the results of the economic evaluation should be treated with a certain amount of caution. The main research priorities are long-term UK-based studies measuring stroke recurrence rates, the efficacy of treatment and the diagnostic accuracy of TTEh and TOE in detecting cardiac abnormalities that respond to treatment.

Study registration

This study is registered as PROSPERO no. CRD42011001353.

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