Diagnostic accuracy and cost-effectiveness of contrast echocardiography on evaluation of cardiac function in technically very difficult patients in the intensive care unit

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Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
The use of four diagnostic procedures for the evaluation of cardiac functions in technically very difficult patients in the intensive care unit (ICU). The four procedures were:

- fundamental imaging transthoracic echocardiography (FTTE),
- harmonic imaging TTE (HTTE),
- harmonic imaging plus contrast TTE (CTTE+H), and
- transoesophageal echocardiography (TEE).

Type of intervention
Diagnosis.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients who presented a technically very difficult study on fundamental echocardiographic imaging, where a TEE was clinically indicated for the evaluation of left ventricular (LV) function. "Technically very difficult" studies were defined as those with non-visualisation of the endocardium in 50% or more of LV segments (at least 8 of the 16 segments). The endocardium was considered "non-visualised" if it could not be seen from all echocardiographic views, including parasternal or apical windows. Exclusion criteria were known or suspected hypersensitivity to blood products or albumin, pregnancy and participation in another clinical trial within 30 days of the study.

Setting
The setting was medical, coronary and surgical ICUs. The economic study was conducted at the Methodist Hospital in Houston (TX), USA.

Dates to which data relate
The dates during which the effectiveness and resource use data were collected were not reported. The price year was not provided.

Source of effectiveness data
The effectiveness evidence was derived from a single study.
Link between effectiveness and cost data
The costing was performed retrospectively on a sample of patients different from that used in the effectiveness study.

Study sample
Power calculations to determine the sample size were not reported. A sample of 32 consecutive eligible patients was enrolled from those admitted to the study hospital. The mean age was 65 (± 16) years and 75% of patients were men. A single group of patients underwent all four diagnostic procedures.

Study design
This was a prospective within-group comparison study, which was conducted in a single centre (the Methodist Hospital in Houston). The patients were not followed after the diagnosis was made and, as such, no loss to follow-up was reported. An experienced reader, who was blinded to all clinical information, interpreted all echocardiographic studies in random order. An independent reader, blinded to all results, reviewed the cases of 9 patients that were randomly selected.

Analysis of effectiveness
All patients included in the initial study sample were taken into account when estimating the effectiveness. The health outcomes used in the analysis were:

- the adequacy of visualisation of regional wall motion (WM);
- the confidence in interpretation;
- the agreement in the exact interpretation of WM (using TEE as the 'gold' standard);
- the agreement in differentiating normal from abnormal territories (using TEE as the 'gold' standard);
- the agreement in detecting any WM abnormality (using TEE as the 'gold' standard);
- the sensitivity and specificity of each procedure relative to the results obtained with TEE;
- a global assessment of LV ejection fraction (LVEF); and
- inter-observer agreement (two observers) when evaluating WM and LVEF.

Effectiveness results
Excellent or adequate endocardial visualisation was reached in 13% of segments with FTTE, in 34% of segments with HTTE, in 87% of segments with CTTE+H, and in 90% of segments with TEE. There was no statistically significant difference between CTTE+H and TEE, whereas FTTE and HTTE were significantly less adequate then CTTE+H or TEE.

The confidence in interpretation was 41% with FTTE, 65% with HTTE, and 98% with CTTE+H and TEE, (p<0.001).

The agreement in the exact interpretation of WM (using TEE as the 'gold' standard) was 48% with FTTE, 58% with HTTE, and 70% with CTTE+H, (p<0.0001).

The agreement in differentiating normal from abnormal territories (using TEE as the 'gold' standard) ranged from 53 to 59% with FTTE, from 56 to 69% with HTTE, and was 72% with CTTE+H.

The agreement in detecting any WM abnormality (using TEE as the 'gold' standard) was 53% with FTTE, (p=0.1), 66% with HTTE (p=0.05), and 78% with CTTE+H, (p<0.001).
The sensitivity was 67% with FTTE, 75% with HTTE, and 89% with CTTE+H. The specificity was 70% with FTTE, 75% with HTTE, and 75% with CTTE+H.

The global assessment of LVEF was possible in 31% of patients with FTTE, 50% of patients with HTTE, and 97% of patients with CTTE+H.

When the multiple diameter method was used, LVEF could be defined in 6% of patients with FTTE, 34% of patients with HTTE, and 75% of patients with CTTE+H, (p<0.001).

EF quantified by CTTE+H correlated best with TEE, (r=0.91).

The agreement between two observers for evaluating WM was 44% with FTTE, 46% with HTTE, and 87% with CTTE+H.

When assessing WM, the correlation between two observers was 0.47 with FTTE, 0.48 with HTTE, 0.83 with CTTE+H, and 0.71 with TEE.

When assessing LVEF, there was no correlation with FTTE and HTTE, whereas the correlation was 0.97 with CTTE+H and 0.93 with TEE (all these correlation values reached statistical significance).

Clinical conclusions
The effectiveness study showed that the use of CTTE+H significantly improved the diagnostic accuracy of procedures used to evaluate cardiac functions in technically very difficult patients.

Measure of benefits used in the economic analysis
The summary benefit measures used in the economic analysis were the accuracy rates for WM and LVEF. Both were obtained directly from the effectiveness analysis.

Direct costs
Discounting was not relevant because the costs were incurred over a short time. The unit costs were analysed separately from the quantities of resources used. The health services included in the economic analysis were diagnostic procedures and ICU stay. The total cost estimates included fixed and variable labour costs, supply, equipment, other direct costs, and allocated overheads. The cost/resource boundary adopted in the study was not explicitly stated, but it appears to have been that of the hospital where the diagnostic procedures were conducted. The procedural costs were estimated using actual data coming from an internal cost-accounting system that provided the unit operating cost of the study diagnostic procedures and the average ICU hospital cost. Resource use was calculated assuming that each patient would undergo all procedures. A hypothetical sample of 100 patients was considered. The price year was not provided, but it seems that the costs have been estimated from a database for 1996 to 1998.

Statistical analysis of costs
The costs were treated deterministically.

Indirect Costs
The indirect costs were not included in the economic analysis.

Currency
US dollars ($).

Sensitivity analysis
Sensitivity analyses were not conducted.

**Estimated benefits used in the economic analysis**
The accuracy rates for WM were 48% for FTTE, 58% for HTTE, and 70% for CTTE+H. The corresponding rates for LVEF were 25% (FTTE), 38% (HTTE) and 84% (CTTE+H), respectively.

**Cost results**
In a sample of 100 patients, the procedural costs to identify WM were $31,087 with FTTE, $30,008 with HTTE, $37,814 with CTTE+H, and $39,115 with TEE. The corresponding costs to identify LVEF were $40,083 (FTTE), $37,831 (HTTE), $32,338 (CTTE+H) and $39,115 (TEE), respectively.

**Synthesis of costs and benefits**
An incremental cost-effectiveness ratio (ICER) was calculated to combine the costs and benefits of the diagnostic strategies.

In a sample of 100 patients, the ICER of FTTE in comparison with TEE was -$154 for each 1% increase in WM accuracy, and -$13 for each 1% increase in LVEF accuracy. The corresponding figures for HTTE relative to TEE were -$217 (WM) and -$21 (LVEF), respectively, and for CTTE+H relative to TEE, -$43 (WM) and -$423 (LVEF).

**Authors’ conclusions**
Harmonic imaging and contrast transthoracic echocardiography (CTTE+H) improved the visualisation of the ventricular endocardium, and increased the diagnostic accuracy of the interpretation of regional and global left ventricular (LV) functions. It also led to cost-savings of 3 to 17% in comparison with transoesophageal echocardiography (TEE).

**CRD COMMENTARY - Selection of comparators**
The rationale for the choice of the comparator was clear. TEE was selected since it represented the most accurate diagnostic procedure for critically ill patients. TTE (both FTTE and HTTE) were the first-line approach for such patients, while CTTE+H represented the technology under evaluation. You should decide whether they represent valid comparators in your own setting.

**Validity of estimate of measure of effectiveness**
The analysis of effectiveness used a prospective within-group comparison study, which was appropriate for the study question. An external comparison group was not required as all of the patients received the four diagnostic procedures. The study sample comprised an unselected group of patients and it appears to have been representative of the study population. The study assessors were blinded to all clinical information. However, there were some drawbacks associated with the study design. For example, factors other than the study interventions, or the sequential order of performing the diagnostic procedures, may have affected the conclusions of the effectiveness analysis. Such issues have to be considered when interpreting the results of the study.

**Validity of estimate of measure of benefit**
The benefit measure was obtained from the effectiveness analysis and was specific to the study procedures. Thus, it would be difficult to compare the benefits of the present study with those of other health care interventions.

**Validity of estimate of costs**
The perspective adopted in the study appears to have been that of the hospital, although it was not explicitly stated. The costs came from the accounting system of the hospital. The unit costs of the diagnostic procedures were reported.
Resource use was estimated on the assumption that each patient would undergo each diagnostic procedure. The price year was not reported, thus making reflation exercises in other settings difficult. The cost estimates were specific to the study setting. No statistical tests were conducted on the quantities or unit costs.

**Other issues**
The authors reported the results of some studies that evaluated the impact of echo contrast in the interpretation of WM and LVEF in ICU patients. However, they stressed that their study was the first to compare the results of several imaging techniques in critically ill patients. The issue of the generalisability of the study results to other settings was not addressed and sensitivity analyses were not conducted. Thus, the external validity of the analysis is likely to be quite low.

**Implications of the study**
The study results suggested that contrast echo may be safely and efficiently used for the diagnostic management of technically very difficult patients in the ICU. However, caution is required when interpreting the results of the analysis due to the limitations of the study design.

**Source of funding**
Supported by an investigator-initiated grant from Molecular Biosystems Inc., San Diego (CA); and Mallinckrodt Inc., St. Louis (MO), USA.

**Bibliographic details**

**PubMedID**
11897214

**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Albumins /economics; Contrast Media /economics; Cost-Benefit Analysis; Echocardiography /economics; Echocardiography, Transesophageal /economics; Endocardium /ultrasonography; Fluorocarbons /economics; Humans; Image Enhancement; Intensive Care Units; Observer Variation; Reproducibility of Results; Sensitivity and Specificity; Stroke Volume /physiology; Ventricular Dysfunction, Left /diagnosis /economics

**AccessionNumber**
22002000651

**Date bibliographic record published**
31/03/2004

**Date abstract record published**
31/03/2004