Use of an intravenous contrast agent (Optison) to enhance echocardiography: efficacy and cost implications

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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
Using Optison, a second-generation intravenous contrast agent with echocardiography, in patients referred to echocardiography laboratory with baseline sub-optimal images.

Type of intervention
Diagnosis.

Economic study type
Cost-effectiveness analysis.

Study population
Patients referred to an echocardiography laboratory with baseline suboptimal images with a minimum of two of six endocardial border segments not being well delineated on the baseline apical four-chamber view.

Setting
Hospital. The economic analysis was carried out in the USA.

Dates to which data relate
The dates for effectiveness and resource use data collection were not reported. The price year was 1996.

Source of effectiveness data
Effectiveness data were derived from a single study.

Link between effectiveness and cost data
Costing was retrospectively performed on the same patient sample as that used in the effectiveness analysis.

Study sample
Power calculations were not stated to have been used in determining the sample size. The study sample consisted of 203 eligible patients, of whom 199 received 3 mL of Optison. 4 were excluded after failing to return for their second exam. The average (SD) age of the study patients was 55 (13) years and most were men (full demographic details are included in the paper). The percentage of study patients with clinically limiting cardiac or pulmonary dysfunction was 36% (74 out of 203). Echocardiographic imaging of the apical four-chamber view was conducted for each Optison injection, plus imaging the apical two-chamber, parasternal short axis, and parasternal long axis views, and then performing Doppler examination of the mitral valve, aortic valve, and pulmonary veins.
Study design
This was a prospective self-controlled trial, carried out in 14 centres. The duration of the follow-up was up to 48 hours after the Optison injection. No loss to follow-up was reported. The monitoring of patients for adverse events was performed during 48 hours after contrast administration.

Analysis of effectiveness
The principle (intention to treat or treatment completers only) used in the analysis of effectiveness was not explicitly specified. The primary clinical outcome measure was the percentage follow-up testing recommended to be necessary for a definitive diagnosis (by the reviewing echocardiographer). Other clinical outcomes were diagnostic yield (as defined by culminating in either a definitive diagnosis or a subsequent change in patient management) and diagnostic accuracy. Independent overread and interpretation of non-contrast and contrast echocardiograms was performed by physicians at a core echocardiography laboratory with discrepancies reviewed by the participating investigators. The criterion used for an echocardiogram being considered as diagnostic was four or more of six segments in the left ventricle being read in the apical four-chamber view. Four grades considered for the image segments were: A not well delineated, B average delineation, C good delineation, and D excellent delineation; as evaluated by the technicians in the core laboratory. In the statistical analysis, dilution and contamination effects were considered in calculating the differences in proportions.

Effectiveness results
The percentage of follow-up testing recommended to be necessary for a definitive diagnosis (by the reviewing echocardiographer) was 42% for the non-contrast and 12% for the contrast (Optison) echocardiograms, (p<0.001).

The corresponding values in terms of diagnostic yield were 87% for the non-contrast, and 49% for the contrast, (p<0.001).

The contrast (Optison) group required an average of 1.05 tests to obtain a diagnosis versus 1.33 in the non-contrast group (p<0.001), culminating in improvement in diagnostic accuracy of 2.7 fold for Optison as compared to non-contrast echocardiogram.

In the subgroup of patients with clinically limiting cardiac or pulmonary dysfunction, the corresponding improvement in diagnostic accuracy was 40%.

Clinical conclusions
To reduce the need for follow-up testing, Optison, as a second-generation intravenous contrast agent, can be used to aid in left ventricular opacification and endocardial border delineation and to augment the Doppler signal for patients whose initial echocardiogram is suboptimal.

Modelling
A decision analytic model was constructed using TREEAGE software version 2.6 to find the least costly diagnostic strategy. The confidence intervals were estimated using Monte Carlo simulations.

Measure of benefits used in the economic analysis
No summary benefit measure was identified in the economic analysis, and only separate clinical outcomes were reported. As such a cost-consequences analysis was performed.

Direct costs
Costs were not discounted due to the short time frame of the study. Some quantities were reported separately from the costs. Cost items were reported separately. Cost analysis covered the diagnostic costs of initial echocardiogram and any follow-up costing. The perspective adopted in the cost analysis was not explicitly specified. Data from adjusted
Medicare charges and a transition-1 microcost accounting system were used to determine costs based on both the "top-down" and "bottom-up" approach. Cost-to-charge ratios were used to adjust Medicare charges. The source of the "bottom-up" microcost data was the study institution. The date of the price data was 1996. Treatment costs were not included in the cost analysis.

**Statistical analysis of costs**
Analysis of variance was used to assess the overall differences in costs.

**Indirect Costs**
Not considered.

**Currency**
US dollars ($).

**Sensitivity analysis**
A series of one-way sensitivity analyses was performed on different cost components, diagnostic accuracy, recommended and observed posttest diagnostic testing. Threshold analysis was performed based on alteration in the cost of Optison (from $0 to $500).

**Estimated benefits used in the economic analysis**
Not applicable.

**Cost results**
The total diagnostic cost was $1,859 for the non-contrast echocardiogram versus $1,590 for Optison, (p<0.001).

**Synthesis of costs and benefits**
Costs and benefits were not combined since the use of G-CSF was the dominant strategy. The threshold value for the cost of Optison was $350 (the current cost of $110 per patient).

**Authors' conclusions**
The use of Optison may improve the effectiveness of echocardiography and decrease the overall costs of obtaining an accurate diagnosis.

**CRD COMMENTARY - Selection of comparators**
The reason for the choice of the comparators is clear.

**Validity of estimate of measure of benefit**
As the effectiveness data were derived from only one phase III clinical trial the internal validity of the estimates of effectiveness measures should be assessed with respect to potential referral bias and the patients' underlying disease, as acknowledged by the authors. The study was a cost-consequences analysis.

**Validity of estimate of costs**
Quantities were not fully reported separately from the costs. Adequate details of methods of cost estimation were given. The outcome variable used in the economic analysis was the physician's recommendations of subsequent tests.
rather than actual test data, which may limit the validity of the result. A good point of the study was the use of charge-
to-cost ratios, which increase the validity and generalisability of the results.

Other issues
The authors' conclusions appear to be reasonably justified given the extensive sensitivity analyses performed to tackle
the potential uncertainties and biases surrounding the parameters of the model. The issue of generalisability to other
settings or countries was addressed by performing sensitivity analysis and appropriate comparisons were made with
other studies.

Implications of the study
The results support the use of contrast agents, in this case Optison, to increase the diagnostic yield of
echocardiography and to reduce downstream costs. The study results also suggest that the use of a contrast agent may
improve patient satisfaction with the overall quality of care. In a recent analysis by Kangarloo et al, patients who had
to return for additional testing after an initially sub-optimal test were less satisfied with their care than those who did
not require follow-up testing.

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Bibliographic details
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Other publications of related interest
Kangarloo H, Ho B K T, Lufkin R B, et al. Effect of conversion from a fee-for-service plan to a capitation
reimbursement system on a circumscribed outpatient radiology practice of 20,000 persons. Radiology 1996;201:79-84.

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