Cost-effectiveness of second-generation contrast agents in stress echocardiography: data from Greek clinical practice


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 a second-generation echo-opaque contrast agent, Levovist, to improve imaging in dobutamine stress echocardiography (DSE) for the evaluation of coronary artery disease (CAD). Patients were administered half a vial of Levovist (4-g vial) at rest, in intravenous infusion at a rate of 2 mL/min of a 300 mg/mL solution, while the remainder was administered at the same infusion rate at peak dobutamine stress. The dobutamine administration protocol included 5 stages of progressively increasing doses (5, 10, 20, 30, 40 microg/kg per minute), with the addition of 1 mg atropine at the end of the infusion if the heart rate achieved was less than the submaximal expected rate.

Type of intervention
Diagnosis.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients undergoing DSE for the detection or evaluation of CAD.

Setting
The setting was a hospital. The economic study was carried out in Greece.

Dates to which data relate
The dates to which the effectiveness and resource use data related were not reported. The price year was also not reported.

Source of effectiveness data
The effectiveness evidence was derived from a single study.

Link between effectiveness and cost data
The costing was not carried out on the same sample of patients as that used in the effectiveness study.

Study sample
Power calculations were not reported. A sample of 132 patients undergoing DSE at the authors' institution was identified and recruited. Patients whose studies were unsatisfactory were divided into two groups. In group A the patients received Levovist, while in group B the patients did not receive a contrast agent. There were 30 patients (21 men) in group A and 10 patients (9 men) in group B. The mean age of the patients was 66 years (age range: 40 - 79) in
group A and 61 years (age range: 49 - 75) in group B. Patients whose DSE results failed to be diagnostic for reasons other than unsatisfactory visualisation of endocardial segments were excluded. A study was considered technically unsatisfactory (suboptimal) when the endocardial borders of two or more neighbouring left ventricle wall segments were not visualised either fully or partially in one or more echocardiographic views. One patient refused the contrast agent.

**Study design**
This was a prospective cohort study, which was presumably carried out at a single centre. Allocation of treatment was based on the availability of the contrast agent in the laboratory. During the 1-month follow-up period, all patients with an unsatisfactory study were referred for myocardial perfusion scintigraphy with thallium-201 or technetium-99m. No patient appears to have been lost to the follow-up assessment.

**Analysis of effectiveness**
All of the patients included in the initial study sample were accounted for in the analysis of effectiveness. The outcomes used were:

- the proportion of patients whose studies were unsatisfactory,
- the improvement of visualisation of the endocardial borders after Levovist was given,
- the proportion of patients undergoing scintigraphy, and
- related outcomes.

The baseline comparability of the study groups was not discussed, although the baseline characteristics were reported. However, the authors stated that there were no quantitative or qualitative differences in the endocardial wall segments that were not visualised satisfactorily.

**Effectiveness results**
The proportion of patients whose studies were unsatisfactory was 30% (40 out of 132). After Levovist was given, an improvement of visualisation of the endocardial borders was observed in 27 of 30 patients (90%).

During the follow-up, 80% of patients in group B and 10% of patients in group A underwent scintigraphy. The percentages of tests positive for ischaemia (or for the existence of viable myocardium) and of negative DSE studies for the whole patient population were, respectively, 52% and 48%.

The addition of a contrast agent raised the percentage of technically satisfactory studies from 70 to 90%.

The results of the analysis suggested that 80% of patients with an unsatisfactory DSE study would normally have been referred for scintigraphy for the investigation of CAD. If those patients were given Levovist, this percentage would be reduced to 10%.

**Clinical conclusions**
The effectiveness analysis showed that use of Levovist improved the rate of satisfactory studies in comparison with DSE without a contrast agent.

**Measure of benefits used in the economic analysis**
The health outcomes were left disaggregated and no summary benefit measure was used in the economic evaluation. In effect, a cost-consequences analysis was carried out.
Direct costs
Discounting was not relevant since the costs were incurred during a short timeframe (1 month). The unit costs were presented separately from quantities of resources used. The health services included in the economic evaluation were the contrast agent and the scintigraphic examination. The cost/resource boundary of the hospital and the third-party payer was adopted. Resource use was estimated from the results of the effectiveness study that were applied to a hypothetical group of 100 patients. The cost of the contrast agent came from the price paid by the hospital, while the cost of the scintigraphic examination was based on the government-recommended charge. A discount granted to those insured with the National Foundation of Social Security Services for the scintigraphic examination was also considered. The price year was not reported.

Statistical analysis of costs
The costs were treated deterministically.

Indirect Costs
The indirect costs were not considered.

Currency
Euros (Euro).

Sensitivity analysis
Sensitivity analyses were not performed.

Estimated benefits used in the economic analysis
See the 'Effectiveness Results' section.

Cost results
The cost calculation showed that in a hypothetical cohort of 100 patients with an unsatisfactory DSE study, the use of Levovist would add Euro 6,747. If 10% of these patients required scintigraphy, the total added cost would be Euro 9,453 (or Euro 95 per patient).

If the same 100 patients did not receive Levovist, the added cost of scintigraphy in 80 patients would be Euro 21,650 (or Euro 216 per patient).

Consequently, the use of Levovist led to a cost-reduction of approximately Euro 121 per patient. If the same calculations were carried out using the discounted charge for scintigraphy, the cost-reduction would be Euro 7 per patient.

Synthesis of costs and benefits
A synthesis of the costs and benefits was not relevant since a cost-consequences analysis was carried out.

Authors' conclusions
The use of contrast agents during dobutamine stress echocardiography (DSE) studies reduced the proportion of studies with low diagnostic value, thus reducing the hospital costs.

CRD COMMENTARY - Selection of comparators
The authors justified the choice of the comparator, stating that DSE without the use of contrast agents represented usual
care at their institution. You should decide whether this is a valid comparator in your own setting.

**Validity of estimate of measure of effectiveness**
The effectiveness analysis was based on an observational study. Treatment was allocated according to the availability of the contrast agent. The lack of randomisation makes it difficult to exclude the potential impact of selection bias and confounding factors. The authors did not discuss the baseline comparability of the study groups. Further, a small sample of patients was considered and there was no evidence of how appropriate the sample size was. The patients were identified at a single institution and it was unclear whether the study sample could be considered representative of the patient population. The authors noted that the absence of angiographic confirmation of CAD in patients where regional left ventricular dysfunction was found represented a limitation of their study.

**Validity of estimate of measure of benefit**
No summary benefit measure was used in the analysis because a cost-consequences analysis was conducted. Please refer to the comments in the 'Validity of estimate of measure of effectiveness' field (above).

**Validity of estimate of costs**
A restricted perspective was adopted in the study and only limited cost categories were included in the economic evaluation. The unit costs and the quantities of resources used were reported, but the price year. The source of the data was provided. The cost estimates were specific to the study setting, but alternative estimates were not explored in the sensitivity analysis. In addition, the costs were treated deterministically.

**Other issues**
The authors stated that their findings corroborate those from published studies. The issue of the generalisability of the study results to other settings was not addressed and sensitivity analyses were not carried out. This reduces the external validity of the analysis. The study referred to patients undergoing a DES study and this was reflected in the authors' conclusions.

**Implications of the study**
The study results supported the use of contrast agents to improve the quality of imaging of endocardial borders in patients undergoing DES studies.

**Source of funding**
None stated.

**Bibliographic details**

**Other publications of related interest**

Subject indexing assigned by CRD

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