Retrospective analysis of the cost-effectiveness of using plasma brain natriuretic peptide in screening for left ventricular systolic dysfunction in the general population

Nielsen O W, McDonagh T A, Robb S D, Dargie H J

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 measurement of brain natriuretic peptide (BNP) was examined in this study. BNP is considered to be a predictor of left ventricular systolic dysfunction (LVSD) and is used to rule out LVSD in individuals in the general population.

Type of intervention
Screening.

Economic study type
Cost-effectiveness analysis.

Study population
The study referred to the general population of individuals aged 25 to 74 years.

Setting
The setting of the study was not explicitly reported. The economic study was carried out in Glasgow, UK.

Dates to which data relate
No dates for the effectiveness or resource use data were reported. The price year was not given.

Source of effectiveness data
The effectiveness evidence came from a single study.

Link between effectiveness and cost data
The costing was performed retrospectively on the same sample of patients as that used in the effectiveness analysis (assuming that each individual would receive one screening test).

Study sample
Power calculations to determine the sample size were not reported. A single group of 1,257 individuals randomly selected from a sample of 2,000 invited individuals, who had attended the Third Glasgow Monica Risk Factor Survey in 1992 and who had an analysable ECHO and a venous blood sample available, were included in the study. The authors stated that individuals participating in the study were comparable with those who did not participate.

Study design
This appears to have been a cross-sectional study in which a single group of patients was evaluated to identify those
with and without the disease. The patients were randomly selected from a wider sample, but the method of randomisation was not reported. The sites where the study was conducted were not reported. The patients were not followed up after the outcome assessment. The patients completed a self-reported questionnaire and a blood pressure reading was obtained. Electrocardiography was also performed. Two readers coded all the electrocardiograms (ECGs) and a third coder adjudicated any discrepancies. For echocardiography, a left ventricular ejection fraction (EF) was used as the 'gold' standard for left ventricular function.

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 study were:

- the number of patients with LVSD;
- the sensitivity, specificity, positive and negative predictive values of the alternative predictors evaluated in the analysis (clinical test, ECG, clinical test plus ECG, and BNP);
- the number of individuals that needed to be examined (NNE) by ECHO to detect one case of LVSD; and
- the prevalence and identification of factors predicting LVSD in three subgroups of patients.

The three subgroups of patients were:

- individuals with ischaemic heart disease (IHD), defined as those with a self-reported myocardial infarction, combined with signs of ischaemia on the ECG or with physician-diagnosed angina and the need for anginal treatment;
- high-risk individuals, defined as those with elevated blood pressure and/or ischaemic changes on the ECG; and
- low-risk individuals, defined as those without the risk factors of the other two groups.

Effectiveness results
The analysis showed that 48 patients (3.8%) had LVSD and 1,209 had an EF of at least 32% (hence, were not at risk of the disease).

In the whole sample, the sensitivity was 85% for the clinical test, 57% for the ECG, 90% for the clinical test plus ECG, and 92% for BNP. The corresponding specificities were 61% (clinical test), 85% (ECG), 56% (clinical test plus ECG) and 53% (BNP), respectively. The positive predictive values were 0.08 for the clinical test, 0.13 for the ECG, 0.07 for the clinical test plus ECG, and 0.07 for BNP. The corresponding negative predictive values were 0.991 (clinical test), 0.980 (ECG), 0.993 (clinical test plus ECG) and 0.994 (BNP), respectively. Thus, LVSD was significantly associated with an abnormal clinical test, ECG abnormalities and elevated plasma BNP.

The NNE was 14%, meaning that 14% ECHOs would be needed to detect one case of LVSD.

When the three subgroups were compared, it was noted that the low-risk group was younger, had more smokers and had less diabetics, cardiovascular medication, cardiac-type dyspnoea and LVSD. It also had a lower median BNP concentration. The prevalence of disease was 0.7% in low-risk patients, 6% in high-risk patients and 19% in ischaemic heart disease patients.

When the predicting factors were analysed, in the subgroup of those with IHD, LVSD was strongly associated with a history of diabetes and modestly with ECG signs of ischaemia. The inclusion of BNP improved the prediction of disease. Among those without symptomatic IHD, diabetes was not associated with LVSD, but high blood pressure and signs of ischaemia on the ECG were significant. The inclusion of BNP also improved disease prediction.

The receiver-operating characteristic curve analysis examined the prediction of LVSD, by BNP, in the three groups. The BNP cut-off point with the highest combination of sensitivity and specificity covered the values from 8 to 19
Clinical conclusions
The effectiveness analysis showed that clinical parameters were effective in identifying those patients at low and high risk of LVSD. Also, BNP was a significant predictor of LVSD.

Measure of benefits used in the economic analysis
The summary benefit measure used in the economic analysis was the number of cases of LVSD detected. This was derived from the effectiveness analysis.

Direct costs
The costs were not discounted because of the short time horizon of the analysis. The health services included in the economic evaluation were the diagnostic tests, such as ECHO and BNP. The unit costs of the tests were reported separately from the quantities of resources used. The cost/resource boundary adopted in the study was not reported. Resource use was estimated on the assumption that each person received one screening test. The source of the unit costs was not reported. The price year was not given.

Statistical analysis of costs
Statistical tests were not used for the analysis of the costs.

Indirect Costs
The indirect costs were not included.

Currency
US dollars ($).

Sensitivity analysis
Sensitivity analyses were not conducted, but three different estimates of the cost of BNP relative to the cost of ECHO were used. It was considered that the ratio of BNP price to ECHO price was 20:100, 10:100 or 5:100. The results for the 10:100 ratio are reported in this abstract.

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

Cost results
The total costs were $82,300 with ECHO and $41,830 with BNP-ECHO in the low-risk group (cost reduction by BNP screening: 49%). The corresponding costs were $26,900 (ECHO) and $19,990 (BNP-ECHO) in the high-risk group (cost-difference: 26%), and $14,000 (ECHO) and $11,300 (BNP-ECHO) in the IHD group (cost-difference: 19%).

Synthesis of costs and benefits
An average cost-effectiveness ratio was calculated to combine the costs and benefits of the two screening strategies. The cost per LVSD case detected was $13,717 with ECHO and $8,366 with BNP-ECHO in the low-risk group (difference: 39%). The corresponding costs per LVSD case detected were $1,681 (ECHO) and $1,333 (BNP-ECHO) in the high-risk group (difference: 21%), and $538 (ECHO) and $471 (BNP-ECHO) in the IHD group (difference: 13%).
Authors' conclusions
An initial simple questionnaire and blood pressure measurement were useful in ruling out left ventricular systolic dysfunction (LVSD) in individuals in the general population. Among those at risk, the use of BNP was cost-effective in selecting persons requiring further evaluation through echocardiography.

CRD COMMENTARY - Selection of comparators
The authors implicitly considered ECHO to be the standard procedure for the identification of patients at risk of LVSD. You should decide whether it represents a valid comparator in your own setting.

Validity of estimate of measure of effectiveness
The analysis of the effectiveness used a cross-sectional study, which, as the authors acknowledged, may not have been the best design for the study question. The individuals involved in the effectiveness study were randomly selected from a wider sample, but the method of randomisation was reported elsewhere. There was no follow-up as the study was not longitudinal. The characteristics of the patients in the three subgroups were reported in detail. Regression analysis was performed to identify the predicting factors. The study sample comprised volunteers and caution is required when extending the results of the effectiveness analysis to other populations. The overall internal validity of the analysis was low.

Validity of estimate of measure of benefit
The benefit measure was derived from the effectiveness analysis (see comments above).

Validity of estimate of costs
The economic perspective adopted in the study was not reported, but only the costs of the tests considered in the study were included (The perspective adopted, however, appears to represent the health care service). The reproducibility of the analysis was high because the authors provided details of the resource consumption and unit costs, which were analysed separately. However, the price year was not reported and the source of the cost data was not mentioned. The costs were treated deterministically. However, three alternatives for the cost of the BNP test were considered to address the issue of variability of the costs across countries and settings.

Other issues
The authors reported the results of other studies that evaluated the diagnostic impact of BNP as a predictor of LVSD. The findings were similar to those observed in the present study. The issue of the generalisability of the study results to other settings was not addressed. Sensitivity analyses were not carried out, but the authors considered the variability in costs and commented on the implications of different sensitivity values for the BNP test. The authors stated that they selected a specific cut-off point for the BNP test, but different cut-off points could be chosen according to the target population. The authors also commented on the impact of performing a chest X-ray as an alternative screening strategy. Some methodological limitations of the analysis were noted. Most of these were related to the instruments used to evaluate the diagnostic accuracy of BNP.

Implications of the study
The authors suggest that future studies of mortality and morbidity should define standardised cut-off points for BNP in order to facilitate the implementation of this procedure in routine clinical practice.

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