Clinical significance of blood brain natriuretic peptide level measurement in the detection of heart disease in untreated outpatients: comparison of electrocardiography, chest radiography and echocardiography

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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
Four diagnostic strategies for the detection of heart disease (HD) in untreated patients were examined. The strategies were blood brain natriuretic peptide (BNP) measurement, electrocardiography (ECG), chest radiography (CR) and echocardiography (ECHO).

Type of intervention
Diagnosis.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised untreated patients with symptoms suggestive of HD, such as palpitation, dyspnoea, chest discomfort, chest pain, low leg oedema and hypertension.

Setting
The setting was an outpatient clinic. The economic study was carried out at the Department of Cardiology and Pneumology, Dokkyo University School of Medicine and the Department of Internal Medicine of two community hospitals in Japan.

Dates to which data relate
The effectiveness and resource use data were gathered from November 1997 to April 2001. The price year appears to have been 2001.

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

Link between effectiveness and cost data
The costing was performed prospectively on the same sample of patients as that used in the effectiveness study.

Study sample
A single group of 130 eligible outpatients attending the three study clinics was enrolled in the study and underwent all four diagnostic approaches. The final condition of having or not having HD was evaluated by performing further examinations (e.g. exercise testing, Holter ECG, cardiac catheterisation and computer tomo-radiography) and follow-up
checks. The authors reported the demographic and clinical characteristics of the patients divided into two groups, those with HD and those without. There were 86 patients with HD, of which 66% were men. The mean age was 69.7 (+/- 11.8) years. There were 44 patients without HD, of which 59% were men. The mean age was 68.7 (+/- 12.5) years. Power calculations do not appear to have been performed.

**Study design**

This was a prospective within-group comparison study, because the same group of patients underwent all diagnostic strategies during the first visit. The diagnostic criteria used for each technique were described. In case of abnormal test results, two or more of the authors (experienced clinical cardiologists) who were unaware of the patient's clinical information gave their opinion on whether the patient had or did not have HD and classified them accordingly. The study was carried out in a teaching hospital and two community hospitals. The length of follow-up was not stated. No loss to follow-up appears to have occurred.

**Analysis of effectiveness**

All of the patients in the initial study sample were accounted for in the effectiveness study. The health outcomes used in the study were the sensitivity, specificity, accuracy, positive predictive value (PPV) and negative predictive value (NPV). Comparability of the study groups was not relevant as a single group of patients was used.

**Effectiveness results**

With BNP, the sensitivity was 0.90, the specificity 0.98, the accuracy 0.92, the PPV 0.99 and the NPV 0.83.

With ECG, the sensitivity was 0.78, the specificity 0.66, the accuracy 0.74, the PPV 0.82 and the NPV 0.60.

With CR, the sensitivity was 0.66, the specificity 0.89, the accuracy 0.74, the PPV 0.92 and the NPV 0.57.

With ECHO, the sensitivity was 0.91, the specificity 1, the accuracy 0.94, the PPV 1 and the NPV 0.85.

All of the values estimated with ECG and CR were significantly lower than those reported with BNP, with the exception of the specificity with CR. There was a significant difference between the values observed with ECHO and BNP.

The authors also reported the positive and negative rates for each test in patients classified according to their diagnosis.

**Clinical conclusions**

The effectiveness analysis showed that the BNP and ECHO strategies had the best diagnostic characteristics in comparison with ECG and CR, in untreated patients with symptoms suggestive of HD.

**Measure of benefits used in the economic analysis**

The summary benefit measures used in the economic analyses were the five outcome measures estimated in the effectiveness study, namely sensitivity, specificity, accuracy, PPV and NPV.

**Direct costs**

Discounting was not relevant because the costs were incurred in a short time period. The unit costs were reported separately from the quantities of resources used. The health services included in the economic evaluation were BNP, ECG, CR and ECHO (including the extra cost of using the Doppler technique). The cost/resource boundary of the study was that of the Japanese NHI system. Resource consumption was estimated using data derived from the sample of patients included in the effectiveness study (from November 1997 to April 2001). The unit costs were based on NHI reimbursement rates at April 2001, which appears to have been the price year.
Statistical analysis of costs
Statistical analyses of the cost-effectiveness ratios were conducted to test the statistical significance of the estimated differences. The 2-sample Wilcoxon rank sum test was performed.

Indirect Costs
The indirect costs were not included.

Currency
Japanese yen (Y).

Sensitivity analysis
Sensitivity analyses were not performed.

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

Cost results
The total costs of each diagnostic strategy were not reported.

Synthesis of costs and benefits
An average cost-effectiveness ratio was calculated for each benefit measure used in the analysis.

The cost-efficacy of each test (in units of Y1,000) was presented according to its sensitivity, specificity, accuracy, PPV and NPV:

with BNP, Y0.53 for sensitivity, Y0.57 for specificity, Y0.54 for accuracy, Y0.58 for PPV and Y0.49 for NPV;
with ECG, Y0.52 for sensitivity, Y0.44 for specificity, Y0.49 for accuracy, Y0.55 for PPV and Y0.40 for NPV;
with CR, Y0.40 for sensitivity, Y0.53 for specificity, Y0.44 for accuracy, Y0.55 for PPV and Y0.34 for NPV;
with ECHO, Y0.09 for sensitivity, Y0.10 for specificity, Y0.09 for accuracy, Y0.10 for PPV and Y0.08 for NPV.

The statistical analyses showed that the cost-effectiveness ratio of BNP was higher than the ratios of almost all the remaining techniques.

Authors' conclusions
Brain natriuretic peptide (BNP) measurement and echocardiography (ECHO) detected a high rate of patients with heart disease (HD) in comparison with chest radiography (CR) and electrocardiography (ECG). However, the cost-benefit ratio associated with BNP was higher relative to the other diagnostic approaches. Thus, BNP should be the first diagnostic option used for untreated patients with symptoms suggestive of HD. The authors, however, noted that the predictive characteristics of each test varied according to the category of HD.

CRD COMMENTARY - Selection of comparators
The rationale for the choice of the comparator was clear. ECHO, ECG, and CR represent routine diagnostic approaches widely used for patients suspected of having HD. BNP measurement was a new approach whose efficacy and efficiency had not yet been defined in all clinical settings. You should decide whether they all represent valid comparators in your
own setting.

**Validity of estimate of measure of effectiveness**
The analysis of effectiveness used a within-group comparison study, which may limit the impact of bias and confounding as the patients acted as their own controls. However, the fact that the study interventions were performed subsequently means that temporal factors other than the study interventions may have had an impact on the estimated outcome measures. The authors noted that the study was carried out in a university hospital and two community hospitals. The study sample of those attending such clinics may not be similar to the whole population of untreated patients with suspected HD. Other bias and confounding factors were not noted.

**Validity of estimate of measure of benefit**
The benefit measures were derived directly from the effectiveness study. However, it is worth noting that all the five benefit measures represent intermediate health outcomes and do not estimate the final effect of the interventions on the patient’s health.

**Validity of estimate of costs**
The perspective adopted in the study was explicitly stated. All the relevant categories of costs appear to have been included in the economic evaluation. The cost estimates were specific to the study setting and sensitivity analyses were not performed. The unit costs and the quantities of resources used were analysed separately and the price year was reported. This facilitates the transfer of the economic results to other settings. However, the estimated total costs were not reported. The resource use data were derived from the same sample of patients as that used in the effectiveness study.

**Other issues**
The authors did not compare their findings with those from other studies. They also did not address the issue of the generalisability of the study results to other settings. Thus, the external validity of the analysis was low. Sensitivity analyses were not performed. The authors noted some limitations of their analysis, which have been highlighted already.

**Implications of the study**
The study results suggest that BNP should be the first diagnostic approach for untreated patients with symptoms suggestive of HD. The authors also noted that a very skilled cardiologist is required to interpret the results of ECHO, which has a predictive value comparable to that of BNP, in order to reach the expected accuracy in HD detection. This is not always possible in all clinical settings.

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