Paper

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CLINICAL

Potential costs of B-type natriuretic peptide for the identification of people with heart failure in primary care in Scotland – a pilot study

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ABSTRACT

Background and Aims: The utility of B-type natriuretic peptide as a screening test for heart failure has been proven in a number of clinical trials. The aims of this study were to assess the utility of the measurement of B-type natriuretic peptide in a 'real life' setting and to estimate the potential costs of implementing its use in primary care in Scotland.

Methods and Results: Eight general practitioner practices with a combined population of approximately 62,000 were invited to participate. During the 9-month study period, 82 samples for B-type natriuretic peptide measurement were requested. The negative predictive value for B-type natriuretic peptide was 96.9%. Compared with electrocardiography, B-type natriuretic peptide reduced the need for echocardiography by 308 tests per million population per year. The estimated cost of implementation in Scotland is approximately £220,000 per annum, equating to £64.93 per patient correctly diagnosed with heart failure, with a potential saving in echocardiography of £110,800.

Conclusion: In this pilot study, measurement of plasma B-type natriuretic peptide in a 'real life' setting in primary care had a similar sensitivity, specificity and negative predictive value to that observed in trial populations. B-type natriuretic peptide aids early diagnosis of heart failure in primary care and may help to facilitate prompt introduction of evidence based therapies to modify patient outcomes. The costs of measuring plasma B-type natriuretic peptide in suspected cases of heart failure are modest, and its use would increase the diagnostic capacity of primary care if supported by local cardiology services.

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BACKGROUND

B-type natriuretic peptide (BNP) is a hormone produced in the heart, causing diuresis, vasodilatation and smooth muscle relaxation.[1] Elevated plasma concentrations of BNP and its precursor pro-N terminal BNP (pro-NT-BNP) are found in conditions which cause cardiac stress including cardiac chamber wall stretch, intravascular fluid expansion, left ventricular hypertrophy and acute myocardial infarction. Plasma concentrations may also be raised where there is reduced clearance of the hormone from the blood such as in renal failure. For these reasons BNP levels are commonly elevated in patients with decompensated heart failure (HF).[2,3]

The utility of BNP and pro-NT-BNP as screening tests for heart failure has been demonstrated in a number of clinical settings including outpatients,[4,5] as a guide to therapy titration in HF programs[6,7] and for investigation of the acutely breathless patient in the emergency room.[8-11] Furthermore, BNP is a predictor of patients at risk of future cardiac events.[12,13]

Several recent HF guidelines supported the use of BNP measurement as a screening test.[14-16] Available evidence was extensively reviewed by NHS Quality Improvement Scotland in 2005.[17] This review included recommendations to implement BNP as a diagnostic test in primary care and possibly secondary care in Scotland. Furthermore BNP is heavily featured in the most recent National Institute for Health and Care Excellent (NICE) guidance on the diagnosis of chronic HF (Table 1). In the light of this recent advice, Lothian Coronary Heart Disease Managed Clinical Network undertook a pilot project to examine the potential use and costs of BNP in primary care.

METHODS

Study population

Selected local general practitioner (GP) surgeries (n=8) in Lothian with a patient population of approximately 62,000 took part in the pilot. These were chosen to represent a variety of socioeconomic areas including city centre, suburbs and small towns in the region. Each was visited by a member of the project team and provided with information which included a flowchart to guide them in the use of BNP testing (Figure 1). GPs were asked to replace an electrocardiogram (ECG) or an echocardiogram with BNP as the first-line test for a patient with suspected HF attending their surgery. Population prevalence figures for coronary heart disease and left ventricular dysfunction were taken from Quality and Outcomes Framework data 2005.[18]

BNP measurement

Specific blood bottles and request forms were provided to GP surgeries. All samples were analysed at the same laboratory (Royal Infirmary of Edinburgh) within 24 hours using a commercially available assay (Bayer Diagnostics plc). Results were reported by a consultant cardiologist with a clinical comment added as guidance to the requesting GP. The first 50 patients had an echocardiogram and ECG performed regardless of the BNP level. Subsequent patients had BNP testing but echocardiography and ECG arranged only if the BNP level was greater than a predetermined cut off of 100pg/ml.[19]

Estimates of cost

Costs of BNP were calculated using standard assay costs for a 50-well plate of £1000 and assumed that all the tests in an assay-kit were used. A laboratory handling charge of £5 was also added for each sample giving a total cost of £25 per sample.

Previous studies have used a cost estimate of between £15 and £30 for point of care BNP testing, and for the purposes of our study we have used a value of £25.[20] For comparison, a standard cost for an ECG was assumed to be £30 and an echocardiogram £72.[21] The number of samples generated within the eight GP surgeries and their associated population was extrapolated to estimate the numbers likely to be generated per million population per year.

Ethics

As BNP is a recognised clinical test included in many national guidelines ethical approval was not deemed necessary.

Statistics

Data were entered into a spreadsheet and analysed using SPSS v11.0 and Excel (Microsoft® Excel 2000).

TABLE 1 Updated NICE guidance on the use of BNP for the diagnosis of chronic heart failure[22]

1. Measure serum natriuretic peptides (B-type natriuretic peptide [BNP] or N-terminal pro-B-type natriuretic peptide [NTproBNP]) in patients with suspected heart failure without previous MI. [new 2010]
2. Refer patients with suspected heart failure and a BNP level above 400 pg/ml (116 pmol/L) or an NTproBNP level above 2000 pg/ml (236 pmol/L) urgently, to have transthoracic Doppler 2D echocardiography and specialist assessment within 2 weeks. [new 2010]
3. Refer patients with suspected heart failure and a BNP level between 100 and 400 pg/ml (29–116 pmol/L) or an NTproBNP level between 400 and 2000 pg/ml (47–236 pmol/L) to have transthoracic Doppler 2D echocardiography and specialist assessment within 6 weeks. [new 2010]
4. Be aware that: a serum BNP level less than 100 pg/ml (29 pmol/L) or an NTproBNP level less than 400 pg/ml (47 pmol/L) in an untreated patient makes a diagnosis of heart failure unlikely.

FIGURE 1 Guidance for use of BNP testing in primary care

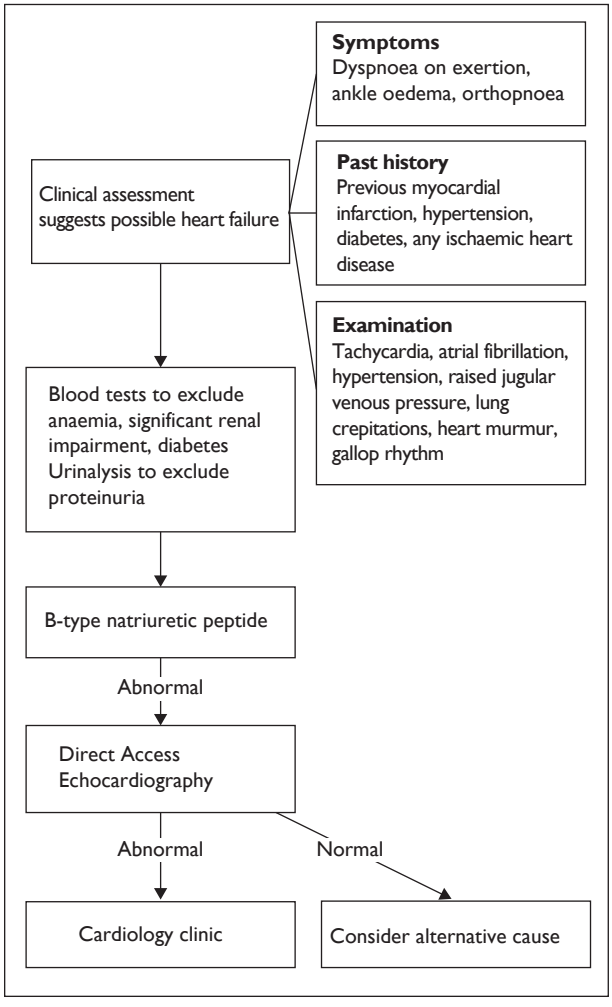

TABLE 2 Number of BNP (n) samples requested during a 9-month period by each GP practice for left ventricular dysfunction (LVD) and coronary heart disease (CHD) prevalence in these practices

GP practice	List size	n-LVD	% LVD	n-CHD	% CHD	CHD+LVD	BNP (n)
1	12,308	58	0.47	592	4.81	650	41
2	8079	58	0.72	408	5.05	466	7
3	6300	61	0.97	250	3.96	311	1
4	3275	30	0.92	167	5.1	197	11
5	7189	28	0.39	312	4.34	340	1
6	5080	38	0.75	255	5.02	293	11
7	8394	33	0.39	324	3.86	357	8
8	11,347	52	0.46	379	3.34	431	2
Subtotal	61,971	297	0.59	2437	4.5	2734	82

Data are expressed as means, standard deviation and range where indicated.

RESULTS

Study population characteristics

GP surgeries included in the pilot (Table 2) cover a population of approximately 62,000 people which represents 8% of the population in NHS Lothian region. The prevalence of left ventricular dysfunction due to coronary heart disease in this cohort was slightly higher than the overall average within Lothian (0.59 vs 0.46%, $p < 0.001$; Chi-square). The average age of the patients sampled was 73 ± 10 years (range 51–88). A total of 38/82 (46%) of the patients were men and two patients died during the study. The average creatinine and urea were 106.8 ± 27.7 µmol/L and 7.6 ± 3.3 mmol/L respectively. The average BNP concentration was 94.9 pg/ml (range 2.5–922; 30/79 samples >100pg/ml).

BNP measurement

During the 9-month study period, 82 samples for BNP measurement were requested. Three of these samples were either sent in the wrong container or were not suitable for analysis. The number of BNP tests requested varied quite widely between GP practices and did not appear to be associated with the background prevalence of either coronary heart disease or left ventricular dysfunction as documented in each practices disease registers (Table 2).

TABLE 3 Relationship between BNP values and left ventricular dysfunction (LVD) in those undergoing echocardiography (n=52)

BNP (pg/mL)	LVD present (n)	No LVD (n)	Totals
>=100	2	18	20
0–99.9	1	31	32

Electrocardiogram and echocardiogram results

Electrocardiogram results were available in 41 patients and echocardiography was performed in 52 patients. An abnormal ECG was found in 23/41 (56%) patients (atrial fibrillation in 24/41 (58.5%), left ventricular hypertrophy in 7/41 (17%), previous myocardial infarction or left bundle branch block in 7/41 (17)% and minor ST-T segment changes in 3/41 (7%). The echocardiographic assessment of left ventricular function revealed normal function in 37/52 (71%), mild left ventricular systolic dysfunction (LVSD) in 11/52 (21%) and moderate or severe LVSD in 4/52 (8%).

Negative predictive value of BNP

The negative predictive value for BNP (that is its ability to rule-out HF) in our primary care population was 96.9% (Table 3).

Estimated potential costs of BNP

The estimated costs per million population of three different strategies for assessing patients with suspected HF in the community are summarised in Table 4. This

assumes that 1760 BNP samples will be generated per million population per year based on the number of samples generated by the eight GP surgeries in our region (over 9 months) with an average background prevalence of coronary heart disease of 4.5%. Clearly, this will vary considerably throughout Scotland. Extrapolation of these figures to Scotland based on population size suggests that the implementation of a BNP test as a diagnostic test for GPs would cost approximately £220,000 per annum. Given that 30/79 (38%) of BNP samples evaluated in our cohort were elevated, this would equate to £64.93 per positive test.

Estimated potential cost-savings for echocardiography

Assuming that 1760 patients present per year per million population with 'suspected heart failure' and an ECG is used as first test, then this would generate approximately 986 echocardiograms per million (56% of 1760). If BNP was used instead of an ECG, this could reduce this number to 678 echocardiograms (38.5% of 1760). The potential cost saving is £22,176 per annum per million, equivalent to £110,880 across Scotland. In this analysis, cost per patient per diagnosis including BNP and subsequent transthoracic echocardiogram would be £136.93.

TABLE 4 Estimated costs per million population of providing BNP in primary care per annum as the screening test prior to echocardiography

	Echo first	ECG then echo	BNP then echo
Unit cost of first test (£)	72	30	25
Cost of first test (£)	126,720	52,800	44,000
Cost of echo if first test positive (£)	-	70,992	48,816
Total cost/ annum/million population (£)	126,720	123,792	92,816

Key: Echo = direct access echocardiography for all patients with suspected heart failure, ECG-echo=ECG first, then echo for patients with an abnormal ECG (56% in our cohort), BNP-echo= BNP first then echo for patients with BNP>100pg/ml (38.5% in our cohort.

DISCUSSION

In this pilot study, measurement of plasma BNP concentration in a 'real life' Scottish population in primary care had a similar sensitivity, specificity and negative predictive value to that in trial populations.[2-5] The estimated costs of measuring plasma BNP for suspected cases of HF in Scotland were approximately £220,000 per annum for BNP itself and £244,080 for echocardiography which would be required to then assess the patients with a positive BNP test (38.5% in this study).

As the vast majority of patients with suspected HF has preserved left ventricular function, the use of BNP has the potential to reduce the number of echocardiograms that are requested for assessment of left ventricular function. Some regions are already providing echocardiography to primary care based on the finding of an abnormal ECG in a patient with suspected HF. This model is not currently supported by NICE guidelines, which recommends BNP alone in those with no prior history of myocardial infarction.[22]

Our study suggests that use of BNP could reduce the number of echocardiograms in these regions by almost one third. In other regions, currently without or with limited primary care access to echocardiography, the use of BNP could result in increased numbers requiring echocardiography. However, it should be noted that echocardiography will not only give information about left ventricular function, but also valve function and the presence of left ventricular hypertrophy.[20]

Further advantages of BNP relate to its convenience and this was highlighted by a number of GPs who took part in this pilot project. Travelling to a hospital or clinic for echocardiography can be difficult for some patients and almost impossible for others, such as the frail elderly, especially those in nursing homes or those in remote or rural populations. A simple blood test such as BNP may be taken in the patient's own home by a generic member of staff. These potential cost savings, often absorbed by the patient and their families, have not been factored into our calculations. In most cases, the test does not depend on further interpretation by the GP, although some understanding is required of the factors which may contribute to a false positive and a false negative test.

Point-of-care (POC) BNP testing has been estimated to cost £25 per sample. As this is identical to our estimates for a conventional laboratory assay, the potential cost benefit may therefore be extrapolated from our data. Previous literature does not appear to have considered the initial outlay costs of equipment purchase, or indeed the cost of ongoing device calibration which would need to be facilitated at a local level.

While POC BNP testing has been shown to correlate well with conventional laboratory analysis, it is less accurate. A study of 150 patients using the iSTAT point of care testing kit (Abbott Diagnostics) and paired laboratory BNP samples showed a correlation coefficient of R=0.977 ($p<0.0001$), however, there was a significant mean negative bias of -36%.[23] It is perhaps too soon for

POC testing to be considered as an option for individual GP practices. The quality assurance process associated with maintaining many assay devices throughout the community is likely to be prohibitive and inefficient.

There remains some uncertainty around the exact impact on primary and secondary care services of implementing BNP measurement in this setting, and debate surrounding cost effectiveness continues. Nevertheless, the measurement of plasma BNP has been included in all recent guidelines for the diagnosis and treatment of chronic HF and is heavily featured in current HF guidelines.[14-16] Despite this it is still not widely available in the UK and is currently only available routinely in one hospital in Scotland. This is likely due to concern about costs and lack of familiarity of the test, coupled to a lack of clinical confidence regarding its impact on clinical decision making and patient care pathways. Clear guidance for primary care staff must be developed in conjunction with local cardiology services to ensure appropriate utilisation of the test in only those with suspected HF, to prevent inappropriate investigations and ensure appropriate resource allocation.

This uncertainty is perhaps reflected in the wide variation in use of BNP in the eight GP practices included in this project which appears unrelated to background prevalence of coronary heart disease within the local population. The average number of samples generated per million population per year was estimated to be around 1760 but this could be as low as 210–230 (practices 3 and 7) or as high as 4400–4500 per million (practices 1 and 4). We note that the prevalence of HF due to coronary artery disease in our population (0.59%) was lower than the quality outcomes framework national average rate (0.80%).

Our small pilot study suggests that net costs would increase after the widespread introduction of a BNP assay in primary care. Our analysis does not incorporate the overall potential costs saved which are difficult to quantify but would include a reduction in inappropriate prescription of HF medication and a reduction in the number of inappropriate referrals to cardiology services. It is likely that costs of the BNP assay itself would fall further if implemented on a national level. Thus although our analysis suggests a modest additional net cost to implementing BNP testing, this estimate is subject to multiple factors – from significantly increasing the cost in the case of widespread, indiscriminate testing, to a potential net saving if unit test costs fall and the benefits of early diagnosis translate into reductions in hospitalisation and inappropriate medication use.

The benefits of increased diagnostic accuracy on future long term patient outcomes and safety are significant. Patients with newly diagnosed HF are at highest risk of mortality within weeks of diagnosis, with 25% of patients dead at three months.[24] BNP offers a rapid avenue to diagnosis, and would provide primary care practitioners with additional diagnostic confidence to introduce evidence based therapy such as angiotensin converting enzyme inhibitors at an earlier stage while awaiting cardiology out-patient review.

CONCLUSIONS

This study suggests that BNP would be used appropriately by GP practices at least within the first 9 to 12 months of introduction. However, on average, in the eight practices included in this pilot study, the use of BNP was not excessive and total estimated costs were less than predicted in the 2005 NHS Quality Improvement Scotland review.[17] The use of BNP in primary care has the potential to reduce the numbers of patients requiring echocardiography by one third when used as a first test in place of the ECG. This clinical pilot study suggests that BNP could provide a similar negative predictive accuracy for diagnosis to that seen in other economic analyses of the utility of BNP.[25] Early exclusion of the diagnosis would potentially reassure the patient quickly. In contrast, patients seen in primary care who are at risk of HF and who have obvious clinical features combined with elevated BNP could be initiated on evidence-based therapies at an earlier stage with the potential of saving lives during this vulnerable period.

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