N-terminal brain natriuretic peptide as a screening tool for heart failure in the pacemaker population

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Aims Assessment of N-terminal brain natriuretic peptide (NT-BNP) as a screening tool for heart failure in patients with a permanent pacemaker.

Methods and results Consecutive patients undergoing a routine permanent pacemaker assessment were enrolled. Patients underwent medical history and examination, echocardiography and blood sampling for NT-BNP. Analysis was performed on 261 patients (132 DDD, 121 VVI, eight others), mean age 73 ± 12 years, range 34–99 years. Seventy two subjects (27%) had heart failure as defined by left ventricular ejection fraction (LVEF) <40% and symptoms of heart failure (NYHA class II, III, or IV). Screening with NT-BNP gave a sensitivity of 73% and specificity of 72% for detecting heart failure in all patients [area under the curve (AUC) 0.76, P < 0.001, 95% CI 0.69–0.83]. This increased in subjects with a DDD type pacemaker (sensitivity 80%, specificity 66%, AUC 0.8, CI 0.7–0.90) and reduced in subjects with a VVI type pacemaker (sensitivity 66%, specificity 61%, AUC 0.68 CI 0.57–0.78).

Conclusion Symptoms of heart failure are common in patients with pacemakers. Screening with NT-BNP is feasible and assists in the detection of important cardiac co-morbidity, particularly in patients with a DDD type pacemaker.

KEYWORDS
Pacemaker; Heart failure; Screening; NT-BNP

Introduction
Permanent cardiac pacemakers are widely used in modern cardiological practice, with implant rates ranging from 250 to 800 per million of the population per annum, leading to 1000–3000 patients undergoing regular follow-up in a typical pacemaker centre.1–3 The prevalence of heart failure is high in this population due to their advanced age,4,5 high prevalence of atrial fibrillation, and prior myocardial infarction,6–9 and perhaps due to the effect of ventricular pacing itself.10–12

Screening for heart failure is particularly appropriate in the pacemaker population for a number of reasons: the cost and logistical considerations are favourable as the patients are under routine hospital-based follow-up. The prevalence of heart failure is high with low pre-existing rates of diagnosis.6–8,13 In addition, conventional right ventricular pacing, by inducing intraventricular dyssynchrony, may worsen pre-existing heart failure.10 Also, it may be difficult to distinguish between heart failure, pacemaker syndrome, chronotropic incompetence, and other co-existing problems that may cause breathlessness such as respiratory disease and obesity.14–17

Few data exist describing the use of natriuretic peptides as a screening tool in patients with pacemakers, in contrast to the large amount of data from the non-paced population.18,19 The haemodynamic effects of pacing make it unsafe to draw inferences on the neurohormonal behaviour of paced subjects based on existing data from non-paced subjects. In part, this is due to the effect of intraventricular dyssynchrony caused by conventional pacing, altering the phase and magnitude of mechanical strain of both ventricles,11,20 the main stimulus for BNP release.18,19 Also, ‘non-physiological’ pacing modes such as single chamber VVI pacing, by interrupting normal atrioventricular synchronization, may lead to altered left ventricular (LV) diastolic filling and loading characteristics, and, therefore, BNP release.5,21–23

For a screening test to become widely applicable, it must be cost-effective, easy to administer and interpret, and the results should guide diagnosis and choice of treatment. Timely diagnosis may lead not only to the initiation of disease modifying agents such as beta-blockers, angiotensin-converting enzyme (ACE)-inhibitors, and aldosterone antagonists, but also put greater focus on optimizing the pacing mode.

Methods

Setting
A regional tertiary referral cardiothoracic centre serving a mixed urban/rural population of 650 000 for the purpose of permanent pacemaker assessment. Patients undergoing a routine permanent pacemaker assessment were enrolled. Routine follow-up includes medical history and examination, echocardiography and blood sampling for NT-BNP. Analysis was performed on 261 patients (132 DDD, 121 VVI, eight others), mean age 73 ± 12 years, range 34–99 years. Seventy two subjects (27%) had heart failure as defined by left ventricular ejection fraction (LVEF) <40% and symptoms of heart failure (NYHA class II, III, or IV). Screening with NT-BNP gave a sensitivity of 73% and specificity of 72% for detecting heart failure in all patients [area under the curve (AUC) 0.76, P < 0.001, 95% CI 0.69–0.83]. This increased in subjects with a DDD type pacemaker (sensitivity 80%, specificity 66%, AUC 0.8, CI 0.7–0.90) and reduced in subjects with a VVI type pacemaker (sensitivity 66%, specificity 61%, AUC 0.68 CI 0.57–0.78).

Conclusion Symptoms of heart failure are common in patients with pacemakers. Screening with NT-BNP is feasible and assists in the detection of important cardiac co-morbidity, particularly in patients with a DDD type pacemaker.
cardiac pacing. The local research Ethics Committee approved the study.

**Patient selection**

During a 12-month period between 1999 and 2000, all patients presenting to one of four routine pacemaker follow-up clinics were considered for the study. The clinic chosen each week altered on a rotational basis. Inclusion criteria included permanent pacing for a period of ≥3 months and age over 18 years. Exclusion criteria were a recent (≤1 month) history of myocardial infarction or cardiac surgery, multi-site or biventricular pacing, or inability to give informed consent. Of 300 patients approached, 279 (93%) consented to participate. Eighteen patients were excluded because they had significant renal impairment on subsequent laboratory analysis, (serum creatinine >177 μmol/L or ≥2.0 mg/dL) leaving 261 patients suitable for analysis. Written informed consent was obtained from all patients.

**Study protocol**

A medical history was taken from all patients by the same physician (ST) to identify the following.

**Pre-existing diagnoses**

All hospital records were screened to look for a discharge or outpatient record of a diagnosis of heart failure. Additionally, in patients who were prescribed a loop diuretic by their general practitioner (GP) or patients who reported a diagnosis of heart failure made at any time, the GP was contacted to establish if a diagnosis of heart failure had been made and its duration. Angina pectoris was defined as a prior or current history of typical cardiac chest pain supported by an objective measure of ischaemia such as treadmill exercise test or perfusion scintigraphy. Myocardial infarction was defined according to World Health Organisation criteria. Ischaemic heart disease was defined as a history of myocardial infarction, unstable angina, or angiographic evidence of >50% stenosis of one or more coronary arteries. Valvular heart disease was defined as echocardiographic or angiographic evidence of a haemodynamically significant valve lesion. Airways disease was classified as chronic obstructive pulmonary disease or asthma diagnosed by a respiratory physician based on spirometry and, for asthma, a combination of L VEF 40% on echocardiographic screening and a positive response to all questions = NYHA class I, a positive response to Q1 only = NYHA class II, a positive response to Q2 = NYHA class III, and a positive response to all questions = NYHA class IV.

**Medication use**

All cardiac and concomitant non-cardiac medications were recorded. Frusemide or bumetanide doses are described in frusemide-equivalent doses, where 1 mg bumetanide = 40 mg frusemide.

**Pacing characteristics**

Duration of pacing, current pacing mode, indication for pacing, and rhythm at implant were recorded. Chronic AF was defined for the purposes of this study as the presence of AF, diagnosed from a 12-lead ECG and lasting for >4 weeks.

**Symptom screening**

Prior to the clinical examination and echocardiogram, each patient was asked set questions, by the same physician, designed to evaluate symptoms of heart failure as follows.

Q1: 'Do you ever experience any of the following symptoms; shortness of breath, fatigue, or exercise limitation when undertaking your normal daily activities or any other activities such as moderate exercise, hobbies, or sport?'

Q2: 'Do shortness of breath or fatigue ever restrict your ability to undertake your activities of daily living, such as washing, dressing, moving around the house, cooking, and cleaning?'

Q3: 'Do you ever experience shortness of breath or fatigue after walking a few yards or at rest?'

A positive response to any of the above questions would be countered with the response 'What symptom exactly is it that limits you in this fashion?' To ensure that it was symptoms referable to heart failure that were responsible.

Responses were categorized according to the New York Heart Association classification of severity of symptoms: a negative response to all questions = NYHA class I, a positive response to Q1 only = NYHA class II, a positive response to Q2 = NYHA class III, and a positive response to all questions = NYHA class IV.

**Blood sampling for N-terminal brain natriuretic peptide**

Blood was taken at the same visit as the clinical and echocardiographic assessment. Following at least 15 min of recumbency, blood sampling was undertaken. Blood specimens were cool centrifuged immediately, and the plasma stored at ~80°C without freeze-thaw cycles until measured. The samples were analysed using a highly sensitive, commercially available, enzyme linked immunoassay (Biomedica Gruppe, Austria) and reported in pmol/L. The lower limits for detection of this assay were 5 pmol/mL. Reported within-run coefficients of variation (CV) are 9.9% mean concentration (MC) 236 pmol/L and 11% at MC, 550 pmol/L, respectively, for low- and high-concentration patient samples, and the respective day-to-day CVs 11% (MC, 238 pmol/L) and 13% (MC, 519 pmol/L), based on multiple calibrations for the Biomedica assay. Laboratory analysis was also performed for serum creatinine from blood samples taken at the same study visit.

**Echocardiographic studies**

All studies were conducted within 14 days of entry into the study using commercially available equipment (Vingmed' Vivid' V with a 3.4 MHz electronic transducer, GE industries, USA). M-mode atrial and ventricular parameters were measured according to the recommendations of the American Society of Echocardiography. Intrinsic beats were used preferentially for echocardiographic analysis. If the patient was pacing intermittently, the three intrinsic beats after a paced beat and the intrinsic beat prior to a paced beat was not used for analysis.

**Echocardiographic data analysis**

Echocardiographic evaluations were performed by two experienced observers (ST & NN) examining the digitized images after the original examination. The images were evaluated in random order with the observers blinded to the patient identity and were analysed by means of a commercially available offline data evaluation package (Echopac, GE Vingmed Ultrasound). Left ventricular ejection fraction (LVEF) was based on a Simpson's bi-plane calculation from an apical four-chamber view and two-chamber view at end systole and end diastole. Endocardial tracings were made manually. A mean from three digital loops was taken (five in AF). Inter-observer differences of >5% in the calculation of LVEF led to repeat analysis by the original observers and a new analysis by a third observer (KW). The mean of all values from all five sets of analyses were then reported as the final value. A value for LVEF 40% was considered indicative of LV systolic dysfunction. This value is at least two standard deviations below the mean for our local non-paced population, derived from an echocardiographic screening survey of the local 'normal' population (n = 300, all >45 years of age). During the study, heart failure was diagnosed with the presence of the combination of LVEF 40% on echocardiographic screening and symptoms of heart failure ≥NYHA Class II.

**Statistical analysis**

All analyses were performed using commercially available software (SPSS). Sensitivity (sens), specificity (spec), likelihood ratios (LR), prevalence and pre/post-test probabilities were calculated using methods previously described. Data are reported as
mean ± standard deviation. Continuous variables between groups were compared by the Student’s t-test for unpaired observations, all tests were two-tailed, multiple groups were compared using ANOVA. Nominal data were compared by the χ² test. In all cases a P-value ≤0.02 was considered as statistically significant to allow for inflation of the experiment-wise Type 1 error. The reliability of the cut-off point used in (1) subsequently was internally validated using the technique of bootstrap resampling, 90% confidence intervals are presented. Bootstrapping analysis was performed using in-house software courtesy of LM University of Munich.

Receiver operator characteristic curve data assessment strategy

Receiver operator characteristic (ROC) curves were used to examine the performance of N-terminal brain natriuretic peptide (NT-BNP) over its entire range of values; the curves represent a plot of sensitivity vs. 1-specificity. The area under the curve (AUC) is derived from the ROC curve, giving an assessment of overall test performance with an AUC of 0.5 indicating no discriminating ability for the test and a value of 1, perfect predictive power. We defined a priori two different assessment strategies leading to varying cut points for NT-BNP value.

(i) A statistically derived value, based on the Youden index, maximizing the sum of the sensitivity and specificity. Such a point weighs true positives and false negatives equally and represents the asymptote of the ROC curve. This cut value allowed for the discriminatory ability of the test to be assessed, but is likely to be less useful clinically.

(ii) NT-BNP cut point leading to a high sensitivity (>95%) in order to rule out a diagnosis of heart failure or asymptomatic LV systolic dysfunction, but to retain enough specificity (33%) to be clinically useful, in effect leading to a one in three yield for detecting major systolic dysfunction on subsequent discriminatory echocardiography. This represents a more clinically useful cut point.

Results

Baseline characteristics

Analysis was performed on 261 patients. The mean age of the patients was 72 ± 12 years and 24% were aged >80 years (4% over 90). Risk factors for ischaemic heart disease were common and equally prevalent in patients with DDD(R) and VVI(R) pacemakers. History of smoking (64%) was the commonest risk factor for coronary disease, followed by hypertension (62%), family history of premature coronary disease (18%), and diabetes (12%). A total 36% of patients had evidence of ischaemic heart disease, while 6.5% had valvular heart disease. A diagnosis of ‘heart failure’ had been made at some time prior to the study in 16% of patients, the majority (11%) after device implantation (Table 1).

Pacing characteristics

A total of 96% of patients had either a VVI(R) or a DDD(R) pacing system [46% VVI(R) vs. 50% DDD(R)]. The mean number of years of pacing was 5.2 ± 4.3 years, range 0.25–40 years, median 5.7 years (interquartile range

| Table 1 | Baseline clinical characteristics for all patients, those with heart failure (LVEF ≤ 40% and NYHA II, III, or IV) and those with significant MR (MR = moderate, moderate to severe, or severe MR) |
|---------|---------------------------------|-----------------|-----------------|-----------------|
|         | All Heart failure Significant MR |
| Number  | 261 72 (27%) 30 (11%) |
| Age (year) | 72 ± 11 75 ± 10 77 ± 8 |
| Risk factors | Smoker, % 64% (7%) 71% (9%) 67% (0%) |
| Smoking (current) | 62 82 75 |
| Hypertension, % | 12 19 14 |
| Diabetes, % | 26.8 ± 4.4 25.4 ± 3.8 26.1 ± 3.7 |
| BMI | 36.2 61 39 |
| Ischaemic heart disease, % | 16.0 27 25 |
| Pre-existing diagnosis of heart failure at screening, % | 34 66 50 |
| Loop diuretic, % | 13 25 19 |
| ACE/ARB, % | 22 30 28 |
| Beta-blocker, % | 33 40 38 |
| Aspirin, % | 24 29 28 |
| Warfarin, % | 5.2 ± 4.2 6.2 ± 5.7 5.1 ± 2.9 |
| Range (years) | 0.25–39.5 0.25–39.5 1.6–10.9 |
| DDD (R)/VVI (R) | 50%/42% 42%/54% 42%/53% |
| Rhythm at implant | Paroxysmal AF, % 6 4 6 |
| Persistent AF, % | 15 22 21 |
| Rhythm at screening | Paroxysmal AF, % 8 5 2 |
| Persistent AF, % | 26 42 64 |
| Absolute increase in incidence of AF between implantation and screening, % | +13 +19 +39 |
| Significant MR, % | 9 19 100 |
| Heart Failure, % | 27 100 43 |
2.4–6.8 years). At the time of implantation, 15% of patients were in chronic AF. More than one in three patients in sinus rhythm (SR) implanted with a VVI(R) system had subsequently developed chronic AF, compared to one in seven of the DDD(R) group \((P < 0.001)\). Patients who were in AF at the time of study had a lower LVEF \((SR: 49 \pm 13\% \text{ vs. } AF: 42 \pm 12\%, P = 0.002)\), higher likelihood of symptoms \((\text{NYHA II–IV: } SR: 49\% \text{ vs. } AF: 66\%, P = 0.005)\) and more loop diuretic use \((SR: 29\% \text{ vs. } AF: 46\%, P = 0.005)\).

**Medication use**

Of all patients, 34% were receiving a loop diuretic, 14% an ACE-inhibitor or an angiotensin receptor blocker (ARB), 22% a beta-blocker, and 3% an aldosterone antagonist.

**Symptom burden**

Of all patients, 54% had symptoms consistent with heart failure that limited exercise capacity \((\text{NYHA Class II–IV})\), with a higher prevalence in those with a VVI(R) pacemaker \((57\%)\) compared to a DDD(R) device \((50\%)\). Twelve per cent of all patients reported a moderate to severe degree of restriction \((\text{NYHA Class III and IV})\).

**Echocardiographic studies**

The quality of echocardiographic images was considered good or moderate in 94% of patients, and graded as poor in 6%.

**Ventricular function and heart failure**

Seventy two patients \((27\%)\) had symptoms compatible with heart failure \((\text{NYHA Class II–IV})\) and \(\text{LVEF} \leq 40\%\), while 50 \((19\%)\) had symptoms of heart failure and an \(\text{LVEF} \leq 35\%\). Only 13 \((19\%)\) of these patients had a pre-existing record of a diagnosis of heart failure. A further 4% of patients had \(\text{LVEF} \leq 40\%\) without symptoms. A total of 72 patients \((27\%)\) had symptoms compatible with heart failure but a \(\text{LVEF} > 40\%\).

**N-terminal brain natriuretic peptide**

Data was analysed on 261 subjects and presented in fmol/mL. Data from 18 patients were not included in the analysis due to the presence of renal impairment. Plasma concentrations of NT-BNP increased with worsening NYHA class \((\text{Figure 1})\). Plasma concentrations of NT-BNP were also higher in patients with a VVI pacing mode compared with DDD mode \((\text{396} \pm 449 \text{ vs. } \text{267} \pm 228 \text{ pmol/mL}; P < 0.001)\). Bootstrapping resampling analysis of the NT-BNP values showed the estimate of the cut-off value to be stable, 90% confidence intervals \(231–303 \text{ pmol/L}\).

**The discriminatory performance of NT-BNP**

Figure 2 shows the ROC curve for NT-BNP and the detection of heart failure due to LV systolic dysfunction in all study patients. Figure 3 shows the ROC curve for the detection of major LV systolic dysfunction \((\text{LVEF} \leq 40\%)\) with or without symptoms and Figure 4 shows separate ROC curves for the detection of heart failure and LV systolic dysfunction in patients with DDD and VVI pacing modes. With the exception of patients in VVI pacing mode, all ROC plots gave an AUC of above 0.75. The discriminatory value of NT-BNP for the detection of LV systolic dysfunction was not improved by excluding asymptomatic patients \((\text{AUC } 0.73, 0.64–0.82)\) or those with little impairment of exercise capacity \((6 \text{ min hall walk distance} > 162 \text{ m}, \text{AUC } 0.74, 0.6–0.87)\). The test appeared more useful in patients < 65 years \((\text{AUC } 0.83, 0.7–0.96)\). Table 2 summarizes the diagnostic performance of NT-BNP in the entire sample and various subgroups.

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**Figure 1** The relationship between NYHA status and NT-BNP level. The plots display the median values (horizontal bars), 25th and 75th percentiles (lower and upper limits of boxes), and the minimum and 99th percentiles (error bars). NT-BNP values for each group are: NYHA Class I: \(231 \pm 157 \text{ pmol/mL}\); NYHA Class II: \(226 \pm 224 \text{ pmol/mL}\); NYHA Class III: \(651 \pm 431 \text{ pmol/mL}\); NYHA Class IV: \(1007 \pm 812 \text{ pmol/mL}\).

**Figure 2** ROC curve for the performance of NT-BNP in detecting heart failure in all study patients. The diagonal line is the 0.5 level guideline at which the test would offer no discriminatory capacity. \(\text{AUC} = 0.77 \left(0.7–0.83\right)\).
'Ruling in' and 'ruling out' a diagnosis of heart failure

The cut-off value derived from the Youden index, giving equal weighting to sensitivity and specificity, was 267 fmol/mL (Table 3). An NT-BNP cut off value of 130 pmol/mL gave a detection rate for heart failure due to LV systolic dysfunction of 95%, i.e. only one in 20 cases would be missed, 37% of patients with a value above this cut-off had heart failure symptoms and LV systolic dysfunction on subsequent echocardiography. In patients who were asymptomatic, an NT-BNP cut-off value of <200 pmol/mL excluded 98% of patients with a LVEF ≤ 40%.

False positives and mitral regurgitation

NT-BNP level increased with increasing severity of mitral regurgitation (MR) (Figure 5). Moderate or severe MR was the only echocardiographic abnormality in 37% of the false positives and was previously undiagnosed in 80% of cases. MR was three times more common in patients with elevated NT-BNP and preserved LV systolic function than in patients who had normal NT-BNP and good LV function (36% vs. 12%, \( P = 0.02 \)).

False negatives and loop diuretic or ACE-inhibitor/ARB therapy

Acute and chronic therapies with loop diuretics and ACE-inhibitors may suppress BNP.\(^{29-31}\) However, no significant differences were seen in loop diuretic, ACE-inhibitor, or ARB use in patients with NT-BNP below the cut-off, but LV systolic dysfunction comparable to those with elevated NT-BNP levels.

Discussion

The usefulness of large scale screening for LV systolic dysfunction with NT-BNP in selected populations has been previously well documented,\(^{32-35}\) with values for AUC ranging
The pacemaker population represents a considerable challenge for clinicians, with a high prevalence of major LV systolic dysfunction, symptoms compatible with heart failure and loop diuretic use, but relatively low rates of diagnosis and appropriate pharmacotherapy.4,5,7 The data presented allow clinicians to adopt one of two strategies in their pacemaker population. First, in patients with no symptoms, the sensitivity of the test allows confident exclusion of significant LV dysfunction in a meaningful portion of the patients. Leading perhaps, to a gap of several years before repeated screening. Secondly, in the remaining patients, the specificity of the test allows targeted use of further, more costly, discriminatory tests such as echocardiography in the anticipation of a reasonable yield. Overall, screening with all pacemaker patients with NT-BNP would allow clinicians to confidently exclude LV systolic dysfunction in one-third, while putting the remaining two-thirds forward for echocardiography. Of those undergoing echocardiography, over half would have prognostically important LV systolic dysfunction (37%) or MR of a significant degree (17%). From a patient base of 1000–3000 people, the ability to avoid 300–1000 echocardiograms makes economic and logistic sense, rather than undertaking echocardiography on the whole population.

Table 2 The diagnostic performance of NT PRO-BNP, areas under the ROC curves (AUC) for detecting heart failure

<table>
<thead>
<tr>
<th></th>
<th>AUC</th>
<th>C/I</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart failure (NYHA II, III, IV and LVEF ≤40%)</td>
<td>0.77</td>
<td>0.7–0.83</td>
</tr>
<tr>
<td>Heart failure (NYHA II, III, IV and LVEF ≤35%)</td>
<td>0.8</td>
<td>0.74–0.86</td>
</tr>
<tr>
<td>LVEF ≤40%</td>
<td>0.77</td>
<td>0.7–0.83</td>
</tr>
<tr>
<td>LVEF ≤35%</td>
<td>0.8</td>
<td>0.73–0.86</td>
</tr>
<tr>
<td>LVEF ≤30%</td>
<td>0.82</td>
<td>0.73–0.9</td>
</tr>
<tr>
<td>LVEF ≤25%</td>
<td>0.85</td>
<td>0.78–0.93</td>
</tr>
<tr>
<td>Heart failure in the DDD group</td>
<td>0.8</td>
<td>0.7–0.9</td>
</tr>
<tr>
<td>Heart failure in the VVI group</td>
<td>0.7</td>
<td>0.6–0.8</td>
</tr>
<tr>
<td>Heart failure (under 65 years of age)</td>
<td>0.83</td>
<td>0.7–0.96</td>
</tr>
<tr>
<td>Heart failure (over 65 years of age)</td>
<td>0.74</td>
<td>0.66–0.81</td>
</tr>
<tr>
<td>Heart failure in those paced over 2 years</td>
<td>0.78</td>
<td>0.7–0.85</td>
</tr>
<tr>
<td>Heart failure or (at least) moderate MR or (at least) moderate aortic regurgitation</td>
<td>0.79</td>
<td>0.7–0.85</td>
</tr>
</tbody>
</table>

Table 3 The utility of NT PRO-BNP in detecting heart failure. Using a cut-off value 267 fmol/mL

<table>
<thead>
<tr>
<th></th>
<th>All patients</th>
<th>DDD</th>
<th>VVI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity (%)</td>
<td>75</td>
<td>64</td>
<td>80</td>
</tr>
<tr>
<td>Specificity (%)</td>
<td>67</td>
<td>77</td>
<td>50</td>
</tr>
<tr>
<td>Positive predictive value (%)</td>
<td>46</td>
<td>43</td>
<td>46</td>
</tr>
<tr>
<td>Negative predictive value (%)</td>
<td>87</td>
<td>89</td>
<td>82</td>
</tr>
<tr>
<td>Likelihood ratio +ve</td>
<td>2.3</td>
<td>2.7</td>
<td>1.6</td>
</tr>
<tr>
<td>Likelihood ratio –ve</td>
<td>0.37</td>
<td>0.47</td>
<td>0.4</td>
</tr>
<tr>
<td>Prevalence (%)</td>
<td>27</td>
<td>21</td>
<td>34</td>
</tr>
<tr>
<td>Pre-test odds ratio</td>
<td>0.36</td>
<td>0.27</td>
<td>0.51</td>
</tr>
<tr>
<td>Post-test odds ratio</td>
<td>0.85</td>
<td>1.45</td>
<td>1.0</td>
</tr>
<tr>
<td>Post-test probability</td>
<td>0.46</td>
<td>0.59</td>
<td>0.50</td>
</tr>
</tbody>
</table>

Figure 5 Boxplot demonstrating the relationship between increasing degrees of MR and NT PRO-BNP level. *P = 0.05, **P = 0.02, in comparison with the group with no MR. No MR (NT-BNP 275 ± 470 pmol/mL), mild MR (NT-BNP 312 ± 209 pmol/mL), mild to moderate MR (NT-BNP 394 ± 308 pmol/mL, P = n/s at 0.05), moderate and moderate to severe (NT-BNP 517 ± 388 pmol/mL, P = 0.02). P-value is for comparison with the group with no MR.

Conclusion

In pacemaker patients, the repetitive nature of hospital follow-up, within a structured setting, lends itself to a technician-lead screening programme based on NT-BNP. Screening with NT-BNP would serve a dual purpose; first, to allow reassurance to be given to pacemaker patients with values below a chosen cut point, secondly, for pacemaker patients with results above a pre-determined range a programme of confirmatory echocardiography will give a high diagnostic yield for prognostically important LV dysfunction. Diagnosis will lead to optimization of pharmacotherapy, pacing modality, atrioventricular synchronization, and perhaps ultimately the decision to upgrade to biventricular pacing.

Limitations

Some important limitations exist with this technique. First, the neurohormonal profile of our selected patients is based on a number of factors which are likely to vary from
population to population leading to some difficulty in extra-
polating normal ranges for NT-BNP values. A multi-centre
study would be necessary to identify the degree of applica-
bility across broader patient groups. The second limitation is
the use of echocardiography as the ‘gold-standard’ diagnos-
tic test for systolic dysfunction. To improve accuracy
Simpson’s biplane method for estimating LV volumes was
employed, it was also felt that echocardiography best
reflects usual clinical practice.

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Conflict of interest: no conflict of interest exists.

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