

## Brain natriuretic peptide based strategy to detect left ventricular dysfunction in Chagas disease: A comparison with the conventional approach<sup>☆</sup>

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### Abstract

**Background:** Left ventricular dysfunction (LVd) is the main predictor of mortality in Chagas disease (ChD).

**Aims:** To compare the diagnostic performance of the conventional approach (ECG and chest X-ray) in the recognition of LVd in ChD, with a new strategy, in which BNP is measured in patients with an abnormal ECG.

**Methods:** Consecutive ChD patients recruited at an Outpatient Reference Center in Belo Horizonte, Brazil, without other systemic diseases, in 1998–99 (sample 1,  $n=165$ ) and in 2001–02 (sample 2,  $n=62$ ) underwent ECG, chest X-ray, BNP measurement and echocardiography.

**Results:** The prevalence of LVd (ejection fraction  $\leq 0.40$ ) was 9.1% in the sample 1. The conventional strategy recognized all patients with LVd (sensitivity: 100%, 95% CI: 79.6–100% and negative predictive value –PV 100%, 92.1–100%), but with low specificity (30%, 95% CI: 23.2–37.8) and +PV (12.5%, 95% IC: 17.7–19.6). The BNP/ECG strategy showed significantly better specificity (96.0%, 95% CI: 91.5–98.2,  $p<0.001$ ) and +PV (66.7%, 95% CI: 43.7–83.7,  $p<0.001$ ), and non-significantly lower sensitivity (80.0%, 95% CI: 54.8–93.0,  $p=0.25$ ) and –PV (98.0%, 95% CI: 94.2–99.3,  $p=0.08$ ). Overall accuracy was improved with the new strategy. (94.5%, 95% CI: 90.0–97.1  $\times$  36.4%, 95% CI: 29.4–43.9,  $p<0.001$ ). Similar results were obtained for the sample 2.

**Conclusions:** The BNP-based strategy was more accurate than the conventional approach in the detection of LVd in ChD patients and should be considered as a valid option.

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**Keywords:** Natriuretic peptides; Cardiomyopathy; Diagnosis; Ventricles; Sensitivity and specificity; Chagas disease

**Abbreviations:** LV, left ventricular; LVSD, LV systolic dysfunction; ECG, electrocardiogram; BNP, brain natriuretic peptide; +PV, positive predictive value; –PV, negative predictive value.

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### 1. Introduction

Chagas disease is a major health challenge in Latin America, where recent estimates indicate an infection prevalence of 13 million, with 3.0–3.3 million symptomatic cases [1]. Left ventricular (LV) systolic dysfunction, which is the main predictor of mortality in Chagas disease, [2] occurs in nearly 15% of this population [3]. In other clinical settings, treatment of LV systolic dysfunction (LVSD) may

reduce the risk of heart failure by as much as 37% in asymptomatic patients [4] and the risk of death in about one fifth [5]. Since LVSD is asymptomatic in approximately 50% of cases, [6] screening for LVSD has been considered to be highly useful by some authors, [7] although this issue is still a matter of debate [8].

Echocardiography is the best non-invasive technique used in the assessment of left ventricular function in Chagas disease. However, there are limitations for its widespread use, especially the difficulty in performing the echocardiogram in rural areas where the disease is endemic, and the need for an experienced examiner. Therefore, the development of alternative screening methods for the detection of LV dysfunction is desirable. ECG and chest X-ray are usually recommended as first-line methods in the recognition of LV dysfunction in Chagas disease [9]. Although the ECG has been recognized as a highly sensitive test, the diagnostic accuracy of a chest X-ray is considered poor [10] and the overall diagnostic performance of this strategy has not been studied. Recently, we demonstrated that an elevation of brain natriuretic peptide (BNP) concentration measured by radioimmunoassay (RIA) in blood, a reliable indicator of systolic left ventricular dysfunction, might be a promising screening method in Chagas disease [11]. This excellent diagnostic performance were confirmed in a subsequent study using a simple and reliable point-of-care commercial kit for BNP measurement, which could be easily used in such distant rural areas [12].

In the present study we compared, using the STARD initiative patterns, the diagnostic accuracy of abnormalities in ECG and/or chest X-ray in the recognition of LV dysfunction (conventional approach) with a new strategy, in which BNP is measured in patients with an abnormal ECG.

## 2. Methodology

The study protocol was approved by the Ethics Committee of the Federal University of Minas Gerais and was conducted at the Chagas Disease Outpatient Center of the University Hospital, a regional reference center for blood banks and primary care units in Belo Horizonte, Minas Gerais, Brazil. The study was planned before data collection (prospective design) and complies with STARD initiative [13]. All examinations were interpreted by investigators blinded to the results of the other diagnostic tests and they were generally performed within the same week. No adverse effect resulting from the diagnostic procedures occurred.

### 2.1. Study design

The two different strategies are described in Fig. 1 and were applied to all study subjects, with no kind of verification bias. The conventional strategy [9] consists of the simultaneous evaluation of the patient by electrocardio-

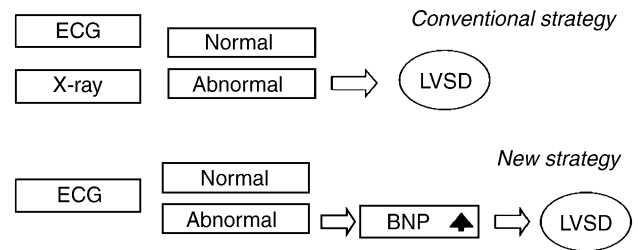


Fig. 1. Diagnostic strategies for detecting LV systolic dysfunction in Chagas disease.

gram and Chest X-ray (ECG/X-ray); those patients with abnormal results in one or both tests are considered to have the cardiac form of the disease and would be candidates to the echocardiographic study. In the new BNP-based strategy (ECG/BNP), a normal ECG obviates the need for further testing for global LV systolic dysfunction; those patients with an abnormal ECG and elevated BNP levels might have LV systolic dysfunction and should undergo an echocardiography study.

### 2.2. Patients

The study population consisted of two distinct samples: a first sample recruited in 1998–99 and a second sample studied during the 2001–2 period, both including consecutive patients (20–70 years of age) with a definite diagnosis of Chagas disease. The diagnosis of Chagas disease was based on the presence of at least two positive serological examinations using distinct techniques (ELISA, indirect hemagglutination or indirect immunofluorescence) in an individual with a relevant epidemiological history. The recruited patients signed an informed consent term and underwent a standardized protocol that included extensive clinical, ECG, laboratory and chest X-ray examinations, echocardiogram and BNP measurement. Exclusion criteria were other significant systemic diseases, alcoholism, or pregnancy.

The study design and the number of patients submitted to the diagnostic procedures are displayed in the flow diagram [13] in Fig. 2. The first sample was selected from a group of 222 consecutive Chagas disease patients without other apparent systemic diseases who underwent a routine medical visit at the Chagas Disease Outpatient Center of the University Hospital. Twenty-nine patients were excluded during the recruitment procedures due to concomitant systemic diseases (hypertension, diabetes or thyroid dysfunction,  $n=18$ ), alcoholism ( $n=1$ ) or impossibility of following the study protocol ( $n=10$ ). For the remaining 193 patients, incomplete data precluded the analysis of 28 subjects, since 19 samples of BNP were lost, seven patients did not undergo a chest X-ray or ECG and two echocardiographic studies were not performed for technical reasons. These patients had general features similar to those of patients included in the study, with a prevalence of left ventricular dysfunction, defined by LV ejection fraction of 40% or less of 15.4% (4/26).

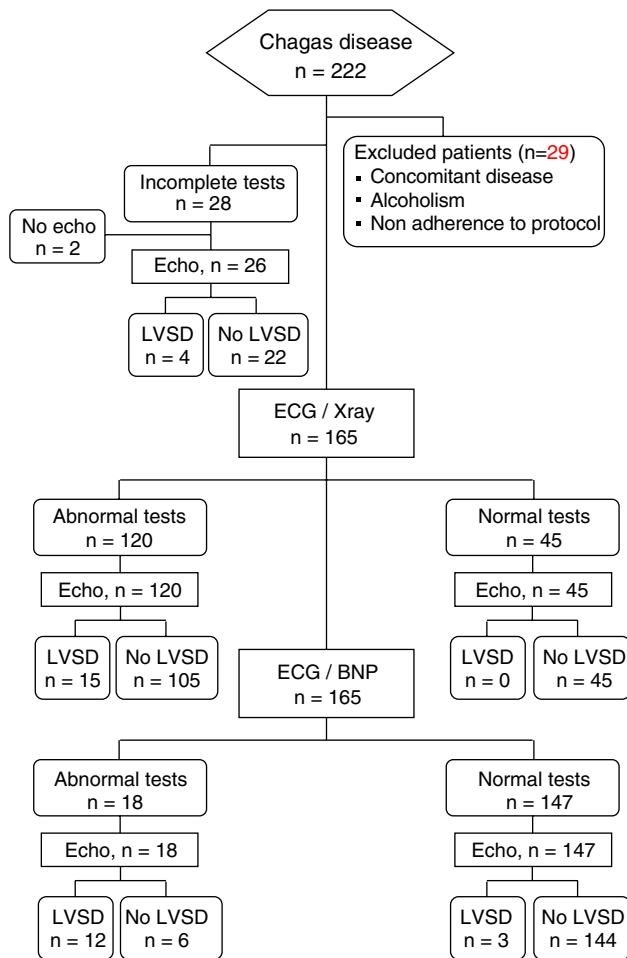


Fig. 2. Flow diagram of the diagnostic study design and the number of patients submitted to the diagnostic procedures in the sample 1. LVSD=Left ventricular systolic dysfunction, Echo=echocardiogram.

The second sample was selected using a similar recruitment procedure. Of 75 patients that satisfied the criteria for inclusion and did not present exclusion criteria, 62 (82.3%) had completed all required tests. The second sample had a clinical profile similar to that of the first, with a 14.5% prevalence of LV systolic dysfunction (nine patients). The general features of both samples patients are shown in Table 1. The 165 subjects in the first study sample were predominantly males (57%), with a mean age of  $42.4 \pm 9.7$  years; the second sample was not significantly different. Most patients in both samples are asymptomatic and only few patients (six in sample 1 and five in sample 2) were in NYHA functional class III or IV.

### 2.3. Procedures

The reference standard of LV systolic function was the LV ejection fraction (LVEF), estimated using the Simpson rule and obtained by a standardized echocardiogram. All studies were performed by an experienced examiner (MVLB) using an ATL HDI 5000 device (Bothell, Washington, USA). Significant left ventricular systolic

dysfunction is considered to be present if LV ejection fraction is  $\leq 0.40$ . This cut-off point was chosen since it has been previously used in several clinical trials performed on patients with LV dysfunction [14].

In all participants, a standard 12 leads ECG was recorded at a paper speed of 25 mm/s with a portable Fukuda Denshi Model FX-2111 electrocardiograph (Fukuda Co., Tokyo, Japan). The tracing was analyzed blindly by a cardiologist experienced in electrocardiology (ALPR) using the Buenos Aires code, specifically designed to be used in Chagas disease, [15] and normal and abnormal ECG were identified. Chest radiography was performed according to the conventional technique used at the Radiological Unit of the University Hospital of UFMG and analyzed by one observer (AAP) supervised by an experienced researcher (MOCR). The cardiac silhouette and the cardiothoracic ratio were assessed as previously reported [10]. Chest radiography with a cardiothoracic ratio greater than 0.50 or an enlarged cardiac silhouette, or both, was considered abnormal.

BNP measurement was performed in venous blood after a supine 20 min rest by different methods in both samples. In the first sample, BNP measurement was performed by a researcher experienced in the natriuretic peptide field (AMR), in the Department of Physiology and Biophysics of the Federal University of Minas Gerais, as previously described [11]. Samples were placed in chilled tubes containing protease inhibitors (EDTA, PMSF and Pepstatin A, all  $10^{-5}$  M, all purchased from Sigma Chemical Co., St Louis, MO, USA). After centrifugation at  $1500 \times g$  for 15 min at  $4^\circ\text{C}$ , plasma was separated and stored at  $-80^\circ\text{C}$ . For BNP extraction, plasma was allowed to pass slowly through a Sep-Pak C18 column (Waters Corp., USA) activated by sequential washes with acetonitrile and 0.2% ammonium acetate, pH 4, and eluted with an acetonitrile:ammonium acetate solution (60:40). The samples were dried in a Speed-Vac apparatus and redissolved in buffer for

Table 1  
General features of Chagas disease patients

Features*	Sample 1 (n=165)	Sample 2 (n=62)	P <sup>†</sup>
Male, %	57.0	50.0	0.37
Age, y	42.4 (9.7)	44.1 (9.3)	0.28
NYHA functional class I, %	60.0	71.0	0.13
Abnormal ECG, %	69.1	64.5	0.52
Cardio-thoracic index	0.47 (0.06)	0.47 (0.05)	0.27
Enlarged cardiac silhouette, %	19.4	25.8	0.36
BNP (pg/ml) ‡	137 (82.8)	20.7 (58.3)	na
Elevated BNP, %	13.9	19.4	0.35
Ejection fraction	56.4 (10.4)	57.8 (12.6)	0.37
LV systolic dysfunction, %	9.1	14.5	0.23
Abnormal ECG or X-ray, %	72.7	66.1	0.33
Abnormal ECG and elevated BNP, %	10.9	19.4	0.12

\*Data are means (SD), unless otherwise indicated, <sup>†</sup>P value refers to the comparison between the two samples. ‡ median (interquartile range), na=not applicable.

assay. BNP was measured by RIA using hBNP as standard, tyr<sup>0</sup>-BNP for iodination and specific hBNP antibody (all purchased from Peninsula Laboratories, USA). Each sample was tested in duplicate and the final result was the mean value; all samples were measured in the same assay. In the second sample, [12] a small amount of blood (5 ml) collected into tubes containing potassium EDTA (1 mg/mL of blood), were centrifuged at 3000 ×g for 10 min and plasma was obtained and frozen at –80 °C until further analysis, performed at Southwestern Medical School, Dallas, Texas. BNP was measured using the Triage BNP test (Biosite Inc., USA), which is a fluorescence immunoassay for the quantitative determination of BNP in plasma specimens. The precision, analytical sensitivity and stability characteristics of the system have been previously described [16]. Each sample was tested in triplicate to minimize variation from single observations and for internal controls and the final results were reported as the mean of the 3 samples.

The diagnostic performance of the BNP values in the diagnosis of LV systolic dysfunction in the Chagas disease population was evaluated using the receiver–operator–characteristic (ROC) curve. The area under the curve was 0.89±0.04 in the first sample [11] and 0.92±0.03 in the second sample [12]. Different cut-off points were obtained for different samples, since the BNP methods used were also different (RIA and fluorescence immunoassay) [17]. Based on the analysis of the ROC curve and aiming at obtaining specificity ≥80%, a BNP cut-off value of 210 pg/ml was chosen for the first sample and a cut-off value of 75 pg/ml was chosen for the second sample. Other cut-off values were tested considering also the ECG results without further improvements of the diagnostic performance.

### 3. Statistical analysis

The number of subjects needed to be examined (NNE) by echocardiography to detect one case of LV systolic dysfunction in both strategies was calculated as 1/prevalence of LV dysfunction in abnormal screening tests [18]. The sensitivity, specificity, accuracy, positive and the negative predictive values and positive and negative like-

lihood ratios (LR) were calculated for each strategy of detection of abnormal LV systolic function [19]. Confidence intervals (95%) were calculated by the method of Wilson [20] using CIA software, version 2.0.0 (Confidence Interval Analysis for Windows, London, 2000). The statistical significance of the differences in diagnostic measurement strategies was assessed by the McNemar test for paired data. All measurements of diagnostic indexes were performed for both strategies also in the sample 2 and compared to those obtained in the sample 1 by the *z* test. A *p*-value of <0.05 was considered significant.

## 4. Results

### 4.1. First study

ECG abnormalities and an enlarged heart silhouette were found in 69.1 and 19.4% of patients of the first sample, respectively (Table 1). The median BNP value was 137.0 pg/ml (Q1–Q3: 97.7–180.7 pg/ml); in the same original study, normal subjects had median values of 144.7 pg/ml (Q1–Q3: 103.9–163.6 pg/ml) [11]. The wide range of distribution of BNP values and the relative low number of patients with systolic dysfunction (15 patients, 9.1%) hinders the interpretation of these numbers. The median BNP value was 131.0 pg/ml (Q1–Q3: 95.4–169.7 pg/ml) in patients with LV ejection fraction >0.40 and 228.7 pg/ml (Q1–Q3: 176.2–360.8 pg/ml, *p*<0.001) in those with LV ejection fraction ≤0.40.

An abnormal ECG or X-ray was observed in 120 patients (72.7%) while elevation of BNP in patients with abnormal ECG occurred in 41 subjects (10.9%). The NNE, calculated as 1/prevalence of LV dysfunction in the abnormal screening test subgroup, was 8.0 [1/(15/120)] by the conventional strategy and 2 [1/(12/18)] by the new strategy.

The conventional strategy (ECG/X-ray) recognized all patients with LV systolic dysfunction (sensitivity: 100%, 95% CI: 79.6–100% and negative predictive value – PV 100%, 92.1–100%), but with low specificity (30%, 95% CI: 23.2–37.8) and positive predictive value (12.5%, 95% CI: 17.7–19.6), yielding an overall accuracy of 36.4% (95% CI: 29.4–43.9, see Table 2).

Table 2  
Diagnostic accuracy of two strategies in the detection of LV systolic dysfunction in Chagas disease patients

	Sample 1 ( <i>n</i> = 165)			Sample 2 ( <i>n</i> = 62)		
	ECG/BNP (95% CI)	ECG/X-Ray (95% CI)	<i>P</i> *	ECG/BNP (95% CI)	ECG/X-Ray (95% CI)	<i>P</i>
Sensitivity(%)	80.0 (54.8–93.0)	100 (79.6–100)	0.25	77.8 (45.3–93.7)	100 (70.1–100)	0.08
Specificity (%)	96.0 (91.5–98.2)	30.0 (23.2–37.8)	<0.001	90.6 (79.7–95.9)	39.6 (27.6–53.1)	<0.001
Positive predictive value (%)	66.7 (43.7–83.7)	12.5 (7.7–19.6)	<0.001	58.3 (32.0–80.7)	22.0 (12.0–36.7)	0.020
Negative predictive value (%)	98.0 (94.2–99.3)	100 (92.1–100)	0.08	96.0 (86.5–98.9)	100 (84.5–100)	0.14
Accuracy (%)	94.5 (90.0–97.1)	36.4 (29.4–43.9)	<0.001	88.7 (78.5–94.4)	48.4 (36.4–60.6)	<0.001
Positive likelihood ratio	20.0 (8.77–45.58)	1.43 (1.37–1.61)	–	8.24 (3.33–20.36)	1.65 (1.51–2.13)	–
Negative likelihood ratio	0.21 (0.07–0.57)	0.00 (0.00–0.69)	–	0.24 (0.07–0.83)	0.00 (0.00–0.78)	–

\**P* value refers to the comparison of the measurements of the diagnostic performance of ECG/BNP and ECG/X-ray.



The BNP/ECG-based strategy was significantly better than the conventional approach (Table 2) in terms of specificity (96.0, 95% CI: 91.5–98.2,  $p < 0.001$ ) and positive predictive value (66.7, 95% CI: 43.7–83.7,  $p < 0.001$ ), displaying non-significantly lower sensitivity (80.0, 95% CI: 54.8–93.0,  $p = 0.25$ ) and negative predictive value (98.0, 95% CI: 94.2–99.3,  $p = 0.08$ ). The overall accuracy was much improved with the new strategy (94.5, 95% CI: 90.0–97.1,  $p < 0.001$ ).

The superiority of using the new strategy can be graphically displayed using the likelihood ratios and a Fagan normogram (Fig. 3). Considering the positive likelihood ratio obtained for the sample 1 (conventional approach, 1.4, 95% CI: 1.37–1.61; new strategy, 20.0, 95% CI: 8.77–45.58) and an estimated 10% pre-test prevalence of left ventricular dysfunction in an outpatient Chagas disease population, an elevated BNP in the presence of an abnormal ECG increases the post-test probability to 68.9%, although the post-test probability after an abnormal ECG or X-ray would be only 13.4%. The negative likelihood ratio was zero (95% CI: 0.00–0.69) in the conventional approach and 0.21 (95% CI: 0.07–0.57) in the

new one, indicating that a negative test in both strategies leads to a very low post-test probability of LV dysfunction, i.e., 0% and 2.3%, respectively.

#### 4.2. Second study

The frequency of abnormal ECG, X-ray and BNP measurement is displayed in Table 1. BNP values were significantly different, reflecting the different methodologies used for BNP measurement. The median BNP value was 11.7 pg/ml (Q1–Q3: 5.6–30.7 pg/ml) in patients with LV ejection fraction  $> 0.40$  and 93.5 pg/ml (Q1–Q3: 66.6–534.5 pg/ml,  $p < 0.001$ ) in those with LV ejection fraction  $\leq 0.40$ .

Both strategies were applied to the second sample and the indexes obtained, displayed in Table 2, were closely similar when compared to those of the first sample. All comparisons between measurements obtained in the two samples revealed absence of statistically significant differences, although a slight degeneration of the diagnostic performance of the new strategy is suggested by a lower positive likelihood ratio (8.24, 95% CI: 3.33–20.36).

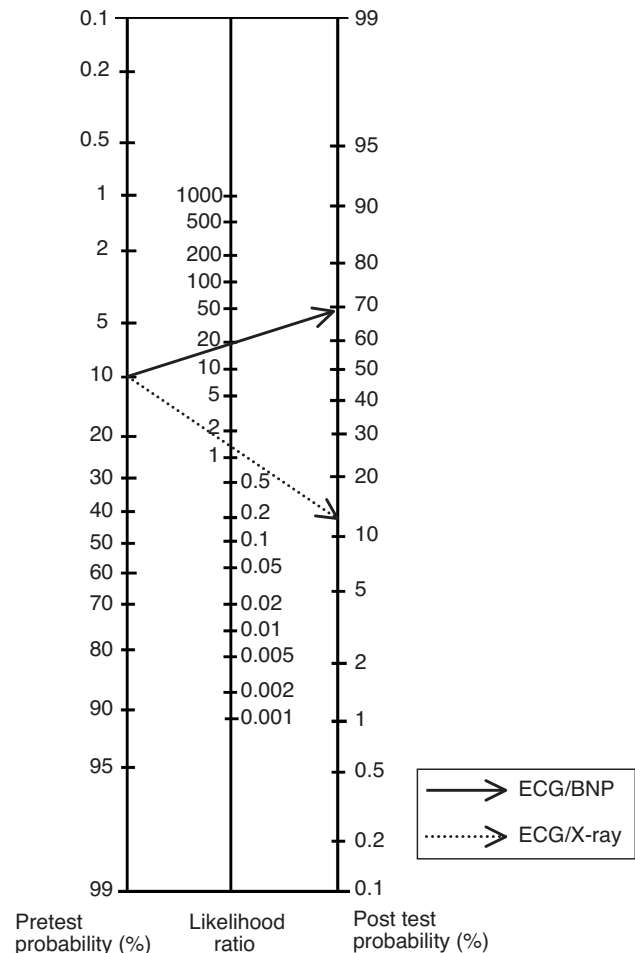


Fig. 3. Post-test probability of LV dysfunction considering the likelihood ratio in the conventional and new strategies.

## 5. Discussion

This study describes the comparison of two strategies for the detection of left ventricular systolic dysfunction in two different groups (first and second samples) of patients with positive serology for Chagas disease, showing that measuring BNP in patients with abnormal ECG is more accurate than performing ECGs and chest X-rays in all patients. To our knowledge, this is the first study that compares these two strategies in patients with Chagas disease and it is one of first reports in tropical medicine field that complies with the STARD initiative recommendations.

The electrocardiogram and chest X-ray have been used in Chagas disease since the original studies by Carlos Chagas [21] and have an established role in the management of Chagas disease patients, with both diagnostic and prognostic importance [9]. Nonetheless, major improvements in the diagnostic capabilities and therapeutic options have occurred in the last decades and it is now clear that left ventricular systolic dysfunction, evaluated non-invasively by echocardiography, is the best predictor of an elevated risk of death in Chagas disease. Moreover, it is now indisputable that pharmacological treatment may halt the progression of LV dysfunction in studies performed at other settings, indicating the urgent need to redefine strategies to recognize and treat these patients.

When the accuracy of this classical strategy was scrutinized using modern evidence-based diagnostic tools, we observed that it was able to detect all patients with significant LV systolic dysfunction, with a sensitivity and negative predictive value of 100% in both samples. However, the specificity, the positive predictive value and

the overall accuracy were relatively low, indicating that a large number of patients would need to be examined by echocardiography in order to detect one that could benefit from pharmacological treatment. We hypothesize that this relatively low accuracy can be attributed to two factors: the use of two diagnostic tests in parallel, which can lower the specificity and positive predictive values, [22] and the poor diagnostic performance of the chest X-ray [10].

Few other studies have addressed the issue of screening to recognize Chagas patients with LV systolic dysfunction [3,23]. Bestetti studied a hospital cohort of 74 Chagas disease patients and found a prevalence of 59% of left ventricular systolic dysfunction, defined as ejection fraction below 55% [23]. The combination of New York Heart Association functional class (2 or more) and a systolic blood pressure below 120 mmHg predicted left ventricular dysfunction with a sensitivity of 59% and a specificity of 77%. ECG variables were not predictive of LV dysfunction and BNP measurement was not performed. Although potentially useful in the hospital setting, this strategy may not be applicable to screening of ambulatory patients, since different clinical profiles and LV dysfunction prevalence may impair the transferability of the diagnostic strategy [24]. It should also be pointed out that the sensitivity of the strategy in the latter study is relatively low, leading to the withholding of the echocardiogram in a large number of patients (41%) that would benefit from the formal evaluation of LV systolic function. More recently, Salles and colleagues, [3] after studying 738 adult outpatients in the chronic phase of Chagas disease, reported that a QT dispersion above 60 ms was associated with LV systolic dysfunction and could be used to predict asymptomatic dysfunction in chronic Chagas' disease. A model considering QT dispersion, the presence of cardiomegaly, frequent PVCs, and male sex had 90% specificity and 71% sensitivity in this population, in which LV systolic dysfunction (ejection fraction < 45%) was observed in 14.7% of cases. Although the diagnostic performance of this strategy was quite good, limitations related to QT dispersion measurements may hamper its use in general practice [3,25].

We evaluated a new strategy, based on sequential tests and the use of a new and promising simple method for the diagnosis of LV systolic dysfunction, i.e., the measurement of BNP in blood samples [11,12]. In the present study, that BNP-based approach was more accurate and superior to the conventional one in terms of specificity and positive predictive value in both samples. A marked and significant increment of accuracy, odds ratio and positive likelihood ratio was detected, with a reduction of the number of patients to be examined by echocardiography from 8 to 2. Since the echocardiogram is not widely available in the public health system in many areas of the Latin America, patients candidate to the echocardiogram by the conventional approach are not actually being submitted to the exam. The marked reduction of the number of cases needed

to be examined by echocardiography using this new strategy may permit that all screened patients would be examined by the echocardiogram, optimizing the use of limited resources.

In fact, the association of ECG and BNP measurement was successful in the detection of LV systolic dysfunction when tested in other clinical settings [18,22,26] and was recommended by the recently released NICE guideline for *Management of Chronic Heart Failure in Adults in Primary and Secondary Care* [27]. Nonetheless, the use of BNP as a diagnostic tool is a recent conquest and there are unsolved issues and problems related to the implementation of its use in clinical practice [28]. Different commercial and experimental measurement techniques are available, with different cut-off points and clinical determinants [29]. In our study, a different methodology was applied to the first and second samples (RIA and fluorescence immunoassay), leading to markedly different cut-off points [17]. More than a limitation, this fact indicates that the excellent performance obtained in the first sample was transferable to the second sample, in which a commercial kit was used. The cost-effectiveness of this strategy is still controversial, although studies have suggested that screening high-risk subjects by BNP before echocardiography could reduce the cost per detected case of LV systolic dysfunction by 26% [18] and may be economically attractive for patient groups with at least 1% prevalence of moderate or greater LV systolic dysfunction [30]. Additionally, commercial BNP measurement was not yet available in many Latin America cities by the time of the writing of this paper (September 2004) and this strategy could be applied only if, as expected, measuring BNP becomes a widespread and low-cost laboratory method in the near future, what could be anticipated by the simplicity and the reliableness of the point-of-care measurement system used in the second sample.

In our study, the new strategy is non-significantly less sensitive and with a lower negative predictive value than the traditional one. Indeed, three out 15 patients with LV dysfunction, in the sample 1, and two out nine, in the sample 2, would be missed by a BNP-based strategy. Since the main aim of a screening test is to be a 'rule out' test, missing target patients could be a limitation of this new strategy. Additionally, relatively wide confidence intervals for the new strategy positive likelihood ratios and predictive values should also be considered a limitation of our findings. Further analysis of the data, using ROC curves and different cut-points (data not shown), did not improve the sensitivity of this strategy without compromising the specificity. Vasan et al. [31] reported limited sensitivity of BNP measurement in recognizing LV systolic dysfunction in a community-based cohort and Tang et al. [32] found that more than 1 in 5 patients with systolic HF and chronic symptoms in specialized outpatient HF clinic had plasma BNP in the "normal" range, suggesting a more limited value of BNP measurement as a screening test in the clinical setting.

A major challenge in global diseases is “to transform new knowledge into cost-effective, equitably affordable interventions and to guarantee their access to the patients and populations of endemic countries” [1]. Effectively screening for LV systolic dysfunction is a major issue in Chagas disease, since it can significantly reduce mortality and morbidity. A BNP-based strategy proved to be accurate and should be considered as an alternative option in the detection of LV systolic dysfunction in Chagas disease. Nonetheless, further studies should be performed to define the best strategy in the management of Chagas disease cardiopathy.

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