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

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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 ≤ 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: I7.7–19.6). 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 × 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.

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

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

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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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 electrocardiogram 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.

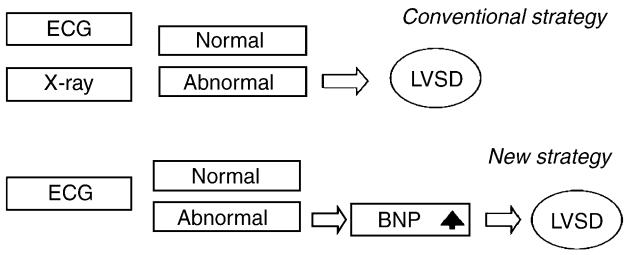

Fig. 1. Diagnostic strategies for detecting LV systolic dysfunction in Chagas disease.

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).