Usefulness of NT-proBNP Level for Diagnosing Left Ventricular Hypertrophy in Hypertensive Patients. A Cardiac Magnetic Resonance Study

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The presence of left ventricular hypertrophy (LVH) is associated with an increase in cardiovascular morbidity and mortality in hypertensive patients. We investigated the diagnostic value of the N-terminal probrain natriuretic peptide (NT-proBNP) level for detecting LVH in hypertensive patients with a conserved left ventricular ejection fraction. The study involved 27 consecutive patients. Cardiac magnetic resonance imaging was performed to determine left ventricular mass and the plasma NT-proBNP level was measured. A significant correlation was found between the NT-proBNP level and left ventricular mass (r=0.598; P=.001). Use of a cut-off point of 35 pg/mL enabled the presence of LVH to be identified with a sensitivity of 100% (95% confidence interval [CI], 69-100) and a specificity of 70.6% (95% CI, 44.1-89.6). The area under the receiver operating characteristic (ROC) curve was 0.867 (95% CI, 0.73-1; P<.05). The plasma NT-proBNP level may be useful for identifying patients with LVH.

Key words: *Arterial hypertension. Ventricular hypertrophy. Cardiac magnetic resonance.*

Utilidad del NT-proBNP en el diagnóstico de la hipertrofia ventricular izquierda en el paciente hipertenso. Estudio mediante resonancia cardiaca

Se ha relacionado a la hipertrofia ventricular izquierda (HVI) con un incremento de la morbimortalidad cardiovascular en el paciente hipertenso. Hemos analizado la utilidad diagnóstica de la fracción N-terminal del péptido natriurético tipo B (NT-proBNP) en la detección de HVI en pacientes hipertensos con fracción de eyección conservada. Se ha estudiado a 27 pacientes consecutivos, a los que se realizó una resonancia cardiaca para el cálculo de la masa ventricular izquierda (MVI) y se determinó la concentración plasmática de NT-proBNP. Se ha encontrado una correlación significativa entre los valores de NT-proBNP y la MVI (r = 0,598; p = 0,001). Un punto de corte de 35 pg/ml permite identificar la HVI con una sensibilidad del 100% (intervalo de confianza [IC] del 95%, 69-100) y una especificidad del 70,6% (IC del 95%, 44,1-89,6). El área bajo la curva ROC fue 0,867 (IC del 95%, 0,73-1; p < 0,05). La concentración plasmática de NT-proBNP puede ser útil para identificar a los pacientes con HVI.

Palabras clave: *Hipertensión arterial. Hipertrofia ventricular. Resonancia cardiaca.*

INTRODUCTION

Left ventricular hypertrophy (LVH) in patients with high blood pressure has been related to an increase in cardiovascular complications and a poorer long-term course of disease. Recent high blood pressure guidelines recommend checks be made for LVH in the initial evaluation of all hypertensive patients.[1] An electrocardiogram (ECG) is the method most commonly used to identify LVH in current clinical practice: the equipment necessary is readily available and the procedure is inexpensive. However, the electrocardiographic criteria employed are of low sensitivity; this method is unlikely, therefore, to identify a great many patients with the problem.[2] Echocardiography is a more sensitive way of diagnosing LVH, but it is commonly unavailable and cannot, therefore, be used with all hypertensive patients.[3] This situation has led to the search for other

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Received November 7, 2007.
Accepted for publication December 18, 2007.

markers that help identify this high cardiovascular risk population.

One of these markers is type B natriuretic peptide (BNP) (a hormone synthesized by the myocardium, the levels of which have been shown related to structural heart disease, and in particular to heart failure) and its N-terminal portion (NT-proBNP).[4] Some studies that have employed echocardiography as the standard for diagnosing LVH have indicated the possible use of these markers in the diagnosis of LVH in hypertensive patients, although the information provided is scant and contradictory.[5-7] The aim of the present work was to determine the usefulness of the plasma NT-proBNP concentration in the diagnosis of LVH by comparing it against the standard of cardiac magnetic resonance imaging. The latter technique is reliable, its results reproducible, and it provides high resolution images, allowing smaller numbers of patients to be examined for significant variations to be noted.[8-10]

METHODS

This study prospectively included 27 patients with a diagnosis of essential high blood pressure referred consecutively to a hospital unit for this condition. All were subjected to a complete analysis including the determination of their plasma NT-proBNP concentrations (ELISA Kit, Roche Diagnostics), ECG, echocardiography (calculating the mass of the left ventricle using the Penn formula), and cardiac magnetic resonance. Patients with a background or symptoms of heart failure were excluded, as were those with an ejection fraction of <50% on echocardiography, or arrhythmias detected by ECG (especially atrial fibrillation).

For the cardiac magnetic resonance study a Philips Intera 1.5 T machine was used, employing the parallel imaging technique. Four and two chamber steady-state free precession (SSFP) cines were acquired during breath-old. A consecutive series of images along the short axis from the base to the apex of the left ventricle was also recorded. Left ventricular variables were measured using specific software (Leonardo, Siemens, Erlangen, Germany). Analysis first required the endocardial and epicardial borders of the left ventricle to be made clear in all the images of the short axis series, along with the papillary muscles at end-diastole.[11] Using these data the program calculated the mass of the left ventricle, adjusting for the body surface area of each patient. Cut-off points of 83 g/m^2 in men and 67 g/m^2 in women[2] were selected for the diagnosis of LVH. The observers who analyzed the magnetic resonance results were blind to the NT-proBNP results and vice versa.

Statistical Analysis

Continuous variables were expressed as means (standard deviation [SD]); qualitative variables are expressed as numbers and percentages. When the distribution of the results was normal the differences between groups were analyzed using the Student *t* test for independent samples; the Mann Whitney *U* test was used when the distribution was not normal. The qualitative variables were analyzed using the χ^2 test or Fisher's exact test. The Pearson correlation coefficient between the plasma NT-proBNP concentration and the left ventricular mass (determined by magnetic resonance and adjusted for body surface area) was also calculated. A ROC curve was plotted to determine the LVH diagnostic reliability of the plasma concentration of NT-proBNP. All calculations were performed using SPSS v.15.0 software (SPSS Inc.). A *P* value less than .05 was considered significant.

RESULTS

The mean age of the population was 54 (12.7) years; men made up 85.2% of the sample. Some 22.2% of the patients were smokers and 14.8% were diabetics. None had any history of cardiovascular disease. Only 3 patients showed ECG criteria for LVH (Sokolov and/or Cornell). Cardiac magnetic resonance diagnosed LVH in 9 patients (33.3%). Table shows the main clinical and echocardiographic characteristics of the patients with LVH and the rest of the study population. Those with LVH had a higher mean age and higher blood pressure (172.2 [27.8] compared to 150.3 [17.2] mm Hg; *P*<.05).

A significant correlation was found between the mass of the left ventricle as determined by magnetic resonance and the plasma NT-proBNP concentration (*r*=0.598; *P*=.001). The area under the ROC curve was 0.867 (95% confidence interval [CI], 0.73-1; *P*=.002). An NT-proBNP cut-off of 35 pg/mL was established for the identification of LVH; sensitivity 100% (95% CI, 69-100) specificity 70.6% (95% CI, 44.1-89.6), positive predictive power 66.7%, negative predictive power 100%.

DISCUSSION

The present study shows the good relationship between the plasma NT-proBNP concentration and the left ventricular mass as determined by cardiac magnetic resonance in hypertensive patients. A cut-off point of 35 pg/mL allowed the identification of patients with LVH with high sensitivity and specificity. An important finding was the high negative predictive power of the plasma NT-proBNP concentration: if this is confirmed in future work, the need to perform an ECG to rule out LVH in asymptomatic hypertensive patients would be obviated in those with a plasma NT-proBNP concentration of <35 pg/mL.

Several studies have examined the usefulness of NT-proBNP as a screening test to detect LVH both in the general population and among hypertensive patients, but the results have been contradictory.[5,7,12] All of these studies

Clinical and Echocardiographic Characteristics of the Studied Population

Antecedents and Clinical Variables	With LVH (n=9)	Without LVH (n=18)	*P*
Age, mean (SD), y	61.9 (12.9)	50 (1.3)	<.05
Male sex	8 (88.9)	15 (83.3)	NS
Diabetes mellitus	1 (11.1)	3 (16.7)	NS
Smoker	1 (11.1)	5 (27.8)	NS
Dyslipidemia	3 (33.3)	7 (38.9)	NS
Weight, mean (SD), kg	88.1 (17.8)	83.7 (12.6)	NS
SBP, mean (SD), mm Hg	172.2 (27.8)	150.3 (17.2)	<.05
DBP, mean (SD), mm Hg	91 (14.6)	91.3 (12.4)	NS
Heart rate, mean (SD), beats/min	65.1 (14.5)	67.2 (14.2)	NS
NT-proBNP, mean (SD), pg/mL	188.9 (165.5)	46.5 (51)	<.05
Echocardiographic variables			
Ejection fraction, mean (SD), %	75 (7.5)	68.7 (9.2)	NS
IVS, mean (SD), mm	13.3 (2.2)	10.9 (1.7)	<.005
DDLV, mean (SD), mm	50.9 (5.6)	46.4 (3.4)	<.05
PW, mean (SD), mm	12.3 (1.9)	10.5 (1.7)	<.05
SDLV, mean (SD), mm	28.3 (6.2)	27.9 (4.8)	NS
Left atrium, mean (SD), mm	42.4 (3.7)	38.6 (4.9)	.05
LVMbsa, mean (SD), g/m^2	135.4 (38.2)	91.7 (17.4)	<.001

DBP: diastolic blood pressure; LVDD: left ventricular diastolic diameter; IVS: interventricular septum; LVMbsa: left ventricular mass adjusted for body surface area; PW: posterior wall; SBP: systolic blood pressure; LVSD, the left ventricular systolic diameter.
Results are expressed as means (standard deviation) or in (%).

determined the ventricular mass via echocardiography as the standard for diagnosing LVH, despite its limitations. Although validated in post mortem studies,[13] echocardiograms are associated with a great deal of inter- and intra-observer variability, with an error of estimation of the ventricular mass of some 27-97 g; neither are the results obtained very reproducible between studies (variation, 22-40 g).[8] A novelty of the present work is the use of cardiac magnetic resonance as a standard. This technique is more reliable and provides more reproducible results than echocardiography in the estimation of the ventricular mass.[8-10] However, its high associated costs, complexity of use and scant availability mean it is not used for this purpose in normal clinical practice, although it is used in research work.

The populations analyzed in earlier studies were very heterogeneous and included patients with symptoms of heart failure, and this may have affected their plasma NT-proBNP concentrations and therefore the final results.[7] The present work, in contrast, involved only hypertensive patients with no background of cardiovascular disease (heart failure or coronary heart disease). Furthermore, all showed sinus rhythm and their ejection fractions were conserved. This homogeneity may have helped avoid possible interferences.

The main limitation of the present work is the small number of patients studied—although it is the only one that has used cardiac magnetic resonance as a reference standard.

In conclusion, the determination of the plasma NT-proBNP concentration could offer a good means of initial screening for LVH in asymptomatic patients with high blood pressure; this would allow the identification of those who would benefit from confirmatory echocardiography. This would provide a better evaluation of cardiovascular risk amongst this population. Studies with larger numbers of patients are required to clarify the role of BNP in the diagnosis of LVH, in the follow-up of patients with high blood pressure, and in the monitoring of the regression of LVH with anti-hypertension treatment.

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