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Prevalence and predictors of left ventricular hypertrophy in patients with hypertension and normal electrocardiogram

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Abstract

Background: Electrocardiography (ECG) has low sensitivity for detecting left ventricular hypertrophy (LVH), while echocardiography cannot be routinely performed.

Design/methods: In this study we evaluate the prevalence of LVH and diastolic dysfunction in hypertensive patients with normal ECG. We excluded patients with cardiovascular (CV) diseases, diabetes, chronic kidney disease, or presenting ECG-LVH or other ECG anomalies. The enrolled 440 hypertensive patients underwent echocardiographic examination (Acuson Sequoia 512); LV mass was indexed by body surface area (LVMI) and LVH was defined as LVMI >125 g/m² in men and >110 g/m² in women. Diastolic function was evaluated by mitral inflow and tissue Doppler imaging (TDI).

Results: The prevalence of LVH was 8.18% (95% confidence interval [CI] 5.97–11.1%). Multiple regression analysis showed that the only variable independently associated with LVH was duration of hypertension (p < 0.001). The receiver operating characteristic (ROC) curve showed that duration of hypertension was a powerful predictor of LVH, with an area under the curve (AUC) of 0.878 and p < 0.0001. Further, in patients with LVH the mean difference of LVMI from the cut-off value for LVH was 12.3 ± 9.19 g/m². Diastolic dysfunction, defined as early diastolic myocardial velocity (Em) <0.08 m/s, was detected only in 3.2% of patients.

Conclusions: The prevalence of LVH among hypertensive patients with normal ECG, free of diabetes and of CV diseases is low; moreover, patients with echocardiographic LVH presented LVMI values that identified mild LVH. Few cases of impaired diastolic function were registered. We suggest that in hypertensive patients with such characteristics the echocardiographic examination should be reserved to those who present with higher duration of hypertension.

Keywords
Left ventricular hypertrophy, hypertension, electrocardiography, echocardiography

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Introduction

Early detection of left ventricular hypertrophy (LVH) in hypertensive patients is of great importance for the correct stratification of cardiovascular (CV) risk, because LVH is associated with increased CV events and mortality.¹

Electrocardiography (ECG) has the advantages of low costs, simplicity and almost ubiquitous diffusion; LVH detected by the Sokolow–Lyon index (SV₁ + RV₅–₆ >38 mm) or by the Cornell voltage...
QRS duration product (>2440 mm*ms) is an independent predictor of CV events, and ECG can also be used to detect patterns of ventricular overload or 'strain' (known to indicate more severe risk). ischaemia, conduction defects and arrhythmias. However, it is well known that the sensitivity of ECG to detect LVH is low, independently of the definition of LVH. Echocardiography is more sensitive than ECG in diagnosing LVH and predicting CV risk, and may help in the more precise stratification of overall risk and in the determination of therapy.

Nevertheless, the routine execution of echocardiographic examination in hypertensive patients, although useful on various grounds, may lead to some difficulties. The correct indication to echocardiography in hypertensive patients is still a matter of debate for several reasons (very high number of patients, cost, availability), particularly in untreated hypertensive patients at low or medium risk.

The aim of this study is to evaluate the prevalence and the predictors of LVH and the prevalence of anomalies of diastolic function in a group of hypertensive patients with normal ECG and free of diabetes and CV diseases.

**Patients and methods**

In accordance with the Declaration of Helsinki and institutional guidelines, the protocol was approved by the local Ethical Committee and subjects were aware of the investigational nature of the study and agreed to participate after informed consent.

**Study population**

The patients were selected among the subjects consecutively attending our Internal Medicine, Nephrology and Hypertension Unit. All subjects underwent a detailed review of their medical history and routine laboratory measurements.

The definition of hypertension was based on the 2007 European Society of Hypertension/European Society of Cardiology (ESH/ESC) Guidelines. Clinic blood pressure (BP) was considered as the average of three consecutive measurements using a mercury sphygmomanometer after the subjects had been supine for 5 minutes.

Glomerular filtration rate (GFR) was estimated using Cockcroft and Gault equation, corrected by body surface area.

The following exclusion criteria were applied:

- age <20 or >75 years;
- diabetes;
- chronic kidney disease (CKD);
- anomalies of ECG;
- history of CV diseases (previous coronary artery disease, history of angina or myocardial infarction, abnormalities of cardiac rhythm, heart failure, ejection fraction <55%, moderate or severe valvular diseases, previous transient ischaemic attack or stroke);
- other major non-CV diseases.

After the application of the exclusion criteria, 440 White hypertensive subjects with normal ECG were included in the study.

**Laboratory methods**

Determination of routine biochemical parameters was performed with standard techniques by using an autoanalyser (Boehringer Mannheim for Hitachi system 911, Germany).

**Electrocardiography**

ECG was performed with a standard 12-lead system with the patient at rest in supine position.

ECG was defined as normal when the following conditions were simultaneously present:

- sinus rhythm;
- absence of conduction abnormalities;
- absence of LVH with Sokolow–Lyon index, Cornell voltage criteria and Cornell voltage QRS duration product;
- absence of left atrial abnormalities;
- absence of ST trait or T-wave abnormalities.

**Echocardiography**

The echocardiographic examination was executed by using an Acuson Sequoia 512 system (Siemens, Mountain View, CA, USA). Images were taken in left lateral decubitus position. Two-dimensional targeted M-mode echocardiography was performed by using the parasternal long-axis acoustic window in order to evaluate left ventricular end-diastolic diameter (LVEDD), left ventricular end-systolic diameter (LVESD), interventricular septum thickness (IVST), and posterior wall thickness (PWT) according to the American Society of Echocardiography (ASE) recommendations.

Only those frames with optimal visualization of interfaces and showing simultaneous visualization of septum, left ventricular diameters and posterior wall were used for readings.

Left ventricular mass (LVM) was determined by using the ASE-corrected cube formula and was
indexed by body surface area (LVMI). In our laboratory, the mean intra-observer variability for LVM was 8.6%.

LVH was defined as LVMI > 125 g/m² in men and > 110 g/m² in women, as suggested by the 2007 ESH/ESC Guidelines. LVMI was used to divide the study population into two subgroups (with and without LVH) and in the main statistical analyses of the results.

The prevalence of LVH was also evaluated indexing LVM by height elevated by a power of 2.7 (LVMH².⁷), in order to provide a more stringent allowance for those who were overweight. In that case LVH was defined as LVMH².⁷ > 51 g/m².⁷ in both sexes.

Relative wall thickness (RWT) was calculated as the ratio of 2PWT/LVEDD. Concentric and eccentric LVH were defined on the basis of RWT above or below 0.45, respectively.

Left ventricular ejection fraction (EF) was assessed by 2D-echo using modified Simpson’s rule. Diastolic function was evaluated by using both mitral inflow and tissue-Doppler echocardiography, performed according to the ASE recommendations. Mitral inflow was assessed in the apical four-chamber view, using pulsed-wave Doppler echocardiography, with the Doppler beam aligned parallel to the direction of flow and the sample volume at the leaflet tips. From the mitral inflow profile, the E-wave (E) and A-wave (A) peak velocities, E/A ratio and E-deceleration time (DT) were measured. Isovolumic relaxation time (IVRT) was calculated between the aortic valve closure and the start of E-wave.

Tissue Doppler imaging (TDI) of the mitral annulus was obtained from the apical four-chamber view, using a 1- to 2-mm sample volume placed in the lateral mitral valve annulus, in order to evaluate early diastolic myocardial velocity (Em).

We decided to evaluate diastolic function principally by means of TDI because parameters measured by TDI are more preload-independent than those calculated by mitral inflow; further, Em is inversely related to myocardial fibrosis.

Echocardiographic data are expressed as the average of five consecutive cardiac cycles. Images were read by a single cardiologist, who was blinded to the patient’s clinical characteristics.

**Statistics**

Data for continuous variables are given as means ± standard deviation (SD).

Differences between groups were evaluated by using the independent-sample Student’s t-test with Bonferroni correction, for continuous variables, and the chi-squared ($\chi^2$) test, with Yates’ correction, for the categorical variables.

The independent correlates of LVH were tested by means of multivariate stepwise logistic regression analysis by calculating odds ratios and 95% confidence intervals (CI).

Receiver operator characteristic (ROC) curves were built to assess the power of independent correlates of LVH to predict it.

The null hypothesis was rejected at a two-tailed $p \leq 0.05$.

The statistical analyses were performed by using the SYSTAT DATA software package, version 5.2 (Systat, Evanston, IL, USA).

**Results**

The main demographic and clinical data of the patients are synthesized in Table 1. Patients with LVH were...
older and presented with longer duration of hypertension, while the subgroups with and without LVH did not differ with regards to gender, body mass index, renal function, or blood pressure.

Table 2 shows the main echocardiographic findings. Patients with LVH showed significantly higher LV wall thicknesses, LV diameters, RWT, and left atrium diameter.

Diastolic function, evaluated by both mitral inflow and TDI, was significantly worse in patients with LVH. The mean (±SD) value of LVMI was 92.3 ± 17 g/m² in the whole group and 62.4 ± 11.3 g/m² in the subgroup with LVH (135.5 ± 7.8 g/m² in males and 123.8 ± 10.1 g/m² in females with LVH). This difference was 12.3 ± 9.19 g/m² in males, and 7.17 ± 9.9 g/m² in females (Figure 1).

The other covariates included in the analysis were: age, sex, body mass index, and systolic blood pressure. Further, the ROC curve showed that known duration of hypertension was also a powerful predictor of the presence of LVH, with AUC of 0.878 and p < 0.0001 (Figure 2). In particular, a known duration of hypertension >66 months had 89.74% sensitivity and 80.5% specificity to detect LVH.

Diastolic function

Diastolic dysfunction, defined as Em < 0.08 m/s, was found only in 14/440 patients (3.18%). Among these 14 patients (8 males and 6 females), 8 had LVH, all with concentric pattern (5 males and 3 females).

Discussion

Our study was aimed at evaluating the prevalence of LVH and diastolic dysfunction in a group of hypertensive patients with normal ECG and free of diabetes, CKD and CV diseases.
The main findings of our study are the following:

- in this sample of low/medium-risk patients the prevalence of LVH was low (8.18% using LVMI, 12.27% using LVMH), particularly in males;
- the values of LVMI in patients with LVH were only a little above the cut-off values that define the presence of LVH;
- the presence of LVH was significantly associated with and predicted by the duration of hypertension;
- the prevalence of diastolic dysfunction was low (3.18%).

These results suggest that the execution of an echocardiographic examination in hypertensive patients with normal ECG may not be very useful or cost/time-effective if routinely performed, due to the low probability of identifying subjects with LVH or improving the stratification of CV risk and the treatment approach.

However, the examination should be reserved for patients with longer duration of hypertension; our data show that in hypertensive patients with normal ECG and free of other associated pathological conditions, a useful threshold to decide whether performing the examination or not may be duration of hypertension longer than 5 years.

The routine execution of echocardiography in hypertensive patients, in fact, is a matter of debate. In the ESH/ESC Guidelines echocardiography is presented as a second-level examination, to be performed only when and where the local conditions are adequate.

A recent Italian multicentre survey showed that hypertension accounts for approximately 30% of echocardiographic examinations currently performed in outpatient hospital or academic echo laboratories. In a study by Cuspidi et al., 580 never-treated patients with grade 1–2 hypertension, free of diabetes, CV diseases, renal insufficiency and ECG-LVH, underwent echocardiography. LVH registered an overall prevalence of only 14.8%. Since in the subgroup of age <50 years echocardiography had a very limited impact on risk stratification and too high costs, the authors concluded that the search for LVH by echocardiography in order to improve CV risk stratification could be optimized on the basis of demographic variables.

Our results are consistent with those of Cuspidi et al., in our sample of hypertensive patients the prevalence of LVH detected by echocardiography was low (8.18%). Moreover, LVMI values generally identified mild LVH, which only in very few cases was accompanied by alterations of LV diastolic function detected by TDI.

An objection to a limited use of echocardiography in hypertension could be the fact that one of our aims is an early detection of target-organ damage, and in fact ECG is not sufficiently sensitive at detecting mild initial forms of left ventricular growth such as LV remodelling. Nevertheless, we should also bear in mind that the treatment of these forms, often having no functional abnormality, is not substantially different from the treatment of hypertensive patients without LVH.
The proposal, advanced both in the past and recently, of a limited echocardiographic examination, performed to detect only some parameters, does not appear as an adequate solution and did not meet with good success, since it does not really shorten the execution time of the examination and entails the loss of very important information (diastolic function).

On the other hand, it is reasonable that echocardiography should be always performed when other pathological conditions are associated with the ‘simple’ hypertension. For example, diabetes or CKD are frequently associated with LV structural and functional changes.

Moreover, we think that the execution of the echocardiographic examination should be recommended if ECG is positive for LVH (Sokolow–Lyons index or Cornell voltage QRS duration product and/or strain pattern): in this case we should not consider echocardiography as a simple duplication or a means to confirm LVH detected by ECG, because it is also possible to quantify LVH, obtain information on geometric changes (concentric or eccentric LVH), evaluate systolic and diastolic function (the latter is often not normal), and receive more accurate prognostic information.

Finally, in this study we mainly used LVMI to evaluate the prevalence and the predictors of LVH, and LVMH was utilized only as a confirmation of the prevalence found by using LVMI. In this regard, we should point out that the LVMI and the cut-offs for LVH we used (≥125 g/m² in men and ≥110 g/m² in women), are the methods suggested by ESH/ESC Guidelines. The best method for the normalization of LVM measurements in adults is still a matter of debate, and different studies agree on the conclusion that the method of indexing LVM does not have a significant impact on the ability to predict CV risk. Finally, the choice of a different indexation method does not influence the low prevalence of diastolic dysfunction found in this study.

Conclusions

In summary, since it is not possible to perform an echocardiographic examination in all hypertensive patients, it seems reasonable to recommend the examination on the basis of a clinically oriented approach (Figure 3). Thus, hypertensive patients with normal ECG and without other pathological conditions should receive an echocardiographic examination not routinely, but on the basis of clinical variables such as known duration of hypertension. Hypertensive patients who do not undergo echocardiography should repeat ECG (for example, once a year) and undergo the examination in the case of new changes of ECG (QRS, ST segment), or in the case of symptoms of left ventricular dysfunction (dyspnoea, oedema).

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Figure 3. Proposed algorithm for a clinically-oriented use of echocardiography in hypertension. *ECG at least every year; echocardiography every 2 years if ECG and clinical status are unchanged. In presence of diastolic dysfunction repeat echocardiography every year.
Conflict of interest
None declared.

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