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Diagnostics

Impact of Baseline Echocardiography on Treatment Outcome in Primary Care Patients With Newly Detected Arterial Hypertension: A Randomized Trial

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Background: The objective of this study was to test whether baseline echocardiography in newly detected hypertension improves left ventricular mass index and blood pressure control. This is a randomized trial with primary care patients.

Methods: After routine clinical work-up 177 consecutive patients with newly detected hypertension were randomized according to result of their echocardiogram (echo group and control group). Treating physicians were encouraged to prescribe angiotensin II receptor antagonist therapy for patients with evidence of hypertensive target organ damage. Mean blood pressure (BP) and echocardiographic left ventricular mass index were measured at baseline and after 6 months of therapy in both groups.

Results: More patients with hypertensive target organ damage were identified in the echo group as compared to the control group (58 of 91 [64%] *v* 42 of 86 [49%] patients (difference 15%, 95% CI 1%–29%). In the echo group, 41 patients (45%) received angiotensin II receptor antagonist therapy as compared to 27 patients (31%) in the control group (difference 14%, 95% CI 0–28%). After 6 months, there were no differences in mean left ventricular mass index, mean diastolic 24-h ambulatory BP monitoring, or mean systolic and diastolic office BP between the two groups.

Conclusions: In patients with newly detected hypertension, baseline echocardiography detects more patients with hypertensive target organ damage, but does not lead to a reduction in left ventricular mass index or improved BP control after 6 months of therapy. Am J Hypertens 2006; 19:1150–1155 © 2006 American Journal of Hypertension, Ltd.

Key Words: Echocardiography, target organ damage, arterial hypertension.

Left ventricular hypertrophy (LVH) is a hypertensive target organ damage and an independent cardiovascular risk factor.[1–3] Importantly, LVH occurs not only in severe but also in mild hypertension.[4–7] In outpatients with mild definite hypertension LVH is encountered in up to 38% of patients.[1]

Most outpatients with newly diagnosed hypertension have mild hypertension. Identifying hypertensive target organ damage is important for early treatment stratification. According to current guidelines,[8–10] patients with mild hypertension and LVH should receive immediate drug treatment. Antihypertensive drug treatment reduces left ventricular mass (LVM),[11–16] and regression of LVH is associated with reduced cardiovascular risk.[11,13] Angiotensin II receptor antagonist therapy is more effective in reducing LVM than β-adrenergic receptor therapy.[12] The Losartan Intervention for Endpoint (LIFE) Reduction in Hypertension Study trial demonstrated the superiority of the angiotensin II receptor antagonist losartan compared to atenolol in reducing cardiovascular end points in hypertensive patients with electrocardiographic[13] and echocardiographic LVH.[17]

Although the value of baseline echocardiography for LVH detection[4–7,18,19] and risk stratification[4,7,18,19] in hypertensive patients has clearly been demonstrated, performing baseline echocardiography for detection of LVH in patients with newly detected hypertension is not recommended in current guidelines.[8–10] Thus, the presence of

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LVH might be missed in patients with mild hypertension.[4,7,18,19]

To our knowledge there are no randomized outcome studies evaluating the impact of baseline echocardiography on treatment outcomes in primary care patients with newly detected essential hypertension. In this prospective randomized trial, we evaluated the impact of baseline echocardiography on LVM index and blood pressure (BP) control in consecutive general medical outpatients from an unselected primary care population with never-treated essential hypertension.

Methods

Consecutive adult general medical outpatients (2615) were screened for office hypertension.

All patients with elevated sitting office BP were deemed eligible for the study (after 5 min of rest, mean of two BP measurements ≥140/90 mm Hg at two different visits, according to standard guidelines).[8] Exclusion criteria were pretreated hypertension, missing study participation consent, severe concomitant illness with the exception of diabetes mellitus, and accepted indications for echocardiography (eg, pericarditis, heart failure, or the presence of a heart murmur suggesting valvular heart disease). The study protocol had been approved by the local ethics committee.

The Medical Outpatient Department of the University Hospital Basel, Switzerland, provides primary care for general medical walk-in patients. Approximately 20% are referred by general practitioners for second opinion or for interdisciplinary ambulatory care. All patients are routinely seen by three- or four-year residents. They are supervised by an attending physician in General Internal Medicine.

Patients with newly detected office hypertension received routine clinical work-up, according to standard guidelines[8] (ie, history, physical examination, routine blood tests, electrocardiogram [ECG] and urinalysis, and 24h ambulatory BP monitoring [24-h ABPM] with validated devices [Spacelabs, Diessenhofen, Switzerland, and Mobilograph, Stolberg, Germany]). Normal mean 24-h ABPM values were defined as <130/80 mm Hg.

After having obtained informed written consent and having ruled out white coat hypertension, patients with definite hypertension were randomized by computer as to make the result of the echocardiogram available to their treating physician (echo group) or to withhold it (control group).

Then all study patients underwent transthoracic echocardiography with a HP 5500 system (Hewlett Packard, Andover, MA) performed by one of two experienced cardiologists who were instructed not to inform patients about the echo findings. Both cardiologists were blinded to the patients' group allocation during the course of the study. Only residents treating patients randomized to the echo group, but not of patients randomized to the control group, obtained a written report about the findings of baseline echocardiography. Results of target organ damage other than LVH were available for the treating physicians of both groups.

Left ventricular mass index was calculated according to the formula: $0.8 \times (1.04 \times [\text{Interventricular septal thickness} + \text{posterior wall thickness} + \text{enddiastolic diameter (EDD)}]^3 - \text{EDD}^3) + 0.6)/\text{m}^2$ body surface area. The LVH was defined conservatively as LVM index >136 g/m^2 for men and >110 g/m– for women, with sufficient sensitivity to diagnose the more severe cases of LVH that are more likely to change the routine treatment decision.

Area-based methods perform as well as height-based methods for normalization of LVM mass for body size[20] in populations with a low rate of obesity such as ours (24%).

Treating residents received a written Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC) VI guideline summary as a general recommendation for antihypertensive treatment decision. They based their treatment decision on the presence of hypertensive cardiac or renal target organ damage. Specifically, renal target organ damage was defined as microalbuminuria (albumin-to-creatinine ratio >2.26 mg/mmol) or proteinuria (protein-to-creatinine ratio >11 mg/mmol), cardiac target organ damage as having electrocardiographic signs of LVH (Sokolow-Lyon index >3.5 mV or Cornell product >2440 mV × msec), or an elevated LVM index in echocardiography (>136 g/m^2 for men and >110 g/m^2 for women). When hypertensive target organ damage was identified (LVH shown by ECG or echocardiography, microalbuminuria, proteinuria, diabetes mellitus, history of cardiovascular events), drug treatment with angiotensin II receptor antagonist therapy (particularly valsartan) was strongly encouraged. In the course of the study, treating resident physicians were free to adjust treatment if necessary. End of study examinations including BP measurements and echocardiography were performed after 6 months.

The primary outcome was the difference in mean LVM index between the two groups. Secondary outcomes were the comparison of mean differences in LVM index, office and 24-h ABPM between the two groups, and the proportion of patients with elevated LVM index in the two groups after 6 months of therapy.

Descriptive statistics were calculated using two sample test of proportions. We conducted analyses of covariance to evaluate between group differences in LVM index at the end of follow-up using baseline LVM index as a covariate, and BP values at the end of follow-up using baseline BP as a covariate. Primary analyses were performed on an intention-to-treat basis. We used the last value carried-forward method for missing values. In addition, we conducted per protocol analyses for the primary outcomes (LVM index and BP values after 6 months of follow-up) to minimize potential masking of changes from baseline that might occur with an intention-to-treat analysis. The