Trends in hypertension control and left ventricular hypertrophy over three years

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Key words:
Blood pressure; Hypertension; Left ventricular hypertrophy.

Background. **The aim of this study was to describe trends in blood pressure (BP) control and in the prevalence of left ventricular hypertrophy (LVH) during 3 years of follow-up in a representative sample of treated hypertensive patients seen in our out-patient hypertension hospital clinic.**

Methods. **Four hundred and sixty-four hypertensive treated patients who took part in a clinical survey at our out-patient clinic during the year 1997 and who had been submitted to a routine follow-up visit 3 years later were included in the study. All patients were subjected to the following procedures: an accurate medical history, physical examination, electrocardiogram, clinical BP measurement. For the diagnosis of LVH we used two different ECG criteria: the Solokow-Lyon voltage and the gender-specific Cornell voltage.**

Results. **During the first survey, 15% of treated patients had a clinical BP < 130/85 mmHg, 25.1% ≥ 130/85 mmHg and < 140/90 mmHg, 33.6% ≥ 140/90 and < 150/95 mmHg, 26.3% ≥ 150/95 mmHg. The corresponding figures in the second survey were 19, 26.7, 33.2 and 21.1%, respectively. Overall, from the first to the second survey the prevalence of an effective BP control (< 140/90 mmHg) rose from 40.1 to 46.7% ($p < 0.01$). At baseline, 40 patients had ECG LVH (8.6%); at the second visit, LVH was found to have regressed in 19 of these patients. Among the 424 patients with a normal baseline electrocardiogram, 3 developed LVH during follow-up. Hence, the prevalence of LVH decreased from 8.6 to 5.1% ($p < 0.01$). In terms of treatment, the prevalence of combination therapy regimens increased from 68.6 to 79.7% ($p < 0.05$).**

Conclusions. **This study demonstrates that in hypertensive patients managed in a hypertension hospital clinic, BP control improved during the long-term follow-up and that this trend was associated with a significant regression in ECG LVH.**

(Ital Heart J 2002; 3 (9): 514-519)

Received July 22, 2002;
accepted August 20, 2002.

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Introduction

Arterial hypertension is a major cardiovascular and cerebrovascular risk factor; this condition is highly prevalent throughout the world involving about 20-25% of the general population[1,2]. As demonstrated in a number of intervention trials, the reduction in blood pressure (BP) in hypertensive patients is accompanied by a significantly lower incidence of cardiovascular complications and death[3,4]. In recent years, however, despite an increased awareness of the importance of aggressively controlling hypertension and despite the availability of several effective and well-tolerated antihypertensive drugs, only one third of treated patients achieve a full normalization of BP[5,6]. An inadequate reduction in BP is probably the main reason why uncontrolled patients have a greater prevalence of target organ damage, morbidity and mortality from coronary heart disease and stroke than well-controlled hypertensive and normotensive subjects[7,8].

All current guidelines for the management of hypertension, published at the end of the '90s, recommend the lowering of BP to values < 140/90 mmHg in the general hypertensive population and to achieve optimal or normal BP values in some specific subgroups such as young, diabetic or nephropatic patients[9,10]. During the last years scientific societies have propagated the recommendations of guidelines worldwide. This, in order to improve the management of hypertensive patients and BP control. The purpose of the present investigation was to compare the prevalence of BP control and left ventricular hypertrophy (LVH) in a cohort of treated hypertensive patients, regularly followed in our out-patient hospital clinic, at the 1997 visit and after 3 years of follow-up.

Methods

Four hundred and sixty-four patients with essential hypertension who took part in a clinical survey at the out-patient clinic of our hypertension center during the year 1997[11], and who had been visited 3 years later (between June 1st and November 15th 2000) were included in the study. Additional inclusion criteria were: 1) a regular follow-up at our hypertension clinic (at least three visits over 3 years), 2) no prolonged withdrawal of therapy during the 6 months preceding the study. In the initial survey, including 700 patients, a large fraction of them had been referred to our center by their general practitioners because of inadequate BP control or in order to exclude secondary forms of hypertension; on the basis of their BP at the time of the first visit, about 60% of the patients had grade II or III hypertension as defined by the WHO/ISH guidelines. In both surveys, after informed consent, all patients were subjected to the following procedures: 1) an accurate medical history with a specific questionnaire filled in, 2) physical examination, 3) standard 12-lead electrocardiogram, 4) clinical BP measurement, 5) blood and urine sampling for routine examinations. The BP was measured by a physician using an appropriately sized arm cuff and a mercury sphygmomanometer (the values at the first and fifth phases of the Koroktoff sounds were rounded to the nearest 2 mmHg and taken as the systolic and diastolic values) with the patient in the seated position for 5-10 min (8.00-12.00 a.m.). Three measurements were taken at 1 min intervals and the average used to define the clinical systolic and diastolic BP. In all patients standard 12-lead electrocardiogram was taken. Compliance to treatment was systematically evaluated during the visits by structured questions on the regularity of drug assumption. BP control was defined as optimal when the systolic and diastolic BP was < 130/85 mmHg and as satisfactory when the BP was between 130/85 and 139/89 mmHg. Borderline control was defined as BP values between 140/90 and 150/95 mmHg. The following criteria were used to assess the presence of other risk factors: marked hypercholesterolemia was defined as a total serum cholesterol level ≥ 6 mmol/l; obesity as a body mass index ≥ 30.0 kg/m^2; diabetes mellitus as a fasting plasma glucose level ≥ 7.0 mmol/l or current antidiabetic therapy. LVH was detected using two different criteria: a Solokow-Lyon voltage (the sum of the S wave amplitude in V_1 and of the R wave amplitude in V_5 or V_6) ≥ 35 mm and the gender-specific Cornell voltage (the sum of the S wave amplitude in V_3 and of the R wave amplitude in aVL) > 20 mm in women and > 28 mm in men. LVH was diagnosed when at least one of these two criteria was present[12].

Statistical analysis. Statistical analysis was performed using the SAS System version 6.12 (SAS Institute Inc., Cary, NC, USA). Data are expressed as mean ± SD or as percentages. Continuous, normally distributed variables in patient groups were compared using the Student's t test for independent samples. Analysis of categorical data was performed using the χ^2 test, or the Fisher's exact test as appropriate. Stepwise multiple regression analysis was used to assess which variables distinguished appropriately controlled patients from those with persistent inadequately controlled hypertension. A two-tailed p value < 0.05 was considered significant.

Results

Patient characteristics and drug used. Of the 464 hypertensive patients included in both surveys, 250 (53.9%) were men and 214 (46.1%) women (Table I). In the first survey, the average age was 58.6 ± 10.4 years and the mean clinical BP under treatment was 139.2 ± 14.8/85.5 ± 9.1 mmHg. With regard to the oth-

Table I. Characteristics of the patients in the two surveys (n = 464).

	First survey	Second survey	p
Clinical characteristics			
Age (years)	58.6 ± 10.4	61.3 ± 10.3	< 0.001
Systolic BP (mmHg)	139.2 ± 14.8	136.6 ± 14.1	< 0.01
Diastolic BP (mmHg)	85.5 ± 9.1	83.6 ± 8.1	< 0.01
Pulse pressure (mmHg)	53.76 ± 13.2	53.13 ± 12.2	NS
Heart rate (b/min)	72.5 ± 13.4	71.8 ± 12.7	NS
Weight (kg)	72.9 ± 13.1	73.1 ± 13.5	NS
BMI (kg/m^2)	26.26 ± 3.53	26.36 ± 3.88	NS
Concomitant cardiovascular risk factors (%)			
Hypercholesterolemia	32.8	26.3	< 0.001
Obesity	16.8	17.03	NS
Diabetes mellitus	6.5	6.9	NS
Smoking	13.1	12	NS
ECG LVH	8.6	5.1	< 0.01

Data are expressed as mean ± SD or as percentages. BMI = body mass index; BP = blood pressure; LVH = left ventricular hypertrophy.

er risk factors, 32.8% of the patients had hypercholesterolemia, 16.8% were obese, 13.1% were current smokers, 8.6% had ECG signs of LVH, 6.5% were diabetics. In the second survey, the mean clinical BP was 136.6 ± 14.1/83.6 ± 8.1 mmHg ($p < 0.001$ for systolic BP and $p < 0.01$ for diastolic BP). With regard to the treatment, 31.4% of the patients were on monotherapy, 38.3% on two drugs, 20.8% on three drugs, and 9.5% on four or more drugs in the first survey and 20.3, 41.6, 25.3 and 12.8% respectively in the second one. The antihypertensive agents used are reported in table II. On the whole, considering both monotherapy and combination therapy, ACE-inhibitors, diuretics, calcium-antagonists and beta-blockers were the drugs most frequently prescribed in both surveys, without any significant time-related changes among these four classes.

The compliance to pharmacological treatment was satisfactory: 87% of patients reported taking the prescribed drugs regularly in the first survey and 88% in the second one. Finally, the demographic and clinical characteristics of non-participants (336 patients) were similar to those of the 464 participants (mean age 59.1 years, mean BP 142/87 mmHg).

Table II. Antihypertensive medications.

	First survey (%)	Second survey (%)	p
Total			
ACE-inhibitors	53.9	50.2	NS
Diuretics	51.3	53.4	NS
Calcium-antagonists	46.5	48.3	NS
Beta-blockers	29.3	35.8	NS
Angiotensin II antagonists	10.8	19.5	< 0.05
Alpha-blockers	9	5.2	NS
$Alpha_2$ central agonists	8.6	8.2	NS
Monotherapy			
ACE-inhibitors	30.0	29.5	NS
Diuretics	7.2	3.3	NS
Calcium-antagonists	25.7	24.6	NS
Beta-blockers	25.7	26.3	NS
Angiotensin II antagonists	7.1	13.4	< 0.05
Alpha-blockers	2.9	1.3	NS
$Alpha_2$ central agonists	1.4	1.6	NS

Blood pressure control. In the initial survey, the clinical BP was < 130/85 mmHg in 70 patients, ≥ 130/85 and < 140/90 mmHg in 116, ≥ 140/90 and < 150/95 mmHg in 156, and ≥ 150/95 mmHg in 122, indicating that BP control was optimal in 15.0%, satisfactory in 25.1%, borderline in 33.6% and unsatisfactory in 26.3% of cases. The corresponding figures in the second survey were 19.0, 27.7, 33.2 and 21.1% respectively. Overall, the percentage of patients with optimal or satisfactory BP control (< 140/90 mmHg) rose from 40.1 to 46.7% ($p < 0.01$) (Fig. 1). Considering the systolic and diastolic BP levels independently, in both surveys the percentage of patients with a satisfactory diastolic BP control (< 90 mmHg) was higher than the percentage of individuals with adequate (< 140 mmHg) systolic BP levels (54 vs 40%, $p < 0.01$ in the first survey; 65 vs 53%, $p < 0.01$ in the second survey). In both surveys the patients with borderline or unsatisfactory BP control compared with those with optimal or satisfactory BP control were more frequently women than men (57 vs 43%, $p < 0.01$ in the first survey; 55 vs 45%, $p < 0.01$ in the second survey) and were older (mean age 60.3 ± 10.1 vs 56.4 ± 10.3 years, $p < 0.01$; 63.6 ± 10.6 vs 59.8 ± 9.8 years, $p < 0.01$ respectively). Patients with borderline or unsatisfactory BP control did not differ from those with optimal or satisfactory BP levels with regard to hypercholesterolemia, obesity and cigarette smoking.

In terms of treatment, the prevalence of BP values < 140/90 mmHg was similar in patients under monotherapy or taking two or three drugs in combination in the first (42, 43 and 42%) as well as in the second survey (47, 49 and 48%); this prevalence was significantly lower in the second survey for patients treated with four or more drugs (29 and 32% respectively, $p < 0.01$).

Left ventricular hypertrophy. At baseline, 40 of the 464 patients were found to have ECG LVH with an

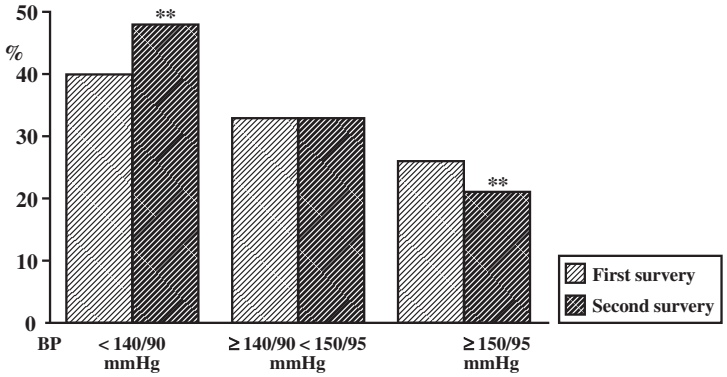

Figure 1. *Prevalence rates of satisfactory (< 140/90 mmHg), borderline (≥ 140/90 and < 150/95 mmHg) and unsatisfactory blood pressure (BP) control (≥ 150/95 mmHg) observed in the first and in the second survey. ** = p < 0.01.*

overall prevalence of 8.6%. Although the majority of cases of LVH occurred among patients with inadequate or unsatisfactory BP control, 32.5% of cases were diagnosed in patients with optimal or satisfactory BP control, according to the clinical BP criteria (Fig. 2). Of these patients, 19 out of 40 (47.5%) showed regression of the ECG LVH at the second survey. Among the 424 patients without LVH at the first survey, 3 were found to have developed LVH at the second one. Overall, the prevalence of ECG LVH decreased from 8.6 to 5.1% ($p < 0.01$) from one survey to the other. A weak, but significant correlation was found between both the Cornell and Solokow voltages and the systolic BP ($r = 0.22$ and $r = 0.16$ respectively, $p < 0.001$ in the first survey; 0.20 and 0.15 respectively, $p < 0.001$ in the second survey) but not with diastolic BP. A non-significant correlation was observed between the mean reduction in systolic BP and ECG voltages (systolic BP/ECG voltages: $r = 0.12$, $p = 0.06$, for the Cornell, and $r = 0.11$, $p = 0.07$ for the Solokow criteria).

Discussion

Our results show that 1) the prevalence of effective BP control in treated hypertensive patients attending a hypertension hospital clinic significantly increased during a period of 3 years and this trend was associated with a marked reduction in ECG LVH; 2) systolic BP control appeared persistently more difficult to achieve than diastolic BP control; 3) the rate of optimal BP levels under treatment still remained very low. The most important finding of this study was the increase in the BP control rate, accompanied by a reduction in the overall prevalence of ECG LVH in selected hypertensive patients referred to a tertiary center clinic; in fact, during this period the fraction of patients with BP values < 140/90 mmHg rose from 40.1 to 46.7% whereas that of patients with ECG LVH decreased from 8.5 to 5.1%.

Several surveys have recently investigated the prevalence of a satisfactory BP control among hypertensive patients in the general population and in general practice[13,14]. In the United States < 30% of hypertensive individuals have BP values < 140/90 mmHg, while in the UK, a study revealed that only 6% of hypertensive patients achieved this target BP level[15]. In a recent survey, Hansson et al.[16] reported, on the basis of the best available data, that one third of the adult population of five European countries (France, Germany, Italy, Sweden, UK) had BP levels above the ideal target BP. The information on BP control in treated hypertensive patients attending a hospital hypertension clinic is very scarce. The only recent data available are those of Chatellier et al.[17] in Paris and our own data[11] regarding a population studied in Milan, indicating a level of control in these selected patients significantly higher than in the general population of hypertensives. It should be pointed out that it is very difficult to compare BP control in the general population, in hospital clinics and in clinical trials. Indeed, whereas on the one hand treatment may be more intensive and successful in a specialized clinic, on the other it is more likely that more severe and complicated, and therefore more resistant hypertensive patients attend hospital clinics. With these limitations in mind, it may be worth noting that the prevalence of patients with a clinical BP < 140/90 mmHg was almost twice as large in specialized clinics as in the population surveys reported by Mancia et al.[6] and by Burt et al.[13]. It should also be mentioned that, in the HOT (Hypertension Optimal Treatment) trial, 91.5% of the patients could achieve a clinical diastolic BP of at least 90 mmHg[18]. Similar results have been obtained in the LIFE (Losartan Intervention For Endpoint reduction in hypertension) study in which a diastolic BP ≤ 90 mmHg was achieved in 89% of patients[19]. However, even in this study, BP levels < 140/90 mmHg were reached in no more than 45% of patients.

Following the publication of the 1999 WHO/ISH guidelines, the results of our study add new information about the changes in BP control. This, since they show that in a selected hypertensive population followed up in an out-patient specialized clinic, the effective BP control rate was significantly improved as the

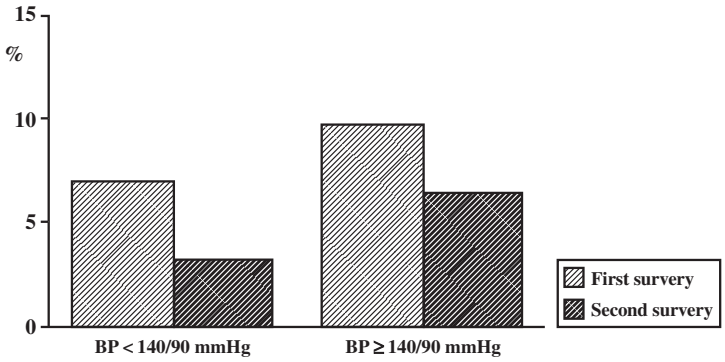

Figure 2. *Prevalence rates of ECG left ventricular hypertrophy according to blood pressure (BP) control (< 140/90 and ≥ 140/90 mmHg) in the first and in the second survey.*

mean reductions in systolic and diastolic values were 2.6 and 1.9 mmHg respectively and the percentage of controlled patients increased by 6.6%. Another notable finding of the study was the significant decrease in the number of patients with ECG LVH signs. The clinical implications of this latter result are particularly relevant in terms of cardiovascular prognosis. It has been recently demonstrated that the prevention or regression of ECG LVH by the ACE-inhibitor ramipril in patients at a high cardiovascular risk was associated with a reduced risk of adverse cardiovascular outcomes independently of the BP status or of the concomitance of coronary artery disease[20]. Despite this favorable clinical trend, it should however be pointed out that more than one half of our patients did not achieve the recommended BP target. Although a full discussion of the multiple causes of the limited control of BP is beyond the object of this paper[21], some of the findings of this study shed some light on the factors that are most likely to be responsible for the unsatisfactory BP response to treatment. Indeed, in this representative sample of patients attending our clinic, those with an unsatisfactory BP control were older, more frequently women and on a more complex antihypertensive therapy. Although it may be assumed that patients prescribed four or more drugs are less compliant than those prescribed simpler treatment regimens, this was not apparent from the patients' replies to specific questions; thus, it is more likely that the insufficient control in patients who were submitted to complex therapeutic regimens indicates a more severe form of hypertension. Some other points deserve comment. First, could it be that as a consequence of the "white coat" phenomenon, office BP evaluation results in a significant underestimation of the true BP control in such a group of treated patients? We cannot exclude this possibility as systematic data regarding the home and ambulatory pressures were not available for all patients. However, in a large subgroup of patients, who regularly underwent home BP monitoring, the prevalence of self-measured BP values < 135/85 mmHg was somewhat greater (56%) than that observed in the clinic. To date, only a limited number of studies have been designed in such a way as to specifically investigate this issue in treated hypertensive patients, and the results obtained seem to be partially discordant[22]. Mancia et al.[6] showed that the poor BP control among individuals receiving antihypertensive treatment was not substantially influenced by the white coat phenomenon. On the contrary, Meja et al.[23], evaluating the role of factors known to induce therapy-resistant hypertension in patients referred to a specialized center, found a pseudoresistance or isolated office resistance in a consistent fraction of subjects. Secondly, the association between an improvement in BP control and the regression in ECG LVH represents an important finding of this survey, although this observation certainly has some limits because we used two simple traditional criteria rather than the more sensitive and accurate Perugia criterion[24] or the product of the QRS duration and the Cornell voltage[25]. On the other hand, it should be remarked that a Solokow-Lyon voltage > 38 mm was accepted as an alternative diagnostic criterion in the LIFE study. Thirdly, this survey indicates an improvement in BP control in selected hypertensive patients during a period of 3 years; among many potential factors involved in this trend, the most important probably was a more intensive therapeutic approach aimed at achieving the recommended BP targets as defined in the WHO/ISH guidelines. In fact, the fraction of patients on monotherapy fell significantly from one survey to the other, without substantial changes in the use of the first line classes of drugs, angiotensin II receptor antagonists being the only exception. The increase in the use of angiotensin II antagonists, however, does not seem to have had, in our study, a clear impact on BP control trends. This, in view of the fact that the prevalence of a satisfactory BP control in patients treated with these new drugs was not greater than in the other patients. Another important factor was a greater awareness, by our patients, of the problems related to hypertension as a consequence of educational meetings and of the distribution of printed material regularly carried out in the last years at our out-patient center[26]. Indeed, despite a tendency towards more complex treatment regimens, the patients' adherence to the antihypertensive treatment was virtually identical to that seen in the previous survey. This evidence seems to reflect a satisfactory physician-patient relation, aimed at obtaining a positive therapeutic result, which is a corner-stone of every successful long-term treatment.

In conclusion, the results of this survey indicate a parallel positive trend in BP control and in the regression of LVH in a representative sample of selected hypertensive patients followed-up in an out-patient hospital clinic during long-term antihypertensive treatment, largely based on multiple combination therapy. Considering that BP normalization and target organ damage regression have been demonstrated to play a pivotal role in preventing cardiovascular events, further efforts should be performed in all hypertensive patients in order to achieve a more effective BP control than the one observed in this survey.

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