Progression of White Coat Hypertension to Sustained Hypertension After 10 Years

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ABSTRACT

Background
The long-term outcome of white coat hypertension (WCH) is still controversial despite the extensive information currently available.

Objective
To evaluate the cumulative incidence of sustained hypertension (SH) among patients with white coat hypertension compared to normotensive patients after 10 years of inclusion in the study.

Methods
Two hundred and fifty patients of both genders were prospectively included in the study with the following office blood pressure (OBP) and 24-hour ambulatory blood pressure monitoring (ABPM) values :

	WCH	Hypertension	Normal BP
OBP (mm Hg)	≥ 140 and/or 90	≥ 140 and/or 90	≤ 140 and/or 90
ABPM (mm Hg)	≤ 135 and 85	≥ 135 and 85	≤ 135 and 85

The patients were divided into two groups: 129 patients with WCH and 121 normotensive patients, and were evaluated after 10 years of follow-up.
Glucose blood level, lipid profile and left ventricular mass index (LVMI) were measured.

Results
Age, gender, smoking habits and glucose blood level were similar at baseline among normotensive patients and patients with white coat hypertension.
However, body mass index, total cholesterol levels, lipid levels and LVMI were significantly greater in white-coat hypertensive patients. Sustained hypertension was developed by 48 patients with WCH and 21 normotensive patients. We found an independent association between WCH and SH at 10 years of follow-up [OR: 2.5 (95% CI 1.2-4.2)].

Conclusion
Progression to sustained hypertension was greater in patients with white coat hypertension compared to normotensive patients.

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Key words > White coat hypertension – Prognosis

Abbreviations >

AHR	Heart rate	**ABPM**	Ambulatory blood pressure monitoring
OHR	Office heart rate	**BP**	Blood pressure
WCH	White coat hypertension	**OBP**	Office blood pressure
SH	Sustained hypertension	**DT BP ABPM**	Daytime blood pressure on ABPM
HT	Hypertension	**DOBP**	Diastolic office blood pressure
BMI	Body mass index	**SOBP**	Systolic office blood pressure
LVMI	Left ventricular mass index		

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White coat hypertension (WCH) is defined as hypertension (HT) in the clinical setting with normal values of home blood pressure (BP) or normal 24-hour ambulatory blood pressure monitoring (ABPM) measurements. (1, 2) The prevalence of WCH varies between 20% and 45% depending on the population studied, the value of office HT, gender and age.

One of the main causes of the real prevalence of WCH is threshold BP used to define HT in ABPM. (4) However, the cutoff value may underestimate or overestimate the diagnosis of WCH.

In general, WCH is considered a benign condition in its outcome and treatment (5). One of the criteria used to characterize this outcome is the greater linear relationship of daytime ambulatory blood pressure compared to office blood pressure (OBP) with respect to target organ damage. However, this relationship should not be the only influence of clinical WCH characterization. This concept has been supported by several studies demonstrating that the outcome of WCH is not as benign as it was thought. (6-8)

Despite ample bibliographic information on the characterization of WCH, it is still unclear if its outcome and prognosis is similar to that of normotension.

The goal of the present study is to evaluate the cumulative incidence of sustained hypertension (SH) among patients with white coat hypertension compared to normotensive patients after 10 years of follow-up in both groups.

METHODS

We conducted a prospective longitudinal study with control group which was approved by the Ethics Committee of the Hospital Santojanni.

The patients were evaluated at baseline and after 10 years. Since de beginning of 1999, patients attending the outpatient clinic at the Hospital Santojanni were invited to participate in the study. The recruitment ended in 2000.

A total of 250 men and women between 45 to 55 years were selected and divided into two groups: 129 with WCH and 121 with normotension. The diagnosis was based on systolic office blood pressure (SOBP) and/or diastolic office blood pressure measurements plus daytime systolic and/or diastolic blood pressures on ABPM.

In 2010, 230 patients of the 250 original participants were examined again, as it was impossible to contact 9 patients with WCH and 11 with normal BP.

The following procedures were performed at the first medical visit and after 10 years of follow-up:

Blood pressure was measured on three different visits using a Baum Manometer mercury sphygmomanometer, following the Argentine Council of Hypertension (9) and the American Heart Association guidelines. (10)

Patients' weight and height were recorded. A 12-lead electrocardiogram was taken to all the patients in order to exclude those with left ventricular hypertrophy, complete left bundle branch block or arrhythmias. These anomalies were neither present during the second exam. At the first visit, the patients were not receiving any medication, including antihypertensive agents.

Patients with diabetes, metabolic syndrome, history of kidney or cardiovascular disease or any systemic condition were excluded from the study.

A smoker was defined as someone smoking at least one cigarette daily during the last month of the visit.

Patients underwent lipid profile determination and ABPM one week after OBP was measured.

Ambulatory blood pressure was measured using the oscillometric Spacelabs 90207 monitor programmed to take readings every 15 minutes during daytime and every 30 minutes during night-time, adjusted according to the sleeping habits of each patient.

Statistical Analysis

Quantitative variables are presented as mean and standard deviation and qualitative variables as percentage. A t test was used for the analysis and comparison of quantitative variables with normal distribution, according to the the Kolmogorov–Smirnov test and homoscedasticity. The non-parametric Kruskall-Wallis test was used when the distribution was not normal. Qualitative variables were analyzed using the chi square test and a p value < 0.05 was considered statistically significant. The percentage of patients with normotension and with white coat hypertension at the beginning of the study who developed SH after 10 years of follow-up was calculated.

A stepwise multivariate analysis was performed to evaluate association among variables. The model used SH after 10 years of follow-up as the dependent variable and OBP, daytime BP on ABPM (DT BP ABPM), body mass index (BMI), smoking habits, hypercholesterolemia, hyperglycemia, LVMI, heart rate (HR), and WCH at baseline as independent variables. A p value < 0.05 was used to determine a significant association. A logistic regression analysis was used to estimate the odds ratio for developing SH including the same variables described in the former model, adjusted for age, BMI and gender.

Statistical analysis was performed using SPSS 17.0 statistical package for Windows (SPSS Inc., Chicago, III, USA). A two-tailed p value < 0.05 was considered statistically significant.

RESULTS

Characteristics of the population

Of the original 250 patients, 20 patients were lost to follow-up in 2010. Sustained hypertension was developed by 48 patients with WCH and by 21 normotensive patients during follow-up (Figure 1).

Age, gender, BP on ABPM, office heart rate (OHR), smoking habits and glucose blood levels were similar in both normotensive and WCH patients at baseline examination (Table 1) and after 10 years evolution (Table 2). However, BMI was greater and triglycerides and total cholesterol levels were higher in patients with WCH compared to those with normotension.

In 2010, patients with SH presented mild to moderate HT, 28 of which were receiving antihypertensive agents (9 patients: enalapril 15 mg, 3 patients: enalapril 10 mg, 4 patients: hydrochlorothiazide 25 mg, 10 patients: enalapril 10 mg + hydrochlorothiazide 25 mg, 2 patients enalapril 20 mg). Treatment was discontinued seven days before undergoing ABPM.

The average time between patient inclusion in the study and the new diagnosis of SH was over five years

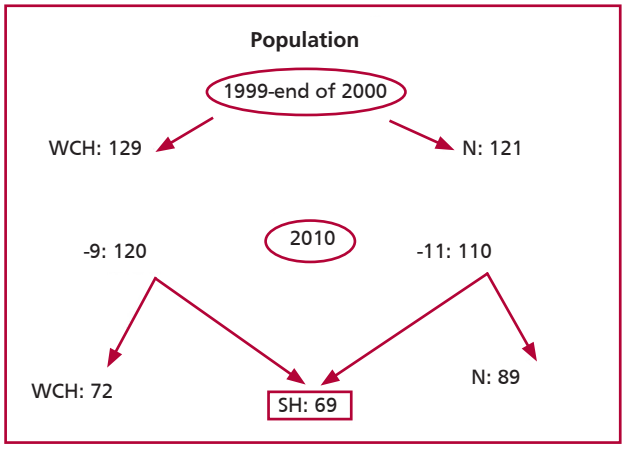

Fig. 1. Progression to sustained hypertension in the population studied. WCH: White coat hypertensive patients. N: Normotension SF: Sustained hypertension. -: Minus. The graph represents the population according to the characteristics of office and ABPM blood pressure from the first medical visit to the 10-year follow-up visit.

Table 1. Characteristics of the population: basal variables analyzed in the first medical visit.

	WCH (n = 120)	N (n = 110)	P
Gender (w/m)	56/73	55/66	ns
	43/57%	45/55%	
Age, years	46.4 ± 3	45.9 ± 3.3	ns
BMI (kg/m^2)	27 ± 3	26 ± 3.2	0.02
SOBP, mm Hg	148 ± 12	118 ± 8	0.001*
DOBP, mm Hg	89 ± 6	78 ± 5	0.001*
DTSBP ABPM,mm Hg	117 ± 7.8	115 ± 6.5	ns
DTDBP ABPM, mm Hg	73.6 ± 4	72.4 ± 4.3	ns
NT SBP ABPM, mm Hg	108 ± 8.1	107 ± 7.2	ns
NT DBP ABPM, mm Hg	66 ± 5	65.8 ± 4.7	ns
OHR, bpm	68 ± 10	66 ± 10	ns
Glucose blood level, mg/dl	92.0 ± 11	93.2 ± 17	ns
TC, mg/dl	233.2 ± 41	210.8 ± 32	0.001
HDL, mg/dl	46.3 ± 11	50 ± 12	ns
TG, mg/dl	127 ± 54	116 ± 56	0.07
Smoking habits	14 w / 10 m	17 w / 9 m	ns
	20%	23.6%	
LVMI, g/m2	112 ± 26	80 ± 30	0.03

WCH: White coat hypertension. N: Normotension. w/m: Women/men. BMI: Body mass index. SOBP: Systolic office blood pressure. DOBP: Diastolic office blood pressure. ABPM: Ambulatory blood pressure monitoring. DT SBP ABPM: Daytime systolic blood pressure on ABPM. DT DBP ABPM: Daytime diastolic blood pressure on ABPM. NT SPB ABPM: Night-time systolic blood pressure on ABPM. NT DPB ABPM: Night-time diastolic blood pressure on ABPM. OHR: Office heart rate. bpm: Beats per minute. TC: Total cholesterol. HDL: High density lipoprotein. TG: Triglycerides. LVMI: Left ventricular mass index. Values are expressed as mean ± standard deviation. Values were analysed using a t test or the Kruskal-Wallis test with a significance level < 0.05. ns: Non significant.

Table 2. Characteristics of population variables analyzed 10 years after the first medical visit

	WCH (n = 120)	N (n = 110)	P
Gender (w/m)	55/65	52/58	ns
	46/54%	47/53%	
Age, years	56.6 ± 3	54.8 ± 2.8	ns
BMI (kg/m2)	26 ± 3	25.4 ± 3	0.05
SOBP, mm Hg	149 ± 13	121 ± 6.8	0.001
DOBP, mm Hg	93 ± 5.4	79 ± 4.6	0.001
OHR, bpm	69 ± 9	66.8 ± 8.6	ns
DT SBP ABPM, mm Hg	130 ± 7	121 ± 5	0.01
DTDBP ABPM, mm Hg	79.3 ± 4	76 ± 5	0.01
Glucose blood level, mg/dl	94 ± 11	88 ± 11	0.001
TC, mg/dl	229 ± 41	211.8 ± 42	0.02
HDL, mg/dl	45.7 ± 11	48 ± 11	ns
TG, mg/dl	127 ± 54	102 ± 49	0.01
Smoking habits	9 w / 14 m	10 w / 12 m	ns
	19.1%	20%	
LVMI, g/m2	115.4 ± 25	90 ± 23	< 0.01

Values are expressed as mean ± standard deviation. WCH: White coat hypertension. SH: Sustained hypertension N: Normotension. ns: Non significant.. BMI: Body mass index. SOBP: Systolic office blood pressure. DOBP: Diastolic office blood pressure. LVMI: Left ventricular mass index. TC: Total cholesterol. HDL: High density lipoprotein. TG: Triglycerides. w/m: Women/men. OHR: Office heart rate. bpm: Beats per minute. ABPM: Ambulatory blood pressure monitoring. DT SBP ABPM: Daytime systolic blood pressure on ABPM.

in all the 69 patients. The information was obtained by anamnesis.

There were no data on the physical examination during the 10-year follow-up.

Anamnesis detected the presence of type 2 diabetes (treated with metformin) in 3 patients with SH, 1 with WCH and 1 with normotension. None of the patients had cardiovascular events as myocardial infarction, heart failure or kidney disease during that period.

The analysis of association among variables identified SOBP [OR: 2.16 (95% CI 1.05-5.4)] and WCH [OR: 2.5 (95% CI 1.7-3.5)] as predictors of SH (Table 3). The other variables, including LVMI (B: 0.612; chi square: 1.8; p = 0.1) did not present a significant association with the development of SH (p > 0.05)

DISCUSSION

There is no agreement about morbidity and mortality in WCH.

In the different studies conducted on this condition some authors found a greater risk of events in this population; (11, 12); however, the predominant concept is that the prognosis of WCH does not differ from that of normotension. (13, 14) Based on our previous results (8) and on those published by other authors, (15) we assume that the clinical situation of

Table 3. Determinants of sustained hypertension by logistic regression analysis

Independent variables	B	Standard error	Chi square test	P
SOBP, mm Hg	0.8415	0.4	3.38	0.03
Presence of WCH	1.4532	0.6	4.902	0.02

SOBP: Systolic office blood pressure. WCH: White coat hypertension B: Regression coefficient.

WCH is intermediate between normotension and SH.

The results of the present study show that 40% (95% CI 31-48) of patients with WCH developed SH compared with 19% (95% CI 18.7-19.27) of those with normotension after 10 years of follow-up.

In general, the factors determining the clinical outcome of WCH are not completely known, generating controversy. For example, daytime ambulatory blood pressure is tightly related with target organ damage as left ventricular hypertrophy, heart failure and kidney failure. In patients with WCH, daytime ambulatory blood pressure is normal and not significantly greater than that of normotensive patients.

The correlation between office blood pressure, another determinant in the outcome of WCH, and target organ damage is lower than that of ambulatory blood pressure. However, a linear relationship between OBP and cardiovascular events has been demonstrated, even in normotensive ranges. This finding agrees with the results of the present study, as SOBP was a predictor of the progression to SH in the studied population.

In the present study, subjects with WCH had higher lipid values compared to normotensive patients since this population is more predisposed to atherogenesis and metabolic syndrome (16, 17). However, the multivariate analysis showed that this was not a major determinant of greater risk to develop SH.

The characterization of WCH as "low risk" is mainly due to the level of daytime BP established as normal by ABPM. This means that the higher the value of chosen normal daytime BP, the greater the likelihood of developing organ damage. On this issue, Staessen et al. (18) defined WCH when daytime BP on ABPM was ≤ 146/91 mm Hg, and Pickering et al. (1) with levels ≤ 134/90 mm Hg.

We considered normal BP when the value of daytime BP on ABPM was ≤ 135/85 mm Hg so as not to overestimate target organ damage in patients with WCH. In this way, we ensured that patients with SH were not included.

Left ventricular mass index, a well-known predictor of target organ damage (19, 20), was estimated in the population and results were similar to those reported by similar studies. (21, 22) In subjects with WCH, LVMI was greater compared to normotensive patients in both baseline and at 10 year determinations, suggesting greater risk in this population. However, this variable was not associated with the development of HT, probably due to the small sample size.

In this study, WCH did not behave as a harmless condition, showing a cardiovascular risk that was different from that of normotension. These results suggest the need for a tight follow-up of these patients in order to achieve a strict control of risk factors and progression to SH.

CONCLUSIONS

In patients with WCH, progression to SH was greater compared with normotensive patients after 10 years of follow-up.

RESUMEN

Hipertensión de guardapolvo blanco: evolución a hipertensión sostenida luego de 10 años de seguimiento

Introducción

No obstante la amplia información en la bibliografía sobre la caracterización de la hipertensión de guardapolvo blanco (HGB), su evolución alejada es hasta el presente tema de controversia.

Objetivo

Evaluar la incidencia acumulada de hipertensión sostenida (HS) en hipertensos de guardapolvo blanco respecto de normotensos a los 10 años de su inclusión en el estudio.

Material y Métodos

Se incorporaron en forma prospectiva 250 pacientes de ambos sexos, según los siguientes valores de presión de consultorio (PC) y de monitoreo ambulatorio de la presión arterial (MAPA) de 24 horas:

	HGB	HS	Normotensión
PC (mm Hg)	≥140 y/o 90	≥140 y/o 90	≤140 y/o 90
MAPA (mm Hg)	≤135 y 85	≥135 y 85	≤135 y 85

Se conformaron dos grupos: 129 hipertensos de guardapolvo blanco y 121 normotensos, los cuales fueron evaluados nuevamente a los 10 años de seguimiento.
Se midieron la glucemia, el perfil lipídico y el índice de masa ventricular izquierda (IMVI).

Resultados

Las variables edad, sexo, tabaquismo y glucemia de normotensos e hipertensos de guardapolvo blanco fueron similares en el examen basal.
Los hipertensos de guardapolvo blanco, por el contrario, presentaron valores significativamente superiores en IMC, colesterol total, hipertrigliceridemia e IMVI. Cuarenta y ocho hipertensos de guardapolvo blanco y 21 normotensos originales evolucionaron a HS. La HGB se asoció en forma independiente con HS a los 10 años de seguimiento [OR: 2,5 (IC 95% 1,2-4,2)].

Conclusión

La evolución a hipertensión sostenida fue mayor en los hipertensos de guardapolvo blanco que en los normotensos.

Palabras clave > Hipertensión de guardapolvo blanco - Pronóstico

REFERENCES

1. Pickering TG, James GD, Boddie C, Harshfield G, Blank S, Laragh J. How common is white coat hypertension? JAMA 1988;259:225-8.
2. Drayer JI, Weber MA, Nakamura DK. Automated ambulatory blood pressure monitoring: A study in age-matched normotensive and hypertensive men. Am Heart J 1985;109:1334-8.

3. 2007 Guidelines for the Management of Arterial Hypertension; The Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). J Hypertens 2007;25:1105-87.
4. Perloff D, Grim C, Flack J, Frohlich E, Hill M, McDonald M, et al. The prognostic value of ambulatory blood pressures. JAMA 1983;249:2792-8.
5. Pierdomenico SD, Cuccurullo F. Prognostic value of white-coat and masked hypertension diagnosed by ambulatory monitoring in initially untreated subjects: an updated meta-analysis. Am J Hypertens 2010;24:52-8.
6. Kario K, Shimada K, Schwartz JE, Matsuo T, Hoshide S, Pickering TG. Silent and clinically overt stroke in older Japanese subjects with white-coat and sustained hypertension. J Am Coll Cardiol 2001;38:238-45.
7. Ohkubo T, Kikuya M, Metoki H, Asayama K, Obara T, Hashimoto J, et al. Prognosis of "masked" hypertension and "white-coat" hypertension detected by 24-h ambulatory blood pressure monitoring 10-year follow-up from the Ohasama study. J Am Coll Cardiol 2005;46:508-15.
8. Majul C, Páez O, De María M, Cragnolino R, López A, Gorosito A y col. Hipertensión por guardapolvo blanco: ¿es una entidad intermedia entre normotensos e hipertensos sostenidos? Rev Argent Cardiol 2001;69:260-6.
9. Consenso de Hipertensión Arterial. Consejo Argentino de Hipertensión Arterial "Dr. Eduardo Braun Menéndez". Rev Argent Cardiol 2007;75(Supl 3).
10. Perloff D, Grim C, Flack J, Frohlich ED, Hill M, McDonald M. Human blood pressure determination by sphygmomanometry. Circulation 1993;88:2460-70.
11. Mancia G, Bombelli M, Facchetti R, Madotto F, Quarti-Trevano F, Polo Friz H, et al. Long-term risk of sustained hypertension in white-coat or masked hypertension. Hypertension 2009;54:226-32.
12. Gustavsen PH, Høegholm A, Bang LE. Kristensen KS. White coat hypertension is a cardiovascular risk factor: a 10-year follow-up study. J Hum Hypertens 2003;17:811-7.
13. Fagard RH, Cornelissen VA. Incidence of cardiovascular events in white-coat, masked and sustained hypertension versus true normotension: a meta-analysis. J Hypertens 2007;25:2193-8.
14. Pierdomenico SD, Lapenna D, Di Mascio R, Cuccurullo F. Short- and long-term risk of cardiovascular events in white coat hypertension. J Hum Hypertens 2008;22:408-14.
15. Palatini P, Mormino P, Santonastaso M, Mos L, Dal Follo M, Zanata G, et al. Target-organ damage in stage I hypertensive subjects with white coat and sustained hypertension. Results from the HARVEST Study. Hypertension 1998;31:57-63.
16. Mulè G, Nardi E, Cottone S, Cusimano P, Incalcaterra F, Palermo A, et al. Metabolic syndrome in subjects with white-coat hypertension: Impact on left ventricular structure and function. J Hum Hypertens 2007;21:854-60.
17. Björklund K, Lind L, Vessby B, Andrén B, Lithell H. Different metabolic predictors of white-coat and sustained hypertension over a 20-year follow-up period: a population-based study of elderly men. Circulation 2002;106:63-8.
18. Staessen JA, Fagard RH, Lijnen PJ, Thijs L, Van Hoof R, Amery A. Mean and range of the ambulatory pressure in normotensive subjects from a meta-analysis of 23 studies. Am J Cardiol 1991;67:723-7.
19. Koren MJ, Savage DD, Casale PN, Laragh JH, Devereux RB. Changes in left ventricular mass predict risk in essential hypertension. Circulation 1990;82:29-32.
20. De Simone G, Devereux RB, Koren MJ, Mensah GA, Casale PN, Laragh JH. Midwall left ventricular mechanics. An independent predictor of cardiovascular risk in arterial hypertension. Circulation 1996;93:259-65.
21. Verdecchia P, Carini G, Circo A, Dovellini E, Giovannini E, Lombardo M, et al. The MAVI Study Group. Left ventricular mass and cardiovascular morbidity in essential hypertension: the MAVI study. J Am Coll Cardiol 2001;38:1829-35.
22. Sega R, Trocino G, Lanzarotti A, Carugo S, Cesana G, Schiavina R, et al. Alterations of cardiac structure in patients with isolated office, ambulatory, or home hypertension: data from the general population (Pressione Arteriose Monitorate E Loro Associazioni [PAMELA] Study). Circulation 2001;104:1385-92.

Disclosure

None declared.