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Original Article

Functional and Structural Heart Conditions Associated With White-Coat Hypertension in Comparison With True Hypertension and Normal Blood Pressure States

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ABSTRACT

Background: This study attempted to evaluate functional and structural cardiac states using echocardiography in patients with white-coat hypertension in comparison with true hypertension and normotensive conditions.

Methods: The study population consisted of 72 individuals, aged 25 to 75 years. The subjects were assigned to 4 groups: white-coat hypertensives (n=20), controlled true hypertensives (n=20), uncontrolled true hypertensives (n=12), and a normotensive group (n=20). Whilst the 4 subgroups in the study exhibited a similar gender distribution, the normotensive subjects were significantly younger; however, there was no discrepancy in the mean age between the white-coat hypertensive group and the other hypertensive subgroups. Univariate comparisons between the functional and structural cardiac parameters of the white-coat hypertensives and the other study groups revealed low deceleration time and E'-wave velocity and high E-wave velocity and left ventricular internal dimension indices compared with the other 2 hypertensive groups.

Results: After adjustment for sex and age, the white-coat hypertensive group revealed differing results in 2 indices of E' wave velocity and interventricular septal thickness (IVST) when compared with the other three. A number of features were identified as the hallmarks of white-coat hypertensives: specific functional and structural cardiac changes such as low IVST in comparison with the uncontrolled hypertensives; presence of diastolic dysfunction, which was not found in the normotensives; and greater cardiac mass than that in the normotensives, less than that in the uncontrolled hypertensives, but closer to that in the controlled hypertensives.

Conclusions: Although the prognosis for patients with white-coat hypertension is not as grave as that for those with true hypertension, it is considerably worse than the prognosis among the normal population. ***(Iranian heart Journal 2018; 19(2): 50-56)***

KEYWORDS: Function, Structure, Heart, White-coat hypertension

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The term "white-coat hypertension" is defined as the elevation of office blood pressure with normal ambulatory blood pressure which might need to be controlled by antihypertensive treatment. [1] This concept was primarily applied by Pickering in 1988 for subjects who were not receiving antihypertensive medications. [2] The exact prevalence of this phenomenon has not been determined, but the usual range in large population-based studies is estimated to be between 18% and 33% across the general hypertensive patient population—with a higher rate among those with persistent hypertension. [3] Nowadays, controversy persists as to whether the nature of white-coat hypertension is a real hypertensive state needing antihypertensive medications or whether it is an unreal state not in need of treatment. In fact, variability of blood pressure in an office or clinic is a challenge for clinicians to manage appropriately. [4] In this context, reduced risk for myocardial infarction, stroke, and heart failure with pharmacotherapy in the affected subjects has recently been suggested. [5] On the other hand, the measurement of blood pressure can not only be affected by technical and observer biases but can also, potentially, be influenced by differing states such as general clinics and emergency wards. [6]

Differences in clinical conditions and outcomes between true and white-coat hypertensives have previously been investigated. Some imaging studies on the carotid artery have shown similar intima-media thickness and the cross-sectional area of this artery in patients with true hypertension and those with white-coat hypertension and that these measurements are higher than those in individuals with a normal blood pressure status. Further, an increased left ventricular mass index has been found in the white-coat hypertension status. [7] A higher serum homocysteine level and a higher left ventricular mass index are 2 major cardiovascular risk parameters which are significantly greater in both true and white-coat hypertension groups than in individuals with a normal hypertension state. [8-9] However, the prognostic value of white-coat hypertension re mains to be debated. Although some recent studies have demonstrated a high risk of cardiovascular mortality and morbidity even after adjustment for potential confounders in the white-coat hypertension group and also sustained hypertensive subjects compared with normotensive subjects, [10] there are only a few published studies which compare structural and functional cardiac conditions between patients with white-coat hypertension and true hypertension. Accordingly, in the present study, we sought to evaluate functional and structural cardiac states using echocardiography in patients with white-coat hypertension and compare the findings with those in patients with true hypertension.

METHODS

Study Population

The study population consisted of 72 individuals, aged 25 to 75 years, who were consecutively referred to the Cardiology Clinic at Shariati Hospital, Isfahan in 2013. Those with any clinical evidence of secondary causes of hypertension, pregnancy, valvular heart disease, identified atrial fibrillation, or working at night shifts were not included in the study. All the participants gave their informed consent from the outset of the study, which was approved by the Review Committee of Islamic Azad University, Najafabad Branch.

Blood Pressure Assessment

Blood pressure was measured using a mercury sphygmomanometer whilst the subjects were in a seated position with their arm placed comfortably at heart level. Blood pressure was measured by the same practitioner twice: once in the outpatient clinic and again in the echocardiography department. Ambulatory blood pressure monitoring was performed for 24 hours using a Spacelab Ambulatory blood pressure monitor. All the patients were evaluated on a working day, and they were instructed to carry out their usual daily activities. The subjects were considered normotensive if they had a blood pressure (BP) less than 140/90 mm Hg and a 24-hour ambulatory BP less than 135/85 mm Hg. White-coat hypertension was defined as office readings of a systolic blood pressure (SBP) of at least 140 mm Hg or a diastolic blood pressure (DBP) of at least 90 mm Hg and average ambulatory BP of less than 135/85 mm Hg (Franklin et al, 2013). In this regard, true hypertension was defined as a clinic SBP of equal to or greater than 140 mm Hg or a clinic DBP of at least 90 mm Hg and an average ambulatory SBP of equal to or greater than 135 mm Hg or an average ambulatory DBP of at least 85 mmHg, or patients undertreated with any antihypertensive treatment without any evidence of secondary hypertension. According to these definitive criteria, the subjects were assigned to the white-coat hypertension group (n=20), controlled true hypertension group (n=20), uncontrolled true hypertension group (n=12), and normotensive group (n=20).

Echocardiography Assessment

All the participants were evaluated via 2D echocardiography for functional and structural heart assessment by an expert fellow of echocardiography. In this regard, both systolic and diastolic cardiac parameters such as left ventricular ejection fraction (LVEF), interventricular septal thickness (IVST), left ventricular internal dimension (LVID), and left ventricular posterior wall thickness (PWT) as well as the diastolic function parameters such as E, E', and deceleration time (DT) were evaluated. The echocardiography measurements were then compared with the normal ranges assessed in some sex- and age-matched normotensive subjects without any evidence of cardiovascular disorders. Additionally, cardiac mass was measured using the following formula:

$$\text{LV mass} = 0.8\,(1.04\,([\text{LVID}+\text{PWT}+\text{IVST}]^3 - [\text{LVID}]^3) + 0.6$$

Statistical Analysis

The results were presented as medians (first and third quartiles) for the quantitative variables and were summarized by absolute frequencies and percentages for the categorical variables. The continuous variables were compared using the ANOVA test and/or nonparametric Kruskal–Wallis test whenever the data did not appear to have normal distributions or when the assumption of equal variances was violated across the 2 groups. The categorical variables were, on the other hand, compared using the χ^2 or Fisher exact test when more than 20% of cells with an expected count of less than 5 were observed. The multivariable linear regression modeling was employed to assess group differences adjusted for baseline variables, including gender and age. For the statistical analysis, the statistical software SPSS, version 19.0, for Windows (SPSS Inc, Chicago, IL) was used. A *P* value of 0.05 or less was considered statistically significant.

RESULTS

The 4 subgroups of participants—comprising white-coat hypertensives, normotensives, controlled true hypertensives, and uncontrolled true hypertensives—were similar in terms of gender distribution (male frequency = 40.0%, 30.0%, 40.0%, and 50.0%—respectively; *P*=0.727). However, the normotensive subjects were significantly younger (mean age = 59.75±9.95 y in the white-coat hypertension group, 38.10±12.27 y in the normotensive group, 59.55±15.62 y in the controlled hypertensive group, and 59.00±12.95 y in the uncontrolled hypertensive group; *P*<0.001), with no discrepancy between the white-coat hypertension group and the other hypertensive subgroups.

As is shown in Table 1, the mean clinic SBP value was significantly high in the white-coat hypertensives by comparison with the normotensives and controlled hypertensives, but not with the uncontrolled hypertensives.

The mean DBP in the white coat-hypertension group was lower than that in the other hypertensive groups; it was high only in comparison with the normotensives. In other words, daytime as well as night-time SBP and DBP values in the white-coat hypertensives were significantly low when compared with the respective values in the uncontrolled hypertensives but were high when compared with the corresponding values in the normotensives or controlled hypertensives.

Univariate comparisons of the functional and structural cardiac parameters between the white-coat hypertensives and the other study groups showed that the median of cardiac mass was high in the white-coat hypertensives compared with the normotensive groups (127.5 vs 101.1; *P*=0.005). With respect to differences in the cardiac left ventricular mass, although the uncontrolled hypertensive group had significantly higher mass than the normal and controlled hypertensive groups, no statistical difference was observed apropos cardiac mass between the controlled hypertensives and the white-coat hypertensives (*P*=0.091). On the other hand, the median of cardiac mass was high in the white-coat hypertensives compared with the normotensive subjects (Table 2). In this context and after adjustment for sex and age, the white-coat hypertensive group revealed differing results in 2 indices of E'-wave velocity and IVST, when compared with the other 3 subgroups (Table 3).

In ventricular measurements, the white-coat group exhibited similar thickness in both the septum and the posterior wall to the controlled hypertensive group but these values were lower than those in the uncontrolled hypertensives and greater than those in the normotensive subjects. In this group, the E-wave velocity was equal to that in the normotensives and higher than that in both controlled and uncontrolled hypertensives; nonetheless, the E'-wave velocity indices were lower than those in the normotensives.

Table 1. Blood pressure variables of the participants in the 4 subgroups examined (median [first and third quartiles])

Variable	White-Coat Hypertensives	Normotensives	Controlled Hypertensives	Uncontrolled Hypertensives	*P* value
Echo-SBP	150 (150 – 160)*	100 (110 – 130)*	132.5 (121.2 – 140) *	150 (150 – 160)	< 0.001
Echo-DBP	90 (80 – 97.5)*	70 (60 – 80)*	80 (70 – 83.7)	90 (80 – 90)	< 0.001
Max-SBP_{day}	145 (138 – 150.7)*	133 (117 – 148)	153.5 (143.2 – 158.0)	176.5 (163.5 – 182)*	< 0.001
Max-DBP_{day}	84 (76.7 – 94.7)*	83 (77 – 95)	88 (76 – 98.7)	106 (93.7 – 116.7)*	0.006
Max-SBP_{night}	125.5 (121.7 – 135.2)*	110 (107 – 128)	124 (116.2 – 137.2)	167.5 (154.2 – 178.5)*	< 0.001
Max-DBP_{night}	69 (64.2 – 81.7)*	70 (64 – 83)	76 (63.5 – 84.7)	93.5 (80.5 – 111.7)*	< 0.001
Min-SBP_{day}	94 (89.2 – 101)*	89 (86 – 101)	96 (90.2 – 100.7)	120 (114.5 – 134.7)*	< 0.001
Min-DBP_{day}	46.5 (41.2 – 60)*	54 (47 – 60)	49.5 (41 – 55.2)	57 (53 – 71.5)*	< 0.001
Min-SBP_{night}	96.5 (91.2 – 102.2)*	93 (88 – 97)	101.5 (93.2 – 110.7)	131.5 (113.2 – 136.5)*	< 0.001
Min-DBP_{night}	49 (44.2 – 54.7)*	49 (46 – 54)	53.5 (46.5 – 58.2)	62 (54 – 69.5)*	< 0.001
Mean-SBP_{day}	116.5 (114.2 – 122)*	108 (99 – 118)*	119 (111.5 – 128)	144 (138.5 – 153.7)*	< 0.001
Mean-DBP_{day}	67 (61.2 – 70.7)*	65 (61 – 73)	66 (60.5 – 75.5)	142.5 (125.5 – 149.7)*	< 0.001
Mean-SBP_{night}	113 (108 – 116.7)*	100 (96 – 110)	113.5 (105.7 – 122.7)	147 (137 – 156)*	< 0.001
Mean-DBP_{night}	62.5 (55 – 67.2)*	59 (55 – 64)	62 (54.7 – 69.7)	79.5 (67.2 – 86.5)*	< 0.001

* Statistically significant difference between the white-coat hypertensives and the other groups
SBP, Systolic blood pressure; DBP, Diastolic blood pressure

Table 2. Echocardiography parameters of the participants in the 4 subgroups examined (median [first and third quartiles])

Variable	White-Coat Hypertensives	Normotensives	Controlled Hypertensives	Uncontrolled Hypertensives	*P* value
LVEF	0.6 (0.55 – 0.6)	0.6 (0.6 – 0.6)	0.6 (0.6 – 0.6)	0.6 (0.55 – 0.6)	0.198
DT	214 (169 – 278)	189 (158 – 215)	229 (177.2 – 285.2)	247 (186.5 – 365.5)	0.039
E wave	0.8 (0.7 – 0.97)	0.86 (0.70 – 1.03)	0.75 (0.64 – 0.92)	0.66 (0.56 – 0.80)	0.038
E' wave	0.06 (0.05 – 0.07)	0.10 (0.09 – 0.11)	0.07 (0.06 – 0.08)	0.06 (0.04 – 0.07)	< 0.001
IVST	0.92 (0.81 – 1.00)	0.72 (0.65 – 0.81)	0.87 (0.72 – 1.03)	1.10 (1.07 – 1.19)	< 0.001
LVID	4.64 (4.07 – 4.88)	4.54 (4.27 – 4.90)	4.3 (3.88 – 4.76)	4.22 (4.07 – 4.82)	0.411
PWT	0.81 (0.78 – 0.96)	0.69 (0.64 – 0.79)	0.80 (0.69 – 1.00)	1.04 (0.87 – 1.10)	< 0.001
LV mass	127.5 (115.2 – 157.5)	101.1 (89.4 – 124.3)	126.0 (82.1 – 150.1)	153.2 (123.6 – 217)	0.005

LVEF, Left ventricular ejection fraction; DT, Declaration time; IVST, Interventricular septal thickness; LVID, Left ventricular internal dimension; PWT, Left ventricular posterior wall thickness

Table 3. Multivariate linear regression model adjusted for sex and age

Variable	Beta	Standard Error	*P* value
DT			
Study group	-1.327	13.101	0.920
Sex	-18.387	27.038	0.499
Age	2.439	0.957	0.013
E wave			
Study group	-0.017	0.024	0.480
Sex	0.081	0.049	0.108
Age	-0.001	0.002	0.459
E' wave			
Study group	-0.005	0.002	0.014
Sex	-0.001	0.005	0.743
Age	0.001	0.001	< 0.001
IVST			
Study group	0.047	0.020	0.020
Sex	-0.139	0.041	0.001
Age	0.003	0.001	0.029
PWT			
Study group	0.034	0.020	0.084
Sex	-0.096	0.041	0.023
Age	0.003	0.001	0.032
Cardiac mass			
Study group	7.275	4.221	0.089
Sex	-39.162	8.907	< 0.001
Age	0.483	0.312	0.126

DT, Declaration time; IVST, Interventricular septal thickness; PWT, Left ventricular posterior wall thickness

DISCUSSION

Assessment of the outcome of white-coat hypertension in recent studies has indicated an unfavorable prognosis for affected patients. As is clearly shown in some recent observations, compared with normotensive individuals, the risk of cardiovascular mortality as adjusted for potential confounders has demonstrated a progressive significant increase in white-coat hypertensives and even this patient group has also exhibited a marked increase in the adjusted risk of developing sustained hypertension over a 10-year time period (Mancia et al, [10] 2013 and de la Sierra et al, [1] 2013). It has been even suggested that measuring home blood pressure levels, along with the other traditional risk factors, may be enough to stratify the cardiovascular risk (Hänninen et al,[7] 2012). A literature review suggests that the increased risk of mortality and morbidity in these patients can be due to various underlying cardiovascular abnormalities and metabolic disturbances, so that compared with normotensives, subjects with white-coat hypertension have been shown to be at increased cardiovascular risk. Thus, it seems that the presence of structural or functional heart disturbance is bi-directionally associated with the progression of white-coat hypertension and results in an unfavorable outcome. The present study was conducted to assess both structural and functional heart states in subjects with white-coat hypertension and compare them with those in normotensives. We have succeeded in clarifying that both structural heart status and diastolic functional status (indicated by a decreased E'-wave index and increased DT) could be impaired in these affected patients when adjusted for sex and age variables.

Taking into account the association between IVST changes and white-coat hypertension; although increased IVST was shown in both controlled and uncontrolled hypertensives compared with normotensives, as was similarly shown by Grossman and colleagues [7] (2008), this index was significantly higher in the white-coat hypertensives than in the normotensives.

We observed that changes in the diastolic function parameters (eg, decreased E'-wave velocity) indicated a higher rate of diastolic dysfunction in the white-coat hypertensives than in the normotensives. In addition and in comparison with the true hypertensive groups, IVST and PWT were both higher in the white-coat hypertensives than in the normal subjects but lower than those in the uncontrolled hypertensives. On the other hand, although the diastolic function was more impaired in the white-coat hypertensives than in the normal subjects, this impairment was not as high as that of the uncontrolled hypertensive group. In other words, diastolic dysfunction in the white-coat hypertensives was somewhere in the range between the normotensives and the controlled subjects but markedly lower than that in the uncontrolled hypertensives.

Therefore, a high IVST and a high rate of diastolic dysfunction compared with those in normal people can be 2 main hallmarks of subjects with white-coat hypertension in comparison with normotensives. The clinical importance of this issue should, however, be evaluated in future studies.

It is also deserving of note that based on our univariate analysis, the median of cardiac mass in the patients with white-coat hypertension was significantly higher than that in the normotensive groups and its value was consistent with that among the patients with controlled hypertension and considerably less than that among those with uncontrolled hypertension.

Although, after we made adjustments for sex and age, this difference was insignificant, the results of the previous studies are conflicting. Hernández del-Rey and colleagues [16] (2003) reported that the left ventricular mass was significantly greater in their patients with white-coat hypertension than in their other grade 1 to 2 hypertensive patients even after adjustment for age, gender, body mass index, and smoking. Contrarily, Rizzo et al [15] (1996) indicated that neither the left ventricular mass index and the left ventricular mass/height nor relative wall thickness was significantly high in white-coat hypertensives when compared with normotensives, but age and sex were associated with the left ventricular mass index, left ventricular mass/height, and relative wall thickness. In total, cardiac mass seems to be more affected by its own hypertension state and also underlying predisposing factors, which may be affected by patients' gender, advanced age, and comorbidities.

In conclusion, white-coat hypertension can be accompanied by both special functional and structural cardiac changes—especially high IVST in tandem with diastolic dysfunction, which can be the major hallmarks of white-coat hypertension and may be associated with unfavorable outcomes in affected patients.

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