What Is the Relationship Between White Coat Hypertension and Dyslipidemia?

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SUMMARY

The prognostic significance of white coat hypertension (WCH) remains controversial. Consecutive patients (955 cases, 566 females) aged between 15 and 70 years were divided into 3 groups, those with sustained normotension (NT), WCH, and hypertension (HT), and the prevalences of obesity, impaired glucose tolerance (IGT) or type 2 diabetes mellitus (DM), coronary heart disease (CHD), and dyslipidemia were compared among the groups. Although the prevalences of all of the disorders showed significant progression from the sustained NT group towards the WCH and HT groups, the prevalence of dyslipidemia was significantly higher in the WCH group ($P < 0.05$ for all). Due to the gradually increased prevalences of obesity, IGT or DM, and CHD from the sustained NT group towards the WCH and HT groups and the highest prevalence of dyslipidemia in the WCH group, WCH should preferentially be accepted as an alarming sign of a deterioration in health rather than being a predisposing factor of HT or atherosclerosis alone. The significantly higher prevalence of dyslipidemia in the WCH group than in the HT group may be explained by the increased amount of adipose tissue in the HT cases, since the prevalence of obesity was the highest in the HT group. Thus, the high prevalence of WCH even in early decades may represent increased susceptibility to future weight gain, and dyslipidemia in patients with WCH may be a preliminary sign of obesity. Therefore, the management of WCH should focus on the prevention of dyslipidemia and excess weight gain. (Int Heart J 2008; 49: 87-93)

Key words: White coat hypertension, Dyslipidemia, Excess weight

WHITE coat hypertension (WCH) is a well-known clinical entity defined as blood pressure (BP) that is persistently elevated in the doctor's office but normal under other conditions, and its prognostic significance remains controversial.[1,2] It was reported in the Ohasama study that WCH is a risk factor for development of home hypertension (HT).[3] Sixty subjects (46.9%) with WCH and 144 (22.2%) with sustained normotension (NT) progressed to home HT in another 8-year follow-up study,[4] and the results demonstrated that WCH is a transitional condition

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eventually terminating with home HT. Additionally, the intima-media thickness and cross-sectional area of the carotid artery were found to be similar in patients with WCH and HT, which were significantly higher than those in cases of sustained NT, leading the authors to conclude that there is target organ damage in WCH, and thus it should not be considered as an innocent trait.[5] Similarly, plasma homocysteine levels were higher and left ventricle mass index was greater in the WCH group compared to the NT cases ($P < 0.001$ in both), but they were significantly lower in the WCH group than in HT cases in another study ($P < 0.001$ and $P = 0.005$, respectively).[6] On the other hand, no evidence that WCH exhibits a clearly higher risk for cardiovascular events in the above 7.4-year follow-up study was found.[2] In another study, complication risks of WCH were not found to be different from those of subjects with sustained NT.[7] Therefore, most existing studies of WCH have only focused on the progression to home HT over time, or whether or not it causes any target organ damage. In contrast, in this study we have attempted to identify other prognostic significances of WCH and to determine any associations with any other health parameters.

METHODS

The study was performed at the Internal Medicine Polyclinic of Dumlupinar University between August 2005 and February 2007. Consecutive patients aged between 15 and 70 years were enrolled to avoid debility induced weight loss in elders. Their medical histories, including smoking habit, diabetes mellitus (DM), dyslipidemia, and medications were determined, and a routine check-up procedure that included fasting plasma glucose (FPG), triglycerides (TG), high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C), and electrocardiography was performed. Current regular smokers who had smoked for at least the last 6 months and cases with a previous smoking history of at least 5 pack-years were accepted as smokers. Cigar and pipe smokers were excluded. Diabetics using insulin and patients with devastating illnesses such as malignancies, acute or chronic renal failure, chronic liver diseases, hyper- or hypothyroidism, and heart failure were excluded in order to avoid their possible effects on weight. The body mass index (BMI) of each case was calculated based on measurements made by the physician rather than information obtained from the subjects. BMI was determined by dividing the weight in kilograms by height in meters squared. Underweight was defined as a BMI less than 18.5, normal weight as 18.5-24.9, overweight as 25-29.9, and obese as a BMI of 30.0 kg/m^2 or greater.[8] Cases with an overnight FPG level of 126 mg/dL or higher on two occasions or who were already taking antidiabetic medications were defined as diabetics. An oral glucose tolerance test with 75-gram glucose was performed in cases

with an FPG level between 110 and 126 mg/dL, and cases with a 2-hour plasma glucose level of 200 mg/dL or higher were diagnosed as having DM and 140-199 mg/dL as impaired glucose tolerance (IGT). Patients with dyslipidemia were also detected, and we used the National Cholesterol Education Program Expert Panel's recommendations for defining dyslipidemic subgroups.[8] Dyslipidemia was diagnosed when LDL-C was 160 or higher and/or TG were 200 or higher and/or HDL-C was lower than 40 mg/dL. Stress electrocardiography was performed in suspected cases and coronary angiography was only conducted in the stress electrocardiography positive cases. Therefore, coronary heart disease (CHD) was diagnosed either angiographically or based on a history of coronary artery bypass graft. Office blood pressure (OBP) was checked after a 5-minute rest in a seated position with a mercury sphygmomanometer on 3 separate visits, and no smoking was permitted during the 2 hours preceeding a blood pressure measurement. A 10-day twice daily measurement of blood pressure at home (HBP) was obtained in all cases, even in those who were normotensive in the office due to the risk of masked HT after a 10-minute educational presentation about proper BP measurement techniques.[9] The presentation included the recommended use of an upper arm device while discouraging wrist and finger devices, using a standard adult cuff with bladder sizes of 12 × 26 cm for arm circumferences up to 33 cm and a large adult cuff with bladder sizes of 12 × 40 cm for arm circumferences up to 50 cm, and taking at least a 5-minute rest in the seated position before a measurement. An additional 24-hour ambulatory blood pressure (ABP) monitoring was obtained only in cases with higher OBP and/or HBP measurements. ABP was performed with oscillometrical equipment (SpaceLabs 90207, Redmond, Washington, USA) set to take a reading every 10 minutes throughout the 24-hour period. Normal daily activities were allowed, and subjects were told to keep the arm relaxed during measurements. HT was defined as a BP of 135/85 mmHg or greater on mean daytime (between 10 AM to 8 PM) ABP.[9] WCH was defined as an OBP of 140/90 mmHg or greater with a mean daytime ABP of < 135/85 mmHg, sustained NT as an OBP of < 140/90 mmHg together with an average HBP of < 135/85 mmHg, and masked HT as an OBP of < 140/90 mmHg or HBP of < 135/85 mmHg with a mean daytime ABP of 135/85 mmHg or greater.[9] The cases were divided into 3 subgroups; sustained NT, WCH, and HT. The mean ages and female ratios and the prevalences of smoking, underweight, normal weight, overweight, obesity, IGT or DM, CHD, and dyslipidemia were determined in each group and compared among the groups. Student's *t*-test was used to analyze the data.

RESULTS

The study included 955 cases (566 females and 389 males). The characteristics of the 3 groups are summarized in Table I. The mean age increased significantly from the sustained NT group towards the WCH and HT groups ($P < 0.01$ in both). The female ratio was slightly but significantly higher in the WCH and HT groups ($P < 0.05$). The prevalence of smoking was the highest in the sustained NT group, however, in the smokers, only 65 of 247 were female, so the prevalence of smoking was nearly 3-fold higher in males. Therefore, the slightly but significantly higher prevalence of smoking habit in the sustained NT group may actually be a result of the lower percentage of females in the sustained NT group rather than a direct effect of smoking on BP. Similarly, although there was no difference according to the gender distribution between the WCH and HT groups,

Table I. Comparison of the Study Cases

Variable	Sustained normotension (n = 510)	P	WCH (n = 324)	P	Hypertension (n = 121)
Mean age and range (years)	39.1 ± 13.2 (15-70)	< 0.01	47.0 ± 13.0 (15-70)	< 0.01	54.8 ± 8.9 (33-70)
Female ratio	56.0%	< 0.05	62.9%	> 0.05	62.8%
Prevalence of smoking	30.7%	< 0.001	18.2%	< 0.01	25.6%
Prevalence of underweight	3.1%	< 0.01	0.0%	> 0.05	0.0%
Prevalence of normal weight	43.3%	< 0.001	13.8%	> 0.05	10.7%
Prevalence of overweight	39.0%	> 0.05	41.9%	< 0.05	36.3%
Prevalence of obesity	14.5%	< 0.001	44.1%	< 0.01	52.8%
Prevalence of IGT or diabetes mellitus	7.2%	< 0.001	17.2%	< 0.001	32.2%
Prevalence of CHD	3.7%	< 0.05	6.1%	< 0.001	22.3%
Prevalence of dyslipidemia	19.6%	< 0.001	41.6%	< 0.05	35.5%

WCH indicates white coat hypertension; IGT, impaired glucose tolerance; and CHD, coronary heart disease.

Table II. Mean Blood Pressure Values of the Study Cases

Variable	Sustained normotension (n = 510)	WCH (n = 324)	Hypertension (n = 121)
Prevalence	53.4%	33.9%	12.6%
Mean OBP	119.3 ± 5.7/79.1 ± 3.3	151.1 ± 4.3/95.1 ± 6.1	165.3 ± 6.7/109.1 ± 3.7
Mean HBP	99.1 ± 10.1/71.5 ± 3.7	123.3 ± 3.7/75.2 ± 4.3	147.2 ± 5.4/96.2 ± 6.4
Mean ABP	Not performed	121.9 ± 4.1/76.2 ± 4.2	145.3 ± 6.7/97.3 ± 6.3
Mean heart rate (beat/minute)	64.3 ± 13.3 (54-128)	78.4 ± 11.2 (59-147)	81.3 ± 10.3 (62-162)

WCH indicates white coat hypertension; OBP, office blood pressure; HBP, home blood pressure; and ABP, 24-hour ambulatory blood pressure monitoring.

smoking was significantly higher in the HT group ($P < 0.01$). Interestingly, there were only 16 detected cases within the underweight group, all of whom were in the sustained NT group. Although the prevalence of normal weight decreased significantly from the sustained NT cases towards the HT cases, the prevalence of obesity also increased significantly in the same direction. The prevalence of overweight was approximately 40% in all the groups. Again, the prevalences of IGT or DM and CHD increased gradually and significantly from the NT group to the WCH and HT groups ($P < 0.001$ in 3 steps and < 0.05 in one). Although all of the parameters indicative of poor health showed a pattern of progression from the sustained NT group towards the HT groups, only the prevalence of dyslipidemia was significantly higher in the WCH group and the reason was unknown ($P < 0.05$). On the other hand, 445 cases with WCH and HT were diagnosed both via HBP and ABP, and no difference was observed between the two methods according to the total number of cases diagnosed. The mean systolic/diastolic OBP, HBP, ABP values and mean heart rates of the groups are summarized in Table II. It was observed on ABP that the white coat effect was initiated by leaving home to come to hospital.

DISCUSSION

In a previous study, we observed very high prevalences of WCH in society; 33.3% in the second decade of life, 46.6% in the third, and 50.0% in the fourth, and the prevalence of HT started to exceed 40% in the sixth decade and reached 75% in the eighth decade of life.[10] On the other hand, the prevalence of HT was only 3% in the third, 8% in the fourth, and 21% in the fifth decade of life in the same study. A high prevalence of WCH in society was also shown in other studies.[11,12] Therefore, as a hypothesis we came to the conclusion that all HT cases, 75% in the eighth decade, may arise from previous WCH cases. However, this process takes a very long period of time, reaching up to the normal life span of a human being. In the present study, we evaluated WCH not only as a cause of HT or atherosclerosis, but also as a coexisting and alarming sign of a deterioration in health since most studies on WCH in the literature only focused on the progression to home HT, or whether or not it had already caused any target organ damage. When we compared the sustained NT, WCH, and HT groups, the prevalences of nearly all of the health problems including obesity, IGT or DM, and CHD showed significant progressions from the sustained NT group towards the WCH and HT groups, with the WCH group being midway in the progression. Except for the prevalence of being overweight, the prevalences of all of the other pathologies were significantly higher in the WCH group than in the sustained NT group. Similar patterns of progression were observed for nearly all of the patho-

logic conditions between the WCH and HT groups, but interestingly only dyslipidemia had a higher prevalence in the WCH group compared to the HT group. The prevalence of dyslipidemia was highest in the WCH group (41.6%) versus 19.6% ($P < 0.001$) in the sustained NT group and 35.5% in the HT group ($P < 0.05$). A previous study reported that serum triglyceride and cholesterol levels did not differ significantly between NT, WCH, and sustained HT cases in male subjects,[13] and we previously reported similar results indicating higher prevalences of dyslipidemia in WCH cases.[14] Thus, the higher prevalence of dyslipidemia in the WCH group may explain the adverse effects of WCH on health, since dyslipidemia is associated with future health problems such as obesity, HT, DM, CHD, and stroke. The lower prevalence of dyslipidemia in the HT group may be explained by the already increased adipose tissue per taken fat in the already HT cases, since the prevalence of obesity was significantly higher in the HT group than in the WCH group ($P < 0.01$). Therefore, the dyslipidemia in the WCH group may represent an increased susceptibility to weight gain. In this way, the higher prevalences of WCH detected even in the second (33.3%) and third decades (46.6%)[10] of life, despite the lower prevalences of excess weight in these age groups, may represent increased susceptibility to future weight gain, and WCH and dyslipidemia may be early warning signs of future excess weight gain and various associated disorders.

It is already known that excess weight leads to both structural and functional abnormalities of many bodily systems, and the risk of death from all causes including cardiovascular diseases and cancers increases throughout the range of moderate to severe weight excess both for men and women in all age groups.[15] We have examined the effects of body weight on BP and reported that the prevalence of sustained NT was significantly lower in underweight (80.3%) than normal weight (64.0%) and overweight cases (31.5%) ($P < 0.05$ for both) .[16] We also found that 55.1% of cases with HT were obese compared with 26.6% of cases with NT ($P < 0.001$).[17] Similarly, the relationship between excess weight and elevated BP is also described under the heading of metabolic syndrome, and clinical manifestations of the syndrome include abdominal obesity, dyslipidemia, HT, insulin resistance, and proinflammatory as well as prothrombotic states. We believe that WCH should also be included in the definition.

In conclusion, we believe WCH should preferentially be accepted as an alarming sign of deteriorating health rather than being a predisposing factor of HT or atherosclerosis alone due to the gradually increased prevalences of obesity, IGT or DM, and CHD from the sustained NT towards the WCH and HT groups and the higher prevalence of dyslipidemia in the WCH group. The significantly higher prevalence of dyslipidemia in the WCH group than in the HT group may be explained by the already increased adipose tissue per taken fat in the HT cases,

since the prevalence of obesity was the highest in the HT group. Thus, the high prevalence of WCH even in early decades may represent increased susceptibility to future weight gain, and the dyslipidemia seen in WCH may be a preliminary sign of obesity. Therefore, the management of WCH should focus on the prevention of dyslipidemia and excess weight gain.

REFERENCES

1. Karter Y, Curgunlu A, Altinişik S, *et al*. Target organ damage and changes in arterial compliance in white coat hypertension. Is white coat innocent? Blood Press 2003; 12: 307-13.
2. Polonia JJ, Gama GM, Silva JA, Amaral C, Martins LR, Bertoquini SE. Sequential follow-up clinic and ambulatory blood pressure evaluation in a low risk population of white-coat hypertensive patients and in normotensives. Blood Press Monit 2005; 10: 57-64.
3. Ohkubo T, Asayama K, Kikuya M, *et al*. How many times should blood pressure be measured at home for better prediction of stroke risk? Ten-year follow-up results from the Ohasama study. J Hypertens 2004; 22: 1099-104.
4. Ugajin T, Hozawa A, Ohkubo T, *et al*. White-coat hypertension as a risk factor for the development of home hypertension: the Ohasama study. Arch Intern Med 2005; 165: 1541-6.
5. Nakashima T, Yamano S, Sasaki R, *et al*. White-coat hypertension contributes to the presence of carotid arteriosclerosis. Hypertens Res 2004; 27: 739-45.
6. Curgunlu A, Karter Y, Uzun H, *et al*. Hyperhomocysteinemia: an additional risk factor in white coat hypertension. Int Heart J 2005; 46: 245-54.
7. Fagard RH, Van Den Broeke C, De Cort P. Prognostic significance of blood pressure measured in the office, at home and during ambulatory monitoring in older patients in general practice. J Hum Hypertens 2005; 19: 801-7.
8. National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. Circulation 2002; 17: 106: 3143-421.
9. O'Brien E, Asmar R, Beilin L, *et al*. European Society of Hypertension recommendations for conventional, ambulatory and home blood pressure measurement. J Hypertens 2003; 21: 821-48. (Review)
10. Helvaci MR, Seyhanli M. What a high prevalence of white coat hypertension in society! Intern Med 2006; 45: 671-4.
11. Hozawa A, Ohkubo T, Kikuya M, *et al*. Blood pressure control assessed by home, ambulatory and conventional blood pressure measurements in the Japanese general population: the Ohasama study. Hypertens Res 2002; 25: 57-63.
12. Celis H, Fagard RH. White-coat hypertension: a clinical review. Eur J Intern Med 2004; 15: 348-57.
13. Björklund K, Lind L, Vessby B, Andren 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.
14. Helvaci MR, Kaya H, Seyhanli M, Cosar E. White coat hypertension is associated with a greater all-cause mortality. J Health Sci 2007; 53: 156-60.
15. Calle EE, Thun MJ, Petrelli JM, Rodriguez C, Heath CW Jr. Body-mass index and mortality in a prospective cohort of U.S. adults. N Engl J Med 1999; 341: 1097-105.
16. Helvaci MR, Kaya H, Yalcin A, Kuvandik G. Prevalence of white coat hypertension in underweight and overweight subjects. Int Heart J 2007; 48: 605-13.
17. Helvaci MR, Ozcura F, Kaya H, Yalcin A. Funduscopic examination has limited benefit for management of hypertension. Int Heart J 2007; 48: 187-94.