White coat hypertension may be an initial sign of an accelerated atherosclerotic process

Mehmet Rami Helvaci (1)
Orhan Ayyildiz (1)
Orhan Ekrem Muftuoglu (1)
Mustafa Yaprak (2)
Abdulrazak Abyad (3)
Lesley Pocock (4)

(1) Professor of Internal Medicine, MD
(2) Assistant Professor of Internal Medicine, MD
(3) Middle-East Academy for Medicine of Aging, MD, MPH, MBA, AGSF, Chairman
(4) medi+WORLD International, Australia

Correspondence:
Mehmet Rami Helvaci, M.D.
Alanya, Antalya,
Turkey
Phone: 00-90-506-4708759
Email: mramihelvaci@hotmail.com

ABSTRACT

Background: Role of white coat hypertension (WCH) is unknown in metabolic syndrome.

Methods: The study was performed in the Internal Medicine Polyclinic.

Results: The study included 1,068 patients (628 females). Prevalence of excess weight increased from the third (28.7%) up to the seventh decades (87.0%), gradually (p<0.05 nearly in all steps), and then decreased in the eighth decade of life (78.5%, p<0.05). The most significant increase was detected during the passage from the third to the fourth decade (28.7% versus 63.6%, p<0.001) parallel to the smoking. Similarly, hypertriglyceridemia, hyperbetalipoproteinemia, dyslipidemia, impaired glucose tolerance (IGT), and WCH increased up to the seventh decade of life and decreased afterwards (p<0.05 nearly in all steps). On the other hand, hypertension (HT), type 2 diabetes mellitus (DM), and coronary heart disease (CHD) always increased without any decrease by decades (p<0.05 nearly in all steps) indicating their irreversible properties.

Conclusion: Probably metabolic syndrome is an accelerated atherosclerotic process all over the body. It includes some reversible parameters such as smoking, alcohol, sedentary lifestyle, animal-rich diet, overweight, hypertriglyceridemia, hyperbetalipoproteinemia, dyslipidemia, impaired fasting glucose, IGT, and WCH for the development of terminal illnesses such as early aging, obesity, DM, HT, peripheral artery disease, chronic obstructive pulmonary disease, cirrhosis, CHD, and stroke. The terminal illnesses are mainly due to the chronic inflammatory process on the arterial endothelial systems due to the much higher blood pressure in them. WCH may be an initial sign of the accelerated atherosclerotic process that can be detected easily.

Key words: White coat hypertension, metabolic syndrome, atherosclerosis, aging.
Introduction

Causative relationships between accelerated atherosclerosis and smoking, alcohol intake, sedentary lifestyle, animal-rich diet, and excess weight have been known for many years under the title of metabolic syndrome (1, 2). The syndrome is characterized by a low-grade chronic inflammatory process on endothelial systems, particularly on the arterial endothelial systems, probably due to much higher blood pressure (BP) in them. The inflammatory process may be slowed down with nonpharmaceutical approaches including lifestyle changes, diet, and regular exercise before the development of end-organ insufficiencies (3, 4). Probably the metabolic syndrome includes reversible parameters such as smoking, alcohol, sedentary life style, animal-rich diet, overweight, hypertriglyceridemia, hyperbetalipoproteinemia, dyslipidemia, impaired fasting glucose (IFG), impaired glucose tolerance (IGT), and white coat hypertension (WCH) for the development of terminal illnesses such as early aging, obesity, type 2 diabetes mellitus (DM), hypertension (HT), peripheral artery disease (PAD), chronic obstructive pulmonary disease (COPD), cirrhosis, coronary heart disease (CHD), and stroke (5). In another definition, the syndrome induced accelerated atherosclerosis may be the leading cause of death in human beings. On the other hand, WCH is a well-known clinical entity defined as the persistently elevated BP in doctor’s office whereas normal at home. It was reported in an Ohasama study that WCH is a risk factor for development of home HT (6). Similarly, intima-media thickness and cross-sectional areas of carotid artery were found similar in patients with WCH and HT, which were significantly higher than the patients with sustained normotension (NT) (7). Additionally, plasma homocysteine levels were higher, and left ventricle mass index was greater in the WCH compared to the sustained NT groups (p<0.001 for both) (7). We tried to understand the role of WCH in the definition of the metabolic syndrome in the present study.

Material and Methods

The study was performed in the Internal Medicine Polyclinic of the Dumlupinar University between August 2005 and March 2007. Consecutive patients at and above the age of 20 years were taken into the study. Their medical histories including smoking habit, DM, dyslipidemia, and already used medication were learnt, and a routine check up procedure including fasting plasma glucose (FPG), triglyceride (TG), high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C), and an electrocardiography were performed. Current smokers with six pack-months and cases with a history of five pack-years were accepted as smokers, and cigar or pipe smokers were excluded. Alcohol was not included due to the very low prevalence of alcohol use in Kutahya region of Turkey. Patients with devastating illnesses including type 1 DM, malignancies, acute and chronic renal failure, decompensated cirrhosis, hyper- or hypothyroidism, and heart failure were excluded to avoid their possible effects on body weight. Body mass index (BMI) of each patient was calculated by the measurements of the same physician instead of verbal expressions. Body weight in kilograms is divided by height in meters squared, and underweight is defined with a BMI of lower than 18.5, normal weight with 18.5-24.9, overweight with 25-29.9, and obesity with a BMI of 30.0 kg/m(2) or higher (8). Patients with an overnight FPG level of 126 mg/dL or greater on two occasions were defined as diabetics. An oral glucose tolerance test with 75-gram glucose was performed in cases with a FPG level between 110 and 125 mg/dL, and diagnosis of cases with a 2-hour plasma glucose level of 200 mg/dL or higher is DM and between 140-199 mg/dL is IGT. Patients with dyslipidemia were detected by using the National Cholesterol Education Program Expert Panel’s recommendations (8). Dyslipidemia is diagnosed when LDL-C is 160 or higher and/or TG is 200 or higher and/or HDL-C is lower than 40 mg/dL. A stress electrocardiography was performed in cases with an abnormal electrocardiography and/or with a history of angina pectoris. Coronary angiography was obtained for the stress electrocardiography positive cases. So CHD was diagnosed either angiographically or with a history of coronary artery stenting and/or coronary artery bypass graft surgery. Office blood pressure (OBP) was checked after a 5-minute rest in seated position with a mercury sphygmomanometer on three visits, and no smoking was permitted during the previous 2 hours. A 10-day twice daily measurement of blood pressure at home (HBP) was obtained in all cases, even in normotensives in the office due to the risk of masked HT after a brief education about proper BP measurement techniques (9). An additional 24-hour ambulatory blood pressure monitoring (ABP) was obtained just in cases with higher OBP and/or HBP measurements. It was performed with oscillometrical equipment (SpaceLabs 90207, Redmond, Washington, USA) set to take a reading every 10 minutes throughout the 24-hours. Normal daily activities were allowed, and subjects were told to keep the arm relaxed during measurements. Eventually, HT is defined as a BP of 135/85 mmHg or higher on mean daytime ABP (between 10 AM to 8 PM) (9). WCH is defined as an OBP of 140/90 mmHg or higher, but mean daytime ABP of <135/85 mmHg (9). Eventually, prevalence of smoking, excess weight, hypertriglyceridemia, hyperbetalipoproteinemia, dyslipidemia, IGT, WCH, DM, HT, and CHD were detected for the decades and compared in between. Comparison of proportions was used as the method of statistical analysis.

Results

The study included 1,068 patients (628 females and 440 males). Due to just 20 patients in the ninth decade, they were not included for the statistical comparison. There were only 1.7% (19) of cases with underweight and 28.7% (307) of cases with normal weight, so 69.4% (742) of cases at and above the age of 20 years had excess weight including overweight and obesity. The prevalence of excess weight increased from 28.7% in the third to 87.0% in the seventh decades, gradually (p<0.05 nearly in all steps), and then decreased to 78.5% in the eighth (p<0.05) and to 60.0% in the ninth decade of life. Interestingly, the prevalence of excess weight showed its most significant increase during the passage from the third to the fourth decades of life (28.7% versus 63.6%, p<0.001). Prevalence of smoking had a significant increase during the passage from the third to the fourth decades of life too (11.0% versus 32.4%, p<0.001). Prevalence of hyperbetalipoproteinemia, hypertriglyceridemia, dyslipidemia, IGT, and WCH had a similar fashion to the excess weight, increasing until the seventh decade of life and decreasing afterwards, significantly (p<0.05 nearly in all steps). On
the other hand, prevalence of HT, DM, and CHD always increased without any decrease by decades, significantly (p<0.05 nearly in all steps), indicating their irreversible properties. On the other hand, 517 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 patients diagnosed. Mean systolic/diastolic OBP, HBP, ABP values and mean heart rates of the groups are summarized in Table 2 (next page).

### Table 1: Characteristics of the study cases

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Third decade</td>
<td>181</td>
<td>11.0%</td>
<td>28.7%</td>
<td>1.6%</td>
<td>5.5%</td>
<td>6.5%</td>
<td>0.5%</td>
<td>23.2%</td>
<td>0.5%</td>
<td>0.0%</td>
</tr>
<tr>
<td>Fourth decade</td>
<td>157</td>
<td>32.4%</td>
<td>63.6%</td>
<td>12.7%</td>
<td>15.2%</td>
<td>26.7%</td>
<td>1.2%</td>
<td>24.2%</td>
<td>24.2%</td>
<td>1.9%</td>
</tr>
<tr>
<td>Fifth decade</td>
<td>246</td>
<td>ns†</td>
<td>ns+</td>
<td>78.4%</td>
<td>15.8%</td>
<td>31.7%</td>
<td>10.1%</td>
<td>33.3%</td>
<td>11.7%</td>
<td>4.0%</td>
</tr>
<tr>
<td>Sixth decade</td>
<td>249</td>
<td>ns</td>
<td>ns</td>
<td>83.1%</td>
<td>19.6%</td>
<td>ns</td>
<td>ns</td>
<td>ns</td>
<td>ns</td>
<td>ns</td>
</tr>
<tr>
<td>Seventh decade</td>
<td>108</td>
<td>31.7%</td>
<td>ns</td>
<td>87.0%</td>
<td>23.1%</td>
<td>ns</td>
<td>ns</td>
<td>ns</td>
<td>ns</td>
<td>ns</td>
</tr>
<tr>
<td>Eighth decade</td>
<td>107</td>
<td>23.3%</td>
<td>ns</td>
<td>78.5%</td>
<td>14.0%</td>
<td>ns</td>
<td>ns</td>
<td>ns</td>
<td>ns</td>
<td>ns</td>
</tr>
</tbody>
</table>

* p<0.05  ** p<0.01  *** p<0.001  † Nonsignificant (p>0.05)  ‡ Impaired glucose tolerance  § Coronary heart disease
Discussion

Probably metabolic syndrome contains a group of reversible parameters for the development of terminal illnesses, those developed due to the accelerated atherosclerotic process all over the body. The accelerated atherosclerosis may be the leading cause of death in human beings. So definition of the syndrome includes reversible parameters such as smoking, alcohol, animal-rich diet, sedentary lifestyle, overweight, WCH, IFG, IGT, hypertriglyceridemia, hyperbetalipoproteinemia, dyslipidemia for the development of terminal diseases such as early aging, obesity, HT, DM, PAD, COPD, cirrhosis, CHD, and stroke (10, 11). Parallel to the excess weight, prevalence of hypertriglyceridemia, hyperbetalipoproteinemia, dyslipidemia, IGT, and WCH increased until the seventh decade of life and decreased afterwards in the present study (p<0.05 nearly in all steps). On the other hand, prevalence of HT, DM, and CHD always continued to increase without any decrease by decades showing their irreversible properties (p<0.05 nearly in all steps). Probably after development of one of the terminal diseases, the nonpharmaceutical approaches will provide little benefit to prevent development of the others due to cumulative effects of the risk factors on endothelial systems for a long period of time, especially on the arterial endothelial systems due to the much higher BP in them (10, 11). Parallel to the excess weight, prevalence of hypertriglyceridemia, hyperbetalipoproteinemia, dyslipidemia, IGT, and WCH increased until the seventh decade of life and decreased afterwards in the present study (p<0.05 nearly in all steps).

WCH is associated with some features of the metabolic syndrome (12), and more than 85% of cases with the syndrome have elevated BP levels (4). We observed high prevalence of WCH even in early decades of life in the present study, for example 23.2% in the third and 24.2% in the fourth decades. The high prevalence of WCH in society was also shown by some other authors in the literature (13-15). When we compared the sustained NT, WCH, and HT groups in another study (16), prevalence of nearly all of the health problems including IGT, obesity, DM, and CHD had significant progressions from the sustained NT towards the WCH and HT groups, and the WCH group was found as a progression step in between. But as an interesting finding, the prevalence of dyslipidemia was the highest in the WCH group, and it was 41.6% among them whereas they were 19.6% in the sustained NT (p<0.001) and 35.5% in the HT groups (p<0.05) (16). Similar results showing the higher prevalence of dyslipidemia among the WCH cases were also observed in another study (17), whereas serum TG and cholesterol levels did not differ significantly between NT, WCH, and sustained HT cases in men in another study (18). The relatively lower prevalence of dyslipidemia in the HT group may be explained by the already increased adipose tissue per taken fat in them, since prevalence of obesity was significantly higher in the HT against the WCH groups (52.8% versus 44.1%, p<0.01) (16). So the detected high prevalences of WCH even in early decades, despite the low prevalences of excess weight in these age groups, may show a trend of weight gain and its terminal consequences. Probably all of the associations are closely related with the metabolic syndrome since WCH and dyslipidemia may be two initial signs of the syndrome. On the other hand, we accept the WCH as a different entity from borderline/mild HT due to the completely normal HBP and ABP measurements in the WCH, whereas they are abnormal in mild HT cases, but both groups of patients will get benefit from life style changes such as cessation of smoking and alcohol, regular physical activity, and animal-poor diet.

Weight gain and smoking may be the major triggering causes of the metabolic syndrome (19). Although smoking may cause some weight loss, its effect is probably due to the chronic endothelial inflammation all over the body, since loss of appetite is one of the initial symptoms of systemic inflammations. In another definition, smoking induced weight loss is an indicator of disease but not health. Similarly, excess weight leads to a chronic and low-grade inflammatory process on the endothelial systems, particularly on the arterial endothelial systems due to the much higher BP in them, and risk of death from all causes.
including cardiovascular diseases and cancers increases parallel to the range of moderate to severe weight excess in all age groups (20). The effects of body weight on BP were also shown previously, that the prevalence of sustained NT was significantly higher in the underweight (80.3%) than the normal weight (64.0%) and overweight groups (31.5%, p<0.05 for both) (21), and 55.1% of cases with HT had obesity against 26.6% of cases with sustained NT (p<0.001) (22). So the weight gain may be the main triggering factor for insulin resistance, dyslipidemia, IGT, and WCH (4). Stopping of weight gain with animal-poor diet, regular exercise, and cessation of alcohol, even in the absence of a prominent weight loss, will result with resolution of many parameters of the syndrome (23-25). But according to our opinion, limitation of excess weight as an excessive fat tissue in and around abdomen under the heading of abdominal obesity is meaningless, instead it should be defined as overweight or obesity via BMI, since adipocytes function as an endocrine organ that produces a variety of cytokines and hormones anywhere in the body (4). The resulting hyperactivity of sympathetic nervous system and renin-angiotensin-aldosterone system is probably associated with chronic endothelial inflammation, elevated BP, and insulin resistance. Similarly, the Adult Treatment Panel III reported that although some people classified as overweight with a large muscular mass, most of them also have excess body fat, and excess weight does not only predispose to CHD and stroke; it also has a high burden of other CHD risk factors including dyslipidemia, type 2 DM, and HT (8).

As a conclusion, metabolic syndrome may be an accelerated atherosclerotic process all over the body. It includes some reversible parameters such as smoking, alcohol, sedentary lifestyle, animal-rich diet, overweight, hypertriglycerideremia, hyperbetalipoproteinemia, dyslipidemia, IFG, IGT, and WCH for the development of terminal illnesses such as early aging, obesity, DM, HT, PAD, COPD, cirrhosis, CHD, and stroke. The terminal illnesses are mainly due to the chronic inflammatory process on the arterial endothelial systems due to the much higher BP in them. WCH may be an initial sign of the accelerated atherosclerotic process that can be detected easily.

References


