Impact of Obesity on 24-Hour Ambulatory Blood Pressure and Hypertension

Vasilios Kotsis, Stella Stabouli, Marshall Bouldin, Annette Low, Savvas Toumanidis, Nikos Zakopoulos

Abstract—The purpose of the present study was to determine the relationship between body mass index (BMI) and parameters derived from 24-hour ambulatory blood pressure monitoring including mean 24-hour daytime and nighttime systolic and diastolic blood pressures, 24-hour daytime and nighttime pulse pressure, mean 24-hour daytime and nighttime heart rate, dipping and nondipping status. 3216 outpatient subjects who visited our hypertension center and were never treated with antihypertensive medication underwent 24-hour blood pressure monitoring. BMI was significantly correlated with clinic systolic and diastolic blood pressures. Significant correlations were also found between BMI and mean 24-hour daytime and nighttime systolic blood pressure, 24-hour daytime and nighttime pulse pressure, and mean 24-hour daytime and nighttime heart rate. In multivariate regression analysis, clinic systolic, diastolic blood pressure, mean 24-hour systolic blood pressure, 24-hour pulse pressure, and high-density lipoprotein were independently correlated with BMI. The incidence of white coat hypertension was higher in overweight and obese patients than in normal weight subjects. Confirmed ambulatory blood pressure hypertension was also found to be higher in overweight and obese individuals compared with normal weight subjects. Our data also highlight the higher incidence of nondipping status in obesity. These findings suggest that obese patients had increased ambulatory blood pressure parameters and altered circadian blood pressure rhythm with increased prevalence of nondipping status. (Hypertension. 2005;45:602-607.)

Key Words: blood pressure monitoring, ambulatory • body mass index • hypertension • obesity

The increasing prevalence of obesity in industrialized countries is an alarming epidemic. Epidemiological studies clearly demonstrate a correlation between body weight and blood pressure in obese populations. In the Framingham Study, 70% of the new cases of essential hypertension were related to excess body fat.1 Population studies have shown that office blood pressure closely correlates with body mass index (BMI) and other anthropometric indices of obesity such as waist-to-hip ratio.2

Experimental studies in animals have also shown that excess weight gain caused by a chronic high-fat diet almost invariably raises blood pressure.3–5 Considerable evidence suggests that excess weight gain is related to human essential hypertension. Currently, 30% to 35% of adults in the United States are obese, and >30% are overweight.6–10 In some groups, such as black women older than age 50, the prevalence of obesity may be as high as 70% to 80%, coinciding with a rate of hypertension of >70%.11

Initially reserved for research purposes, ambulatory blood pressure monitoring has gradually become a widely used clinical tool for diagnostic purposes and for assessment of treatment efficacy. Evidence is available that 24-hour day or nighttime average blood pressure values correlate with subclinical organ damage more closely than office values.12 Evidence is also available that the same ambulatory values are more predictive of cardiovascular risk than office values,13–16 and that improvement of left ventricular hypertrophy is more closely related to treatment-induced changes in average ambulatory than office blood pressures.17–19

Also, combined office and ambulatory blood pressure measurements have been used to identify a condition characterized by a persistently elevated office blood pressure and a persistently normal ambulatory blood pressure, one referred to as isolated office (white coat) hypertension.20,21 With ambulatory blood pressure monitoring, it is also possible to study dipping and nondipping status, blood pressure and heart rate variabilities, and finally the circadian 24-hour blood pressure profile of the patients.22,23

In the present study, we explored possible correlations among BMI and parameters of 24-hour ambulatory blood
pressure monitoring in a large population database, one of the biggest 24-hour blood pressure monitoring database available. To our knowledge, there are no previous studies of the impact of body mass index on ambulatory blood pressure monitoring parameters and the 24-hour circadian rhythm.

**Methods**

**Study Population**

All patients gave their written consent to participate in the study. The institutional review board approved the human research protocol. The study population consisted of 3216 outpatient subjects (53% men and 47% women) who visited our hypertension center (Department of Clinical Therapeutics, Alexandra University Hospital, Athens, Greece) from January 1996 until January 2004 and were never previously treated with antihypertensive medication or were not taking other drugs. Subjects were referred to us for possible hypertension by their primary health care providers (60%) or visited our hospital outpatient clinic for a routine check-up. All patients who are visiting our center volunteer to undergo 24-hour ambulatory blood pressure monitoring as a routine procedure. Body weight was measured with the subjects in light clothing without shoes. BMI was calculated as weight (kg)/height (m²). Hematocrit, fasting serum glucose, fasting serum cholesterol, high-density lipoprotein (HDL), low-density lipoprotein (LDL), and triglycerides were also measured.21,22

**Clinic Blood Pressure Measurements**

Clinic blood pressures were measured 3 times in each subject using a mercury sphygmomanometer (standard cuff applied around the nondominant arm and systolic and diastolic values identified from the first and fifth phase of Korotkoff sounds). During the measurements, the participant remained seated with the arm comfortably placed at the heart level. The same doctor obtained the sphygmonometric measurements.

**Ambulatory Blood Pressure Monitoring**

All subjects underwent 24-hour ambulatory blood pressure monitoring on a usual working day. They were instructed to act and work normally. The Spacelabs 90217 ambulatory blood pressure monitor (Spacelabs Inc, Redmond, Wash) was used. The appropriate sized cuff was placed around the nondominant arm and 3 blood pressure determinations were made, along with sphygmonanometric measurements to verify that the average of the 2 sets of values did not differ by >5 mm Hg. Readings were obtained automatically at 15-minute intervals throughout the 24-hour study period. All subjects included in the study had at least 3 valid readings per hour. The resulting 80 to 96 pairs of systolic and diastolic blood pressure readings per recording with the corresponding time of measurements were used to calculate blood pressure derivatives. All subjects were instructed to rest or sleep between 10:00 PM and 6:00 AM and to maintain their usual activities between 6:00 AM and 10:00 PM (daytime).21,22 Shift workers were excluded from our population. All patients that are not resting or sleep at night were also excluded from the analysis.

**Statistical Analysis**

The SPSS 10.0 (SPSS Inc, Chicago, Ill) statistical package was used to analyze the data. Standard descriptive statistics, 2-tailed Student’s t test, bivariate correlation analysis, multivariate linear regression analysis (stepwise criteria: Probability of F to enter ≤0.050, probability of F to remove ≥0.100), and χ² test were used when appropriate. P<0.05 was considered statistically significant.

**Results**

Demographic data of the 4 groups are listed in Table 1 as mean±standard deviation (SD). We studied possible correlation for the parameters of ambulatory blood pressure monitoring with BMI. The results are listed in Table 2.

**BMI** was significantly correlated with clinic systolic blood pressure and clinic diastolic blood pressure. Parameters of 24-hour ambulatory blood pressure monitoring were also significantly correlated with BMI: Mean 24-hour systolic blood pressure, mean daytime systolic blood pressure, and mean nighttime systolic blood pressure were significantly correlated
with BMI. The 24-hour pulse pressure, daytime pulse pressure, and nighttime pulse pressure were also significant correlated with BMI. Mean 24-hour heart rate and mean nighttime heart rate were also correlated with BMI. BMI was also correlated with hematocrit, fasting serum glucose, HDL, LDL, and triglycerides levels (Table 2).

In multivariate regression analysis clinic systolic, diastolic blood pressure ($P<0.001$, $F=19.75$ and $P<0.001$, $F=36.77$, respectively), mean 24-hour systolic blood pressure ($P<0.0001$ and $F=15.99$), 24-hour pulse pressure ($P<0.0001$ and $F=17.91$), and HDL ($P<0.0001$ and $F=25.06$) were independently correlated with BMI. Parameters that were excluded from the model were hematocrit, fasting serum glucose, fasting total cholesterol, triglycerides, SDs of 24-hour systolic and diastolic blood pressures.

According to NIH criteria, patients were underweight if their BMI was <18.49, normal weight if their BMI was between 18.5 and 24.9, overweight if their BMI was between 25 and 29.9, and obese if their BMI was $>$30. Isolated office (white coat) hypertension was increased in higher BMI levels. The incidence of white coat hypertension was 12.5% in underweight patients, 22% in normal weight patients, 31.7% in overweight patients, and 35.3% in obese patients. The high prevalence of isolated clinic hypertension in obese subjects emphasizes the importance of the 24-hour ambulatory blood pressure monitoring in those patients.

“Normotensive” was determined as subjects with both office blood pressure values <140/90 mm Hg and ambulatory blood pressure values for 24-hour systolic and 24-hour diastolic blood pressures <125/80 mm Hg. Of our normotensives had normal weight, 31.3% were overweight, and 10.6% were obese. However, from our hypertensive patients, 23.4% had normal weight, 32.9% were overweight, and 43.7% were obese.

The circadian systolic blood pressure profiles of our normal weight, overweight, and obese subjects are shown in Figure 1. Each hour includes the mean values of 3 to 4 valid measurements calculated from 24-hour measurements of 3216 patients; 231 552 to 308 736 measurements of blood pressures were used to format the curve. Similar curves were obtained for diastolic blood pressure, pulse pressure, and heart rate (Figures 2, 3, and 4). Systolic and diastolic blood pressures of obese subjects were higher during all hours of day and night compared with systolic and diastolic blood pressures of lean subjects. During the night, systolic and diastolic blood pressures of lean subjects declined more than in obese subjects. Also, nighttime pulse pressures were greater in obese than in lean subjects. Heart rate of obese patients was higher during daytime. Although the difference was less during the night, both day and nighttime values for heart rate were higher in obese compared with lean subjects.

Dippers were defined as subjects whose nighttime blood pressures decreased $>$10% compared with their daytime blood pressures; 55% of normal weight subjects were dippers, whereas only 35% of obese subjects were dippers, a difference that was statistically significant $P<0.05$ ($\chi^2$). In our

<table>
<thead>
<tr>
<th>Variables</th>
<th>R</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>clinic SBP</td>
<td>0.207</td>
<td>0.000</td>
</tr>
<tr>
<td>clinic DBP</td>
<td>0.252</td>
<td>0.000</td>
</tr>
<tr>
<td>SBP 24</td>
<td>0.083</td>
<td>0.000</td>
</tr>
<tr>
<td>mean HR 24</td>
<td>0.058</td>
<td>0.01</td>
</tr>
<tr>
<td>PP 24</td>
<td>0.093</td>
<td>0.000</td>
</tr>
<tr>
<td>mean SBP day</td>
<td>0.069</td>
<td>0.002</td>
</tr>
<tr>
<td>mean HR day</td>
<td>0.046</td>
<td>0.05</td>
</tr>
</tbody>
</table>
“normotensive” subjects, 60% of underweight and 58.6% of our normal weight subjects were dippers but only 30.6% of overweight and 28.6% of obese were dippers. In our “hypertensive” subjects, 50.9% of underweight and 38.5% of normal weight subjects were dippers but only 30.5% of overweight and 27.3% of obese were dippers.

Discussion
In this study, we examined possible associations among obesity and parameters of ambulatory blood pressure. Obese patients had increased office and ambulatory blood pressures. Most population studies assess cardiovascular risk in terms of the manifestations of obesity, such as hyperlipidemia, diabetes, and hypertension. These disorders usually occur together and are often referred to as the metabolic syndrome, although they are almost always initiated by excess weight gain. Studies have shown that office blood pressure closely correlates with BMI, results that are in accordance with our results. Risk estimates from the Framingham Heart study suggest that ≈78% of hypertension in men and 65% in women can be directly attributed to excess body weight. In our population, there was an increase in the incidence of hypertension in overweight and obese subjects compared with normal weight subjects. Thus, data from multiple population studies suggest that excess weight gain is a consistent predictor for subsequent development of essential hypertension.

Clinical studies have repeatedly demonstrated the therapeutic value of weight loss in reducing blood pressure. Studies in animal models have also highlighted the impact of excess weight gain in hypertension by providing mechanistic insights. Abnormal renal sodium and water reabsorption and impaired pressure natriuresis appear to play a major role in obesity-related hypertension. To maintain sodium balance, obese subjects present increased arterial pressure. In addition, they have elevated glomerular filtration rate and renal plasma flow, as has been demonstrated in many studies. Another possible mechanism of obesity-induced hyper-
tension is activation of the sympathetic nervous system, which also acts to alter pressure natriuresis. Activation of sympathetic nervous system may be important in explaining the variations in blood pressure observed in our studies. Our obese subjects had higher heart rate variabilities, higher day and nighttime heart rates, and impaired nighttime decrease in blood pressure.

There is a great deal of evidence showing that the onset of cardiovascular events exhibits a prominent circadian rhythmicity with a marked peak in the morning and the lowest frequency during the night. Little attention has been drawn to a second peak in the incidence of cardiovascular events, which has been shown to occur in some studies late in the afternoon or early in the evening. Muller et al showed that there is a second peak in the incidence of sudden cardiac death at 6:00 to 7:00 PM. The same investigators found a similar evening peak in myocardial infarction onset determined by the creatine phosphokinase method, and this was later confirmed in the Cardiac Arrhythmia Suppression Trial (CAST). Muller et al also showed that the evening peak in stroke onset, together with an acceleration of activity on rising from the afternoon sleep. The 2 blood pressure peaks morning and evening occur in our lean and obese subjects; however, the peak blood pressure values were significantly higher in obese subjects (Figure 1).

Left ventricular hypertrophy, silent cerebrovascular disease, microalbuminuria, and progression of renal damage were found greater in nondippers subjects. A meta-analysis by Fagard et al suggests that the day–night blood pressure difference accounts for 15% of left ventricular mass. O’Brien et al also reported a more frequent history of stroke in nondippers than in dippers. In the analysis of the Syst-Eur study, the night/day ratio of systolic ambulatory blood pressure was an independent predictor of cardiovascular events. Thus, clinical studies with ambulatory blood pressure monitoring have shown that cardiovascular complications of essential hypertension such as left ventricular hypertrophy, stroke, and progression of renal damage tend to be more frequent in patient with nondipping circadian blood pressure profile. Our data extend this observation and highlight the higher incidence of nondipping status in obesity.

Limitations of the present study may include bias as a result of subject selection and limits in generalizing the findings to other populations. In our hypertension center’s population, we found that obese patients had higher 24-hour blood pressure values and altered circadian blood pressure rhythm. No differences in BMI were observed between subjects referred to us for possible hypertension by their primary health care providers and subjects who visited our hospital outpatient clinic for a routine check-up. Further studies are needed to confirm these observations in other populations.

Perspectives
We studied the impact of BMI in 24-hour ambulatory blood pressure monitoring parameters in a very large hypertension center’s population database. This is the first study to our knowledge of the association of BMI with 24-hour blood pressure profile and also with the 24-hour circadian blood pressure rhythm. We found that BMI positively correlated with 24-hour blood pressure parameters. Obese patients had increased ambulatory blood pressures and increased prevalence of isolated office hypertension and nondipping status, which emphasizes the importance of ambulatory blood pressure monitoring in obese patients. Future studies must be focused on the differences in target organ injury between obese and normal weight hypertensive subjects and also obese normotensive subjects.

Acknowledgments
I wish to thank Prof John E. Hall from the Department of Physiology and Biophysics and Center of Excellence in Cardiovascular-Renal Research, University of Mississippi Medical Center, Jackson, for assistance in writing this manuscript.
References

Impact of Obesity on 24-Hour Ambulatory Blood Pressure and Hypertension
Vasilios Kotsis, Stella Stabouli, Marshall Bouldin, Annette Low, Savvas Toumanidis and Nikos Zakopoulos

Hypertension. 2005;45:602-607; originally published online February 21, 2005;
doi: 10.1161/01.HYP.0000158261.86674.8e
Hypertension is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2005 American Heart Association, Inc. All rights reserved.
Print ISSN: 0194-911X. Online ISSN: 1524-4563

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://hyper.ahajournals.org/content/45/4/602

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Hypertension can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Hypertension is online at:
http://hyper.ahajournals.org//subscriptions/