Blunted Nighttime Blood Pressure Dipping in Postmenopausal Women

Andrew Sherwood, Rebecca Thurston, Patrick Steffen, James A. Blumenthal, Robert A. Waugh, and Alan L. Hinderliter

Blunting of the normal drop in blood pressure (BP) from day to night is emerging as a strong prognostic indicator of cardiovascular morbidity and mortality. This study evaluated the effects of natural menopause on BP dipping in African American and white women. A total of 112 women (62 premenopausal and 50 postmenopausal) took part in the study. Pre- and postmenopausal groups were comparable in terms of clinic BP, body mass index, and ethnic composition. Ambulatory BP was recorded over 24 h during a typical workday, with measurements programmed to be taken every 15 min during waking hours and every 30-minutes during sleeping hours. Nocturnal BP dipping was defined as the difference between waking and sleep BP. Waking BP did not differ by menopausal status. However, nocturnal systolic BP (SBP) and diastolic BP (DBP) dipping were attenuated in postmenopausal women, with both SBP ($P < .05$) and DBP ($P < .05$) higher during nighttime sleep in postmenopausal than in premenopausal women. Ethnicity was also related to BP dipping, with African American women tending to show blunted SBP dipping ($P = .055$) compared with white women; BP dipping was most blunted in postmenopausal African American women. These observations suggest that blunted nighttime BP dipping may contribute to increased cardiovascular disease risk in postmenopausal women. Am J Hypertens 2001;14:749–754 © 2001 American Journal of Hypertension, Ltd.

Key Words: Nighttime blood pressure; blood pressure dipping; ambulatory blood pressure; menopause; ethnicity.

Ambulatory blood pressure (ABP) monitoring technology has made it possible to record BP during routine daily activities, including sleep. Compared with standard clinic BP readings, ABP measurements show a stronger correlation with hypertensive target organ damage, including left ventricular mass index. ABP studies clearly illustrate the marked diurnal variation in BP, with pressures typically highest at work and lowest during sleep. A number of studies have documented that work ABP is a strong predictor of hypertensive target organ damage. More recently, relatively large-scale studies have shown that nighttime ABP and, particularly, the absence of a normal drop in systolic blood pressure (SBP) from day to night, is an especially strong prognostic indicator of cardiovascular morbidity and mortality in both normotensive and hypertensive populations. The night:day ratio of SBP has been found to be predictive of heart failure, stroke, and myocardial infarction, as well as sudden death in elderly patients with systolic hypertension. Furthermore, a lack of nocturnal decline, or dip, in BP has been associated with increased left ventricular mass and wall thickness in adults and in adolescents with high BP.

Studies of individual differences in diurnal ABP variations provide further evidence for the clinical significance of nighttime BP dipping. In the United States, African Americans have significantly higher rates of hypertension as well as mortality associated with cardiovascular diseases (such as heart disease, stroke, and end-stage renal disease) than those in the general population. A growing number of ABP studies have reported that African Americans show less of a nocturnal drop in BP than Americans of European origin. Gender is another individual difference factor related to both cardiovascular disease risk and BP. Premenopausal women have a lower incidence of cardiovascular disease compared to their male counterparts, but postmenopausal women are at increased risk compared with men. Blood pressure rises
with age in both men and women; however, although BP in premenopausal women is typically lower than in men, by the sixth decade of life BP in women exceeds that in men.\textsuperscript{23–25} For women, the more dramatic rise in BP associated with age appears to be related to the effects of menopause, and may contribute to the postmenopausal increase in cardiovascular morbidity and mortality.\textsuperscript{22,25,26} Recent studies indicate that postmenopausal women may exhibit a significantly attenuated nocturnal decline in BP.\textsuperscript{27,28} This evidence is consistent with the possibility that an attenuation of BP dipping may contribute to the increased cardiovascular disease risk associated both with ethnicity and, in women, with the effects of menopause.

The present study examined the effects of natural menopause on 24-h ABP in a biracial sample of women with normal and mildly elevated BP. Pre- and postmenopausal women were matched on a variety of demographic variables, including body mass index and clinic BP. It was hypothesized that postmenopausal women would exhibit a reduction in nighttime BP dipping compared with premenopausal women. The relationship of ethnicity to menopausal status and BP dipping was also examined.

### Methods

#### Subjects

Subjects were 112 employed women, aged 48 to 55 years, recruited by advertisements in local newspapers. Initially, self-report was used to exclude women currently experiencing menopause (ie, perimenopausal), whereas women who reported regular menstruation were considered premenopausal and women who had not menstruated in at least 9 months (median, 26 months) were considered postmenopausal. Reproductive hormone (follicle-stimulating hormone) assays were used to further document menopausal status. Women taking hormone replacement therapy (HRT) were excluded from the study. Other exclusion criteria were clinic SBP > 179 mm Hg or DBP > 99 mm Hg, surgical menopause, current prescription cardiovascular medications, and use of tobacco products.

All assessment procedures were reviewed and approved by the Duke University Medical Center Institutional Review Board. Before participating in the study, subjects gave informed consent.

#### Clinic Blood Pressure Measurement

Clinic BP measurements were taken on three separate visits, each approximately 1 week apart. On each visit, three seated BP readings were taken 2 min apart, using an appropriate sized occlusion cuff, mercury column sphygmomanometer, and stethoscope. The SBP was recorded coincident with the first occurrence of Korotkoff sounds (phase I) and DBP with their disappearance (phase V). Clinic SBP and DBP values were computed as the mean of the nine readings taken over the three visits.

### Ambulatory Blood Pressure Measurement

Ambulatory blood pressure monitoring was conducted during a typical workday. The AccuTracker II ABP Monitor (Suntech AccuTracker II, Raleigh, NC) was worn for approximately 24 h, starting usually between 8 and 10 AM until the same time the following morning. The AccuTracker II measures BP noninvasively, based on the auscultatory technique. It was programmed to take four BP measurements hourly at random intervals ranging from 12 to 28 min apart. Participants were instructed to follow their normal schedule and to complete a diary entry indicating posture, activity, and location at each BP reading. The same procedure was followed in the evening waking hours. Sleep was defined by diary activity ratings, which included an indication of “going to sleep.” The ABP monitor was programmed to take only two BP readings hourly during sleeping hours, customized to subjects’ sleep habits. All BP readings were reviewed and artifactual readings were deleted according to criteria previously described.\textsuperscript{29} Mean SBP and DBP values were computed based on all valid readings, and were obtained during waking hours and during nighttime sleep.

#### Reproductive Hormones

Blood (2 mL) was drawn from an antecubital vein and collected into a serum-separator tube and refrigerated. The sample was analyzed within 12 h of collection using immunochemoluminometric assay (Labcorp Inc, Burlington, NC) to determine concentrations of estrogen, progesterone, follicle stimulating hormone, and luteinizing hormone.

#### Data Reduction and Analysis

Blood pressure dipping was defined by subtracting the mean nighttime sleep BP from the mean daytime waking BP. Student t tests and \( \chi^2 \) tests were used to assess whether there were any menopausal and ethnic differences in demographic characteristics. Correlational and \( \chi^2 \) analyses were used to examine the relationships between BP dipping and demographic variables. Two-factor (menopause \( \times \) ethnicity) analysis of variance (ANOVA) and analysis of covariance (ANCOVA) tests were employed to assess the effects of menopausal status and ethnicity on waking BP, sleep BP, and BP dipping, with waking BP serving as a covariate for ANCOVA of BP dipping. All statistical analyses were conducted using SAS software (SAS Institute, Cary, NC) with \( \alpha \) set at .05.

### Results

#### Sample Characteristics by Menopausal Status

The study sample consisted of 62 premenopausal and 50 postmenopausal women. Demographic, anthropometric, and other characteristics are described in Table 1 according to menopausal status. Height, weight, body mass index
Menopausal Status and Ambulatory Blood Pressure

Ambulatory BP levels and BP dipping are presented by menopausal status in Table 2. Waking ambulatory SBP and DBP were similar in pre- and postmenopausal women. However, sleep BP differed significantly between the two groups, with postmenopausal women exhibiting higher SBP (F [1,109] = 4.78, P < .05) and DBP (F [1,109] = 6.14, P < .05) during sleep than premenopausal women. Menopausal status was also a significant determinant of nighttime BP dipping, with postmenopausal women exhibiting a reduced nocturnal decline in SBP (F [1,108] = 10.16, P < .01) and DBP (F [1,108] = 4.28, P < .05) compared with premenopausal women.

Sample Characteristics by Ethnicity

The study sample consisted of 76 white and 36 African American women. Demographic, anthropometric, and other characteristics are described in Table 3 according to ethnicity. The two ethnic groups were similar in every respect except for alcohol use; 61% of the white women drank alcohol, compared with 13% of the African American women.
Table 3. Baseline clinical characteristics of study participants according to ethnicity

<table>
<thead>
<tr>
<th>Ethnicity</th>
<th>White</th>
<th>African American</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>76</td>
<td>36</td>
<td></td>
</tr>
<tr>
<td>Age (y)</td>
<td>50.3 ± 2.0</td>
<td>50.4 ± 2.3</td>
<td>NS</td>
</tr>
<tr>
<td>Clinic SBP (mm Hg)</td>
<td>117 ± 14</td>
<td>113 ± 11</td>
<td>NS</td>
</tr>
<tr>
<td>Clinic DBP (mm Hg)</td>
<td>77 ± 9</td>
<td>74 ± 8</td>
<td>NS</td>
</tr>
<tr>
<td>Height (in)</td>
<td>63.8 ± 2.4</td>
<td>64.5 ± 3.1</td>
<td>NS</td>
</tr>
<tr>
<td>Weight (lb)</td>
<td>150.7 ± 23.3</td>
<td>160.1 ± 33.5</td>
<td>NS</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>25.9 ± 3.7</td>
<td>26.9 ± 4.1</td>
<td>NS</td>
</tr>
<tr>
<td>Postmenopausal (%)</td>
<td>47</td>
<td>39</td>
<td>NS</td>
</tr>
<tr>
<td>Sleep duration (h)</td>
<td>6.7 ± 1.4</td>
<td>6.3 ± 1.5</td>
<td>NS</td>
</tr>
<tr>
<td>Number of children at home</td>
<td>0.7 ± 0.8</td>
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<td>Alcohol users (%)</td>
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<tr>
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<td></td>
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<tr>
<td>Median household income</td>
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</tbody>
</table>

Abbreviations as in Tables 1 and 2.

Ethnicity and Ambulatory Blood Pressure

Ambulatory BP levels and BP dipping are presented by ethnicity in Table 4. Waking and sleep SBP and DBP were similar in African American and white women. However, there was a marginally significant effect of ethnicity on SBP dipping, with African American women exhibiting a reduced nocturnal decline in SBP (F [1,108] = 3.76, P = .055) and a trend toward a smaller decline in DBP (F [1,108] = 2.75, P < .1) than white women. Although African American and white women differed in the likelihood of their drinking alcohol, BP dipping was found to be unrelated to alcohol use. Controlling for alcohol use by including it as a covariate in the statistical analyses did not alter the findings for ethnic effects on BP dipping.

Menopausal Status by Ethnicity Effects on Ambulatory Blood Pressure

There were no significant interactions between ethnicity and menopausal status on BP or BP dipping. Thus, the effects of menopause on BP dipping were evident in both African American and white women. However, because ethnicity also was related to dipping, it is notable that the greatest nocturnal decline in SBP occurred in premenopausal white women (mean dipping 20 mm Hg), whereas in postmenopausal African American women, SBP dipping (mean 12 mm Hg) was most blunted (Fig. 1).

Discussion

The present study found that both menopausal status and ethnicity were related to diurnal BP variability, and especially to nighttime BP dipping. Waking BP levels were similar in pre- and postmenopausal women, but postmenopausal women showed less of a fall in BP during sleep. Similarly, waking BP levels were comparable in African American and white women, but African American women tended to show less of a nocturnal decline in BP. These findings were generally more robust for SBP than DBP.

The finding that BP dipping is blunted in postmenopausal women is an important verification of only two studies published on this topic. Li et al., who examined diurnal ABP variations in 24 premenopausal and 40 postmenopausal women with normal BP, found that postmenopausal women showed attenuated dipping, but only for DBP. Schillaci et al. also have reported that postmenopausal women showed an attenuated nocturnal decline in BP that is independent of their clinic BP status. Our findings show that the effects on BP dipping were evident relatively soon (median, 26 months) after menopause. The present study is also the first to demonstrate this phenomenon in a study conducted in the United States and, moreover, in a biracial study sample comprised of both African Americans and Americans of European descent. The effects of ethnicity and menopause on BP dipping were found to be independent and additive, with BP dipping most attenuated in postmenopausal African American women. Therefore, menopause may mark an increased cardiovascular risk for both white and African American women, but the additional risk may be especially significant for the latter.

Our observations with regard to ethnicity are consistent with a number of reports, recently reviewed by Profant andDimsdale, that individuals of African origin and, espe-
cially, African Americans, typically exhibit an attenuated nocturnal decline in SBP compared with whites. However, the present study extends the previous findings by being the first to document blunted BP dipping in African Americans in a study sample comprised exclusively of women. Blunted BP dipping may contribute to the high levels of cardiovascular morbidity and mortality in African Americans, who, as a group, are predisposed to develop left ventricular hypertrophy.29,30 Interestingly, in a recent study, 24-h ABP was related to left ventricular mass index in both African Americans and whites, but nondipping was found to be associated with increased left ventricular mass index only in African Americans.31

The mechanisms accounting for individual differences in BP dipping are poorly understood. In terms of the plausible physiological mechanisms, African Americans have been found to show higher levels of systemic vascular resistance than whites, a hemodynamic profile associated with concentric left ventricular remodeling and hypertrophy.32 African Americans with normal BP also may be characterized by structural changes in precapillary resistance vessels that are consistent with the early stages of vascular hypertrophy.33 These structural changes may contribute to both elevated nocturnal BP and to the development of left ventricular hypertrophy in African Americans. With regard to menopause, effects upon BP have been largely attributed to the postmenopausal decline in female reproductive hormones, and particularly in estrogen. In postmenopausal women, oral or transdermal estrogen treatment, with or without the addition of progesterone, has been found to produce a decrease in mean 24-h ABP levels, and an increase in BP dipping.34–38 Estrogen is thought to potentiate endothelium-dependent vasodilation by stimulating the release of nitric oxide and the production of nitric oxide synthase.39 Other indirect vascular benefits of estrogen include decreasing the concentration of renin and angiotensin converting enzyme, and stimulating the opening of calcium-activated potassium channels.40 One manifestation of the deterioration of these vascular regulatory mechanisms may be a blunted nocturnal decline in BP in postmenopausal women, which may further contribute to their increased risk for cardiovascular disease.

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