Stress, menopausal status and nocturnal blood pressure dipping patterns among hypertensive women

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BACKGROUND: A less than 10% decline in blood pressure during the night is known as a nondipping blood pressure (BP) pattern. Nondipping BP has been shown to be associated with target organ damage and poorer cardiovascular outcomes. Additionally, some evidence suggests that hypertensive nondipping women are at greater risk for target organ damage than hypertensive nondipping men.
OBJECTIVE: To determine whether stress, demographics, menopausal status or sleep quality are associated with nondipping BP among hypertensive women.
METHODS: A cross-sectional study design was used to describe the relationship between stress and dipping status among a sample of hypertensive women and to describe the sample by age, ethnicity, marital status, menopausal status, current medications and sleep quality.
RESULTS: The study sample consisted of 47 women (mean [± SD] age 57±13.9 years) with essential or office hypertension who underwent 24 h ambulatory BP monitoring, and completed stress and sleep quality measurements. Thirty-one women (66%) were classified as dippers and 16 (34%) were classified as nondippers. Nondippers were older (P=0.04), postmenopausal (P=0.003) and had lower stress scores (P=0.02) than their dipper counterparts. Postmenopausal status significantly predicted nondipping (OR 16; 95% CI 1.9 to 136.4).
CONCLUSION: These findings were of interest given that some women had a nondipping BP pattern and significantly lower stress scores. It is possible that there are fundamentally different physiological mechanisms that explain this nondipping phenomenon. In the future, the identification of specific hemodynamic mechanisms associated with nondipping could potentially influence the choice of antihypertensive treatment regimens for nondipper hypertensive patients.

Key Words: *Ambulatory blood pressure monitoring; Blood pressure; Hypertension; Nondipping*

Le stress, l'état ménopausique et les baisses nocturnes de tension artérielle chez les femmes hypertendues

HISTORIQUE : La diminution nocturne de la tension artérielle inférieure à 10 % est désignée absence de baisse nocturne de la tension artérielle (TA). Cette absence de baisse nocturne de la TA s'associe à une atteinte des organes cibles et à des issues cardiovasculaires plus négatives. De plus, selon certaines données probantes, les femmes hypertendues sans baisse nocturne de la TA sont plus vulnérables à une atteinte des organes cibles que les hommes dans la même situation.
OBJECTIF : Déterminer si le stress, la démographie, l'état ménopausique ou la qualité du sommeil s'associent à une absence de baisse nocturne de la TA chez les femmes hypertendues.
MÉTHODOLOGIE : Une étude transversale a permis de décrire la relation entre le stress et la baisse nocturne de la TA au sein d'un échantillon de femmes hypertendues et de décrire cet échantillon selon l'âge, l'ethnie, la situation familiale, l'état ménopausique, la prise courante de médicaments et la qualité du sommeil.
RÉSULTATS : L'échantillon à l'étude se composait de 47 femmes (âge moyen [±ÉT] de 57±13,9 ans) présentant une hypertension essentielle ou en cabinet et ayant subi une surveillance ambulatoire de la TA pendant 24 heures ainsi que des mesures du stress et de la qualité du sommeil. Trente et une femmes (66 %) étaient classées comme ayant une baisse nocturne et 16 (34 %) comme n'en ayant pas. Celles-ci étaient plus âgées (P=0,04), postménopausées (P=0,003) et présentaient un indice de stress (P=0,02) inférieur à celui de leurs camarades présentant une baisse nocturne de la TA. L'état postménopausique avait une valeur prédictive significative d'absence de baisse nocturne de la TA (RRR 16; 95 % IC 1,9 à 136,4).
CONCLUSION : Ces constatations étaient intéressantes puisque certaines femmes présentaient une absence de baisse nocturne de la TA et des indices de stress beaucoup plus faibles. Il est possible que des mécanismes physiologiques fondamentalement différents expliquent ce phénomène. À l'avenir, le dépistage de mécanismes hémodynamiques précis associés à l'absence de baisse nocturne de la TA pourrait influer sur le schéma posologique d'antihypertenseurs sélectionnés pour les patientes hypertendues ne présentant pas de baisse nocturne de la TA.

Cardiovascular disease is a leading cause of death of men and women in Canada (1). Cardiovascular disease-related deaths account for 34% of all deaths among Canadian women and 32% of all deaths among Canadian men (1).

Hypertension is strongly and independently related to cardiovascular morbidity and mortality (2). In Canada, hypertension is more common in women older than 55 years of age than in age-matched men (3). According to the Heart and Stroke Foundation of Canada (3), more than one-third of postmenopausal Canadian women have hypertension. Although the explanation for hypertension in menopause is not fully understood, estrogen depletion, general aging and/or body weight are believed to contribute to the blood pressure (BP) changes (4).

Ambulatory BP monitoring (ABPM) is a noninvasive technology used for the evaluation of individuals with suspected and established hypertension (5). ABPM has revealed a diurnal variation in BP. The normal variation in BP is characterized by a 10% or greater reduction in BP from day to night (6). Individuals with this nighttime dip in BP are known as dippers and those who do not dip are known as nondippers. Nondippers have a less than 10% reduction in BP during sleep (7).

Although controversial, evidence suggests that individuals with a nondipping BP profile are at risk for greater cardiovascular morbidity and poorer outcomes (8-15). Some researchers have also reported greater target organ damage among hypertensive nondipping women than among hypertensive nondipping men (16). It has been estimated that 25% of essential hypertensive patients have a nondipping BP pattern (17).

The exact mechanisms of action responsible for nondipping BP are not fully understood. It is believed that the autonomic nervous system – in particular, the sympathetic nervous system – has an effect on circadian BP variation. Researchers have demonstrated that during the night, nondippers have increased sympathetic nervous system

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activity (18,19) and decreased parasympathetic nervous system activity (19,20). Accordingly, data suggest that nondippers have higher nighttime levels of epinephrine and norepinephrine than dippers (18). The physiology of the stress response also involves increased sympathetic nervous system activity and higher levels of epinephrine and norepinephrine release (21,22). Although the stress response can be triggered by physical stress, psychological stress or a combination of both, in today's society, individuals are exposed more often to psychological stress than to physical stress (22). Therefore, it is possible that there is an association between psychological stress and nondipping BP.

In the present study, women were chosen as research subjects because stress and BP dipping status have not been studied in hypertensive women and in Canada, hypertension affects more women older than 55 years of age than age-matched men (3). Additionally, much of the hypertension research has been primarily conducted using men as the research subjects, and hypertension in women is less understood (23). An awareness of the demographic and psychosocial factors associated with nondipping BP is important because it may aid in the identification of individuals at high risk for this altered BP pattern as well as possible end organ damage.

The primary purpose of the present cross-sectional study was to investigate whether stress is associated with nondipping BP among hypertensive women. The secondary aim of the study was to investigate whether demographics, menopausal status and sleep quality were associated with nondipping BP in women with hypertension.

METHODS

Subjects

The study was performed in women scheduled for 24 h ABPM for the investigation and evaluation of essential hypertension. All subjects had either a previous diagnosis of essential hypertension or had systolic BP (SBP) readings of greater than 140 mmHg and/or diastolic BP (DBP) readings of greater than 90 mmHg on three or more occasions in the office of their primary care physician. Sequential sampling was performed, in which all women who met the inclusion criteria were invited to participate in the study.

The study inclusion criteria were female sex; office or essential hypertension; ability to read, write and communicate in English; ability to provide informed consent; and an appointment scheduled for 24 h ABPM in the hypertension unit of an Atlantic Canada Regional Health Authority. The study exclusion criteria were diagnosis of secondary hypertension, diabetes mellitus or renal dysfunction; and a history of myocardial infarction, congestive heart failure, cardiac valve diseases, sleep apnea and cerebrovascular disease. Individuals with these acute and chronic conditions were excluded because these conditions may affect BP patterns differently during sleep, as well as at different stress levels. Shift workers were also excluded due to the potential impact shift work has on sleep and BP patterns.

Ethical considerations

The study was reviewed and approved by the Health Authority Research Ethics Board, and all subjects provided written informed consent before participation. All measurement techniques were noninvasive; therefore, the risks of injury during the study were minimal.

Measures

Demographic and medical history data: The following demographic data were recorded for each participant: age, ethnicity, marital status, menopausal status and current medications (BP, hormone replacement therapy [HRT] and sleeping aids). A woman was considered to be premenopausal if she reported having a menstrual period within the past 12 months and was considered postmenopausal if she did not report having a menstrual period within the past 12 months or had a hysterectomy, with both ovaries removed. Data concerning diagnosis, comorbidities and medications were collected from the medical records and by self report.

ABPM: The 24 h BP was measured with the Spacelabs ABPM (model 90207; Spacelabs Medical, USA), after validation of its readings against those of the BpTRU oscillometric monitor (VSM MedTech Ltd, Canada). Both monitors have been validated for BP measurement, with the BpTRU validated for office BP measurement (24) and the Spacelabs ABPM approved for 24 h ABPM (25). The ABPM was set to obtain BP readings at 30 min intervals during the day (07:00 to 22:00) and 60 min intervals during the night (22:00 to 07:00) as per the hypertension unit's policy. This information was recorded by the monitor and transferred by a direct connection to the computer analysis system. Initially, the ABPM recordings for each person were automatically scrutinized to edit out artefactual readings. The predetermined editing criteria were an SBP of greater than 240 mmHg or less than 70 mmHg, or a DBP of greater than 150 mmHg or less than 40 mmHg. Additionally, to be included in the analysis, each ABPM dataset was required to include a minimum of two-thirds of the SBP and DBP measurements during both the daytime and nighttime periods. This was in accordance with the practice guidelines for ambulatory BP measurement (26).

All ABPM sessions were performed during a weekday and subjects were instructed to attend to their usual daily activities, but to hold their arm stationary during BP readings. Subjects recorded the time they retired to asleep and awoke for the day. Additionally, subjects recorded whether they were out of bed during the night (eg, to use the bathroom, etc) and the approximate time(s). Dipping status was calculated manually. Daytime and nighttime mean SBPs were calculated using the patient-reported sleep and awake times. In the present study, BP dipping was defined as a 10% or greater reduction in mean SBP from day to night. Nondipping BP was defined as a less than 10% reduction in mean SBP from day to night.

Sleep diary: Sleep diaries are often used in sleep research studies to monitor subjective reports of sleep over time, such as quantitative estimates of sleep onset, duration and latency (27). There is evidence to suggest that using arbitrary nighttime and daytime definitions, as opposed to actual asleep and awake hours, can result in dipping status misclassifications (28). Therefore, in the present study, subjects reported the time they went to sleep and the time they awoke. These times were needed to determine the nighttime period and dipping status. Additionally, subjects recorded the approximate time they were out of bed during the night; this time was accorded with the closest BP measurement and removed from the mean nighttime SBP calculation. This information was required because researchers have also shown that nighttime activity may influence the results of ABPM, thereby affecting the classification of individuals as dippers or nondippers (29).

Sleep quality visual analogue scale: Evidence suggests that sleep affects dipping status (30). To control for the impact of sleep, participants were asked to rate the preceding night's sleep quality on a 100 mm sleep quality visual analogue scale (VAS). The distance of the subject's mark from the zero end of the scale was measured. The number of millimetres from the zero end of the scale to the subject's mark was used as a continuous measure, or rating, of the perceived quality of sleep (27).

Perceived stress scale 14: The perceived stress scale (PSS) 14 (31) is a 14-item, five-point Likert scale that measures the degree to which individuals appraise their life as stressful (in which a score of 0 is 'never', 1 is 'almost never', 2 is 'sometimes', 3 is 'fairly often' and 4 is 'often'). This tool was chosen to measure a person's appraised level of stress during the past month to determine whether a person's stress level affected their BP dipping pattern.

The PSS14 scale was scored by reversing the scores (0=4, 1=3, 2=2, 3=1, 4=0) on the positive items (items 4, 5, 6, 7, 9, 10 and 13) and then summing across all 14 items (31). This scale has been validated in hypertensive individuals (32) and there is evidence that the scale is internally consistent, as reflected by the Cronbach's alpha value of 0.86 (32). In the present study, the PSS14 Cronbach's alpha was 0.71. The PSS is a commonly used measure of global distress (33) and researchers have found that PSS scores are associated with biological markers of stress and risk factors for coronary artery disease (34).

Sample size justification

Stress, measured with the PSS14 (31), was considered to be the most important predictor variable for dipping status. The psychometric properties of the PSS14 used in a study of treated hypertensive women (32) were used to calculate the sample size. It was estimated that a sample size of 56 patients was needed to detect a mean drop of two points or a 10% difference in the response scores on the PSS14 at the 0.05 level of significance with a power of 80%. A preliminary data analysis revealed a statistically significant difference in the stress scores of dippers and nondippers; therefore, the study was closed with 47 women enrolled. The statistical power of the study was calculated to be 86.4% at the 0.05 level of significance.

Data collection procedure

The hypertension unit's patient educator screened potential participants for eligibility, and the primary investigator (FSR) obtained informed consent and collected demographic and medical data. The patient educator instrumented subjects with the ABPM. Subjects used a sleep diary to record the time they went to sleep for the night, times they were out of bed during the night and the time they awoke for the day. Subjects completed the stress questionnaire and sleep VAS in their homes the following day. The time commitment for the questionnaire was approximately 10 min. Subjects received $25 and a parking validation ticket for participation in the study.

Statistical analysis

Continuous variables were analyzed using Student's *t* test for independent variables to calculate the mean values for dippers and nondippers. Values are expressed as means ± SDs. Categorical variables were analyzed using cross tabulation to calculate χ^2 (if the cell count of the 2×2 table was five or higher) or Fisher's exact test values (if the cell count of the 2×2 table was less than five). Correlations among the variables were also computed. Multicollinearity (strong correlations among the independent variables) was examined with the collinearity diagnostic statistics (tolerance and variance inflation factor). Tolerance and variance inflation factor statistics are commonly used to measure the extent of multicollinearity of the *i*th independent variable with the other independent variables in a regression model (35). The tolerance statistic is the proportion of an independent variable's variance not accounted for by other independent variables in the model. The tolerance of an independent variable is 1 minus the proportion of variance it shares with the other independent variables in the analysis. The variance inflation factor is the reciprocal of the tolerance (35). Variance inflation factor values of greater than 2.5 or a tolerance of less than 0.4 may indicate concern for multicollinearity in logistic regression models (36). The independent variables included in the model to test for multicollinearity were stress, age, menopausal status, marital status, receiving or not receiving BP medication, sleep quality and number of times out of bed. HRT, sleep medication, ethnicity and specific BP medication category were not included because of the small sample size and the small number of patients in each category.

Logistic regression was used to describe the relationship of multiple independent variables with a dichotomous dependent variable (dipper or nondipper). For each of the independent variables (stress, age, marital status, menopausal status, receiving or not receiving BP medication, sleep quality and number of times out of bed), the logistic regression yielded an OR and 95% CI. The OR described the unique impact of each of the independent variables on dipping status, after controlling for the influence of the other independent variables. The logistic regression was performed using the enter method, in which all independent variables were entered into the logistic regression. The -2_{log} likelihood ratio test of the χ^2 difference between models was used for model refinement. SPSS version 14.0.1 for Windows (SPSS Inc, USA) was used to analyze the data.

RESULTS

Study population

Between February 13, 2006, and July 14, 2006, 61 adult women with office or essential hypertension who were scheduled for 24 h ABPM at the hypertension unit of a Regional Health Authority in Atlantic Canada were invited to participate in the study. Eleven subjects declined to participate, stating they had too much to do, had no time, were too stressed or returned blank questionnaires. Two subjects had consented to participate in the study but each removed the ABPM in the evening, stating that it was too uncomfortable to wear. One subject wore the ABPM twice, but on both occasions, ABPM recordings were invalid. Consequently, the study sample was comprised of 47 subjects who wore the 24 h ABPM and completed the questionnaires. The subjects had a mean of 38.34±2.53 valid readings (ranging from 29 to 42) for the 24 h period. This resulted in a total of 1802 valid readings from the 47 subjects.

TABLE 1
Age, blood pressure and heart rate (HR) measurements in dippers and nondippers

	Dippers (n=31)		Nondippers (n=16)		
Variable	Mean	SD	Mean	SD	P
Age, years	54.03	14.95	62.69	9.80	0.04
24 h ABPM					
SBP, mmHg	131	7.92	131	10.74	0.97
DBP, mmHg	77	9.26	76	10.79	0.76
MAP, mmHg	97	6.62	97	9.0	0.91
HR, beats/min	72	8.69	74	9.81	0.58
SBP, mmHg					
Daytime*	138	9.04	133	10.84	0.062
Nighttime*	116	7.76	126	11.75	0.001
DBP, mmHg					
Daytime*	83	10.34	78	10.57	0.15
Nighttime*	65	7.80	71	11.09	0.061
MAP, mmHg					
Daytime*	104	7.80	99	8.18	0.061
Nighttime*	84	7.40	92	10.80	0.008
HR, beats/min					
Daytime*	75	9.75	77	11.15	0.70
Nighttime*	66	8.91	68	7.94	0.60

*The P-value is the level of significance at α=0.05. *Based on subject's self-recorded awake/asleep periods. ABPM Ambulatory blood pressure monitoring; DBP Diastolic blood pressure; MAP Mean arterial pressure; SBP Systolic blood pressure*

The 47 women who participated in the study had a mean age of 57±13.9 years (Table 1). Thirty-four of the women were diagnosed with essential hypertension, and 13 had office hypertension and were undergoing a diagnostic 24 h ABPM test for hypertension. Although all women did not have an initial diagnosis of hypertension and were not receiving antihypertensive medication at the time of enrolment in the study, based on the Canadian Hypertension Education Program recommendations for the management of hypertension (37), individuals may be considered as hypertensive if the mean awake SBP is 135 mmHg or greater, the mean awake DBP is 85 mmHg or greater, the mean 24 h SBP is 130 mmHg or greater, or the mean 24 h DBP is 80 mmHg or greater. According to these criteria, women not receiving antihypertensive therapy could be considered as hypertensive (Table 2).

The sample consisted of 31 women (66%) who were classified as dippers and 16 (34%) who were classified as nondippers based on their 24 h ABPM records and self-reported awake and asleep periods. Additionally, the dipping status of subjects who reported getting out of bed at night was re-evaluated based on the removal of the BP measurement associated with the time that they were out of bed. However, removing the nighttime BP measurement that accorded with a woman getting out of bed at night did not affect the classification of dipping status. Therefore, the mean BP values represent all BP recordings throughout the 24 h period (Table 1).

TABLE 2
Ambulatory blood pressure (ABP) and antihypertensive therapy

	Antihypertensive therapy	
ABP, mmHg	Yes (n=29)	No (n=18)
Awake SBP	137	136
Awake DBP	77	87
Asleep SBP	122	116
Asleep DBP	65	71
24 h SBP	132	129
24 h DBP	73	82

Data presented as the mean. DBP Diastolic blood pressure; SBP Systolic blood pressure

TABLE 3
Demographic characteristics of dippers and nondippers

Variable	Dippers (n=16)	Nondippers (n=31)	P
Ethnicity, n (%)			0.65
Caucasian	27 (87.1)	15 (93.8)	
Non-Caucasian*	4 (12.9)	1 (6.2)	
Marital status, n (%)			0.46
Partner†	20 (64.5)	12 (75)	
No partner‡	11 (35.5)	4 (25)	
Menopausal status, n (%)			0.003
Postmenopausal§	15 (48.4)	15 (93.8)	
Premenopausal¶	16 (51.6)	1 (6.2)	
Antihypertensives, n (%)			0.18
Receiving	17 (54.8)	12 (75)	
Not receiving	14 (45.2)	4 (25)	
Diuretic, n (%)			0.6
Receiving	13 (41.9)	8 (50)	
Not receiving	18 (58.1)	8 (50)	
Calcium channel blocker, n (%)			0.08
Receiving	5 (16.1)	7 (43.8)	
Not receiving	26 (83.9)	9 (56.2)	
Beta blocker, n (%)			0.24
Receiving	4 (12.9)	5 (31.2)	
Not receiving	27 (87.1)	11 (68.8)	
Angiotensin-converting enzyme inhibitor, n (%)			0.50
Receiving	9 (29)	3 (18.8)	
Not receiving	22 (71)	13 (81.2)	
Angiotensin II receptor blocker, n (%)			0.10
Receiving	6 (19.4)	7 (43.8)	
Not receiving	25 (80.6)	9 (56.2)	
Hormone replacement therapy, n (%)			1.0
Receiving	2 (6.4)	1 (6.3)	
Not receiving	29 (93.5)	15 (93.7)	
Sleeping aids, n (%)			1.0
Receiving	2 (6.4)	1 (6.3)	
Not receiving	29 (93.5)	15 (93.7)	

*The P-value is the level of significance at α=0.05. *Non-Caucasian represents African Nova Scotians and other ethnicities; †Married or common-law partner; ‡Single, divorced, separated or widowed; §Did not have a menstrual period within the past 12 months or had a hysterectomy with both ovaries removed; ¶Had a menstrual period within the past 12 months*

On univariate analysis, nondippers were found to be significantly older than dippers (P<0.05). Additionally, the mean nighttime SBP and daytime and nighttime mean arterial pressures were significantly higher among nondippers than dippers (Table 1). Nondipping was also associated with menopausal status (P<0.005). No significant differences in ethnicity, marital status or current medications (BP, HRT, sleeping aids) were observed between dippers and nondippers (Table 3).

TABLE 4
Perceived stress, sleep quality and dipping status

	Dippers (n=31)	Nondippers (n=16)	P
Perceived stress score, mean ± SD	21.6±5.80	17.7±6.0	0.036
Sleep quality visual analogue scale, mm, mean ± SD	57.2±26.8	59.8±24.8	0.67
Sleep quality visual analogue scale (categories)*, n (%)			0.47
Quartile 1	10 (32.2)	2 (12.5)	
Quartile 2	7 (22.6)	6 (37.5)	
Quartile 3	7 (22.6)	4 (25.0)	
Quartile 4	7 (22.6)	4 (25.0)	
Bed status, n (%)			0.58
Not out of bed	11 (35.5)	7 (43.8)	
Out of bed once or more	20 (64.5)	9 (56.2)	

*The P-value is the level of significance at α=0.05. *Quartiles were computed by a frequency analysis (quartile 1 ranges from 0 mm to 39.0 mm; quartile 2 ranges from 39.1 mm to 62.0 mm; quartile 3 ranges from 62.1 mm to 79.0 mm; and quartile 4 ranges from 79.1 mm to 100 mm)*

The mean stress scores reported by dippers were significantly (P<0.05) higher than the mean scores reported by nondippers. There were no significant differences in sleep quality observed between dippers and nondippers. Additionally, the number of times the subjects were out of bed during the night (eg, using the bathroom) was not significantly different between dippers and nondippers (Table 4).

Correlational analysis was performed (data not shown). All of the correlations (r) were less than 0.5, except for the correlation between age and menopausal status, which yielded r=0.715 and supports the intuitive relationship between these factors. However, Paulson (38) has noted that correlation values of 0.90 and higher potentially indicate correlation problems, but often, the correlations do not become severe until r>0.95. Therefore, based on the correlation between age and menopausal status, collinearity is not a problem. Additionally, collinearity diagnostic statistics (tolerance and variance inflation factor) were used to detect collinearity in the regression model. The collinearity statistics were greater than 0.4 for tolerance and less than 2.5 for variance inflation factor. These values suggest that multicollinearity was not a concern among the independent variables.

Postmenopausal status was found to be a significant (P<0.05) predictor of nondipping status in the logistic regression. Based on this analysis, postmenopausal women were 16 times more likely to be nondippers than premenopausal women (Table 5).

An interaction between age and menopausal status was considered in the logistic regression. To create an interaction term for age and menopausal status, age was converted into a categorical variable (based on 10-year intervals) and included in the logistic regression analysis along with the other independent variables. However, the interaction term was not found to significantly contribute to the model.

DISCUSSION

A total of 47 women with office or essential hypertension who were referred to the hypertension unit of a Regional Health Authority in Atlantic Canada participated in the present study. Twenty-four hour ABPM and patient-recorded awake and asleep times were used to determine BP dipping status. Subjects also completed questionnaires to measure stress and sleep quality. Data from these questionnaires were used to examine the ability of stress and sleep quality to predict nighttime BP dipping status. Demographic data regarding age, ethnicity, marital status, menopausal status and current medications (BP, HRT, sleeping aids) were examined, revealing that dippers and nondippers differed significantly by age and menopausal status. Women with a nondipping BP pattern were significantly older and more likely to be postmenopausal.

The mean age of the hypertensive women with a dipping BP pattern was 54.0 years. The mean age of the hypertensive women with a nondipping BP pattern was 62.7 years (P<0.05). A tendency for nondippers to be older than their dipper counterparts is consistent with the results of several cross-sectional studies (11,39,40) and a retrospective analysis of a large international (n=7860) database (4).

In the present study, dippers and nondippers differed significantly by menopausal status (P=0.003). Additionally, menopausal status was the only independent variable found to significantly predict nondipping status. Postmenopausal women were 16 times more likely for nondipping than premenopausal women (OR 16; 95% CI 1.9 to 136.4). The large CI reflects the small size of the study sample. However, it should be noted that although the CI is wide, it is significant. Even at the lower end of the CI, postmenopausal women were almost twice as likely to be nondippers. Considering that when compared with a normotensive dipping group, hypertensive nondippers, hypertensive dippers and normotensive nondippers have been found to have relative hazard ratios for cardiovascular mortality of 10.4, 5.98 and 5.41, respectively, we believe that our finding is clinically significant (14).

In a study by Sherwood et al (41) that studied pre- and postmenopausal women with normal and slightly elevated BP, postmenopausal women were also found to experience a smaller dip in nighttime BP. It is known that after menopause, women experience more drastic BP increases than men of the same age, suggesting that the changes in estrogen levels accompanying menopause may have an effect on age-related BP elevation (42). It is possible that changes in estrogen levels associated with menopause may have had an effect on dipping status in the present study.

Researchers have also reported that postmenopausal hypertensive women receiving HRT experienced more frequent nocturnal BP dipping than women not receiving HRT (42). In the present study, no differences were observed in nocturnal BP dipping status between HRT users and nonusers. However, only three of the 15 (20%) postmenopausal women in the present study were receiving HRT. In view of the small number of women receiving HRT, it is not surprising that no differences in dipping status were observed between women taking HRT and those not taking HRT.

We hypothesized that stress had a direct relationship with nondipping BP. The PSS14 (31) was used to measure stress because it measures perceived stress. The results of the statistical analysis found that stress did not have a direct relationship with nondipping BP. In the present study, women with office or essential hypertension who exhibited a nocturnal BP dipping pattern had significantly greater perceived stress scores than those who exhibited a nocturnal nondipping BP pattern (P<0.05). This finding is contradictory to the results of other studies, which found that nondippers have increased physiological measures of stress including greater urinary epinephrine (18) and norepinephrine levels (18,20) throughout the night. It should be noted that in the present study, psychological stress, rather than physiological stress, was examined. Additionally, in a study of social support and ambulatory BP, Piferi (43) found that college students who reported greater social support also had greater nighttime BP dipping and less stress. However, a significant relationship between stress and a nighttime nondipping BP pattern was not reported. Ituarte et al (44) also examined stress and nondipping, and found that, among normotensive subjects, greater stress was associated with greater nighttime nondipping of heart rate but not of BP.

In light of these findings, there is reason to suspect that there are fundamentally different physiological mechanisms that explain this nondipping phenomenon. There is debate surrounding the hemodynamic variations in individuals with dipping or nondipping BP patterns (45,46). Future research should focus on the underlying hemodynamic mechanisms of dipping status. The identification of specific hemodynamic mechanisms associated with the nondipper BP pattern could influence the choice of antihypertensive medication regimens. It may be possible for treatments to be tailored to individuals with a nondipping BP pattern. In this way, antihypertensive medication would not only treat hypertension but also potentially restore a dipping BP pattern. Additional research is also needed to determine whether restoration of dipping status is associated with reduced cardiovascular morbidity and mortality.

TABLE 5
Prediction of dipping status based on logistic regression analysis

Variable	β	SEM	Wald	df	P	OR	95% CI
Menopausal status*	2.773	1.094	6.428	1	0.011	16.0	1.876–136.441
Constant	–2.773	1.031	7.235	1	0.007	0.063	

*The P-value is the test of significance of the Wald statistic (calculated as ratio of the estimated coefficient (β) to SEM²). *Premenopausal=0; postmenopausal=1. df Degrees of freedom*

In the present study, dipping and nondipping women did not differ in their rating of sleep quality. This finding is in contrast to those reported in other studies in which poorer sleep quality was associated with nondipping BP, as determined by actigraphic (30) and polysomnographic data (47). Additionally, individuals with a nondipping BP pattern have also been found to report poorer sleep quality on subjective measures of perceived sleep (48). One possible reason for this inconsistent finding may be that the sleep quality VAS used in the present study was not a standardized assessment tool (44).

It is acknowledged that antihypertensive therapy can be a confounder of dipping status. There is evidence to suggest that nighttime dosing (49-51) and diuretic therapy (52) may alter the nighttime BP pattern. However, researchers of population-based studies examining the prognostic implications of ambulatory BP have found that a less than 10% decline in nighttime BP is associated with an increased risk of all-cause mortality (15) and cardiovascular mortality (14). In both prognostic studies, between 30% (14) and 58% (15) of the subjects were receiving antihypertensive therapy.

It was deemed unethical to take patients off of their medication for participation in the present study. The study was designed to examine nondipping status among hypertensive women as they are normally found when referred to the hypertension clinic for ABPM. The study was not powered to find a difference among antihypertensive therapies with regard to dipping status. Exclusion criteria were used to control for some variability.

Limitations

Limitations of the present study should also be noted. One of the major limitations is that only women were included in the study, and data analysis was based on cross-sectional data. Therefore, results are not generalizable to men or normotensive women. Additionally, the present study included the use of questionnaires to evaluate subjective measures of stress and sleep quality. Although questionnaires are the oldest established method of investigation of psychological characteristics, they are subjective measures and retrospective in nature (53).

Access to all participants' medical charts was not possible because many of the participants were referred to the hypertension unit for ABPM by their family physician and/or had not previously received treatment at this Regional Health Authority in Atlantic Canada. The health history was often based on self-reports and therefore, was subject to recall bias.

Another limitation of the study was that daytime sleeping was not documented. It is possible that daytime sleeping could interfere with assessment of dipping status. In the study, BP was recorded every 30 min during the daytime period (07:00 to 22:00) and every 1 h during the nighttime period (22:00 to 07:00) as per the policy of the hypertension unit where the study took place. It is possible that more frequent ABPM recordings, especially during the night, could capture the effect of activity on dipping status. Although there is no consensus on the frequency of ABPM recordings, several researchers have used 15 min to 30 min intervals during the day and 20 min to 30 min intervals during the night

(48,54). However, a recent study reported no significant difference in mean BP if one, two or three recordings per hour were used (55).

Additionally, of the 61 women invited to participate in the study, 11 (18%) refused to participate and three did not complete the study. It is possible that the women who chose not to participate or complete the study would have had different results from the women who chose to participate in the study.

A further limitation of the study was the small sample size. As with most studies, the sample size is based on the primary outcome. The primary outcome variable of the study was stress. The statistical power of the study was calculated to be 86.4% at the 0.05 level of significance. The study had enough power to detect the smallest worthwhile effect between stress and dipping status 86.4% of the time. Therefore, the type II error rate (false-negative rate) was 13.6% for rejecting an effect between stress and dipping status. However, the smaller the sample size for a study, the more likely it is that a type II error will occur. Similar to other studies, the present study was not powered to examine differences between each secondary independent variable and dipping status. Therefore, we may have committed some type II errors and accepted that there were no differences, when there were actually differences among the secondary independent variables and dipping status.

CONCLUSION

A total of 47 women with office or essential hypertension wore an ABPM to record BP for 24 h. For each participant, nocturnal BP dipping status was evaluated based on self-reported awake and asleep times, and nighttime activity. Thirty-one women were classified as having a dipping BP pattern and 16 were classified as having a nondipping BP pattern. The dipper and nondipper groups were compared with regard to stress, age, ethnicity, marital status, menopausal status, current medications and sleep quality. Nondippers tended to be older and postmenopausal, and had lower stress scores than their dipping counterparts. A logistic regression analysis revealed that postmenopausal status significantly predicted nondipping BP status. The findings of the present study suggest that this nondipping phenomenon may not be explained by psychosocial factors. Therefore, it is possible that dippers and nondippers have fundamentally different physiological mechanisms that explain nighttime BP patterns. In the future, identification of specific hemodynamic mechanisms associated with nondipping could potentially influence the choice of antihypertensive treatment regimens for nondipper hypertensive patients.

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