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Hemoglobin A1c and C-Reactive Protein are Independently Associated with Blunted Nocturnal Blood Pressure Dipping in Obesity-Related Prediabetes

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Abstract

Blunted nocturnal dipping in blood pressure (BP) is associated with increased cardiovascular disease (CVD) risk in middle-aged/older adults. The prevalence of blunted nocturnal BP dipping is higher in persons with obesity and diabetes, conditions that are also associated with elevated aortic stiffness and inflammation. Therefore, we hypothesized that elevated glycemia, inflammation and aortic stiffness would be inversely associated with the magnitude of nocturnal systolic BP dipping among middle-aged/older adults with obesity at elevated CVD risk. Twenty-four-hour ambulatory

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Conflicts of interest: None

BP monitoring, aortic stiffness (carotid-femoral pulse wave velocity, CF-PWV), hemoglobin A1c (HbA1c) and inflammation (c-reactive protein, CRP) were measured in 86 middle-aged/older adults with obesity and at least one other risk factor for CVD (age 40–74 yrs; 34M/52F; BMI=36.7 ± 0.5 kg/m^2; HbA1c=5.7 ± 0.04%). In the entire cohort, CRP (β=0.40 ± 0.20, p=0.04), but not HbA1c or CF-PWV was independently associated with BP dipping percent (Model R^2=0.07, p=0.12). In stratified (i.e., presence or absence of prediabetes) multiple linear regression analysis, HbA1c (β=6.24 ± 2.6, p=0.02) and CRP (β=0.57 ± 0.2, p=0.01), but not CF-PWV (β=0.14± 2.6, p=0.74), were independently associated with BP dipping percent (Model R^2=0.32, p<0.01) in obese adults with prediabetes but were absent in obese adults without prediabetes (Model R^2=0.01 p=0.95). However, nocturnal systolic BP dipping percent (p=0.65), CF-PWV (p=0.68) and CRP (p=0.59) were similar between participants with and without prediabetes. These data suggest that impaired long-term glycemic control and higher inflammation may contribute partly to blunted BP dipping in middle-aged/older adults with obesity-related prediabetes.

Keywords

inflammation; ambulatory blood pressure monitoring; pulse wave velocity

Introduction

A decline in systolic blood pressure (BP) ≥10% at night during sleep is a normal physiological phenomenon referred to as nocturnal BP “dipping”. A blunted decline in nocturnal systolic BP (i.e., ‘non-dipping’) is associated with target organ damage such as increased left ventricular mass and central arterial stiffness [1–3] and heightened cardiovascular disease (CVD) mortality, independent of average 24-hr systolic BP [4]. However, the mechanisms underlying blunted nocturnal systolic BP dipping remain unclear.

The nocturnal non-dipping BP pattern is more prevalent in obesity [5] and the prevalence of non-dipping in individuals with diabetes may be as high as 30% [6]. In addition, individuals with obesity are more likely to exhibit higher systemic inflammation compared to normal weight adults [7, 8]. This is important because inflammation likely contributes to the development of CVD in obesity in part because of insulin resistance and vascular dysfunction including aortic stiffness [8, 9], a robust independent predictor of CVD risk in middle-aged/older adults [10, 11]. Moreover, the combination of obesity and metabolic dysfunction results in the greatest risk for CVD and death, underscoring the importance of glycemic control for CVD risk management in obese adults with early stage type 2 diabetes (i.e., prediabetes) [12].

Given that 86 million Americans have prediabetes [13], more than double the number with diagnosed type 2 diabetes [13, 14], it is important to identify modifiable risk factors to attenuate CVD risk in this group. However, whether the prevalence of blunted nocturnal systolic BP dipping is higher in obese adults in the presence or absence of prediabetes is unknown. Furthermore, the intermediary mechanisms that might contribute to abnormal systolic BP dipping in obesity-related prediabetes have not been explored.

The purpose of the study was to determine whether systemic inflammation, recent glycemic control and aortic stiffness were independently associated with nocturnal BP dipping in a cohort of middle-aged/older adults with obesity and at high CVD risk. We hypothesized that elevated glycemia (hemoglobin A1c, HbA1c), inflammation (c-reactive protein CRP), and aortic stiffness (carotid-femoral pulse wave velocity, CF-PWV) would be inversely associated with the magnitude of nocturnal systolic BP dipping (dipping percent) among middle-aged/older adults with obesity. Second, we also hypothesized that the associations between HbA1c, CRP and CF-PWV would be selective to obese persons with prediabetes. This is clinically important because this would provide evidence that impaired long-term glycemic control, inflammation and arterial stiffness may contribute to blunted nocturnal systolic BP dipping which has been linked to subclinical and overt CVD [1, 2, 4]) in obesity.

Research Design and Methods

Study Design

Ninety-nine middle-aged/older adults were recruited but complete data were available in 86 of these individuals (34 male/52 female) for analyses. The analyses used baseline data in 86 middle-aged/older adults (age 40–75 years) with obesity who were recruited as part of a pharmacological weight loss study (Clinical Trials.gov study NCT01351753) and 24 hour ambulatory BP monitoring was done at baseline. Participants were included in the study if they were obese, defined as having a body mass index (BMI) ≥ 30 kg/m^2, and had at least one additional CVD risk factor such as hypertension, hyperlipidemia, hyperglycemia or metabolic syndrome or who were being treated for a CVD risk factor with anti-hypertensive medications or anti-hyperlipidemia medications. Participants were excluded if they had a history of smoking cessation within the past 3 months, had a diagnosed atherosclerotic event within the past 6 months, had congestive heart failure (WHO class III or IV), had renal impairment defined as serum creatinine ≥1.4 mg/dL (females) or ≥1.5 mg/dL (males), or if they were currently involved in any weight loss or formal vigorous exercise program. All women were postmenopausal of whom eight were on hormone replacement therapy: transdermal patch and removed the patch 24 hours prior to the experimental visit (n=3); oral hormone replacement therapy and went off for one month prior to measurements (n=2); intravaginal cream or tablets for postmenopausal symptoms (n=3). Fifteen participants were taking levothyroxine with doses ranging from 50–150 mcg/day and had normal TSH concentrations at time of study. The study was approved by the University of Iowa Institutional Review Board and all participants signed written informed consent.

Experimental visit

Participants reported to the University of Iowa Institute for Clinical and Translational Science Clinical Research Unit after an overnight 8-hr fast. Height and weight were measured and a fasting venous blood sample was obtained. Following 15 min of supine rest, blood pressure and aortic stiffness using pulse wave analysis were measured (see below for details). Participants were fitted and started to wear a 24-hr ambulatory BP monitor at the end of the visit and instructed to wear the monitor for 24 hours. As a result of scheduling, in some instances participants wore the 24-hr ambulatory BP monitor prior to the experimental visit.

Body Mass Index

Height and weight were measured with participants wearing a standard gown and no shoes and after participants emptied their bladder. Measurements were done using a stadiometer and a digital scale by a trained nurse. Body mass index (BMI) was calculated by dividing weight (in kg) by height (in m^2).

24-hour Ambulatory Blood Pressure

Ambulatory BP monitoring (ABPM) was performed for 24-hr with a cuff on the non-dominant arm (Space Labs, Inc.). Participants were instructed to record their activities and sleep periods for the 24-hr monitoring period. Blood pressure was measured every 30 min during the day from 0600–2300 and nighttime (i.e., "nocturnal") BP was recorded every 60 min from 2300–0600. Daytime and nocturnal BPs were determined from these fixed times. Participants had to have at least 10 daytime readings and 5 nighttime readings and at least 80% successful readings of planned measurements over the 24 hours. The percent (%) of nocturnal systolic BP dipping was calculated as:

$$\frac{\text{Nocturnal systolic BP} - \text{Daytime systolic BP}}{\text{Daytime systolic BP}} \times 100\%.$$

Aortic stiffness

Carotid-femoral PWV, the 'gold standard' measurement of aortic stiffness, was obtained non-invasively by applanation tonometry (Sphygmocor, AtCor Medical, Inc.) as previously described [15, 16]. ECG-gated pulse waveforms of the carotid, femoral and radial arteries were recorded sequentially and PWV was calculated as path length (L) divided by time delay (t) between sites (PWV=L/t). L was calculated as distance from the suprasternal notch to femoral minus the distance from the suprasternal notch to carotid artery. The peak of the R wave from the simultaneously recorded ECG was used as a timing marker. Within-subject coefficient of variation for cfPWV in our laboratory is 2.1% for 9 adults measured on two visits separated by one week.

Circulating factors

Circulating concentrations of fasting insulin, glucose, HbA1C, cholesterol, and triglycerides were measured in venous blood sample by the University of Iowa Diagnostic Laboratory by standard techniques. C-reactive protein (CRP) was measured by the University of Iowa Diagnostic Laboratory by a high-sensitivity turbidimetric method with a minimal detection level of 0.2 mg/L. Prediabetes was defined as an HbA1C value ≥ 5.7 and not being treated with any antidiabetic drugs. HOMA-IR was calculated as follows: insulin (mU/ml) * glucose (mg/dl) / 405.

Risk of Obstructive Sleep Apnea

Because nocturnal BP and metabolic health[17] can be influenced by presence of obstructive sleep apnea (OSA), we used the Berlin Survey to determine whether participants had high risk of OSA. This survey has been validated and used in other cohort studies. Briefly, participants were categorized as high or low risk for OSA based on their responses to

questions regarding snoring, daytime sleepiness, and CV risk factors as previously described [18]. Complete data on likelihood of OSA at the time of vascular measurements and ABPM was available in 42 participants.

Statistics

Normality of distribution for variables of interest was assessed using Shapiro-Wilkes tests. Differences between adults with and without prediabetes were evaluated using un-paired t-tests or Wilcoxon rank-sum tests for non-normally distributed variables and chi-square tests for categorical variables. Univariate correlations of nocturnal systolic dipping percent and established CVD risk factors were assessed using Spearman correlations. Associations between arterial stiffness, circulating factors, and nocturnal systolic BP dipping were evaluated using multivariable regression, first in the entire cohort and then stratified by pre-diabetes status because of the well-characterized effect of diabetes on nocturnal systolic BP dipping [19, 20]. A third multivariable model was constructed to adjust for known modifiers of BP and nocturnal dipping. We also tested for associations between these factors and average nocturnal systolic BP as nocturnal BP is associated the CV and non-CV mortality. A residuals versus fitted plot was constructed for each significant predictor variable to assess the assumptions of linearity and homoscedasticity. A sensitivity analysis was performed on a subset of participants that excluded those with possible undiagnosed diabetes (HbA1c ≥ 6.5%) and CRP level >2 SD from the mean. Significance was set at $P<0.05$ and STATA version 14 (College Station, TX) was used for all statistical analyses.

Results

Participants

Characteristics of the cohort of the eighty-six individuals with obesity and at least one CVD risk factor (34 male/52 female) used for analyses are listed in Table 1. Thirty-eight percent of all participants were taking renin-angiotensin-aldosterone system (RAAS) antagonists. However, the proportion of participants taking RAAS antagonists was the same (38%) in participants with and without prediabetes (p=1.00).

Bivariate Correlational and Regression Analyses in Entire Cohort

No traditional CVD risk factors significantly correlated with nocturnal systolic BP dipping percent in our cohort (p>0.13 for all). Among our hypothesized predictors, CRP (r=0.25, p=0.015) but not CF-PWV (r=0.11, p=0.29) or HbA1c (r=0.13, p=0.215) was correlated with nocturnal systolic BP dipping in the entire cohort. In a multivariable analysis including CRP, HbA1c, and CF-PWV conducted in the entire cohort, only CRP was associated with nocturnal systolic BP dipping percent (β=0.40, p=0.04) (Table 2).

Participants Stratified by the Presence or Absence of Prediabetes

Of the 86 participants, 50 had prediabetes, defined as HbA1C ≥ 5.7 % and not taking antidiabetic medication [21], and 36 did not have prediabetes (Table 3). Participants with prediabetes were slightly older than participants without prediabetes (p=0.01), but BMI did not differ by prediabetes status (p=0.59). Clinic, daytime, and nocturnal BP and CF-PWV were similar in adults with and without prediabetes (all p>0.05, Table 3). Nocturnal systolic

BP dipping percent was the same in adults with (−10.5 ± 6.4%) and without (−9.9 ± 6.1%) prediabetes (p=0.65, Table 3). Three participants with prediabetes and one participant without prediabetes were “risers”, i.e., their nocturnal systolic BP was higher than their daytime systolic BP and their dipping was positive. Four participants with prediabetes and one participant without prediabetes were extreme dippers; their systolic BP dipped more than 20% at night. There was no difference in the proportion of participants with either pattern by prediabetes status (p>0.47 for both comparisons).

Fourteen participants without prediabetes and 15 participants with prediabetes had high risk of OSA (p=0.12 for difference between groups).

Bivariate Correlational and Regression Analyses in Participants With or Without Prediabetes

In individuals with prediabetes, CRP (r=0.34, p=0.015) and HbA1c (r=0.26, p=0.05), but not CF-PWV (r=0.09, p=0.51), were correlated with nocturnal systolic BP dipping percent in bivariate correlational analysis. In contrast, in individuals without prediabetes none of the hypothesized predictors correlated with nocturnal systolic BP dipping percent: CRP (r= −0.15, p=0.36) HbA1c (r=0.01, p=0.95), CF-PWV (r= −0.05, p=0.79). In the stratified unadjusted regression analysis with HbA1c, CRP and CF-PWV in the model, HbA1c (β=6.24, p=0.02) and CRP (β=0.57, p=0.01), but not CF-PWV (β=0.14, p=0.74), were independently associated with nocturnal systolic BP dipping percent in adults with prediabetes (Table 4A). These associations were absent in middle-aged/older adults without prediabetes (Table 4B). In a third stratified model in which we controlled for age, sex, average 24-hr systolic BP, and anti-hypertensive and lipid-lowering medication usage, the associations between CRP (β=0.57, p=0.12) and HbA1c (β=7.35, p=0.19) with nocturnal systolic dipping percent remained significant (Table 4C).

To investigate whether indices of short-term glucose/insulin control or OSA were also associated with nocturnal systolic BP dipping percent, fasting insulin (β=0.32, p=0.612), fasting glucose (β=0.15, p=0.267), fasting HOMA-IR (β= −1.5, p=0.571) were not associated with nocturnal systolic BP dipping percent in the whole cohort, with similar findings in stratified analyses (Supplemental Table 1). OSA status was not associated with nocturnal systolic BP dipping percent in the whole cohort (β=0.35 ± 2.2, p=0.87) or in stratified analyses.

Because we had 3 statistical outliers (>2 SD from the mean) for our CRP measurement, one individual with an extreme reverse dipping pattern (+15% compared to daytime systolic BP), and 2 individuals with HbA1c>6.5%, the cut-off for diabetes, we conducted a sensitivity analysis by performing the regression with these individuals omitted (n=80, 35 without prediabetes and 45 with prediabetes). Our results remained the same: HbA1c (β=9.87, P=0.027) and CRP (β=0.97, p=0.006) but not CF-PWV (β=0.02, p=0.96), were independently associated with nocturnal systolic BP dipping percent in adults with prediabetes (Model R^2=0.26, p=0.006). These associations remained absent in adults without prediabetes, neither HbA1c (β= −2.38, p=0.41), CRP (β=0.07, p=0.78), nor CF-PWV (β=0.16, p=0.71) associated with nocturnal dipping percent (Model R^2=0.03, p=0.82).

There was no association between clinic systolic BP and nocturnal systolic dipping percent(β=0.14 ± 0.04, p=0.76). Finally, to test whether CRP, HbA1c, and CF-PWV were also associated with average nocturnal systolic BP, in a multivariable model including age, sex, BMI, anti-hypertensive medication usage, CRP, HbA1c, and CF-PWV, only CF-PWV was associated with average nocturnal systolic BP; β=1.97 ± 0.8, *p*=0.01 in the whole cohort, driven by the prediabetes group in stratified analyses (Supplemental Table 2).

Discussion

The primary findings of the current study are that higher HbA1c and circulating CRP concentrations are independently associated with less nocturnal systolic BP dipping % only in individuals with obesity and prediabetes even after adjusting for age, sex, average 24-hr systolic BP, and anti-hypertensive medication usage. There was no relation between systolic BP dipping percent with short-term indices of glycemia (fasting glucose) or insulin resistance (fasting insulin and HOMA-IR) among obese adults without prediabetes. These findings suggest that CVD risk conferred by impaired longer-term glycemic control (HbA1c) not only directly contributes to elevated arterial stiffening and daytime BP as previously described [22], but that elevated glycemia may also interfere with normal physiological nocturnal BP dipping in obesity. Furthermore, these results indicate that once middle-aged/older adults with obesity have prediabetes, small incremental increases in HbA1c may be associated with significantly more blunting of nocturnal systolic BP dipping compared to those without prediabetes. It reasons that even small improvements in HbA1c may improve nocturnal systolic BP dipping in middle-aged/older persons with obesity-related prediabetes. The study also supports the role of systemic inflammation as either a mediator of blunted nocturnal BP dipping or an identifier of overall higher risk among this sub-group of obese adults with prediabetes. Thus, whether reducing systemic inflammation would also attenuate blunted nocturnal systolic BP dipping in this group will require additional studies to test these hypotheses.

Blunted nocturnal systolic BP dipping is more common in persons with obesity [5] and the prevalence of blunted nocturnal systolic BP dipping in type 2 diabetes is over 30% [6]. Nighttime systolic BP is also predictive of CV mortality in individuals with diabetes [23], but whether this is true for adults with prediabetes is unclear. Surprisingly, in the current cohort we found that the nocturnal BP dipping percent was not different between obese adults with and without prediabetes. However, among the obese persons with prediabetes defined as an HbA1C ≥5.7%, HbA1C was independently associated with blunted nocturnal systolic BP dipping (β=7.35, P=0.010), suggesting that impaired long-term glycemic control may affect systolic BP dipping in obese persons with prediabetes. Consistent with this, biomarkers associated with short-term glucose control (e.g., fasting glucose, insulin, HOMA) were not associated with nocturnal systolic BP dipping in our whole cohort or by prediabetes status. This suggests that longer-term, and not short-term glycemic control, potentially modulates nocturnal systolic BP dipping in obese adults with prediabetes. This finding is not entirely unexpected as short-term biomarkers are highly variable and may be affected by the patient's recent dietary intake, physical activity or length of fasting.

Circulating CRP, a biomarker of systemic inflammation and CVD risk, is elevated in persons with obesity [24]. In addition, higher CRP is associated with increased arterial stiffness in middle-aged/older adults [25] that are both elevated in individuals with obesity [24]. Anti-inflammatory therapy is associated with reductions in aortic stiffness and aortic inflammation supporting the idea that inflammation plays a key role in aortic remodeling and stiffness [26]. Arterial stiffness is associated with less nocturnal systolic BP dipping among adults with hypertension [1, 27], but prior to our study it was unknown if higher inflammation and arterial stiffness could be potential intermediary mechanisms that modulate alterations in nocturnal BP dipping among older adults with obesity. Taken together, our results and others indicate that systemic inflammation among obese adults with prediabetes may be one intermediary mechanism for blunted nocturnal BP dipping but prospective studies with follow up or anti-inflammatory intervention studies will be needed to confirm this finding.

Because of the association of average nocturnal systolic BP and CVD risk, we investigated whether HBA1c, CRP and CF-PWV were associated with average nocturnal systolic BP itself (as opposed to just percent dipping). There was an independent association between aortic stiffness and average nocturnal systolic BP, independent of age and BMI. Given that aortic stiffness has been purported to precede incident hypertension and aortic stiffness improves risk prediction for CV events in models with traditional CV risk factors, these results are not unprecedented [11, 28]. There was no association between clinical systolic BP and nocturnal dipping in our study, underscoring the importance of monitoring 24 hr blood pressure to assess CV risk. Our study suggests that higher aortic stiffness may contribute to overall CVD risk in part through its influence on nocturnal BP, but further studies are required to test this hypothesis.

A limitation of our study is the use of data collected at a single time point in a relatively small sample. This may have limited our ability to detect small to mid-sized effects. We included information regarding the likelihood of sleep apnea in our study, but we did not obtain this measurement on all participants. Therefore, we may not have captured the true prevalence of sleep apnea in our cohort. The cross-sectional design does not allow us to determine cause and effect between HbA1c or CRP with nocturnal systolic BP dipping in the cohort with prediabetes. Longitudinal data would be useful to assess how changes in HbA1c and CRP at multiple time points alter nocturnal systolic BP dipping profiles within the same person. We are unable to determine whether blunted nighttime systolic BP dipping is associated with mortality in obese persons with prediabetes, therefore, this should be examined in future investigations in prospective studies. Lastly, we did not record the timing of anti-hypertensive medication usage although most participants likely take the medications in the morning. Whether or not participants took medication immediately before bedtime may have affected their nocturnal BP. A strength of our study is the similarity of the well characterized cohort of persons with obesity at high CVD risk, and multivariable stratified models adjusting for important confounders.

In conclusion, in middle-aged/older adults with obesity and at least one other CVD risk factor, higher HbA1c and CRP are independently associated with less nocturnal systolic BP dipping selectively among those persons with prediabetes (defined by elevated HbA1c).

Prediabetes status itself did not affect the magnitude of nocturnal systolic BP dipping among obese adults. Our study has demonstrated that longer-term glycemic control and inflammation may contribute to CVD risk through their association with nocturnal BP dipping. Future studies are needed to determine if improvements in HbA1c and CRP in early stages of type 2 diabetes may improve normal physiological dipping of nighttime systolic BP and decrease CVD risk in this high-risk group.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Participant characteristics

n	86
Age (yrs)	56 ± 1
Female, n (%)	52 (60)
Prediabetes, n (%)	50 (58)
Body Mass Index (kg/m^2)	36.7 ± 0.5
Clinic Systolic Blood Pressure (mmHg)	128 ± 2
Clinic Diastolic Blood Pressure (mmHg)	73 ± 1
24 hr ABPM Daytime SBP (mmHg)	126 ± 1
24 hr ABPM Nocturnal SBP (mmHg)	114 ± 1
Antihypertensive Medication, n (%)	60 (70)
Lipid-lowering Medication, n (%)	31, 36
Nocturnal Systolic BP Dipping (%)	−10 ± 1
Carotid-Femoral PWV (m/s)	9.2 ± 0.2
Hemoglobin A1c (%)	5.7 ± 0.4
C-reactive Protein (mg/L)	4.0 ± 0.4
Total Cholesterol (mg/dL)	197 ± 4
LDL-C (mg/dL)	116 ± 4
HDL-C (mg/dL)	55 ± 2
Triglycerides (mg/dL)	142 ± 7
Insulin (mcU/ml)	15 ± 1
Fasting Glucose (mg/dL)	97 ± 1
HOMA-IR	3.6 ± 0.2
High Risk of OSA, n. (%)	29 (34)

Data are Mean ± SE or n (%). ABPM, ambulatory blood pressure monitoring; LDL, low-density lipoprotein; HDL, high-density lipoprotein; HOMA-IR, homeostatic model of insulin resistance; OSA, obstructive sleep apnea.

Table 2

Multivariable associations between nocturnal systolic blood pressure dipping percent and hemodynamic and clinical variables in entire cohort.

Predictor	B (SE)	*p*-value
HbA1c (%)	1.80 (1.7)	0.28
C-reactive Protein (mg/L)	0.40 (0.2)	0.04*
Carotid-femoral PWV (m/sec)	−0.02 (0.4)	0.99
		Model R^2=0.07, p=0.12

B, unstandardized regression coefficient; BP, blood pressure.

*P<0.05 variable significantly associated with nocturnal systolic blood pressure dipping percent .

Table 3

Clinical Characteristics of Study Participants Stratified by Prediabetes Status

	No Prediabetes (n=36)	Prediabetes (n=50)	*p*-value
Age (yrs)	53 ± 1	57 ± 1*	0.01
Female, n (%)	23 (68)	29 (58)	0.48
Body Mass Index (kg/m^2)	36.4 ± 0.9	37.0 ± 0.6	0.59
Clinic Systolic BP (mmHg)	130 ± 3	127 ± 2	0.40
Clinic Diastolic BP (mmHg)	74 ± 2	72 ± 1	0.19
24 hr ABPM Daytime Systolic BP (mmHg)	129 ± 1	125 ± 2	0.06
24 hr ABPM Nocturnal Systolic BP (mmHg)	116 ± 2	111 ± 2	0.07
Anti-hypertensive Medication, n (%)	27 (65)	33 (61)	0.72
Nocturnal Systolic BP Dipping (%)	−9.9 ± 1	−10.5 ± 1	0.64
Nocturnal Non-dippers, n (%)	16 (39)	27 (48)	0.37
Carotid-Femoral PWV (m/s)	9.1 ± 0.2	9.3 ± 0.3	0.82
Hemoglobin A1c (%)	5.40 ± 0.04	5.95 ± 0.05*	<0.001
C-reactive protein (mg/L)	3.6 ± 0.4	4.3 ± 0.6	0.58
Total cholesterol (mg/dL)	201 ± 6	196 ± 6	0.10
LDL-cholesterol (mg/dL)	116 ± 6	116 ±5	0.27
HDL-cholesterol (mg/dL)	57 ± 4	52 ± 2	0.63
Triglycerides (mg/dL)	136 ± 10	147 ± 9	0.47
Insulin (mU/ml)	12 ± 1.0	17 ± 1*	<0.01
Glucose (mg/dL)	94 ± 1	99 ± 2*	0.04
HOMA-IR	2.76 ± 0.25	4.25 ± 0.37*	<0.01
High Risk for OSA, n (%)	14 (39)	15 (30)	0.12

Data are mean ± SE. BP, Blood pressure; ABPM, ambulatory BP monitoring; PWW, pulse wave velocity; Anti-HT medication, use of anti-hypertension medication; HOMA, homeostatic model of insulin resistance, used to assess β-cell function and insulin resistance; OSA, obstructive sleep apnea.

*P<0.05 vs. prediabetes.

Table 4

Minimally adjusted associations between nocturnal systolic blood pressure dipping percent and hypothesized predictors in obese middle-aged/older adults with prediabetes (A) without prediabetes (B).

A. Prediabetes

Predictor	B (SE)	*p*-value
HbA1c (%)	6.24 (2.6)	0.02 *
C-reactive Protein (mg/L)	0.57 (0.2)	0.01 *
Carotid-femoral PWV (m/sec)	0.14 (0.4)	0.74
		Model R^2=0.22 p=0.009 *

B. No Prediabetes

Predictor	B (SE)	*p*-value
HbA1c (%)	0.43 (4.5)	0.93
C-reactive Protein (mg/L)	0.00 (0.4)	0.99
Carotid-femoral PWV (m/sec)	−0.37 (0.7)	0.58
		Model R^2=0.01 P=0.95

C. Multivariable adjusted associations between hypothesized predictors and nocturnal systolic blood pressure dipping percent in middle-aged/older adults with prediabetes

Predictor	B (SE)	*p*-value
HbA1c (%)	7.59 (2.8)	0.01 *
C-reactive Protein (mg/L)	0.58 (0.2)	0.02 *
Age (yrs)	−0.04 (0.01)	0.79
Sex (male)	−1.07 (2.2)	0.64
Body mass index (kg/m^2)	0.03 (0.2)	0.89
Average 24-hr systolic BP (mmHg)	−0.03 (0.07)	0.67
Lipid-lowering medication treatment (yes/no)	−1.76 (2.2)	0.42
Antihypertension medication treatment (yes/no)	0.38 (2.0)	0.85
		Model R^2=0.27 p=0.03 *

B: unstandardized regression coefficient; PWV: pulse wave velocity.

* P<0.05 variable or model significantly associated with noctumal systolic blood pressure dipping percent.