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Telemedicine Home Blood Pressure Measurements Predict Progression of Albuminuria in Elderly People with Diabetes

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Abstract

We assessed whether home blood pressure monitoring improved the prediction of progression of albuminuria when added to office measurements, and compared it to ambulatory blood pressure monitoring in a multiethnic cohort of older people (n=392) with diabetes mellitus, without macroalbuminuria, participating in the telemedicine arm of the Informatics for Diabetes Education and Telemedicine (IDEATel) study. Albuminuria was assessed by measuring the spot urine albumin-to-creatinine ratio at baseline and annually for three years. Ambulatory sleep/wake systolic blood pressure ratio was categorized as dipping (ratio≤0.9), non-dipping (ratio>0.9 -1), and nocturnal rise (ratio>1). In a repeated measures mixed linear model, after adjustment that included office pulse pressure, home pulse pressure was independently associated with higher follow-up albumin-to-creatinine ratio (p=0.001). That association persisted (p=0.01) after adjusting for 24-hour pulse pressure, and nocturnal rise, which were also independent predictors (p=0.02 and p=0.03, respectively). Cox proportional hazards models examined progression of albuminuria (n=74) as defined by cutoff values used by clinicians. After adjustment for office pulse pressure the hazards ratio (95% CI) per 10 mmHg increment of home pulse pressure was 1.34 (1.1-1.7), p=0.01. Home pulse pressure was not an independent predictor in the model including ambulatory monitoring data—a nocturnal rise was the only independent predictor (p=0.035). However, Cox models built separately for home pulse pressure and ambulatory monitoring exhibited similar calibration and discrimination. In conclusion, home blood pressure

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adds to office measurements and may substitute for ambulatory monitoring to predict worsening of albuminuria in elderly people with diabetes.

Keywords

Albuminuria; Diabetes mellitus; Home Blood Pressure; Ambulatory Blood Pressure

Introduction

Albuminuria is independently associated with cardiovascular morbidity and mortality in people with and without diabetes mellitus.[1-6] An increase in albuminuria is associated with higher cardiovascular morbidity and mortality,[7] whereas a decrease achieved through drug therapy is associated with better outcomes.[8] Albuminuria is prevalent in older and middle-aged people with type 2 diabetes mellitus,[9-11] in whom cardiovascular and renal complication rates are the highest.[12-14] Thus, it is of particular importance to identify predictors of worsening albuminuria in older people with diabetes mellitus.

Ambulatory Blood Pressure Monitoring (ABPM) predicts progression of albuminuria better than office blood pressure (BP) in people with diabetes,[15-19] and 24-hour pulse pressure (PP) and a nocturnal increase in blood pressure (BP) are the most informative variables in elderly diabetics.[18,19] However, ABPM is not yet considered standard of care for the management of hypertension. On the other hand, a growing number of patients are successfully monitoring their BP at home using oscillometric devices.[20,21] In longitudinal studies home monitoring outperformed office BP measurements in predicting cardiovascular events in hypertensive patients,[22-24] As noted above, progression of albuminuria is independently associated with cardiovascular risk, and may help identify patients at need for more aggressive clinical management. Therefore, it is important to determine whether home BP improves the prediction of worsening albuminuria in people with diabetes when added to office BP measurements, and how it compares to ABPM in that regard. Although cross-sectional studies have shown that the association of prevalent albuminuria with home BP is stronger than with office blood pressure[26] and comparable to that with ABPM,[27] to the best of our knowledge there have been no longitudinal studies examining the association with worsening albuminuria. We therefore tested the hypothesis that home BP improves the prediction of worsening albuminuria in people with diabetes above and beyond office BP, and compared the predictive information provided by home BP to that provided by ABPM. We carried out this study in a multiethnic cohort of people with diabetes, who performed self-monitoring of home BP as part of a telemedicine diabetes care intervention in a randomized controlled trial, and underwent ABPM at their baseline examination visit.

Methods

Study Participants

We studied participants enrolled in the intervention (telemedicine) arm of the multi-center Informatics for Diabetes Education and Telemedicine (IDEATel) Study, which has been described in detail elsewhere,[28] and which evaluates telemedicine as a means of managing the care of Medicare beneficiaries with diabetes.

This study analyzed relationships between blood pressure data obtained at the baseline exam, , and urinary albumin, measured by spot urine albumin-to-creatinine ratio, at three consecutive annual follow up visits. Only intervention participants who completed at least two follow-up visits and provided urine albumin measurements were included (n = 392). Details of the IDEATEL protocol are described in the online supplement.

Home BP Monitoring

Home BP was measured using an oscillometric device (UA-767 ; A&D Medical; Milpitas, CA). Participants were fitted with the appropriate-sized cuff during the baseline visit, and trained in the use of the BP monitor,. Participants were encouraged to take their BP measurements several times a day (at least twice) at different times, and while taking their usual antihypertensive medications. For these analyses we utilized home BP measurements obtained within 60 days of the office and ambulatory BP measurements.

Office BP Measurement

Office BP was measured at the baseline visit using the Dinamap Pro 100 (Critikon, Tampa, FL) automated oscillometric device. Participants were instructed to take their antihypertensive medications as usual the morning of the examination. Three measurements were obtained at one minute intervals in a seated position after 5 minutes of rest in a quiet room, using a standardized protocol.[29] The average of the second and third measurements was recorded as the resting BP. Office PP was defined as the difference between systolic and diastolic resting BP.

Ambulatory BP Monitoring

ABPM was performed at the baseline visit using a Spacelabs 90207 monitor (SpaceLabs, Redmond, WA) following a published protocol.[30] BP was recorded every 20 minutes for a 24hour period.. Sleep and wake intervals were defined from diary entries, and confirmed by a telephone interview on the morning when monitoring ended. A minimum of 6 valid wake readings and 4 valid sleep readings were required for the computation of wake and sleep averages (31). A reading was accepted as valid if it was non-artifactual and within physiologic range. The mean (SD) number of measurements per participant was 64.5 (8.3), while the minimum number was 32 (in one participant). Ambulatory 24-hour PP was defined as the mean difference between all systolic and diastolic BP readings. Nocturnal dipping was defined as a ratio of mean sleep to mean wake systolic BP (SBP) of 0.90 or lower (a decrease in sleep SBP of at least 10% relative to wake SBP). Non-dipping was defined as a ratio > 0.9 to 1.0, and a nocturnal rise was defined as a ratio > 1.0.[33]

Albumin-to-Creatinine Ratio

Albumin-to-creatinine ratio (ACR, milligrams of albumin per gram of creatinine) was calculated from a morning spot urine sample. Urine albumin excretion was categorized into normoalbuminuria (ACR < 17 in men, and < 25 in women), microalbuminuria (ACR 17-250 in men, and 25-355 in women), and macroalbuminuria (ACR > 250 in men, and > 355 in women); these thresholds are designed to identify people with urinary albumin excretion rates > 30 mg/24 hours and > 300 mg/24 hours, respectively [34]. Participants who had macroalbuminuria at baseline were excluded from this study. Progression of albuminuria was defined as a persistent increase in ACR to a higher category. In those with normoalbuminuria at baseline, progression was defined as microalbuminuria or macroalbuminuria at follow-up. In those with microalbuminuria at baseline, progression was defined as macroalbuminuria at follow-up. In participants with microalbuminuria at baseline, improvement in albuminuria was defined as having persistent measurements within a lower albuminuria category at follow-up visits,. In all statistical analyses this group was combined with those without progression. Thus, our analyses compared participants with progression of albuminuria to those without progression.

Statistical Analysis

Variables that were positively skewed, including ACR, were log transformed in order to better approximate a normal distribution. Comparisons of baseline characteristics according

to category of progression of albuminuria were made using chi-squared or Fisher's exact tests (when any expected cell frequency was <5) for categorical variables, Student's t for continuous variables approximating a normal distribution, and the Mann-Whitney U test for continuous variables that were not normally distributed. Correlations were assessed using Pearson's or Spearman's, as appropriate. Receiver operating characteristic (ROC) curves were used to identify the cutoff point for home PP that best predicted progression of albuminuria,.[35,36]

The goal of the multivariate analyses was to test the independent association of home BP with follow-up urine albumin excretion after adjustment for other covariates, including office and 24hour BP. Two types of multivariate analyses were performed: repeated measures mixed linear models, which considered ACR as a continuous variable, and Cox proportional hazards models, which considered albuminuria as a categorical dichotomous variable. PP measurements were selected as predictors for these models because we previously found them to be the strongest predictors of progression of albuminuria in this population.[18,37] Office and home PP were the BP variables entered in the first set of multivariate models, whereas ambulatory 24-hour pulse pressure, nocturnal BP patterns, and home PP were entered in the second model. All predictor variables were considered fixed at baseline (i.e., none was treated as time-dependent).

Repeated measures mixed linear model analyses were performed with all available ACR measurements from the annual follow up visits as the dependent variable, including baseline ACR and adjusting for clustering within physician panels in the study. The following covariates, assessed at baseline, were included in the mixed linear models because of their biologically plausible association with urine albumin excretion: age, gender, race, body mass index, use of ACE inhibitors or ARB, number of antihypertensive medications, current smoking, duration of diabetes mellitus, hemoglobin A1c, serum triglycerides, and HDL-cholesterol. Collinearity between BP variables was assessed by calculating the tolerance for each of them in the full models. None of them exhibited tolerance values below 0.20, which would have indicated, excessive, collinearity.[38]

Given the relatively small number of events (n = 74), the Cox models were adjusted for baseline ACR and those covariates that reached statistical significance in the mixed linear models, as follows: race, body mass index, duration of diabetes mellitus, and current smoking. Correctness of the proportional hazards assumption was verified using the Harrell and Lee modification of the Schoenfeld goodness of fit test.[39] First, we assessed the value of home PP when added to multivariate adjusted Cox models that included office BP on one hand, and ABPM variables on the other. Secondly, we built separate Cox models for home BP and ABPM variables and compared those models in terms of goodness of fit (calibration) and discrimination.[40] Calibration was measured using the -2 Log-Likelihood statistic and compared using the likelihood ratio test, whereas discrimination of each model was estimated calculating the c-statistic (area under the ROC curve) and its 95% confidence interval. Statistical analyses were performed using SPSS, version 15.0 (SPSS, Chicago, IL) and SAS, version 9.1 (SAS Institute Inc., Cary, NC).

Results

There were 497 IDEATel participants in the telemedicine arm with complete baseline data. Of those, 47 were excluded because they had macroalbuminuria at baseline, and 58 because they had less than two follow-up ACR measurements, leaving 392 participants for analysis. The mean follow-up time was 32.1 ± 8.4 months. Of the 103 participants who had microalbuminuria at baseline, 40 exhibited improvement during follow-up. The 74 participants who exhibited worsening of albuminuria were older (table 1), with a longer

history of diabetes,. higher home SBP and pulse pressure, higher 24-hour pulse pressure, and a more frequent nocturnal rise in SBP.

The median [Inter-Quartile Range] number of home BP measurements obtained by the participants was 51 [28-63], and the median time from the baseline examination to the first home BP measurement was 18 [15-25] days. Home SBP and PP tended to be lower than the corresponding office measurements, but the diastolic pressure was higher. The 24 hour ABP levels were the lowest. Home BP measurements were significantly correlated with office and ambulatory measurements (see table in online supplement).

The proportion of people who exhibited progression of albuminuria in different BP categories is summarized in table 2. When BP control was defined based on cutoff values of systolic and diastolic BP, the proportion of participants with progression of albuminuria was similar in those with controlled and uncontrolled BP. On the other hand, when a home PP of 60 mm Hg or higher (the cutoff value selected through ROC curve analysis) was present, 24% exhibited progression of albuminuria, as compared to 14% of those with home PP less than 60 mm Hg ($p = 0.014$). Similar trends were observed for office and 24-hour pulse pressure (data not shown).

The mixed linear models (table 3) showed that, adjusting for other baseline characteristics, both office and home PP were independently associated with higher urine ACR at follow-up ($p = 0.018$ and 0.001, respectively). When ABPM variables were introduced into the model, home PP was independently associated with ACR ($p = 0.011$), as were 24-hour PP, and a nocturnal BP rise. Other variables independently associated with higher ACR in both mixed models were black and Hispanic ethnicity, active smoking, duration of diabetes mellitus, and a lower body mass index.

Cox proportional hazards models (table 4) were adjusted for baseline urine ACR and those covariates that reached statistical significance in the mixed models. In model 1, which adjusted for those covariates and office pulse pressure, only home PP was an independent predictor of progression of albuminuria ($p = 0.013$). The hazard ratio (95% CI) per 10 mm Hg of home PP was 1.36 (1.07, 1.74). In the second model, which included as predictors home PP and ABPM measurements (but not office pulse pressure), only a nocturnal BP rise was an independent predictor ($p = 0.03$).

Finally, a third multivariate-adjusted Cox model was fitted. It included the ABPM variables (24hour PP and nocturnal BP patterns) as predictors, and adjusted for office pulse pressure, but did not include home pulse pressure. This model was compared with model 1. Their calibration, as measured by the -2 Log- Likelihood (-2LL) statistic was similar. The -2LL was 779.01 for the home PP model, and 775.46 for the ABPM model ($p = 0.169$ for the likelihood ratio test). Both models also performed similarly In terms of discrimination. The c-statistic (95% CI) was 0.71, (0.64 to 0.79) for the model with home pulse pressure, and 0.70 (0.62 to 0.78) for that with 24hour PP and nocturnal BP patterns.

Discussion

Home monitoring adds significantly to office BP measurements to predict progression of albuminuria in elderly people with diabetes, and may constitute an adequate substitute to ABPM in that regard. Systolic and diastolic BP were not as informative as pulse pressure, a common observation in longitudinal studies of elderly populations.[49] This is probably because PP reflects arterial stiffness, which is very prevalent in this age group. Home PP was independently associated with higher ACR at follow up in fully adjusted mixed linear models. In Cox proportional hazards models, the addition of home PP resulted in improved prediction of progression of albuminuria when the multivariate model included office BP,

but failed to improve the model if ABPM variables were considered. This apparent discrepancy between the two types of multivariate analyses is probably due to lesser statistical power in the Cox models caused by the relatively small number of events, and the dichotomization of the urine albumin-to-creatinine ratio, a continuous variable, which may also have reduced the statistical power due to some loss of information.[41,42] In addition, when home measurements and ABPM were assessed in separate Cox models, those models exhibited similar calibration and discrimination, suggesting that even if home BP does not add to ABPM, it may adequately substitute for it to predict progression of albuminuria.

Our findings also confirm the importance of a nocturnal BP rise, assessed by ABPM, in predicting progression of albuminuria, as we have previously reported in this cohort,[19] and as previously shown in patients with type-1 diabetes mellitus.[17]

Home monitoring allows the acquisition of larger numbers of measurements than the office setting, is not subject to the white coat effect,[44] and correlates better than office measurements with ABPM.[6]

This is an observational study nested within the intervention arm of a randomized controlled trial, and there might be concerns that the association of BP measurements with albuminuria may have been confounded by changes in medications prompted by higher BP values. However, such confounding would have decreased the observed association of BP with worsening albuminuria, as participants with higher BP should have been targeted for more intensive antihypertensive treatment. In addition, both office and home BP data were known to participants and their primary care providers, and were thus subject to the same potential confounding by increased antihypertensive treatment.

Several limitations are noteworthy. First, ACR was measured using a single spot urine sample, whereas a 24-hour urine collection, or three measurements instead of one, would have provided a more accurate assessment of renal albumin excretion. However, assessment of albuminuria in a spot urine sample has been accepted as a valid alternative in large studies,[50-53] and there is no reason to expect that misclassification of albuminuria caused by our measurement procedure would be differential with respect to the predictors. Second, our sample was composed of older subjects, with long standing diabetes, prevalent end-organ damage, and advanced arterial, stiffness at the time of the evaluation. Thus, our findings may not generalize to younger patients, and particularly to those with type-1 diabetes. Third, like all observational studies, ours is subject to the risk of residual confounding due to poorly measured or unmeasured confounders. In addition, although medication use may be used as a covariate, it could not be analyzed as a predictor itself, due to the potential confounding by indication. Finally, the IDEATel baseline exam did not include an assessment of renal function, such as a serum creatinine measurement. Patients with advanced renal failure were excluded, but we do not know whether the addition of a serum creatinine measurement would have substantially changed our results.

The strengths of this study include a longitudinal design and a large sample that was well-characterized, elderly, multiethnic, and had adequate representation of women. Home BP measurements were acquired systematically as part of a telemedicine intervention, and ambulatory BP monitoring was performed utilizing a well validated methodology.[54]

Perspectives

Our main finding is that home BP monitoring adds significantly to office BP, and more modestly to ABPM, to predict worsening of albuminuria in elderly people with type-2 diabetes. Our data also suggests that home BP monitoring may constitute an adequate substitute to ABPM for that purpose. These findings are clinically relevant because

progression of albuminuria is associated with a higher risk of major cardiovascular events. In addition, home BP monitoring carries a lower cost than ABPM, and is rapidly gaining acceptance among patients.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Selected Baseline Characteristics of 392 Participants Categorized by Progression of Albuminuria during Follow-Up. IDEATel Study, New York, 2000-2005

Characteristic	Without Progression (n = 318)	With Progression (n = 74)	*P* Value
Age, years	70 ± 6	72 ± 6	0.013
Female, %	63	51	0.08
Race/ethnicity, %			0.79
White	46	49	
Hispanic	13	11	
African-American	41	40	
Body Mass Index, kg/m2	32 + 6	31 + 6	0.25
Office systolic blood pressure, mm Hg	140 ± 22	139 ± 23	0.72
Office diastolic blood pressure, mm Hg	71 ± 11	69 ± 10	0.27
Office pulse pressure, mm Hg	69 ± 17	69 ± 18	0.79
Proportion taking ACE-I/ARB, %	61	67	0.35
Albumin-to-creatinine ratio (log_{10}-transformed),			
mg/g. Baseline (n=392)	1.4 ± 0.5	1.5 ± 0.5	0.17
1-year (n=382)	1.3 ± 0.5	1.7 ± 0.6	<0.001
2-year (n=387)	1.3 ± 0.5	1.8 ± 0.5	<0.001
3-year (n=301)	1.2 ± 0.5	1.7 ± 0.6	<0.001
Duration of diabetes, years	8 [3, 15]	10 [6, 19]	0.036
Hemoglobin A1c	7.3 ± 1.3	7.3 ± 1.4	0.57
HDL cholesterol, mg/dl	47± 14	44 ± 11	0.10
Triglycerides, mg/dl	169 + 100	190 + 119	0.13
Currently smoking, %	6.9	6.6	0.96
Home systolic blood pressure, mm Hg	137 ± 14	141 ± 16	0.035
Home diastolic blood pressure, mm Hg	76 ± 9	76± 10	0.82
Home pulse pressure, mm Hg	60 ± 12	64 ± 12	0.018
24-hour systolic blood pressure, mm Hg	132 ± 14	133 ± 14	0.41
24-hour diastolic blood pressure, mm Hg	69 ± 8	68 ± 9	0.14
24-hour pulse pressure, mm Hg	62 ± 11	65 ± 11	0.03
Nocturnal blood pressure pattern, %*			0.036
Dipping	32	22	
Flat (non-dipping)	50	52	
Rise	18	26	

Data are mean ± SD, median [interquartile range] or percentages.

*P for linear trend.

ACE-inhibitors = angiotensin converting enzyme inhibitors; ARB = angiotensin receptor blockers. Comparisons were made, as appropriate, using the chi-squared or Fisher's exact tests for categorical variables, and Student's t or Mann-Whitney U test for continuous variables.

Table 2

Percentage of Participants Exhibiting Progression of Albuminuria at Follow-up, within Blood Pressure Categories (n = 392). IDEATel Study, New York, 2000-2005

Blood Pressure Variable	Progression of Albuminuria	*P* value
Office blood pressure*		
Controlled (n = 145)	20%	0.69
Uncontrolled (n = 247)	18%	
24-hour blood pressure†		
Controlled (n = 104)	18%	0.97
Uncontrolled (n = 288)	19%	
Home blood pressure‡		
Controlled (n = 63)	20%	0.97
Uncontrolled (n = 329)	19%	
Home Pulse Pressure		
< 60 mm Hg (n = 194)	14%	0.014
≥ 60 mm Hg (n = 198)	24%	

*Uncontrolled office blood pressure was defined as systolic blood pressure > 130 mm Hg or diastolic blood pressure > 80 mm Hg.

†Uncontrolled 24-hour blood pressure was defined as mean systolic blood pressure > 120 mm Hg or mean diastolic blood pressure > 70 mm Hg.

‡Uncontrolled home blood pressure was defined as mean systolic blood pressure > 125 mm Hg, or mean diastolic blood pressure > 75 mm Hg. Comparisons were made with the chi-square or Fisher's exact test, as appropriate.

Table 3

Results of Mixed Linear Models for Progression of Albuminuria in 392 Participants without Macroalbuminuria at Baseline. Model 1: Selected Characteristics, Office Pulse Pressure, and Home Pulse Pressure. Model 2: Selected Characteristics, Home Pulse Pressure, 24-Hour Pulse Pressure, and Nocturnal Pattern. IDEATel Study, New York, 2000-2005

Variable	Model 1		Model 2	
	β Coefficient (SE)	*P* Value	β Coefficient (SE)	*P* Value
Age, years	−0.001 (0.003)	0.89	−0.001 (0.003)	0.75
Gender (female)	0.026 (0.048)	0.59	0.019 (0.048)	0.70
Body mass index, kg/m^2	−0.009 (0.003)	0.008	−0.009 (0.002)	0.014
Race/ethnicity				
White (reference)				
Black	0.162 (0.069)	0.021	0.178 (0.70)	0.012
Hispanic	0.099 (0.041)	0.043	0.106 (0.488)	0.03
Current smoker	0.098 (0.042)	0.018	0.095 (0.041)	0.022
Duration of diabetes, years	0.007 (0.002)	0.003	0.007 (0.002)	0.002
Number of antihypertensive medications	0.031 (0.023)	0.18	0.028 (0.023)	0.22
ACE-inhibitor / ARB use	−0.010 (0.049)	0.83	−0.016 (0.049)	0.74
Hemoglobin A1c, %	0.027 (0.015)	0.08	0.022 (0.015)	0.15
HDL-cholesterol, mg/dl	0.001 (0.002)	0.80	0.001 (0.001)	0.42
Triglycerides, mg/dl	0.001 (0.001)	0.002	0.001 (0.000)	0.002
Office pulse pressure, 10 mm Hg	0.036 (0.015)	0.018		
Home pulse pressure, 10 mm Hg	0.068 (0.02)	0.001	0.059 (0.023)	0.011
24-hour pulse pressure, 10 mm Hg			0.060 (0.025)	0.021
Nocturnal blood pressure pattern				
Dipping (reference)				
Flat			0.040 (0.046)	0.38
Rising			0.129 (0.061)	0.035

ACR = albumin-to-creatinine ratio; ACE-inhibitor = angiotensin converting enzyme inhibitor; ARB = angiotensin receptor blocker. All covariates are listed in the table.

Table 4

Results of Proportional Hazards Model for Progression of Albuminuria in 392 Participants without Macroalbuminuria at Baseline. Model 1: Selected Characteristics, Office Pulse Pressure, and Home Pulse Pressure. Model 2: Selected Characteristics, Home Pulse Pressure, 24-Hour Pulse Pressure, and Nocturnal Pattern. IDEATel Study, New York, 2000-2005

Variable	Model 1		Model 2	
	Hazards Ratio (95% CI)	*P* Value	Hazards Ratio (95% CI)	*P* Value
Baseline ACR (log_{10}-transformed), mg/g	1.24 (0.71 to 2.17)	0.44	1.09 (0.63 to 1.89)	0.77
Body mass index, kg/m^2	0.98 (0.94 to 1.02)	0.41	0.99 (0.95 to 1.03)	0.59
Race/ethnicity				
White (reference)				
Black	1.49 (0.65 to 3.4)	0.35	1.68 (0.76 to 3.73)	0.19
Hispanic	0.73 (0.43 to 1.24)	0.24	0.62 (0.37 to 1.07)	0.09
Duration of diabetes, years	1.01 (0.99 to 1.04)	0.34	1.02 (0.99 to 1.04)	0.15
Current smoker	1.03 (0.41 to 2.59)	0.95	1.11 (0.44 to 2.80)	0.83
Office pulse pressure, 10 mm Hg	0.88 (0.74 to 1.05)	0.16	---	---
Home pulse pressure, 10 mm Hg	1.36 (1.07 to 1.74)	0.01	1.08 (0.82 to 1.41)	0.59
24-hour pulse pressure, 10 mm Hg			1.09 (0.82 to 1.46)	0.52
Nocturnal blood pressure pattern				
Dipping (reference)				
Flat			1.7 (0.96 to 3.18)	0.06
Rising			2.2 (1.08 to 4.35)	0.03

ACR = albumin-to-creatinine ratio. All covariates are listed in the table.