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The association of antihypertensives with postural blood pressure and falls among seniors residing in the community: a case control study

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Abstract:

Background: A drop in postural blood pressure(BP) may contribute to falls, while antihypertensives have been considered to induce postural drop or orthostatic hypotension (OH) and falls among older people. However, this relationship between antihypertensives, postural BP and the risk of falls has never been evaluated in a single study.

Objective: To examine the association of postural BP changes and BP therapy with the risk of falls among community-dwelling older people in a case-control manner.

Method: Cases(n=202) included participants aged ≥65years with two falls or one injurious fall while controls(n=156) included participants ≥65years with no falls in the preceding 12months. Antihypertensives usage and medical history were recorded. Supine blood pressure measurements were obtained at 10minutes' rest and at 1,2 and 3 minutes after standing. Orthostatic hypotension was defined as a reduction in BP of 20mmHg/10mmHg within 3 minutes of standing.

Results: Individual antihypertensive classes were not associated with falls. Minimal standing systolic BP(SBP) was significantly lower among fallers [128(±27.3)vs.135.7(±24.7)mmHg;p=0.01], but fallers were not more likely to fulfil the diagnostic criteria for OH. Diuretics were associated with OH and α-blockers were associated with minimal standing SBP. The use of ≥2 antihypertensives was significantly associated with recurrent and injurious falls [OR,1.97;CI,1.2-3.1], which was not attenuated by adjustment for either OH or minimal standing SBP, but was no longer significant after adjustment for age and number of comorbidities [OR, 1.6; CI, 0.95-2.6].

Discussion: Minimal standing SBP or a lower SBP at 2 or 3 minutes standing was associated with falls rather than OH using consensus definition, while the association between ≥2 antihypertensives and falls was attenuated by age and comorbidities but not by OH or minimal standing SBP, challenging previous assumptions that antihypertensives are associated with OH related falls. Future studies should now seek to link these findings prospectively with falls in order to guide decision-making for BP lowering therapy among older patients.

Keywords:

Antihypertensives, Falls, Orthostatic hypotension, Aged

Introduction:

Among community-dwelling seniors, 28-35% over 64 years and 32%-42% of those over 70 years fall each year[1]. Falling, therefore, is a serious problem among the older population with potentially devastating long term consequences of increased morbidity and mortality. The risk of recurrent falls and fall-related complications tend to multiply in older adults after their first fall. Therefore, falls guidelines have recommended identification of modifiable extrinsic and intrinsic risk factors and their subsequent minimization in individuals presenting with recurrent falls or a single fall with gait abnormalities[2].

The consumption of antihypertensives as a group has been reported to be independently associated with falls among older adults [3]. However, in their meta-analysis of studies evaluating falls risk associated with cardiac medications, Leipzig et al found that only diuretics were associated with falls [4]. Butt and colleagues suggested that falls risk increases during the first few weeks of initiation of blood pressure lowering therapy irrespective of drug class[5] while recent studies by Callisaya et al and Tinetti et al[6, 7] recounted an increased daily dosage of antihypertensives to be associated with falls.

Orthostatic hypotension (OH) is considered a commonly documented adverse effect of antihypertensive treatment[8] with studies demonstrating alpha-blockers, beta-blockers and diuretics to be frequently associated with OH[3, 9]. It is therefore assumed that antihypertensive therapy results in falls through the side-effects of OH or hypotensive episodes. Rubenstein et al[10] suggested OH to be one of the primary causes of falls, while Craig et al[11] found falls to be the most common presentation for OH patients with medication induced OH being associated with 33% of these falls. However, these studies have evaluated fallers unilaterally without the inclusion of a control population.

Available large studies [6, 7] on the association between antihypertensives with falls have employed medication databases or cohort study information which did not include postural blood pressure measurements. Furthermore, previous studies had not considered evaluating the triangular relationship between antihypertensive use, postural blood pressure changes and the risk of falls. We hypothesized that postural blood pressure drop is a mediating factor for falls associated with antihypertensive use. Therefore, the objectives of this study were to examine the associations of antihypertensives with postural blood pressure drop among older individuals with and without a history of falls, and subsequently employing statistical modelling to evaluate the role of postural blood pressure changes in falls associated with antihypertensive use.

Methodology:

Reporting of the study conforms to STROBE Statement along with references to STROBE and the broader EQUATOR guidelines [12].

Study Population:

The sample consisted of participants recruited into the Malaysian Falls Assessment and Intervention Trial (MyFAIT) conducted in a large teaching hospital in Kuala Lumpur, Malaysia, between September 2013 to September 2014. Details of the trial have been described elsewhere [13]. Briefly, subjects aged ≥65 years who attended the departments of Emergency Medicine, Primary Care clinics and Geriatric Medicine clinics due to falls and discharged were invited to attend the 'falls clinic' for evaluation. Those with at least two falls or one injurious fall over the past 12 months were included into the study as cases because these factors were shown to be strongly associated with high risk of future falls [2]. Non-fallers (controls) from the hospital catchment area were recruited through media and word-of-mouth advertising and included community dwelling volunteers with no falls over the past 12 months. The exclusion criteria (both cases and controls) were clinical diagnosis of dementia, severe physical disabilities (unable to stand) and a major psychiatric illness or psychosis. A sample size of 352 participants was considered to provide 80% power to detect an effect size of 0.30 which is small to medium effect size (G*Power 3.1). This study was approved by the University Malaya Medical Centre Medical Ethics Committee (925.4). Written informed consent was obtained from all study participants.

Study Variables:

Medication Classification: Participants were asked to bring their written prescriptions and actual medications in order to collect a complete record of prescribed and over the counter medicines. The data on drugs were obtained via face-to-face interviews using a standardised case record form. Medications were subsequently classified according to the British National Formulary, 67 Edition [14]. Blood pressure lowering drugs were divided into the following main classes: angiotensin-converting enzyme inhibitors (ACE-I), angiotensin II receptor antagonists (A2RA), beta blockers (β-blockers), calcium channel blockers (CCBs), thiazide diuretics and other drugs used for cardiac diseases e.g. alpha-adrenergic receptor antagonists (α-blockers) and vasodilators (e.g. nitrates). Combination drugs were separated into their respective discrete classes (e.g. Diovan HCT which contained Valsartan and Hydrochlorothiazide was classified into both A2RA and thiazide diuretic groups and counted as 2 antihypertensive medications). Multiple antihypertensives use was defined as the consumption of two or more antihypertensives (≥2antihypertensives) [15].

Baseline Measurements: Falls were defined according to the consensus definition as "an unexpected event in which the person comes to rest on the ground, floor or lower level"[16]. Both cases and controls were evaluated with a structured history, which included enquiry regarding falls occurrence, mechanism and time, related symptoms and the complications of falls. Sociodemographic details and medical history were also obtained.

At baseline, participants were interviewed by a geriatrician. An established diagnosis of hypertension was recorded if the participant reported physician diagnosed hypertension and/or was on existing BP lowering therapy, regardless of the recorded blood pressure at the time of assessment. All other medical conditions were identified through self-report of previous diagnosis of specific conditions by participants, and verified by the attending geriatrician. Uncertainties were addressed by cross-checking with participants' previous medical records if available, or through written correspondence with participants' doctor. Circulatory disease was defined as the presence of any diagnosis of myocardial infarction, angina, stroke, TIA or peripheral artery disease. Eye diseases included cataract and glaucoma. Height and weight measurements were also obtained and body mass index (BMI) was calculated.

Blood Pressure Measurements: Blood pressure was measured at the falls clinic between the hours of 1.00pm to 4.00pm and participants were advised to take their regular prescribed medications on the day of assessment. One recumbent reading was obtained after 10 minutes of supine rest. Three standing readings were obtained at 1 minute, 2 minutes and 3 minutes after assuming the erect posture. All blood pressure measurements were obtained with an automated blood pressure machine (Omron HEM-7200). Orthostatic hypotension (OH) was diagnosed if a systolic blood pressure drop of 20mmHg or greater or diastolic blood pressure drop of 10 mmHg or greater was observed within three minutes of standing according to the consensus definition [17]. Minimal standing SBP was the lowest recorded SBP measurement amongst the three BP recordings obtained at 1, 2 and 3 minutes after assuming the erect posture.

Statistical Analysis:

Continuous data were evaluated with histogram plots and the Kolmogorov-Smirnov test to determine normal distributions. These were then expressed as means with standard deviation (SD) in parentheses, and comparisons were made between fallers and non-fallers using the independent t-test. Categorical data were expressed as frequencies with percentages in parentheses with differences between groups expressed as odds ratios with 95% confidence intervals, and the statistical significance of these nominal variables was tested with the Chi-squared test. For categorical outcomes of OH and falls, multivariate logistic regression methods were used to control for potential confounders. As minimal SBP was a continuous variable, independent t test was applied to test statistical significance and mean differences in minimal SBP were adjusted for confounders using linear regression methods. A p-value of <0.05 was considered statistically significant. Statistical modelling using binary logistic regression analysis method was employed to determine the mediation effects of postural blood pressure changes on falls associated with antihypertensive use. This was determined by examining the associations by step-wise adjustment of potential confounders. If the independent variable (antihypertensive use) was no longer statistically significant after the addition of a new variable (OH or minimal standing SBP) within the model, then the new variation was considered a potential mediator for the relationship between the independent variable and dependent variable. All statistical analysis was conducted using the Statistical Package for Social Science (SPSS) version 21.0 (Chicago, IL, USA).

Results

Recruitment and baseline demographics

A total of 442 participants were assessed initially. Eighty participants were excluded as they either did not meet the inclusion criteria or fulfilled exclusion criteria. Blood pressure data was incomplete for four individuals, who were then excluded from the analyses. Data on medication and blood pressure measurements from a total of 358 participants which included 202 fallers and 156 non-fallers were subsequently analyzed. Fallers were significantly older than non-fallers and they had significantly more comorbidities, with diabetes, eye diseases and circulatory diseases being significant among fallers. There was no significant difference between fallers and non-fallers with regards to gender, body mass index, hypertension, osteoporosis, depression, thyroid diseases and other chronic conditions (Table 1).

Blood Pressure Measurements

Table 2 summarises the supine and erect blood pressure measurements of the participants. In the supine position, the systolic blood pressure (SBP) of fallers was significantly lower than non-fallers, which was no longer significant following adjustment for age and comorbidities. After assuming the upright posture, there was no significant difference in standing SBP measurement at 1 min, but SBP at 2 and 3 minutes were significantly lower among fallers than non-fallers. These remained significant after adjustment of age and number of comorbidities. There was no significant difference in supine and standing diastolic blood pressure (DBP) at any time point between fallers and non-fallers. There was no significant difference in the prevalence of OH [fallers, 52(25.7) vs. nonfallers, 28(17.9); p=0.08] between the two groups using the pre-defined criteria; however mean minimal SBP during standing was significantly lower in fallers (Table 1).

Antihypertensive Medications and Falls

Among the total sample, 126 fallers and 77 non-fallers were taking at least one antihypertensive drug (OR=1.7; 95%CI, 1.1-2.5; p=0.01). With univariate analyses of individual classes of antihypertensives, α-blockers and A2RAs were associated with falls. However, this finding was no longer significant following adjustment for age difference alone (Table 3). Fallers were significantly more likely to be on two or more antihypertensives following univariate analysis (OR=1.97; 95%CI, 1.2-3.1; p=0.005), but this was not statistically significant after adjustment for age and number of co-morbidities (OR=1.6; 95% CI, 0.95-2.6; p=0.07) (Table 3).

Antihypertensives versus Orthostatic Hypotension and Minimal standing SBP

Regardless of the history of falls, individuals with OH were significantly more likely to be on diuretics even after adjustment for age (p=0.02), but no significant decrease in minimal SBP was observed with diuretic use. While the use of α-blockers is associated with significantly lower minimal standing SBP (p=0.01), OH was not associated with α- blocker use. The antihypertensive classes of β-blockers, CCBs, ACE-Inhibitors and A2RAs were not associated with OH or decreased minimal standing SBP. There was no significant difference in the number of anti-hypertensives used between individuals with and without OH. Similarly the minimal standing SBP did not differ with number of antihypertensives (Table 3).

Multivariate Analyses

Multivariate analysis was employed to determine the influence of OH and minimal standing SBP on the relationship between the antihypertensive use and falls (Table 4). Model 1 confirms that the relationship between the use of any antihypertensive drug and falls was unattenuated by the presence of OH, while Model 2 confirms that the presence of OH did not alter the significant association between the use of 2 or more antihypertensives and falls. Model 3 denotes that both the use of any antihypertensive and minimal standing SBP were independently associated with falls and Model 4, similarly indicated that the use of two or more antihypertensives and minimal standing SBP were also independently associated with falls. Model 5 indicates that minimal standing SBP remained an independent predictor for falls despite the inclusion of age or comorbidities in the model.

Discussion:

Our case-control study uniquely examined the relationships between BP lowering therapy with recurrent or injurious falls and postural blood pressure variations. Treatment with medications from any antihypertensive drug class was not associated with falls; instead use of multiple antihypertensives exhibited significant association with falls, which was only attenuated by the age and number of comorbidities. Orthostatic hypotension, according to the existing consensus definition, was not associated with the risk of recurrent or injurious falls. Minimal standing SBP, however, was significantly lower among fallers as compared to controls. The increased risk of falls observed with antihypertensive use was not mediated by OH or minimal standing SBP, but was influenced by the inevitable age differences between our fallers and non-faller controls.

By opting to select cases from individuals with recurrent or injurious falls and controls from those with no history of falls in the previous year, we excluded those with a history of only one non-injurious fall in the previous year. As the risk factors for one time fallers and recurrent fallers (two or more) differ, it is the recurrent faller who would benefit to the greatest extent from fall prevention efforts and from the negative outcomes associated with multiple falls[2, 18, 19], therefore this study only focused on the latter group of older adults.

Although orthostatic hypotension has formerly been reported as a risk factor of falls [10, 11, 20], this study suggests that it is the presence of a lower SBP while standing rather than the presence of OH alone that determines the risk of recurrent or injurious falls. A recent meta-analysis demonstrated that in spite of lower cardiovascular morbidity and mortality among older hypertensive adults on antihypertensive therapy than those without treatment, mild treatment was effective for all ages over 65years and strict SBP control presented no added advantage [21]. Our study superimposes this report by suggesting that use of antihypertensives is only beneficial with mild consumption whereas a strict SBP control, may present higher risk for falls. While the prevalence of hypertension increases markedly with age [22], age-related decline in blood pressure is also prominent in older adults, which is the marker of poor or deteriorating health [23] and may be associated with syncope [24] and recurrent falls [8]. One longitudinal study found that among older adults, the changes in blood pressure are related to health, with a rise of 1.5mmHg per year among healthy elderly while a drop among the older adults with multiple co-morbidities and this co-morbidity related drop was more prominent with SBP than DBP [25]. The prevalence of lower SBP while standing among our fallers might then be explained by the significant number of comorbidities. Furthermore, the report by Odden et al suggested that frail older adults might benefit from slightly higher blood pressure, to overcome age-related loss of vascular elasticity and sustain perfusion of vital organs [26]. Of note, the difference in standing SBP among our fallers was only observed if standing SBP was measured at 2minutes and beyond. Our findings support that of Kario et al who reported that individuals with a history of falls and a standing SBP below 140 mmHg had an increased risk of falling[27]. Before further conclusions can be drawn, prospective evaluation of the relationship between minimal standing SBP at 2 or 3minutes and falls occurrence is warranted, in order to develop a clear cut-off for minimal standing SBP or an accurate predictive score while taking into account minimal standing SBP, age, history of recurrent and injurious falls alongside other potential predictors for falls.

Our study has provided a deeper insight into the link between postural blood pressure and antihypertensives among older fallers. The measurement of standing SBP may represent a useful parameter in determining how aggressively SBP should be treated among geriatric population, with increasing age and history of falls currently being the only available decision aid[28]. Our findings contradict those of a previous study that various classes of antihypertensives are associated with falls [29] and choosing one class over the other may reduce the risk of falls. On the contrary, our results indicate that the use of two of more antihypertensives regardless of class of medication might be associated with high risk of falls.

Callisaya et al[6] stated that increased antihypertensive burden, calculated by the ingested dose of each antihypertensive divided by the recommended maximal daily dose, increases the risk of falls, independent of drug classes. While our study supports this finding, it suggests that the simple method of counting number of antihypertensives may also be effective in predicting falls risk. The association of multiple antihypertensives with falls was attenuated with age adjustment, as reported by Gu and colleagues [30] that the use of multiple antihypertensives increases with increasing age. A multicentre longitudinal study found that lower SBP along with use of two or more antihypertensives significantly contributed to mortality among their institutionalized octogenarians [15]. Although we did not find the association of use of two or more antihypertensives with SBP but as the authors suggested that the safety of using multiple antihypertensives in elderly patients with lower SBP “raises a cautionary note”, our findings do suggest that 2 or more antihypertensives and lower standing SBP are independently linked with falls and if they co-exist they may amplify falls risk.

While orthostatic hypotension was related with uncontrolled blood pressure as suggested by the findings of the British Women Heart and Health study (BWHHS), the number of antihypertensives and use of β-blockers were not associated with OH in our study. Instead, diuretic use was linked with OH, unlike that reported by the BWHHS[31]. In addition, using currently agreed definitions for OH, there was no significant relationship between OH and falls. While this suggests that the use of multiple blood pressure lowering agents may be associated with higher-risk of future falls through currently unexplained mechanisms, it also suggests that the diagnostic criteria for OH may require revision[32].

The limitations of the study are as follows. As a case-control study, it was unable to determine any causal relationship between antihypertensive therapy and falls, which will be a subject of a future prospective study which, however, requires larger sample sizes for adequate statistical power. Falls in our study were identified through retrospective recall, the prospective study will therefore need to consider the use of fall diaries to minimize recall bias[33].

To our knowledge, our study was the first to include the evaluation of postural blood pressure measurements, antihypertensive use and falls in the same participants. Individuals with a history of at least two falls or one injurious fall, had significantly lower standing SBP obtained 2-3 minutes after assuming the upright posture rather than immediately. Orthostatic hypotension was not associated with recurrent or injurious falls. While falls were also associated with the regular use of two or more antihypertensive drugs as compared to non-faller controls, this was not mediated by minimal standing SBP, challenging previous assumptions that antihypertensive are linked to falls through their blood pressure lowering effects. A prospective study evaluating actual falls outcome with regards to blood pressure changes among older individuals prescribed antihypertensive therapy is now warranted to accurately identify factors associated with increased risk of falls, which will be invaluable for effective blood pressure lowering among the older population.

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Table 1. Comparison of Baseline Characteristics of Fallers and Non-fallers

Characteristics	Fallers[†] (n=202)	Non-Fallers[‡] (n=156)	p-value
Age (Years), mean ± SD	75.2 ±7.1	72.2(±5.5)	<0.001[***]
Male Gender, n(%)	65(32.2)	51(32.7)	0.92
Body Mass Index (kg/m2), mean ± SD	24.2 ±3.7	24.5(±4.0)	0.48
Smoker, n(%)	7(3.5)	7(4.5)	0.61
Alcohol, n(%)	15(7.4)	15(9.6)	0.45
Medical History, n(%)			
Diabetes	69(34.2)	30(19.2)	0.002[**]
Hypertension	115(56.9)	77(49.4)	0.17
Respiratory disorders	9(4.5)	6(3.8)	0.78
Arthritis	44(21.8)	40(25.6)	0.37
Osteoporosis	19(9.4)	15(9.6)	0.93
Hearing disorders	14(6.9)	7(4.5)	0.33
Depression	6(3)	2(1.3)	0.47
Thyroid diseases	13(6.4)	16(10.3)	0.18
Eye diseases	95(47)	52(33.3)	0.009[**]
Circulatory diseases	41(20.8)	18(11.5)	0.03[*]
Neoplasm	4(2)	9(5.8)	0.05[*]
No. of co-morbidities, mean ± SD	2.3(±1.6)	1.8 (±1.5)	0.01[**]
Min SBP[a] (mmHg). mean ± SD	128(±27.3)	135.7(±24.7)	0.01[**]
Min DBP[b] (mmHg), mean ± SD	67(±16.7)	69.8(±17.3)	0.13

SD=standard deviation
[***]p≤.001, [**]p≤.01, [*]p≤.05
[†]Recurrent or injurious falls in the past 12-months
[‡]No falls in the past 12 months
[a]Minimal standing SBP was the lowest recorded reading of SBP amongst the three standing
[b]Minimal standing DBP was the lowest recorded reading of DBP amongst the three standing measurements

Table 2: Postural Blood Pressure Measurements Among Fallers and Non-Fallers

Blood Pressure	**Fallers**[†] **(n=202)**	**Non-Fallers‡ (n=156)**	**Mean Difference (95%CI)**	**Unadjusted p-value**	**Adjusted Mean Difference**[§] **(95%CI)**	**Adjusted p-value**[§]
Supine (mmHg), mean (±SD)						
Baseline SBP	130(24.8)	135.6(20.3)	4.6(0.05-9.2)	0.04*	4.5(0.23 to 9.2)	0.06
Baseline DBP	66.2(15)	66.6(15.0)	0.4(-2.6 to 3.5)	0.78	0.73(-2.4-3.9)	0.65
Standing (mmHg), mean (±SD)						
SBP at 1 min	134.2(27.9)	139.6(26.5)	5.3(-0.33 to 11.1)	0.06	5.3(-0.56 to 11.2)	0.07
SBP at 2 min	139.1(26)	146.2(24.0)	7.1(1.7-12.3)	0.009**	7.7(2.3-13.2)	0.006**
SBP at 3 min	139.1(27)	146.5(24.2)	7.3(1.9-12.8)	0.008**	7.6(2.1-13.3)	0.007**
DBP at 1 min	71.1(17)	72.2(18.2)	1.6(-2.0 to 5.3)	0.37	0.32(-3.3 to 4.1)	0.86
DBP at 2 min	72.8(17)	75.2(16.2)	2.4(-1.1 to 5.9)	0.17	1.1(-2.4 to 4.6)	0.54
DBP at 3 min	72.8(16.2)	75.7(15.3)	2.8(-0.47 to 6.1)	0.09	1.3(-1.9 to 4.6)	0.43

SBP=systolic blood pressure, DBP=diastolic blood pressure; OH= orthostatic hypotension; CI= Confidence Interval
***p≤0.001, **p≤0.01, *p≤0.05
[†]Recurrent or injurious falls in the past 12-months
[‡]No falls in the past 12 months
[§]adjusted for age and number of comorbidities using linear regression

Table 3: The Association between Antihypertensive Classes and Falls, Orthostatic Hypotension and Min SBP

	Falls		Orthostatic Hypotension		Minimal SBP	
Antihypertensives	**Unadjusted OR(95%CI)**	**Adjusted OR§ (95%CI)**	**Unadjusted OR(95%CI)**	**Adjusted OR§ (95%CI)**	**Mean difference[c] (95%CI)**	**Adjusted mean difference† (95%CI)**
α-blockers	2.7(1.1-7.0)***	2.2(0.82-5.81)	1.9(0.83-4.5)	1.83(0.75-4.4)	13.5(3.6 to 23.4)***	14.1(3.3 to 24.8)***
β-blockers	1.3(0.75-2.3)	0.98(0.54-1.8)	1.5(0.81-2.7)	1.28(0.67-2.5)	3.7(-3.5 to11.0)	3.7(-3.3 to 11.4)
ACE-I	1.1(0.63-2.0)	1.1(0.61-2.1)	1.3(0.69-2.5)	1.29(0.65-2.6)	0.05(-8.2 to 8.3)	0.59 (-8.3 to 7.2)
A2RAs	2.1(1.1-4.0)***	1.7(0.9-3.5)	1.2(0.6-2.3)	1.09(0.53-2.2)	3.1(-4.3 to10.5)	3.7(-4.3 to 11.7)
CCBs	1.3(0.84-2.1)	1.0(0.63-1.73)	0.98(0.56-1.7)	0.86(0.48-1.5)	-0.77(-6.7 to 5.2)	-0.53(-6.9 to 5.8)
Diuretics	1.5(0.78-3.1)	1.5(0.78-3.2)	2.2(1.1-4.4)*	2.2(1.1-4.4)***	-1.3(-10.7 to 8.1)	-1.1(-9.9 to 7.7)
Nitrates	1.6(0.46-5.3)	0.89(0.24-3.2)	1.7(0.52-6.1)	1.6(0.45-5.8)	-6.0(-21.3 to 9.2)	-5.8 (-21.5 to 9.9)
Any antihypertensive	1.7(1.1-2.5)	1.4(0.94-2.3)	1.5(0.93-2.6)	1.6(0.8-3.3)	4.4 (-1.1 to 9.9)	4.4(-1.2 to 10.2)
≥2 antihypertensives	1.97(1.2-3.1)**	1.6(0.95-2.6)	1.5(0.85-2.5)	1.37(0.79-2.3)	2.8(-3.1 to 8.8)	3.4(-3.0 to 9.9)

ACE-I, Angiotensin converting enzyme inhibitors; A2RA, angiotensin II receptor antagonists; CCB, calcium channel blockers;
***p≤0.001, **p≤0.01, *p≤0.05; OR= Odds Ratio; CI= Confidence Interval
§adjusted for age and number of comorbidities using binary logistic regression.
† adjusted for age and number of comorbidities using linear regression.

Table 4. Logistic Regression Models to Determine the Influence of Postural Blood Pressure Changes on the Relationship between Antihypertensives and Falls
OR=odds ratio, CI=confidence interval, Min SBP=Minimal systolic blood pressure

Models	**Adjusted OR (95%CI)**	**p-value**	**R^2**
Orthostatic Hypotension and Antihypertensive Use			
Model 1			0.03
Any hypertensive	1.6(1.1-2.5)	0.02*	
Orthostatic hypotension	1.5(0.89-2.5)	0.12	
Model 2			0.04
≥2 antihypertensives	1.9(1.2-3.1)	0.008**	
Orthostatic hypotension	1.5(0.9-2.6)	0.12	
Minimal SBP and Antihypertensive Use			
Model 3			0.04
Any hypertensive	1.6(1.1-2.5)	0.02*	
Min SBP (per mmHg)	0.99(0.98-0.99)	0.02*	
Model 4			0.05
≥2 antihypertensives	1.9(1.2-3.2)	0.007 **	
Min SBP (per mmHg)	0.99(0.08-0.99)	0.02*	
Model 5			0.102
Age (per year's increase)	1.1(1.0-1.1)	0.001***	
No. of comorbidities	1.0(0.91-1.2)	0.45	
≥2 antihypertensives	1.5(0.91-2.6)	0.10	
Min SBP (per mmHg increase)	0.99(0.98-0.99)	0.01**	

***p≤0.001, **p≤0.01, *p≤0.05