



Associated factors of orthostatic hypotension in the elderly essential hypertension patients and relationship between orthostatic hypotension and early renal damage

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Background: This study sought to explore the related factors of orthostatic hypotension (OH) in elderly patients with essential hypertension, and analyze the relationship between early renal damage and OH in elderly hypertensive patients.

Methods: The demographic and clinical data of 511 elderly patients with essential hypertension (EH) were collected from September 2017 to September 2018. These patients were divided into group with OH and group without OH. The data were compared between the two groups to analyze correlations between OH and early renal damage indicators [urine microalbumin (mAlb) >30 mg/L].

Results: In the study, 118 were in the OH+ group, and 393 were in the OH- group. The proportion of patients with coronary heart disease, atherosclerosis, grade 3 hypertension, persistent rapid atrial fibrillation, left ventricular diastolic dysfunction, and left ventricular hypertrophy in OH+ group was significantly higher than in OH- group ($P < 0.05$). Further, logistic regression analysis showed that coronary heart disease, carotid atherosclerosis, and grade 3 hypertension are independent associated factors for OH in elderly EH patients. In the 511 patients, 249 had urine mAlb >30 mg/L, and 262 had urine mAlb \leq 30 mg/L. The 24-hour systolic blood pressure (SBP)-coefficient of variation (CV), the 24-hour diastolic blood pressure (DBP)-coefficient of variation (CV), the drop difference of both SBP and DBP from supine to standing position in 3-minute were higher in patients with urine mAlb >30 mg/L than in patients with urine mAlb \leq 30 mg/L ($P < 0.05$). The urine mAlb of patients with OH was higher than that of patients without OH, and the urine mAlb of patients with elevated blood pressure variability (BPV) was also higher than that in patients with normal BPV ($P < 0.05$). Further groupings revealed that patients with both OH and elevated BPV had the highest urine mAlb levels ($P < 0.05$).

Conclusions: Coronary heart disease, atherosclerosis, and grade 3 hypertension are independent associated factors of OH in elderly EH patients. In elderly hypertensive patients with both OH and elevated BPV, the urine mAlb is much higher than that in patients with OH or elevated BPV alone. OH is associated with early renal damage.

Keywords: Essential hypertension (EH); orthostatic hypotension (OH); influencing factors; urine microalbumin

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Introduction

Orthostatic hypotension (OH), a common condition among the elderly, is characterized by abnormal blood pressure (BP) regulation. Diagnosis of OH is made with a decrease of 20 mmHg or more in systolic blood pressure (SBP) and/or a decrease of 10 mmHg or more in diastolic blood pressure (DBP), complicating with various hypoperfusion symptoms or not, within 3 min of changing from supine to standing position. Risk factors of OH include age, cardiovascular diseases (hypertension, heart failure, aortic stenosis, etc.), nervous system diseases (autonomic neuropathy, Parkinson's disease, Alzheimer's disease, multiple system sclerosis), endocrine system diseases (diabetes, abnormal aldosterone levels, adrenocortical insufficiency, hypothyroidism, etc.), drug factors (vasodilators, diuretics, combination of multiple antihypertensive drugs, sedatives, tricyclic antidepressants, etc.), insufficient capacity, etc.

Elderly hypertension patients are prone to OH, 22% elderly hypertension patients have OH (1). Whether different blood pressure grade has an impact on OH, and which common cardiovascular complications are associated with OH, has not been discussed in previous studies, so this article will focus on them. In elderly patients, OH not only causes falls, fractures, headaches, memory loss, dementia, syncope, disability, etc., but is also one of the independent risk factors for death in patients with cardiovascular and cerebrovascular diseases (2). To date, clinical research on the damage of OH to target organs has largely focused on damage to the cardiovascular and cerebrovascular organs. Research has confirmed that OH is a risk factor for some cardiovascular events, including heart failure, myocardial ischemia, myocardial infarction, and stroke (3). However, as an important target organ, the damage of OH on kidney is rarely concerned. It is speculated that reduce of renal vascular perfusion, damage of vascular endothelial function, release of inflammatory cytokines and activating RAAS system may lead to kidney damage. Therefore, urinary microalbumin (mAlb) is used as an indicator of early renal damage, and determined in this study. This study purposely selected elderly patients with both essential hypertension and OH, and analyzed their clinical data to gain further insights into OH. The results of this study will prove helpful in the effective clinical prevention and comprehensive management of OH. We present the following article in accordance with the STROB reporting checklist (available at <http://dx.doi.org/10.21037/apm-20-2265>).

Methods

All procedures performed in this study involving human participants were in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by Ethics Committee of Sichuan Provincial People's Hospital (No. 2017156) and informed consent was taken from all the patients.

Research object

The sample size was calculated by the formula, the factors such as intolerance to BP examination, loss of data, refusal to accept examination, etc., were also considered, so we expanded the sample size to 3,000. The participants in this study were selected from 2,980 patients with essential hypertension who underwent physical examinations from September 2017 to March 2018 and who were aged 65 years and over. Patients' past medical histories and physical examination data were collected in the examinations. Of the 2,980 patients, 511 met the inclusion and exclusion criteria (for further details, see below) of this study, 2,469 patients were excluded. BP measurement of standing position was interrupted in 5 patients due to hypoperfusion, however, all of them tolerated the second BP measurement after rest. Among them, 231 had grade 1 hypertension, 177 had grade 2 hypertension, and 103 had grade 3 hypertension. Of the 511 patients, 313 were males and 198 were females. The patients had an average age of 72 years (range, 69–76 years). Of the 230 normal control patients who participated in this study, 131 were males and 99 were females with an age of 71.94 ± 3.16 years. There was no statistically significant difference in the demographic characteristics between the two groups ($P < 0.05$).

To be eligible to participate in the study, the patients had to meet the following inclusion criteria: (I) meet the hypertension diagnostic criteria under the "Chinese Guidelines for the Prevention and Treatment of Hypertension 2010" (4); (II) be aged ≥ 65 years; (III) have undertaken repeated blood pressure measurements in the past or the presently described physical examination to meet the diagnostic criteria for essential hypertension; (IV) have a clear consciousness and be able to cooperate with medical staff to complete the supine and standing blood pressure measurements; and (V) be able to cooperate to complete a 24-hour ambulatory blood pressure check.

The exclusion criteria were the following: (I) renal

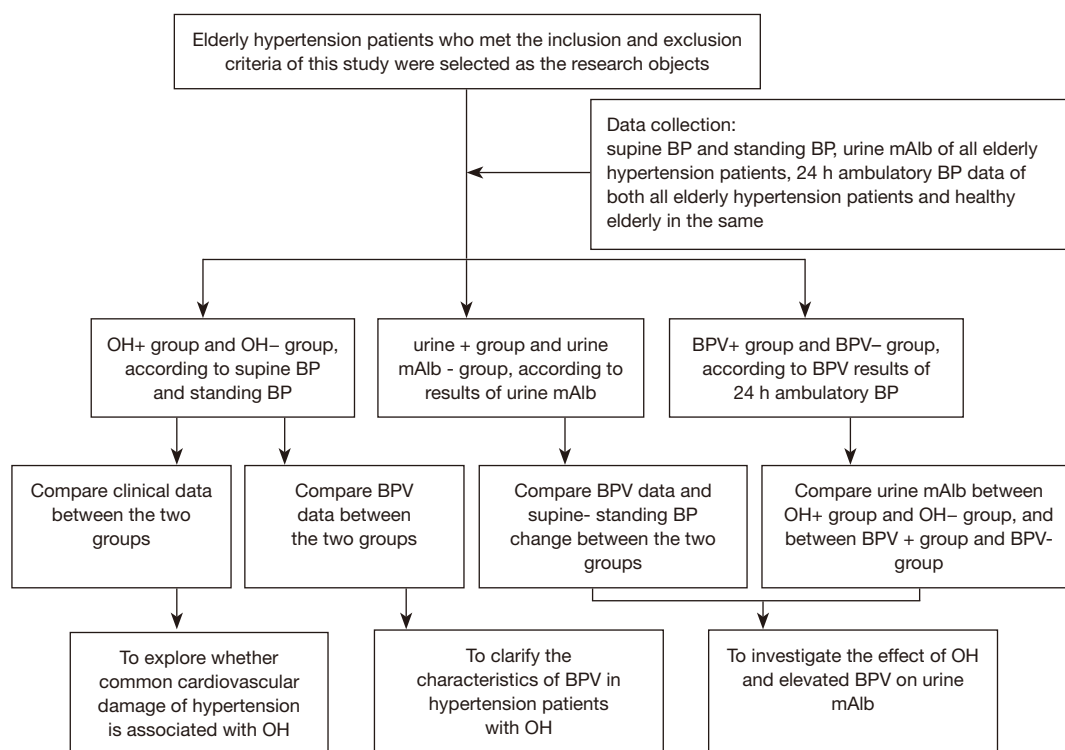


Figure 1 The flow chart of method of this study. OH, orthostatic hypotension; BPVs blood pressure variability; mAlb, microalbumin.

artery stenosis, adrenal gland space-occupying lesion; (II) heart failure or aortic valve stenosis; (III) endocrine system diseases (diabetes, hypothyroidism), serious systemic diseases, anemia, or autoimmune diseases; (IV) hypovolemia; (V) elevated serum creatinine levels (of $>106 \mu\text{mol/L}$ for males and $>97 \mu\text{mol/L}$ for females); (VI) recent use of drugs which maybe cause OH; (VII) diseases or drugs which maybe affect urinary mAlb level.

Methods

The flow chart of method of this study is shown in *Figure 1*.

Data collection

The data were collected by researchers who had been uniformly trained. The researchers were aware of the implementation steps and clinical significance of this study and were able to proficiently and correctly perform blood pressure measurements. The researchers also knew how to fill out the questionnaire and the clinical data collection form, which included questions to gather data about each patient's name, gender, age, contact information, smoking history, hypertension, past diseases, and recent

medications.

Blood pressure measurement

Diagnosis of OH is made with a decrease of 20 mmHg or more in SBP and/or a decrease of 10 mmHg or more in diastolic blood pressure (DBP), complicating with various hypoperfusion symptoms or not, within 3 min of changing from supine to standing position. The German Schiller ambulatory blood pressure monitor was used to detect coefficient variation (CV) of BP. All subjects were tested to determine their ambulatory blood pressure on the next day of the physical examination. Patients had to wear a cuff on their ipsilateral arm to enable their blood pressure measurements to be taken in lying and standing positions. Patients' blood pressure was recorded every 30 minutes. In terms of the blood pressure detection data, over 90% of the data were valid. The CV of blood pressure was calculated as follows: $\text{CV} = [\text{standard deviation (SD) of mean blood pressure} / \text{mean blood pressure}] \times 100\%$. The 24-hour SBP-coefficient of variation (24 h SBP-CV) and the 24-hour diastolic blood pressure-coefficient of variation (24 h DBP-CV) were selected as observation indicators for BPV. Due to the lack of normal reference values of 24 h SBP-CV and

24 h DBP-CV for the elderly in China, this study used the 24 h SBP-CV and 24 h DBP-CV of healthy elderly patients who participated in physical examinations at the same time and who had been matched for gender as a reference. The mean + 2SD was used as the upper cutoff value for the normal range of BPV (5). Under this standard, if a patient's 24 h SBP-CV or/and 24 h DBP-CV exceeded the upper limit of this parameter, that patient was regarded as elevated blood pressure variability (BPV+), and if it was less than or equal to this upper limit, that patient was regarded as normal (BPV-).

Laboratory index testing

The participants were instructed not to consume any greasy food or drink any alcohol for 3 days before their examination. All patients had an empty stomach for more than 12 hours before blood sampling. In the morning, venous blood was taken in a test tube, and blood lipids and blood creatinine levels were measured after centrifugation.

Observation indicators

The occurrence of OH and BPV in all patients with essential hypertension were recorded. The binary logistic regression model was used to analyze the occurrence of OH in elderly patients with hypertension and its influencing factors. The relationship between elderly patients with both hypertension and OH and early renal damage was also analyzed. The 1996 diagnostic criteria of the American Autonomic Society (AAS) and the American Academy of Neurology (AAN) (6) were adopted to determine OH.

Kidney damage assessment

As stated above, 511 elderly hypertensive patients and 230 normal control patients participated in this study. The first urine specimens were taken on an empty stomach in the morning, and urine mAlb was measured using the immunoturbidimetric method. The kit was provided by Ningbo Yijie Biotech Co. Ltd. For the purposes of the present study, a normal range of urinary mAlb was classified as 0–30 mg/L; a urinary mAlb >30 mg/L was classified as urinary mAlb (+), which indicates early renal damage.

Statistical methods

SPSS18.0 was used to analyze the data, the normal count data are expressed as mean ± SD, and a homogeneity of variance test was performed. The data of normal distribution and the homogeneity of variance were tested

by a *t*-test. For data with a normal distribution but uneven variance, the Kruskal-Wallis H rank-sum test was used to make comparisons among multiple groups, and after correction, the Mann-Whitney U test, was used to make further comparisons between the two groups. The count data are expressed in percentages and were tested using the χ^2 method. The multivariate analysis adopted a binary logistic regression model. A P value <0.05 indicated that the difference was statistically significant.

Results

This study shows that coronary heart disease, carotid atherosclerosis, hypertension grade, persistent rapid atrial fibrillation, left ventricular diastolic dysfunction and LVH are associated with OH in elderly hypertension patients. BPV of hypertension patients with OH is significantly higher than those without OH, and elevation of BPV is more obvious with higher blood pressure grade. Both OH and elevated BPV are associated with early renal damage.

Analysis of clinical characteristics and related factors of OH in elderly hypertensive patients

Of the 511 patients, 118 patients had OH (OH+ group), and 393 patients did not have OH (OH- group). All the clinical data and BP data were collected without missing. The proportion of patients with horizontal blood pressure, grade 3 hypertension, coronary heart disease, carotid atherosclerosis, persistent rapid atrial fibrillation, left ventricular diastolic dysfunction, and left ventricular hypertrophy in the OH+ group was higher than that in the OH- group ($P < 0.05$), while the blood pressure of the standing SBP in the OH+ group was lower than that of the OH- group ($P < 0.05$). There were no significant differences between the two groups in relation to gender, age, body mass index (BMI), duration of hypertension, smoking, total cholesterol (TC), triglyceride (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-c), and serum creatinine (see *Table 1*).

Analysis of independent associated factors for elderly hypertension patients with OH

The results of the multivariate logistic regression analysis showed that coronary heart disease, carotid atherosclerosis, and hypertension were all independent related factors of OH in patients with primary hypertension (see *Table 2*).

Table 1 Basic data analysis of the OH+ group and OH- group

Clinical information	n	OH- group (n=393), n (%)	OH+ group (n=118), n (%)	$\chi^2/t/H$	P
Sex					
Male	313	238 (60.55)	75 (63.56)	0.344	0.558
Female	198	155 (39.44)	43 (36.44)		
Age (years)		72 [69–76]	72 [68–77]	0.121	0.728
BMI (kg/m ²)		22.18±0.37	22.19±0.45	0.016	0.987
Course of hypertension (years)		3.30 [2.30–3.50]	3.15 [2.50–3.63]	3.854	0.051
Hypertension classification					
Level 1	231	198 (50.38)	33 (27.97)	18.490	<0.01
Level 2	177	134 (34.10)	43 (36.44)	0.220	0.639
Level 3	103	61 (15.52)	42 (35.59)	22.718	<0.01
Smoking	208	157 (39.95)	51 (43.22)	0.402	0.526
Coronary heart disease	249	171 (43.51)	78 (66.10)	18.537	<0.01
Carotid atherosclerosis	207	141 (35.88)	66 (55.93)	15.145	<0.01
Persistent rapid atrial fibrillation	9	3 (0.76)	6 (5.08)	7.456	0.012
Abnormal left ventricular diastolic function	350	256 (65.14)	94 (79.66)	11.134	<0.01
Left ventricular hypertrophy	187	132 (33.59)	55 (46.61)	6.633	0.010
Blood creatinine (μmol/L)		72.83±12.05	72.43±12.01	0.313	0.755
TC (mmol/L)		4.66±0.34	4.59±0.35	1.910	0.057
TG (mmol/L)		1.38±0.19	1.35±0.19	1.500	0.134
HDL-C (mmol/L)		1.31±0.17	1.27±0.17	1.882	0.060
LDL-C (mmol/L)		2.80±0.31	2.84±0.41	1.483	0.139
Supine SBP (mmHg)		159 [150–173]	171 [157–192]	39.878	<0.01
Supine DBP (mmHg)		68 [65–73]	76 [70–84]	45.758	<0.01
Standing 3-min SBP (mmHg)		161 [152–177]	148 [135–163]	61.889	<0.01
Standing 3-min DBP (mmHg)		68 [65–73]	67 [62–74]	1.841	0.175

BMI, body mass index; TC, total cholesterol; TG, triglyceride; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; SBP, systolic blood pressure; DBP, diastolic blood pressure.

Comparison of demographic and clinical data between the urine mAlb+ group and the urine mAlb- group

The average level of urine mAlb of the 511 elderly hypertensive patients was higher than that of the normal control group ($P<0.05$). Patients with a mAlb of 0–30 mg/L were classified as falling into the urine mAlb- group, and patients with a urine mAlb of >30 mg/L were classified as falling into the urine mAlb+ group. Of the 511 elderly hypertensive patients, 249 fell into urine mAlb+ group, and

262 patients fell into the urine mAlb- group.

The supine blood pressure, 3-minute blood pressure in the standing position, 24 h SBP-CV, 24 h DBP-CV, 3-minute SBP difference in the supine-standing position, and 3-minute DBP difference in the supine-standing position in the urine mAlb+ group were higher than that in the urine mAlb- group. Besides, in the urine mAlb+ group, proportion of patient with OH or BPV+ were higher than that in urinary mAlb+ group (see *Table 3*).

Table 2 Analysis of independent related factors of elderly essential hypertensive patients with OH

Independent variable	β	SE	wald	I	OR	95% CI
Coronary heart disease	0.855	0.230	13.778	0.000	2.352	1.123–2.030
Carotid atherosclerosis	0.837	0.225	13.799	0.000	2.309	1.485–3.590
Grade 3 hypertension	0.755	0.262	8.329	0.004	2.127	1.274–3.553

Table 3 Comparison of basic data of patients in the urine mAlb+ and urine mAlb- groups

Clinical information	n	Urine mAlb+ group (n=249), n (%)	Urine mAlb- group (n=262), n (%)	$\chi^2/t/H$	P
Sex				0.409	0.523
Male	313	149 (59.84)	164 (62.60)		
Female	198	100 (40.16)	98 (37.40)		
Age (year)		72 [69–76.5]	72 [68–76]	0.207	0.649
BMI (kg/m ²)		22.18±0.40	22.20±0.38	0.587	0.557
A course of hypertension (year)		3.00 [2.4–3.6]	3.00 [2.2–3.5]	1.602	0.206
Smoking	208	101 (40.56)	107 (40.84)	0.004	0.949
Coronary heart disease	249	121 (48.59)	128 (48.85)	0.003	0.953
Carotid atherosclerosis	207	104 (41.77)	103 (39.31)	0.319	0.572
Persistent rapid atrial fibrillation	9	5 (2.01)	4 (1.53)	0.171	0.679
Abnormal left ventricular diastolic function	350	198 (79.52)	152 (57.25)	27.354	<0.01
Left ventricular hypertrophy	187	108 (43.37)	79 (28.63)	9.717	<0.01
Blood creatinine (μ mol/L)		73.32±12.91	72.18±11.31	2.518	0.113
Supine SBP (mmHg)		170 [154–187.5]	155 [149–170]	51.649	<0.01
Supine DBP (mmHg)		72 [67–79]	67 [65–72]	37.720	<0.01
Standing 3-min SBP (mmHg)		163 [151–177]	155 [147–170]	15.820	<0.01
Standing 3-min DBP (mmHg)		68 [65–78]	67 [64–72]	7.243	0.007
OH+	118	79 (31.73)	39 (14.89)	20.389	<0.01
BPV+	224	146 (58.63)	78 (29.77)	43.201	<0.01
24h SBP-CV (%)		11.48 [10.18–13.11]	10.23 [9.51–11.35]	54.889	<0.01
24h DBP-CV (%)		10.28 [9.35–11.37]	9.26 [8.71–10.22]	58.225	<0.01

BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; OH, orthostatic hypotension; BPV, blood pressure variability; SBP-CV, systolic blood pressure coefficient of variance; DBP-CV, diastolic blood pressure coefficient of variance.

Comparison of urine mAlb levels between the OH+ group and the OH- group, BPV+ group and BPV- group

Patient with 24 h SBP-CV >11.42% and 24 h DBP-CV >10.29% was regarded as elevated BPV (BPV+). Of the 511 patients, 224 patients had elevated BPV (BPV+ group), and 287 patients did not have elevated BPV (BPV- group). A comparison of urine mAlb between the OH+ group and

OH- group revealed that the urine mAlb level of the OH+ group was higher than that of the OH- group ($P<0.01$). Further, the proportion of patients with OH+ combined with urine mAlb+ was higher than that of the OH- group ($P<0.01$). A comparison of urine mAlb between the BPV+ group and the BPV- group revealed that the urine mAlb level of the BPV+ group was higher than that of the BPV-

Table 4 Comparison of urine mAlb levels among the four groups (i.e., the OH- BPV-, OH+ BPV-, OH- BPV+, and OH+ BPV+ groups)

Group	n	Urine mAlb (mg/L)
OH- BPV- group	251	27.37±7.54
OH+ BPV- group	36	31.25±11.31*
OH- BPV+ group	142	32.08±9.92*
OH+ BPV+ group	82	37.97±10.02* ^{#&}
H		57.994
P		<0.01

Compared with the OH- BPV- group, *P<0.05; compared with the OH+ BPV- group, #P<0.05; compared with the OH- BPV+ group, &P<0.05. OH, orthostatic hypotension; BPV, blood pressure variability.

group (P<0.01). Moreover, the proportion of patients with BPV+ combined with urine mAlb+ was higher than that of the BPV- group (P<0.01).

Comparison of urine mAlb levels in patients with OH and/or elevated BPV

Further comparisons were made of the urinary mAlb levels among the OH- BPV- group, the OH+ BPV- group, the OH- BPV+ group, and the OH+ BPV+ group. The results were statistically significant (P<0.01), and showed that the OH+ BPV+ group had the highest mAlb level and that the level was significantly higher than the levels of the OH- BPV+ group, the OH+ BPV- group, and the OH- BPV- group (P<0.01). Additionally, the mAlb levels in the OH- BPV+ group and the OH+ BPV- group were higher than those in the OH- BPV- group (P<0.01); however, the difference between the OH+ BPV- group and the OH- BPV+ group was not statistically significant (P>0.05; see Table 4 and Figure 2).

Discussion

Analysis of the prevalence of elderly essential hypertensive patients with OH

OH is more common in the elderly, but elderly patients often do not receive sufficient attention in clinical work. Presently, the reason why OH is more likely to occur in the elderly is not fully understood; however, it is considered to be closely related to the pathological changes that occur

with age. Méndez (7) have found that the prevalence of OH was only 7% in people without known risk factors for OH. The results of another study showed that the prevalence of OH in the middle-aged population was approximately 6.2%, and the prevalence in the elderly population rose to 26.5%, the prevalence of OH in the elderly hypertensive population could be as high as 32.1%, and the prevalence of OH further increased with age (8). It is evident that elderly patients with essential hypertension are prone to OH. This study showed that the prevalence of OH in elderly patients with essential hypertension was 23.09%, which is slightly higher than the 22% reported by Ruscica *et al.* (9). In this study, elderly hypertension patients were included from a single health examination center, there may be some selection bias. Besides, diabetes and heart failure can lead to the increase of urinary mAlb, this study did not include elderly hypertension patients with heart failure, diabetes mellitus in order to avoid the interference on the determination of urine mAlb, which had impact on prevalence of OH.

Analysis of associated factors of elderly essential hypertensive patients with OH

Previous research on OH risk factors have found that hypertension is one of the independent risk factors for OH (10,11). This study separately determined the ratio of OH+ patients to OH- patients with different blood pressure grades. Notably, the proportion of OH+ patients in the grade 3 hypertension group was higher than the proportion of OH- patients (P<0.01), and grade 3 hypertension was found to increase the risk of OH. Compared to patients with grade 1 to 2 hypertension, patients with grade 3 hypertension displayed a significant increase in long-term blood pressure, which can cause vascular endothelial damage, hypoxia of myocardial cells, and the proliferation of collagen cells, resulting in increased heart mass and left ventricle hypertrophy and decreased myocardial compliance, which in turn leads to the limited diastolic filling of the heart, decreased response to preload, and decreased cardiac output. At the same time, long-term high blood pressure also causes the body's baroreceptor sensitivity to decrease, and the appearance of abnormal autonomic nervous regulation, which together weakens the body's ability to compensate for the lowering of blood pressure; thus, it is more likely to cause the occurrence of OH. However, it should be noted that other mechanisms need to be studied further (12). Sarikhani *et al.* (13) analyzed the differences

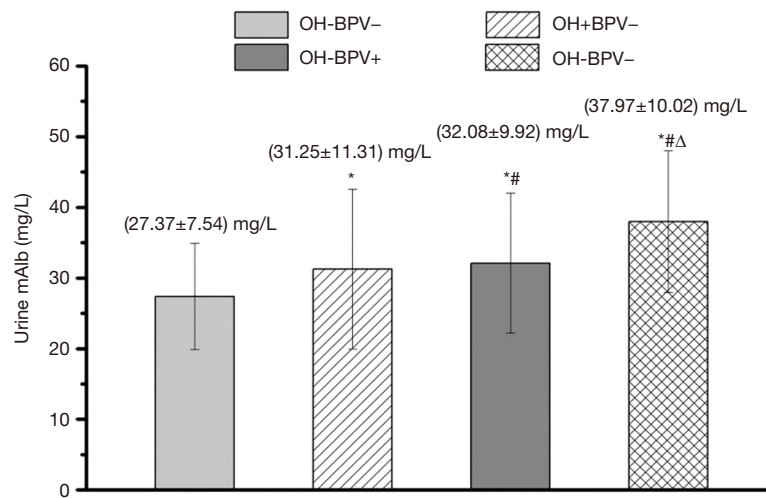


Figure 2 Comparison of urine mAlb levels among the four groups of patients. Compared with the OH- BPV- group, * $P < 0.05$; compared with the OH+ BPV- group, # $P < 0.05$; compared with the OH- BPV+ group, $\Delta P < 0.05$. OH, orthostatic hypotension; BPV, blood pressure variability; mAlb, microalbumin.

in risk factors for OH in men and women and identified a SBP ≥ 180 mmHg in the supine position as a risk factor for OH in both male and female patients. Another foreign epidemiological study showed that patients with the higher supine blood pressure are more likely to have OH; thus, consistent with the results of the present study, grade 3 of supine blood pressure is an important associated factor for OH (14). So, good blood pressure control may prevent OH.

This study also found that coronary heart and carotid atherosclerosis are independent associated factors for OH in elderly patients with essential hypertension. Seok *et al.* (15) analyzed the relationship between OH and coronary heart disease in a coronary heart disease study of 12,433 Black and White individuals in the community and found a correlation between coronary heart disease and OH. Mahdi *et al.* (16) believe that patients with coronary heart disease may have cardiovascular compensatory dysfunction, which, if combined with systemic vasoconstriction and relaxation dysfunction will result in drops in blood pressure and increase the risk of OH. Atherosclerosis is an important pathological basis for cardiovascular events. Fedorowski *et al.* (17) found that patients with carotid atherosclerosis had vascular stenosis, which caused a decrease in baroreceptor sensitivity and a weakened adjustment reflex to orthostatic blood pressure, especially in the severity of atherosclerosis in the elderly and patients in the lying position. There was a positive correlation between the drop in orthostatic blood pressure and atherosclerosis, which indicates that this may

be one of the potential mechanisms of OH. There was also a positive correlation between the severity of atherosclerosis and the decrease in blood pressure in the supine-standing position, particularly among the elderly. Thus, atherosclerosis may be one of the potential mechanisms of OH. Notably, Biaggioni *et al.* (18) drew the same inferences in their study in which the atherosclerosis index was used as an index to evaluate atherosclerosis, and they found that the increase of atherosclerosis index of carotid artery and aorta would decrease sensitivity of arterial baroreceptor and lead the occurrence of OH.

The relationship between OH or elevated BPV and renal damage

The clinical significance of urinary mAlb

At present, there are many indicators of renal damage, such as blood creatinine, urea nitrogen, and urinary mAlb (19). Urinary mAlb passes through the glomerular filtration membrane and remains in a relatively constant state; however, when the structure and function of the kidney change, the kidney's filtering function of albumin can be affected, which can lead to an increase in the level of urine mAlb. Compared with other indicators of renal function, urinary mAlb has an important diagnostic value in identifying early renal damage. Alagiakrishnan *et al.* (20) noted that the level of urinary mAlb is positively correlated with the degree of early renal damage.

The effects of OH or/and elevated BPV on urine mAlb

To clarify the effects of OH and BPV increase on urine mAlb when the two factors exist alone and at the same time, this study also compared the difference in urine mAlb among the four groups: the OH- BPV- group, OH+ BPV- group, OH- BPV+ group, and OH+ BPV+ group. The results showed that patients in the OH+ BPV+ group had the highest urine mAlb levels, followed by patients in the OH- BPV+ group and then the OH+ BPV- group; the OH- BPV- group had the lowest urine mAlb level. Among the four subgroups, patients in the OH+ BPV+ group had the highest urine mAlb. Given that patients in this group have both increased OH and BPV, the autonomic nerve function may be the most impaired. Further, as these two factors are jointly involved in kidney damage, there might be an additive effect. However, it should be noted that there was no significant difference in the urine mAlb level between the OH+ BPV- group and the OH- BPV+ group. Thus, the increase in OH and BPV may essentially be related to the impairment of autonomic nerve function, such that when the autonomic nerve damage of the two groups is similar, there may be no significant difference in the degree of kidney damage. Due to the small sample size, no further linear correlation analysis was made between the decrease of BP from supine to standing position and the increase of urinary mAlb, further attention will be paid in the following research.

In summary, combined coronary heart disease, carotid atherosclerosis, and grade 3 hypertension are independent associated factors for OH in elderly hypertension patients. Good blood pressure control may prevent OH in elderly hypertension patients. In hypertension patients with both OH and elevated BPV, the early renal damage is more serious than that in patients with OH or elevated BPV only. OH is not only a risk factor for cardiovascular and cerebrovascular events, but also is associated with early kidney damage. In the following study, Cystatin C will be determined. Combined determination of urine mAlb and cystatin C will be helpful for doctor to detect early kidney damage in elderly hypertension patients with OH, and early use angiotensin-converting enzyme inhibitor (ACEI) or angiotensin receptor blocker (ARB) may delay kidney damage in these patients.

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study involving human participants were in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by Ethics Committee of Sichuan Provincial People's Hospital (No.2017156) and informed consent was taken from all the patients.

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