Journal of Geriatric Cardiology (2016) 13: 239–243

Research Article **· Open Access ·**

The association between orthostatic hypertension and all-cause mortality in hospitalized elderly persons

Avraham Weiss[1,2], Yichayaou Beloosesky[1,2], Alon Grossman[2,3], Agata Shlesinger[1,2], Nira Koren-Morag[2,4], Ehud Grossman[2,5]

[1]*Department of Geriatrics, Rabin Medical Center, Beilinson Hospital, Petach Tikvah, Israel*
[2]*Sackler Faculty of Medicine, Tel Aviv University, Israel*
[3]*Department of Internal Medicine E, Rabin Medical Center, Beilinson Hospital, Petach Tikvah, Israel*
[4]*Department of Epidemiology and Preventive Medicine, Tel Aviv University, Israel*
[5]*Internal Medicine Department and Hypertension Unit, Chaim Sheba Medical Center, Tel Hashomer, Israel*

Abstract

Background Little is known about the prevalence of orthostatic hypertension (OHT) and its effect on long-term mortality in the elderly. We evaluated the prevalence of OHT and its effect on mortality in hospitalized elderly patients. **Methods** Out of 1852 patients admitted between 31/12/1999 and 31/12/2000 to an acute geriatric ward, 474 patients (48% males) with a mean age of 81.5 ± 6.8 years were enrolled in this study. Blood pressure (BP) was measured three times during the day in a supine and standing position. Patients with at least one increase in systolic or diastolic BP levels upon standing were diagnosed with OHT. Medical history, physical examination and laboratory parameters were retrieved from the medical records. Mortality data until 18th June 2014 were retrieved from the computerized system of the Ministry of the Interior. **Results** Four hundred and seven patients (86%) were diagnosed with OHT. Those without OHT had a lower body mass index and were more likely males, smokers, had a higher rate of Parkinson's disease and less congestive heart failure compared with those with OHT. Patients with OHT had a better survival rate than those without OHT ($P = 0.024$). Hazard ratios (HRs) for mortality in those with OHT adjusted to age and multiple risk factors were: 0.67 [95% confidence interval (CI): 0.51–0.87] and 0.73 (95% CI: 0.55–0.97), respectively; a similar tendency was noticed in a sensitivity analysis by gender. **Conclusion** Hospitalized elderly patients with OHT had a better survival rate than those without OHT.

J Geriatr Cardiol 2016; 13: 239–243. doi:10.11909/j.issn.1671-5411.2016.03.004

Keywords: Hypertension; Mortality; Orthostatic; The elderly

1 Introduction

Orthostatic hypotension (OH) is a common and disturbing problem among the elderly and is especially prevalent among hospitalized patients.[1] Data as to the opposite phenomenon, orthostatic hypertension (OHT) is scarce. There is a dearth of information relating to the prevalence of OHT among the elderly and hardly any knowledge as to its clinical significance and implications.[2] Aries, *et al*.[3] found a favorable outcome in patients with acute stroke if a significant blood pressure (BP) rise occurred during early upright positioning. The fact that OH presents considerable risks to afflicted individuals, particularly the elderly,[4–6] may suggest that OHT may provide a protective effect. We therefore evaluated the prevalence of OHT and its effect on survival in a cohort of hospitalized elderly patients in an acute geriatric setting.

2 Methods

Data for this study was retrieved from a previous study in which OH was evaluated in a cohort of hospitalized patients.[1] All patients consecutively admitted to an acute geriatric department from January 1, 1999 to December 31, 2000 were evaluated. Patients were included in the study if they were at least 60 years old, able to get out of bed alone or with minor assistance and were able to stand up alone for at least 5 min. Patients were studied during their convalescence and three days before their planned discharge from

Correspondence to: Ehud Grossman, MD, Internal Medicine Department and Hypertension Unit, the Chaim Sheba Medical Center, Tel-Hashomer 52621, Israel. E-mail: gross-e@zahav.net.il
Telephone: +972-3530-2834 **Fax:** +972-3530-2835
Received: October 11, 2015 **Revised:** January 12, 2016
Accepted: January 22, 2016 **Published online:** March 27, 2016

the hospital. Of the 1852 patients hospitalized during this period, 474 were included in the study. The study was approved by the local Helsinki committee. Patients were followed until June 2014.

2.1 BP measurements and orthostatic test

BP and heart rate were measured with a device (Vital Signs Monitor 52 NTP model, Welch Allyn Protocol, Inc., Beaverton, Ore USA) checked every day for accuracy against a mercury sphygmomanometer. Measurements were taken in a supine and standing position, three times a day, 30 min after meals and three days before planned discharge. BP was measured in a supine position after at least 5 min of complete bed rest and then after 2 min of standing. BP was measured twice, 1 min apart in each position and subsequently, the average of the two measurements was recorded.

OHT was defined when either systolic or diastolic BP levels upon standing were greater than the supine levels. Patients were classified as either OHT^+ when OHT was exhibited in at least in one measurement or OHT^- when OHT was not exhibited on all three measurements.

2.2 Data collection

Detailed medical history, standard physical examination, and routine blood chemistries were performed in all patients. Cause of hospitalization and prescribed medications were recorded. In addition to age, height and weight were also recorded. Body mass index (BMI) was calculated as weight (kg) divided by height (m^2). Hypertension was diagnosed if the patient had been treated with antihypertensive medications or if the systolic BP was >140 mmHg and/or diastolic BP > 90 mmHg.

Dyslipidemia was defined as serum total cholesterol levels ≥ 200 mg/dL. Diabetes mellitus (DM) was diagnosed if the patient was taking hypoglycemic agents or if fasting plasma glucose was recorded as higher than 126 mg/dL on at least two occasions. Chronic kidney disease was diagnosed when serum creatinine values ≥ 1.5 mg/dL. Coronary heart disease was diagnosed when a history of angina pectoris, myocardial infarction, coronary catheterization with balloon dilatation or coronary artery bypass graft operation, was recorded. Other medical conditions retrieved from the medical records were atrial fibrillation, chronic obstructive pulmonary disease and senile dementia. Prescribed medications were categorized as diuretics, renin angiotensin system blockers (angiotensin converting enzyme inhibitor/angiotensin receptor blocker), calcium channel blockers, beta blockers, aspirin, and hypoglycemic agents.

Mortality data until 18th June 2014 were taken from the Bureau of Population Registry of the Ministry of Interior.

2.3 Statistical analysis

Data were analyzed with SPSS software version 22.0. (SPSS Inc. Headquarters, 233 S. Wacker Drive, 11th floor Chicago, Illinois 60606, USA). The significance level was set at 0.05. Data were presented as mean ± SD for continuous variables and as frequency and percentage for categorical variables. Chi-square tests and independent *t*-tests compared the two OHT groups for categorical and continuous variables, respectively. Survival was calculated as time from screening to death or time from screening to the end of follow-up (June 18, 2014). Cox regression analyses were performed separately for each conventional risk factor, adjusted to age, to analyze its HR for mortality.

Multivariate analysis using the Cox regression model for survival was performed with conventional risk factors. Conventional risk factors for mortality were selected for the final model on the basis of an association with mortality in the univariate analysis or findings of significant associations in previous studies. The covariates were age, gender, BMI, cerebrovascular accident, atrial fibrillation, ischemic heart disease, congestive heart failure, chronic renal failure, diabetes mellitus, Parkinson's disease and dementia. Cumulative survival curves were computed and demonstrated using the Cox regression models.

3 Results

3.1 Study population

The study population consisted of 474 subjects (48% male) with a mean age of 81.5 ± 6.8 years. Four hundred and seven patients (86%) exhibited OHT at least in one of the three measurements and were defined as OHT^+. Table 1 summarizes patients' characteristics by OHT group. OHT^+ patients had a higher BMI, were less likely males, were smokers, had a lower rate of Parkinson's disease and congestive heart failure compared with those who were OHT^-.

3.2 Mortality rate and survival

A total of 425 deaths occurred in the entire cohort over a mean follow-up of 5.7 ± 4.7 years (range 0.1 to 15.3 years). The mortality rate was 15.8 per 100 person-years and was lower in those with OHT^+ (15.1 per 100 person-years) than in those with OHT^- (21.3 per 100 person-years), (P = 0.010).

Female gender and higher BMI were associated with a lower rate of mortality, whereas diabetes mellitus, chronic renal failure, congestive heart failure, ischemic heart disease and senile dementia were associated with a higher rate of mortality (Table 2).

Table 1. Patients' characteristics.

	Total	Orthostatic hypertension		*P*
		No	Yes	
	n = 474	*n* = 67	*n* = 407	
Males	229 (48%)	43 (64%)	186 (46%)	0.005
Age, yrs	81.5 ± 6.8	81 ± 6.1	82 ± 6.9	0.652
Body mass index, kg/m^2	25.2 ± 4.5	24 ± 3.6	25.5 ± 4.5	0.002
Smokers	75 (16%)	20 (32%)	55 (14%)	< 0.001
Hypertension	298 (63%)	39 (58%)	259 (64%)	0.367
Diabetes mellitus	140 (29.5%)	23 (34%)	117 (29%)	0.353
Hyperlipidemia	178 (40%)	22 (35.5%)	156 (41%)	0.398
Chronic renal failure	116 (24.5%)	21 (31%)	95 (23%)	0.158
Chronic heart failure	147 (31%)	12 (18%)	135 (33%)	0.012
Ischemic heart disease	268 (57%)	42 (63%)	226 (56%)	0.302
Stroke	152 (32%)	25 (37%)	127 (31%)	0.334
Parkinson's disease	61 (13%)	14 (21%)	47 (12%)	0.036
Plasma glucose, mg/dL	121 ± 47	126 ± 43	120 ± 48	0.357
eGFR, mL/min	56.2 ± 17.7	53 ± 17	57 ± 18	0.150
Medications				
Diuretics	163(34%)	18 (27%)	145 (36%)	0.162
ACEI/ARB	149 (31%)	21 (31.3%)	128 (31.4%)	0.986
β-blockers	85 (18.4%)	12 (18%)	73 (18%)	0.996
Calcium antagonists	143 (30%)	17 (25.4%)	126 (31%)	0.356

Data are presented as mean ± SD or *n* (%). ACEI: angiotensin converting enzyme inhibitor; ARB: angiotensin receptor blocker; eGFR: estimated glomerular filtration rate.

Table 2. Risk of mortality by clinical and laboratory parameters and orthostatic hypertension.

	Adjusted age, HR (95% CI)	#Adjusted multivariate, HR (95% CI)
Female gender	0.62 (0.51–0.75)	0.69 (0.56-0.86)
High body mass index*	0.95 (0.93–0.97)	0.95 (0.93–0.97)
Diabetes mellitus	1.35 (1.08–1.67)	1.29 (1.03–1.61)
Chronic renal failure	1.93 (1.55–2.40)	1.54 (1.21–1.95)
Congestive heart failure	1.56 (1.26–1.91)	1.41 (1.09–1.81)
Ischemic heart disease	1.40 (1.14–1.71)	1.25 (1.01–1.55)
Atrial fibrillation	1.35 (1.07–1.71)	1.20 (0.92–1.57)
Stroke	1.23 (1.00-1.51)	0.98 (0.79–1.22)
Chronic obstructive pulmonary disease	1.27 (1.01–1.59)	1.20 (0.95–1.52)
Parkinson's disease	1.51 (1.14–1.99)	1.06 (0.79–1.42)
Dementia	1.97 (1.57–2.49)	1.91 (1.50–2.45)
Orthostatic hypertension	0.67 (0.51–0.87)	0.73 (0.55–0.97)

*Per 1 kg/m^2; #Adjusted for age, gender, body mass index stroke, atrial fibrillation, ischemic heart disease, congestive heart failure, chronic renal failure, diabetes mellitus, Parkinson's disease and dementia.

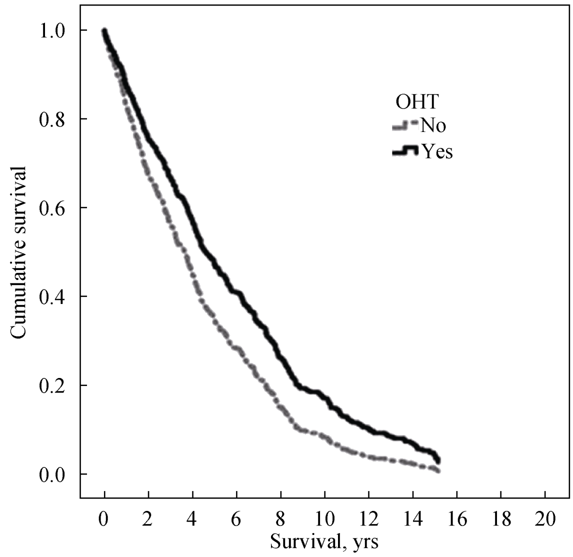

Figure 1. Survival curves in patients with and without OHT. Survival curves by OHT adjusted for age, gender, body mass index, stroke, atrial fibrillation, ischemic heart disease, congestive heart failure, chronic renal failure, diabetes mellitus, Parkinson's disease and dementia (P = 0.041). OHT: orthostatic hypertension.

In comparison to the OHT$^-$ group, the HR for mortality during the follow-up period in the OHT$^+$ group adjusted for age and known risk factors was: 0.67 [95% confidence interval (CI): 0.51–0.87] and 0.73 (95% CI: 0.55–0.97), respectively (Table 2). The survival rate was significantly better amongst the OHT$^+$ group compared to the OHT$^-$ group (5.9 ± 4.9 *vs*. 4.7 ± 3.7 years, respectively; P = 0.024). Females had a better survival rate than males (6.5 ± 4.9 and 4.8 ± 4.3 years, respectively; P < 0.001). In both genders, OHT$^+$ patients had better survival rates then OHT$^-$ patients. Differences in cumulative survival curves between the two OHT groups are presented in Figure 1.

4 Discussion

In this historical-prospective study, it was shown that elderly patients whose BP increased above the supine position at least once in three BP measurements during the day were at a lower risk of mortality, even after adjustments for known risk factors. This finding seems to contradict our previous analysis of this cohort where no association was found between OH and all-cause mortality.[7] However, the interpretation of the orthostatic tests was different in our previous analysis. Herein, orthostatic tests were performed three times a day. In our previous analysis, patients were diagnosed with OH when they had a fall in BP in two out of the three measurements. In the present analysis, OHT was defined when exhibited in at least one measurement. Thus, some patients who had been diagnosed with OH in our former study, experienced OHT only on the third measurement and were thus included in our OHT group.

In accordance with our present findings, Lagro, *et al*.[8] found a survival advantage in patients attending a fall clinic when their BP fell upon standing, recovering to at least 80% of its supine levels in one minute. Aries, *et al*.[3] showed that stroke patients in whom BP rose after upright repositioning had a better outcome compared to stroke patients whose BP did not rise. Lindqvist, *et al*.[9] demonstrated in a relatively young cohort of diabetic patients that increased BP after rising to a standing position was associated with preserved autonomic function. These observations, together with our findings, may suggest a favorable outcome in elderly patients with OHT. It seems that an effective mechanism to overcome a gravitational challenge, especially when rising from a supine position to a standing position, presents a better prognosis in the elderly.

Yet, other investigators reported that OHT was associated with 'masked hypertension' and thus considered a risk factor for mortality.[10,11]

A possible explanation for the different observations can be the varied populations studied and the magnitude of BP elevation upon standing. It is possible that the 'autonomic reserve' manifested by OHT may be protective in the elderly, fragile populations such as the one evaluated in our study. In addition, when BP elevation upon standing is mild (≤ 20 mmHg), it may indicate preserved autonomic function, whereas when BP elevation upon standing is remarkable (≥ 20 mmHg), it may uncover 'masked hypertension' and be associated with increased mortality.

In the present study, the majority of patients were defined as having OHT. This may be related to the flexible criteria we used when defining OHT as any rise or no change in systolic or diastolic BP upon assuming an upright posture from a lying position, even once during the day. It is noteworthy that we used three measurements during the day to identify those with at least one episode of OHT. We prefer to use flexible criteria in identifying all patients with even a minimal ability to maintain or increase BP levels while standing.

The mechanism underlying the survival benefit of elderly persons with OHT is somewhat unclear and several mechanisms have been proposed. We believe that the main mechanism in the elderly is the agile and tonic reaction of the autonomic sympathetic systems as suggested by previous studies.[2,12–16]

Our study has some limitations. Firstly, we included only hospitalized elderly patients; however, BP was measured towards the end of the hospitalization when the patient's medical condition had stabilized. In addition, co-morbidities and dispensed medications in the study cohort were similar to the community-dwelling elderly. Nevertheless, we should be careful and emphasize that our observation may not be applicable to elderly healthy subjects. Secondly, the cause of mortality was unknown to us; therefore, we did not know whether the increased mortality rate was related to cardiovascular mortality.

In conclusion, hospitalized elderly patients in whom BP levels increase or remain unchanged upon standing from a supine position at least once during the day, have a favorable survival rate. Several measurements may be required for diagnosing OHT.

Acknowledgments

The authors thank Mrs. Phyllis Curchack Kornspan for her editorial services. There are no competing commercial interests in relation to the submitted work.

References

1 Weiss A, Grossman E, Beloosesky Y, *et al*. Orthostatic hypotension in acute geriatric ward: is it a consistent finding? *Arch Intern Med* 2002; 162: 2369–2374.

2 Fessel J, Robertson D. Orthostatic hypertension: when pressor reflexes overcompensate. *Nat Clin Pract Nephrol* 2006; 2: 424–431.

3 Aries MJ, Bakker DC, Stewart RE, *et al*. Exaggerated postural blood pressure rise is related to a favorable outcome in patients with acute ischemic stroke. *Stroke* 2012; 43: 92–96.

4 Gupta V, Lipsitz LA. Orthostatic hypotension in the elderly: diagnosis and treatment. *Am J Med* 2007; 120: 841–847.

5 Shibao C, Lipsitz L A, Biaggioni I, *et al*. Evaluation and treatment of orthostatic hypotension. *J Am Soc Hypertens* 2013; 7: 317–324.

6 Regan CO, Kearney PM, Cronin H, *et al*. Oscillometric measure of blood pressure detects association between orthostatic hypotension and depression in population based study of older adults. *BMC Psychiatry* 2013; 13: 266.

7 Weiss A, Beloosesky Y, Kornowski R, *et al*. Influence of orthostatic hypotension on mortality among patients discharged from an acute geriatric ward. *J Gen Intern Med* 2006; 21: 602–606.

8 Lagro J, Schoon Y, Heerts I, *et al*. Impaired systolic blood pressure recovery directly after standing predicts mortality in older falls clinic patients. *J Gerontol A Biol Sci Med Sci* 2014; 69: 471–478.

9 Lindqvist A, Torffvit O, Rittner R, *et al*. Artery blood pressure oscillation after active standing up: an indicator of sympathetic function in diabetic patients. *Clin Physiol* 1997; 17: 159–169.

10 Barochiner J, Cuffaro PE, Aparicio LS, *et al*. Predictors of

masked hypertension among treated hypertensive patients: an interesting association with orthostatic hypertension. *Am J Hypertens* 2013; 26: 872–878.
11 Kario K, Eguchi K, Nakagawa Y, *et al*. Relationship between extreme dippers and orthostatic hypertension in elderly hypertensive patients. *Hypertension* 1998; 31: 77–82.
12 Kario K, Eguchi K, Hoshide S, *et al*. U-curve relationship between orthostatic blood pressure change and silent cerebrovascular disease in elderly hypertensives: orthostatic hypertension as a new cardiovascular risk factor. *J Am Coll Cardiol* 2002; 40: 133–141.
13 Robertson D, Hollister AS, Biaggioni I, *et al*. The diagnosis and treatment of baroreflex failure. *N Engl J Med* 1993; 329: 1449–1455.
14 Ketch T, Biaggioni I, Robertson R, *et al*. Four faces of baroreflex failure: hypertensive crisis, volatile hypertension, orthostatic tachycardia, and malignant vagotonia. *Circulation* 2002; 105: 2518–2523.
15 Manger WM. Baroreflex failure—a diagnostic challenge. *N Engl J Med* 1993; 329: 1494–1495.
16 Jordan J, Shannon JR, Black BK, *et al*. Raised cerebrovascular resistance in idiopathic orthostatic intolerance: evidence for sympathetic vasoconstriction. *Hypertension* 1998; 32: 699–704.