

## Prevalence and Clinical Implications of Orthostatic Hypotension in Elderly Inpatients

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### Abstract

**Background:** Prevalence of orthostatic hypotension (OH) has been investigated in many studies, mainly on selected samples of subjects. We aimed to assess the prevalence of OH and its association with incidence of adverse events among older medical inpatients.

**Methods:** OH was evaluated according to current guidelines at admission and at discharge among older medical inpatients admitted to a Geriatric acute ward of an university-teaching hospital. A comprehensive clinical (CIRS, Cumulative Illness Rating Scale), functional (ADL, Activities of Daily Living; IADL, Instrumental Activities of Daily Living Scale, TUG, Timed Up and Go) and cognitive (SPMSQ, Short Portable Mental Status Questionnaire) evaluation was performed. Length of stay-in and adverse events (death, institutionalization, falls, syncope, post-traumatic fractures, cardiovascular events) were evaluated at discharge and at 6 months.

**Results:** Among 343 patients admitted, 195 (mean age  $80.1 \pm 7.2$ ) were enrolled. Prevalence of OH at admission was 52.3%; patients with OH had higher systolic and diastolic blood pressure values ( $p=0.001$  both) and lower heart rate ( $p=0.02$ ) than patients without OH. Although several conditions were associated with presence of OH, only history of neurological and coronary artery disease were slightly independently associated with OH ( $p=0.03$  and  $p=0.02$ , respectively). Prevalence of OH at discharge was 49%. OH was not significantly associated with any adverse event, nor during the hospital stay nor after discharge.

**Conclusion:** OH is extremely common among elderly inpatients, but it was not associated with adverse events. Our results question the utility of routinely screening older medical inpatients for OH.

**Keywords:** Orthostatic hypotension; Elderly; Inpatients; Coronary artery disease

### Introduction

Orthostatic hypotension (OH) is defined as a decline in systolic or diastolic blood pressure of at least 20 and 10 mmHg respectively, while standing up from a lying position within 3 minutes of observation [1]. Its prevalence among home-dwelling elderly has been reported to vary from 6 to 30% [2-11], reflecting differences in samples studied and measurements protocols [12]. Similarly, among nursing-home residents a wide range of prevalence has been reported (18-50%) [13,14]. Few studies focused their attention on elderly inpatients: Shibao et al, analyzing discharge data from the American Nationwide Inpatient Sample, found that among patients over 75 years the incidence of OH-related hospitalizations was 233 on 100000 [15], but the prevalence seems to be much higher in acute geriatric medical wards [16]. In a retrospective study conducted in a veterans' geriatric clinic OH affected up to 55% of the men admitted to the hospital [17]. Similar findings were reported in one other small-cohort study [18].

Despite the high prevalence of OH reported in these studies, there are contrasting evidences on clinical implications of OH among elderly subjects. Although some studies demonstrated that OH is associated with adverse events, including myocardial infarction,

coronary artery disease, incident heart failure, recurrent falls, overall and cardiovascular death [2,4,10,11,19-22], several other studies have reported negative results [4,6,9,10,19,23-25]. However, most of these studies have been performed on selected samples of subjects, mainly on community-dwelling hypertensive or diabetic individuals with few other co morbidities. To the best of our knowledge, there are very few studies [16-18,26,27] investigating prevalence and clinical implications of OH among elderly contemporary hospitalized patients. "We hypothesized that, in such a frail and vulnerable sample of patients, there should be a high prevalence of OH," thereby consenting to evaluate whether this condition is consistently associated with adverse events during the hospital stay and at short term after discharge. In the present study we aimed primarily to evaluate the prevalence of, and the clinical conditions associated with, OH in a sample of elderly medical inpatients admitted to a Geriatric Unit of a University-teaching hospital, and secondly to investigate whether OH was associated with length of stay and with greater incidence of adverse events (including syncope, falls, post-traumatic fractures, re-hospitalization, institutionalization, death and cardiovascular events) during the hospital stay and at six months after discharge.

### Methods

During the period December 2011-March 2012, patients aged  $\geq 65$  years consecutively attending the Geriatric Acute Ward of San

Giovanni Battista-Molinette University Hospital in Turin (Italy) were recruited for this study. Subjects were asked to give an informed consent before to join the study. We excluded terminal patients and those unable to reach and keep the standing position on their own.

Prevalence of OH was investigated at admission and at discharge. Blood pressure (BP) measurement was made according to the current European guidelines for arterial hypertension [28] using a manual mercury sphygmomanometer with an appropriate sized cuff. BP was recorded in a lying position after 5 minutes of bed rest, then after 30 seconds, 1 and 3 minutes of standing. We extended the length of time test to 5 minutes in order to find delayed forms following the most recent indications for the OH diagnosis [29]. BP measurements were made during the day at least thirty minutes after meals. The cardiovascular response was investigated by recording the peripheral heart rate whilst supine and upright as suggested by the current European OH guidelines [30].

For each patient demographic variables (age/gender) and medical history of congestive heart failure, coronary artery disease (CAD), hypertension, arrhythmia, valvular disease, neurological disease and diabetes were considered at admission. We recorded both the overall number of medications and the main drugs categories such as antihypertensive (calcium channel antagonists, angiotensin receptor blockers, angiotensin converting enzyme inhibitors, beta or alpha blockers, diuretics), analgesics/opioids, benzodiazepine, neuroleptics, atypical antipsychotics and anticholinergics. The following measures were obtained: height (meters), weight (kilograms), Body Mass Index [BMI, calculated according to the formula weight (kilograms)/height (square meters)]. Previous falls and syncope were investigated. Indexes of co morbidity and global physical health (CIRS, Cumulative Illness Rating Scale) [31], cognitive status (SPMSQ, Short Portable Mental Status Questionnaire) [32], functional autonomy (ADL, Activities of Daily Living; IADL, Instrumental Activities of Daily Living Scale) [33,34], and mobility (Timed Up and Go) [35] were carefully assessed in each patient. Length of stay-in (measured in days), survival and adverse events (including syncope, falls, post-traumatic fractures, re-hospitalization, institutionalization, death and cardiovascular events) were recorded at discharge and after 6 months through telephone interview. For those patients we have not been able to contact after discharge we addressed to the Demographical Services of residence Communes to verify their alive status: these subjects were included into the survival analysis but excluded from the other ones.

### Statistical Analysis

The Statistical analysis was performed via the Software SPSS 19.0 for Windows. For the continuous variables the mean and the standard deviation have been evaluated; for the Boolean variables percentage has been calculated. The Boolean variables have been analyzed through the  $\chi^2$  test; the continuous variables by using the t-test for paired data. Stepwise multiple linear regression analysis was performed introducing variables achieving the level of significance at the simple analysis. The survivals curves have been evaluated using the Kaplan-Meier method with Log Rank of significance.

### Results

During the period of observation 343 patients were admitted to our ward; 148 patients were excluded: 118 were unable to stand or keep the upright position, 26 were terminal patients, and 4 were in an advanced stage of dementia, with low compliance with the operators. The final

sample studied was therefore composed by 195 subjects (101 women and 94 men, mean age  $80.1 \pm 7.2$  years). Because of prevalence of OH did not change at the 5-minute test, results will be referred to the standard 3-minute test. In the overall sample only 44 patients were steadily OH free both at entry and at discharge. The main clinical characteristics of the patients according to the presence of OH are shown in Table 1.

Characteristics and Co morbidities	With OH (n=102) Mean $\pm$ SD/% <sup>†</sup>	Without OH (n=93) Mean $\pm$ SD/% <sup>†</sup>	P-Value
Age	79.7 (7.5)	80.6 (6.9)	0.35
BMI (Kg/m <sup>2</sup> )	24.7 (5.6)	24.9 (5.0)	0.86
Gender (male/female)	55/39	47/54	0.09
ADL score (n° lost functions)	1.6 (1.6)	1.3 (1.6)	0.32
IADL score	7.73 (4.1)	8.05 (4.1)	0.59
SPMSQ score	2.5 (2.3)	2.35 (2.6)	0.06
CIRS Severity Index	1.9 (1.1)	1.77 (0.3)	0.46
CIRS Comorbidity Index	3.6 (1.6)	3.7 (1.5)	0.65
Baseline SBP (mmHg)	134.2 (17.2)	126.8 (17.1)	0.001*
Baseline DBP (mmHg)	79.8 (10.1)	75.4 (10.7)	< 0.001*
Baseline HR (beats/min)	75.3 (11.9)	80.0 (14.7)	0.02*
HR 1' (beats/min)	81.9 (13.9)	84.7 (15.1)	0.19
HR 3' (beats/min)	79.3 (15.8)	83.8 (15.2)	0.05*
Number of drugs	7.1 (3.35)	6.35 (3.1)	0.11
Cardiovascular disease	91.2	82.8	0.08
Congestive heart failure	5.9	6.5	0.87
Coronary artery disease	32.4	18.3	0.02*
Hypertension	79.4	73.1	0.3
Arrhythmia	41.2	38.7	0.72
Valvular disease	16.1	12.7	0.5
Neurological disease	37.3	21.5	0.02*
TIA/Stroke	5.9	3.2	0.38
Diabetes	36.3	25.8	0.11
Previous syncope	13.7	16.1	0.64
Previous fall	33.3	36.5	0.64

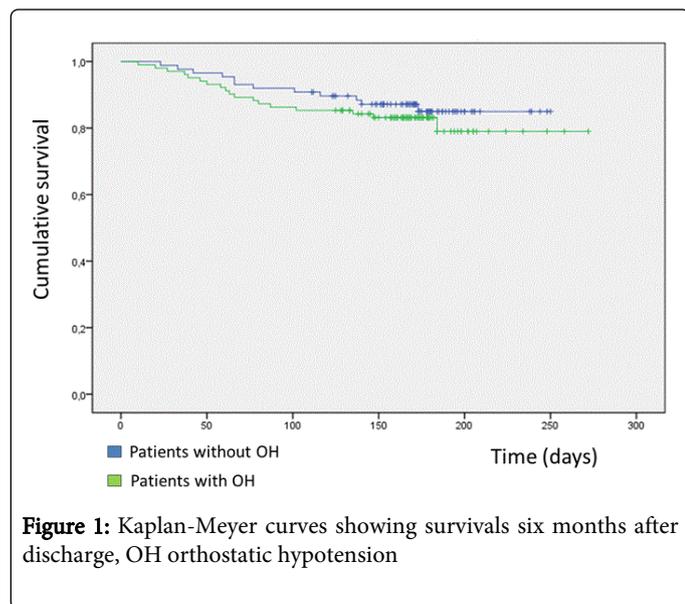
**Table 1:** Characteristics and co morbidities of the sample investigated, OH orthostatic hypotension, SBP systolic blood pressure, DBP diastolic blood pressure, HR hearth rate, TIA transient ischemic attack. \* Variables reaching the step for significance set at P<0.05, <sup>†</sup> Booleans variables are reported in the table expressed as percentage

Prevalence of OH at entry was 52.3%. At discharge it was not possible to perform the orthostatic test in 73 subjects who had been evaluated at admission: 55 were no more able to stand or keep the

upright position on their own, 6 were transferred to other wards, 6 were dead and 10 were not cooperating. Among the remaining 122 patients, prevalence of OH was 49%. Subjects showing OH at baseline and at discharge were not systematically the same: OH was observed in both circumstances in 44 cases, 16 patients presented OH just at entry while 18 patients were diagnosed with OH at discharge only.

At baseline subjects with OH had higher systolic and diastolic blood pressure values ( $p=0.001$ ,  $p<0.001$ , respectively) and showed a lower heart rate both at baseline and after 3 minutes of standing ( $p=0.02$ ,  $p=0.05$ ). Among all the clinical and multidimensional variables considered, including drug categories and classes of blood pressure lowering drugs (Table 1) OH was weakly associated only with history of coronary artery disease (CAD;  $p=0.02$ ) and neurological disease ( $p=0.02$ ). After multivariate adjustment these variables were independently associated with OH ( $p=0.02$ ,  $p=0.03$ ).

There was no difference in incidence of syncope, falls, length of stay and mortality between patients with and without OH. The six-month Kaplan Meyer survival curves (Figure 1) did not show any difference between patients with and those without OH, as well as there was no difference in the incidence of each adverse event between patients with and without OH (Table 2).



Adverse events	With OH (n=94)	Without OH (n=80)	P Value
Falls	12	11	0.85
Syncope	1	-	0.27
Fracture	1	5	0.06
Hospitalization	31	24	0.67
Institutionalization	14	9	0.5
Myocardial infarction	2	1	0.66
TIA/Stroke	-	1	0.27

**Table 2:** Adverse events considered six months after discharge, OH orthostatic hypotension, TIA transient ischemic attack

## Discussion

Orthostatic hypotension is described as a common disorder in the elderly, particularly in the acute medical setting. We observed that about half of the older patients admitted to an acute Geriatric Ward were diagnosed with OH and therefore our results confirm the high prevalence of OH reported in those few other studies which investigated hospitalized elderly inpatients [16-18,27]. Despite a large and comprehensive evaluation, OH was found to be independently associated only with medical history of neurological disease (but not with stroke or transient ischemic attack) and CAD. Although this later observation may be a casual finding, a previous study among community-dwelling older subjects population reported that participants with OH were more likely to have a medical history of myocardial infarction [5]. Subjects with OH had higher systolic blood pressure values at baseline. Raised blood pressure values in patients affected by OH have been reported in previous studies either in community-dwelling, nursing-home population and in hospital inpatients [4,6,8,9,12,17].

Although we performed a careful multidimensional evaluation we didn't find any association between OH and the several variables potentially involved in the pathogenesis of OH. Moreover, the test repetition at discharge showed that OH is a not-reproducible disease. Therefore, it seems likely that in older acute medical inpatients several physiopathological factors and therapeutic measures can contribute to the pathogenesis of OH during the hospital stay. This complex interplay between physiopathological conditions and therapeutic variations makes extremely hard to analyze the potential impact on OH of variations in drug therapy between admission and discharge. Indeed, in the older patient acute events as well as therapeutic interventions can precipitate an already impaired compensatory response to standing. Age-related changes that can affect the normal blood pressure regulation in the elderly include decreased baroreflex sensitivity, alpha-1-adrenergic vasoconstrictor response, parasympathetic activity and renal salt and water conservation, an increased vascular stiffness and a reduced left ventricular diastolic filling [36]. Many factors can influence OH development in the acute medical setting, mainly concerning causes of low circulating volume such as arrhythmia, myocardial infarction, acute heart failure, dehydration, diarrhea, vomiting, fever and hemorrhage. The resolution of the acute phase and a fluid volume expansion could lead to a restoration of the normal circulating volume with a more efficient compensatory response to standing. On the contrary prolonged bed rest can promote the development of the OH. The genesis of the bed rest deconditioning involves multiple mechanisms. With the loss of the head-to-foot hydrostatic pressure gradient, the blood shift from the peripheral to the central veins increases the right and the left ventricular transmural pressure. After a transient increase in diastolic filling and stroke volume, the activation of the short-term regulatory volume mechanism results in the establishment of a new hemodynamic steady state, set to a lower circulating plasma volume. A ventricular remodelling over time during longer bed rest was also suggested to contribute to the OH development [37], as well as a decrease carotid-cardiac baroreflex [38]. During the stay in hospital, furthermore, a changing in or a revision of the pharmacological therapy can impair or improve the regulatory reflex to orthostatic stress. Nevertheless, other studies previously performed on an elderly outpatients' population find that OH is often a not-reproducible disease. On subsequent occasions in the morning, Ward et al monitored OH up to two minutes after standing in a sample of forty outpatients symptomatic for syncope, fall or postural symptoms.

Orthostatic hypotension was confirmed only in the 67.5% of subjects on different occasions [39]. Similarly, in an Italian study performed on 3858 outpatients randomly recruited by general practitioners the OH presence on a second visit after seven days was confirmed in 36.5% and in 25.7% of cases considering systolic OH and both systolic and diastolic OH [40]. Moreover the OH reproducibility seems to be low over time the same day [16].

We did not observe a greater incidence of adverse events among patients with OH than in those without either during the hospital stay and at the follow up. These findings are consistent with the results of a long term follow up (until 3.5 years after discharge) on a sample of 502 elderly inpatients, with no evidence of association with OH and all-cause mortality [26]. To our knowledge there are no other prospective data on elderly inpatients in an acute care setting. Although potentially of clinical utility and interest for selected older patients, our study adds to the evidence that the evaluation of OH is not predictive of adverse outcomes in short and medium terms in this setting of frail and vulnerable medical older patients. Therefore these results raise some doubts about the clinical utility of a routine investigation for OH among elderly medical inpatients. Recently, new evidence on OH from unselected older general population cohorts question whether, even in that contest, OH should be considered a real cardiovascular risk factor [9].

This study has several strengths. First it is an observational-prospective study. Second, the patients underwent a full comprehensive geriatric assessment and results were controlled for a great number of confounders. Finally the entire patient evaluation was performed by qualified medical staff. The present study has also some limitations. Our sample size wasn't very large and the number of the adverse events considered was small, which could have impaired our statistical analysis.

## Conclusion

This study showed a high prevalence of OH among elderly medical inpatients, which was not systematically present in the same patients either at admission or at discharge. Moreover we could not find any association between clinical variables and OH, as well as between the presence of OH and adverse outcomes either during the hospital stay or after discharge. Our findings raise some doubts about the utility to look for OH routinely in all older medical hospital inpatients. More studies on larger clinical samples are needed to confirm the clinical significance of OH among older patients.

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