



## Protocol paper

## When should orthostatic blood pressure changes be evaluated in elderly: 1st, 3rd or 5th minute?

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## ABSTRACT

Detection of orthostatic hypotension (OH) is very important in geriatric practice, since OH is associated with mortality, ischemic stroke, falls, cognitive failure and depression. It was aimed to determine the most appropriate time for measuring blood pressure in transition from supine to upright position in order to diagnose OH in elderly. Comprehensive geriatric assessment (CGA) including Head up Tilt Table (HUT) test was performed in 407 geriatric patients. Orthostatic changes were assessed separately for the 1st, 3rd and 5th minutes (HUT<sub>1</sub>, HUT<sub>3</sub> and HUT<sub>5</sub>, respectively) taking the data in supine position as the basis. The mean age, recurrent falls, presence of dementia and Parkinson's disease, number of drugs, alpha-blocker and anti-dementia drug use, and fasting blood glucose levels were significantly higher in the patients with versus without OH; whereas, albumin and 25-hydroxy vitamin D levels were significantly lower ( $p < 0.05$ ). However, different from HUT<sub>3</sub> and HUT<sub>5</sub>, Charlson Comorbidity Index and the prevalence of diabetes mellitus were higher, the use of antidiabetics, antipsychotics, benzodiazepine, opioid and levodopa were more common ( $p < 0.05$ ). Statistical significance of the number of drugs and fasting blood glucose level was prominent in HUT<sub>1</sub> as compared to HUT<sub>3</sub> ( $p < 0.01$ ,  $p < 0.05$ ). Comparison of the patients that had OH only in HUT<sub>1</sub>, HUT<sub>3</sub> or HUT<sub>5</sub> revealed no difference in terms of CGA parameters. These results suggests that orthostatic blood pressure changes determined at the 1st minute might be more important for geriatric practice. Moreover, 1st minute measurement might be more convenient in the elderly as it requires shorter time in practice.

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## 1. Introduction

The prevalence of orthostatic hypotension (OH) increases with age and it is 10–30% in elderly (Low, 2008). Deficiency in arterial baroreflex sensitivity and venomotor control along with aging, as well as cardiac hypertrophy, decrease in renin-angiotensin aldosterone level and the sensitivity to these hormones make the management of postural blood pressure difficult (Low & Tomalia, 2015; Low, 2008; Okada et al., 2012). Besides, Parkinson's disease (PD), diabetes mellitus (DM), dehydration and malnutrition, which are common comorbidities in elderly patients, and accordingly frequent use of antihypertensive drugs, levodopa, antidepressants and benzodiazepines might enhance tendency toward OH (Low & Tomalia, 2015; Press, PUNCHIK, & Freud, 2015). In addition to typical symptoms such as dizziness, blackout,

temporary loss of conscious, weakness, nausea and drowsiness, the patients may also present with atypical symptoms such as falls and head, neck and low back pain. Asymptomatic OH, in fact, is more common in older adults than considered by the clinicians; 1/3 of the patients have OH although they have no complaint (Arbogast, Alsheklee, Hussain, McNeeley, & Chelimsky, 2009). Detection of OH in elderly is of great importance; because, numerous studies have demonstrated association of OH with mortality, ischemic stroke, falls, cognitive failure and depression (Chou et al., 2015; Gangavati et al., 2011; Jodaitis et al., 2015). For these reasons, evaluation of orthostatic blood pressure changes (OBPC) should necessarily be a part of the comprehensive geriatric assessment (CGA).

According to the consensus statement on the definition of orthostatic hypotension published in 1996, the diagnosis of OH is made in the event of at least 20 mmHg decrease in systolic blood pressure (SBP) and/or at least 10 mmHg decrease in diastolic blood pressure (DBP) within the first 3 min of standing up (The Consensus Committee of the American Autonomic Society and the American Academy of Neurology, 1996). Although

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measurements at the 1st and 3rd minutes of standing are recommended for the diagnosis of OH, there is yet no consensus on the optimum time of measurement for diagnosis (Campos et al., 2015; Maurer, Rivadeneira, & Bloomfield, 1998; Yasuharu et al., 2005). Delayed OH is another concept relevant to this subject and is defined as OH that develops after the 3rd minute; however, data about the prevalence and importance of this situation in elderly is limited (Podoleanu et al., 2009).

The present study aimed to determine the optimum time for clinical significance of blood pressure measurement in transition from supine to upright position while evaluating OBPC in elderly.

## 2. Materials and methods

### 2.1. Study design

A total of 407 elderly patients, who admitted to the geriatric clinic in a university hospital between January 2014 and August 2015, were included in this prospective and cross-sectional observational study. CGA including Head up Tilt Table (HUT) was performed in those geriatric patients after obtaining their informed written consents.

### 2.2. Inclusion criteria

The patients who were over the age of 65 years, presented to our center for any reason, and had none of the exclusion criteria.

### 2.3. Exclusion criteria

Patients with severe anemia (hemoglobin <10 g/dL), critical mitral and/or aortic valve stenosis, acute or chronic renal insufficiency, decompensated cardiac and/or hepatic insufficiency, severe carotid artery stenosis and/or coronary artery stenosis, history of cerebrovascular accident, myocardial infarction or lower extremity fracture in the last week, hypotensive shock, bradycardia or tachycardia during examination, dehydration, electrolyte imbalance, acute hemorrhage, severe metabolic acidosis, sepsis, and similar severe comorbid conditions, all of which are the contraindications for Head up Tilt Table test (HUT), were excluded (Moya et al., 2009).

### 2.4. Patient characteristics

Demographic data (age, gender, education status) of the patients, history of falls (according to the information obtained from the patient or patient's relatives, presence of more than one falls not associated with seizure or acute stroke in the last year) and presence of postural symptoms such as dizziness, blackout, nausea, sweating and imbalance in upright position were asked and recorded. Personal history of chronic disease (hypertension, DM, coronary artery disease, congestive heart failure, cerebrovascular disease, hyperlipidemia, peripheral vascular disease, depression, PD, and dementia), drugs they have been using, and the number of drugs were questioned in detail. In addition, comorbid conditions of the patients were assessed using Charlson Comorbidity Index (CCI). The patients underwent CGA including Mini-Mental State Examination (MMSE), Cognitive State Test (COST) (Babacan-Yildiz et al., 2013), Yesavage's geriatric depression scale (GDS), and Tinetti Performance-Oriented Mobility Assessment (POMA), Barthel activities of daily living index (ADL), Lawton-Brody instrumental activities of daily living (IADL), and Mini Nutritional assessment Short form (MNA-SF).

### 2.5. Laboratory findings

Certain laboratory tests were done to assess the biochemical, metabolic and nutritional status of the patients. Thus, laboratory recordings were obtained for complete blood count, kidney and liver functions, cholesterol levels, thyroid-stimulating hormone (TSH), HbA1c, vitamin D, vitamin B12, and folic acid levels. All of these biochemical tests were carried out on Diagnostic Modular Systems autoanalyzer (Roche E170 and P-800). Serum 25-Hidroksi-Vitamin D [25(OH)D] was measured by radioimmunoassay.

HUT Test was performed for the diagnosis of OH. The test was performed in the morning after the patients received their daily medications and attention was paid for the patients not smoke, intake caffeine, or exercise within 30 min prior to the test. HUT was performed by tilt Table (Gemesan<sup>®</sup> Tilt TableG-71, Turkey). Monitoring over the course of HUT was performed by Biolight<sup>®</sup> BIOM69 (Australia) with reusable adult arm cuff. After allowing the patients to have a rest in a silent room with temperature of 20–24 °C for at least 10 min in supine position, the tilt Table was rapidly and fluently raised up to an angle of 60–80°. The patients were monitored via blood pressure, mean arterial blood pressure, heart rate, electrocardiogram (ECG), and pulse oximeter over the course of HUT (Parry et al., 2009). The data of monitoring at the 1st, 3rd and 5th minutes (HUT<sub>1</sub>, HUT<sub>3</sub> and HUT<sub>5</sub>, respectively) were recorded, and the patients were questioned whether they had postural symptoms such as dizziness, blackout and nausea.

The diagnosis of OH was made in the event of 20 mmHg and higher decrease in systolic pressure and/or 10 mmHg and higher decrease in diastolic pressure during transition from supine position to at least 60° head-up position during HUT (Parry et al., 2009; The Consensus Committee of the American Autonomic Society and the American Academy of Neurology, 1996). According to this definition, OBPC at the 1st, 3rd and 5th minutes were evaluated taking the data of supine position as the basis.

### 2.6. Postural tachycardia syndrome

Postural tachycardia syndrome was defined as an increase in heart rate (>120 beat/min or an increase more than 30 beat/min as compared to baseline values) without OH during HUT test (Low, Sandroni, Joyner, & Shen, 2009).

### 2.7. Statistical analysis

Continuous variables were presented as mean ± standard deviation and evaluated by Kolmogorov-Smirnov test for normal distribution. Normally distributed continuous variables with normal distribution were analyzed by paired sample *t*-test. In case of non-normal distribution, continuous variables were evaluated by Mann-Whitney *U* test. Differences between categorical variables were evaluated by Chi-square and Fisher's exact Chi-square tests. The Cochran's Q test was used to compare proportions within groups. Comparison of the patients that had OH only in HUT<sub>1</sub>, HUT<sub>3</sub> or HUT<sub>5</sub> were assessed by Kruskal-Wallis Test. A probability <0.05 was considered significant. All statistical analyses were done using SPSS 15.0 (SPSS Inc.) package program. Adequate sample size was calculated (298 patients for 95% confidence interval).

### 2.8. Ethics

The study was conducted in conformity with the Declaration of Helsinki and was approved by the ethics committee of the School of Medicine, Dokuz Eylül University in Izmir, Turkey (2013/23-08).

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