Original Article

Time point of blood pressure drop in patients with orthostatic hypotension in the emergency department

Kyeongmin Jang[a,*], Miri Park[a,*], and Hack-Lyoung Kim[b]

Objective: The purpose of this study was to identify the time of blood pressure (BP) drop in the orthostatic hypotension test, and to propose a realistic and appropriate duration in the orthostatic hypotension test.

Methods: A total of 879 consecutive patients (61-year-old and 44% women) with positive on the orthostatic hypotension test in the emergency department were retrospectively reviewed. Orthostatic hypotension was defined as drop in standing SBP of at least 20 mmHg or standing DBP of at least 10 mmHg from their supine values after standing for 5 min. BP measurements was made at 1, 3, and 5 min after standing.

Results: Six hundred and eighty-four (77.8%), 152 (17.3%) and 43 (4.9%) patients had BP drop meeting orthostatic hypotension criteria at 1, 3, and 5 min, respectively. In multivariable analysis, older age (≥60 years) and higher blood urea nitrogen (BUN) (≥15.5 mg/dl) were independently associated with early BP drop at 1 min, and younger age (<40 years) was independently associated with later BP drop at 5 min even after controlling for potential confounders.

Conclusion: To measure orthostatic BP for orthostatic hypotension diagnosis at emergency department, older patients (≥60 years) with high BUN (≥15.5 mg/dl) should be monitored carefully as BP can drop quickly within 1 min. On the contrary, in younger people (<40 years), BP drop occurred slowly after 3 min, suggesting that clinicians measure BP for a longer time.

Keywords: blood pressure drop, emergency department, orthostatic hypotension, time point

Abbreviations: BP, blood pressure; BUN, blood urea nitrogen; CNS, central nervous system; CRP, C-reactive protein; IRB, institutional review board; MDRD, Modification of Diet in Renal Disease; ROC, receiver operating characteristic; SD, standard deviation

INTRODUCTION

Position change from supine or seated to upright is associated with a rapid movement of 500–1000 ml of blood from the thorax into the lower extremities and splanchnic vasculature. Under a normal condition, our body can sustain sufficient blood supply to the central nervous system by the action of the reflex system to maintain blood pressure (BP). However, when malfunction of reflex response of the cardiovascular and autonomic nervous system or conditions leading to hypovolemia occurs, BP drops in the standing position, and blood is not properly supplied to the brain causing dizziness or fainting [1,2]. This abnormal fall in BP on standing from a supine or sitting position has been described as orthostatic hypotension. Orthostatic hypotension is associated with older age, comorbidities and medications [3,4]. The recognition and diagnosis of orthostatic hypotension are clinically important as orthostatic hypotension is associated with higher morbidity, mortality and reduced quality of life [3–8]. One recent meta-analysis indicated that orthostatic hypotension increased the risk of overall mortality by 36% in affected individuals [9].

The most widely used diagnostic criteria for orthostatic hypotension is a reduction in SBP of at least 20 mmHg or DBP of at least 10 mmHg or more within 3 min after resting in the lying position for at least 5 min and then changing to the upright position [3,10–12]. Over the last decade, these criteria have been used as the research standard for many epidemiological and investigative studies [4–6,8]. However, some have criticized this diagnostic guide. It appears to be arbitrary but not evidence-based, and lacks clear evidence on how to measure. Of note, when applying these diagnostic criteria, it is possible to miss clinically significant orthostatic hypotension patients with BP drop within 1 min or after 3 min of standing [13–19].

As orthostatic BP measurement is simple and important for differential diagnosis, it is frequently performed for patients who visit the emergency department with dizziness or syncope [20]. However, orthostatic BP measurement in the emergency department may be stressful to both patients and medical staffs. In particular, patients who visited the emergency department are often elderly having multiple comorbidities; thus, raising them up for several minutes is

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difficult and there is also a high risk of falling during the test. In addition, nurses or clinicians have to spend a lot of time on staying close to the patients during the orthostatic hypotension test in a busy emergency department [21]. Moreover, clinically important point is that orthostatic hypotension is highly prevalent [4,22], and that there are many patients who visit emergency department with dizziness or fainting. Many of them need orthostatic vital signs. Therefore, orthostatic BP measurement can be a great burden for medical staffs who care for patients in an urgent emergency department environment.

In this context, the authors raised question about how long should patients stand during the orthostatic hypotension test not only for proper diagnosis but also for the efficient use of medical resources at emergency department. Thus, this study was performed to investigate the time point of BP drop during orthostatic hypotension test according to the characteristics of patients, and sought to find out the clinical factors of patients who need to change the test time in the emergency department. Our hypothesis is that orthostatic hypotension test time could be adjusted flexibly for patients with certain clinical characteristics at emergency department.

METHODS

Study population

This single-center study was conducted at a general hospital in the city (Seoul, Korea). Consecutive patients who visited the emergency department with dizziness, presyncope or syncope and then underwent the orthostatic hypotension test were retrospectively reviewed. In cases with obvious causes of dizziness or fainting (emotional stress, hyperventilation, blood loss, seizure, cerebral contusion, transient ischemic attack, stroke, acute coronary syndrome and cardiac arrhythmia), the orthostatic hypotension test was not performed. From January 2014 to December 2018, a total of 4251 patients underwent the orthostatic hypotension test in the emergency department. Of these patients, 879 (20.6%) had positive test results on the orthostatic hypotension test, and they were analyzed in this study. The protocol of this study was approved by the Institutional Review Board (IRB) of Boramae Medical Center (Seoul, Korea) (IRB number, 16-2017-15), and we followed the Declaration of Helsinki. Due to the retrospective design of the study and the routine nature of the information collected, the IRB of our hospital waived written consent from the patients.

Data collection

Information on cardiovascular risk factors, including hypertension, diabetes mellitus, dyslipidemia and smoking status, was obtained. Smokers was defined as those with the history of tobacco smoking in the last 12 months. The previous history of coronary artery disease, heart failure and stroke was evaluated. Patients with myocardial infarction or coronary revascularization were considered as having coronary artery disease. Heart failure was defined as a case of hospital admission for heart failure treatment. Stroke includes both cerebral infarction and hemorrhage, which is defined as the case of lesions identified by imaging tests with neurological abnormalities. Whether there was syncope at the time of emergency department visit was reviewed. Syncope was defined a transient loss of consciousness with return to baseline neurological function without medical interventions. The presence of atrial fibrillation was confirmed on electrocardiogram. Random blood concentrations of hemoglobin, hematocrit, glucose, blood urea nitrogen (BUN), creatinine, uric acid, total protein, albumin, and C-reactive protein (CRP) were collected. Estimated glomerular filtration rate was calculated using the four-component Modification of Diet in Renal Disease (MDRD) study equation incorporating age, race, sex and serum creatinine level [23]. Data on concomitant medications, such as vasoactive medications, diuretics and agents acting on central nervous system (CNS) were also reviewed. Vasoactive medications included alpha blockers, beta blockers, calcium channel blockers, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers and nitrates. CNS drugs included anxiolytics, sedatives, hypnotics, antidepressants and antipsychotics.

Measurement of orthostatic blood pressure and definition of orthostatic hypotension

Orthostatic BP was measured after bed rest for 5 min or more in the supine position. The measurements were made at 1, 3, and 5 min after standing up. SBP and DBP and heart rate were measured in the right upper arm by a trained nurse using an automatic sphygmomanometer (DINAMAP; Woodley Equipment Company Ltd, Lancashire, BL6 7NY, United Kingdom). If the patient complained of fainting or severe dizziness during the measurement, the test was stopped immediately. Orthostatic hypotension was defined as a reduction of SBP of at least 20 mmHg or DBP of at least 10 mmHg within 5 min of standing.

Statistical analysis

Continuous variables are expressed as mean ± standard deviation (SD), and categorical variables are expressed as percentages. In comparing the differences between the two groups, Student's *t*-test was used for continuous variables and the chi-square test for noncontinuous variables. Receiver operating characteristic (ROC) curve analysis was performed to identify cut-off value of continuous variables for the prediction of orthostatic hypotension. Logistic regression analysis was used to determine the association between orthostatic hypotension and clinical variables. Variables that were statistically significant in the mean or frequency comparison between the two groups were used as independent variables in simple logistic regression analysis. Multivariable logistic regression analysis was sequentially performed using variables that were statistically significant in the simple logistic regression analysis as independent variables. Continuous variables were converted to binary variables using cut-off values identified through ROC curve analysis and used for logistic regression analysis. A P value of less than 0.05 was considered statistically significant. All analyses were two-sided. All data were analyzed using SPSS for Windows 23.0 (IBM, Armonk, New York, USA).

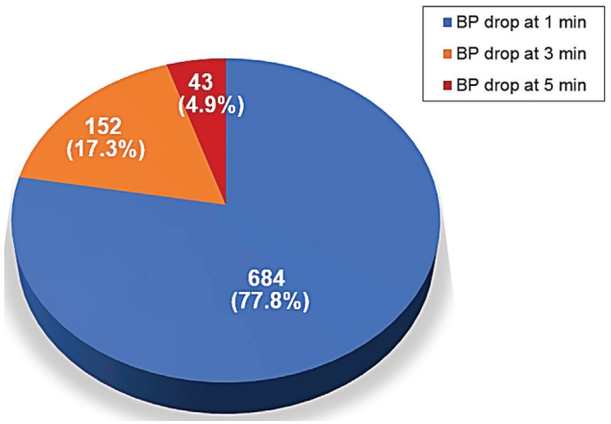

FIGURE 1 Distribution of study patients according to BP drop fulfill criteria of orthostatic hypotension. BP, blood pressure.

RESULTS

In total study patients ($n = 879$), mean age was 61.1 ± 20.7 years and 390 (44.4%) were female. Six hundred and eighty-four (77.8%), 152 (17.3%) and 43 (4.9%) patients had BP drop meeting orthostatic hypotension criteria at 1, 3, and 5 min, respectively (Fig. 1). Only 43 (4.9%) patients met the criteria for diagnosing orthostatic hypotension based on DBP, all of whom had a BP drop occurring at 1 min of standing. Others were diagnosed with orthostatic hypotension based on SBP reduction. The changes in SBP and DBPs and heart rate during the test are demonstrated in Fig. 2.

TABLE 1. Comparisons of clinical characteristics between patients with BP drop at 1 and 3 or 5 min

Characteristic	BP drop at 1 min ($n = 685$)	BP drop at 3 or 5 min ($n = 194$)	*P* value
Age, years	65.7 ± 18.6	45.0 ± 19.8	<0.001
Female sex	272 (39.7)	118 (60.8)	<0.001
Risk factors			
Hypertension	341 (49.8)	46 (23.7)	<0.001
Diabetes mellitus	179 (26.1)	20 (10.3)	<0.001
Dyslipidemia	102 (14.9)	21 (10.8)	0.091
Smoking	37 (7.1)	4 (3.1)	0.061
Previous history			
Coronary artery disease	91 (13.3)	9 (4.6)	<0.001
Heart failure	12 (1.8)	1 (0.5)	0.181
Stroke	94 (13.7)	5 (2.6)	<0.001
Syncope at admission	264 (38.5)	105 (54.1)	0.001
Atrial fibrillation	22 (3.2)	6 (3.1)	0.575
Laboratory findings			
Hemoglobin (g/dl)	12.6 ± 2.2	13.2 ± 2.2	0.002
Hematocrit (%)	37.6 ± 6.1	39.5 ± 5.1	<0.001
Glucose (mg/dl)	143 ± 57	124 ± 30	<0.001
BUN (mg/dl)	20.1 ± 12.4	14.8 ± 7.5	<0.001
Creatinine (mg/dl)	1.3 ± 1.8	0.9 ± 1.0	<0.001
GFR (ml/min per 1.73 m^2)	73.6 ± 29.8	92.1 ± 25.1	<0.001
Uric acid (mg/dl)	5.3 ± 1.9	4.9 ± 2.2	0.116
Total protein (mg/dl)	6.5 ± 0.8	6.8 ± 0.6	<0.001
Albumin (mg/dl)	3.9 ± 0.4	4.1 ± 0.3	<0.001
C-reactive protein (mg/dl)	1.4 ± 3.6	0.7 ± 2.4	0.004
Medications			
Vasoactive medications	340 (49.7)	45 (23.1)	<0.001
Diuretics	17 (2.5)	2 (1.0)	0.275
CNS drugs	146 (21.4)	16 (8.2)	<0.001

Numbers are expressed as mean ± SD or *n* (%). BP, blood pressure; BUN, blood urea nitrogen; CNS, central nervous system; GFR, glomerular filtration rate.

Comparisons of clinical characteristics between patients with blood pressure drop at 1 and 3 or 5 min

Table 1 shows the clinical characteristics of the patients with BP drop at 1 min and 3 or 5 min. Patients with early BP drop at 1 min were older, were less frequently women, and had more cardiovascular risk factors, including hypertension and diabetes mellitus, than those with BP drop at 3 or 5 min. The history of coronary artery disease and stroke were more frequently observed in patients with BP drop at 1 min compared with those with BP drop at 3 or 5 min. Syncope less frequently occurred in patients with BP drop at 1 min. The results of blood tests were more unfavorable (lower levels of hemoglobin, hematocrit, GFR, total protein and albumin, and higher levels of glucose, BUN, creatinine and CRP) in patients with BP drop at 1 min than in those with BP drop at 3 or 5 min. Patients with BP drop at 1 min took more vasoactive medications and drugs acting on the CNS than those with BP drop at 3 or 5 min.

Predictors of early blood pressure drop at 1 min

Predictors of early BP drop at 1 min during orthostatic hypotension BP measurement are demonstrated in Table 2. All variables that differed in the comparisons of the two groups as shown in Table 1 were also significant in the

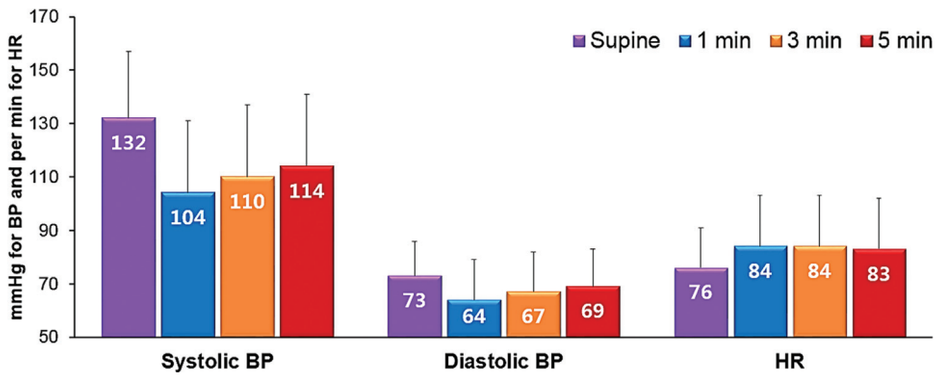

FIGURE 2 The changes of SBP and DBP and heart rate during the test. BP, blood pressure.

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TABLE 2. Predictors for BP drop at 1 min

Variable	Univariable		Multivariable	
	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Age at least 60 years	8.06 (5.57–11.6)	<0.001	10.35 (5.26–20.36)	<0.001
Female sex	0.43 (0.31–0.59)	<0.001	0.97 (0.58–1.61)	0.916
Syncope	0.61 (0.46–0.83)	0.001	0.85 (0.54–1.35)	0.508
Hypertension	3.23 (2.25–4.65)	<0.001	0.68 (0.22–2.12)	0.511
Diabetes mellitus	3.12 (1.90–5.11)	<0.001	0.73 (0.34–1.55)	0.418
Coronary artery disease	3.17 (1.56–6.41)	0.001	0.95 (0.33–2.73)	0.927
Stroke	6.20 (2.48–15.4)	<0.001	2.39 (0.75–7.66)	0.140
Hematocrit at least 38.3%	0.48 (0.34–0.68)	<0.001	1.12 (0.64–1.95)	0.674
Random glucose at least 125 mg/dl	2.45 (1.76–3.42)	<0.001	1.32 (0.79–2.19)	0.277
BUN at least 15.5 mg/dl	3.29 (2.30–4.71)	<0.001	1.84 (1.02–3.31)	0.042
GFR at least 80 ml/min per 1.73 m^2	0.22 (0.15–0.32)	<0.001	0.68 (0.36–1.26)	0.225
Total protein at least 6.3 mg/dl	0.44 (0.29–0.66)	<0.001	0.83 (0.43–1.58)	0.579
Albumin at least 4.0 mg/dl	0.29 (0.20–0.42)	<0.001	0.71 (0.36–1.38)	0.315
CRP at least 0.18 mg/dl	2.03 (1.44–2.85)	<0.001	0.84 (0.51–1.40)	0.523
Vasoactive medication	3.29 (2.28–4.74)	<0.001	1.16 (0.38–3.50)	0.786
CNS-acting medication	2.86 (1.29–6.35)	0.009	1.60 (0.62–4.11)	0.326

BP, blood pressure; BUN, blood urea nitrogen; CI, confidence interval; CNS, central nervous system; CRP, C-reactive protein; GFR, glomerular filtration rate; OR, odds ratio.

univariable logistic analysis. However, only older age (≥60 years) [odds ratio (OR), 10.35; 95% confidence interval (CI), 5.26–20.36; $P < 0.001$] and higher BUN (≥15.5 mg/dl) (OR, 1.84; 95% CI, 1.02–3.31; $P = 0.042$) were independently associated with early BP drop at 1 min in multiple binary logistic regression analysis.

TABLE 3. Comparisons of clinical characteristics between patients with BP drop at 5 and 1 or 3 min

Characteristic	BP drop at 5 min ($n = 43$)	BP drop at 1 or 3 min ($n = 836$)	*P* value
Age (years)	38.7 ± 20.6	62.3 ± 20.1	<0.001
Female sex	28 (65.1)	362 (43.3)	0.004
Syncope at admission	26 (60.5)	343 (41.0)	0.035
Risk factors			
Hypertension	6 (14.0)	381 (45.6)	<0.001
Diabetes mellitus	3 (7.0)	196 (23.4)	0.006
Dyslipidemia	4 (9.3)	119 (14.2)	0.256
Smoking	4 (3.1)	37 (7.1)	0.061
Previous history			
Coronary artery disease	0	100 (12.0)	0.005
Heart failure	0	13 (1.6)	0.519
Stroke	2 (4.7)	97 (11.6)	0.117
Atrial fibrillation	1 (2.3)	27 (3.2)	0.597
Laboratory findings			
Hemoglobin (g/dl)	13.2 ± 2.0	12.7 ± 2.2	0.159
Hematocrit (%)	39.3 ± 4.8	38.0 ± 6.0	0.154
Random glucose (mg/dl)	114 ± 20	140 ± 53	<0.001
BUN (mg/dl)	12.9 ± 4.3	19.0 ± 11.9	<0.001
Creatinine (mg/dl)	0.8 ± 0.2	1.2 ± 1.7	0.086
GFR (ml/min per 1.73 m^2)	99.6 ± 23.6	76.6 ± 29.7	<0.001
Uric acid (mg/dl)	5.4 ± 3.7	5.2 ± 1.8	0.492
Total protein (mg/dl)	6.7 ± 0.5	6.6 ± 0.7	0.088
Albumin (mg/dl)	4.2 ± 0.3	4.0 ± 0.4	0.033
C-reactive protein (mg/dl)	1.1 ± 4.0	1.2 ± 3.3	0.752
Medications			
Vasoactive medications	6 (14.0)	379 (45.3)	<0.001
Diuretics	0	19 (2.3)	0.999
CNS-acting drugs	3 (7.0)	70 (8.4)	0.746

Numbers are expressed as mean ± SD or *n* (%). BP, blood pressure; BUN, blood urea nitrogen; CNS, central nervous system; GFR, glomerular filtration rate.

Comparisons of clinical characteristics between patients with blood pressure drop at 5 min and 1 or 3 min

Table 3 shows the clinical characteristics of patients with BP drop at 5 min and 1 or 3 min. Patients with later BP drop at 5 min were younger, were more frequently female individuals, and had less cardiovascular risk factors, including hypertension and diabetes mellitus, than those with BP drop at 1 or 3 min. The history of coronary artery disease was less frequently observed in patients with BP drop at 5 min compared with those with BP drop at 1 or 3 min. Syncope more frequently occurred in patients with BP drop at 5 min. The results of blood tests were more favorable (lower levels of glucose and BUN, and higher levels of GFR and albumin) in patients with BP drop at 5 min than in those with BP drop at 1 or 3 min. Patients with BP drop at 5 min took less vasoactive medications than those with BP drop at 1 or 3 min.

Predictors of late blood pressure drop at 5 min

The predictors of later BP drop at 5 min during orthostatic hypotension BP measurement are demonstrated in Table 4. Most of the variables that differed in the comparisons of the 2 groups as shown in Table 3 were also significant in the univariable logistic analysis. However, only younger age (<40 years) was independently associated with later BP drop at 5 min in multiple binary logistic regression analysis (OR, 2.90; 95% CI, 1.15–7.30; $P = 0.023$).

DISCUSSION

In this study, we analyzed a large number of emergency department patients with positive results of the orthostatic BP test, and identified several important findings, as follows: in almost all cases (95.1%), BP drop occurred within 3 min, but in some cases (4.9%) it occurred at 5 min after standing, patients with earlier BP drop at 1 min (77.9%) were older and had more cardiovascular risk factors, compared with those with BP drop at 3 or 5 min, older age (≥60

TABLE 4. Predictors for blood pressure drop at 5 min

Variable	Univariable		Multivariable	
	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Age <40 years	8.26 (4.31–15.85)	<0.001	2.90 (1.15–7.30)	0.023
Female sex	2.44 (1.28–4.64)	0.006	1.27 (0.62–2.60)	0.510
Syncope	1.72 (0.99–3.01)	0.054	–	–
Hypertension	0.19 (0.08–0.46)	<0.001	0.89 (0.13–5.85)	0.904
Diabetes mellitus	0.24 (0.07–0.79)	0.019	1.33 (0.33–5.39)	0.683
Random glucose less than 130 mg/dl	6.39 (2.48–16.42)	<0.001	0.37 (0.12–1.09)	0.071
BUN less than 14 mg/dl	3.98 (2.01–7.89)	<0.001	1.39 (0.64–3.05)	0.401
GFR at least 86 ml/min per 1.73 m^2	5.85 (2.84–12.0)	<0.001	1.85 (0.76–4.45)	0.170
Albumin at least 4.0 mg/dl	3.99 (1.75–9.10)	0.001	1.52 (0.61–3.80)	0.366
Vasoactive medication	0.19 (0.08–0.46)	<0.001	0.74 (0.12–4.58)	0.749

BP, blood pressure; BUN, blood urea nitrogen; CI, confidence interval; GFR, glomerular filtration rate; OR, odds ratio.

years) and higher BUN (≥15.5 mg/dl) were independently associated with early BP drop at 1 min even after controlling for potential confounders, patients with later BP drop at 5 min were younger and showed better cardiovascular risk profiles, compared with those with BP drop at 1 or 3 min, and younger age (<40 years) was independently associated with later BP drop at 5 min even after controlling for potential confounders. To the best of our knowledge, this is the first study to characterize emergency department patients based on the positive time point of the orthostatic hypotension test.

Our study showed that orthostatic hypotension was detected in 20.6% of patients with dizziness, presyncope and syncope who underwent orthostatic BP measurement in the emergency department, which is in line with previous studies [24,25]. There are inconsistencies on the timing of postural changes before BP measurement for orthostatic hypotension diagnosis. Several studies have reported that orthostatic hypotension can be detected within 2 min of standing in most cases [25–27]. Atkins *et al.* [25] showed that among 61 patients who met definition of orthostatic hypotension (≥20 mmHg), a decline in BP of at least 20 mmHg occurred within 2 min of standing in 54 patients (81.9%), and mean time to reach minimum BP was 2.4 min. In a study of 66 patients who fulfilled the orthostatic hypotension criteria, 88, 99 and 100% of study patients developed orthostatic hypotension within 1, 2, and 3 min of the upright position during tilt-table testing, respectively [27]. In another study, 83.5% of BP drop satisfied the orthostatic hypotension diagnosis occurred within 3 min of standing [28]. Consistent with these findings, 77.8% of patients developed orthostatic hypotension by 1 min of standing and with additional 17.3% developing orthostatic hypotension by 3 min of standing in our study. For the diagnosis of orthostatic hypotension, recent guidelines also recommend repeat BP measurements after standing 1 and 3 min. However, more than 3 min of standing was needed for orthostatic hypotension diagnosis in other cases [29]. It has been reported that about a half of patients diagnosed with orthostatic hypotension had a significant BP drop after 3 min in tilt-table testing [19,30]. The studies have suggested the necessity of additional measurement of BP even after 3 min of standing. However, it will not be necessary to stand all patients undergoing orthostatic BP measurement for longer than 3 min. It would be effective to selectively spend more time only on patients suspected of having a delayed response. Therefore, it is very important to find out the clinical characteristics of the patients according to the time point of a significant BP drop. However, most previous studies have failed to address this important issue as their study sample size was relatively small [19,25–30]. In this regard, our study deserves clinical attention as we enrolled a large number of patients who were positive on the orthostatic hypotension test and presented the clinical characteristics according to the time point of BP drop.

Earlier blood pressure drop at 1 min

As orthostatic hypotension is associated with physiological changes in normal aging and comorbidities of cardiovascular and neurodegenerative diseases, it is highly prevalent in the elderly, which is reported around 18% [4]. Among institutionalized patients, the prevalence of orthostatic hypotension can be up to 50%, and orthostatic hypotension itself also needs frequent hospitalization [22]. Given the rapidly aging society of the Korean population, contribution of orthostatic hypotension to a social burden as well as morbidity and mortality of individuals will increase. Therefore, it is important to recognize the importance of orthostatic hypotension, and efforts should be made to accurately diagnose orthostatic hypotension. Although guidelines provide criteria for orthostatic hypotension diagnosis [3,10–12], these diagnostic criteria may not be adequate to some patients. However, previous studies have failed to suggest the time point of BP drop according to the clinical characteristics of patients because of the small number of study patients. Our study enrolled a large number of patients who were positive on the orthostatic hypotension test and presented the clinical characteristics according to the time point of BP drop. Our study showed that patients with earlier BP drop at 1 min were older and had more comorbidities, and that age at least 60 years and elevated BUN (≥15.5 mg/dl) were independent factors determining BP drop at 1 min. This suggests that autonomic pathways are more damaged in these groups of patients, and that BP drop response develops rapidly. In older patients with age at least 60 years, a sudden BP drop can occur in 1 min and should be monitored carefully especially when they have higher BUN. The exact underlying pathophysiology linking the association between higher BUN and orthostatic hypotension has not been well understood.

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As a possible mechanism, an increase in BUN is associated with decreased plasma volume, impaired renal function, or heart failure, all of which are risk factors for orthostatic hypotension [3,4]. In addition, it has been suggested that BUN elevation contributes to the occurrence of orthostatic hypotension caused by the inability to synthesize norepinephrine, conversely, reduced GFR with BUN elevation is more frequently accompanied especially in case of orthostatic hypotension caused by autonomic failure [31]. Further research on this issue seems to be necessary to uncover the exact mechanism.

Later blood pressure drop at 5 min

In studies involving patients with dizziness or fainting, little is known about risk factors for delayed orthostatic hypotension that cause BP to drop after 3 min. In our study, patients with BP drop at 5 min were younger and healthier patients with fewer cardiovascular risk factors compared with those with BP drop within 3 min, and young age less than 40 years was an independently associated with BP drop at 5 min even after controlling for potential confounders. Gibbons *et al.* [19] also showed that patients with delayed orthostatic hypotension were significantly younger than those with classic orthostatic hypotension, although the number of study patients is small and only univariable comparisons were performed. These findings can explain the clinical observation of many young patients who complain of orthostatic hypotension symptoms only after prolonged standing, suggesting that more time for the orthostatic BP measurement is needed in these patients. A more prolonged orthostatic stress leads to progressive peripheral venous pooling, increased fluid transudation and combined failure of neuro and cardiovascular reflexes that counter the redistribution of blood volume cause delayed orthostatic hypotension [1,2]. It has also been suggested that delayed orthostatic hypotension may be a mild or early manifestation of autonomic dysfunction [19]. Diagnostic strategies and clinical consequences of delayed orthostatic hypotension should be more addressed in further research.

Clinical implications

Checking for orthostatic vital signs in such a hectic emergency department situation is uncomfortable for both patients and medical staff [20]. Patients are at risk of falling or syncope while standing for a long time, and medical staff spend much time on the orthostatic hypotension test with supervision. Therefore, it would be beneficial to know about the time point of BP drop according to the characteristics of patients and to consequently adjust the time duration of the orthostatic hypotension test. More specifically, defining the minimum duration of standing for orthostatic vital signs is of considerable importance especially in the emergency department. On the basis of our findings, we suggest that the 1-min test may be possible for patients at at least 60 years of age and with BUN at least 15.5 mg/dl, whereas 5-min or longer test may be needed for younger patients under 40 years of age in a busy emergency department. These customized approaches will make much more efficient use of emergency medical resources without missing clinically significant orthostatic hypotension. A more well designed prospective study will be needed to confirm our suggestion.

Study limitations

In addition to the retrospective design, there are several limitations to our study. First, there were some missing medical records for the underlying disease or medications being taken. In a busy emergency department, some of this information may not have been properly documented. Second, this study did not include analysis for measurements after 5 min. Tests at more than 5 min of standing may be needed in some patients with special conditions, such as Parkinson's disease or heart failure [14,15]. Even without these diseases, it has been reported that a substantial portion of patients had BP fall after 10 min of head-up tilt [19]. Third, since patients who participated in our study were tested for fainting or dizziness, applying our results to other situations, such as the orthostatic hypotension test for evaluation of body fluid volume, should be cautious. Lastly, our cross-sectional analysis did not provide information on the causes and treatment options of orthostatic hypotension. Our findings need to be extended into a sufficiently powered longitudinal study.

In conclusion, in patients with dizziness, presyncope or syncope who visited the emergency department, measurement of BP change while standing for 3 min can detect the vast majority of patients with orthostatic hypotension (95.1%). Older people ($\geq$60 years) or patients with high BUN ($\geq$15.5 mg/dl) should be monitored carefully as BP can drop rapidly within 1 min. On the contrary, in young people ($<$40 years), BP may drop slowly after 3 min, so it is necessary to take a longer time to measure BP for orthostatic hypotension diagnosis.

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Conflicts of interest

There are no conflicts of interest.

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