Original Article

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Blood pressure reduction cut-points for orthostatic hypotension in stroke survivors using a sit-up test: a multicentre cross-sectional study

Kazuaki Oyake[a,b], Takaki Tateishi[b], Jun Murayama[b], Naoki Shijima[c], Tasuku Sekizuka[d], Yohei Otaka[b,e], and Kimito Momose[a]

Objective: The sit-up test is used to assess orthostatic hypotension in stroke survivors who cannot stand independently without using a tilt table. However, no study has identified the optimal cut-points for orthostatic hypotension using the test. Therefore, this study aimed to examine the decrease in SBP and DBP during the sit-up test to detect orthostatic hypotension in individuals with stroke.

Methods: Thirty-eight individuals with stroke, recruited from three convalescent rehabilitation hospitals, underwent the sit-up and head-up tilt tests. Systolic and diastolic orthostatic hypotension was defined as a decrease of at least 20 and 10 mmHg in the SBP and DBP, respectively, during the head-up tilt test. The receiver operator characteristic curve with the Youden Index was used to identify the optimal cut-points.

Results: Eight and three participants showed systolic and diastolic orthostatic hypotension, respectively. The optimal cut-points for orthostatic hypotension using the sit-up test were a decrease of 10 mmHg in SBP [sensitivity = 87.5% (95% confidence interval: 47.4–99.7), specificity = 96.7% (82.8–99.9)] and 5 mmHg in DBP [sensitivity = 100.0% (29.2–100.0), specificity = 88.6% (73.3–96.8)].

Conclusion: Compared with the conventional cut-points, smaller cut-points of a decrease in SBP and DBP may be better to identify orthostatic hypotension in individuals with stroke using the sit-up test. The findings of this study may provide valuable information for the clinical application of the sit-up test.

Keywords: blood pressure, cerebrovascular disease, receiver operator characteristic curve, sensitivity, specificity

Abbreviations: AUC, area under the receiver operating characteristic curve; CI, confidence interval; MMSE, Mini-Mental State Examination; ROC, receiver operating characteristic

INTRODUCTION

Stroke is one of the main causes of disability and requires continued care. Stroke is also a recurrent disease, with a reported cumulative recurrence rate of approximately 40% within 12 years after the initial stroke onset [1]. Furthermore, individuals with recurrent stroke achieve less functional gains than those with first-ever stroke [2]. Several factors are associated with stroke recurrences, such as older age, atrial fibrillation, hypertension and smoking [3–5]. In addition, orthostatic hypotension, which is defined as a decrease in SBP of at least 20 mmHg or DBP of 10 mmHg within 3 min of standing or head-up tilt to at least 60° on a tilt table [6], has also been shown to be associated with increased recurrent stroke risk as well as vascular events and all-cause death in individuals with stroke [7]. The prevalence of orthostatic hypotension in these individuals is reportedly 13.0–52.1% [8–12]. However, many individuals with orthostatic hypotension are asymptomatic or only mildly symptomatic [13]. Therefore, the assessment of postural blood pressure changes is essential to provide appropriate interventions to minimize the occurrence of orthostatic hypotension.

Orthostatic hypotension has been assessed with a head-up tilt or an active standing test [6,14,15]. Of these two tests, the head-up tilt test is particularly useful for stroke survivors with limited ability to attain and maintain a standing position, because it uses passive postural changes by the tilt table. However, the tilt table is a specialized equipment, which limits the usability of the head-up tilt test in clinical settings. To overcome the limitations of the head-up tilt test, a sit-up test was developed and has been used to identify the presence of orthostatic hypotension in individuals with stroke [16].

In the sit-up test, participants are passively moved from the supine to the sitting position with the assistance of an

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[a]Department of Physical Therapy, School of Health Sciences, Shinshu University, Nagano, [b]Department of Rehabilitation Medicine, Tokyo Bay Rehabilitation Hospital, Chiba, [c]Department of Physical Therapy, Saku Central Hospital, [d]Department of Rehabilitation, Kakeyu-Misayama Rehabilitation Center Kakeyu Hospital, Nagano and [e]Department of Rehabilitation Medicine I, School of Medicine, Fujita Health University, Aichi, Japan

Correspondence to Kimito Momose, PT, PhD, Department of Physical Therapy, School of Health Sciences, Shinshu University, 3-1-1 Asahi, Matsumoto, Nagano 390-8621, Japan Tel: +81 263 37 3453; fax: +81 263 37 3453; e-mail: kmomose@shinshu-u.ac.jp

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assessor. Changes in blood pressure during the test have demonstrated substantial day-to-day reliability [17]. Although the same cut-points for orthostatic hypotension applied to conventional orthostatic tests have been applied to the sit-up test [16–18], the orthostatic decreases in blood pressure that are elicited during the sit-up test may be smaller than those elicited during the head-up tilt test due to the reduced acute change in gravitational stress [19,20]. Therefore, we hypothesized that the optimal cut-points for orthostatic hypotension using the sit-up test are smaller than the conventional cut-points using the head-up tilt test. However, there have been no reports to support this hypothesis. This study aimed to evaluate a decrease in SBP and DBP during the sit-up test to identify the presence of orthostatic hypotension in individuals with stroke.

MATERIALS AND METHODS

Study design

This is a multicentre cross-sectional study. The study protocol was approved by the appropriate ethics committees of Shinshu University (approval number: 4851), Tokyo Bay Rehabilitation Hospital (approval number: 257), Saku Central Hospital (approval number: R-202010-09) and Kakeyu-Misayama Rehabilitation Center Kakeyu Hospital (approval number: 2020015). All participants provided written informed consent before enrolment in the study. The study was performed in accordance with the 1964 Declaration of Helsinki, as revised in 2013.

Participants

Participants were recruited from three convalescent rehabilitation hospitals in Japan between December 2020 and December 2021. The inclusion criteria comprised the following: age 40–90 years; within 180 days of first-ever stroke; and a Mini-Mental State Examination (MMSE) score of at least 24 points [21]. The exclusion criteria were as follows: limited range of motion and/or pain that affects the sit-up and head-up tilt tests; bilateral hemiparetic stroke; unstable medical conditions, such as arrhythmias or uncontrolled diabetes mellitus; and any comorbid neurological disorders. Demographic and clinical data, such as age, type of stroke and functional outcomes, were obtained from medical records.

Protocols

The experimental protocol consisted of the sit-up and head-up tilt tests, with a 10-min rest period between the tests. The order of the tests was randomized for each participant. The tests were performed by two trained assessors in a quiet room at a comfortable temperature. The participants were instructed to refrain from eating and consuming caffeinated products for at least 2 h and to avoid vigorous exercise for at least 12 h prior to each test [14,15]. The tests were performed between 1600 and 1800 h.

In both tests, the participants remained in a resting supine position on a motorized tilt table for 10 min before the postural change [14,16,17]. In the sit-up test, participants were passively moved from the supine to the sitting position within 30 s and then, were maintained in the sitting position for 3 min with the assistance of an assessor [16]. They were also instructed not to assist with the manoeuvre during the test. The height of the tilt table was adjusted such that both feet of the participants were on the floor while sitting. In the head-up tilt test, the participants were supported by belts at the levels of the waist, thighs and lower legs and by a footrest. After the supine rest for 10 min, the tilt table was elevated to an angle of 70° for approximately 30 s and was maintained for 3 min [14]. If a participant demonstrated a severe symptom such as presyncope, the test was terminated immediately, and the participant was returned to a supine position [16]. Self-reported symptoms associated with orthostatic hypotension, such as dizziness, lightheadedness or blurred vision, during each test were recorded at the end of the test.

Blood pressure was measured on the nonparetic arm using an automated sphygmomanometer (HEM-907; Omron Co., Ltd., Kyoto, Japan). In the supine position, SBP and DBP were measured twice within 1 min after the 10 min of rest. After the postural change, blood pressure variables were measured every minute for 3 min in the upright position. Blood pressure measurements in the supine position were defined as the mean values of the two readings. The changes in SBP and DBP were calculated by subtracting the measurements in the supine position from the minimum values in the upright position, which was the primary outcome of the present study [16,17].

Statistical analysis

The R software version 4.0.3 (R Foundation for Statistical Computing, Vienna, Austria) with the MKpower package was used to calculate the sample size required for the sensitivity and specificity analysis [22]. The sensitivity and specificity values adopted within the alternative hypothesis are expected to be at least 80%, indicating that the instrument is fairly good as a diagnostic tool [23]. The required sample size was estimated to be 24, considering a power of 95%, an alpha level of 5%, the estimated sensitivity and specificity of 80%, the lower 95% confidence limit of sensitivity and specificity of 50% and an expected prevalence of 50%. Syntaxes in R for calculating the sample size for the sensitivity and specificity analyses are provided in Appendixes 1 and 2 (Supplemental Digital Content, http://links.lww.com/HJH/C83), respectively.

Systolic and diastolic orthostatic hypotension were defined as a drop of at least 20 and 10 mmHg in SBP and DBP, respectively. Furthermore, participants with orthostatic hypotension were identified as those exhibiting either systolic or diastolic orthostatic hypotension during the head-up tilt test [6]. Demographic and clinical characteristics were compared between participants with and without orthostatic hypotension using the unpaired *t*-test for continuous variables, Mann–Whitney *U* test for ordinal variables and Fisher's exact test for dichotomous variables. The measured blood pressure variables in the supine position and the changes in SBP and DBP during the tests were also compared between the tests using the paired *t*-test. We used the receiver operating characteristic (ROC) curves to find the cut-points for the sit-up test to identify participants diagnosed with orthostatic hypotension using the head-up tilt test. We also calculated diagnostic characteristics, including sensitivity, specificity, positive and negative predictive values, and positive and negative likelihood ratios, at the various blood pressure cut-points. Furthermore, the

Youden Index was calculated as the sum of sensitivity and specificity minus one to identify the blood pressure cut-point that optimized sensitivity and specificity. The optimum cut-points were determined by those with the highest Youden Index. These comparative and ROC analyses were performed using GraphPad Prism version 7.00 for Windows (GraphPad Software, San Diego, California, USA). Statistical significance was set at a P value less than 0.05.

RESULTS

Participants

A flow chart of the participants enrolled in the present study is shown in Fig. 1. Although 276 individuals with stroke were assessed for eligibility, 238 were excluded from the study. The main reason for exclusion was having an MMSE score of less than 24 points ($n = 157$). Consequently, data of 38 participants were included in the analysis. Table 1 lists the participants' characteristics.

Although all the participants were asymptomatic during both the sit-up and head-up tilt tests, a total of nine participants (23.7%) met either the SBP or DBP criteria for orthostatic hypotension during the head-up tilt test. Specifically, eight showed systolic orthostatic hypotension, while three exhibited diastolic orthostatic hypotension. Two participants with orthostatic hypotension met the systolic and diastolic criteria for orthostatic hypotension.

The comparative analysis revealed that participants with orthostatic hypotension had significantly greater body weight [mean difference = 13.7, 95% confidence interval (95% CI) = 5.1–22.3, $P = 0.003$] and BMI (mean difference = 2.4, 95% CI = 0.7–5.8, $P = 0.014$) compared with participants without orthostatic hypotension, while no significant differences were observed in the other participants' characteristics between participants with and without orthostatic hypotension ($P > 0.05$).

Comparisons of haemodynamic variables between the sit-up and head-up tilt tests

The blood pressure responses to the sit-up and head-up tilt tests are shown in Fig. 2. Table 2 illustrates blood pressure variables obtained from each test. In the supine position, there were no significant differences in both SBP (mean difference = −1.3, 95% CI = −3.2 to 0.7, $P = 0.188$) and DBP (mean difference = −0.7, 95% CI = −2.0 to 0.5, $P = 0.261$) between the tests. The decrease in SBP during the sit-up test was significantly smaller than that during the head-up tilt test (mean difference = 5.1, 95% CI = 2.1–8.0, $P = 0.001$). The decrease in DBP during the sit-up test also tended to be smaller than that during the head-up tilt test, although the difference was not significant (mean difference = 2.1, 95% CI = 0.0–4.2, $P = 0.051$).

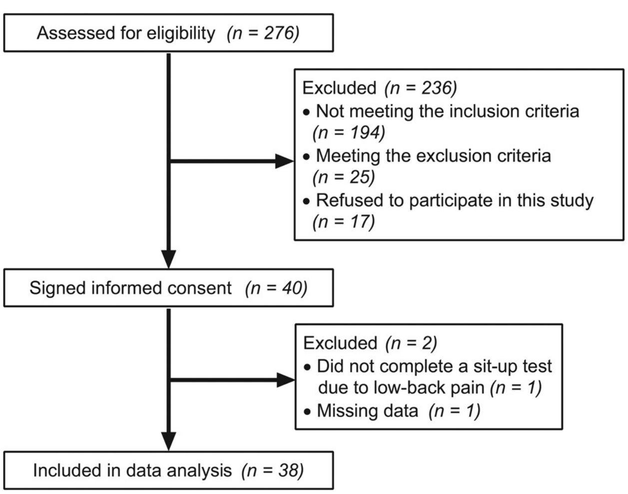

FIGURE 1 Flow diagram of participant enrolment.

Receiver operator characteristic curve analysis

Figure 3 presents the results of the ROC analyses, illustrating the diagnostic characteristics for the sit-up test across all hypothetical cut-points for the reductions in SBP and DBP. Both the ROC curves for identifying participants with systolic orthostatic hypotension [area under the ROC curve (AUC) = 0.915, standard error = 0.064, $P < 0.001$] and with diastolic orthostatic hypotension (AUC = 0.938, standard error = 0.040, $P = 0.013$) were significant.

Table 3 summarizes the diagnostic characteristics of the sit-up test at the conventional cut-points (a change of −20 and −10 mmHg in SBP and DBP, respectively) as well as at different cut-points. In addition, Fig. 4 illustrates the relationships between the Youden Index and cut-points for systolic and diastolic orthostatic hypotension. At the conventional cut-point for systolic orthostatic hypotension (−20 mmHg), we found a sensitivity of 37.5% (95% CI = 8.5–75.5), specificity of 96.7% (95% CI = 82.8–99.9) and Youden Index of 0.342. At the conventional cut-point for diastolic orthostatic hypotension (−10 mmHg), we found a sensitivity of 33.3% (95% CI = 0.8–90.6), specificity of 97.1% (95% CI = 85.1–99.9) and Youden Index of 0.305. The Youden Index for a reduction in SBP was maximum at 0.842, and the corresponding cut-point, sensitivity and specificity were −10 mmHg, 87.5% (95% CI = 47.4–99.7), and 96.7% (95% CI = 82.8–99.9), respectively. In addition, the Youden Index for a reduction in DBP was maximum at 0.886, and the corresponding cut-point, sensitivity and specificity were −5 mmHg, 100.0% (95% CI = 29.2–100.0) and 88.6% (95% CI = 73.3–96.8), respectively.

DISCUSSION

The sit-up test provides a practical bedside assessment for orthostatic hypotension, which could easily be implemented in the clinical setting. To our knowledge, this multicentre cross-sectional study is the first to examine the cut-points of a decrease in blood pressure for identifying orthostatic hypotension using the sit-up test. Utilizing a multicentre approach allows for improved generalizability of our results. This study found that a threshold of 10 mmHg for a decrease in SBP and 5 mmHg for a decrease in DBP produced the optimal diagnostic characteristics as assessed with the Youden Index. These results support our hypothesis that the optimal cut-points of the decreases in blood pressure during the sit-up test for identifying orthostatic hypotension are smaller than the conventional cut-points. The findings of this study may have important implications for the clinical application of the sit-up test for identifying stroke survivors with orthostatic hypotension.

TABLE 1. Participants' characteristics

Variable	Overall ($n = 38$)	With OH ($n = 9$)	Without OH ($n = 29$)	*P*
Age (years)	60.5 ± 12.6	63.6 ± 8.1	65.4 ± 13.7	0.704
Sex, male/female	17/21	6/3	11/18	0.249
Body weight (kg)	57.5 ± 12.4	68.0 ± 4.1	54.3 ± 2.0	0.003
BMI (kg/m^2)	22.5 ± 3.6	24.9 ± 4.2	21.7 ± 3.0	0.015
Type of stroke, ischemic/haemorrhage	20/18	6/3	14/15	0.454
Side of motor paresis, right/left	25/13	6/3	19/10	0.999
Time since stroke onset (days)	80.9 ± 36.1	75.7 ± 36.5	82.6 ± 36.4	0.622
Antihypertensive medicine				
Alpha-blocker	2	0	2	0.999
Angiotensin-converting enzyme inhibitor	1	0	1	0.999
Angiotensin II receptor blocker	11	1	10	0.237
Calcium channel blocker	24	6	18	0.999
Diuretics	2	0	2	0.999
Comorbidities				
Diabetes mellitus	8	2	6	0.999
Heart diseases	5	1	4	0.999
Hyperlipidaemia	9	2	7	0.999
Hypertension	34	9	25	0.555
Stoke Impairment Assessment Set motor score (points)	17.00 (9.75, 22.25)	16.00 (9.00, 23.00)	18.00 (9.50, 22.50)	0.966
Functional Independence Measure motor score (points)	71.50 (46.75, 88.25)	78.00 (45.00, 89.50)	70.00 (50.50, 87.00)	0.913
Functional Independence Measure cognitive score (points)	30.50 (26.75, 34.00)	33.00 (27.50, 35.00)	30.00 (26.00, 33.00)	0.147

Values are presented as mean ± standard deviation, number or median (interquartile range).
P values indicate significant differences between the groups with OH and without OH.
OH, orthostatic hypotension.

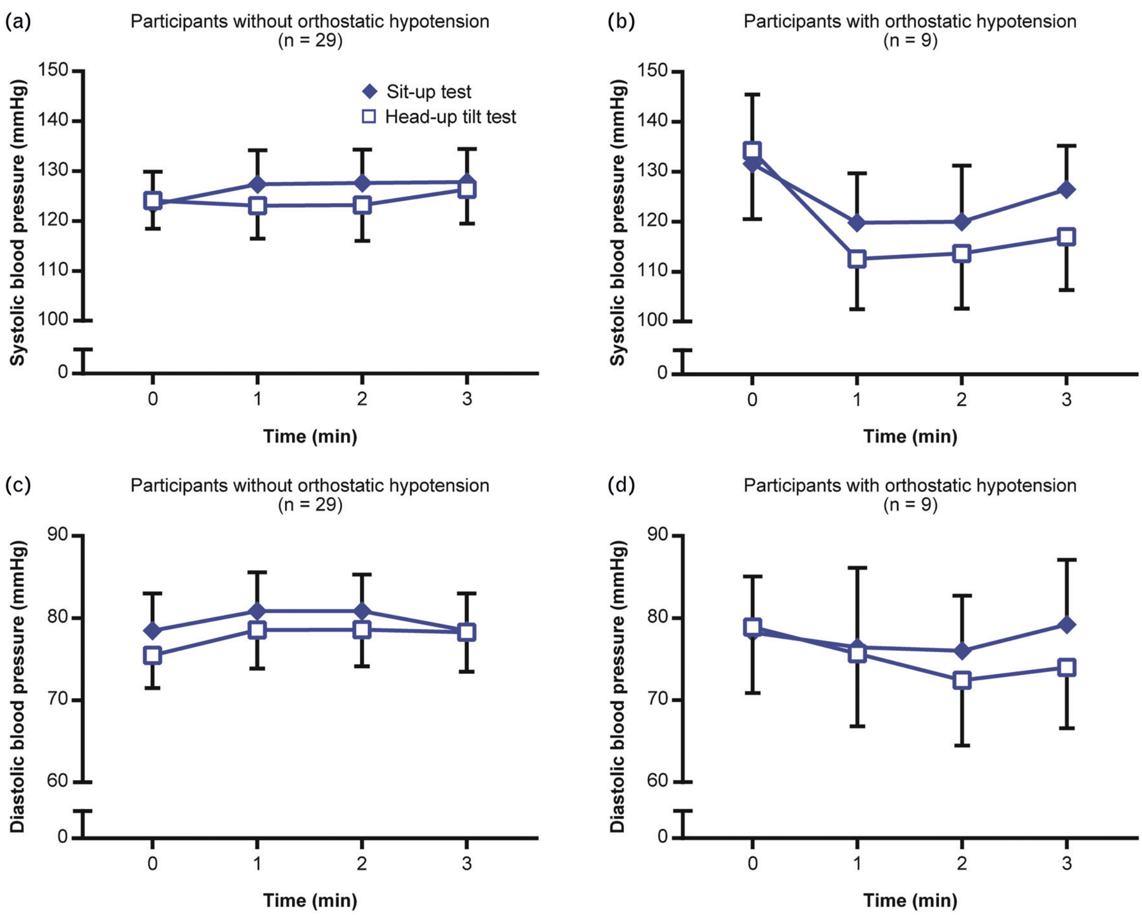

FIGURE 2 Blood pressure response to the sit-up and head-up tilt tests. (a) SBP changes during the sit-up and head-up tilt tests in participants without orthostatic hypotension and (b) in those with orthostatic hypotension. (c) DBP changes during the sit-up and head-up tilt tests in participants without orthostatic hypotension and (d) in those with orthostatic hypotension. Diamonds and squares represent the mean blood pressure values during the sit-up and head-up tilt tests, respectively. Vertical bars indicate 95% confidence intervals. As the x-axis represents the time after postural change, data at 0 on the x-axis correspond to data in the supine position.

TABLE 2. Comparisons of haemodynamic variables between the sit-up and head-up tilt tests

Variable	Sit-up test	Head-up tilt test	95% CI	*P*
SBP in the supine position (mmHg)	125.2 ± 16.9	126.5 ± 15.3	−3.2 to 0.7	0.188
Change in SBP during testing (mmHg)	−2.9 ± 10.8	−8.0 ± 11.7	2.1–8.0	0.001
DBP in the supine position (mmHg)	75.6 ± 10.3	76.3 ± 10.5	−2.0 to 0.5	0.261
Change in DBP during testing (mmHg)	1.1 ± 7.4	−1.1 ± 6.5	0.0–4.2	0.051

Values are presented as mean ± standard deviation.
P values indicate significant differences between the sit-up and head-up tilt tests.

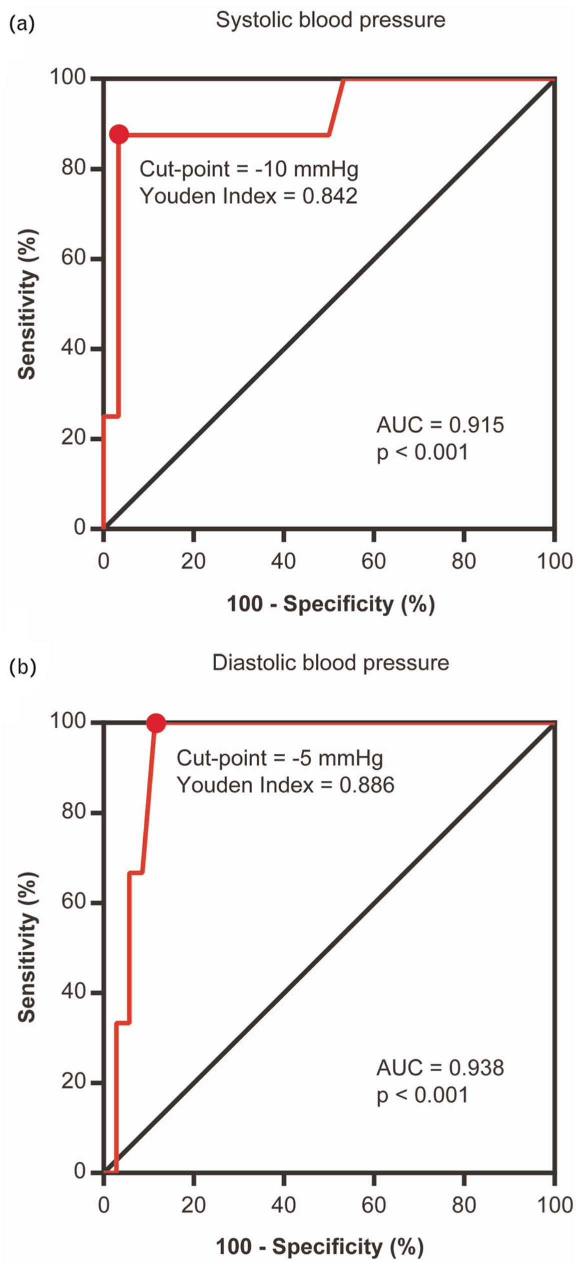

FIGURE 3 Receiver operator characteristic curves for the decrease in blood pressure during the sit-up test for the detection of (a) systolic and (b) diastolic orthostatic hypotension. The red lines are the plot of the sensitivity against (100−specificity). The diagonal lines represent the line of no-discrimination. The thick dots are the cut-points with the highest Youden Index.

In this study, a lower prevalence of orthostatic hypotension (23.7%) was observed among the participants compared with that reported among individuals undergoing in-hospital stroke rehabilitation (38.5 versus 52.1%) [10,11]. A cohort study reported that of the 35 individuals with stroke who had orthostatic hypotension on admission to the rehabilitation centre, 23 had an improvement in orthostatic hypotension at approximately 1 month after admission [11]. In this study, the mean time since stroke onset was approximately 80 days, although it was less than 30 days as reported in two previous studies [10,11]. The discrepancy in prevalence rates between the studies may be attributed to the difference in the time duration since stroke onset. We also found that the body weight and BMI were greater in participants with orthostatic hypotension than in those without, although the mean BMI in participants with orthostatic hypotension was within the normal weight range [24]. These results support the findings of Tang *et al.* [16] who reported that stroke survivors with orthostatic hypotension tended to be heavier in body weight and demonstrated greater dyslipidaemia levels than those without orthostatic hypotension. Obesity and orthostatic hypotension are well established risk factors for stroke [25–29]. In contrast, studies have reported that being overweight or obese was not associated with increased recurrent stroke risk [30–32]. Further studies are warranted to examine the association between orthostatic hypotension and body weight.

As a rest period of at least 5 min is considered sufficient to establish a stable baseline [14,15], the sit-up and head-up tilt tests were conducted randomly with a 10-min rest period between each test. These procedures may help reduce order bias and carryover effects, resulting in no significant differences in SBP and DBP in the supine position between the tests. A smaller decrease in SBP was observed during the sit-up test than that observed during the head-up tilt test. The decrease in blood pressure after transferring from the supine to the upright position is associated with a reduction in venous return and stroke volume [33]. We also previously reported that the decrease in stroke volume during the sit-up test was smaller than that during the head-up tilt test in healthy young individuals [20]. Compared with the sitting position, more blood is pooled in the lower extremities due to gravitational forces in the standing position, which results in a smaller venous return and stroke volume in the standing position than in the sitting position [34]. These findings can explain the difference in the reduction of SBP between the tests.

The AUC is an effective measure to summarize the overall diagnostic accuracy of a test [35]. Shaw *et al.* [19] examined the optimal blood pressure cut-points to identify

TABLE 3. Diagnostic characteristics for the sit-up test across different cut-points for orthostatic hypotension

Variables	Cut-point (mmHg)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	LR+	LR−	Youden Index
SBP	*−20*	*37.5 (8.5–75.5)*	*96.7 (82.8–99.9)*	*75.0*	*85.3*	*11.25*	*0.65*	*0.342*
	−15	62.5 (24.5–91.5)	96.7 (82.8–99.9)	83.3	90.6	18.75	0.39	0.592
	−10	**87.5 (47.4–99.7)**	**96.7 (82.8–99.9)**	**87.5**	**96.7**	**26.25**	**0.13**	**0.842**
	−5	87.5 (47.4–99.7)	70.0 (50.6–85.3)	43.8	95.5	2.92	0.18	0.575
DBP	*−10*	*33.3 (0.8–90.6)*	*97.1 (85.1–99.9)*	*50.0*	*94.4*	*11.67*	*0.69*	*0.305*
	−7	66.7 (9.4–99.2)	94.3 (80.8–99.3)	50.0	97.1	11.67	0.35	0.610
	−5	**100.0 (29.2–100.0)**	**88.6 (73.3–96.8)**	**42.9**	**100.0**	**8.75**	**0.00**	**0.886**
	−3	100.0 (29.2–100.0)	71.4 (53.7–85.4)	23.1	100.0	3.50	0.00	0.714

The values in italics represent the diagnostic characteristics of the conventional cut-points.
The bold values indicate the diagnostic characteristics at the highest Youden Index value.
Values in parenthesis indicate 95% confidence intervals.
PPV, positive predictive value; NPV, negative predictive value; LR+, positive likelihood ratio; LR−, negative likelihood value.

orthostatic hypotension using the sit-to-stand test and reported that the AUC for systolic and diastolic orthostatic hypotension was 0.916 and 0.930, respectively. These AUC values are similar to the results of this study. An AUC of at least 0.900 is considered outstanding [35]. Therefore, the sit-up test appears to be a good alternative to identify orthostatic hypotension in situations wherein the head-up tilt test cannot be easily performed. Furthermore, the sit-up test may be more useful than the sit-to-stand test in clinical settings because it can be performed for individuals who cannot perform the sit-to-stand manoeuvre due to balance impairment or difficulty in transferring to a standing position.

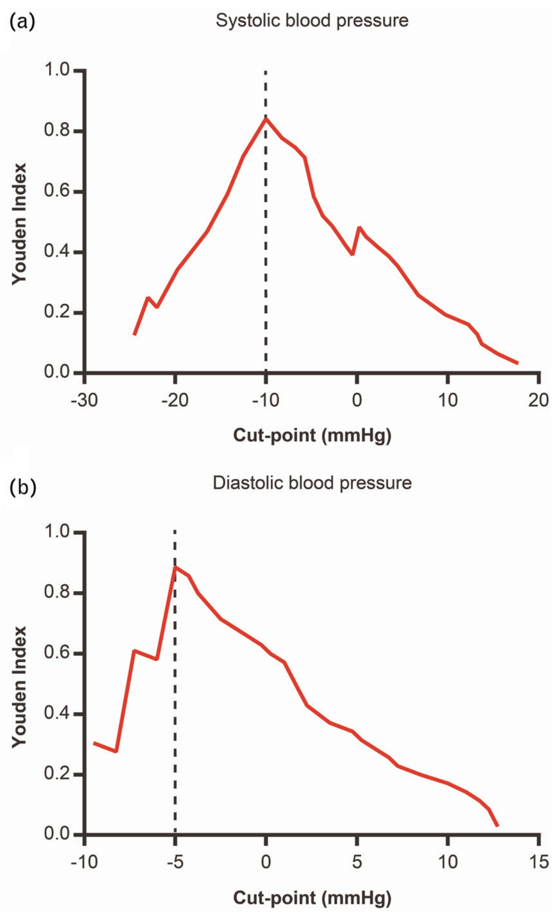

FIGURE 4 Relationships between the Youden Index and cut-points for (a) systolic and (b) diastolic orthostatic hypotension. The red lines are the plot of the Youden Index against cut-points. The vertical dashed lines indicate the optimal cut-points corresponding to the highest Youden Index.

Study limitations

The major limitation of this study was the relatively small sample size, given that in a previous study, 831 participants were included to determine the optimal cut-points for orthostatic hypotension using the sit-to-stand test [19]. Although the power calculation assumed comparable distribution between participants with and without orthostatic hypotension, the distribution observed in this study was markedly different. Accordingly, we performed the additional post-hoc power analyses for the sensitivity analysis. For detecting participants with systolic orthostatic hypotension, considering the sensitivity of 87.5% and a prevalence of 21%, the required sample size was estimated to be 48 individuals. In addition, for identifying participants with diastolic orthostatic hypotension, a sample size of 63 individuals was calculated using the sensitivity of 100.0% and a prevalence of 8%. These syntaxes are presented in Appendixes 3 and 4 (Supplemental Digital Content, http://links.lww.com/HJH/C83), respectively. Because of the small sample size, the sensitivity had large CIs. Further studies with a large sample size, including community-dwelling individuals with stroke and other conditions, such as spinal cord injury, are needed to confirm the robustness of our findings. Second, of the individuals with stroke assessed for eligibility, 238 (86.2%) were excluded from the study. Many were excluded because they had an MMSE score of less than 24 points. Therefore, generalization of the finding to these individuals should be made with caution. Finally, the tests were performed in the evening. Orthostatic hypotension occurs more frequently in the morning than later in the day [36]. Therefore, this study may have underestimated the prevalence of orthostatic hypotension.

In conclusion, the sit-up test allows the assessment of orthostatic hypotension in individuals with stroke who cannot stand independently without the use of specialized equipment such as a tilt table. This study suggests that compared with the conventional cut-points for orthostatic hypotension, smaller cut-points of a decrease in SBP and DBP can better identify orthostatic hypotension in individuals with stroke using the sit-up test. The findings of this study provide valuable information for the clinical application of the sit-up test.

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Conflicts of interest

There are no conflicts of interest to declare.

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