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Decreased Stroke Volume and Venous Return in School Children with Postural Tachycardia Syndrome

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In postural tachycardia syndrome (POTS), a subtype of orthostatic intolerance, the changes in hemodynamics due to postural changes are poorly understood. We speculated that inappropriate venous return, which may occur in the upright position in patients with school-aged POTS, could be detected by echocardiography. Our prospective study was conducted with 100 POTS patients (45 boys and 55 girls), aged 13.1 ± 1.5 years and 52 age- and sex-matched healthy subjects (control). Echocardiography was performed in the supine and sitting positions. Cardiac parameters [stroke volume index, cardiac index, heart rate, and the maximum inferior vena cava diameter (max IVC)] were evaluated in addition to pulse pressure. Unlike the control subjects, POTS patients demonstrated decreased stroke volume index ($P = 0.02$) and max IVC ($P < 0.01$) irrespective of posture. The rates of max IVC change did not differ between control and POTS groups. The enrolled POTS patients were divided into two subgroups [dilatation (n = 57) and contraction (n = 43)] based on whether the change rate of max IVC was less than zero or not. The contraction group showed a significantly higher heart rate than the dilatation group with respect to posture ($P = 0.03$), indicating the poor response of peripheral vessels in the lower limbs only in the contraction group. In conclusion, echocardiographic assessment detected decreased stroke volume and venous return in POTS. The changes in max IVC in response to postural changes may indicate an underlying pathophysiology in POTS.

Keywords: echocardiography; inferior vena cava; orthostatic intolerance; postural tachycardia syndrome; posture
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Introduction

Postural tachycardia syndrome (POTS) is classified as a major subtype of orthostatic intolerance. Orthostatic intolerance can be a trigger of school refusal and disturb the daily school activities (Tanaka et al. 2009). POTS patients suffer from symptoms of recurrent headache, general fatigue, nausea, abdominal pain, and sleep disturbance in addition to the typical complaints of morning tiredness and orthostatic dizziness (Singer et al. 2012; Sheldon et al. 2015; Bryarly et al. 2019). A head-up tilt table test alone is not sufficient for evaluating the underlying pathophysiology because of its heterogenous causes. The non-invasive beat-to-beat blood pressure and a heart rate monitoring device (Finometer/Portapres, Finapres Medical Systems, Netherlands) have advanced the understanding of POTS by revealing hemodynamic abnormalities related to postural change (Tanaka 2012). However, the underlying pathophysiology of excessive tachycardia without obvious hypotension in the upright posture is poorly understood. Thoracic hypovolemia during orthostasis is believed to be the basis of the symptoms in POTS (Stewart and Montgomery 2004). We speculated that inappropriate venous return, which may occur in the upright position in patients with POTS, could be detected by echocardiography. Reports suggest that changes in the diameter of the inferior vena cava (IVC) in response to postural changes could be a parameter for understanding the compensatory mechanisms for orthostatic stress in children with orthostatic intolerance (Fujii et al. 2011).

This study aimed to use echocardiographic parameters to assess circulatory responses in the sitting posture and

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compare them with those in the supine position; it also aimed to investigate the characteristics of hemodynamic responses to postural changes in school-aged POTS.

Materials and Methods

Study population

We performed this prospective study on 177 subjects who attended the Department of Pediatrics and Child Health, Nihon University Itabashi Hospital, Tokyo, Japan for symptoms of orthostatic intolerance between April 2016 and March 2018. Subjects were only enrolled if they met the criteria of the Japanese screening test for orthostatic intolerance (Table 1) (Tanaka et al. 2009). The 65 subjects were recruited as control (CTRL) among children referred for heart murmurs, chest pain, palpitations, suspicion of an abnormal electrocardiogram, and follow-up for Kawasaki disease. We excluded 13 patients (20%) who were found to have heart disease (n = 7: atrial septal defect 2, ventricular septal defect 1, bicuspid aortic valve 1, mild aortic regurgitation 1, mitral valve prolapse/mitral valve regurgitation 2) or abnormal electrocardiograms (n = 6: Wolff-Parkinson-White syndrome 3, premature ventricular contraction 3) after cardiac screenings. The subjects who had a history of Kawasaki disease were selected only when they were confirmed to have no cardiac complications for more than 10 years since their disease onset. We also confirmed that all of the control patients did not meet the diagnostic criteria of orthostatic intolerance (Table 1). Finally, 52 subjects were eligible to participate in the age- and sex-matched CTRL cohort. Informed consent was obtained from all enrolled children and their parents prior to inclusion in this study. All protocols were approved by the institutional review board of the Nihon University Itabashi Hospital (RK-150609-20). The study methods were carried out in accordance with the relevant guidelines and regulations.

Protocol

Echocardiography was performed in the morning in all subjects. The medications were discontinued for 3 days prior to participation in this study, that correspond to at least 5 times of the half-life periods of the drugs, such as midodrine hydrochloride. All participants continued normal diet and POTS patient did not take any special dietary advices of water drinking or salt supplementation. Echocardiography was performed in the sitting and supine positions. The subjects were asked to raise their upper body to a 90-degree sitting position with their legs stretched on the bed. This position was maintained for at least one minute before measurement to allow for stabilization after initial orthostatic hypotension. Blood pressure was checked at the beginning and end of the test in the supine and sitting positions, respectively. The pulse pressure was calculated by subtracting the diastolic from systolic blood pressure. The diagnosis in all orthostatic intolerance patients was confirmed by a screening active-standing test using non-invasive continuous blood pressure monitoring instruments that enabled beat-by-beat blood pressure measurement using the tonometry method. The equipment was changed from BP-608 Evolution II CS (OMRON HEALTHCARE Co., Ltd., Kyoto, Japan) to TFM-3040M Task Force™ hemodynamic monitor CNSystems (NIHON KOHDEN Co., Ltd., Tokyo, Japan) in January 2017. The orthostatic intolerance group was classified into instantaneous orthostatic hypotension (n = 25), POTS (n = 100), vasovagal syncope (n = 7), delayed orthostatic hypotension (n = 18), hyper-response type (n = 19), and non-typeable (n = 8) subgroups based on the active-standing response (Tanaka et al. 2009; Tanaka 2012). The diagnosis of POTS is based on an increased heart rate of ≥ 40 beats/min or a maximum heart rate of ≥ 120 bpm while standing, in the absence of orthostatic hypotension (> 20 mmHg drop in systolic blood pressure) (Singer et al. 2012; Li et al. 2015; Sheldon et al. 2015). Only patients with POTS were selected for the study.

Echocardiography

Echocardiography was performed using an Artida cardiac ultrasound machine equipped with a 2.5-5 MHz transducer (CANON Medical Systems, Tochigi, Japan). The left ventricular ejection fraction was calculated using the modified Simpson's method (Lang et al. 2015). The ratio of peak mitral E to A wave velocity was detected from the left

Table 1. Screening checklist for orthostatic intolerance in Japan.

- Susceptibility to vertigo and dizziness on standing
- A tendency to faint in the standing position, which in severe cases leads to a fall
- Nausea on taking a hot bath or on encountering unpleasant experiences
- Palpitation and/or dyspnea after mild exercise
- Difficulty getting out of bed
- Pallor
- Anorexia
- Occasional umbilical colic (severe abdominal pain)
- Fatigability
- Frequent headache
- Motion sickness

ventricular inflow waveforms in the apical four-chamber view (Nagueh et al. 2016). The cardiac structure and its performance were normal in the supine position; this was confirmed in all subjects. The stroke volume was calculated using power doppler in the apical five-chamber view as the product of cross-sectional area (cm^2) and the velocity-time integral (cm) of the left ventricular outflow tract (Porter et al. 2015). The images of these method were shown in Fig. 1. The cardiac output (L/min) was calculated using the formula: stroke volume × heart rate. The stroke volume and cardiac output were corrected using body surface area for calculating the stroke volume index and cardiac index, respectively. The body surface area was calculated using the formula of DuBois (Du Bois and Du Bois 1989). The maximum IVC diameter (max IVC) was assessed at 1 to 2 cm from the junction of right atrium in the expiratory phase.

Statistical analyses

All data have been presented as means ± standard deviation. Normality tests were performed for each continuous variable using the Kolmogorov-Smirnov method. The categorical variables were assessed using the Fisher's exact or Chi-square tests, as appropriate. Differences between CTRL and POTS groups were tested for statistical significance using the Student's *t*-test. Repeated measures analysis of variance (ANOVA) was used to evaluate the cardiac parameters for effects of group and posture, and to assess the interaction between group and posture. A P value < 0.05 was considered statistically significant. All data were collected and analyzed by the same observer throughout the study. Intra- and inter-observer reproducibility of echocardiography findings were assessed using the intraclass correlation coefficient and Bland-Altman analysis. The 21 subjects (11 CTRL and 10 POTS) were randomly selected. Intra-observer variability was tested by an experienced echocardiographer who was blinded to the first measurement. Inter-observer variability was assessed independently by a different researcher. All statistical analyses were performed using commercially available software, EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan) (Kanda 2013) and the R software package (version 3.4.0.; The R Foundation for Statistical Computing Vienna, Austria).

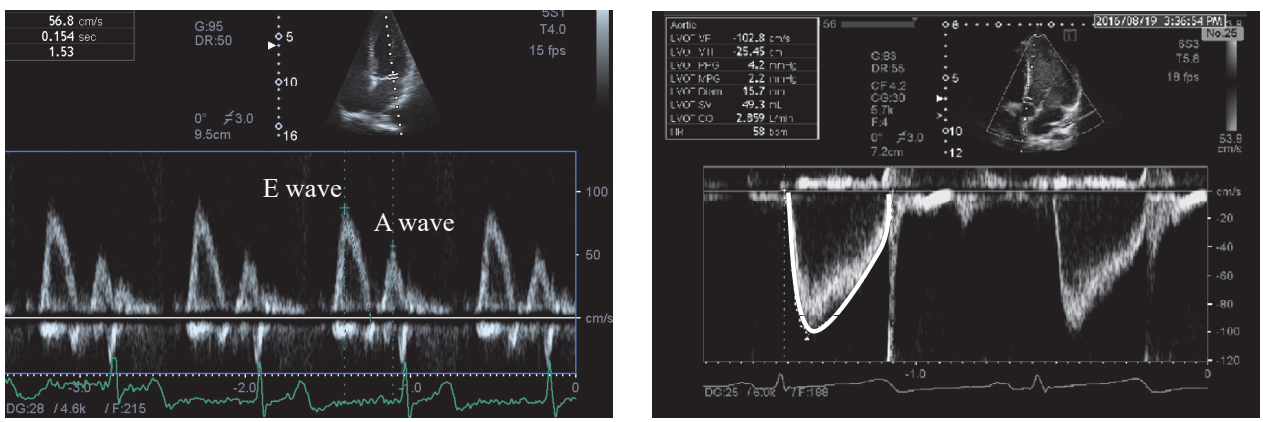
Results

Patient demographic and echocardiographic data (CTRL vs. POTS)

The characteristics of patients in this study are shown in Table 2. There were no differences between patients in the CTRL and those in the POTS groups in terms of age, sex, supine blood pressure, and supine heart rate. With respect to left ventricular function, the left ventricular ejection fraction and the ratio of peak mitral E to A wave velocity were normal, and did not significantly differ between the both groups. No significant differences were observed between the two groups in terms of the rates of change of all cardiac indices (stroke volume index, cardiac index, and heart rate).

Effects of posture on hemodynamic parameters in CTRL vs. POTS patients

Fig. 2 shows the hemodynamic effect of postural changes on cardiac parameters, namely, stroke volume index, cardiac index, max IVC, and pulse pressure. In the sitting position, the max IVC increased (P = 0.01) while



A **B**

Fig. 1. Cardiac parameters recorded with a pulsed-wave doppler.
A) Mitral flow as recorded with a pulsed-wave doppler in a four-chamber view. A wave: late diastolic atrial contraction flow, E wave: early diastolic rapid filling flow.
B) Left ventricular outflow tract velocity-time integral as recorded with a pulsed-wave doppler in a five-chamber view. Velocity-time integral was determined by tracing the spectral doppler envelope. To obtain the stroke volume, the aortic valve diameter was measured. Assuming that the left ventricular outflow tract is circular, the cross-sectional area of the aortic valve was calculated with the formula $\pi \times (\text{diameter}/2)^2$. Stroke volume was determined using left ventricular outflow tract velocity-time integral × cross-sectional area of the aortic valve.

Table 2. Characteristics of the participants.

	CTRL (n = 52)	POTS (n = 100)	P
Clinical characteristics			
Age (years)	13.2 ± 2.1	13.1 ± 1.5	0.54
Body surface area (m^2)	1.4 ± 0.2	1.4 ± 0.2	0.88
Women, n (%)	25 (48)	55 (55)	0.49
Systolic blood pressure (mmHg)	109.7 ± 9.8	108.5 ± 8.6	0.44
Diastolic blood pressure (mmHg)	61.0 ± 7.8	60.9 ± 7.4	0.95
Heart rate (bpm)	65.2 ± 11.4	67.9 ± 11.7	0.16
Left ventricular functions in the supine position			
Ejection fraction (%)	77.4 ± 4.9	78.2 ± 5.6	0.37
E/A	1.91 ± 0.6	1.83 ± 0.4	0.25
Change rate from the supine position to the sitting position			
Stroke volume index (%)	−21.3 ± 12.5	−22.8 ± 11.9	0.46
Cardiac index (%)	−0.1 ± 0.2	−0.1 ± 0.2	0.95
Heart rate (%)	29.3 ± 19.8	33.8 ± 20.0	0.19

Values are expressed as mean ± standard deviation or number (percentage).
CTRL, control; E/A, the ratio of peak mitral E wave velocity to peak mitral A wave velocity; POTS, postural tachycardia syndrome.

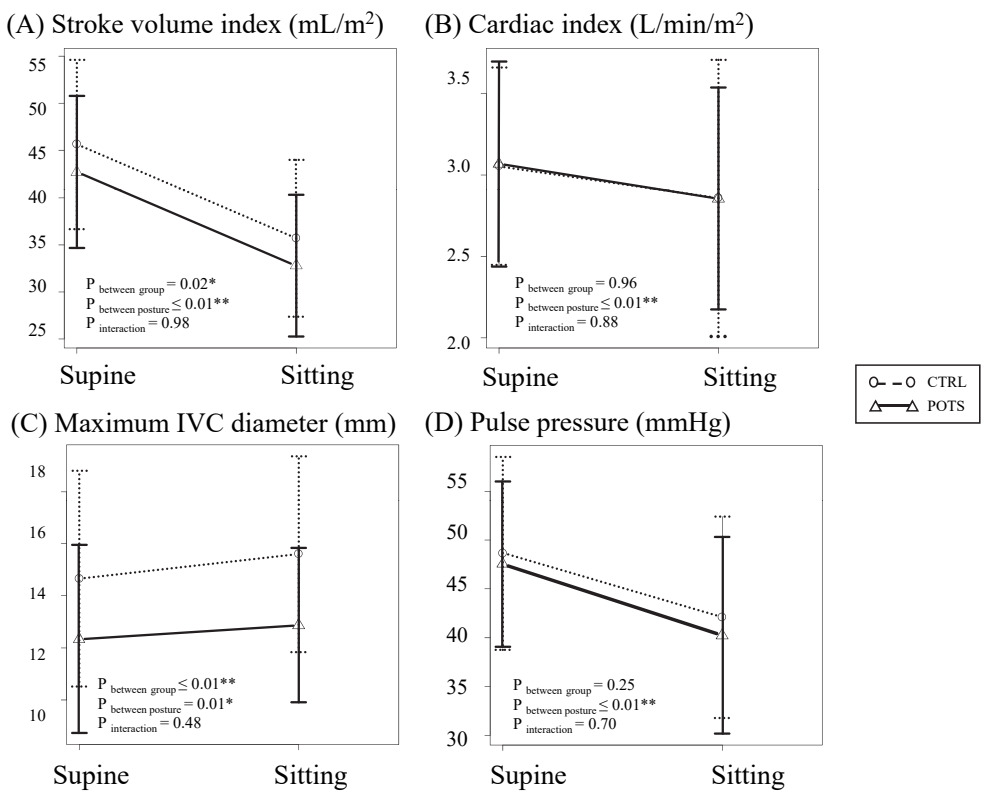


Fig. 2. Changes in hemodynamic parameters related to postural change between the CTRL (n = 52) and the POTS groups (n = 100).
Repeated measures ANOVA for stroke volume index (A), cardiac index (B), maximum IVC diameter (C), and pulse pressure (D) between both groups (CTRL vs. POTS) before and after assuming the sitting position. Open circles and triangles denote the CTRL and POTS groups, respectively. There was no interaction between posture and the groups for each parameter. * $P < 0.05$, ** $P < 0.01$.
ANOVA, analysis of variance; CTRL, control; IVC, inferior vena cava; POTS, postural tachycardia syndrome.

other indices decreased (P < 0.01). Compared to the CTRL group, the stroke volume index and the max IVC were significantly lower in patients in the POTS group (P = 0.02, P ≤ 0.01, respectively). However, the degree of changes was not found by the postural change between the POTS and CTRL groups. (There were no crossed lines on the graphs, which suggested no interaction effect).

Differences in the rate of change of max IVC between CTRL and POTS patients

As shown in Fig. 3, no significant differences were observed between the two groups in terms of the rate of change of max IVC (P = 0.97). The wide range of the rate of change of max IVC in the POTS group was classified as follows: > 0: dilatation group (n = 57), ≤ 0: contraction group (n = 43). The CTRL group was also classified into two subgroups, based on the presence of a contracted IVC (cCTRL: n = 18) or a dilated IVC (dCTRL: n = 34). The representative echocardiograms are shown in Fig. 4.

Effects of posture on hemodynamic parameters in the POTS group (contraction vs. dilation group)

As shown in Fig. 5, the POTS subgroups were compared in terms of stroke volume index, cardiac index, heart rate, and pulse pressure. Postural changes affected all parameters, as the heart rate increased (P < 0.01) and other indices decreased (P < 0.01). No significant differences were observed between the contraction and dilatation groups in all parameters. A significant interaction between posture and the subgroups was found in terms of heart rate (P = 0.03).

Effects of posture on hemodynamic parameters in CTRL (cCTRL vs. dCTRL)

As shown in Fig. 6, all differences in hemodynamics in the CTRL group, with respect to changes of IVC diameter between the cCTRL and dCTRL subgroups, were assessed. The impact was due to the posture on all parameters. No differences were found between the groups, except in heart rate. The heart rate was significantly higher in the dCTRL subgroup than in the cCTRL subgroup (P = 0.04). There were no significant effects of posture and group interaction on all parameters.

Assessment of reproducibility

The intra- and inter-observer agreements for the rate of max IVC changes and stroke volume measurements in the 21 randomly selected subjects were evaluated and found to be excellent (Table 3).

Discussion

POTS is characterized by the orthostatic intolerance,

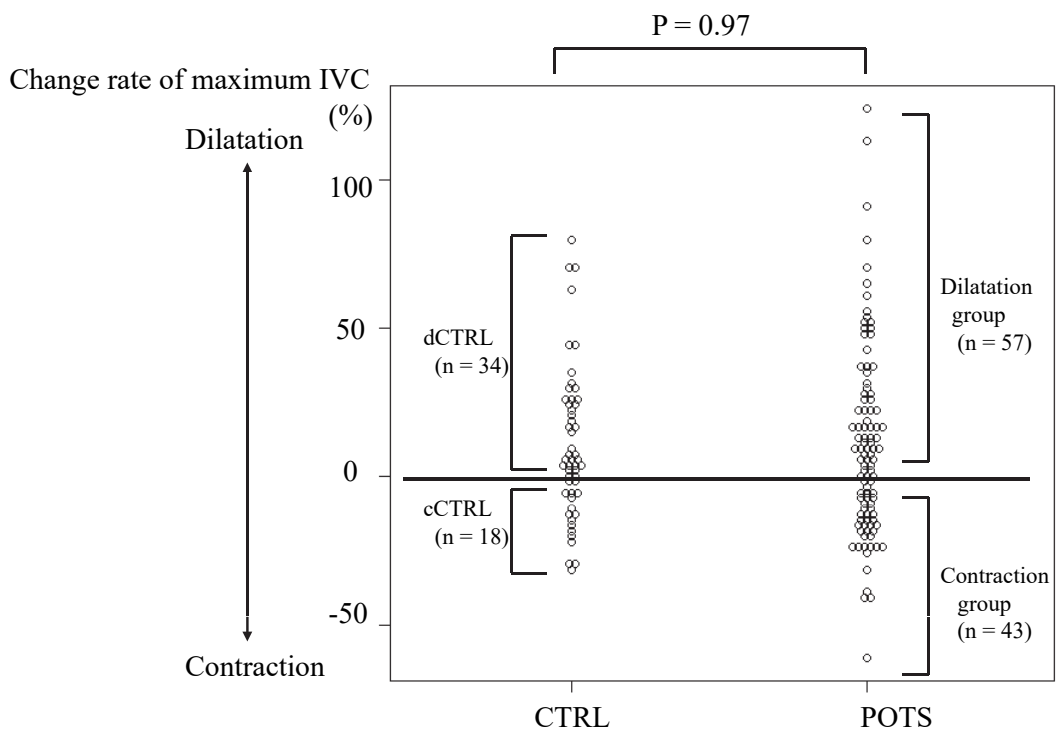


Fig. 3. The rate of change of maximum IVC diameter in the CTRL and the POTS groups.
The dotted plot indicates the rate of maximum IVC diameter change in the CTRL and the POTS groups. There was no difference between the two groups (P = 0.97). A change rate value above 0 is suggestive a dilated IVC after postural change. POTS patients were divided into two subgroups, namely, contraction (≤ 0; n = 43) and dilatation (> 0; n = 57) groups. The CTRL were divided into two groups with reference to POTS, cCTRL (n = 18) and dCTRL (n = 34).
cCTRL, the subgroup with a contracted IVC in the CTRL group; CTRL, control; dCTRL, the subgroup with a dilated IVC in the CTRL group; IVC, inferior vena cava; POTS, postural tachycardia syndrome.

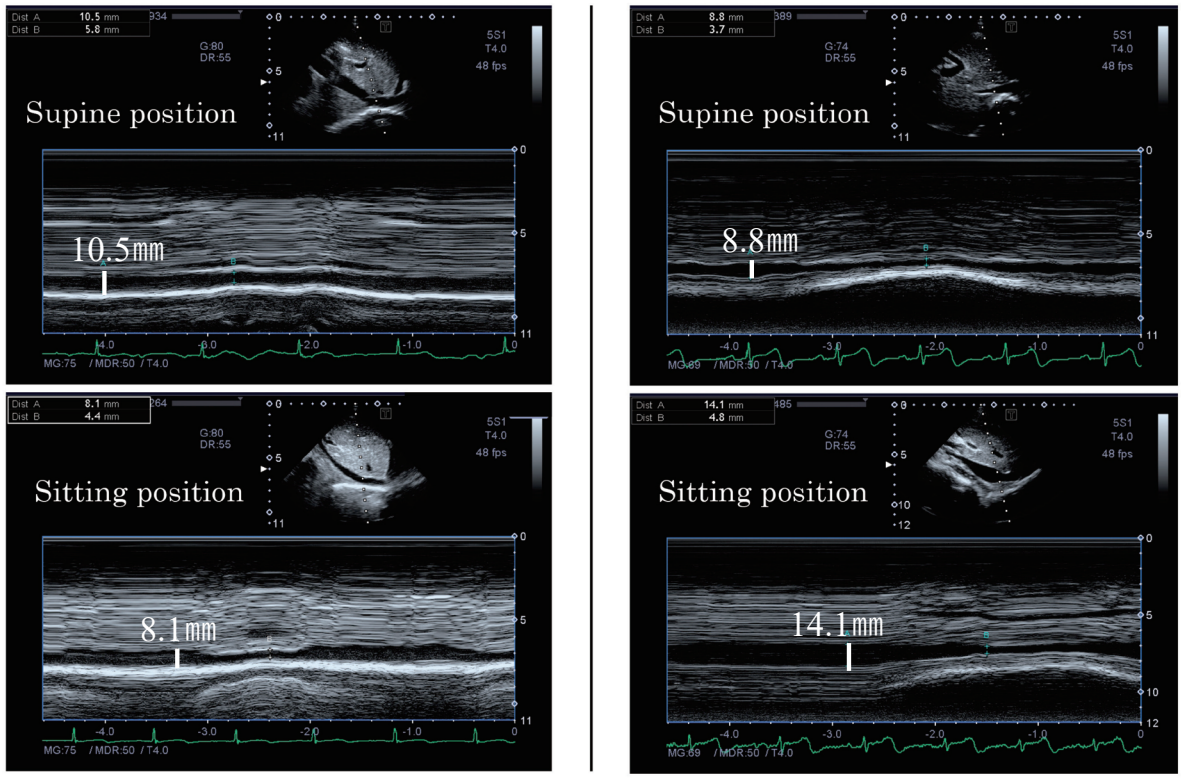


Fig. 4. The changes in the maximum IVC diameter with postural changes on representative echocardiograms in POTS patients.
The top and bottom panels represent the supine and sitting positions, respectively. A: contraction group (change rate = −23%). B: dilatation group (change rate = +60%).
IVC,inferior vena cava; POTS, postural tachycardia syndrome.

palpitations, presyncope, and lightheadedness. Those symptoms need to exclude cardiac abnormalities (Garland et al. 2015; Arnold et al. 2018). Although echocardiography is sometimes performed in POTS for differential diagnosis, there were no reports regarding the hemodynamics with postural change using echocardiography in school-aged POTS patients. This study reported the characteristics of hemodynamic responses to postural change in patients with POTS; they tended to have low stroke volume index and decreased max IVC compared to CTRL subjects, irrespective of posture. With respect to changes in max IVC based on posture, POTS was classified into two groups, namely, contraction (the rate of max IVC change was 0 or less) and dilatation (the rate of max IVC change exceeded 0) groups. In our cohort, the contraction group showed a more remarkable increase in heart rate than the dilatation group. In addition, in the sitting position, the decreased pulse pressure in the contraction group tended to be insufficient compared to that in the dilatation group. Accelerated heart rate may suggest compensatory reactions of the contraction group, which have the problem of vascular response to postural change in lower extremity (Fig. 7).

The venous system plays an important role in propelling venous blood from the systemic circulation to the heart. The compliance of a systemic vein is approximately 24 times that of its corresponding artery (Guyton and Hall 2000). The sympathetic discharge increases when an individual moves from the supine to the upright position; this increases arterial resistance, heart rate, myocardial contractility, and decreases venous capacity. An increase in venous return may be achieved by this reflex (Gelman 2008). We speculated that the postural change findings seen on echocardiography in the sitting position would be useful for understanding cardiac responses; additionally, the compensatory peripheral vein responses consequent to decreased thoracic volume may cause the max IVC change observed with change in posture.

Our study found that the stroke volume index in POTS patients was lower than that of the CTRL subjects; this may be considered to be indicative of a hypovolemic status or thoracic hypovolemia owing to the characteristic poor response of peripheral vessels in POTS. The findings of decreased max IVC in POTS are consistent with this hypothesis. Previous reports have speculated that the blood volume is lower in POTS patients compared to that of CTRL subjects (Stewart and Montgomery 2004; Stewart et al. 2009; Li et al. 2015).

Two different types of reactions of max IVC were

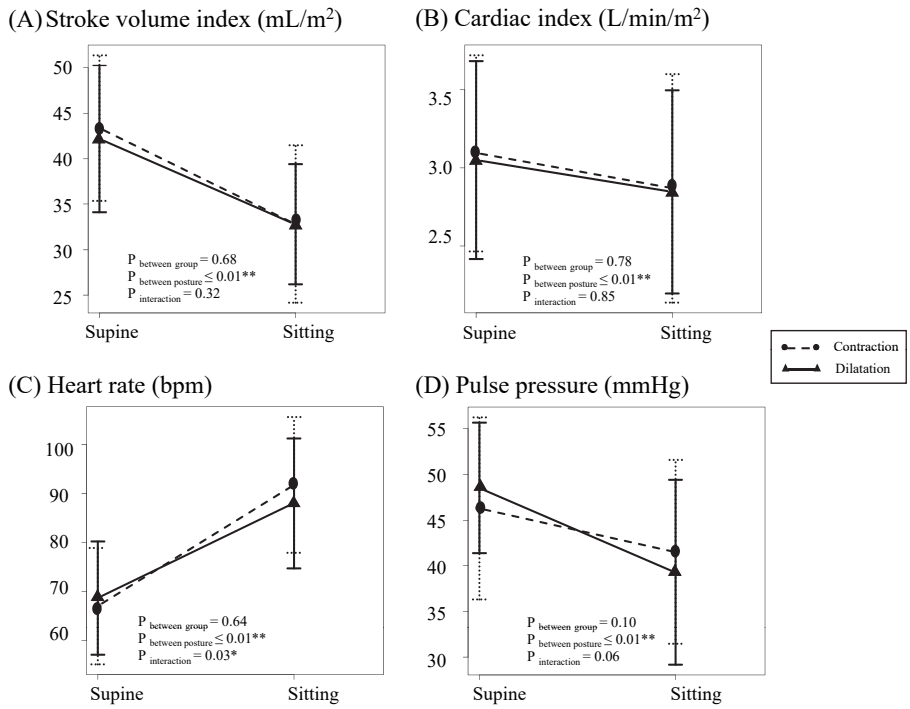


Fig. 5. Change in hemodynamic parameters related to postural change between the contraction and dilatation subgroups in the POTS group.
Repeated measures ANOVA for stroke volume index (A), cardiac index (B), heart rate (C), and pulse pressure, (D) between groups (contraction vs. dilatation) in POTS before and after sitting position. The filled circles and triangles indicate the contraction and the dilatation groups, respectively. *P < 0.05, **P < 0.01. ANOVA, analysis of variance; POTS, postural tachycardia syndrome.

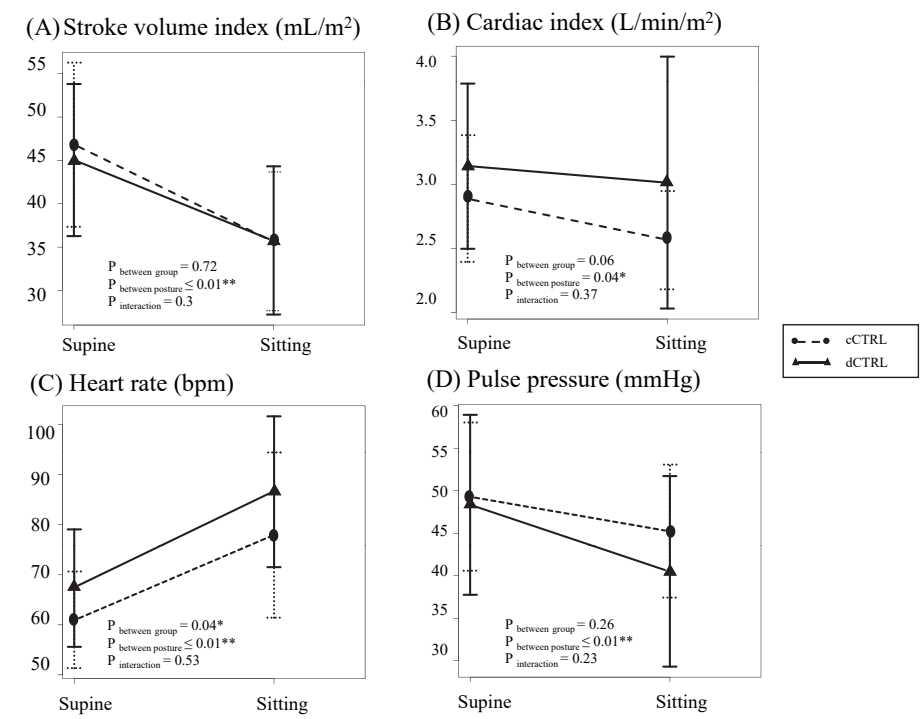


Fig. 6. Change in hemodynamic parameters in relation to postural changes between the cCTRL and the dCTRL groups.
Repeated measures ANOVA for stroke volume index (A), cardiac index (B), heart rate (C), pulse pressure, (D) difference between groups (cCTRL vs. dCTRL) before and after assuming the sitting position. Filled circles and triangles indicate the cCTRL and the dCTRL, groups respectively. *P < 0.05, **P < 0.01. ANOVA, analysis of variance; cCTRL, the group with a contracted IVC in the CTRL group; CTRL, control; dCTRL, the group with a dilated IVC in the CTRL group.

Table 3. Intra-observer and inter-observer variability.

	Intra-observer			Inter-observer		
Variable	ICC	95% CL	Bias ± LOA	ICC	95% CL	Bias ± LOA
Change rate of max IVC	0.974	0.938 ~ 0.989	0.90 ± 10.12	0.945	0.871 ~ 0.977	−1.67 ± 15.32
Stroke volume	0.989	0.972 ~ 0.995	0.42 ± 4.2	0.974	0.909 ~ 0.991	1.65 ± 5.16

CL, confidence limits; ICC, Intraclass correlation coefficient; IVC, inferior vena cava; LOA, limits of agreement.

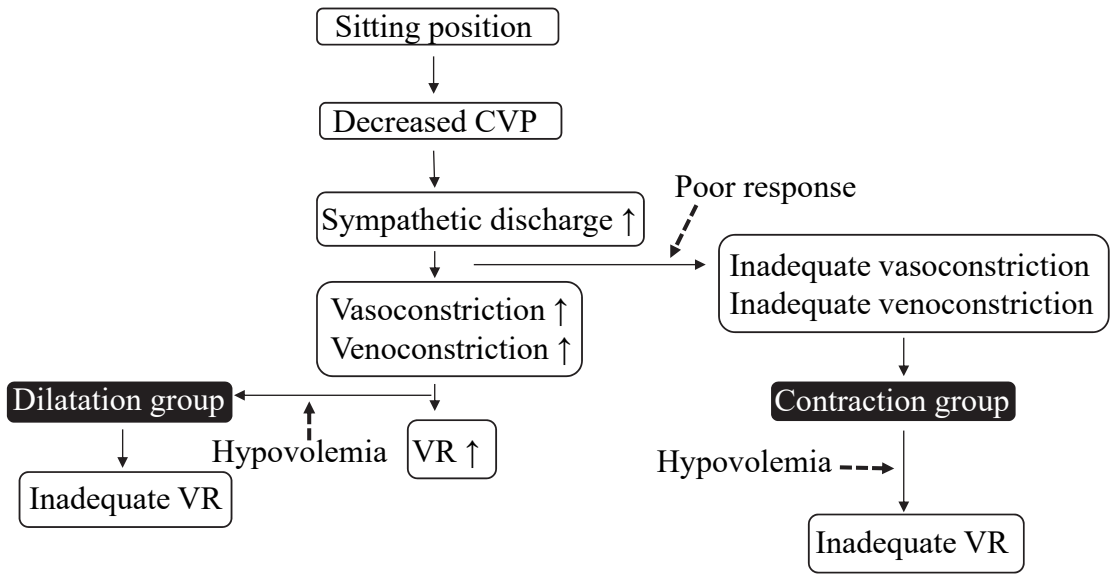


Fig. 7. Physiological causes of contraction and dilatation patients with POTS.
Both the contraction and dilatation groups have hypovolemia compared to the CTRL group. A poor vascular response to sympathetic discharges coexists in the contraction group. The dotted arrows show the factors that lead to various pathological reactions.
CTRL, control; CVP, central venous pressure; VR, venous return.

observed in response to postural change in this study. According to previous reports, the dilatation group would be considered to correspond to POTS owing to a marked increase in heart rate on head-up tilt table testing (Fujii et al. 2011); however, contraction of the IVC was also noted in response to postural change in our study.

The CTRL group was also amenable to the classification into two groups, similar to POTS. The heart rate in dCTRL was higher than that of the cCTRL group. These findings suggest differences in adrenergic status between the cCTRL and dCTRL groups even in healthy subjects; they also indicate the existence of certain factors that increase sitting heart rate in the contraction group of POTS. Compared to the dilatation group, the pulse pressure in the contraction group was less narrow in the sitting position. In the contraction group, a poor peripheral venous tone might force to drive heart rate to maintain the venous return.

It is well known that the pathophysiology of POTS is not homogeneous (Bryarly et al. 2019). It has been proposed that peripheral sympathetic denervation (neuropathic), a norepinephrine transporter deficiency (hyperadrenergic), low plasma volumes, excessive mast cell activation, or autoimmune disorder (a disorder of autoantibodies to adrenergic receptors or ganglionic acetylcholine receptor) can induce POTS. Indeed, these conditions are sometimes overlapped. Furthermore, POTS shows various symptoms, such as visceral pain and dysmotility, which could not be simply explained (Benarroch 2012; Garland et al. 2015; Arnold et al. 2018; Zadourian et al. 2018).

In this study, a part of these POTS subtypes, i.e., peripheral sympathetic reaction and plasma volumes, were evaluated using the measurement of IVC diameter with postural change. Stewart et al. (2002, 2004, 2009) proposed that the classification of POTS may be based on the quantification of blood volume in the lower limbs (low flow, normal flow, and high flow POTS). In other classifications, the categories include hyperadrenergic POTS with increased peripheral vasoconstriction and neuropathic POTS with decreased peripheral vasoconstriction (increased venous pooling) (Stewart 2012; Bryarly et al. 2019). Beta adrenoreceptor blockers and alpha adrenoreceptor agonists are considered effective in hyperadrenergic and neuropathic POTS, respectively. Some of the subjects in the contraction group in our study might be alleviated by the histamine receptor antagonists if they have orthostatic symptoms with the recurrent allergic symptoms, because the excessive acti-

vation in mast cells would lead to increase in sympathetic activity by releasing histamines and vasodilators (Kohn and Chang 2020). We were unable to classify each group into these categories in our study. Further investigations are also needed to evaluate whether the two types of IVC reactions could help identify patients who require alpha adrenoreceptor agonists. Moreover, the observation with loading conditions after water drinking, salt supplementation, and exercising would be well worth consideration in the same manner of this study, as these are highly recommended as the non-pharmacological treatment for POTS (Bryarly et al. 2019).

This study has certain limitations. First, the hemodynamic responses to postural change were assessed in the sitting rather than the standing position. This was performed as participants found it easier to cooperate and the echocardiographic views were immediately available, as positional change requires little time. All patients completed the examination sequence, including children with a predisposition to orthostatic intolerance. However, certain differences in physiological changes between the sitting and standing positions require discussion. The pathophysiology of the sitting position has been discussed in the field of anesthesia (Marshall et al. 1983; Buhre et al. 2000). In these reports, before the induction of anesthesia in the sitting position, the heart rate increased by 12%, total peripheral resistance increased by 12%, and stroke volume decreased by 11% (Marshall et al. 1983), when measured using an indicator dye dilution technique; however, 14% of the blood volume shifted from the intra- to extra-thoracic space after change from the supine to the sitting position (Buhre et al. 2000). It is known that during change from the supine to the standing position, the heart rate and total peripheral resistance both increase by 30%, and the stroke volume decreases by 40% (Schmidt and Thews 1983). Therefore, such remarkable changes were not likely to be observed in this study. In addition, any impact of physical abdominal compression on IVC in the sitting compared to the standing position was beyond the scope of our study. Second, there were inevitable factors of sampling bias which might have been introduced in our study. We diagnosed with POTS based on the result of the head-up tilt table testing, however, it has been pointed out that there are overlap of heart rate increment between healthy subjects and POTS, or vasovagal syncope and POTS (Singer et al. 2012; Medow et al. 2017). Further, the result of head-up tilt table testing could not necessarily reflect the active standing on clinical situation, as reported that 15% to 40% of normal subjects developed syncope during head-up tilt table testing (de Jong-de Vos van Steenwijk et al. 1995; Petersen et al. 2000). Moreover, as the late cardiac complications of Kawasaki disease have been noted in the previous studies (Kato et al. 1996; Ozawa et al. 2013; Brogan et al. 2020), the CTRL who had a history of Kawasaki disease could not be concluded that they had no potential inflammation in this stage. Finally, other data including peripheral adrenergic tone (e.g., plasma norepinephrine levels and muscle sympathetic nerve activity), which would support our hypothesis were lacking. No previous reports have focused on the IVC diameter with respect to postural changes as a parameter of venous tone in POTS; however, further studies using other quantitative modalities would be needed to substantiate the differences in peripheral sympathetic nerve function between the two groups, prior to clinical application of this method. Although the maximum IVC diameter was selected as the parameter of deriving the pressure, the pair of maximum IVC diameter and collapsibility index has been recommended as to define central venous pressure, because there are some causes for IVC enlargement in the presence of normal central venous pressure (Beigel et al. 2013). Hence, it would be more preferable to measure the minimum IVC diameter, right atrial volume, right ventricular volume, or left ventricular volume in addition to the maximum IVC diameter to evaluate the precise venous return in the future study.

In conclusion, echocardiographic assessment detected decreased stroke volume and venous return in POTS. The changes in max IVC in response to postural changes may indicate an underlying pathophysiology in POTS. Further studies on larger cohorts are needed to validate our findings.

Acknowledgments

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Conflict of Interest

The authors declare no conflict of interest. Outside the submitted work, Ichiro Morioka has received lecture fees from MSD Co., Ltd. and AbbVie LLC; and study grants from Atom Medical Corp.

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