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Myocardial Performance Index in Subjects Susceptible to High-Altitude Pulmonary Edema

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Abstract

Objective A recent study concerning high-altitude pulmonary edema (HAPE), a non-cardiogenic pulmonary edema, suggested that it is initially a hydrostatic-type pulmonary edema. We suspect that some extent of cardiac insufficiency may likely relate to the mechanism of the development of this disease.

Methods By Doppler echocardiography, the Tei index (a new quantitative index proposed for the evaluation of global myocardial performance) and the systolic pulmonary artery pressure (sPAP) were measured before and after 30 minutes of hypoxic breathing.

Patients Eleven HAPE-susceptible subjects (HAPE-s) and nine HAPE-resistant subjects (HAPE-r).

Results The results of Tei index indicated an enhanced left myocardial performance but an impaired right performance in HAPE-s during hypoxic breathing. The sPAP of HAPE-s was significantly increased after hypoxic breathing, which was not correlated with the heart functions such as right ventricular (RV) Tei index, cardiac index (CI), percent ejection fraction (EF%) and percent fractional shortening (FS%) under hypoxic condition. Comparatively, the HAPE-r subjects did not show such significant changes of Tei index after hypoxic breathing. The results suggested that a paradoxical myocardial performance, in a format of an augmented left ventricular (LV) in contrast to an attenuated RV, was observed in the HAPE-s exposed to acute hypoxia.

Conclusion The responses of the left and right myocardial performances to hypoxia may be involved in the pathogenesis of HAPE.

Key words: Doppler examination, hypoxia, myocardial performance, pulmonary hypertension, Tei index

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Introduction

High-altitude pulmonary edema (HAPE) is a rare life-threatening condition, which occurs in healthy persons after rapid exposure to altitudes in excess of 2,500 meters (m) above sea level. It is a non-cardiogenic pulmonary edema and characterized by a hypoxic pulmonary hypertension with a normal range of pulmonary artery wedge pressure (1). Meanwhile, it is recognized as a hydrostatic-type pulmonary edema in initial stage because the subjects with HAPE had high pulmonary artery pressures that lead to a protein-rich and mildly hemorrhagic edema, with normal levels of leukocytes, cytokines, and eicosanoids (2). Evidences proved that the HAPE is initially caused by an increase in capillary pressure (3) and the acute hypoxic pulmonary hypertension impacted on left ventricular (LV) diastolic function in healthy mountaineers at high altitude (4). Indeed, the cardiac performance is determined by the net result of preload, afterload and contractility and further influenced by many other factors including high-altitude environment (5). We hypothesize that the response of the myocardial performance to hypoxia may also be involved with the pathogenesis of HAPE.

The Tei index, a conceptual new myocardial performance index, has been widely used to quantitatively assess myocardial performance (6). It is more reflective of overall cardiac function than systolic or diastolic function alone, and applied to independently assess the myocardial performance of left and right ventricles (6, 7). In addition, the advantages of

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the index are less dependency on heart rate, afterload and independence of geometric changes of the ventricles (8). To investigate the role of myocardial performance in the pathophysiology of HAPE, the present study was designed and conducted to measure the Tei index by noninvasive Doppler echocardiography in subjects susceptible to HAPE before and after acute hypoxic stress, and to compare the results with those measured in subjects resistant to HAPE.

Materials and Methods

Study populations

We investigated 11 male Japanese HAPE-susceptible subjects (HAPE-s) whose susceptibilities to HAPE were known because they had previously developed at least one episode of HAPE while climbing an area of the Japan Alps which ranges from 2,758 to 3,190 m above sea level. They were admitted to our hospital and diagnosed clinically and radiographically with HAPE from July 1979 to January 2003 by the well known standard criterion (9). All of them promptly recovered with hospitalization. The cardiovascular examinations were conducted in-hospital after their recovery in order to exclude any preexisting cardiopulmonary diseases. They were all discharged from our hospital after complete recovery and returned to their locations elsewhere in Japan. We recruited them to come to our institute for the present study. The averages for age, body weight, height and body surface area (BSA) at the time of present study were 50.9 ± 13.2 (SD) years old (y), 62.1 ± 8.2 kilograms (kg), 166.3 ± 6.5 centimeters (cm), and 1.68 ± 0.13 square meters (m^2), respectively. They were all in physical good health condition at the time of the present study.

A group of HAPE-resistant controls (HAPE-r) was recruited, which consisted of 9 Japanese men matched with the HAPE-s group in terms of the averages for age (53.1 ± 13.4 y), body weight (65.3 ± 7.5 kg), height (165.0 ± 6.6 cm) and BSA (1.73 ± 0.13 m^2). Their resistance to HAPE was known because all of them were elite Japanese mountaineers and they repeated alpine-style climbing to peaks above 2,800 m without any symptoms of HAPE or other acute mountain illnesses. The medical histories and physical examinations performed during the recruitment excluded any preexisting cardiopulmonary disorders in HAPE-r controls.

This study was carried out in our institute at Matsumoto City, Japan, at an elevation of 610 m above sea level. All subjects were unrelated natives of Japan living at low altitudes less than Matsumoto City. None of the subjects received any medication during the two weeks before the experiment. The procedures of the study were in accordance with the recommendations found in Helsinki Declaration of 1975. The investigational protocols were approved by the Ethics Committee of Shinshu University School of Medicine for human studies and an appropriate written informed consent was obtained from each subject after a full explanation before the study.

Hypoxic exposure

The current hypoxic exposure was induced by breathing a hypoxic gas mixture containing oxygen (O_2), nitrogen (N_2) and carbon dioxide (CO_2) through a mouthpiece. The end-tidal O_2 pressure (P_{ETO2}) and CO_2 pressure (P_{ETCO2}) of the subjects were controlled at 60 mmHg and 40 mmHg, respectively, through a purpose-made computerized system (Duograph, Chest Inc., Tokyo, Japan) that can regulate each gas concentration. The arterial oxygen saturation (SpO_2) was monitored by a pulse oximeter via a finger probe to the subjects, which was designed around 80-75% over the time course of hypoxia, corresponding to an altitude about 4,000 m. The hypoxic exposure was terminated after 40-45 minutes of the hypoxic breathing. The subjects were in a comfortable seated position throughout the experiment.

Study sequence

The echocardiography and Doppler examinations were performed in subjects under room air at the elevation of 610 m above sea level (Normoxia). Subsequently, the hypoxic exposure was administered to the subjects by breathing the hypoxic gas mixture. After 30 minutes of the hypoxic breathing, the similar Doppler echocardiography was then repeated in the subjects while breathing the hypoxic gas (Hypoxia). As soon as the measurements were completed, the hypoxic breathing was terminated. A short observation was followed to the subjects after the experiment in case any unexpected acute hypoxic illnesses happened.

Echocardiography and Doppler examinations

Complete M-mode, two-dimensional, pulsed-wave, continuous-wave, and color flow examinations were carried out as described previously (10-12) by a commercial available ultrasound instrument (Sonos 5,500, Philips Ultrasand System, Andover, MA, USA) with a probe of 2.5 MHz. The measurements were performed online and recorded on paper at a speed of 100 mm/second as well as on videotape for later confirmation offline if necessary. Because the subjects were connected to the hypoxic breathing system via a mouthpiece, they had to be in a sitting position rather than the left decubitus position that is generally required for the measurements of echocardiograph. The echocardiography and Doppler examinations were performed by an experienced cardiologist (Dr. Kogashi) who was blind to the clinical data of each subject.

Assessment of cardiac systolic function

The heart rate (HR) was measured simultaneously. The parameters for calculating cardiac systolic function were measured in M-mode and two-dimensional echocardiography for which the left parasternal long-axis and the short-axis views at the mid-left ventricular level were obtained. The end-systolic volume (ESV) and end-diastolic volume (EDV) were obtained by Teichholz's formula (13). The stroke volume (SV) was calculated by subtracting the ESV

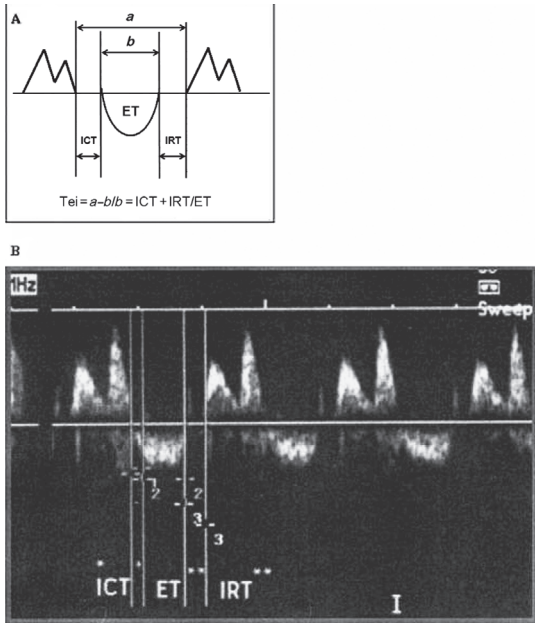

Figure 1. **A: The schema of measurements of each parameter for calculating the Tei index. *a* = isovolumetric contraction time (ICT) + ejection time (ET) + isovolumetric relaxation time (IRT); *b* = ET. Tei Index = (ICT+IRT)/ET = (*a*-*b*)/*b* (see the text in detail). B: The pulsed Doppler diagram showing the time intervals for calculating the left ventricular (LV) Tei index in mitral inflow and the LV outflow recordings.**

from EDV (SV = EDV-ESV). Then the cardiac output (CO) was the result of SV multiplying by HR (CO = SV × HR). The cardiac index (CI) was the CO adjusted by BSA. Lastly, the percent ejection fraction (EF%) was obtained through dividing SV by EDV (EF%=SV/ED ×100). The percent fractional shortening (FS%) was obtained by subtracting the left ventricular (LV) end-systolic dimension (LVESD) from the end-diastolic dimension (LVEDD) and then dividing by LVEDD [FS%=(LVEDD-LVESD)/LVEDD ×100] (13).

Assessment of left ventricular Tei index

In Doppler examinations, the mitral inflow velocity pattern was recorded from the apical long-axis view with pulsed wave Doppler sample volume positioned at the tip of the mitral leaflet during LV diastole. The LV outflow velocity pattern was recorded from the apical long-axis view with the pulsed wave Doppler sample volume positioned just below the aortic valve. Then the time intervals for calculating the LV Tei index were measured from the mitral inflow and the LV outflow recordings (8) (Fig. 1). Four consecutive beats were measured and averaged for each parameter. In the schema in Fig. 1, the time from the cessation to the onset of mitral inflow (*a*) represents the interval between the mitral valve closure and opening, which is equal to the sum of isovolumic contraction time (ICT), ejection time (ET) and isovolumic relaxation time (IRT). The ET (*b*) of the LV was measured in the LV outflow velocity pattern. Tei index is defined as the sum of the ICT and IRT and then divided by the ET, thus, the LV Tei index was determined in *(a-b)/b* (7).

Assessment of right ventricular Tei index

Similar to the assessment of LV Tei index, the right ventricular (RV) Tei index was determined in *(a-b)/b* in tricuspid inflow and RV outflow patterns. The tricuspid inflow pattern was recorded from the parasternal long-axis view with pulsed wave Doppler sample volume positioned at the tip of the tricuspid leaflet during RV diastole. And the RV outflow pattern was recorded from the parasternal short-axis view with the pulsed wave Doppler sample volume positioned just proximal to the pulmonary valve. The time from the cessation to the onset of tricuspid inflow (*a*) represents the interval between the tricuspid valve closure and opening. The ET (*b*) of the RV was measured by the RV outflow pattern (7).

Measurement of pulmonary artery pressure

The systolic pulmonary artery pressure (sPAP) was determined by the time from the onset to the peak velocity of RV ejection flow (acceleration time; AcT) in RV outflow pattern (14). The empiric regression of sPAP with the AcT is curvilinear, making the estimation of very high or very low sPAP. To overcome this problem, the AcT against the logarithm of the sPAP [$\log_{10}$ (sPAP)=*-0.0068 x* AcT+2.1 mmHg] was used to correct it to a liner correlation (14).

Statistical analysis

Continuous data are expressed as mean ± SD. The alterations of the measurements from normoxia to hypoxia were calculated and expressed in percentage format. The comparisons of the parameters between normoxia and hypoxia within the group were made by the paired Student's *t* test. And the comparisons of the measurements between HAPE-s and HAPE-r groups were made by the unpaired Student's *t* test. The correlation coefficients of the RV Tei index to the sPAP, CI, EF% and FS% for the HAPE-s under hypoxia was calculated (15). A probability value less than 0.05 was considered significant.

Results

Hypoxic status of the subjects

As shown in Table 1, the SpO_2 did not show significance between the HAPE-s and HAPE-r groups under room air at 610 m (98.4 ± 0.9% vs. 98.4 ± 1.0%, p >0.05). After 30 minutes of hypoxic breathing, the SpO_2 was significantly reduced to 79.6 ± 3.4% in the HAPE-s (p <0.0001 vs. normoxia) and to 80.8 ± 3.3% in the HAPE-r group (p <0.0001 vs. normoxia) at the time of echocardiograph. There was no significant difference of the SpO_2 between the two groups under hypoxic status (p >0.05).

Table 1. Parameters Regarding the sPAP, SpO_2 and Cardiac Systolic Function in HAPE-s and HAPE-r

Parameters	HAPE-s			p value*	HAPE-r			p value*
	Normoxia	Hypoxia	Alteration in percentage (%)		Normoxia	Hypoxia	Alteration in percentage (%)	
SpO_2	98.4±0.9	79.6±3.4	-23.9±5.8	<0.0001	98.4±1.0	80.8±3.3	-21.9±5.7	<0.0001
HR (beats/min)	60.0±9.6	75.4±11.5	26.4±12.9	<0.0001	65.0±8.0	76.0±6.3	18.2±14.9	0.002
EDV (mL)	102.6±30.7†	101.5±23.9	9.1±37.6	0.92	71.3±29.7	88.8±37.9	13.4±35.4	0.30
ESV (mL)	38.5±15.7	33.9±7.8	-7.7±73.7	0.46	36.6±14.2	31.6±21.6	-9.4±42.9	0.58
SV (mL)	64.1±17.8†	68.8±17.8	12.5±32.5	0.28	43.3±6.9	57.3±18.2	32.2±32.5	0.04
CI ($L/min/m^2$)	2.2±0.5†	2.8±0.5	33.8±37.9	0.06	1.6±0.3	2.4±0.9	47.8±48.2	0.03
EF (%)	64.1±9.5	67.2±3.2	4.4±15.8	0.6	59.2±11.1	67.6±10.3	20.1±17.4	0.01
FS (%)	35.2±7.1	37.3±2.6	6.9±23.7	0.7	31.6±7.8	37.8±7.6	28.9±24.9	0.01
sPAP(mmHg)	24.2±8.9	33.5±11.5	43.4±33.4	<0.0001	27.5±9.8	30.9±5.9	32.5±71.9	0.4

Data are expressed as mean ± SD. p value*: compared between normoxia and hypoxia; †: $p < 0.05$ compared with the HAPE-r.
CI indicates cardiac index; EDV, end-diastolic volume; EF, ejection fraction; ESV, end-systolic volume; FS, fraction of shortening; HAPE-r, high-altitude pulmonary edema-resistant subjects; HAPE-s, HAPE-susceptible subjects; HR, heart rate; sPAP, systolic pulmonary artery pressure; SpO_2, oxygen saturation; SV, stroke volume.

Table 2. The LV and RV Tei Indexes in HAPE-s and HAPE-r

Parameters	HAPE-s		p value*	HAPE-r		p value*
	Normoxia	Hypoxia		Normoxia	Hypoxia	
LV Tei index						
ICT+IRT (msec)	180.8±79.8	164.1±72.8	0.03	137.8±29.8	142.7±24.1	0.60
ET (msec)	257.8±27.7	263.9±28.1$^{(p=0.04)}$	0.04	246.1±27.4	235.5±24.6	0.34
Tei index	0.61±0.10	0.54±0.07	0.02	0.57±0.18	0.61±0.14	0.54
RV Tei index						
ICT+IRT (msec)	96.4±36.3	124.2±39.0$^{(p=0.01)}$	0.001	84.2±37.5	80.6±28.7	0.75
ET (msec)	284.0±31.6$^{(p=0.05)}$	273.4±43.5	0.16	256.9±25.3	260.3±31.1	0.73
Tei index	0.34±0.13	0.47±0.18$^{(p=0.05)}$	0.008	0.34±0.18	0.32±0.15	0.76

Data are expressed as mean ± SD. The numbers in the superior brackets indicate the significant p values compared with that of the HAPE-r group under corresponding environmental conditions. p value*: compared between normoxia and hypoxia.
ET indicates ejection time; HAPE-r, high-altitude pulmonary edema-resistant subjects; HAPE-s, HAPE-susceptible subjects; ICT, isovolumic contraction time; IRT, isovolumic relaxation time; LV, left ventricle; RV, right ventricle.

Cardiac systolic function

Regarding the cardiac systolic function, as expected, the HR increased significantly under hypoxic stress compared to that in normoxia in both groups. There were no significant alterations after hypoxic stress in terms of EDV, ESV and SV, resulting in no significant enhancements of CI, EF and FS under hypoxic condition in the HAPE-s group (Table 1). However, the SV was significantly increased during hypoxic breathing compared to that under normoxia in the HAPE-r group (p=0.04), in spite of no significant differences of the EDV and ESV between normoxia and hypoxia. As a result, the CI, EF and SF were significantly enhanced by the hypoxic stress in the HAPE-r group (Table 1). Moreover, although the EDV, SV, and CI were significantly larger in HAPE-s than in HAPE-r under normoxia (p=0.03, 0.004 and 0.04, respectively), the magnitudes of alterations of the EDV, ESV, SV, CI, EF, and FS from nomoxia to hypoxia were all stronger in HAPE-r than in HAPE-s (Table 1). These comparisons and analyses indicated that the potential enhancement of cardiac function by hypoxic stress was significantly stronger in HAPE-r group than in HAPE-s group.

LV and RV Tei indexes

Table 2 shows the detailed information about the LV and RV Tei indexes in both groups. In the HAPE-s group under hypoxic condition, the RV Tei index significantly increased (p=0.008) due to a significant prolongation of the sum of ICT and IRT (p=0.001), while the LV Tei index significantly decreased (p=0.02) due to a significant shortening of the sum of ICT and IRT (p=0.03) and a significant prolongation of ET (p=0.04) compared to those in normoxia. In contrast, both the LV and RV Tei indexes did not change significantly after hypoxic breathing compared to those in normoxia in the HAPE-r group (p=0.54, 0.76, respectively), indicating the potential resistant power to hypoxia in both LV and RV of the HAPE-r subjects. In addition, the RV Tei index was significantly higher in HAPE-s than HAPE-r under hypoxic condition, indicating an absolute impairment of RV performance in HAPE-s under hypoxic condition.

Pulmonary artery pressure

As expected, the sPAP was significantly increased in the HAPE-s under hypoxic condition compared to that under normoxic condition (Table 1, p <0.001). However, HAPE-r group did not show such a significant hypoxic increase in sPAP (Table 1, p=0.4). Moreover, the increase magnitude of sPAP was larger in the HAPE-s (43.4 ± 33.4%) than the HAPE-r (32.5 ± 71.9%). The hypoxic increased sPAP of the HAPE-s did not show significant correlations with RV Tei index and other heart function measurements, such as CI, EF and FS in the HAPE-s group under hypoxia (Fig. 2).

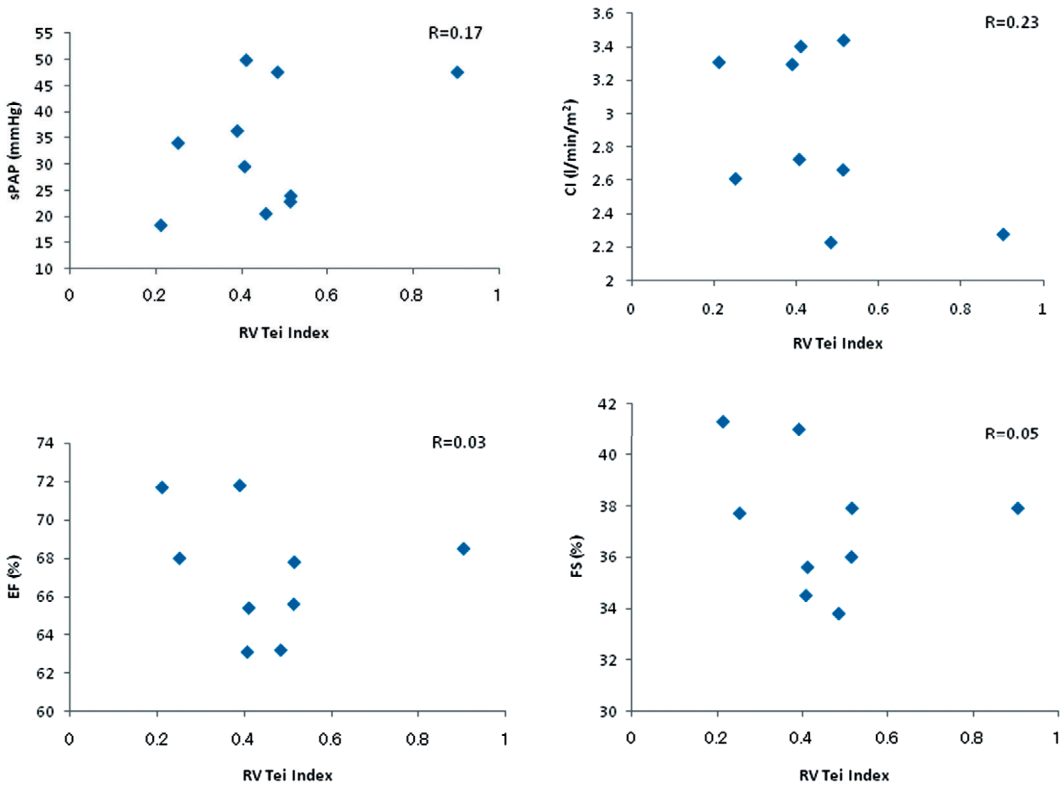

Figure 2. **The correlations of the right ventricular (RV) Tei index to the systolic pulmonary artery pressure (sPAP), cardiac index (CI), percent ejection fraction (EF%) and percent fractional shortening (FS%) in high-altitude pulmonary edema-susceptible subjects (HAPE-s) under hypoxic condition. The increased sPAP induced by hypoxia in the HAPE-s did not show significant correlations with RV Tei index and other heart function measurements, such as CI, EF% and FS% in the HAPE-s group under hypoxia.**

Discussion

The findings of the current noninvasive echocardiographic-Doppler investigation in the HAPE-s under acute hypoxic stress are that the cardiac systolic function was not enhanced significantly and that the RV performance was impaired while the LV performance was enhanced, resulting in paradoxical performances in the LV and RV. We propose that when HAPE-s challenge acute hypoxia, the unbalanced myocardial performance may abnormally interfere with the pulmonary circulation and play a secondary role in the development of HAPE.

Although HAPE is a non-cardiogenic pulmonary edema, hypoxia at high altitude can directly impact cardiac function because the heart critically depends on oxygen availability itself. The electrocardiograph (ECG) of HAPE patients showed sinus tachycardia, slight peaked P wave, tall R wave in $_aV_R$, right-axis deviation and clockwise rotation with positive displacement of the S-T segment and T-wave inversion in leads V_1-V_5, suggesting RV overload and enlargement (16). Allemann et al. demonstrated that in healthy mountaineers, the high-altitude-induced pulmonary hypertension was quantitatively related to RV pressure overload, which led to LV diastolic dysfunction. They proposed that the LV diastolic dysfunction would be more marked in HAPE-s and could, in turn, contribute to the pathogenesis of pulmonary edema (4). Coincidently, we found that the cardiac systolic function of the HAPE-s did not respond to the acute hypoxia, for example, their SV, CI, EF and FS did not show any significant enhancements compared with those under hypoxic stress in contrast to those observed in HAPE-r. Although the EDV was significantly larger in HAPE-s than in HAPE-r under normoxic condition, the magnitude of the increase of the EDV from normoxia to hypoxia was larger in the HAPE-r group than in the HAPE-s group. This seems to be the major reason to lead to significant increases of the SV and CI in the HAPE-r group from normoxic to hypoxic conditions. We believe it is an acclimatization response of the cardiovascular system to the acute hypoxia by "functional sympatholysis" in which the HR and CI increases (17).

The recently proposed myocardial performance index (Tei index) has been proved to be a sensitive indicator of the LV and RV performances independently in various myocardial diseases (6) and in primary pulmonary hypertension (7). The ICT and IRT are important considerations in the assessment of systolic and diastolic myocardial performances, because calcium influx and efflux secondary to ATP utilization occur during these periods (8). The Tei index increases with ven-

tricular dysfunction due to prolongation of ICT and IRT and shortening of ET. The present data revealed that the LV Tei index of the HAPE-s was significantly reduced after hypoxic breathing, suggesting an enhancement in LV performance by hypoxic stress. This result is in accordance with other reports elsewhere. The Operation Everest I-III projects (18-20) and human hypoxic studies (21, 22) showed that the left heart tolerates hypoxia. In healthy volunteers during stimulated ascent to Mt. Everest the ECG showed no significant changes in arrhythmias or conduction defects and no ST depression or T-wave inversion (23). In the meantime, the echocardiography also revealed an enhancement of the LV cardiac systolic function in healthy volunteers under high-altitude hypoxia (18-22). It is thought that the acute hypoxia stimulates the sympathetic nervous system contributing to the enhancement in LV contractility (24). The putative advantage of the enhancement of cardiac systolic function at high altitude, especially at extreme high altitude, will output the maximum amount of blood for transferring sufficient oxygen to support metabolic demands of the body challenging the hypoxic stress. Unfortunately, the present data did not show the enhancements of SV, CI, EF, and FS in the HAPE-s group by hypoxic stress due to the large EDV under normoxic condition, and subsequently, there was a slight increase in EDV by hypoxic stress.

The Tei index is superior to any other current noninvasive measurements for the assessment of RV function which is difficult and challenging owing to its anatomical characteristics as compared with the measurements of LV function (7, 8). The RV Tei index is clinically useful and reliable to assess the RV impairment before the development of RV insufficiency (25, 26) and it is not influenced by changes in HR, right ventricular pressure, right ventricular dilation, or tricuspid regurgitation (7). In contrast to the LV function exposed to high altitudes, little is known about the RV function under hypoxic stress. The RV is sensitive and vulnerable to hypoxia. The typical examples are the subacute mountain sickness in immigrated susceptible infants (27) and the high-altitude heart disease in immigrated susceptible adults at high land (28). Both the syndromes are characterized by right heart failure in clinical manifestations and marked right ventricular hypertrophy as a pathological feature. The present results revealed that the RV Tei index was significantly increased in HAPE-s exposed to acute hypoxia, indicating an impaired RV performance. This impairment is caused by hypoxic impact but it is less likely secondary to the increased sPAP and other heart systolic functions, such as CI, EF, and FS because the hypoxia-induced increase of RV Tei index was the result of the prolongation of ICT and IRT by hypoxic stress and it was not correlated with the sPAP, CI, EF, and FS in the HAPE-s group under hypoxic condition.

The big obstacle in the present measurements by echocardiography and Doppler is that the subject had to be in a sitting position because of the connection with the hypoxic breathing system (Duograph, Chest Inc., Tokyo, Japan) by mouthpiece, which reduced preload, lengthened the isovolume time, and shortened the ejection time, as a result, the Tei index increased (29). The partial preload dependence is a major limitation of the Tei index (30). Preload reduction in normal subjects by the Valsalva maneuver significantly increases Tei index primarily as a result of a decrease in ejection time (31). However, the Tei index value (0.54 ± 0.07) measured in the present study was relatively similar to the Tei index value (0.54 ± 0.14) measured by Voon et al. in seated normal subjects (29). As an original study of Tei index in the HAPE-s under hypoxic stress, we emphasize that the present values of Tei index measured in the seated subjects only functioned to serve as a comparison between groups for research purpose. Nevertheless, a relatively longer hypoxic period with confidential safety of subjects under hypoxic exposure may be necessary to apply to a future study to confirm the results of the present study. Lastly, although we adjusted the regression of sPAP with the AcT by logarithm to a liner correlation, the accuracy of a sPAP value measured by echocardiograph is still controversial (14).

In summary, a paradoxical myocardial performance with an augmented LV in contrast to an attenuated RV in the HAPE-s under hypoxic condition may induce a disturbance of the two cardiac pumps breaking the balance of the LV and RV outputs. The responses of the left and right myocardial performances to hypoxia may be involved in the pathogenesis of HAPE. Furthermore, measurement and evaluation of the alteration of RV Tei index by hypoxic stress might be one of the means to screen the subjects prone to HAPE before they attempt exposure to a high altitude.

The authors state that they have no Conflict of Interest (COI).

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