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Effect of Low-Grade Exercise on Echocardiographic Indexes in Healthy Young Adults

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Abstract **Background:** Low-grade exercise echocardiography is required in some clinical situation: however, echocardiographic data of low-grade exercise have not been available. To study the effect of low-grade exercise on echocardiographic parameters, we performed echocardiographic examination at rest and 5 minutes after 20 watts load exercise by supine bicycle ergometer. **Methods:** Subjects consisted of 24 young healthy volunteers (12 men and 12 women) aged 23±3 years old. Heart rate, systolic and diastolic blood pressure, systolic and diastolic echo indexes, estimated pulmonary artery pressure, and right heart function including global and free wall right ventricular strain are compared between at rest and during 5 minutes exercise. **Results:** Heart rate, systolic and diastolic blood pressure were significantly increased by low-grade exercise. Though stroke volume, left atrial volume index, and right ventricular end-diastolic diameter were not changed, left ventricular ejection fraction, cardiac output, and cardiac index increased significantly. Also, estimated peak systolic and mean pulmonary arterial pressure increased significantly. However, all the indexes were within the reported normal reference ranges. **Conclusions:** Although the strength of exercise is limited low for healthy young subjects, the low-grade exercise echocardiography may be a useful tool for patients with limited exercise tolerance, such as latent pulmonary hypertension in patients with collagen disease. Short duration, limited load, and easy enforcement exercise is convenient not only to patients, but also to echo-laboratory staffs. The results of this study would be useful as reference values for responses of patients with latent cardiovascular dysfunction.

Key words: bicycle ergometer, cardiac function, stress echocardiography, exercise

Introduction

Exercise echocardiography is a useful tool for diagnose or decision making of myocardial ischemia, valvular dysfunction, or latent pulmonary hypertension.[1-4] However, we sometime feel difficulty to perform exercise echocardiography on some patients because of their fragility or setting-up of echo-laboratory by means of staffs, limited room and equipment. We recently consider convenient and useful exercise echocardiography in echo-laboratory. Namely, we introduced low-grade exercise as 5 minutes of 20 watts supine bicycle ergometer for patients. However, before we apply this exercise protocol on patients, we need to obtain the cardiovascular responses in healthy normal. Therefore, we observed changes of heart rate (HR), systolic and diastolic blood pressure (SBP and DBP) as well as usual echocardiographic parameters including estimated mean pulmonary arterial pressure (e-mPAP) and right ventricular function.

Methods

Subjects. Subjects were 24 healthy volunteers who ascertained the objects of the study and they give us written informed consent between 2016 May and 2016 December. Exclusion criteria were who have any of the following conditions: organic heart disease, pulmonary disease, unable to pedaling bicycles, resting left ventricular (LV) ejection fraction (LVEF) <50%, or resting e-mPAP ≥25 mmHg.

Echocardiography. Echocardiography was performed with a commercially available echo machine (Vivid 7, GE Medical Systems, Milwaukee, WI, USA) equipped with a M3S (1.8-3.4MHz) probe. Firstly, echocardiography was performed at rest, and exclusion criteria were checked. All echocardiographic data were stored on the echo machine for later analysis by a dedicated software (EchoPAC, GE Medical Systems, Princeton, NJ, USA).

Exercise. After echocardiography at rest, low-grade exercise was performed with a supine exercise ergometer (Echo Stress Table 750EC, LOAD, Groningen, Netherland) at 20 watts for 5 minutes. Exercise echocardiography was done with attendance of a medical doctor, and electrocardiography, blood pressure, and SpO_2 were monitored during exercise.

Data analysis. The following parameters were obtained at rest and during exercise: HR, SBP, DBP, end-diastolic LV internal diameter (LVDd), end-systolic LV internal diameter (LVDs), LVEF, stroke volume (SV), cardiac index (CI), left atrial (LA) volume index (LAVI), E and A waves of transmitral flow (TMF-E and TMF-A), early diastolic mitral annular velocity (e'), right ventricular (RV)-right atrial (RA) pressure gradient (RV-RA PG), estimated systolic pulmonary pressure (e-SPSP), e-mPAP, end-diastolic RV diameter (RVDd), end-systolic RA area (RA area), tricuspid annular plane systolic excursion (TAPSE), RV fractional area change (RV FAC), systolic tricuspid annular velocity (TA-s'), RV global longitudinal strain (RV GLS), and RV free wall strain (FW strain).

SV was calculated as SV = CSA x VTI = (LVOTd/2)2 × 3.14 x VTI , where LVOTd was the diameter of LV outflow tract (LVOT), and VTI was the velocity-time integral of LVOT Doppler flow signal. CI was derived from CO divided by body surface area (BSA). LAVI was derived as LA volume/BSA.

RV-RA PG was obtained by simplified Bernoulli equation as shown in Figure 1. SPAP was obtained as sum of RV-RA PG and right atrial (RA) pressure. RA pressure was assumed as constant at 5 mmHg throughout

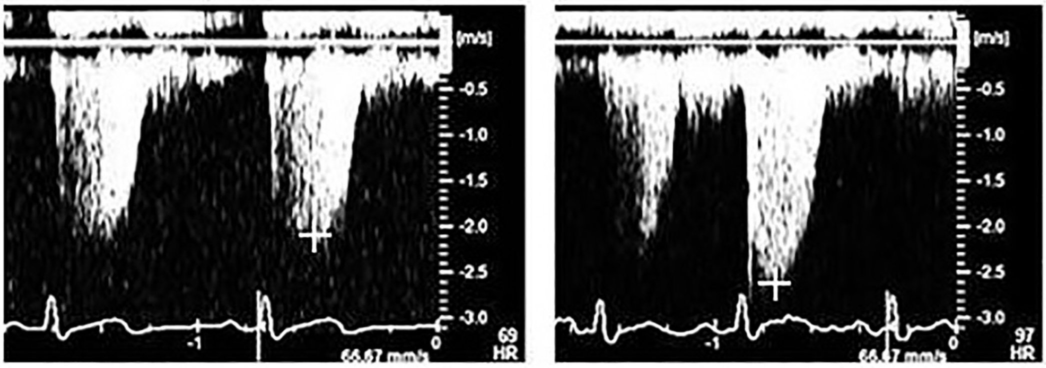

Fig. 1 RV-RA PG at rest and during low-grade exercise.

Maximum tricuspid regurgitation (TR) velocity is measured at the peak (+) of TR tracing. By the simplified Bernoulli equation, RV-RA PG at rest is 18 mmHg (left panel) and that of during low grade exercise (right panel) is 28 mmHg.

the study because the subjects are all healthy normal. Then, e-mPAP was calculated with a formula "mPAP = 0.61 × SPAP + 2" appeared in a reference.[5] Pulmonary hypertension was defined as mPAP>25 mmHg at rest[6] or mPAP>30 mmHg during exercise.[7] RV FAC was calculated as (end-diastolic RV area − end-systolic RV area)/(end-diastolic RV area). RV strain was obtained as RV GLS (mean strain including both of RV free wall and septum) and FW strain (RV free wall only). In both of the strain indexes, RV apex and tricuspid annulus were excluded from calculation because of signal instability.

Statistics. Continuous data were described as mean±SD. Indexes at rest and during exercise were compared with Wilcoxon analysis. The p value <0.05 was assumed as statistical significance.

Ethical issue. This study was approved by Ethical Review Board of Yamaguchi University Graduate School of Medicine, Faculty of Health Sciences (# 373).

Results

The characteristics of subjects are shown in Table 1. Hemodynamics and echocardiographic variables are shown in Table 2, and graphs of these variables are shown in Figure 2a-2d for readers' convenience.

HR, SBP, and DBP were increased significantly by low-grade exercise (HR of 68±12 vs 91±14 beats/min, p<0.01, SBP of 111±12 vs 128±14 mmHg, p<0.01, and DBP of 61±12 vs 66±13 mmHg, p<0.05).

According to the echocardiographic indexes, LVDd, and LVDs were significantly decreased during low-grade exercise, LVEF and CI were significantly increased during exercise (LVDd of 47±4 vs 46±4 mm, p<0.01, LVDs of 31±3 vs 28±4 mm, p<0.01, LVEF of 63±4% vs 69±4%, p<0.01, and CI of 2.7±0.5 vs 3.8±0.7 L/min/m^2, p<0.01). However, SV did not change significantly.

As the diastolic indexes, TMF-E, TMF-A, and e' were significantly increased, however, E/A and E-DcT were significantly decreased (TMF-E of 83±20 vs 98±19 cm/s, p<0.01, TMF-A of 38±9 vs 54±16 cm/s, p<0.01, e' of 13.1±1.7 vs 15.4±2.1cm/s, p<0.01, E/A of 2.4±1.0 vs 1.9±0.5, p<0.05, and E-DcT of 195±21 vs 179±23 ms, p<0.01). LAVI did not change statistically.

Finally, e-mPAP, TAPSE, TA-s', RV FAC, RV GLS, and FW Strain were significantly increased during exercise, on the other hand, RA area were significantly decreased during exercise (mPAP of 15.5±1.3 vs 18.2±2.2 mmHg, p<0.01, TAPSE of 22±2 vs 23±2 mm, p<0.01, TA-s' of 12.5±1.4 vs 14.4±2.1 cm/s, p<0.01, RV FAC of 46±3% vs 53±5%, p<0.01, RV GLS of 24.4±2.4% vs 28.0±3.4%, p<0.01, FW Strain of 29.8±3.2% vs 34.2±4.2%, p<0.01, and RA area of 13±3 vs 12±2 cm2, p<0.01). RVDd did is not change statistically.

Discussion

We studied the effect of the low-grade exercise on echocardiographic indexes including systolic, diastolic, right ventricular function, and pulmonary artery pressure. Because exercise echocardiography was originally applied to diagnose ischemic heart disease like angina pectoris, a treadmill or a bicycle ergometer with a multistage symptom-limited protocol was popular. With such an exercise protocol, echocardiographic indexes at rest and peak exercise stage were well studied, however, the effects of low-grade exercise

Table 1 Characteristics of Subjects

Normal subject characteristics(n=24)	
age (yrs)	23 ± 3
male	12
BSA (m2)	1.6 ± 0.2
Baseline hemodynamics	
HR (beats/min)	68 ± 12
SBP (mmHg)	111 ± 12
DBP (mmHg)	61 ± 12
Exercise hemodynamics	
HR (beats/min)	91 ± 14
SBP (mmHg)	128 ± 14
DBP (mmHg)	66 ± 13
Values are mean ± SD or n	

BSA body surface area, *HR* heart rate, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *SD* standard deviation

Table 2 Hemodynamic and echocardiographic data

Normal subjects			
	Baseline	Exercise	P value*
Hemodynamics			
HR (beats / min)	68 ± 12	91 ± 14	<0.01
SBP (mmHg)	111 ± 12	128 ± 14	<0.01
DBP (mmHg)	61 ± 12	66 ± 13	<0.05
LV systolic function			
LVDd (mm)	47 ± 4	46 ± 4	<0.01
LVDs (mm)	31 ± 3	28 ± 4	<0.01
LVEF (%)	63 ± 4	69 ± 4	<0.01
SV(ml)	66 ± 11	68 ± 14	NS
CI (L / min / m^2)	2.7 ± 0.5	3.8 ± 0.7	<0.01
LV diastolic function			
LAVI (ml / m^2)	22.0 ± 5.6	21.1 ± 5.3	NS
TMF - E (cm / s)	83 ± 20	98 ± 19	<0.01
TMF - A (cm / s)	38 ± 9	54 ± 16	<0.01
E/A	2.4 ± 1.0	1.9 ± 0.5	<0.05
E - DcT (ms)	195 ± 21	179 ± 23	<0.01
e' (cm / s)	13.1 ± 1.7	15.4 ± 2.1	<0.01
PH and RV function			
e-mPAP (mmHg)	15.5 ± 1.3	18.2 ± 2.2	<0.01
RVDd (mm)	33 ± 4	32 ± 4	NS
RA area (cm^2)	13 ± 3	12 ± 2	<0.01
TAPSE (mm)	22 ± 2	23 ± 2	<0.01
TA - s' (cm / s)	12.5 ± 1.4	14.4 ± 2.1	<0.01
RV FAC (%)	46 ± 3	53 ± 5	<0.01
RV GLS (%)**	24.4 ± 2.4	28.0 ± 3.4	<0.01
FW Strain (%)**	29.8 ± 3.2	34.2 ± 4.2	<0.01

Values are mean ± SD.
* Statistical significance was set at p value < 0.05
** Displayed as absolute value.

HR heart rate, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *LV* left ventricle, *LVDd* end-diastolic LV internal diameter, *LVDs* end-systolic LV internal diameter, *LVEF* LV ejection fraction, *SV* stroke volume, *CI* cardiac index, *LAVI* left atrial volume index, *TMF-E* early diastolic flow velocity of transmitral flow, *TMF-A* late diastolic flow velocity of transmitral flow, *E/A* ratio TMF-E/TMF-A, *E-DcT* deceleration time of TMF-E, *e'* early diastolic mitral annular velocity, *PH* pulmonary hypertension, *RV* right ventricle, *e-mPAP* estimated mean pulmonary arterial pressure, *RVDd* end-diastolic RV diameter, *RA* area right atrial area, *TAPSE* tricuspid annular plane systolic excursion, *TA-s'* systolic tricuspid annular velocity, *RV-FAC* RV fractional area change, *RV-GLS* RV global longitudinal strain, *FW* strain RV free wall strain, *SD* standard deviation

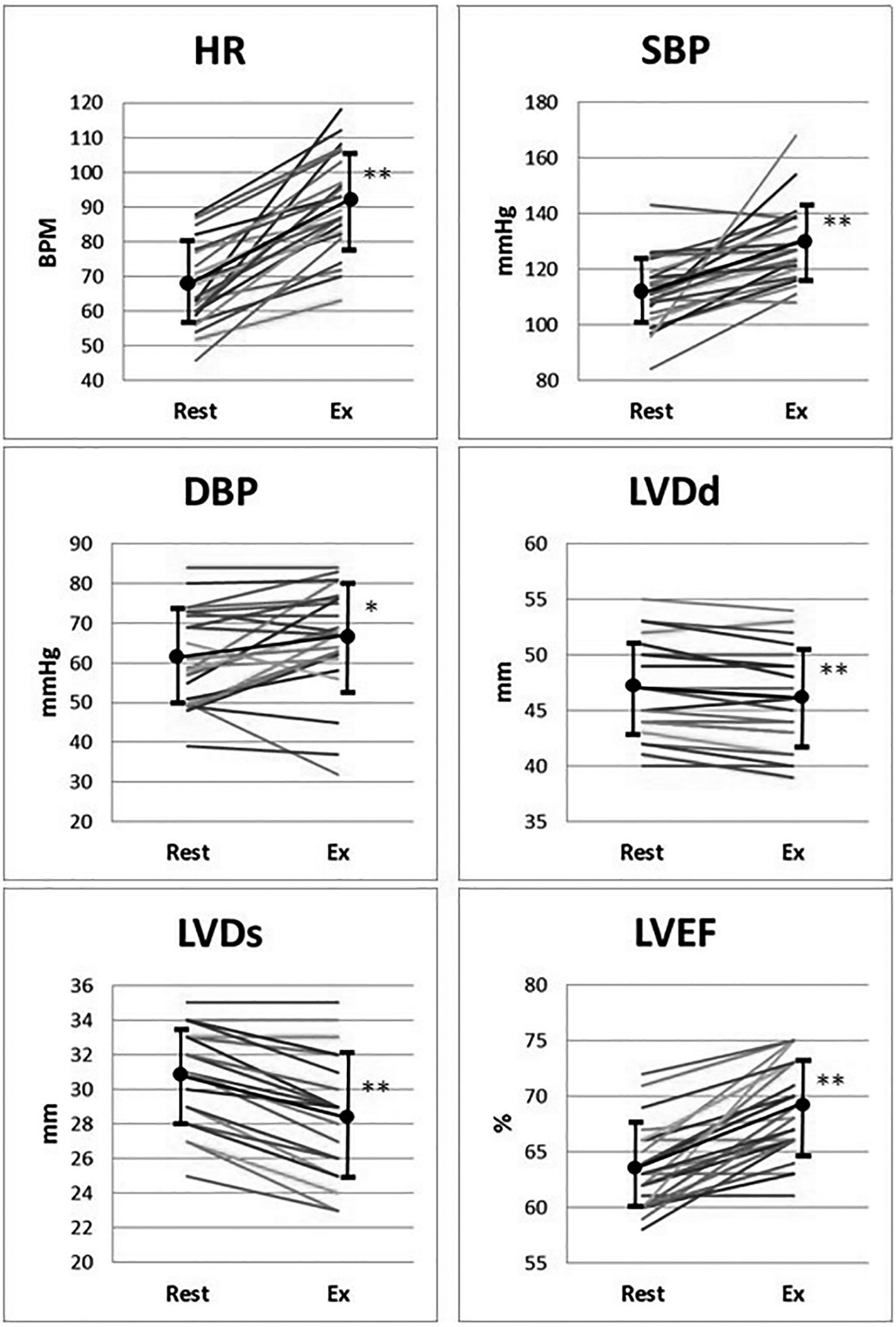

Fig. 2a Changes of indexes by low-grade exercise.
*, $P < 0.05$; **, $P < 0.01$. *Rest* at Rest, *Ex* low-grade exercise, *HR* heart rate, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *LVDd* end-diastolic LV internal diameter, *LVDs* end-systolic LV internal diameter, *LVEF* LV ejection fraction

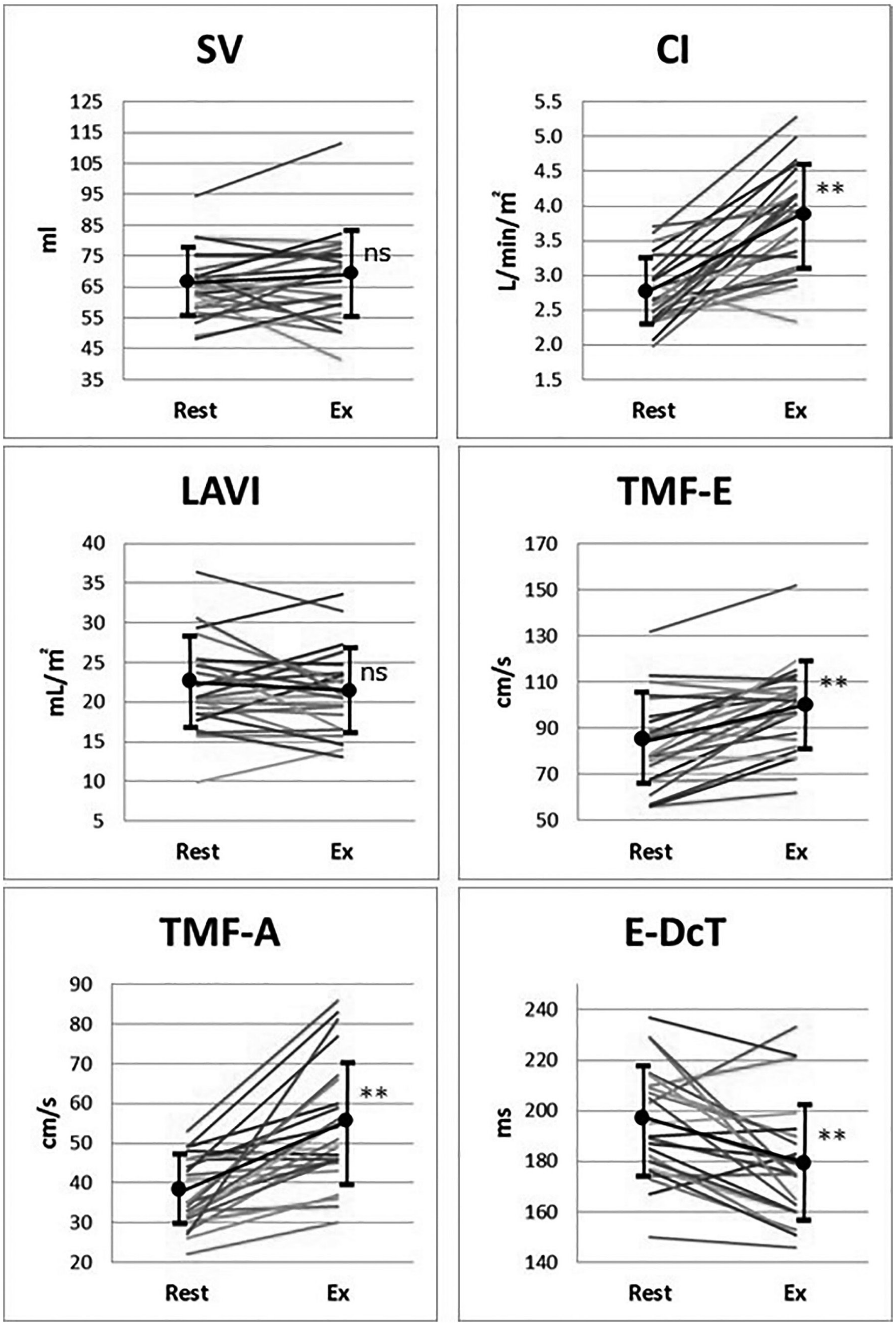

Fig. 2b Changes of indexes by low-grade exercise.
ns not significant, * $P < 0.05$, ** $P < 0.01$, *Rest* at Rest, *Ex* low-grade exercise, *SV* stroke volume, *CI* cardiac index, *LAVI* LA volume index, *TMF-E* early diastolic flow velocity of transmitral flow, *TMF-A* late diastolic flow velocity of transmitral flow, *E-DcT* deceleration time of TMF-E

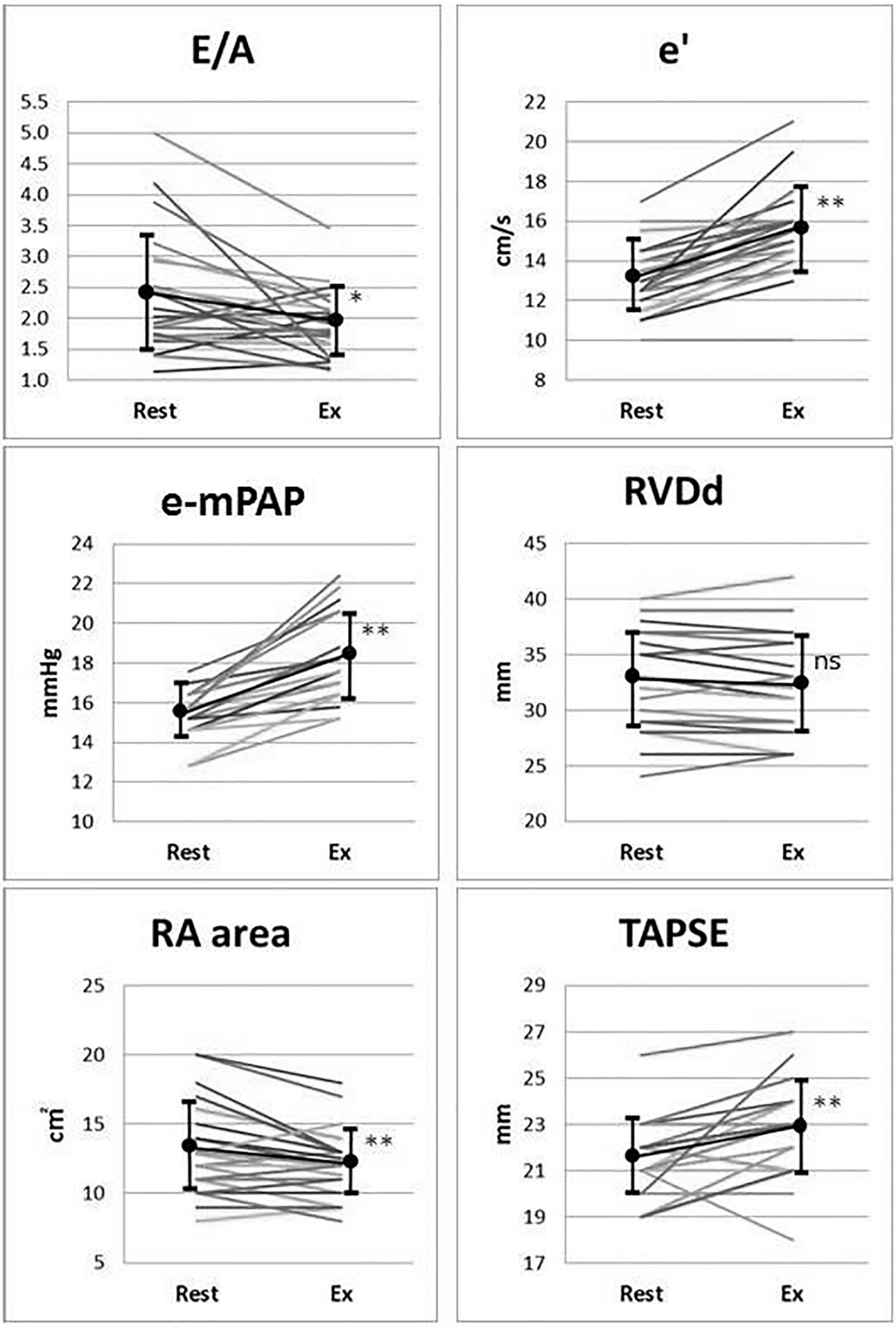

Fig. 2c Changes of indexes by low-grade exercise.
ns not significant, * P < 0.05, ** P < 0.01, *Rest* at Rest, *Ex* low-grade exercise, *E/A* ratio TMF-E/TMF, *e'* early diastolic mitral annular velocity, *e-mPAP* estimated mean pulmonary arterial pressure, *RVDd* end-diastolic RV diameter, *RA* area right atrial area, *TAPSE* tricuspid annular plane systolic excursion

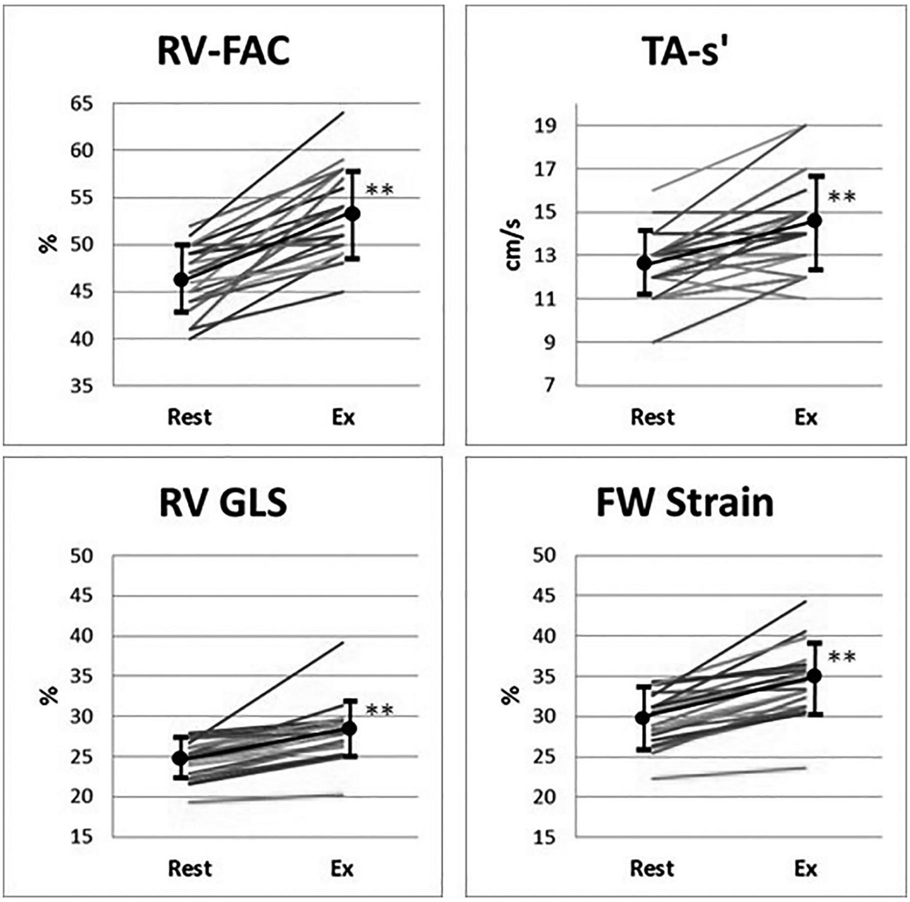

Fig. 2d Changes of indexes by low-grade exercise.
* P < 0.05, ** P < 0.01, *Rest* at Rest, *Ex* low-grade exercise, *RV-FAC* RV fractional area change, *TA-s'* systolic tricuspid annular velocity, *RV-GLS RV* global longitudinal strain, *FW Strain* RV free wall strain

on echocardiographic indexes were not well studied. Therefore, we need the data obtained in this study in healthy young subjects before applying this low-grade exercise protocol on some patients.

Even if the load was low-grade, HR was increased, cardiac function was slightly accelerated, mean and peak pulmonary arterial pressure was elevated, though all of them was within normal range reported elsewhere.[8-11] These responses to low-grade exercise are considered normal in healthy young individuals.

Augmentation of systolic echocardiographic indexes like HR, SBP, and LVEF were reflecting the driving of sympathetic nerve system during low-grade exercise. Augmentation of TMF-E, TMF-A and shortened TMF-DcT were reflecting the augmentation of diastolic recoil as a result of augmentation of systolic function, indicating well preserved systolic and diastolic function reserve in healthy young subjects.

Echocardiography is one of the important noninvasive modalities to reveal the pulmonary arterial hypertension (PAH).[12] However, we are ready to overlook the diagnosis of PAH by only using echo examination at rest. In such a situation, stress echocardiography could prevent missing the correct diagnosis. To perform stress echocardiography, simple low-grade exercise is much easier than time-consuming multistage symptom-limit stress protocol. Also, 6 minutes' walk is reported for detecting PAH in patients with collagen disease.[13]

The significant increase in mPAP during low-grade exercise is due to increasing pulmonary arterial flow with increasing in CI. This normal response in healthy young subjects suggests the preserved function in pulmonary small arteries and arterioles during low-grade exercise and no lesion or no sclerosis nor stenosis on pulmonary vascular bed.

Although RVDd did not change significantly by low-grade exercise, significant decrease in RA area and significant increase in TAPSE, TA-s', and RV FAC indicated the acceleration of the right heart systolic function. Also, RV GLS and FW strain increased significantly in healthy young subjects, which could be a reference when the application of the low-grade exercise on the patients.[14]

Clinical implication: Since all of the averaged echocardiographic indexes by low-grade exercise in this study were within normal reference values reported elsewhere,[5-8] these data would be a practical reference data set when we apply the low-grade exercise protocol on some patients. However, further investigation is needed for precise diagnostic value of this low-grade exercise echocardiographic technique.

A possible application is that on patients with scleroderma or other collagen disease without finding of PAH at rest. It is expected for early diagnosis of PAH by applying this low-grade exercise echocardiography on such patients.

Limitation

Firstly, we studied only in the healthy young subjects. The data in middle-age or senile are required for age-match to practical patients. Secondly, we tried only one load strength (20 watts during 5 minutes) for low-grade exercise. Study on a lighter or a heavier load as low-grade exercise protocol may be potentially required. Thirdly, we could not completely rule out the PAH caused by left sided heart dysfunction by this method when we apply on some patients suspected PAH. Because we focused on right heart and PH during exercise, it is difficult to rule out the left heart dysfunction at the same time.

Conclusion

We showed the responses to low-grade exercise on healthy young adults. We hope these data are useful as a fundamental reference for the application to the patients with fragile or limited exercise tolerance or latent pulmonary hypertension.

Human right statement and informed consent:

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1964 and later version. Informed consent was obtained from all participants for being included in the study.

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Conflict of interest

The authors declare no conflict of interest.

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