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# Respiratory and Circulatory Responses during Low-intensity Resistance Exercise Training Using a KAATSU Device in Male Patients with Cardiovascular Disease

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#### Summary

**Purpose**: This study examined respiratory and circulatory responses during low-intensity resistance exercise using a KAATSU device, which results in moderate blood flow restriction, in both healthy male adults and male patients with cardiovascular disease.

**Methods**: Healthy males (n = 10, 29.8  $\pm$  7.0 years) and male patients in cardiac rehabilitation (n = 10, 76.9  $\pm$  3.4 years) performed leg extensions (3 sets of 15 repetitions at low-intensity [20% of a 1-repetition maximum]) not using and using a KAATSU device. We measured expiratory gas and impedance cardiography before (baseline) and during exercise, as well as dyspnea and rate of perceived exertion (RPE) during knee extensor effort immediately after each set of repetitions.

**Results**: The patients were older than the healthy participants. At baseline, although heart rates and ventilatory equivalents did not differ between groups, oxygen uptake, carbon dioxide output, and left cardiac work index (LCWi) were lower in patients than in healthy participants. There were no GROUP  $\times$  KAATSU interactions in terms of respiratory and circulatory responses during low-intensity resistance exercise. Dyspnea and RPE increased with exercise set repetitions and the KAATSU device augmented the RPE in both groups.

**Conclusions**: There were no patient-specific changes in respiratory and circulatory responses, dyspnea, and responses to knee extensor effort using the KAATSU device during low-intensity resistance exercise, despite patients being older than healthy participants and exhibiting a lower respiratory function and LCWi at baseline than them. These results suggest that low-intensity resistance exercise using a KAATSU device can be a safe and useful training method for cardiac rehabilitation.

**Key Words**: KAATSU, low-intensity resistance exercise, expiratory gas analysis, cardiac output, dyspnea, rate of perceived exertion (RPE)

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# Introduction

Patients often experience a decrease in muscle strength and size because of cardiovascular disease (CVD) and medical treatment<sup>1)</sup>. Human skeletal muscle strength and mass can be improved by high-intensity resistance exercise ( $\geq$ 60-70% of a 1-repetition maximum [1-RM])<sup>2.3</sup>; however, patients with cardiovascular disease (CVD) can increase their risk of arrhythmias and heart failure when they perform high-intensity resistance exercise<sup>4)</sup>.

Blood flow restriction (KAATSU) training is a method which subjects perform an exercise while their proximal end of the limb is compressed by a special device<sup>5</sup>. Previous studies reported that low-intensity KAATSU resistance exercise facilitates increases of muscle strength compared with low-intensity no-KAATSU resistance exercise, induces muscle hypertrophy similarly with high-intensity no-KAATSU resistance exercise<sup>6</sup>. The main mechanisms of KAATSU-induced increases in muscle strength and hypertrophy are explained by increase of stimulation of growth hormone production, insulin-like growth factors, cell swelling, reactive oxygen species such as nitric oxide and heat shock protein, recruitment of fasttwitch muscle fibres, and accumulation of metabolites such as protons and lactate in the muscle interstitium<sup>3</sup>. Resistance training using a KAATSU device has been shown to improve muscle strength and mass, even when performed at low intensity (20-30% of a 1-RM) by healthy adults<sup>7</sup>, the elderly<sup>8</sup>, and patients who have had CVD<sup>9</sup>. This suggests that low-intensity resistance training using a KAATSU device can be a suitable method for those individuals who find it difficult to perform high-intensity resistance training.

Although low-intensity KAATSU resistance training is expected to safely induce increases of muscle strength and mass in healthy elderly<sup>10</sup>, respiratory and circulatory responses during such exercise modality should be examined to consider whether it can be also safely applied to cardiac rehabilitation. Previous study reported that ischemia induces sympathoexcitatory pressure elevation reflex in skeletal muscle, increases systolic blood pressure and cardiac output, and may induce abnormal cardiovascular responses in elderly with high cardiovascular risk and cardiovascular patients<sup>11)</sup>. Indeed, KAATSU increases heart rate, systolic blood pressure, and heart rate-blood pressure product<sup>12</sup>, but the magnitude of increase in each response is within normal range in healthy adults<sup>13</sup>. Our previous report found that there were no severe muscular and subcutaneous side effects, and cardiac symptoms after 3 months low-intensity KAATSU resistance training intervention in cardiovascular patients9. However, characteristics in respiratory and circulatory responses during low-intensity KAATSU resistance exercise in cardiovascular patients are still not unclear. Thus, respiratory and circulatory responses during such exercise in cardiovascular patients should be examined to scientific evidence whether add low-intensity KAATSU resistance exercise can be safely applied to cardiac rehabilitation. Therefore, the purpose of this study was to compare KAATSU-induced changes in respiratory and circulatory responses during lowintensity resistance exercise between healthy adults and cardiovascular patients. We also examined dyspnea and knee extensor effort to consider subjective burden during such exercise.

# Methods

# Participants

Healthy males (n = 10) and male patients recovering from CVD (n = 10) participated in this study (Table 1). The patients were undergoing outpatient cardiac rehabilitation at Dokkyo Medical University Hospital 1 day per week or every other week. A single training session in cardiac rehabilitation consisted of a resistance tube exercise, a bodyweight-bearing exercise, and an aerobic exercise using a bicycle ergometer for 60 minutes. The patients comprised individuals with myocardial infarction (n = 5), heart failure (n = 2), valvular disease (i.e. transcatheter aortic valve implantation for aortic stenosis, n = 1; aortic valve and mitral valve replacement and tricuspid annuloplasty for mitral regurgitation, n = 1; and percutaneous mitral valve clipping for mitral regurgitation, n = 1). The experiment was conducted under the supervision of a physician and a gualified KAATSU instructor.

After obtaining the approval of the Research Ethics Review Committee of Dokkyo Medical University Hospital (approval number: 27074), and in accordance with the Declaration of Helsinki, all participants were in-

Healthy males Male patients in cardia	iac rehabilitation
(n = 10) $(n = 10)$	))
Age, years $29.8 \pm 7.0$ $76.9 \pm 3.4^{*}$	*
Body height, cm $172.5 \pm 4.1$ $162.7 \pm 3.2^{*}$	*
Body weight, kg $64.6 \pm 16.3$ $64.1 \pm 6.6$	5
BMI, kg/m <sup>2</sup> $21.8 \pm 5.5$ $24.3 \pm 3.0$	)
Estimated 1-RM, kg 118.1 ± 20.4 61.4 ± 18.7	.7*
20% 1-RM, kg 23.5 $\pm$ 4.0 12.6 $\pm$ 3.7*	7 %
METs (mL/min/kg) $1.12 \pm 0.14$ $1.03 \pm 0.2$	2
HR (bpm) $65.8 \pm 8.4$ $71.4 \pm 11.3$	.3
VO <sub>2</sub> (mL/min/kg) $271.6 \pm 45.5$ $228.4 \pm 41.6$	.6*
VCO <sub>2</sub> (mL/min/kg) 236.8 ± 32.4 195.8 ± 42.9	.9*
VO <sub>2</sub> /HR (mL/min/beat) $4.1 \pm 0.5$ $3.3 \pm 0.6^{\circ}$	<b>*</b>
VE (L/min) 9.13 ± 0.98 11.3 ± 2.6	5
VE/VO <sub>2</sub> (mL/mL) $34.5 \pm 3.9$ $49.4 \pm 9.4^{\circ}$	*
VE/VCO <sub>2</sub> (mL/mL) $39.2 \pm 3.5$ $58.9 \pm 11.7$	.7*
R $0.87 \pm 0.05$ $0.87 \pm 0.06$	06
RR (bpm) $14.3 \pm 2.8$ $17.2 \pm 4.9$	)
TV-I (mL) $656.3 \pm 99.5$ $682.9 \pm 111$	1.2
TV-E (mL) $653.4 \pm 102.2$ $675.9 \pm 110$	0.7
PETCO <sub>2</sub> (mmHg) $39.9 \pm 3.5$ $29.6 \pm 3.6^{\circ}$	<b>;</b> *
ETO <sub>2</sub> (%) $14.7 \pm 0.6$ $15.9 \pm 0.4$ *	*
ETCO <sub>2</sub> (%) $5.7 \pm 0.5$ $4.3 \pm 1.4^{*}$	*
EE (kJ/d) 1891.8 ± 302.9 1598.8 ± 304	4.5*
SV (mL) 81.6 ± 17.2 66.6 ± 16.4	.4
SVi (mL/m <sup>2</sup> ) $44.9 \pm 8.6$ $39.6 \pm 10.0$	.0
CI $(l/min/m^2)$ 3.0 ± 0.7 2.8 ± 0.5	)
CTI 191.4 ± 80.0 138.5 ± 80.1	.1
VET (ms) 338.8 ± 97.6 358.0 ± 87.4	.4
LCWi (kg/m/m <sup>2</sup> ) $3.6 \pm 1.2$ $3.1 \pm 0.6^{\circ}$	<b>*</b>
SVRi (dyn·s/cm <sup>5</sup> ·m <sup>2</sup> ) $2465.9 \pm 633.4$ $2561.5 \pm 653$	3.3
SVR (dyn·s/cm <sup>5</sup> ) $1377.3 \pm 439.3$ $1521.5 \pm 378$	8.7
EDV (mL) $155.2 \pm 57.1$ $126.8 \pm 16.7$	.7
EF (%) 56.6 ± 13.4 52.6 ± 11.1	.1

 Table 1
 Participant characteristics and respiratory and circulatory responses at baseline

BMI: body mass index; 1-RM: 1-repetition maximum; METs: metabolic equivalents; HR: heart rate; VO<sub>2</sub>: oxygen uptake; VCO<sub>2</sub>: carbon dioxide output; VO<sub>2</sub>/HR: oxygen pulse; VE: minute ventilation; VE/VO<sub>2</sub>: ventilatory equivalent for oxygen; VE/VCO<sub>2</sub>: ventilatory equivalent for carbon dioxide; R: respiratory exchange ratio; RR: respiratory rate; TV-I: inspiratory tidal volume; TV-E: expiratory tidal volume; PETCO<sub>2</sub>: partial pressure of end-tidal carbon dioxide; ETO<sub>2</sub>: end-tidal oxygen; ETCO<sub>2</sub>: end-tidal carbon oxide; EE: energy expenditure; SV: stroke volume; SVi: stroke volume index; CI: cardiac index; CTI: contractility index; VET: ventricular ejection time; LCWi: left cardiac work index; SVRi: systemic vascular resistance index; SVR: systemic vascular resistance; EDV: end-diastolic volume; EF: ejection fraction. \*Significant difference (P < 0.05) compared with baseline of healthy males.

formed verbally about the study and provided with written materials about it before their written informed consent was obtained.

# KAATSU

Blood flow restriction was achieved using a KAATSU device (KAATSU nano, KAATSU Global, U. S.A.). Pneumatic cuffs (5-cm wide) were attached at the proximal end of thighs of the participants before being

inflated for the purpose of restricting blood flow to both lower limbs. The mounting pressure of the KAATSU belt was set to 20 standard KAATSU unit (SKU), and the set pressure gradually was increased up to 200 SKU. To help familiarize the participants with the device, 30 repetitions of ankle plantar flexion and dorsiflexion were performed before measurement.

# **Experimental exercise**

A leg extension machine was used in this study (PREFIT GX-320, OG Wellness, Tokyo, Japan). The machine seat and backrest position were adjusted to each participant's physique; the center of rotation of the participant's knee joint was matched to the center of rotation for the machine lever. At least 1 day before the experiment, we measured each participant's estimated 1-RM based on maximal repetition numbers at a submaximal load<sup>14</sup>. The exercise intensity was set at 20% of the 1-RM.

Participants performed leg extensions (3 sets of 15 repetitions) not using and then using the KAATSU device. Each leg extension was performed over a 2-second period (knee extension for 1 second and flexion for 1 second). One supervisor of the exercise session counted aloud "1, 2" in front of the participant in time with a 60 Hz metronome click sound to facilitate performance of the leg extensions at a constant pace. Another supervisor verbally counted the number of leg extensions so that exactly 15 repetitions were performed per set.

#### **Respiratory responses**

We measured expiratory gas during the experiment using a gas analyzer (AE-100i, Minato Medical Science, Osaka, Japan). The parameters analyzed by gas analyzer were as follows: metabolic equivalents (METs), heart rate (HR), oxygen uptake (VO<sub>2</sub>), carbon dioxide output (VCO<sub>2</sub>), oxygen pulse (VO<sub>2</sub>/HR), minute ventilation (VE), ventilatory equivalent for oxygen (VE/VO<sub>2</sub>), ventilatory equivalent for carbon dioxide (VE/VCO<sub>2</sub>), respiratory exchange ratio (R), respiratory rate (RR), inspiratory tidal volume (TV-I), expiratory tidal volume (TV-E), partial pressure of end-tidal oxygen (PETO<sub>2</sub>), partial pressure of end-tidal carbon dioxide (PETCO<sub>2</sub>), end-tidal oxygen (ETO<sub>2</sub>), end-tidal carbon dioxide (ETCO<sub>2</sub>), and energy expenditure (EE). Each value was averaged over 30 s for use in our analysis.

#### **Circulatory responses**

We measured cardiac output during the experiment using a noninvasive impedance cardiography device (PhysioFlow<sup>®</sup> Q-Link<sup>™</sup>, Manatec, Paris, France). We attached two electrodes to the left-frontal side of the neck in a lengthwise arrangement; 1 electrode went to the lower point of the right clavicle, 1 electrode went to the lowest point of the left-frontal side of the rib, 1 electrode went to the xiphisternum, and 1 electrode went to the lower-right point of the xiphisternum. Before attaching electrodes, we wiped the skin of each participant with an alcohol swab to reduce impedance. The parameters analyzed by impedance cardiography were as follows: stroke volume (SV), stroke volume index (SVi), cardiac index (CI), contractility index (CTI), ventricular ejection time (VET), left cardiac work index (LCWi), systemic vascular resistance index (SVRi), systemic vascular resistance (SVR), end-diastolic volume (EDV), and ejection fraction (EF). During the experiment, signal quality exceeding 80% was used in the analysis.

# **Experimental protocol**

Fig. 1 shows the experimental protocol. To establish a baseline, the respiratory and circulatory responses from participants were recorded while they were at rest for 60 s in a seated position. Participants performed leg extensions while not using (Control) and then using the KAASTU device. Exercise type was in block-random order for each participant. There was at least a 5-min rest between exercise sessions to ensure respiratory and circulatory responses were similar to those at baseline before starting exercise afresh. We asked participants to immediately rate their perceived respiratory distress (dyspnea) and their rate of perceived exertion (RPE) in relation to their knee extensor fatigue using the Borg scale after each set of repetitions. Participants were instructed to point to the Borg scale score with their finger because a verbal response could affect their respiratory status.

# Statistical analysis

All data are presented as the mean  $\pm$  standard deviation. Data normality was evaluated using the

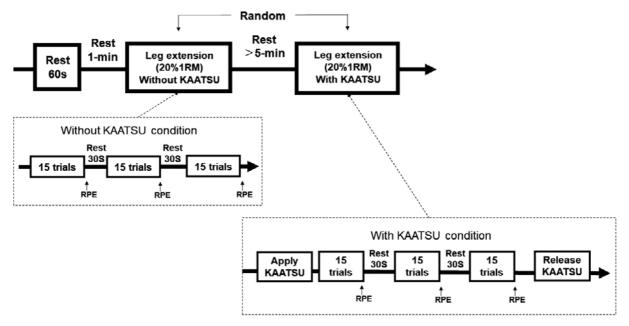


Figure 1 Experimental protocol. 1-RM: 1-repetition maximum; Reps: repetitions; RPE: rate of perceived exertion

Shapiro-Wilk test. Participant characteristics and baseline data between groups were compared using an independent *t*-test or Mann-Whitney U-test. To evaluate the accumulative exercise-induced effects on respiratory and circulatory responses, each value during the third exercise set was analyzed using a 2-way mixeddesign (Group × KAATSU) analysis of variance (ANOVA). To evaluate changes in dyspnea and RPE during the course of an exercise set, recorded values were analyzed using a 3-way mixed-design (GROUP × KAATSU × TIME) ANOVA. When a significant interaction or main effect was observed, a post-hoc Bonferroni procedure was performed. A software package (SPSS Ver.27, IBM) was used for statistical analysis and the level of significance was set at P < 0.05.

## Results

Participant characteristics and respiratory and circulatory responses at baseline are shown by group in Table 1. The male patients with a history of CVD and who were in cardiac rehabilitation were older, shorter, and they had less muscle strength than the group of healthy males. In respiratory responses at baseline, VO<sub>2</sub>, VCO<sub>2</sub>, VO<sub>2</sub>/HR, PETCO<sub>2</sub>, ETCO<sub>2</sub>, and EE were lower, and VE/VO<sub>2</sub>, VE/VCO<sub>2</sub>, and ETO<sub>2</sub> were higher in the patients than in the healthy males (all P < 0.05). In circulatory responses at baseline, only LCWi was lower in patients than in healthy males (P < 0.05). Respiratory responses during the third set of exercises are summarized by group and exercise without (Control) and with use of the KAATSU device (Table 2). No significant GROUP × KAATSU interaction or KAATSU main effect was detected. GROUP main effects were revealed for all parameters such as METs (F = 19.78), VO<sub>2</sub> (F = 27.85), VCO<sub>2</sub> (F = 28.73), VO<sub>2</sub>/HR (F = 31.64), VE/VO<sub>2</sub> (F = 42.50), and VE/VCO<sub>2</sub> (F = 38.25) (all P < 0.001).

Circulatory responses during the third set of exercises by group and use of a KAATSU device are shown in Table 3. There was no significant GROUP  $\times$  KAATSU interaction or GROUP or KAATSU main effect.

The results for dyspnea and knee extensor effort in each set are shown by group and use of the KAATSU device (Table 4). There was GROUP × KAATSU × TIME interaction (F = 4.78, P = 0.032). Dyspnea was higher during the third exercise set compared with the other sets in both groups (P < 0.05 each) and in the patients when the KAATSU device was used. Dyspnea did not differ between heathy participants and the patients during the exercise sets without and with the KAATSU device. There was a KAATSU (F = 44.89, P< 0.001) and a TIME main effect (F = 51.51, P < 0.001) in RPE. RPE increased over the course of the exercise

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	Healthy males		Male patients in cardiac rehabilitation		
-	Control	KAATSU	Control	KAATSU	
METs (mL/min/kg), G	$2.43 \pm 0.56$	$2.53 \pm 0.51$	$2.15 \pm 0.59$	$1.96 \pm 0.51$	
HR (bpm)	$79.7 \pm 13.6$	$80.4 \pm 9.6$	$84.4 \pm 9.1$	$86.6 \pm 7.9$	
VO <sub>2</sub> (mL/min/kg), G	$583.5 \pm 153.1$	$606.3 \pm 139.9$	$380.8 \pm 136.0$	$358.3 \pm 128.0$	
VCO <sub>2</sub> (mL/min/kg), G	$532.6 \pm 131.5$	$558.9 \pm 130.1$	$333.6 \pm 126.9$	$325.5 \pm 133.9$	
VO <sub>2</sub> /HR (mL/min/beat), G	$7.2 \pm 1.2$	$7.3 \pm 0.8$	$4.8 \pm 1.8$	$4.4 \pm 1.5$	
VE (L/min)	$17.26 \pm 3.75$	$18.64 \pm 3.65$	$19.0 \pm 5.3$	$19.8 \pm 5.3$	
VE/VO2 (mL/mL), G	$30.6 \pm 2.1$	$32.0 \pm 1.6$	$52.4 \pm 16.2$	$57.2 \pm 16.5$	
VE/VCO <sub>2</sub> (mL/mL), G	$34.5 \pm 3.1$	$34.7 \pm 3.3$	$61.7 \pm 19.8$	$65.8 \pm 21.9$	
R	$0.96 \pm 0.07$	$0.88 \pm 0.08$	$0.94 \pm 0.06$	$0.92 \pm 0.11$	
RR (bpm)	$21.1 \pm 3.3$	$21.8 \pm 3.9$	$22.4 \pm 4.4$	$23.0 \pm 4.4$	
TV-I (mL)	$815.7 \pm 107.7$	$850.9 \pm 101.4$	$842.0 \pm 206.3$	$867.7 \pm 237.6$	
TV-E (mL)	$820.2 \pm 116.7$	$852.3 \pm 109.6$	$853.5 \pm 204.2$	$874.4 \pm 234.7$	
PETCO <sub>2</sub> (mmHg), G	$43.0 \pm 3.2$	$39.6 \pm 9.3$	$43.6 \pm 68.2$	$30.8 \pm 4.2$	
ETO <sub>2</sub> (%), G	$14.3 \pm 0.2$	$14.6~\pm~0.3$	$15.8 \pm 0.7$	$16.1 \pm 0.6$	
ETCO <sub>2</sub> (%), G	$6.1 \pm 0.5$	$6.0 \pm 0.5$	$4.5 \pm 1.4$	$4.4 \pm 0.6$	
EE (kJ/d), G	$4202.6 \pm 1073.4$	$4353.9 \pm 950.3$	$2719.7 \pm 991.8$	$2625.0 \pm 1088.5$	

 Table 2
 Respiratory responses during the third set of leg extensions while not using (Control) and using a KAATSU device

METs: metabolic equivalents; HR: heart rate; VO<sub>2</sub>: oxygen uptake; VCO<sub>2</sub>: carbon dioxide output; VO<sub>2</sub>/HR: oxygen pulse; VE: minute ventilation; VE/VO<sub>2</sub>: ventilatory equivalent for oxygen; VE/VCO<sub>2</sub>: ventilatory equivalent for carbon dioxide; R: respiratory exchange ratio; RR: respiratory rate; TV-I: inspiratory tidal volume; TV-E: expiratory tidal volume; PETCO<sub>2</sub>: partial pressure of end-tidal carbon dioxide; ETO<sub>2</sub>: end-tidal oxygen; ETCO<sub>2</sub>: end-tidal carbon dioxide; EE: energy expenditure; G: Group main effect in third set (P < 0.001).

 Table 3 Circulatory responses at baseline and during the third set of leg extensions while not using (Control) and using a KAATSU device

	Healthy males		Male patients in cardiac rehabilitation			
	Baseline	Control	KAATSU	Baseline	Control	KAATSU
SV (mL)	$81.6 \pm 17.2$	87.4 ± 11.7	$84.5 \pm 16.1$	$66.6 \pm 16.4$	$80.2 \pm 28.5$	84.7 ± 21.2
SVi (mL/m²)	$44.9 \pm 8.6$	$48.3 \pm 6.2$	$46.6 \pm 8.4$	$39.6~\pm~10.0$	$47.7 \pm 10.9$	$50.2 \pm 12.0$
CI (l/min/m²)	$3.0 \pm 0.7$	$4.2~\pm~0.9$	$4.4 \pm 1.1$	$2.8~\pm~0.5$	$4.4 \pm 1.2$	$4.6 \pm 1.5$
CTI	$191.4 \pm 80.0$	$206.2 \pm 86.2$	$192.8 \pm 95.9$	$138.5 \pm 80.1$	$175.8 \pm 76.7$	$189.0 \pm 86.1$
VET (ms)	$338.8 \pm 97.6$	$158.3 \pm 65.2$	$272.2 \pm 39.9$	$358.0 \pm 87.4$	$262.6 \pm 55.2$	$289.4 \pm 89.4$
LCWi (kg/m/m <sup>2</sup> )	$3.6 \pm 1.2$	$5.1 \pm 1.5$	$5.4 \pm 1.7$	$3.1 \pm 0.6*$	$4.9 \pm 1.5$	$5.2 \pm 1.8$
SVRi (dyn·s/cm <sup>5</sup> ·m <sup>2</sup> )	$2465.9 \pm 633.4$	$1719.9 \pm 353.1$	$1705.0 \pm 500.9$	$2561.5 \pm 653.3$	$1595.8 \pm 474.5$	$1558.5 \pm 534.7$
SVR (dyn·s/cm <sup>5</sup> )	$1377.3 \pm 439.3$	$952.6 \pm 211.2$	$946.2 \pm 340.0$	$1521.5 \pm 378.7$	$951.3 \pm 298.3$	$929.1 \pm 334.6$
EDV (mL)	$155.2 \pm 57.1$	$166.6 \pm 73.9$	$158.9 \pm 48.7$	$126.8 \pm 16.7$	$143.3 \pm 18.3$	$149.1 \pm 13.5$
EF (%)	$56.6 \pm 13.4$	$57.7 \pm 14.1$	$56.3 \pm 14.9$	$52.6 \pm 11.1$	$56.7 \pm 11.5$	$57.2 \pm 12.2$

SV: stroke volume; SVi: stroke volume index; CI: cardiac index; CTI: contractility index; VET: ventricular ejection time; LCWi: left cardiac work index; SVRi: systemic vascular resistance index; SVR: systemic vascular resistance; EDV: end-diastolic volume; EF: ejection fraction. \*Significant difference (P < 0.05) compared with baseline of healthy males.

set and use of the KAATSU device augmented RPE in both groups (all P < 0.001).

#### Discussion

This study examined three categories, (1) respira-

tory responses, (2) circulatory responses, and (3) subjective burden (dyspnea and muscle fatigue) of lowintensity resistance exercise training using a KAATSU device in patients rehabilitating from CVD and in healthy participants. Although the patients were older

	Healthy males		Male patients in cardiac rehabilitation		
	Control	KAATSU	Control	KAATSU	
Dyspnea, G $\times$ K $\times$ T					
Exercise set					
First	$9.4 \pm 1.6$	10.9 ± 1.3 †	$9.5 \pm 1.7$	$10.9 \pm 1.6$	
Second	$10.4 \pm 1.1$	10.8 ± 1.4 †	$11.3 \pm 0.8$	$11.2 \pm 1.8$	
Third	$11.6 \pm 1.3*$	$11.2 \pm 1.5$	$12.5 \pm 1.1*$	$12.1 \pm 1.9*$	
RPE, K, T					
Exercise set					
First	$10.6 \pm 1.3$	$10.9 \pm 1.6$	$10.4 \pm 1.1$	$11.8 \pm 1.6$	
Second	$10.8 \pm 1.4$	$11.2 \pm 1.8$	$11.5 \pm 1.9$	$13.1 \pm 2.2$	
Third	$11.2 \pm 1.5$	$12.1 \pm 1.9$	$12.5 \pm 2.1$	$14.2 \pm 2.3$	

 Table 4
 Dyspnea and knee extensor effort (RPE) in each set performed while not using (Control) and using a KAATSU device

 $G \times K \times T$ : GROUP × KAATSU × TIME interaction (P < 0.05); RPE: rate of perceived exertion; K: KAATSU, main effect (P < 0.05); T: TIME, main effect (P < 0.05). \*Significant difference (P < 0.05) between the first and second set, or between the second and third set. †Significant difference (P < 0.05) between Control and KAATSU during the same exercise set within the group.

than the healthy participants and exhibited a lower respiratory function and LCWi, their respiratory and circulatory responses, dyspnea, and knee extensor effort were similarly affected when using the KAATSU device during low-intensity resistance exercise.

A KAATSU device used in combination with a lowintensity resistance exercise regimen can increase muscle strength and mass in the elderly<sup>7,15</sup> and in patients with CVD9; thus, as a training modality it is expected to be effective in cardiac rehabilitation. In a previous study, metabolic stress gradually increased with repetition number during a set of low-intensity resistance exercises when healthy adults used a KAATSU device<sup>16)</sup>. Because heart function is compromised in patients with CVD compared with healthy adults<sup>17</sup>, there is potential for the patient's respiratory and circulatory dynamics to respond more specifically to the use of KAATSU technology during lowintensity resistance exercise training. Indeed, the present results showed that respiratory functions and LCWi at baseline were lower in the patients than in the healthy participants (Table 1). In respiratory response, VE/VO<sub>2</sub> and VE/VCO<sub>2</sub> are affected by stroke volume, vascular endothelial cell function, autonomic activity, breathing pattern, and gas exchange in the lungs<sup>18)</sup>, and increase if breathing pattern is shallow and fast<sup>19</sup>. Therefore, decrease in cardiac output (CO) and/or pulmonary blood flow may be main causes of lowering in respiratory functions at baseline in cardiovascular male patients. Our results showed that VE at baseline did not differ between groups, suggesting that the breathing patterns were similar between both groups. Therefore, a decrease in CO and/or pulmonary blood flow may have represented the main causes of lower respiratory function at baseline in the patients with a history of CVD. Because aging decreases respiratory function<sup>20)</sup> and left ventricular compliance<sup>21)</sup>, not only a history of cardiac disease, but also aging for the older patients may be implicated in the lower respiratory and circulatory functions of patients compared with healthy participants in this study. Nonetheless, results of this study showed that there was no KAATSU main effect in respiratory and circulatory responses during the low-intensity leg extension exercises (Table 2 and 3). Thus, KAATSU exercise-induced effects on respiratory and circulatory responses during lowintensity resistance exercises may not depend on baseline respiratory and circulatory functions and age. According to the guidelines for cardiac rehabilitation<sup>22</sup>, the HR of patients using the KAATSU device during the low-intensity resistance exercises in our study did not exceed the upper range of safe exercise intensity (resting HR +30 bpm); therefore, we suggest this type of exercise may be of a safe intensity during cardiac rehabilitation in males.

We estimated the 1-RM of patients based on the

number of repetitions managed at a submaximal load<sup>14</sup> and we observed lower METs in our patients with CVD than in the healthy participants (Table 2). Thus, male patients with CVD may subjectively underscore their maximum exercise intensity because of their potential skeletal muscle fatiguability and lower limb exercise intolerance<sup>23</sup>. This possibility suggests that relative exercise intensity dependent on the estimated 1-RM may be lower in patients with CVD compared with healthy participants. The lower values for VO<sub>2</sub> during exercise without and with the use of a KAATSU device in patients versus healthy participants (Table 2) may support this possibility. Given the lack of a GROUP main effect in circulatory responses (Table 3), and with respiratory responses that were lower in patients compared with healthy participants, the possibility exists that relative exercise intensity was lower in the patient group than in the healthy participant group. Therefore, 20% of the estimated 1-RM may be a safe intensity for resistance exercise training using the KAATSU device in male patients with CVD from the perspective of respiratory and circulatory responses.

Subjective burden also gradually increases with progress of repetition during low-intensity KAATSU resistance exercise in healthy adults<sup>24</sup>. In this study, dyspnea and knee extensor effort increased with repetition number during an exercise set in both groups, although knee extensor effort was slightly higher in the patient group than in the healthy participant group (Table 4). Therefore, the subjective exercise intensity may have been higher in the patients than in the healthy males, despite relative exercise intensity based on estimated 1-RM may be lower in patients than in healthy males. HR did not differ between patients and healthy males (Table 2), but differences of relative value to predicted maximal heart rate<sup>25)</sup> in patients (54.7-56.2%) and healthy males (42.6-43.0%) might a reason for an inconsistency between physical and subjective burden in patients with CVD. The average Borg scale scores for dyspnea and knee extensor effort were 12.1 and 14.2, respectively, indicating that the subjective burden was in the "slightly severe" category. Thus, low-intensity resistance exercise regimens that use a KAATSU device will be a training method that is unlikely to reach the "severe" threshold in terms of the subjective burden in male patients with CVD. The maximal Borg scale score observed for dyspnea and knee extensor effort for an individual patient with CVD was 17 (for both parameters) when a KAATSU device was used during exercise. Clinicians should remain mindful of the potential for individual differences in terms of the subjective burden whenever lowintensity exercise training is performed using a KAATSU device for cardiac rehabilitation. Ishizaka et al. reported that KAATSU increases muscular activation during very low-intensity (10% of 1 RM) in cardiovascular patients<sup>20</sup>, thus an exercise intensity lower than 20-30% of 1 RM which often prescribes for healthy adults<sup>7)</sup> may be safe and suitable intensity for cardiovascular patients while there are no cardiovascular patient-specific effects on respiratory and circulatory responses and do not severely increase subjective burden during KAATSU resistance exercise.

Three study limitations came to our attention. First, we recruited only male patients with CVD. Although exercise-induced effects in combination with the use of a KAATSU device have been determined to be similar between healthy males and females<sup>27</sup>, a future study to examine the effects in female patients with CVD is warranted. Second, we were able to measure circulatory responses using noninvasive impedance cardiography for all the healthy participants, but we were unable to obtain measurements for four out of the 10 patients with CVD. We cannot offer a reason for this inability, although we propose that technical improvements should solve this issue in the future. Third, we applied a KAATSU pressure of 200 SKU for all participants. Brandner et al. (2017) report that subjective burdens during low-intensity exercise for which a KAATSU device is used are affected by the intensity of the pressure at which the device is applied<sup>28</sup>; however, a recent systematic review did not find support for such a relationship<sup>29)</sup>. There is no standard or preferred pressure setting for a KAATSU device used by patients with CVD. This opens the door for future studies to examine whether the pressure intensity applied using a KAATSU device changes respiratory and circulatory responses as well as subjective burdens during low-intensity resistance exercise training in patients with CVD.

# Conclusions

We examined the effects of using a KAATSU device on respiratory and circulatory responses as well as subjective burdens during low-intensity (20% of 1-RM) resistance exercise in male patients with CVD. There were no patient-specific device use-related effects on respiratory and circulatory responses nor severe subjective burdens during low-intensity resistance exercise training. Thus, low-intensity resistance exercise regimens that use a KAATSU device may provide a safe and useful training method for cardiac rehabilitation.

# Author contributions

HI, YM, AU, TT, and TN designed the study; HI, YM, TT, and TN executed the experiment; HI analyzed the data; HI, TF, AU, and TN drafted and edited the manuscript; TM, ST, and TN supervised the study. All authors reviewed and approved the final manuscript.

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# **Conflict of interest**

All authors have no conflict of interest in this study.

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