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ORIGINAL ARTICLE

Association between skeletal muscle quality assessed by phase angle, peak oxygen uptake and anaerobic threshold in male patients with coronary artery disease: a cross-sectional study

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Abstract

Objective: This study aimed to elucidate the relationship of phase angle (PhA) with peak oxygen uptake (VO_2) and anaerobic threshold (AT) in male patients with coronary artery disease (CAD).

Methods: In this cross-sectional study, male patients with CAD who had been treated with percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG) were included. At discharge, the PhA was measured using bioelectrical impedance analysis, and the peak VO_2 and AT were measured by cardiopulmonary exercise testing (CPET). A multiple linear regression model with peak VO_2 and AT as dependent variables was used to analyze their association with PhA. Covariates included age, skeletal muscle index, left ventricular ejection fraction, blood hemoglobin concentration, type of revascularization, geriatric nutritional risk index, and dosage of β-blockers.

Results: This study analyzed 90 patients. The results of our analysis showed that PhA was an independent related factor of peak VO_2 (b: 0.335, 95% confidence interval [CI]: 0.037–0.633, P-value: 0.028) and AT (b: 0.336, 95% CI: 0.007–0.664, P-value: 0.046), even after adjusting for covariates.

Conclusion: PhA was related factor of peak VO_2 and AT in male patients with CAD.

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Key words: phase angle; cardiopulmonary exercise testing; peak oxygen uptake; anaerobic threshold; coronary artery disease.

Introduction

In patients with coronary artery disease (CAD), peak oxygen uptake (peak VO_2) measured by cardiopulmonary exercise testing (CPET) is an independent predictive factor of all-cause and cardiovascular mortality[1]. Thus, a primary goal of cardiac rehabilitation (CR) for patients with CAD is to improve their peak VO_2.

Physiological factors that determine peak VO_2 have been summarized by Fick's equation: Peak VO_2 = stroke volume × heart rate (HR) × arteriovenous oxygen content difference (c(A-V)O_2 diff)[2]. The c(A-V)O_2 diff is associated with skeletal muscle mass[3, 4]. However, the skeletal muscle mass exhibits only slight changes over a short period of time[5], making it difficult to adequately assess the effects of short-term

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exercise intervention. Meanwhile, c(A-V)O_2 diff can be influenced by the quality of skeletal muscle. Muscle quality, more responsive to short-term changes than muscle mass[5], can be non-invasively assessed using phase angle (PhA) through bioelectrical impedance analysis (BIA)[6]. Previous studies have suggested a relationship between decreased muscle quality, resulting from structural changes in muscles due to accumulation of intramuscular fat[7, 8], which results in reduced muscle output[9, 10], and decreased peak VO_2 independently of the skeletal muscle mass[11]. Positive associations between PhA and peak VO_2 have been found in diverse populations, including children and adolescents[12], adults with obesity[13], and patients with human immunodeficiency virus[14]. Despite this, no studies have explored the relationship between PhA and exercise tolerance in patients with CAD.

Elucidation of the association between PhA and exercise tolerance in patients with CAD may contribute to selecting effective exercise therapy programs aimed at improving exercise tolerance and evaluating their efficacy. Therefore, the present study aimed to elucidate the relationship of skeletal muscle quality, as assessed by PhA, with peak VO_2 and anaerobic threshold (AT), as measured by CPET, in patients with CAD.

Materials and Methods

This was a cross-sectional study of patients with CAD who had been admitted to Iwate Prefectural Central Hospital (which is the affiliation of the first author) and had undergone CR from July 2017 to December 2022. The inclusion criterion was patients who had undergone CPET and BIA at the time of discharge. The exclusion criteria were as follows: (1) female sex; (2) presence of a bone/joint or neurological disease that limits the implementation of CPET; (3) presence of a respiratory disease affecting the results of CPET; (4) history of dialysis; (5) presence of a cognitive dysfunction or mental illness that hinders communication; (6) history of implantation for pacemaker, implantable cardioverter defibrillator; (7) history of surgery for artificial joint replacement; (8) history of combined heart valve surgery; (9) gas exchange ratio (peak respiratory exchange ratio [RER]) <1.10 or a Borg scale score <17 during exercise load[15]; and (10) difficulty in identifying the AT.

Data collection

We collected demographic data for the following parameters: age; body mass index (BMI); diagnosis; type of revascularization (percutaneous coronary intervention [PCI]); off-pump coronary artery bypass grafting (off-pump CABG) or on-pump CABG; acuity (emergency or non-emergency revascularization); number of days from revascularization to assessment; smoking history; and history of hypertension, dyslipidemia, diabetes mellitus, atrial fibrillation, and heart failure. Additionally, the following information was collected from the records obtained at the closest date from BIA and CPET assessments: echocardiographic parameters (left ventricular ejection fraction [LVEF] and E/e'), laboratory data (blood hemoglobin [Hb] concentration, serum creatinine [Cre], and estimated glomerular filtration rate [eGFR]), nutritional status [Geriatric Nutritional Risk Index (GNRI)], and medication status (β-blockers, angiotensin-converting enzyme inhibitor-angiotensin II receptor blocker, and diuretics).

Body composition

Body composition was measured using a body composition analyzer (InBody S10; InBody, Tokyo, Japan) immediately before CPET. At the analysis, the participants were asked to rest in

the standing position for 5 min. During the body composition analysis, the participants were instructed to stand with both shoulders abducted at a 15° angle from the trunk and with feet placed approximately shoulder-width apart. Eight electrodes were placed between both hands (thumb and middle finger), ankle bones, and heels.

PhA, which was obtained as an index of skeletal muscle quality, is defined as the angle formed by the reactance (Xc), which reflects the capacitance of the cell membrane and the cell size, and the resistance (R), which reflects the conductivity through the ionic solution. Thus, the PhA increases with higher structural integrity of the cell and higher physiological function[16]. PhA was defined by the following formula: PhA (°) = arctangent (Xc) / (R)) × (180/π). The PhA was calculated using Xc and R at 50 kHz. As indicators of skeletal muscle mass, data on appendicular skeletal muscle mass (ASM) and skeletal muscle index (SMI) were collected. ASM represents the total skeletal muscle mass of the limbs and can be converted to SMI by dividing it by the square of the height (kg/m^2).

Cardiopulmonary exercise testing

For CPET, a cycle ergometer (Strength Ergo 8 BK-ERG-121; Mitsubishi Electric Engineering Co., Ltd., Tokyo, Japan) and an expiration gas analyzer (Aero Monitor AE-310; Minato Medical Science Co., Ltd., Osaka, Japan) were used. The exercise protocol comprised 2 min of rest on the ergometer, 4 min of warm-up (10 W, 60 rpm), and ramp exercise loading (10–15 W/min). Discontinuation criteria for CPET were as follows: discontinuation requested by patient, occurrence of abnormal physiological responses, Borg scale score ≥17, and achievement of maximum workload[15]. Peak VO_2 was defined as the highest VO_2 value during CPET, with a peak RER of ≥1.10[15]. AT was defined as the value synthetically determined from the gas exchange standard and V-slope analysis (VCO_2-VO_2 plot) at the time point where the equivalent ventilation increased non-linearly[17]. The obtained VO_2 values were smoothed using a 9-breath moving average[18] and corrected for body weight. CPET and BIA were conducted by different examiners.

Statistical analysis

The Shapiro–Wilk test was used to confirm the normal distribution of each variable. Categorical data are expressed as percentages. Normally distributed data are expressed as mean ± standard deviation, and non-normally distributed data are expressed as median and interquartile range (IQR). In addition, a multiple linear regression model was used to analyze the relationship of PhA with peak VO_2 and AT. The covariates selected were age, SMI, LVEF, blood Hb concentration, type of revascularization (CABG or PCI), GNRI, and dosage of β-blockers. These were selected as explanatory variables, which were considered important in relation to peak VO_2 and AT based on previous studies and clinical considerations. Multicollinearity was assessed using the variance inflation factor (VIF). Moreover, Pearson's correlation coefficient was calculated to examine the association of PhA with peak VO_2 and AT according to type of revascularization and acuity. All statistical analyses were performed using R ver. 4.2.1 (R Software for Statistical Computing, Vienna, Austria), and the significance level was set at 5%.

Ethical consideration

This study was approved by the Ethics Review Board of Iwate Prefectural Central Hospital (approval number: 1350) and the Ethics Review Board of Hirosaki University Graduate School of Health Sciences (approval number: 2022-033), and consent was obtained using an opt-out method. This study was conducted in accordance with the ethical guidelines of the Declaration of Helsinki.

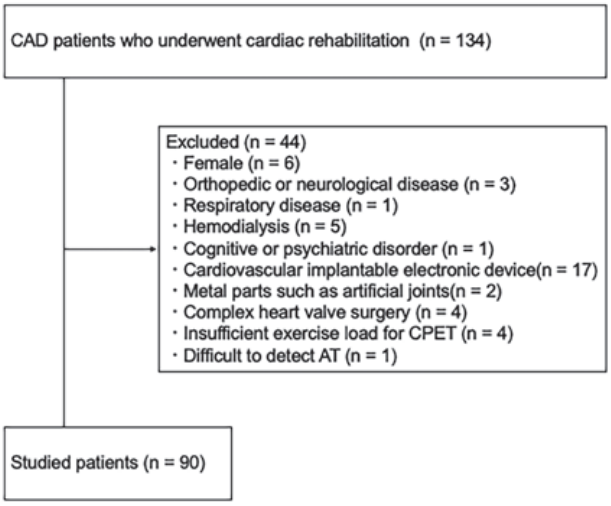

Figure 1 Flow chart of the study population.
AT, anaerobic threshold; BIA, bioelectrical impedance analysis; CAD, coronary artery disease; CPET, cardiopulmonary exercise test; n, number of patients; VO_2, oxygen uptake.

Results

Participants

Of the 134 eligible patients, female participants (n=6) as well as those with a bone/joint or neurological disease that limited the implementation of CPET (n=3), the one with a respiratory disease affecting the results of CPET (n=1), those undergoing dialysis (n=5), the one with history of cognitive dysfunction or mental illness that hinders communication (n=1), those with history of implantation for pacemaker, implantable cardioverter defibrillator contraindicated for BIA (n=17), those with history of surgery for artificial joint replacement affecting the results of BIA (n=2), those with history of combined heart valve surgery (n=4), those with insufficient exercise load (n=4), and the one with difficulty in identifying AT (n=1) were excluded. Finally, 90 patients were included (Figure 1).

Demographic characteristics

Table 1 summarizes the patient's characteristics. The mean age of the patients was 61.5±10.0 years and mean BMI was 25.4±3.3 kg/m^2. There were 41 (46%) and 79 (88%) patients with diabetes mellitus and dyslipidemia, and 83 (92%) patients were receiving β-blockers (92%). There were 57 (63%), 11 (12%), and 22 (24%) patients who had undergone PCI, CABG, and on-pump CABG, respectively. The mean LVEF was 51.8±9.5%. PhA, according to the histogram, exhibited a normal distribution with a mean of 5.68±0.88° (Figure 2). Regarding indices of skeletal muscle mass, the patients had a median ASM of 29.2 (IQR: 26.2–32.2) kg and a mean SMI of 8.07±0.92 kg/m^2. They had a mean peak VO_2 of 15.5±4.0 mL/min/kg and a mean AT of 10.4±2.3 mL/min/kg. In CPET, the median peak RER was 1.15 (IQR: 1.13–1.17), confirming the application of sufficient exercise load. Moreover, reasons for CPET discontinuation were insufficient rotation speed owing to lower limb fatigue and a Borg scale score ≥17, with no occurrence of arrhythmia or abnormal vital signs.

Association of PhA with peak VO_2 and AT

Table 2 shows the results of the multiple linear regression model analysis. The minimum and maximum VIF values were 1.073 and 2.792, respectively, indicating no problem of

Table 1. Patient characteristics

	Total (n=90)
Age, years	61.5 ± 10.0
Height, cm	168.4 [164.0-171.0]
Weight, kg	71.3 [63.9-76.9]
Body mass index, kg/m^2	25.4 ± 3.3
Days from revascularization to assessment	12 [8-17]
Co-morbidity, n (%)	
Hypertension	69 (77)
Diabetes mellitus	41 (46)
Dyslipidemia	79 (88)
Atrial fibrillation	4 (4)
Smoking history	68 (76)
History of heart failure	13 (14)
Diagnosis	
AMI	50 (56)
UAP	14 (16)
EAP	26 (29)
Type of revascularization, n (%)	
PCI	57 (63)
Off-pump CABG	11 (12)
On-pump CABG	22 (24)
Acuity, n (%)	
Emergency CABG	3 (3)
Non-emergency CABG	30 (33)
Emergency PCI	55 (61)
Non-emergency PCI	2 (2)
Intraoperative and postoperative variables in CABG	
Operation time, min	336.4 ± 65.7
Bleeding, mL	333.0 [295.0-371.0]
Cardiopulmonary bypass time, min	115.0 [0-153.0]
Mechanical ventilation time, min	2875.0 [1475.0-5539.0]
Length of ICU stay, day	4.0 [3.0-6.0]
Medication, n (%)	
β-blockers	83 (92)
ACE-I or ARB	62 (69)
Diuretics	8 (9)
β-blockers, mg/day	5 [2.5-5.0]
Echocardiographical measurements	
LVEF, %	51.8 ± 9.5
E/e'	10.1 [8.2-12.5]
Blood examination	
Blood Hb concentration, g/dL	12.8 [11.3-14.2]
Serum creatinine, mg/dL	0.92 [0.79-1.06]
eGFR, mL/min/1.73m^2	66.2 ± 17.1
GNRI, points	93.8 ± 7.8
Body composition	
ASM, kg	29.2 [26.2-32.2]
SMI, kg/m^2	8.07 ± 0.92
PhA, °	5.68 ± 0.88
Cardiopulmonary exercise testing	
Peak VO^2, mL/min/kg	15.5 ± 4.0
AT, mL/min/kg	10.4 ± 2.3
Peak RER	1.15 [1.13-1.17]

Values are presented as means (standard deviations), medians [interquartile ranges], or n (%). AMI, acute myocardial infarction; ACE-I, angiotensin-converting enzyme inhibitor; ASM, appendicular skeletal muscle; ARB, angiotensin II receptor blocker; AT, anaerobic threshold; CABG, coronary artery bypass graft; e', mitral annular early diastolic velocity; E, mitral early diastolic inflow velocity; EAP, effort angina pectoris; eGFR, estimated glomerular filtration rate; GNRI, geriatric nutritional risk index; HR, heart rate; Hb, hemoglobin; ICU, intensive care unit; LVEF, left ventricular ejection fraction; PCI, percutaneous coronary intervention; PhA, phase angle; RER, respiratory exchange ratio; SMI, skeletal muscle mass index; UAP, unstable angina pectoris; VO_2, oxygen uptake.

multicollinearity[19]. The results of the multivariate analysis showed that PhA was an independent related factor of peak VO_2 (b: 0.335, 95% CI: 0.037–0.633, P-value: 0.028) and AT (b: 0.336, 95% CI: 0.007–0.664, P-value: 0.046).

Association of PhA with peak VO_2 and AT by type of revascularization and acuity

Figure 3 shows the correlation of PhA with peak VO_2 and AT by type of revascularization and acuity. When analyzed by type of

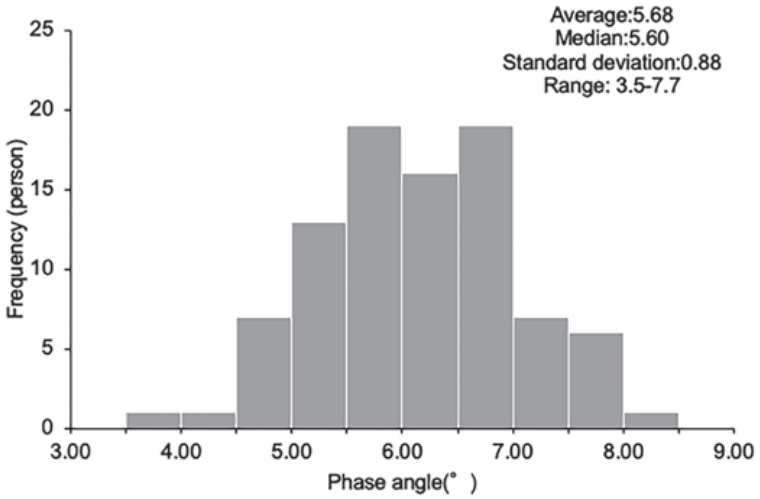

Figure 2 Distribution of phase angle in the study population.

Table 2. Multiple linear regression model with peak VO_2 and AT as dependent variables

Dependent variables	Independent variables	B	b	95%CI (lower, upper)	P-value	VIF
Peak VO_2 (mL/min/kg)	PhA, °	1.505	0.335	(0.037, 0.633)	0.028	2.792
	Age, years	−0.100	−0.255	(−0.196, −0.003)	0.042	1.903
	SMI, kg/m^2	−0.750	−0.177	(−0.395, 0.041)	0.110	1.490
	GNRI, points	−0.040	−0.078	(−0.346, 0.190)	0.563	2.261
	Blood Hb concentration, g/dL	0.403	0.182	(−0.111, 0.474)	0.221	2.698
	LVEF, %	0.059	0.144	(−0.041, 0.328)	0.125	1.073
	β-blockers, mg/day	−0.177	−0.139	(−0.324, 0.046)	0.140	1.079
	CABG	1.196	0.148	(−0.129, 0.425)	0.291	2.417
AT (mL/min/kg)	PhA, °	0.876	0.336	(0.007, 0.664)	0.046	2.792
	Age, years	−0.020	−0.087	(−0.359, 0.184)	0.523	1.904
	SMI, kg/m^2	−0.642	−0.260	(−0.500, −0.020)	0.034	1.491
	GNRI, points	−0.006	−0.019	(−0.315, 0.276)	0.898	2.261
	Blood Hb concentration, g/dL	0.238	0.185	(−0.139, 0.508)	0.259	2.698
	LVEF, %	0.027	0.113	(−0.090, 0.317)	0.272	1.073
	β-blockers, mg/day	−0.052	−0.107	(−0.311, 0.098)	0.302	1.079
	CABG	0.269	0.057	(−0.248, 0.363)	0.710	2.417

b, standardized partial regression coefficient; B, partial regression coefficient; CI, confidence interval; VIF, multicollinearity diagnosis; AT, anaerobic threshold; CABG, coronary artery bypass graft; GNRI, geriatric nutritional risk index; Hb, hemoglobin; LVEF, left ventricular ejection fraction; PhA, phase angle; SMI, skeletal muscle mass index; VO_2, oxygen uptake.

revascularization, a significant positive correlation was found between PhA and peak VO_2 in patients treated with PCI (P=0.007, r=0.356) and those with CABG (P=0.006, r=0.471) (Figure 3a). A significant positive correlation was also found between PhA and AT in patients treated with CABG (P=0.040, r=0.359), but the correlation was not observed in patients treated with PCI (P=0.145, r=0.196) (Figure 3b). When analyzed by acuity, a significant positive correlation was found between PhA and peak VO_2 in patients who had undergone emergency revascularization (P<0.001, r=0.446) and those who had undergone non-emergency revascularization (P=0.010, r=0.447) (Figure 3c). A significant positive correlation was also found between PhA and AT in patients who had undergone emergency revascularization (P=0.019, r=0.306), but the correlation was not observed in those who had undergone non-emergency revascularization (P=0.069, r=0.325) (Figure 3d).

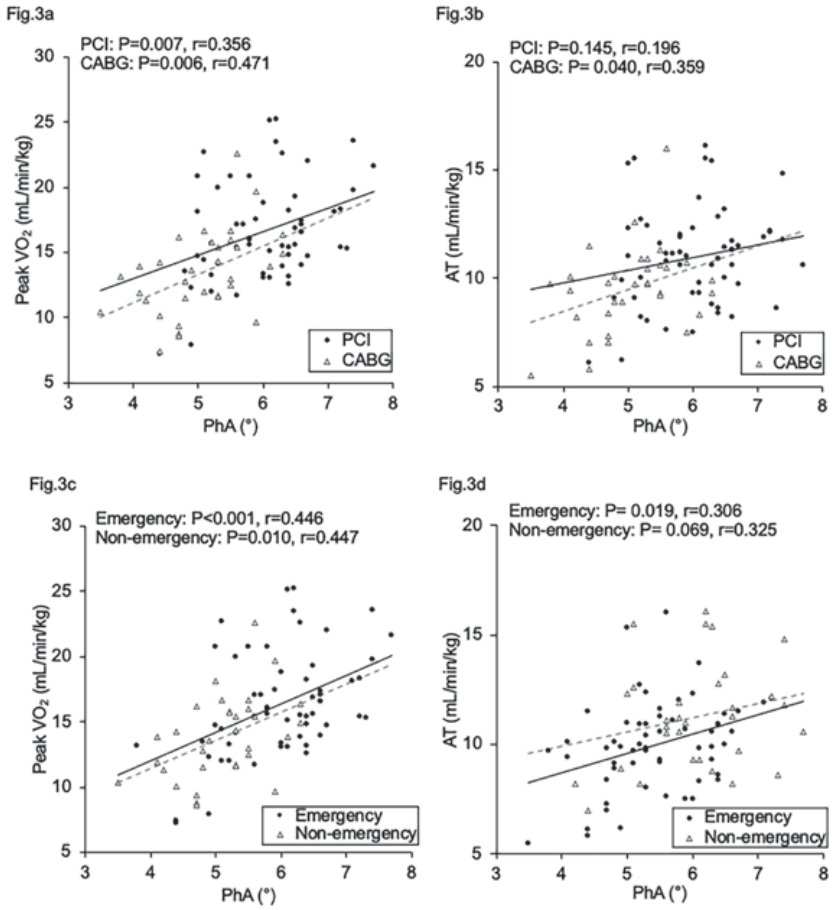

Figure 3 Correlative relationship of PhA with peak VO_2 and AT by type of revascularization and acuity
Simple linear regression is shown as dashed line in CABG and continuous line in PCI. (Figure 3a and 3b). Simple linear regression is shown as dashed line in non-emergency revascularization and continuous line in emergency revascularization. (Figure 3c and 3d).
AT, anaerobic threshold; CABG, coronary artery bypass graft; PCI, percutaneous coronary intervention; PhA, phase angle; VO_2, oxygen uptake.

Discussion

To our best knowledge, this study is the first to show that PhA is an independent related factor of peak VO_2 and AT in male patients with CAD. The results of this study suggest that improving the quality of skeletal muscle as indicated by PhA contributes to improvement in exercise tolerance in patients with CAD. Therefore, PhA is a useful index for developing appropriate exercise prescriptions aimed at improving exercise tolerance and determining the efficacy of exercise therapy.

The results of multivariate analysis showed that PhA was independently related to peak VO_2 and AT, even after adjusting for known covariates. PhA reflects infiltration of fat into the skeletal muscle[20], and infiltration of fat into muscle tissue reduces perfused oxygen supply[7]. Thus, PhA is associated with muscle output per unit mass of skeletal muscle[21], which is an index of skeletal muscle quality. Moreover, PhA reflects both the quality and quantity of skeletal muscle[22], making it a potentially more comprehensive indicator of muscle function compared to the more limited SMI.

Interestingly, the correlation between PhA and AT varies based on the type of revascularization

and its acuity. Compared to PCI, CABG tends to cause skeletal muscle disorders owing to increased catabolism resulting from surgical invasion[23] and delayed ambulation[24] and leads to a higher degree of deterioration in cardiopulmonary function because of surgical invasion[25]. In contrast, PCI is generally characterized by milder skeletal muscle dysfunction and improved cardiorespiratory function than CABG due to allowing for earlier ambulation and releases myocardial ischemia. In addition, patients can be treated in a more stable state with non-emergency revascularization than with emergency revascularization, often resulting in a more stable postoperative state[26]. Therefore, the influence of PhA on AT might have been relatively strong in patients who had undergone CABG or emergency revascularization, in whom decreased muscle function cannot be compensated for by cardiopulmonary function. In contrast, PhA was positively correlated to peak VO_2 regardless of the type of revascularization or acuity. In this study, the reason for all CPET discontinuations was a lower limb fatigue, and the patients had achieved R ≥1.10 at the end of CPET. Therefore, the present study could determine the overall sub-maximum value of cardiopulmonary and muscular function with sufficient exercise load, and we observed a significant positive correlation between peak VO_2 and PhA.

Our findings suggest the usefulness of PhA as an index for determining the efficacy of exercise therapy. PhA responds to exercise intervention and discontinuation more quickly than does skeletal muscle mass[27]. Thus, PhA, which can repeatedly determine the efficacy of exercise therapy over a short period of time, may serve as a useful objective index of exercise tolerance and skeletal muscle quality. Furthermore, our findings may contribute to selection of effective exercise programs for patients with CAD. In this study, PhA was found to have a significant positive correlation with peak VO_2, regardless of the type of revascularization or acuity, but its significant relationship with AT was not observed in patients who had undergone PCI or non-emergency revascularization. Therefore, depending on the patient's characteristics, an exercise program aimed at improving skeletal muscle mass and/or cardiorespiratory function may contribute more to improving exercise tolerance than an exercise program aimed at improving muscle quality.

This study has three limitations. First, as this was a cross-sectional study, the causal relationship between improvements in skeletal muscle quality and improvements in peak VO_2 and AT was unclear. However, our findings indicating a certain association between skeletal muscle quality and exercise tolerance are important as they may contribute to the development of exercise therapy programs for patients with CAD. Second, as female individuals were excluded from the analysis, caution should be taken when interpreting the generalizability of the findings. Previous studies have shown that female individuals have lower skeletal muscle mass[28], pulmonary function[29], and PhA[30], which are determining factors of exercise tolerance, than male individuals. Therefore, studies related to exercise tolerance should ideally be analyzed separately for males and females, but this study had very few female participants; therefore, females were excluded. Third, it was unclear to what extent PhA reflected the quality of skeletal muscle in patients with CAD. Previous studies have shown that PhA was associated with skeletal muscle density, as assessed by computed tomography[31], and skeletal muscle echo-intensity, as measured by ultrasound[32]. Thus, to widely apply our findings, further assessments and examinations through histological analyses are needed.

Conclusion

PhA, an index of skeletal muscle quality, was

found to be independently associated with peak VO_2 and AT in male patients with CAD. Our findings may contribute to the development of appropriate exercise prescriptions aimed at improving exercise tolerance and indices for determining the efficacy of exercise therapy.

Disclosure statement

The authors declare that they have no conflict of interest.

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References

1) Keteyian SJ, Brawner CA, Savage PD, Ehrman JK, Schairer J, Divine G, Aldred H, et al. Peak aerobic capacity predicts prognosis in patients with coronary heart disease. Am Heart J. 2008;156:292-300.

2) Poole DC, Hirai DM, Copp SW, Musch TI. Muscle oxygen transport and utilization in heart failure: implications for exercise (in) tolerance. Am J Physiol Heart Circ Physiol. 2012;302:H1050-H1063.

3) Haykowsky MJ, Brubaker PH, Stewart KP, Morgan TM, Eggebeen J, Kitzman DW. Effect of endurance training on the determinants of peak exercise oxygen consumption in elderly patients with stable compensated heart failure and preserved ejection fraction. J Am Coll Cardiol. 2012;60:120-8.

4) Haykowsky MJ, Brubaker PH, Morgan TM, Kritchevsky S, Eggebeen J, Kitzman DW. Impaired aerobic capacity and physical functional performance in older heart failure patients with preserved ejection fraction: role of lean body mass. J Gerontol A Biol Sci Med Sci. 2013;68:968-75.

5) Taaffe DR, Henwood TR, Nalls MA, Walker DG, Lang TF, Harris TB. Alterations in muscle attenuation following detraining and retraining in resistance-trained older adults. Gerontology. 2009;55:217-23.

6) Kyle UG, Bosaeus I, De Lorenzo AD, Deurenberg P, Elia M, Gomez JM, Heitmann BL, et al. Bioelectrical impedance analysis-part II: utilization in clinical practice. Clin Nutr. 2004;23:1430-53.

7) Kitzman DW, Brubaker P, Morgan T, Haykowsky M, Hundley G, Kraus WE, Eggebeen J, et al. Effect of caloric restriction or aerobic exercise training on peak oxygen consumption and quality of life in obese older patients with heart failure with preserved ejection fraction: a randomized clinical Trial. JAMA. 2016;315:36-46.

8) Heinonen I, Bucci M, Kemppainen J, Knuuti J, Nuutila P, Boushel R, Kalliokoski KK. Regulation of subcutaneous adipose tissue blood flow during exercise in humans. J Appl Physiol (1985). 2012;112:1059-63.

9) Kent-Braun JA, Ng AV, Young K. Skeletal muscle contractile and noncontractile components in young and older women and men. J Appl Physiol (1985). 2000;88:662-8.

10) Goodpaster BH, Carlson CL, Visser M, Kelley DE, Scherzinger A, Harris TB, Stamm E, et al. Attenuation of skeletal muscle and strength in the elderly: The Health ABC Study. J Appl Physiol (1985). 2001;90:2157-65.

11) Haykowsky M, Kouba EJ, Brubaker PH, Nicklas BJ, Eggebeen J, Kitzman DW. Skeletal muscle composition and its relation to exercise intolerance in older patients with heart failure and preserved ejection fraction. Am J Cardiol. 2014;113:1211-6.

12) Langer RD, da Costa KG, Bortolotti H, Fernandes GA, de Jesus RS, Gonçalves EM. Phase angle is associated with cardiorespiratory fitness and body composition in children aged between 9 and 11 years. Physiol Behav. 2020;215:112772.

13) Streb AR, Hansen F, Gabiatti MP, Tozetto WR, Del Duca GF. Phase angle associated with different indicators of health-related physical fitness in adults with obesity. Physiol Behav. 2020;225:113104.

14) Martins PC, de Lima LRA, Silva AM, Petroski EL,

Moreno YMF, Silva DAS. Phase angle is associated with the physical fitness of HIV-infected children and adolescents. Scand J Med Sci Sports. 2019;29:1006-12.

15) Balady GJ, Arena R, Sietsema K, Myers J, Coke L, Fletcher GF, Forman D, et al. Clinician's guide to cardiopulmonary exercise testing in adults: a scientific statement from the American Heart Association. Circulation. 2010;122:191-225.

16) Norman K, Stobaus N, Pirlich M, Bosy-Westphal A. Bioelectrical phase angle and impedance vector analysis-clinical relevance and applicability of impedance parameters. Clin Nutr. 2012;31:854-61.

17) Yasuda S, Nakao K, Nishimura K, Miyamoto Y, Sumita Y, Shishido T, Anzai T, et al. The current status of cardiovascular medicine in Japan: Analysis of a large number of health records from a nationwide claim-based database, JROAD-DPC. Circ J. 2016;80:2327-35.

18) Nakao K, Yasuda S, Nishimura K, Noguchi T, Nakai M, Miyamoto Y, Sumita Y, et al. Prescription rates of guideline-directed medications are associated with in-hospital mortality among Japanese patients with acute myocardial infarction: A report From JROAD-DPC Study. J Am Heart Assoc. 2019;8: e009692.

19) Poole DC, Musch TI. Capillary-mitochondrial oxygen transport in muscle: Paradigm shifts. Function (Oxf). 2023;4:zqad013.

20) Kato M, Okada Y, Nakano W, Takagi D, Ochi M, Ohyagi Y, Igase M, et al. Bioimpedance phase angle is independently associated with myosteatosis: The Shizuoka study. Clin Nutr. 2023;42:793-9.

21) Cunha PM, Tomeleri CM, Nascimento MA, Nunes JP, Antunes M, Nabuco HCG, Quadros Y, et al. Improvement of cellular health indicators and muscle quality in older women with different resistance training volumes. J Sports Sci. 2018;36: 2843-8.

22) Akamatsu Y, Kusakabe T, Arai H, Yamamoto Y, Nakano K, Ikeue K, Ishihara Y, et al. Phase angle from bioelectrical impedance analysis is a useful indicator of muscle quality. J Cachexia Sarcopenia Muscle. 2022;13:180-9.

23) Iida Y, Yamazaki T, Kawabe T, Usui A, Yamada S. Postoperative muscle proteolysis affects systemic muscle weakness in patients undergoing cardiac surgery. Int J Cardiol. 2014;172:595-7.

24) Tsuchikawa Y, Tokuda Y, Ito H, Shimizu M, Tanaka S, Nishida K, Takagi D, et al. Impact of early ambulation on the prognosis of coronary artery bypass grafting patients. Circ J. 2023;87: 306-11.

25) Jelinek HF, Huang ZQ, Khandoker AH, Chang D, Kiat H. Cardiac rehabilitation outcomes following a 6-week program of PCI and CABG patients. Front Physiol. 2013;4:302.

26) Kurki TS, Kataja M, Reich DL. Emergency and elective coronary artery bypass grafting: comparisons of risk profiles, postoperative outcomes, and resource requirements. J Cardiothorac Vasc Anesth. 2003;17:594-7.

27) Dos Santos L, Cyrino ES, Antunes M, Santos DA, Sardinha LB. Changes in phase angle and body composition induced by resistance training in older women. Eur J Clin Nutr. 2016;70:1408-13.

28) Chen LK, Woo J, Assantachai P, Auyeung TW, Chou MY, Iijima K, Jang HC, et al. Asian Working Group for Sarcopenia: 2019 consensus update on sarcopenia diagnosis and treatment. J Am Med Dir Assoc. 2020;21:300-7.

29) Chen HI, Kuo CS. Relationship between respiratory muscle function and age, sex, and other factors. J Appl Physiol. 1989;66:943-8.

30) Bosy-Westphal A, Danielzik S, Dörhöfer RP, Later W, Wiese S, Müller MJ. Phase angle from bioelectrical impedance analysis: Population reference values by age, sex, and body mass index. JPEN J Parenter Enteral. Nutr. 2006;30: 309-16.

31) Looijaard WGPM, Stapel SN, Dekker IM, Rusticus H, Remmelzwaal S, Girbes ARJ, Weijs PJM, et al. Identifying critically ill patients with low muscle mass: Agreement between bioelectrical impedance analysis and computed tomography. Clin Nutr. 2020;39:1809-17.

32) Primo D, Izaola O, Gomez JJL, Luis de D. Correlation of the phase angle with muscle ultrasound and quality of life in obese females. Dis Markers. 2022;7165126.