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Original Article

Knee extensor muscle strength as a predictor of peak oxygen uptake in patients with heart disease

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Abstract. [Purpose] The mortality rate increases when peak oxygen uptake is less than 5 metabolic equivalents, and peak oxygen uptake correlates with knee extensor muscle strength. This study aimed to determine the knee extensor muscle strength at peak oxygen uptake corresponding to 5 metabolic equivalents. [Participants and Methods] We enrolled 45 consecutive patients (29 males and 16 females; average age, 63.6 ± 13.7 years) with heart disease receiving outpatient rehabilitation with us. We performed cardiopulmonary exercise testing with a bicycle ergometer to measure peak oxygen uptake. We investigated the relationship between peak oxygen uptake and isometric knee extensor muscle strength divided by the body weight (kgf/kg). The cutoff value for knee extensor muscle strength with peak oxygen uptake corresponding to 5 metabolic equivalents was calculated. [Results] Knee extensor muscle strength was significantly positively associated with peak oxygen uptake. The cutoff value for knee extensor muscle strength at peak oxygen uptake corresponding to 5 metabolic equivalents was 0.46 kgf/kg. [Conclusion] In this study, the cutoff value for knee extensor muscle strength for achieving peak oxygen uptake corresponding to 5 metabolic equivalents in patients with heart disease was 0.46kgf/kg.
Key words: Heart disease, Peak oxygen uptake, Knee extensor muscle strength

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INTRODUCTION

Heart disease patients with a peak oxygen uptake (Peak VO_2) of less than 5 metabolic equivalents (METs) are classified in the moderate risk group[1)]. In addition, it has been reported that the mortality increases when Peak VO_2 becomes 5 METs or less in both heart disease patients and healthy individuals, and the knee extensor muscle strength (KEMS) is correlated with Peak VO_2 and related to all cause of deaths and cardiac death[2–6)]. However, there are few reports that set the target value of KEMS where Peak VO_2 is at the 5 METs, and there are no reports that have used cardiopulmonary exercise testing (CPX) with a bicycle ergometer.

In the present study, we investigated the relationship between KEMS and Peak VO_2 measured by CPX with a bicycle ergometer in patients with heart disease, and we determined the cutoff value of KEMS equivalent to a Peak VO_2 at the 5 METs.

PARTICIPANTS AND METHODS

We conducted a retrospective and cross-sectional study. Patients who underwent cardiac rehabilitation in the outpatient rehabilitation department after being admitted to our hospital due to acute myocardial infarction, unstable angina pectoris, or

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acute exacerbation of chronic heart failure were examined. Exclusion criteria were patients who could not perform evaluation of motor function and laboratory examination during the month before or after the day of CPX; patients who performed CPX using a treadmill; patients who did not properly perform CPX (Respiratory Quotient (R) at rest is 0.7 or less or 1.0 or more, VO_2 at rest is less than 200 mL/min or 500 mL/min or more, R at Peak VO_2 is less than 1.10) ; patients with CPX discontinued due to ischemic attack; patients with complications of arteriosclerosis obliterans of Fontaine II to IV. From June 9, 2017 to November 30, 2017, out of 68 consecutive patients, 45 were enrolled in this study (29 males, 16 females, average age 63.6 ± 13.7 years, average height 161.3 ± 9.1 cm, average weight 60.4 ± 12.0 kg).

Based on the Declaration of Helsinki, data extraction and analysis were conducted so that individuals can't be identified. There is no invasion or intervention in this study. Based on the guidelines of Ministry of Health, Labor and Welfare in Japan, the information and informed consent on the research is disclosed on our homepage and approved by the ethics committee of Aso Iizuka Hospital (Fukuoka, Japan). The approved number of this study was 17179, and the approved date of this study was December 18, 2016.

Measurement of KEMS was performed by a standardized method using a handheld dynamometer (μTas F-1, Anima Co. Ltd., Tokyo, Japan), following the instructions of Anima Co., Ltd[7]. We attached a dynamometer to the legs of the bench. The patient sat on the bench and the knee joint and hip joint were bent 90 degrees and the dynamometer was fixed to the distal part of his lower leg. Maximum isometric KEMS was measured three times for both lower limbs. The maximum values of the left and right muscular strengths were measured. The right and left KEMS values were averaged and divided by body weight (unit: kgf/kg). We measured CPX using a bicycle ergometer (BK-ERG-121, Fukuda Denshi Co., Ltd., Tokyo, Japan) and expiration gas analysis (Cpex-1, Inter Reha Co. Ltd., Tokyo, Japan). After resting for 1 minute, warm-up was carried out at 0W and the pedal rotation number was 50 rpm for 4 minutes, then loading was gradually increased with a ramp load. We extracted Peak VO_2 and ventilation efficiency (VE/VCO_2 slope).

We extracted the following variables from our hospital medical records, using the variables that were most recent to CPX. We extracted age, male or female, height, weight and body mass index (BMI) as background factors.

We conducted multiple regression analysis with Peak METs as the objective variable, KEMS as the explanatory variable, and age, gender and VE/VCO_2 slope as the adjustment variables. In addition to the KEMS, we selected variables as explanatory variables that were related to Peak VO_2 and KEMS, and that were not intermediate variables. Receiver operating characteristic (ROC) analysis was conducted to determine the optimal cutoff value of KEMS where Peak VO_2 is at the 5METs. The optimal cutoff value was obtained from the Youden index [maximum (sensitivity + specificity −1)]. Stata version 14.2 (Statacorp LLC) was used as analysis software. The statistical significance level was set at 5%, and it was assumed that there was a significant difference when $p<0.05$.

RESULTS

The clinical characteristics of the overall participants are presented in Table 1. The ratio of the ischemic heart disease patients and non-ischemic heart disease patients were almost the same. Median of KEMS was 0.53 kgf/kg. Median of Peak METs was 5.3 METs which was nearly the same as the target value in this study.

Table 2 shows the results of the multiple regression analysis on association between KEMS and Peak METs. After adjusting for all the adjustment variables, KEMS was significantly positively associated with Peak METs (R^2=0.68, adjusted R^2=0.64, Mean VIF=1.49).

We created the ROC curve for KEMS as a predictor of Peak VO_2 at the 5 METs. The area under the curve was 0.86. The cutoff value of KEMS with Peak VO_2 at the 5METs was 0.46 kgf/kg. The sensitivity was 92.86%, and the specificity was 76.47%, respectively.

Table 1. Clinical characteristics of participants

		Overall (n=45)
Age (years)		63.6 ± 13.7
Male (%)		29 (64.7)
Body Mass Index (kg/m^2)		16.6 ± 3.6
Underlying cause	Ischemic heart disease (%)	22 (48.9)
	Non-ischemic heart disease (%)	23 (51.1)
Motor function	Handgrip strength (kgf)	30.0 ± 9.9
	KEMS (kgf/kg)	0.53 ± 0.2
Cardiopulmonary exercise testing	Peak oxygen uptake (METs)	5.3 ± 1.6
	VE/VCO_2 slope (l/min / ml/min)	30.3 ± 5.8

Table 2. Multiple regression analysis with peak oxygen uptake with peak oxygen uptake as the objective variable

Explanatory factor	Regression coefficient	Standard error	t value	95% Confidence interval		p value	VIF
				Lower limit	Upper limit		
KEMS	3.161	1.03	3.07	1.078	5.244	0.004	1.75
Age	−0.04	0.01	−3.29	−0.066	−0.016	0.002	1.44
Gender (Male)	0.557	0.35	1.58	−0.154	1.267	0.121	1.45
VE/VCO_2 slope	−0.063	0.03	−2.30	−0.119	−0.008	0.027	1.31

DISCUSSION

In the present study, the cutoff value of KEMS was 0.46 kgf/kg for acquiring Peak VO_2 at the 5 METs evaluated by CPX using a bicycle ergometer in patients with heart disease.

Reportedly, the grip strength is related to Peak VO_2[8, 9]. However, we selected the target value of KEMS as an indicator of lower limb muscular strength in our study because the lower limb muscle strength declines more rapidly than upper limb muscle strength with aging, and upper limb exercise activates the sympathetic nervous system more than lower limb exercise dose[10, 11]. The rise in VE/VCO_2 slope reflects a decrease in ventilation efficiency due to ventilatory blood flow ratio imbalance associated with heart failure, and a decrease in the skeletal muscle mass caused by heart failure and disuse after acute period treatment[12, 13]. The VE/VCO_2 slope also related to Peak VO_2 and KEMS[3–5], therefore, in the multiple regression analysis, we added VE/VCO_2 slope as a covariate variable. The results showed that KEMS was significantly related to Peak VO_2 and it was a predictor of Peak VO_2 with adjusted by age, gender and VE/VCO_2 slope.

In participants with ischemic heart disease of a previous study, using the treadmill CPX, the KEMS of 0.46 kgf/kg was indicated to acquire Peak VO_2 at the 5 METs[5]. Although CPX performed using a treadmill has a 5 to 10% higher in Peak VO_2 than that using a bicycle ergometer[14], the results of our study showed the same numerical values of KEMS. In another previous study, the cutoff value of KEMS for independent ADL was shown as 0.29 kgf/kg, and for walking independence as 0.30 kgf/kg or 0.3 to 0.4 kgf/kg were shown[15–17]. Since all participants in our study were capable of independent walking, the KEMS of 0.46 kgf/kg exceeded that of 0.29 to 0.40 kgf/kg. Kaneko et al. reported that the ratio of independent climbing stairs was 93% above 0.45 kgf/kg and 100% above 0.50 kgf/kg in elderly patients with internal disease[18]. These values were close to the results of our study. Thus, compared to the previous study, the cutoff value of KEMS was not overly contradictory.

Our study has several limitations. It was a retrospective and cross-sectional study; therefore, to investigate the causal relationship between Peak VO_2 and KEMS, it is necessary to conduct a cohort study. We weren't able to verify the disease specificity by subdividing heart disease, to verify by age difference and gender difference, or to compare the importance of KEMS with other exercise functions (grip strength etc.).

In conclusion, KEMS was significantly positively associated with Peak VO_2, and the cutoff value of KEMS was 0.46 kgf/kg for acquiring Peak VO_2 at the 5 METs in patients with heart disease. Therefore, KEMS was a predictor of Peak VO_2 at the 5 METs in patients with heart disease.

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Conflict of interest

The authors declare that there is no conflict of interest.

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