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Comparison of Predicted Exercise Capacity Equations in Adult Korean Subjects

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Disclosure
The authors have no potential conflicts of interest to disclose.

ABSTRACT

Background: Maximal oxygen uptake (VO_2 max) is a useful index to assess exercise capacity. However, there is no reference value for Koreans. This study aimed to compare actual VO_2 max and predicted VO_2 max using exercise capacity equations in Korean subjects.
Methods: This retrospective study enrolled 383 patients who underwent cardiopulmonary exercise test (CPET) with incremental maximal cycle ergometer test at Asan Medical Center from January 2020 to May 2021. Stage 1 and 2 lung cancer patients with normal lung function and healthy persons of 50 subjects who had maximal CPET were analyzed.
Results: The subjects were aged 65 ± 13 years and predominantly male (74%). CPET results were as follows: absolute VO_2 max, 1.2 ± 0.3 L/min; body weight referenced VO_2 max, 20 ± 3.9 mL/kg/min; peak work rate, 94 ± 24 watts; peak heart rate, 142 ± 21 bpm; peak O_2 pulse, 10 ± 3 mL/beat; minute ventilation, 59 ± 14 L/min; peak respiratory rate, 34 ± 6 breaths per minute; and peak breathing reserve, 41 ± 18%. There was significant discordance between the measured and predicted absolute VO_2 max using the Jones, Hansen, and Wasserman prediction equations developed for Caucasian population ($P < 0.001$). Agreement using Bland-Altman test between true and predicted absolute VO_2 max was the best in Chinese equation (−0.03, 2SD = 0.55) compared to Jones (0.42, 2SD = 1.07), Hansen (0.44, 2SD = 0.86), and Wasserman (0.42, 2SD = 0.86) equations.
Conclusion: The reference value and prediction equation from studies including primarily Caucasians may not be appropriate for Koreans. Since the mean difference is the lowest in Chinese equation, the Chinese equation might be used for the Korean adult population.

Keywords: VO_2 Max; Cardiopulmonary Exercise Test; Exercise Capacity Equation

INTRODUCTION

Cardiopulmonary exercise test (CPET) is a widely used tool to evaluate the physiological response associated with cardiopulmonary disease, and its clinical usefulness has recently been demonstrated in respiratory diseases.[1] Physiological responses of metabolic, cardiovascular, and ventilation systems that affect exercise ability can be evaluated by CPET, thus aiding in the diagnosis and treatment of patients. CPET is useful in the evaluation of the therapeutic effect and prognosis of respiratory diseases and in the diagnosis of dyspnea with unknown cause.

Author Contributions

Conceptualization: Lee JS, Jeong DH. Data curation: Oh YM, Lee SW, Lee SD. Formal analysis: Jeong DH. Investigation: Oh YM, Lee SW, Lee SD. Methodology: Lee JS, Jeong DH. Writing - original draft: Jeong DH. Writing - review & editing: Lee JS.

Maximal oxygen uptake (VO_2 max) is a useful index for the assessment of exercise capacity, as it can powerfully predict outcomes of cardiac and pulmonary disorders.[2-7] VO_2 max can be directly measured by CPET. Exercise capacity indicated by VO_2 max can help in estimating cardiopulmonary risk, thus making the selection of normal reference value essential for interpretation.[8]

Different race and countries have various reference values due to the influence of factors such as age, sex, physical activity, and ethnicity.[9] The American Thoracic Society/American College of Chest Physicians (ATS/ACCP) recommends selecting proper reference value that reflects the characteristics of the population. Most reference values and prediction equations are available for the Caucasians only.[10-13] In contrast, there are few reference values for the Asians[14-16] and no reference value of VO_2 max for Koreans. There are no reliable exercise capacity equations for VO_2 max applicable to Koreans. We therefore compared measured VO_2 max and predicted VO_2 max using exercise capacity equations.

METHODS

Study subjects

This retrospective study was performed between January 2020 and May 2021, including 383 patients who underwent CPET with incremental maximal cycle ergometer test at Asan Medical Center, a 2,700-bed tertiary care center in Korea. The study group primarily consisted of patients being evaluated for pre-operative risk of lung cancer or dyspnea. Of these 383 patients, we selected 29 stage 1 and 2 lung cancer patients with normal lung and cardiac function and 21 healthy subject who had maximal CPET (**Fig. 1**). Healthy subjects were tested for unexplained dyspnea, but had no underlying medical conditions and no abnormal findings on chest X-ray, electrocardiograph (ECG), spirometry, and CPET. Maximal

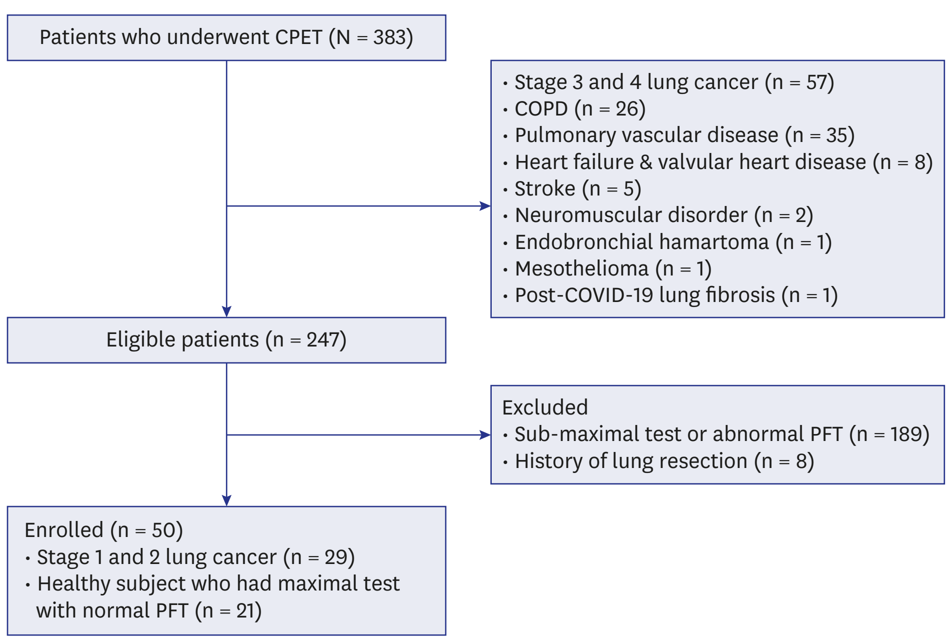

Fig. 1. The study flowchart.
CPET = cardiopulmonary exercise test, COPD = chronic obstructive pulmonary disease, COVID-19 = coronavirus disease 2019, PFT = pulmonary function test.

CPET was defined as the fulfillment of at least one of the following conditions: 1) Patients reached predicted VO_2 max (> 85% predicted), 2) patients achieved predicted maximal heart rate (> 90% predicted), 3) patients had evidence of ventilatory limitation (breathing reserve < 20%), or 4) patients exhaustion was observed (Borg scale rating 9–10). The exclusion criteria were as follows: (1) patients who had sub-maximal CPET; and (2) patients who had lung resection surgery. The physical activity extent was graded according to international physical activity questionnaire.[17]

CPET protocol

CPET were performed on graded exercise using incremental protocol with cycle ergometer (VIAsprint 150P; Carefusion, San Diego, CA, USA),[12] under physician's supervision with defined criteria for termination: ischemic ECG changes, fall in systolic pressure > 20 from peak during test, and severe desaturation. CPET had four stages: resting, warm-up, exercise, and recovery stage. In the resting stage, subjects rested for 2 minutes before the test. In the warm-up stage, we collected sufficient baseline data such as oxygen saturation, heart rate, blood pressures, ECG, and expired gas analysis. Subject performed unloaded pedaling at 30–40 rpm for 1 minute and 30 seconds. In the exercise stage, considering general condition or pulmonary function results, subjects performed maximal exercise with pedaling at 60 rpm while increasing the load to 5–15 watts/min. During exercise, Borg dyspnea scale was recorded for all subjects. The test was stopped on the subject's wishes or in case of an abnormal finding in medical monitoring. If the subject requested discontinuation of the test, the subject proceeds to the recovery stage. Finally, in the recovery stage, the subjects performed unloaded pedaling at 30–40 rpm for 2 minutes and we acquired physiologic data such as oxygen saturation, heart rate, blood pressures, and expired gas analysis until subject's heart rate is stable.

Predicted exercise capacity equations

VO_2 max was recalculated using different prediction equations. A detailed information of prediction equations is presented in **Table 1**.

Jones et al.[10][a]

$$VO_2\ (L/min) = 0.046 \times Height - 0.021 \times Age - 0.62 \times Sex - 4.31$$

Hansen et al.[11][b]

$$\text{Male: } VO_2\ (L/min) = Weight \times [50.75 - (0.37 \times Age)]/1{,}000$$
$$\text{Female: } VO_2\ (L/min) = (Weight + 43) \times [22.78 - (0.17 \times Age)]/1{,}000$$

Wasserman[12][c]

$$\text{Male: } VO_2\ (L/min) = Weight \times [50.72 - (0.372 \times Age)]/1{,}000$$
$$\text{Female: } VO_2\ (L/min) = (Weight + 42.8) \times [22.78 - (0.17 \times age)]/1{,}000$$

Table 1. Main characteristics of predicted exercise capacity equations

Authors (year)	Sample size (M/F)	Age, yr	Ethnic group	Equipment	Ref.
Jones et al. (1989)	50 M/50 F	15–71	Canadian	Cycle	10
Hansen et al. (1994)	77 M	34–74	American	Cycle	11
Wasserman (1999)	77 M	34–74	American	Cycle	12
Dun et al. (2021)	558 M/406 F	18–70	Chinese	Cycle	14

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Dun et al.[14][d]

$$VO_2\ (L/min) = (1{,}532.58 - 328.244 \times Sex - 9.951 \times Age + 11.593 \times Weight)/1{,}000$$

[a] *Sex*, male = 0, female = 1; *age*, years; *height*, centimeters.

[b,c] *Age*, years; *Weight,* kilograms. Predicted weight men: 0.78 × Height (cm) − 60.7, Predicted weight women: 0.65 × Height (cm) − 42.8, when actual weight > predicted, the predicted weight should be used in the equations.

[d] *Sex*, male = 1, female = 2; *age*, years; *height*, centimeters.

Statistical analysis

Data are presented as mean ± SD for continuous variables and numbers (%) for categorical variables. Cardiopulmonary responses at maximal exercise between genders were analyzed by student's *t*-test. We compared actual VO_2 max with predicted VO_2 max using repeated-measures ANOVA test with Bonferroni post hoc test. Bland-Altman test was applied to assess agreement between actual measured VO_2 max and predicted VO_2 max for each prediction equations. All tests were two-sided, and P value < 0.05 was considered statistically significant. We performed all analyses using SPSS software (version 24.0; SPSS, Chicago, IL, USA).

Ethics statement

The study protocol was approved by the Institutional Review Board (IRB) of the Asan Medical Center (IRB No. 2021-0915), which waived the requirement of informed consent because of the retrospective nature of the analysis.

RESULTS

Clinical characteristics of study subject

In this study, 50 patients (mean age, 65 ± 13 years, 74% [37/50] males) fulfilled the enrolled criteria. Smoking history was noted: non-smokers, 19 (38%); current-smokers, 12 (24%); and ex-smokers, 19 (38%). The study group comprised of subjects with lung cancer (n = 29, 58%) and healthy person (n = 21, 42%). Of them, 4% were underweight (body mass index [BMI] < 18.5 kg/m^2) and 28% were overweight (BMI > 25 kg/m^2). The subjects resting respiratory function results were normal. **Table 2** shows the gender-based characteristics of the study subjects.

Variables at maximal exercise

CPET results were as follows: absolute VO_2 max, 1.2 ± 0.3 L/min; body weight referenced VO_2 max, 20 ± 3.9 mL/kg/min; peak work rate, 94 ± 24 watts; peak heart rate, 142 ± 21 bpm; peak O_2 pulse, 10 ± 3 mL/beat; minute ventilation, 59 ± 14 L/min; peak respiratory rate, 34 ± 6 breaths per minute; and peak breathing reserve, 41 ± 18%. VO_2 max, peak work rate and peak O_2 pulse were higher in male than in female, but not statistically significant (**Table 3**). Minute ventilation was significantly higher in male than in female. There were no statistically significant difference in VO_2 max, peak heart rate, peak O_2 pulse, minute ventilation and peak breathing reserve except for peak work rate and peak respiratory rate between lung cancer patients and healthy subjects (**Table 4**).

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Table 2. Baseline characteristics of patients

Variables	Male (n = 37)	Female (n = 13)	Total (N = 50)
Age, yr	67 ± 13	60 ± 14	65 ± 13
Height, cm	165 ± 7	157 ± 5	163 ± 7.4
Weight, kg	64.8 ± 12.4	60.2 ± 10.9	64 ± 12.1
Ideal weight, kg	70 ± 5.5	59.4 ± 3.2	67 ± 6.8
BMI, kg/m^2	23.7 ± 3.7	24.3 ± 3.8	23.9 ± 3.7
FVC, L	3.6 ± 0.6	3 ± 0.5	3.5 ± 0.6
FVC % predicted	86.2 ± 9.8	94.4 ± 13.3	88.3 ± 11.2
FEV_1, L	2.7 ± 0.5	2.3 ± 0.4	2.6 ± 0.5
FEV_1 % predicted	92.2 ± 7.9	98.5 ± 11.6	93.8 ± 9.3
FEV_1/FVC, %	77.3 ± 7.2	81.4 ± 5.3	78.4 ± 7
VC, L	3.5 ± 0.8	2.5 ± 0	3.4 ± 0.8
MVV, L/min	118 ± 77	96 ± 20	112 ± 68
Activity level, %			
Low	56.8	61.5	58
Moderate	40.5	30.8	38
High	2.7	7.7	4

Values are expressed as the mean ± SD and activity level are graded by international physical activity questionnaire, which is expressed as percentage.
BMI = body mass index, FVC = forced vital capacity, FEV_1 = forced expiratory volume in one second, VC = vital capacity, MVV = maximal voluntary ventilation.

Table 3. Cardiopulmonary responses at maximal exercise on cycle ergometry in subjects

Variables	Male (n = 37)	Female (n = 13)	*P* value
VO_2 max, L/min	1.3 ± 0.4	1.1 ± 0.3	0.109
VO_2 max, mL/kg/min	20 ± 3.9	18 ± 3.7	0.195
Peak WR, watts	97 ± 25	86 ± 21	0.126
Peak HR, bpm	140 ± 20	146 ± 21	0.385
% predicted maximal HR	87 ± 11	88 ± 13	0.739
Peak O_2 pulse (mL/beat)	10 ± 4	8 ± 3	0.090
VE	61 ± 16	53 ± 8.4	0.031
Peak RR	34 ± 6	34 ± 6	0.879
Peak BR, %	39 ± 19	45 ± 13	0.294

Values are expressed as the mean ± SD or number (%).
WR = work rate, HR = heart rate, VE = minute ventilation, RR = respiratory rate, BR = breathing reserve.

Table 4. Cardiopulmonary responses at maximal exercise on cycle ergometry between lung cancer patients and healthy subjects

Variables	Lung cancer (n = 29)	Healthy subject (n = 21)	*P* value
VO_2 max, L/min	1.2 ± 0.3	1.1 ± 0.3	0.148
VO_2 max, mL/kg/min	19 ± 3.7	18 ± 3.7	0.612
Peak WR, watts	88 ± 19	86 ± 21	0.032
Peak HR, bpm	139 ± 22	146 ± 21	0.372
Peak O_2 pulse, mL/beat	9 ± 2	8 ± 3	0.227
VE	58 ± 14	53 ± 8.4	0.519
Peak RR	32 ± 6	34 ± 6	0.009
Peak BR, %	41 ± 17	45 ± 13	0.973

Values are expressed as the mean ± SD or number (%).
WR = work rate, HR = heart rate, VE = minute ventilation, RR = respiratory rate, BR = breathing reserve.

Comparison between actual absolute VO_2 max and predicted absolute VO_2 max

Fig. 2 illustrates the marked difference between actual and predicted absolute VO_2 max ($P < 0.001$). Except for predicted absolute VO_2 max using Yaoshan prediction equation developed using the Chinese equation, predicted absolute VO_2 max were significantly overestimated compared with actual measured absolute VO_2 max. Agreement using Bland-Altman test between actual absolute VO_2 max and predicted absolute VO_2 max was the best in Yaoshan equation (−0.03, 2SD = 0.55) compared to Jones (0.42, 2SD = 1.07), Hansen (0.44, 2SD = 0.86) and Wasserman (0.42, 2SD = 0.86) equations.

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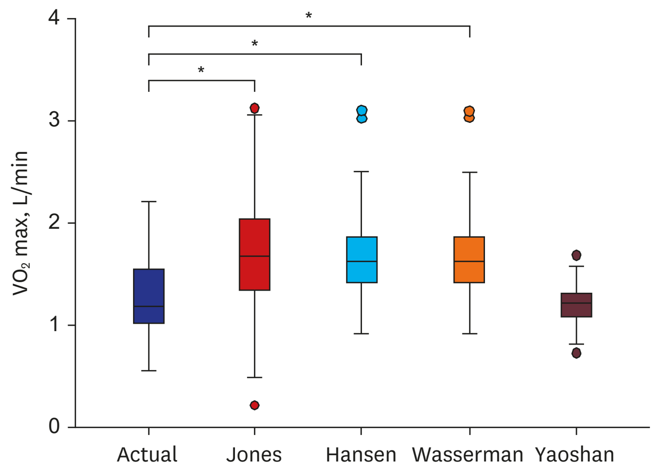

Fig. 2. Comparison of actual and predicted absolute VO_2 max among subjects. Figure shows significant overestimation of predicted VO_2 max compared with actual VO_2 max in our population except for predicted VO_2 max using Yaoshan equation.
*$P < 0.001$ for analysis of variance with Bonferroni post hoc pairwise analysis.

DISCUSSION

To the best of our knowledge, this is the first study to select fitted prediction equations for VO_2 max by comparing actual absolute VO_2 max and predicted absolute VO_2 max in Korean adults. We showed that predicted absolute VO_2 max using Yaoshan equation was similar to actual absolute VO_2 max. Furthermore, most prediction equations for VO_2 max developed by primarily Caucasian population overestimated VO_2 max in our population.

The value of VO_2 max is affected by many factors such as age, sex, height, weight, and physical activity. Thus, the ATS/ACCP for CPET recommends selecting proper reference value that reflects characteristics of their population tested.[8] In our study, among various prediction equations, the Yaoshan equation developed using a Chinese population was the most suitable. Because the anthropometric features of Chinese population is similar to those of the Korean population, Yaoshan equation might be appropriate for VO_2 max in our study. According to recommendations by ATS/ACCP for CPET, prediction equation by Jones et al.[10] and Hansen et al.,[11] which were two most generally used equations of reference values, should be applied clinically. However, in our study, predicted absolute VO_2 max by Jones et al.[10] and Hansen et al.[11] was overestimated compared to the actual absolute VO_2 max. As in our study, Ahmadian et al.[18] showed significant overestimation of predicted VO_2 max compared with actual VO_2 max using prediction equations by Jones et al.[10] and Hansen et al.[11] It is necessary to select appropriate sets of reference values for each institution.

Because the most of prediction equation are based on weight and height, VO_2 max is greatly affected by anthropometric characteristics. Anthropometric features such as weight and height of the Caucasian and Asian population are different. For example, height, weight and BMI of subjects in an Asian population[14,16,19-23] were similar to those of the present study, but lower than those of primarily Caucasians.[12,13,18] As above, the predicted VO_2 max using Yaoshan equation using the Asian population had good agreement with our study. The most plausible explanation for good agreement is that the anthropometric characteristics are similar. Therefore, when selecting reference value, it is important to select a reference value that reflects the characteristics of each population well.

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In the present study, actual VO_2 max was lower than that of other studies by Caucasian population.[13,18,24] This is consistent with a previous study that reported that VO_2 max in an Asian-Indian population was lower than in a Caucasian population.[25] It is crucial to apply reference values specific to different population as VO_2 max are affected by ethnic groups. In addition to difference of height and weight, physiology of skeletal muscle, parenchymal lung and chest wall anatomy could have affected to exercise capacity from other ethnicities. In some study with Asian population, lung volumes such as total lung capacity and functional residual capacity are lower than those for Caucasian population.[26,27]

The limitations of this study must be considered. First, this was a retrospective study conducted in a single tertiary referral center in Korea. Because the anthropometric characteristics of subjects may differ depending on the regions of residence, our results cannot be readily applied to the general population in Korea. Second, the possibility of selection bias should be considered because the study population included healthy subjects and early lung cancer patients. The study population may be less healthy than the general population. But early lung cancer patients had normal lung function and normal cardiopulmonary function. Third, most of the enrolled patients were elderly. Fourth, the sex ratio in this study was not 1:1 and the number of included subjects was small. The results of our study may not be generalized to the general population because the number of patients was small, study population is mainly older people, and gender ratio is not 1:1. Further multicenter studies with larger numbers of subject and subjects with all age ranges are warranted to validate our results.

In conclusion, most prediction equations for VO_2 max based on Caucasian population yield overestimated VO_2 max compared with actual VO_2 max. The predicted VO_2 max using equation developed using the Chinese population was similar to actual VO_2 max. These results imply that the reference value and prediction equation from studies in which populations were primarily Caucasians may not be appropriate for Koreans. Since the mean difference is the lowest in Chinese equation, the Chinese equation might be used for the Korean adult population.

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