



Influence of age in estimating maximal oxygen uptake

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Abstract

Objective To assess the influence of age on the error of estimate (EE) of maximal oxygen uptake (VO_2max) using sex and population specific-equations in cycle ergometer exercise testing, since estimated VO_2max is associated with a substantial EE, often exceeding 20%, possibly due to intrinsic variability of mechanical efficiency. **Methods** 1850 adults (68% men), aged 18 to 91 years, underwent maximal cycle ergometer cardiopulmonary exercise testing. Cardiorespiratory fitness (CRF) was assessed relative to sex and age [younger (18 to 35 years), middle-aged (36 to 60 years) and older (> 60 years)]. VO_2max [$\text{mL}\cdot(\text{kg}\cdot\text{min})^{-1}$] was directly measured by assessment of gas exchange and estimated using sex and population specific-equations. Measured and estimated values of VO_2max and related EE were compared among the three age- and sex-specific groups. **Results** Directly measured VO_2max of men and women were $29.5 \pm 10.5 \text{ mL}\cdot(\text{kg}\cdot\text{min})^{-1}$ and $24.2 \pm 9.0 \text{ mL}\cdot(\text{kg}\cdot\text{min})^{-1}$ ($P < 0.01$). EE [$\text{mL}\cdot(\text{kg}\cdot\text{min})^{-1}$] and percent errors (%E) for men and women had similar values, 0.5 ± 3.2 and $0.4 \pm 2.9 \text{ mL}\cdot(\text{kg}\cdot\text{min})^{-1}$, and $-0.8 \pm 13.1\%$ and $-1.7 \pm 15.4\%$ ($P > 0.05$), respectively. EE and %E for each age-group were, respectively, for men: younger = $1.9 \pm 4.1 \text{ mL}\cdot(\text{kg}\cdot\text{min})^{-1}$ and $3.8 \pm 10.5\%$, middle-aged = $0.6 \pm 3.1 \text{ mL}\cdot(\text{kg}\cdot\text{min})^{-1}$ and $0.4 \pm 10.3\%$, older = $-0.2 \pm 2.7 \text{ mL}\cdot(\text{kg}\cdot\text{min})^{-1}$ and $-4.2 \pm 16.6\%$ ($P < 0.01$); and for women: younger = $1.2 \pm 3.1 \text{ mL}\cdot(\text{kg}\cdot\text{min})^{-1}$ and $2.7 \pm 10.0\%$, middle-aged = $0.7 \pm 2.8 \text{ mL}\cdot(\text{kg}\cdot\text{min})^{-1}$ and $0.5 \pm 11.1\%$, older = $-0.8 \pm 2.3 \text{ mL}\cdot(\text{kg}\cdot\text{min})^{-1}$ and $-9.5 \pm 22.4\%$ ($P < 0.01$). **Conclusion** VO_2max were underestimated in younger age-groups and were overestimated in older age groups. Age significantly influences the magnitude of the EE of VO_2max in both men and women and should be considered when CRF is estimated using population specific equations, rather than directly measured.

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1 Introduction

Cardiorespiratory fitness (CRF) is an important health indicator that is typically expressed as maximal oxygen uptake (VO_2max).^[1–3] Accordingly, VO_2max is routinely used as a diagnostic and prognostic index.^[4–10] Ideally, VO_2max is directly measured during maximal cardiopulmonary exercise testing (CPX), as it provides the most valid and reliable assessment of aerobic fitness.^[11] Nevertheless, for varied reasons, most clinical exercise testing labs do not regularly perform ventilatory gas analyses and CPX. Consequently, clinicians often rely on estimated VO_2max values using equations which combine exercise duration and maximal

workload achieved during standard electrocardiographic (ECG) exercise stress testing.^[12,13] Estimated VO_2max assessments have been validated relative to directly measured VO_2max values, but for a given subject there may be a large magnitude of error, signified by the error of estimate (EE).^[14,15] The associated EE has been reported to often exceed 20%.^[1] The imprecision of these estimates may negatively impact related clinical decisions regarding patient management and risk stratification.

Large EE may be partially attributed to differences in mechanical efficiency, as reflected by the ability to perform work through the utilization of oxygen consumption.^[13] Sex is one variable that may also influence mechanical efficiency and the associated EE.^[14–17] Considering the growing number of elderly subjects worldwide, it is of critical importance to delineate factors affecting peak or symptom-limited exercise testing and the key assessments it provides.^[18] Furthermore, as the majority of the equations used to estimate VO_2max were developed based in young and

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middle-age individuals, it is important to assess the outcome of estimating VO_2max in older ones. Therefore, in this study, we hypothesized that older age exacerbates the EE when using population-specific equations to estimate VO_2max , due to intrinsic variability of mechanical efficiency. Therefore, we assessed EE underlying the estimation of VO_2max in progressive age groups (i.e., younger, middle-aged, older) of men and women.

2 Methods

2.1 Sample

Our study population included voluntary adult subjects in a private clinic who underwent maximal cycle ergometer CPX between January 2008 and December 2014. All subjects provided informed consent and authorized the de-identified use of their collective data for research purposes. The study protocol and retrospective data analysis were approved by the institutional ethics committee.

After excluding subjects that were previously tested at this clinic, those who had undergone treadmill testing, individuals who did not meet criteria for a maximal CPX, and additional subjects with incomplete data, the final study population included 1850 subjects.

2.2 Anthropometric measurements

Body weight was measured without shoes to the nearest 0.1 kg in subjects wearing light clothing. Height was measured to the nearest 0.1 cm. Body mass index (BMI) was calculated by the ratio of body weight and the square of height (kg/m^2).

2.3 Maximal cardiopulmonary exercise testing

Maximal CPX was conducted using an electromagnetically-braked cycle ergometer (Inbrasport CG-04, Inbrasport, Brazil) following a ramp protocol that was tailored to each individual's clinical history, body habitus and exercise habits to achieve volitional exhaustion between 8 and 12 min.^[19,20] All CPXs were performed under direct medical supervision in a properly equipped laboratory.^[21] Subject seat height, body position and leg extension were carefully adjusted on the cycle ergometer to provide a standardized, natural and comfortable cycling movement.

One lead CM5 or CC5 digital ECG continuous monitoring (ErgoPC Elite, Micromed, Brazil) was obtained at rest, during exercise and throughout the 5-min recovery period. Resting, exercise and post exercise measurements of heart rate (HR) and blood pressure were obtained during each minute, respectively, from ECG recordings and by auscultation of the right brachial artery.

During CPX, subjects wore a nose clip and breathed through a mouthpiece with an embedded Prevent pneumotachograph (MedGraphics, United States) to provide respiratory measurements. Ventilatory gases were analyzed with a VO2000 Medgraphics metabolic cart (MedGraphics, United States) that was calibrated prior to each study. Throughout the CPX, expired gases were initially averaged at 10 s intervals and later consolidated minute-by-minute for further analysis. VO_2max was signified by the highest oxygen uptake value attained, expressed as $\text{mL}\cdot(\text{kg}\cdot\text{min})^{-1}$.

CPX was defined as maximal if it was terminated due to fatigue, despite strong verbal encouragement, rather than having been prematurely stopped due to abnormal signs or symptoms, or by having fulfilled selected physiological criteria,^[22] such as a peak respiratory exchange ratio (RER) ≥ 1.05 and/or exceeding the ventilatory threshold.^[23] Additionally, measures of perceived exertion were obtained to assess somatic exhaustion, including a 10-score on the 0–10 Borg scale,^[24] which was further substantiated by the inability to maintain the required pedal cadence (65–75 rev/min).

2.4 Predicted VO_2max and HR

To better characterize the study's sample, VO_2max values were predicted by sex-specific equations: $60 - 0.55 \times \text{age}$ (years) for men and $48 - 0.37 \times \text{age}$ (years) for women.^[25] Maximum values of HR were age-predicted by a previously validated equation derived from a similar population, where HRmax (beats/min) = $208 - 0.7 \times \text{age}$ (years).^[26]

2.5 Estimated VO_2max

VO_2max [$\text{mL}\cdot(\text{kg}\cdot\text{min})^{-1}$] was estimated by sex-specific equations that were previously validated in our exercise lab.^[17] For men and women, VO_2max was estimated as [maximal workload (watts)/weight (kg)] $\times 10.79 + 7$ and [maximal workload (watts)/weight (kg)] $\times 9.82 + 7$, respectively.

2.6 Comparing measured and estimated VO_2max

To compare measured versus estimated VO_2max values, adults were categorized by both sex and age as: younger (18 to 35 years), middle-aged (36 to 60 years) and older (> 60 years). VO_2max per kilogram of body weight, EE (measured VO_2max – estimated VO_2max) in $\text{mL}\cdot(\text{kg}\cdot\text{min})^{-1}$ and percent error (%E) – [(measured VO_2max – estimated VO_2max)/measured VO_2max] $\times 100$ – were calculated. Negative values of EE and %E signified that estimated VO_2max was higher than directly measured VO_2max .

2.7 Data analysis

Descriptive statistics were expressed as mean \pm SD or as

percent. Results for demographic and CPX variables as well as EE and %E were compared by one-way ANOVA-Bonferroni test (three age-groups), *t*-test (male and female subjects) or chi-square test depending of the nature of variable distribution. Pearson product-moment correlation coefficients were also calculated for measured and estimated VO₂max in men and women. Statistical analysis employed Prism software 6.02 (GraphPad, USA), having < 5% probability as the criterion for statistical significance.

3 Results

A total of 1850 subjects, including 1262 men and 588 women, were studied. Our subjects ranged in age from 18 to 91 years, and men and women averaged 53 ± 15 and 50 ± 15 years ($P < 0.01$), respectively. Using BMI criteria, 41.1% of the subjects were overweight (BMI 25.0–29.9 kg/m²) and 23.5% were classified as obese (BMI ≥ 30.0 kg/m²). Accordingly, 27.2% of the men and 22.1% of the women were obese, whereas 1.6% and 1.2% of all men and women, respectively, were morbidly obese (BMI ≥ 40.0 kg/m²). In men, all three age-groups had similar BMIs ($P > 0.05$), whereas in women BMI was higher in older subjects ($P < 0.05$). Major demographic characteristics and selected CPX results are shown in Tables 1 and 2. Associated clinical conditions and regularly prescribed medications for men and women are depicted in Tables 3 and 4.

The duration of CPX averaged 10 ± 2 min with 70.1% of all tests lasting between 8 and 12 min. Maximal attained workload averaged 173 ± 71 and 111 ± 45 watts, respectively, in men and women ($P < 0.01$), with the sex-differences persisting when values were expressed relative to body weight — 2.04 ± 0.86 watts/kg for men and 1.71 ± 0.75 watts/kg for women ($P < 0.01$). Directly measured VO₂max values of men and women were 29.5 ± 10.5 mL·(kg·min)⁻¹ and 24.2 ± 9.0 mL·(kg·min)⁻¹ ($P < 0.01$), ranging from 5.8 to 73.3 mL·(kg·min)⁻¹ in men and from 4.1 to 60.1 mL·(kg·min)⁻¹ in women. When related to age-predicted values, men achieved higher values ($96.9\% \pm 26.8\%$) of VO₂max as compared with women ($81.3\% \pm 24.5\%$) ($P < 0.01$). Younger men achieved the lowest value ($86.9\% \pm 21.9\%$, $P < 0.01$) with middle-aged and older men attaining similar relative values — $98.1\% \pm 26.1\%$ and $98.5\% \pm 28.7\%$, respectively ($P > 0.05$). Different results were observed in women; the middle-aged cohort achieved the highest values of percent of age-predicted VO₂max ($86.4\% \pm 26.5\%$; $P < 0.05$) whereas younger and older women demonstrated similar values, $78.7\% \pm 20.6$ and $71.5\% \pm 17.8\%$ ($P > 0.05$), respectively.

Relative to the EE and %E of VO₂max, men and women had similar values, 0.5 ± 3.2 mL·(kg·min)⁻¹ and 0.4 ± 2.9

Table 1. Major demographics and CPX results according to age-groups - men (n = 1262).

Age groups	Younger (n = 155)	Middle-aged (n = 683)	Older (n = 424)	P
Characteristics				
Age (yrs)	29 ± 5	49 ± 7	69 ± 7	< 0.01
Weight (kg)	86.1 ± 16.6	88.3 ± 15.0	82.2 ± 13.6	< 0.01
Height (cm)	177.2 ± 6.5	176.9 ± 6.2	171.9 ± 6.9	< 0.01*
BMI (kg/m ²)	27.4 ± 5.0	28.2 ± 4.3	27.8 ± 3.9	> 0.05
Predicted VO ₂ max [mL·(kg·min) ⁻¹]	44.1 ± 2.6	33.2 ± 4.0	21.8 ± 3.7	< 0.01
Predicted HRmax (bpm)	188 ± 3	174 ± 5	159 ± 5	< 0.01
β-blocker usage (%)	6.5	21.2	41.3	
CPX Results				
Duration (min)	10 ± 2	10 ± 2	9 ± 3	< 0.01 [#]
HRmax (bpm)	184 ± 11	166 ± 18	135 ± 24	< 0.01
HRmax measured/ predicted (%)	98.0 ± 6.0	95.3 ± 9.5	84.9 ± 14.0	< 0.05
Maximum workload (Watts)	229 ± 57	199 ± 5.9	110 ± 43	< 0.01
Maximum RER	1.14 ± 0.10	1.14 ± 0.09	1.11 ± 0.13	< 0.01*
Measured VO ₂ max [mL·(kg·min) ⁻¹]	38.3 ± 9.5	32.5 ± 9.2	21.4 ± 7.0	< 0.01
Measured/predicted VO ₂ max (%)	86.9 ± 21.9	98.1 ± 26.1	98.5 ± 28.7	< 0.01 [€]
Estimated VO ₂ max [mL·(kg·min) ⁻¹]	36.4 ± 8.2	28.4 ± 7.2	21.6 ± 5.7	< 0.01
Error of estimate [mL·(kg·min) ⁻¹]	1.9 ± 4.1	0.6 ± 3.1	-0.2 ± 2.7	< 0.01
Percent error (%E)	3.8 ± 10.5	0.4 ± 10.3	-4.2 ± 16.6	< 0.01

*non significant when comparing Younger and Middle-aged groups; [#]significant when comparing Middle-aged and Older groups; [€]non significant when comparing Middle-aged and Older groups. BMI: Body Mass Index; CPX: cardiopulmonary exercise testing; HR: heart rate; RER: respiratory exchange ratio.

mL·(kg·min)⁻¹ ($P > 0.05$) and $-0.8 \pm 13.1\%$ and $-1.7 \pm 15.4\%$ ($P > 0.05$), respectively. In reference to the age-groups for both men and women, VO₂max was similarly underestimated in the younger age-groups — %E $3.8 \pm 10.5\%$ and $2.7 \pm 10.0\%$ ($P > 0.05$), and generally overestimated in the older male and female subjects, $-4.2 \pm 16.6\%$ and $-9.5 \pm 22.4\%$ ($P < 0.01$). Men and women had similar results for EE in the middle-aged group, 0.6 ± 3.1 mL·(kg·min)⁻¹ and 0.7 ± 2.8 mL·(kg·min)⁻¹ ($P > 0.05$) and for %E, $0.4 \pm 10.3\%$ and $0.5 \pm 11.1\%$ ($P > 0.05$) (Figure 1).

4 Discussion

Although the use of CPX has increased in recent years, for

Table 2. Major demographics and CPX results according to age-groups – women (n = 588).

Age groups	Younger (n = 101)	Middle-aged (n = 338)	Older (n = 149)	P
Characteristics				
Age (yrs)	28 ± 5	48 ± 7	70 ± 7	< 0.01
Weight (kg)	63.5 ± 12.8	66.7 ± 12.2	69.6 ± 12.8	< 0.05*
Height (cm)	164.0 ± 5.6	163.7 ± 6.2	158.9 ± 5.9	< 0.01*
BMI (kg/m ²)	23.5 ± 4.4	24.9 ± 4.5	27.6 ± 5.0	< 0.05
Predicted VO ₂ max [mL·(kg·min) ⁻¹]	38.2 ± 3.2	30.4 ± 2.8	22.1 ± 2.8	< 0.01
Predicted HRmax (bpm)	188 ± 4	174 ± 5	159 ± 5	< 0.01
β-blocker usage (%)	4.0	42.6	33.6	
CPX Results				
Duration (min)	9 ± 2	10 ± 3	7 ± 2	< 0.01*
HRmax (bpm)	184 ± 10	166 ± 17	137 ± 24	< 0.01
HRmax measured/predicted (%)	97.6 ± 4.9	95.0 ± 9.3	86.1 ± 13.7	< 0.01*
Maximum workload (Watts)	136 ± 34	123 ± 42	67 ± 22	< 0.01
Maximum RER	1.15 ± 0.08	1.15 ± 0.12	1.15 ± 0.11	> 0.05
Measured VO ₂ max [mL·(kg·min) ⁻¹]	29.9 ± 7.3	26.2 ± 8.4	15.8 ± 4.5	< 0.01
Measured/predicted VO ₂ max (%)	78.7 ± 20.6	86.4 ± 26.5	71.5 ± 17.8	< 0.05 ^c
Estimated VO ₂ max [mL·(kg·min) ⁻¹]	28.6 ± 5.9	25.6 ± 6.8	16.6 ± 3.2	< 0.01
Error of estimate (EE) [mL·(kg·min) ⁻¹]	1.2 ± 3.1	0.7 ± 2.8	-0.8 ± 2.3	< 0.01*
Percent error (%E)	2.7 ± 10.0	0.5 ± 11.1	-9.5 ± 22.4	< 0.01*

Data are expressed as mean ± SD. *non significant when comparing Younger and Middle-aged groups; ^c non significant when comparing Younger and Older groups. BMI: Body Mass Index; CPX: cardiopulmonary exercise testing; HR: heart rate; RER: respiratory exchange ratio.

the vast majority of exercise testing labs VO₂max is still indirectly estimated by applying equations that rely on the workloads achieved, and their duration.^[27] In our study, by using specific equations for our population of men and women, VO₂max was consistently overestimated in older subjects and underestimated in the younger cohort, with the largest %E observed in the former.

There are some plausible physiologic mechanisms to explain our findings. One possibility is related to net VO₂, that is, the oxygen uptake associated with a given exercise bout.^[28] Because the percentage of type I fibers influences mechanical efficiency during cycling, changes in fiber type may alter the linear relationship between workload and oxygen consumption.^[29] According to Tevald, *et al.*^[30] and Venturelli, *et al.*,^[31] the loss of muscle fibers with aging is fiber specific, occurring primarily with type II fibers or fast-twitch fibers, with an

Table 3. Major clinical conditions and prescribed medications - men (n = 1262).

Age Groups	Younger (n = 155)	Middle-aged (n = 683)	Older (n = 424)
Major clinical conditions (%)			
Coronary artery disease	1.9	14.3	40.1
Acute myocardial infarction	1.3	7.8	18.4
Percutaneous coronary intervention	1.3	10.1	23.8
Coronary artery bypass graft	0.0	4.1	17.0
Hypertension	7.7	30.5	55.4
Dyslipidemia	12.3	38.7	56.1
Obesity	12.3	17.6	17.2
Diabetes	0.6	7.5	17.0
Medication use (%)			
β-blockers	6.5	21.2	41.3
Calcium channel blocker	1.9	6.4	16.7
Angiotensin-converting enzyme inhibitor	3.9	8.5	16.0
Angiotensin receptor antagonist	5.8	26.1	42.0
Diuretic	3.9	10.0	29.5
Vasodilator	0.6	3.8	14.2
Cholesterol lowering	6.5	39.5	67.9
Antiplatelet	3.2	23.7	59.2
Antiarrhythmic	0.6	3.5	15.6

Table 4. Major clinical conditions and prescribed medications – women (n = 588).

Age Groups	Younger (n = 101)	Middle-aged (n = 338)	Older (n = 149)
Major clinical conditions (%)			
Coronary artery disease	0.0	4.1	18.1
Acute myocardial infarction	0.0	3.0	6.0
Percutaneous coronary intervention	0.0	3.6	8.1
Coronary artery bypass graft	0.0	0.6	6.0
Hypertension	5.0	15.7	44.3
Dyslipidemia	4.0	22.5	46.3
Obesity	4.0	9.5	19.5
Diabetes	0.0	3.6	12.1
Medications in use (%)			
B-blockers	4.0	13.0	33.6
Calcium channel blocker	2.0	2.7	18.8
Angiotensin-converting enzyme inhibitor	1.0	2.1	8.1
Angiotensin receptor antagonist	3.0	13.6	50.3
Diuretic	4.0	5.3	34.2
Vasodilator	0.0	0.6	8.7
Cholesterol lowering	0.0	19.8	61.7
Antiplatelet	0.0	8.3	40.3
Antiarrhythmic	0.0	5.0	14.8

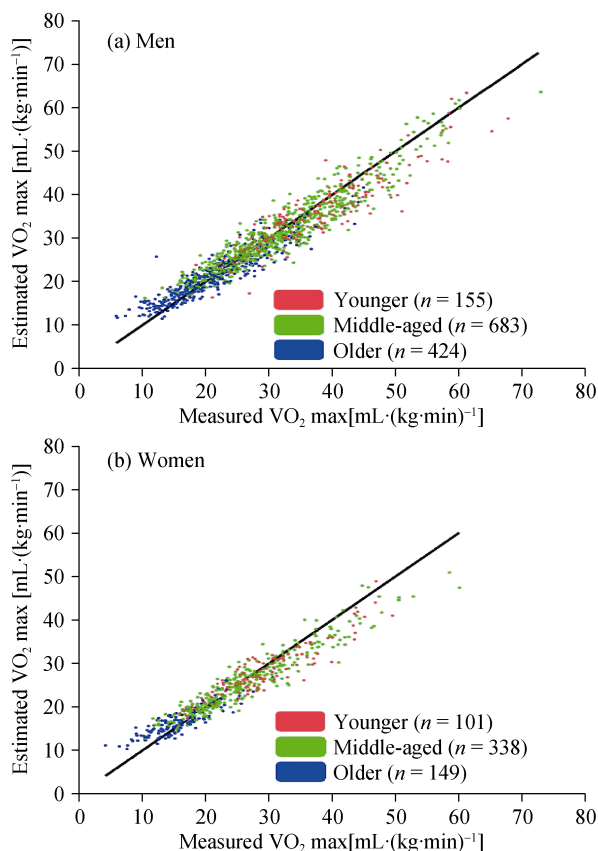


Figure 1. Relationship between measured and estimated VO_2max in three age-groups (younger, middle-aged, older) in men (a) and women (b).

increase in percentage of type I fibers, or slow-twitch fibers, contributing to differences in mechanical efficiency seen between younger and older subjects.

In addition, equations commonly used to estimate VO_2max often employ the added constant value of $7 \text{ mL}\cdot(\text{kg}\cdot\text{min})^{-1}$ to represent the oxygen consumption at rest [$3.5 \text{ mL}\cdot(\text{kg}\cdot\text{min})^{-1}$] plus the energy cost of unloaded pedaling [also $3.5 \text{ mL}\cdot(\text{kg}\cdot\text{min})^{-1}$]. However, in one study, values of oxygen consumption at rest between 2.0 and $4.4 \text{ mL}\cdot(\text{kg}\cdot\text{min})^{-1}$ were reported in 125 healthy men aged 17 to 38 years.^[32] Kwan, *et al.*^[33] found that resting VO_2 was significantly lower in elderly people, suggesting that the conventional value of $3.5 \text{ mL}\cdot(\text{kg}\cdot\text{min})^{-1}$ probably overestimates their energy expenditure at rest. In accordance with this latter study, a recent review of 397 reports noted that the resting value of VO_2 decreased with age in both sexes, leading to its systematic overestimation in older subjects.^[34] Therefore, it is possible that differences in resting VO_2 may have contributed to the increasing EE of VO_2max seen in our study comparing three progressive age groups.

Likewise, the value of oxygen consumption of unloaded pedaling used in our sex-specific equations was derived from a study of 60 healthy men aged 19 to 39 years.^[14] With respect

to net VO_2 , it is also possible that the oxygen consumption for pedaling an unloaded cycle ergometer is age dependent and, therefore, influences the EE of VO_2max mostly in older subjects. Thus, routinely using a constant added value of $7 \text{ mL}\cdot(\text{kg}\cdot\text{min})^{-1}$ to our prediction equations may have influenced our observed EE for VO_2max .

Because this was a retrospective study, we were not able to assess values of resting VO_2 nor VO_2 for pedaling an unloaded cycle ergometer, as these measurements are not routinely obtained in our lab or others. Moreover, there remain controversies regarding the accurate assessment of resting VO_2 , making it difficult to incorporate this variable when equations to estimate VO_2max are used in clinical practice.^[28]

Our study has some methodological limitations. First, we did not evaluate the previous or current history of physical activity, exercise and sports practice of our subjects. Admittedly, regular physical activity can alter skeletal muscle fiber typing, thus influencing our subject's mechanical efficiency, regardless of age. As previously reported, older individuals (mean age, 62 years) that participated in a supervised exercise program showed greater improvement in functional capacity, as measured by the workload (watts)/weight (kg) ratio, than in VO_2max , suggesting that regular exercise may improve mechanical efficiency.^[35] Moreover, it remains unclear whether some co-morbid conditions, such as cardiovascular diseases, and commonly prescribed medications, including statins, can influence mechanical efficiency.^[36,37] Accordingly, future studies are needed to address these potential confounding variables.

In conclusion, the magnitude of EE of VO_2max is directly influenced by age in both men and women. The EE is probably related to age-related differences in mechanical efficiency, oxygen cost of unloaded cycling, basal metabolic rate, or combinations thereof. Thus, estimating VO_2max simply based on the peak workload achieved during CPX may lead to larger errors in older subjects.

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