Determination of Maximal Oxygen Uptake Using Seismocardiography at Rest

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Abstract

Introduction: *Assessment of maximal oxygen consumption ($\dot{V}O_2max$) is an important clinical tool when examining both healthy and unhealthy populations, as a low $\dot{V}O_2max$ is associated with cardiovascular disease and all-cause mortality.* ***Aim:*** *This study investigated the accuracy of a non-exercise test for assessment of $\dot{V}O_2max$ using seismocardiography (SCG).* ***Methods:*** *97 participants (20-45 years, 50 males) underwent a non-exercise test using SCG at rest in the supine position (SCG $\dot{V}O_2max$) and a graded exercise test to voluntary exhaustion on a cycle ergometer with indirect calorimetry (IC $\dot{V}O_2max$). An interim analysis was applied after 50 participants had completed testing (SCG $\dot{V}O_2max$ 1.0) allowing for the algorithm to be modified (SCG $\dot{V}O_2max$ 2.1).* ***Results:*** *SCG $\dot{V}O_2max$ 2.1 (n=47, test set) estimation was significant 3.5 ± 1.8 $ml \cdot min^{-1} \cdot kg^{-1}$ ($p<0.001$) lower compared to IC $\dot{V}O_2max$, with a Pearson correlation of $r=0.65$ ($p<0.0001$) and a standard error of estimate of 7.1 $ml \cdot min^{-1} \cdot kg^{-1}$. The coefficient of variation between tests was 8 ± 1%.* ***Conclusion:*** *The accuracy of $\dot{V}O_2max$ assessment using seismocardiography requires optimization prior to clinical application, as SCG $\dot{V}O_2max$ was systematically lower than IC $\dot{V}O_2max$, and a moderate correlation together with considerable variations were observed between tests.*

1. Introduction

Cardiorespiratory fitness (CRF) are positively associated with self-rated health [1] and inversely correlated with a high risk of cardiovascular disease (CVD) and all-cause mortality [2,3]. In 2016, the scientific statement from the American Heart Association [4] clearly recognised the importance of CRF assessment in clinical practice in order improve patient management and CVD risk prediction. The gold standard method for quantifying CRF is a direct measurement of cardiorespiratory gas exchange during a maximal exercise test for obtainment of maximal oxygen consumption ($\dot{V}O_2max$) [4]. Even though some of the proposed barriers with this method (cost associated with equipment and trained professionals) are becoming less problematic [5], it still requires a maximal effort from an individual, which is not always possible. The potential of non-exercise-based estimations are huge as it provides a rapid and inexpensive method of estimating $\dot{V}O_2max$ in public health and clinical settings [4]. However, the validity of non-exercise test are not yet satisfying [6,7]. In 2020, a clinical non-exercise method using seismocardiography (SCG) for estimation of $\dot{V}O_2max$ was proposed [8]. SCG is a recording of the cardiac vibrations on the chest wall produced by the beating heart, with an accelerometer [9]. New advances in low-cost lightweight sensors, signal processing and machine learning [10] has made this technique suitable for optimization of non-exercise based estimations. Sørensen and colleagues showed that features (aortic valve closing, AC) derived from the SCG signal was highly correlated to $\dot{V}O_2max$ ($r=0.80$) and that a regression model using BMI, sex, age together with mean AC peak to peak amplitude had a correlation of $r=0.90$ with gold standard measurement of $\dot{V}O_2max$ in a relatively small sample size of 26 [8]. Therefore, the purpose of the current study was to investigate the accuracy of a clinical non-exercise test for assessment of $\dot{V}O_2max$ using SCG in a larger cohort.

2. Methods

2.1. Participants

One hundred participants (50 males) aged between 18 and 45 years were included in the study. Data from 97 participants (50 males) are included, as three participants had invalid data regarding the non-exercise $\dot{V}O_2max$ estimation. Exclusion criteria were current or previous cardiovascular disease, chronic medication, pregnancy or conditions that prevented maximal effort testing. Participants received both oral and written information about experimental procedures and possible risks associated with the study, before signing a written informed consent. The study was approved by the Science Ethical Committee of the greater region of Copenhagen,

Denmark (H-17008748), and adhered to the principle of the Helsinki Declaration. The study is prospectively registered at Clinical Trial (NCT03504306).

2.2. Study design

An interim analysis was conducted after the first 50 participants had completed testing (25 females / 25 males). Thus, allowing for adjustment in the algorithm before a blinded analysis of the last 47 participant was performed. Hereby the first 50 participants were used as a training set and the remaining 47 as a test set.

The participants arrived at the laboratory at the University of Copenhagen after at least 4 hours fasting and without vigorous exercise performed within the last 24 hours before testing. The participants then underwent following measurements in chronological order. Anthropometrics was measures and body composition determined by DXA scan (Lunar iDXA, GE Healthcare) after voiding and wearing minimal clothing. Three measures of blood pressure (Boso-medicus control, Jungingen, Germany) were performed each separated by 2 minutes rest with an initial 5 minutes resting period. A 5 ml resting blood sample was obtained from the antecubital vein for assessment of HbA1c, haemoglobin, and haematocrit.

Table 1. Participant characteristics

	All, n=97
Age, yrs.	31 ± 1 [20-45]
Height, cm	175 ± 2 [155-202]
Weight, kg	73.0 ± 2.3 [47.6-99.3]
BMI, $kg \cdot m^{-2}$	23.8 ± 0.5 [18.5-32.2]
Body fat, %	23.2 ± 1.4 [7.0-43.0]
Systolic BP, mmHg	125 ± 3 [92-165]
Diastolic BP, mmHg	76 ± 2 [56-96]
Resting HR, bpm	57 ± 2 [37-87]
Hemoglobin, mmol/L	8.6 ± 0.1 [7.2-10.3]
Hematocrit, %	41.2 ± 0.5[b] [35.0-49.0]
HbA1c, mmol/mol	32 ± 0 [25-39]
$\dot{V}O_2$max, $mL \cdot min^{-1} \cdot kg^{-1}$	
- Estimated	44.0 ± 1.1 [22.4-57.8]
- Measured	46.1 ± 1.4 [26.9-64.7]

Note: Data are presented as mean ± 95% CI and [range].
BMI, body mass index; BP, blood pressure; HR, heart rate; HbA1c, glycated hemoglobin. [b] n=95.

A non-exercise $\dot{V}O_2$max estimation using seismocardiography (SCG VO_2max) in the supine position following 5 minutes of bed rest was then conducted as previously described [8]. In brief, an ultra-sensitive accelerometer (Silicon Design 1521-002), with a resolution of ± 2 g, low noise at 7 µg / √ Hz and a frequency response 0-300 Hz, was placed on the lower part of sternum with double adhesive tape for recording of the SCG signal. The accelerometer measured 19 mm in width, 21 mm in length and 11 mm in height and weighed 5 grams including the electronic components and the ABS plastic housing. Resting ECG (a three lead ECG, with four electrodes placed on the right and left shoulder and right and left iliac crests) and SCG were recorded for 5 minutes using an iWorx IX-228/s (IWORX, Dover, New Hampshire) connected to a PC, acquisition unit sampling at 5000 Hz. LabScribe recording software (Version 3. Dover, New Hampshire) was used. Lastly, after a 5 minute warm-up at 75W participants performed a graded exercise test with 25W increments every minute until voluntary exhaustion on a cycle ergometer (Monark 839E, Monark Exercise AB). Pulmonary gas exchange breath-by-breath measurements were obtained continuously during exercise and sampled in 10-s intervals by an automated online system (Quark CPET, COSMED). Gas analysers were calibrated with a compressed gas mixture (5% CO_2 and 16% O_2) and the digital flowmeter calibrated using a 3 L calibration syringe (COSMED) before each test. The $\dot{V}O_2$max criteria was O_2 levelling off and a respiratory exchange ratio (RER) > 1.15.

2.3. Signal Processing

The ECG and SCG recordings were exported from the iWorx system and processed in MATLAB (2018a. MathWorks, Inc.) The signal processing was performed manually and this has previously been described [8]. The company behind the SCG $\dot{V}O_2$max estimation model, VentriJect Aps, performed the signal processing and was blinded to the measured $\dot{V}O_2$max value, but did receive demographic data (weight, height and age) of the participants.

2.4. $\dot{V}O_2$max prediction models

The features included in the two prediction models are presented below:

- **SCG 1.0 $\dot{V}O_2$max** = $44.1 - 0.465 \cdot BMI + 6.79 \cdot SEX - 0.187 \cdot AGE + 0.292 \cdot ACpp$

- **SCG 2.1 $\dot{V}O_2$max** = $-65.895 + 0.06 \cdot ACpp + 0.176 \cdot tACp\_p + 0.625 \cdot FriendsAlgo - 155.4 \cdot tIVCTRoustrr + 0.542 \cdot S2FrequencySpec$

The SCG 1.0 refer to the previously described model [8] and SCG 2.1 to the adjusted model. The abbreviations for the included features are: ACpp; peak to peak amplitude in SCG diastolic complex, tACp_p; time intervals between peaks in SCG diastolic complex, FriendsAlgo [11]; an algorithm based on sex, age and body weight for prediction of $\dot{V}O_2$max, tIVCTRoustrr; robust estimation of isovolumetric contraction time normalised against the average duration of heart beats, S2FrequencySpec; frequency of the average SCG diastolic complex quantified

using PCA. The SCG $\dot{V}O_2$max 2.1 model was fitted to the data obtained previously [8] (n=43) and the initial 50 participants from this study, with a built-in function of MATLAB (stepwiselm) using both forward and backward stepwise regression. Independent variables were included or removed from the model based on statistical significance of the change in the sum of squared errors. The criteria was $p < 0.05$ for addition and $p < 0.10$ for removal. This process was repeated until no more parameters could be added or removed.

2.5. Statistics

Data are presented as mean ± 95% confidence intervals (CI) with significance set at an α level of 0.05. Systematic difference in measured values between the initial 50 and the last 47 participants were analysed with an unpaired *t* test. Inter-method validity were analysed with a paired *t* test, Pearson correlation coefficient r, coefficient of variation (CV), standard error of estimate (SEE) [8]. The agreement was assessed by a Bland-Altman plot with 95% limits of agreement (LoA). Pearson correlation coefficients were interpreted as follows: very high >0.90, high 0.70-0.90, moderate 0.50-0.70, low 0.30-0.50 and little if any 0.00-0.30 [12]. Statistical analyses were performed and figures constructed in GraphPad Prism 9.2.0 (Software Inc.) and Microsoft Excel (Microsoft Corporation).

3. Results

A systematic difference between the initial 50 participants and the last 47 was observed in the HbA1c measurement (33 ± 1 and 32 ± 1 mmol/mol, respectively) and IC $\dot{V}O_2$max value (44.4 ± 1.6 and 47.9 ± 2.2 ml·min^{-1}·kg^{-1}, respectively) ($p<0.05$).

3.1. Interim analyses and performance in training set

For SCG 1.0 a significant bias of -1.7 ± 1.5 ml·min^{-1}·kg^{-1} together with 95% LoA ranging ±10.3 ml·min^{-1}·kg^{-1} was found compared to IC $\dot{V}O_2$max ($p=0.028$). The correlation analysis revealed a correlation of $r=0.60$ ($p<0.0001$), with a SEE of 5.6 ml·min^{-1}·kg^{-1}. The intra-individual CV was 7 ± 1%. For SCG 2.1 a non-significant bias of -0.9 ± 1.3 ml·min^{-1}·kg^{-1} with 95% LoA between 8.1 and -9.9 ml·min^{-1}·kg^{-1} was found compared to IC $\dot{V}O_2$max ($p=0.172$). The correlation was $r=0.70$ and with a SEE of 4.7 ml·min^{-1}·kg^{-1}. The CV was 6 ± 1%.

3.2. Test set $\dot{V}O_2$max estimation

SCG $\dot{V}O_2$max 2.1 was 7% lower ($p<0.001$) compared with IC $\dot{V}O_2$max (Figure 2), with a moderate Pearson correlation observed ($p<0.0001$) between test (Figure 1).

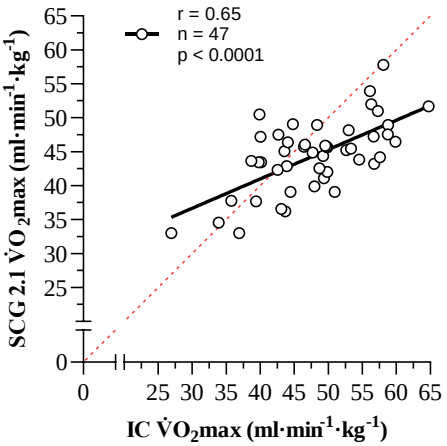

Figure 1. Scatterplot of the correlation between $\dot{V}O_2$max estimated with a non-exercise model using seismocardiography (SCG 2.1) and directly measured with indirect calorimetry (IC).

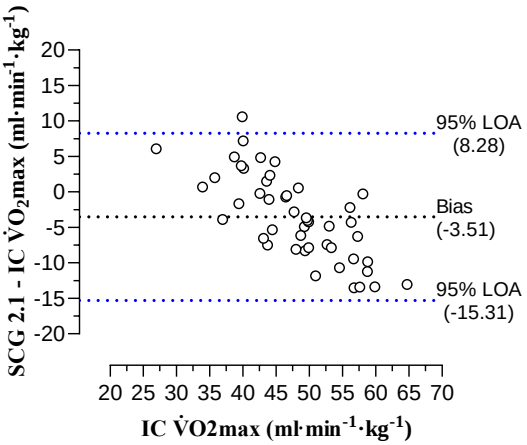

Figure 2. A Bland-Altman plot of the agreement between $\dot{V}O_2$max estimated with a non-exercise model using seismocardiography (SCG 2.1) and directly measured with indirect calorimetry (IC).

Results from the accuracy assesment of the $\dot{V}O_2$max estimation models compared with gold standard IC $\dot{V}O_2$max are presented in table 2.

Table 2. Accuracy of the $\dot{V}O_2$max estimation models compared with IC $\dot{V}O_2$max.

	FriendsAlgo	SCG 1.0	SCG 2.1
Pearson, r	0.51	0.57	0.65
Bias, ml·min^{-1}·kg^{-1}	-6.4±2.1	-4.2±1.9	-3.5±1.8
SEE, ml·min^{-1}·kg^{-1}	9.6	7.9	7.1
CV, %	12 ± 2	9 ± 2	9 ± 2

Note: Data (n=47, test set) are presented as mean ± 95% CI. SEE; standard error of estimate, CV; coefficient of variation, IC; indirect calorimetry. FriendsAlgo [11].

4. Discussion

The accuracy of $\dot{V}O_2$max determination using seismocardiography at rest was investigated in the present study. The interim analysis of the first 50 participants using the SCG 1.0 model revealed beside a significant bias, a moderate correlation of r=0.60 compared with IC $\dot{V}O_2$max, which is lower compared to results previously obtained with that model (high, r=0.90) [8]. The SEE was also higher in the present study compared to previously (5.6 vs. 3.2 $ml \cdot min^{-1} \cdot kg^{-1}$, respectively) [8]. The participants included in the present study constituted a broader representative of the normal population in regards to $\dot{V}O_2$max values compared with the participants being solely in the low to moderate $\dot{V}O_2$max category in the previous study [8]. $\dot{V}O_2$max estimation accuracy in the training set were improved with the modified SCG 2.1 model, as no significant bias was found together with a high correlation and smaller variations between test. When applied in the test set, the SCG 2.1 revealed only a moderate correlation together with a significant bias and larger variations between tests. In addition, the Bland-Altman plot is showing a negative proportional bias (Figure 2), which taken together with a significantly higher measured $\dot{V}O_2$max between the initial 50 and the last 47 participants, reduces the accuracy and thus makes the SCG 2.1 model less accurate when estimated in a more representative extract of the population with higher $\dot{V}O_2$max values. However, when the SCG 2.1 test set is compared with the FriendsAlgo estimation (which include a training set of 7783 subjects and validation set of 1287 subjects), the accuracy was higher as both systematic bias, correlation and variations were improved (Table 2). Nevertheless, further acquisitions of $\dot{V}O_2$max data from a broad population are required in order to improve accuracy of the prediction model.

5. Conclusion

The accuracy of $\dot{V}O_2$max assessment using seismocardiography requires further optimization prior to clinical application, as SCG 2.1 $\dot{V}O_2$max was systematically lower than the gold standard measurement with indirect calorimetry, and a moderate correlation together with considerable variations were observed between tests. Ongoing development of the prediction model is in progress in order to improve the accuracy of $\dot{V}O_2$max estimation using seismocardiography.

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