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Accuracy of a Clinical Applicable Method for Prediction of VO_2max Using Seismocardiography

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ABSTRACT

Cardiorespiratory fitness measured as $\dot{V}O_2$max is considered an important variable in the risk prediction of cardiovascular disease and all-cause mortality. Non-exercise $\dot{V}O_2$max prediction models are applicable, but lack accuracy. Here a model for the prediction of $\dot{V}O_2$max using seismocardiography (SCG) was investigated. 97 healthy participants (18–65 yrs., 51 females) underwent measurement of SCG at rest in the supine position combined with demographic data to predict $\dot{V}O_2$max before performing a graded exercise test (GET) on a cycle ergometer for determination of $\dot{V}O_2$max using pulmonary gas exchange measurements for comparison. Accuracy assessment revealed no significant difference between SCG and GET $\dot{V}O_2$max (mean ± 95 % CI; 38.3 ± 1.6 and 39.3 ± 1.6 ml · min^{-1} · kg^{-1}, respectively. P = 0.075). Further, a Pearson correlation of r = 0.73, a standard error of estimate (SEE) of 5.9 ml · min^{-1} · kg^{-1}, and a coefficient of variation (CV) of 8 ± 1 % were found. The SCG $\dot{V}O_2$max showed higher accuracy, than the non-exercise model based on the FRIENDS study, when this was applied to the present population (bias = − 3.7 ± 1.3 ml · min^{-1} · kg^{-1}, p < 0.0001. r = 0.70. SEE = 7.4 ml · min^{-1} · kg^{-1}, and CV = 12 ± 2 %). The SCG $\dot{V}O_2$max prediction model is an accurate method for the determination of $\dot{V}O_2$max in a healthy adult population. However, further investigation on the validity and reliability of the SCG $\dot{V}O_2$max prediction model in different populations is needed for consideration of clinical applicability.

Introduction

Cardiorespiratory fitness (CRF) is a powerful factor in the risk prediction of cardiovascular disease (CVD), within both healthy and sick populations [1]. This is supported by an inverse relationship between CRF and the risk of CVD and all-cause mortality [2, 3]. Therefore, the American Heart Association stated the significance of incorporating CRF assessment into clinical practice to improve CVD risk prediction and overall patient management in their scientific position statement from 2016 [1]. There are different methods for assessing CRF, the gold standard being the direct measure of maximal oxygen consumption ($\dot{V}O_2$max) using pulmonary gas exchange measurements during an exercise test to exhaustion [4]. However, this methodology is not always suitable or possible, as it is time-consuming and requires maximal effort and expensive equipment. Alternatively, non-exercise prediction models are used [1]. A disadvantage of non-exercise prediction models is the lower accuracy. This especially applies, when used in cohorts different from the one originally assessed [5]. The FRIENDS study addresses the current need for $\dot{V}O_2$max reference standards [6] with an applicable prediction model (age, sex, and weight), which is built and

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validated based on a very large population sample [7]. However, a recently developed and validated $\dot{V}O_2max$ prediction model using seismocardiography (SCG) at rest and demographic data is now available [8, 9]. SCG is a technique that measures the vibrations on the chest wall caused by the beating heart [10], and SCG has been shown to correlate to characteristic events in the cardiac cycle [11]. The SCG $\dot{V}O_2max$ prediction model has recently been adjusted from the previous version of the SCG prediction model. It is within the nature of prediction models to be adjusted when more data are acquired to improve accuracy. The main purpose of this study was to investigate the validity of a model for the prediction of $\dot{V}O_2max$ using SCG compared to the gold standard $\dot{V}O_2max$ determination in a healthy adult population. Additionally, the SCG $\dot{V}O_2max$ prediction model was compared to other non-exercise models using the demographic data from the present study to evaluate, whether the SCG $\dot{V}O_2max$ prediction model performs better than the FRIENDS study [7] and/or the Jones et al. [12] prediction models in this sample.

Materials and Methods

The current study was planned as an external validation of an algorithm for the prediction of $\dot{V}O_2max$, as recommended when developing new machine-learning methods [13]. This study only compares predicted and measured $\dot{V}O_2max$ values performed in a clinical setting, and it is not directed toward improving and/or changing the algorithm behind the prediction models. In addition, this study was part of another research project aiming to develop a biological age model and investigate its clinical applicability [14]. The study was approved by the Science Ethical Committee of the Greater Region of Copenhagen, Denmark (H-18031350), and adhered to the principles of the Helsinki Declaration. The study was registered as a clinical trial (NCT03680768).

Participants

One hundred healthy participants (51 women) with ages ranging from 18 to 65 years were included in the study. Three male participants were excluded from data analyses as their SCG recordings were invalid due to excessive signaling noise. The exclusion criteria were; current or previous cardiovascular disease, chronic medication, pregnancy, or conditions that prevented maximal effort testing on a bicycle ergometer. Before volunteering and signing a written consent, the participants received both oral and written information about the experimental procedures and possible risks associated with the study.

Experimental design

A cross-sectional study design was applied, and the full 2-hour examination protocol used has previously been described [14]. Relevant to the current study, the participants arrived at the laboratory in the morning after an overnight fast, water excluded. Initially, participants were encouraged to empty their bladder, before body composition was determined by a DXA scan (Lunar, iDXA, GE Healthcare, USA). Hereafter, a $\dot{V}O_2max$ prediction was performed at rest in the supine position using seismocardiography (SCG $\dot{V}O_2max$) as previously described [8, 9]. In brief, a five-minute recording of a three-lead ECG and SCG was performed using an iWorx IX-228/s (IWORX, USA), connected to a PC, applying a unit sampling at 5000 Hz in LabScribe recording software (version 3, IWORX, USA). The ECG electrodes were placed on the right and left shoulder and the right and left iliac crest. The SCG signal was recorded with an ultra-sensitive accelerometer (Silicon Design 1521–002), placed on the lower part of the sternum with double adhesive tape. The accelerometer had a resolution of ± 2 g, a low noise at 7 μg / √ Hz, and a frequency response of 0–300 Hz. The accelerometer measured 19 mm in width, 21 mm in length, and 11 mm in height and the total weight of the accelerometer including the electronic components and the ABS plastic housing was five grams. Following the resting measurements, the participants performed a graded exercise test (GET) on a bicycle ergometer (Corival, Lode, Netherlands). The exercise protocol started with a five-minute warm-up at 50 W for women and 100 W for men and was followed by a 25 W increment every minute until voluntary exhaustion. Pulmonary gas exchange measurements were continuously obtained breath-by-breath by an automated online system (Quark, CPET, Cosmed, Italy). Breath-by-breath measurements were analyzed using 30-s rolling averages, and $\dot{V}O_2max$ was determined as the highest 30-s $\dot{V}O2$ value. Heart rate (HR) was measured continuously throughout the test (Vivoactive, Garmin, USA) and the highest value determined HRmax. Furthermore, the participants' perceived exertion on the Borg's 6–20 scale [15] was assessed directly following the termination of the test. The credibility of the $\dot{V}O_2max$ value was assessed and accepted, if a $\dot{V}O_2$ plateau was obtained, or if two out of the three secondary criteria were met. The $\dot{V}O_2$ plateau was defined as less than 2.1 $ml \cdot min^{-1} \cdot kg^{-1}$ increase in VO_2 with increasing workload [16]. The secondary criteria were; a respiratory exchange ratio > 1.10, HRmax within 10 bpm of age-predicted HRmax (220-age), and ≥ 18 on the Borg 6–20 scale [17, 18]. In 78 out of 97 tests a $\dot{V}O_2$ plateau was obtained, and all the remaining 19 tests fulfilled at least two out of three secondary criteria.

Signal processing

The resting ECG and SCG measurements were performed at our laboratory. Subsequently, the recording was sent to the company, VentriJect Aps, together with the age, weight, height, and sex of each participant, for analysis. The ECG and SCG recordings were exported from the iWorx system and processed in MATLAB (2018a. MathWorks, USA). Firstly, the signal processing was performed automatically and was afterward checked and verified manually as previously described [8, 11]. Hereafter, a $\dot{V}O_2max$ value was received from VentriJect and validated against the $\dot{V}O_2max$ value obtained from the GET. VentriJect was blinded to the measured $\dot{V}O_2max$ value during the whole process.

SCG non-exercise prediction model

The present version of the SCG $\dot{V}O_2max$ prediction model (SCG 4.3) is based on linear regression. Features selection and training were done in independent data from two previous studies [8, 9]. The current model is therefore an updated version of the previous developed SCG models: SCG 1.0 [8] and SCG 2.1 [9]. The SCG 4.3 include the following features and fiducial points:

SCG 4.3 $\dot{V}O_2max$ = (− 15.108) + (− 0.122 · S2FrequencySpec) + (0.371 · S2Morphology) + (0.001 · RR) + (0.247 · S1FrequencySpec) + (0.701 · FRIENDS study prediction model) + (143.4 · amp_Dd) +

(− 159.45 · amp_Ks) + (− 0.042 · SYSRV_STD) + (− 87.583 · amp_Ls) + (42.993 · amp_Fs)

Abbreviations: S2FrequencySpec; frequency of the average SCG diastolic complex quantified using principal component analysis. S2Morphology; morphology of the average SCG diastolic complex quantified using principal component analysis. RR; Average duration of heartbeat in milliseconds. S1FrequencySpec; frequency of the average SCG systolic complex quantified using principal component analysis. FRIENDS study prediction model [7]; an algorithm based on sex, age, and body weight for prediction of $\dot{V}O_2max$. Amp_Dd; SCG value at the Dd fiducial point (▶ **Figure 1**). Amp_Ks; SCG value at the Ks fiducial point (▶ **Figure 1**). SYSRV_STD; variation in systolic duration caused by respiration. Amp_Ls; SCG value at the Ls fiducial point (▶ **Figure 1**). Amp_Fs; SCG value at the Fs fiducial point (▶ **Figure 1**). A more detailed description of the features and their units is presented in Table S1 in the supplementary.

Other non-exercise prediction models

The following equations from the FRIENDS study [7] and Jones et al. [12] were applied to the raw data of the participants in the present study for comparison of the different prediction models. **FRIENDS study**: $\dot{V}O_2max$ (ml · min$^{−1}$ · kg$^{−1}$) = 79.9 – (0.39 x age) – (13.7 x sex [0 = men; 1 = women]) – (0.127 x weight [lbs])

Jones et al.: $\dot{V}O_2max$ (L · min$^{−1}$) = 0.046 x height [cm] – 0.021 x age – sex [4.31 = men; 4.93 = women]

Statistics

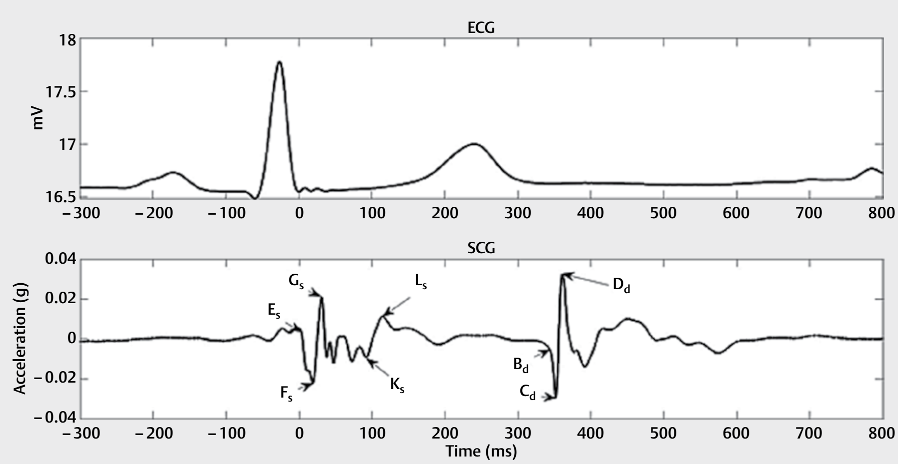
Data are presented as mean ± 95 % confidence intervals (CI). All data were checked for normal distribution with Shapiro-Wilk tests. Data was analysed as one group as the main outcome and divided by sex and age groups to assess if the algorithm was performing differently between sexes and within different age groups as a secondary outcome. Systematic difference in $\dot{V}O_2max$ between SCG and GET within sexes and within age groups was analysed with two-way ANOVA repeated measures tests. A post-hoc Šidák's multiple comparison test was applied, when a significant effect of the test or interaction of group x test was found. Inter-method validity was analysed with Pearson correlation coefficient r, coefficient of variation (CV), standard error of estimate (SEE), and mean absolute percentage error (MAPE). The interpretation of Pearson correlation coefficients was; 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 [19]. SEE was calculated using:

$$SEE = \sqrt{\sum(Y - Y')^2 / (n - 2)},$$

with Y and Y' representing the GET $\dot{V}O_2max$ and SCG 4.3 $\dot{V}O_2max$ values respectively. The SEE interpretation was: very good < 4.0 ml · min$^{−1}$ · kg$^{−1}$, good 4.0–6.0 ml · min$^{−1}$ · kg$^{−1}$, fair 6.0–8.0 ml · min$^{−1}$ · kg$^{−1}$, poor 8.0–10.0 ml · min$^{−1}$ · kg$^{−1}$, and > 10.0 ml · min$^{−1}$ · kg$^{−1}$ very poor. The SEE interpretation is based on previous non-exercise models using only objective measures such as weight, height, age, and sex [7, 20] or together with subjective measures of activity level or physiological work capacity [20, 21]. A MAPE ≤ 10 % was chosen as the criteria level for the prediction model to be considered clinically relevant. A Bland-Altman plot with 95 % limits of agreement (LoA) was applied to assess agreement between methods. Statistical analyses were performed, and figures were constructed in GraphPad Prism 9.3.1 (GraphPad Software, USA) and Microsoft Excel (Microsoft Office 2016, USA).

Results

Demographic data of the participants are presented in ▶ **Table 1** and the measured and predicted $\dot{V}O_2max$ values in ▶ **Table 2**.



▶ **Figure 1** Illustration of a filtered signal from a participant. Signals are means of simultaneously recorded electrocardiography (ECG) and seismocardiography (SCG) recordings. The arrows indicate the different fiducial points used in the SCG 4.3 $\dot{V}O_2max$ prediction model with annotation of fiducial points following what is previously used in a normal SCG signal [11]. Es: Mitral valve closure. Fs: Aortic valve opening minimum point. Gs: Aortic valve opening maximum point. Ks: Systolic outflow minimum point. Ls: Systolic outflow maximum point. Bd: Aortic valve closure. Cd: Aortic valve closure minimum point and Dd: Aortic valve closure maximum point.

SCG 4.3 $\dot{V}O_2$max prediction

For the entire population, no systematic difference in $\dot{V}O_2$max was observed between SCG 4.3 and GET (P = 0.075). The inter-method validity assessment revealed a high Pearson correlation (▶ **Figure 2**), together with a good SEE and an acceptable intra-individual CV (▶ **Table 3**). Further, a reasonable agreement between test methods was observed, as a small and non-significant bias was found, despite considerable 95 % LoA (▶ **Figure 3**). However, a linear regression plot revealed that the bias was not consistent through the range of the data (▶ **Figure 3**). The MAPE was higher than the criteria specified for clinical application (▶ **Table 3**).

Within-group differences in SCG 4.3 $\dot{V}O_2$max prediction

When data was analysed categorized by sex, a significantly lower SCG 4.3 $\dot{V}O_2$max compared with GET $\dot{V}O_2$max was observed for men (n = 46, P = 0.028), but not for women (n = 51, P = 1.00). The inter-method validity assessment showed a moderate Pearson correlation for men, whereas it was high for women (▶ **Table 4**). Furthermore, the SEE was 66 % and CV 43 % higher for men compared with women (▶ **Table 4**). The agreement between test methods was poor for men with a significant bias and 95 % LoA ranging from − 15.82 to 11.58 ml · min^{-1} · kg^{-1}, whereas for women, a good agreement was observed with a non-significant bias and smaller 95 % LoA ranging from − 8.54 to 8.57 ml · min^{-1} · kg^{-1}. However, a linear regression plot revealed that the bias was not consistent through the range of the data for either men or women (▶ **Figure 3**).

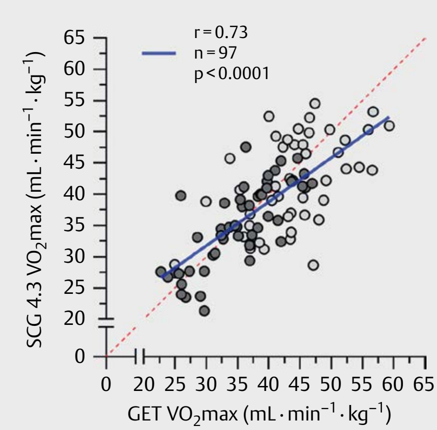
When data were analysed according to age, no differences between SCG 4.3 and GET $\dot{V}O_2$max were found for the age group 18–33 yrs. (n = 34) and 34–49 yrs. (n = 31), but SCG 4.3 was significantly lower for the age group 50–65 yrs. (n = 32) (▶ **Table 4**).

Other non-exercise prediction models

Application of both the FRIENDS study and Jones et al. $\dot{V}O_2$max prediction models resulted in significantly lower $\dot{V}O_2$max compared with GET (▶ **Table 3**). Both prediction models showed a high correlation when compared to GET $\dot{V}O_2$max, together with a fair SEE for the FRIENDS study and a poor SEE for the Jones et al. prediction model (▶ **Table 3**). The MAPE of both prediction models was higher than the specified criteria for clinical application (▶ **Table 3**).

Discussion

In the present study, the validity of an adjusted $\dot{V}O_2$max prediction model using seismocardiography was compared with the gold standard $\dot{V}O_2$max measurement in a healthy adult population. The main finding was that SCG 4.3 $\dot{V}O_2$max prediction on group level



▶ **Figure 2** Scatterplot of the correlation between $\dot{V}O_2$max estimated with a prediction model using seismocardiography (SCG 4.3) and gold standard measurement of $\dot{V}O_2$max applying a graded exercise test (GET) until exhaustion with pulmonary gas exchange. The dark grey data point illustrates women and the light grey data point illustrates men. The dotted red line is the identity line (r = 1.0). The blue line is the regression line for all participants.

▶ **Table 1** Characteristics of the participants

	All, n = 97	Women, n = 51	Men, n = 46
Age, yrs.	41 ± 3 [18–64]	41 ± 4 [21–64]	41 ± 4 [18–64]
Height, cm	175 ± 2 [156–196]	169 ± 2 [156–181]	181 ± 2 [169–196]
Weight, kg	75.4 ± 2.6 [47.3–116.8]	69.2 ± 3.5 [47.3–116.8]	82.4 ± 2.8 [64.4–106.0]
BMI, kg · m^{-2}	24.6 ± 0.7 [17.3–37.1]	24.2 ± 1.1 [17.3–37.1]	25.1 ± 0.8 [20.1–32.5]
Body fat, %	26.9 ± 1.7 [10.3–47.3]	31.9 ± 1.8 [16.5–47.3]	21.4 ± 1.8 [10.3–36.9]
Resting HR, bpm	59 ± 2 [37–86]	62 ± 3 [46–85]	56 ± 3 [37–86]

Data are presented as mean ± 95 % CI and [range]. BMI, body mass index; HR, heart rate.

▶ **Table 2** Measured and predicted $\dot{V}O_2$max values from the participants

	GET ml · min^{-1} · kg^{-1}	SCG ml · min^{-1} · kg^{-1}	FRIENDS study ml · min^{-1} · kg^{-1}	Jones et al. ml · min^{-1} · kg^{-1}
All (n = 97)	39.3 ± 1.6 [22.7–59.3]	38.3 ± 1.6 [21.3–54.5]	35.5 ± 1.6 [19.5–52.0]	33.7 ± 1.6 [15.5–51.5]
Sex				
Men (n = 46)	44.1 ± 2.0 [25.0–59.3]	42.0 ± 2.1 [28.7–54.5]	40.8 ± 1.9 [29.1–52.0]	38.8 ± 1.9 [29.8–51.5]
Women (n = 51)	34.9 ± 1.8 [22.7–47.0]	34.9 ± 1.8 [21.3–47.6]	30.8 ± 1.7 [19.5–44.5]	29.2 ± 1.7 [15.5–43.4]
Age				
18–34 yrs. (n = 34)	41.9 ± 2.5 [22.7–59.3]	43.7 ± 2.1 [27.6–53.2]	41.6 ± 2.3 [24.6–52.0]	39.0 ± 2.5 [24.7–51.5]
34–50 yrs. (n = 31)	39.8 ± 2.9 [25.0–56.6]	38.6 ± 2.6 [23.5–54.5]	35.4 ± 2.2 [22.9–48.6]	32.6 ± 2.6 [16.1–49.8]
50–65 yrs. (n = 32)	35.2 ± 2.7 [23.8–52.4]	32.3 ± 1.7 [21.3–44.1]	29.1 ± 1.9 [19.5–38.3]	29.2 ± 2.1 [15.5–39.2]

Data are presented as mean ± 95 % CI and [range]. GET; graded exercise test. SCG; $\dot{V}O_2$max prediction model using seismocardiography version 4.3. FRIENDS study; application of the prediction model from the FRIENDS study [7]. Jones et al.; application of the prediction model from Jones et al. [17].

▶ **Table 3** Inter-method validity assessment of $\dot{V}O_2$max prediction models compared with gold standard measured $\dot{V}O_2$max.

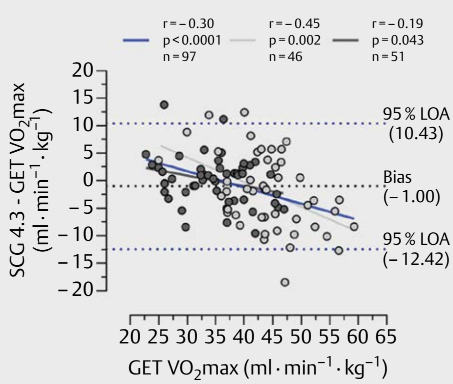
	Pearson r	Bias ml · min⁻¹ · kg⁻¹	SEE ml · min⁻¹ · kg⁻¹	MAPE %	CV %
SCG 4.3	0.73	− 1.0 ± 1.2	5.9	12.3	8 ± 1
FRIENDS study	0.70	− 3.7 ± 1.3***	7.4	18.3	12 ± 2
Jones et al.	0.72	− 5.5 ± 1.2***	8.3	22.6	14 ± 2

Data are presented as mean ± 95 % CI. n = 97. SCG 4.3; $\dot{V}O_2$max prediction model using seismocardiography version 4.3. FRIENDS study; application of the prediction model from the FRIENDS study [7]. Jones et al.; application of the prediction model from Jones et al. [17]. SEE; standard error of estimate. MAPE; mean absolute percentage error. CV; coefficient of variation. ***significant difference between SCG 4.3 and GET (p < 0.0001).

▶ **Table 4** Within group validity assessment of SCG 4.3 $\dot{V}O_2$max prediction model compared with GET.

	Pearson r[1]	Bias ml · min⁻¹ · kg⁻¹	SEE ml · min⁻¹ · kg⁻¹	MAPE %	CV %
Sex					
Men (n = 46)	0.55	− 2.1 ± 2.1*	7.3	15.3	10 ± 2
Women (n = 51)	0.81	0.0 ± 1.2	4.4	9.6	7 ± 2
Age					
18–34 yrs. (n = 34)	0.71	1.8 ± 1.9	5.7	9.9	7 ± 2
34–50 yrs. (n = 31)	0.78	− 1.3 ± 2.0	5.6	11.0	8 ± 2
50–65 yrs. (n = 32)	0.69	− 3.7 ± 2.0**	6.9	16.1	10 ± 3

Data are presented as mean ± 95 % CI. SCG 4.3; VO_2max prediction model using seismocardiography version 4.3. GET; graded exercise test. SEE; standard error of estimate. MAPE; mean absolute percentage error. CV; coefficient of variation. *(p < 0.05) and **(p < 0.001) denotes significant difference between SCG 4.3 and GET.



▶ **Figure 3** A Bland-Altman plot of the agreement between $\dot{V}O_2$max estimated with a prediction model using seismocardiography (SCG 4.3) and gold standard measurement of $\dot{V}O_2$max applying a graded exercise test (GET) until exhaustion with pulmonary gas exchange. The dark grey data point illustrates women and the light grey data point illustrates men. LoA; limits of agreement. n = 97. The blue line represents the regression line for all participants. The dark grey line and the light grey line represent the regression line for women and men, respectively.

demonstrated as an accurate method for determination of $\dot{V}O_2$max, as no systematical difference, a high correlation, a good SEE, and an acceptable CV % were observed.

Comparisons of $\dot{V}O_2$max predictions

To compare SCG 4.3 with other non-exercise prediction models, the FRIENDS study [7] and the model proposed by Jones et al. [12] were chosen, mainly because the same objective variables (weight and age) were included in their models. The strength of the FRIENDS study prediction model is that it is built on data from 7783 subjects and validated in 1278 subjects, showing a Pearson's r of 0.79 and a SEE of 7.2 ml · min⁻¹ · kg⁻¹[7]. When the FRIENDS study prediction model was applied to our participants (▶ **Table 3**), it showed very similar results compared with the original data. The results were more deviating (▶ **Table 3**), when the Jones et al. [12] prediction was applied. The FRIENDS study prediction model is therefore considered an acceptable reference model for comparison of the accuracy for the present prediction model. The SCG 4.3 revealed better overall accuracy compared with the FRIENDS study prediction, indicating that the objective SCG measurements included indeed improved performance of the prediction model. Especially the improvement seen in SEE, MAPE, and CV could make the SCG prediction model interesting in a clinical setting in the future. From a physiological perspective, adding information on the cardiac function to the $\dot{V}O_2$max prediction model is logical. It is generally accepted that $\dot{V}O_2$max primarily is limited by the rate of oxygen delivery to the muscles, where maximal cardiac output is the main limiting factor, especially within the normal population [22, 23]. The Frank-Starling law indicates that a faster relaxation and increase in the diastolic filling would lead to an increase in cardiac output and stroke volume and thereby improve $\dot{V}O_2$max. This emphasizes the importance of improvements in the diastolic complex when aiming for a larger cardiac output and thus $\dot{V}O_2$max. Further, the increase in $\dot{V}O_2$max following a prolonged exercise training period has been shown to be associated with an increase in both maximal cardiac output and stroke volume, due to cardiac morphological adaptations, and especially an improvement in the diastolic function [24]. A faster relaxation would result in a more rapid pressure drop in the left ventricle and thereby create a greater difference between left ventricular and ascending aortic pressure. This would generate a larger amplitude in the SCG signal around the aortic valve closure area (Fiducial point Dd in ▶ **Figure 1**) and give a higher $\dot{V}O_2$max prediction with the model. The fiducial points in the SCG signal have previously been shown to correlate to cardiac events such as peak early ventricular filling [11]. Additionally, cross-sectional data shows that endurance-trained individuals have enhanced early diastolic left ventricular filling and a more rapid filling of the heart during high-intensity exercise compared to untrained individuals [25]. Furthermore, systolic SCG information has also previously been linked with cardiac contractility [26, 27], and therefore both measures of diastolic relaxation and systolic contraction are included in the SCG prediction model. Here, it is shown that adding SCG information to the non-exercise prediction model resulted in an improved and accurate $\dot{V}O_2$max prediction in a healthy adult population. Additionally, the SCG constitutes an easy measurement technique of cardiac function at rest. Therefore, the SCG model shows potential as a relevant method for implementing $\dot{V}O_2$max assessment in the clinical practice and thereby improve both CVD risk prediction and overall patient management. However, much more data are required in different populations, together with more validity and reliability assessments of the SCG prediction model in future studies.

Within-group comparison of SCG 4.3 $\dot{V}O_2$max prediction

Performance of the SCG 4.3 prediction model showed discrepancies regarding sex, as a difference was observed between SCG 4.3 and GET $\dot{V}O_2$max for men, but not women. The first SCG prediction model (SCG 1.0) was built and validated in a cohort with mostly women (65 %) [8], and this could be a reason for the discrepancy in performance. Conversely, the further added data for the development of prediction model versions 2.1 and 4.3 was composed of approximately 50 % men and 50 % women. In contrast, a large bias between the FRIENDS study and GET $\dot{V}O_2$max was seen for both women and men when applied to the present study population (▶ **Table 2**). This deviates from the original data in the FRIENDS study where no difference was observed between the sexes when compared to the measured peak $\dot{V}O_2$ value. This could indicate that some of the discrepancy is related to the investigated population. The SCG 4.3 prediction model and the FRIENDS study both lack consistency throughout the data, with the prediction models underestimating more with higher VO_2max values. This especially applies for the men. In this study, the training status of the participants is better compared with the subjects from the FRIENDS study [7]. Approximately 50 % of the men have a $\dot{V}O_2$max above 45 ml · min^{-1} · kg^{-1}, which could explain some of the discrepancies in regards to sex observed in this study. These findings, however, suggest that an adjustment in the prediction model regarding prediction in males is needed to increase accuracy and thereby applicability. Regarding performance within different age groups, the SCG 4.3 prediction model showed no difference in $\dot{V}O_2$max compared with GET within the two age groups ranging from ages 18 to 50, but it was significantly lower in the 50–65 year-old age group. Still, the $\dot{V}O_2$max prediction was numerically higher in the 18–34 year-old age group and numerically lower in the 34–50 year-old age group, indicating that the prediction model may require an adjustment coupled with the age variable. That said, the development of the SCG 4.3 prediction model was based on data from subjects mainly younger than age 50, with a substantial part being below 40 yrs. However, the measured $\dot{V}O_2$max values are low in the young age group and high in the oldest age group when compared to the values from the FRIENDS study [7]. These findings further emphasize the importance of a large and heterogeneous sample size for the development of $\dot{V}O_2$max prediction models [5].

Study limitations

A limitation of the study is the lack of knowledge on the influence of the independent variables within the SCG prediction model. When applying 12 independent variables there is a risk of overfitting the model, which would result in lower performance in an independent dataset as in the current study. Furthermore, studies should analyze the influence of the individual model variables in order to potentially improve the model performance. Another limitation of this study is the lack of reliability measurements of the SCG $\dot{V}O_2$max prediction model. This would have strengthened the assessment of validity. Furthermore, even though the recording of the SCG signal with the iWorx box and the connected PC is easy to perform, it still requires the necessary equipment. When compared to other non-exercise prediction models, this is a limitation.

Conclusion

Overall the SCG 4.3 $\dot{V}O_2$max prediction model proved to be an accurate method for determination of $\dot{V}O_2$max in a healthy adult population. No systematical difference, a high correlation, a good SEE, and an acceptable CV % were observed when compared to the gold standard determination of $\dot{V}O_2$max. However, the accuracy of the SCG 4.3 prediction model was superior in women compared to men, and the model systematically underestimated $\dot{V}O_2$max in participants above 50 years of age. The SCG 4.3 $\dot{V}O_2$max prediction model performed better when compared to the application of the non-exercise model based on the FRIENDS study. The improved accuracy together with automatic signal processing achieved in the SCG 4.3 prediction model is of interest, when aiming at clinical relevance and applicability. However, further validity and reliability assessments in different subgroups of the population are needed before being considered clinically relevant.

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Conflict of Interest

The authors declare that SES and KS hold significant shares in VentriJect Aps and have worked part-time as Chief Scientific Officer and Head of Software in VentriJect Aps in the past 3 years, respectively. There was no restriction on publication.

References

[1] Ross R, Blair SN, Arena R et al. Importance of assessing cardiorespiratory fitness in clinical practice: a case for fitness as a clinical vital sign: a scientific statement from the american heart association. Circulation 2016; 134: e653–699

[2] Blair SN, Kohl HW 3rd, Paffenbarger RS Jr et al. Physical fitness and all-cause mortality. a prospective study of healthy men and women. JAMA 1989; 262: 2395–2401

[3] Kodama S, Saito K, Tanaka S et al. Cardiorespiratory fitness as a quantitative predictor of all-cause mortality and cardiovascular events. JAMA 2009; 301: 2024–2035

[4] Fletcher GF, Ades PA, Kligfield P et al. Exercise standards for testing and training: a scientific statement from the american heart association. Circulation 2013; 128: 873–934

[5] Malek MH, Housh TJ, Berger DE et al. A new nonexercise-based $\dot{V}O_{2max}$ equation for aerobically trained females. Med Sci Sports Exerc 2004; 36: 1804–1810

[6] Kaminsky LA, Arena R, Beckie TM et al. The importance of cardiorespiratory fitness in the united states: the need for a national registry: a policy statement from the american heart association. Circulation 2013; 127: 652–662

[7] Myers J, Kaminsky LA, Lima R et al. A reference equation for normal standards for VO_2Max: analysis from the fitness registry and the importance of exercise national database (FRIEND Registry). Prog Cardiovasc Dis 2017; 60: 21–29

[8] Sørensen K, Poulsen MK, Karbing DS et al. A clinical method for estimation of VO_2max using seismocardiography. Int J Sports Med 2020; 41: 661–668

[9] Hansen MT, Grønfeldt BM, Rømer T et al. Determination of maximal oxygen uptake using seismocardiography at rest. In: computing in cardiology 2021. IEEE 2021; 48–51

[10] Mounsey P. Praecordial ballistocardiography. Br Heart J 1957; 19: 259–271

[11] Sørensen K, Schmidt SE, Jensen AS et al. Definition of fiducial points in the normal seismocardiogram. Sci Rep 2018; 8: 15455

[12] Jones NL, Makrides L, Hitchcock C et al. Normal standards for an incremental progressive cycle ergometer test. Am Rev Respir Dis 1985; 131: 700–708

[13] König IR, Malley JD, Weimar C et al. Practical experiences on the necessity of external validation. Stat Med 2007; 26: 5499–5511

[14] Husted KLS, Fogelstrøm M, Hulst P et al. A biological age model designed for health promotion interventions: protocol for an interdisciplinary study for model development. JMIR Res Protoc 2020; 9: e19209

[15] Borg GA. Psychophysical bases of perceived exertion. Med Sci Sports Exerc 1982; 14: 377–381

[16] Taylor H, Henschel A, Buskirk E. Maximal oxygen intake as an objective measure of cardio-respiratory performance. J Appl Physiol 1955; 8: 73–80

[17] Edward T. Howley, David R. Bassett, JR. and HGW. Criteria for maximal oxygen uptake: review and commentary. Med Sci Sport Exerc 1995; 27: 1292–1301

[18] Edvardsen E, Hem E, Anderssen SA. End criteria for reaching maximal oxygen uptake must be strict and adjusted to sex and age: A cross-sectional study. PLoS One 2014; 9: 18–20

[19] Hinkle DE, Wiersma W, Jurs SG. Correlation: A measure of relationship. In: Hinkle DE, Wiersma W, Jurs SG, (Eds). Applied statistics for the behavioral sciences. Boston, USA: Houghton Miffin Company; 1994: 103–128

[20] Malek MH, Berger DE, Housh TJ et al. Validity of $\dot{V}O_{2max}$ Equations for aerobically trained males and females. Med Sci Sports Exerc 2004; 36: 1427–1432

[21] Wier LT, Jackson AS, Ayers GW et al. Nonexercise models for estimating $\dot{V}O_{2max}$ with waist girth, percent fat, or BMI. Med Sci Sports Exerc 2006; 38: 555–561

[22] Levine BD. $\dot{V}$O2max: What do we know, and what do we still need to know? J Physiol 2008; 586: 25–34

[23] Bassett DR, Howley ET. Limiting factors for maximum oxygen uptake and determinants of endurance performance. Med Sci Sports Exerc 2000; 32: 70–84

[24] Arbab-Zadeh A, Perhonen M, Howden E et al. Cardiac remodeling in response to 1 year of intensive endurance training. Circulation 2014; 130: 2152–2161

[25] Hellsten Y, Nyberg M. Cardiovascular adaptations to exercise training. Compr Physiol 2016; 6: 1–32

[26] Zanetti JM, Tavakolian K. Seismocardiography: past, present and future. Annu Int Conf IEEE Eng Med Biol Soc 2013; 2013: 7004–7007

[27] Morra S, Pitisci L, Su F et al. Quantification of cardiac kinetic energy and its changes during transmural myocardial infarction assessed by multi-dimensional seismocardiography. Front Cardiovasc Med 2021; 8: 603319