SUPPLEMENTAL MATERIAL FOR:

Validity and reliability of Seismocardiography for the Estimation of Cardiorespiratory Fitness

Authors:

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Short Title: Validity and Reliability of SeismoFit for Estimation of Cardiorespiratory Fitness

Key Words: SeismoFit, seismocardiography, VO_2peak estimation, validity and reliability, cardiopulmonary exercise test.

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Experimental design and measurements

The recruitment strategy is shown in supplementary Table 1. The participants reported to the laboratory in the morning between 7 and 11 a.m. (27 ± 5 min, mean ± SEM) after an overnight fast (>10 h) and at the same time on the three test days. Firstly, after voiding, the height, weight, and body composition of the participants were determined. Body composition was determined by a dual-energy X-ray absorptiometry (DXA) scan (Lunar Prodigy Advance, iDXA, GE Healthcare, United States) on test day one and measured with a bio-impedance scale (MC-780MA, Tanita, Japan) on all three test days. The participants were hereafter laid in the supine position in a hospital bed for the following measurements. Firstly, blood pressure was measured in triplicate with two minutes between measurements (UA-1020, A&D Medical, Japan). This was followed by a $\dot{V}O_2$peak estimation of SeismoFit 1 and hereafter SeismoFit 2 and Polar Fitness Test (PFT) performed in randomised order. Subsequently, a small venous blood sample was collected in a specialised syringe (SafePICO Aspirator, Radiometer, Denmark) and immediately analysed using an automatic analyser (ABL800 Flex, Radiometer, Denmark). The blood sample was applied to control for pre-exercise haematocrit and haemoglobin levels across the three test days. Finally, a gold standard cardiopulmonary exercise test (CPET) for the determination of $\dot{V}O_2$peak was performed on a cycle ergometer.

Non-exercise estimation of $\dot{V}O_2$peak

The SeismoFit system used for the recording of SCG and estimation of $\dot{V}O_2$peak is a patented and CE-marked medical device for measuring cardiorespiratory fitness (VentriJect Aps, Denmark). The SeismoFit contains a three-axis digital output accelerometer (LIS3DHH, ST Microelectronics, Switzerland) for SCG recording. The SCG $\dot{V}O_2$peak was performed by placement of the SeismoFit two centimetres proximal to processus Xiphoideus on the sternum attached with adhesive tape for the repeated estimation on each test day (**Supplementary Figure 1**).

Supplementary Figure 1.

Shows the SeismoFit device attachment on a participant.

Cardiorespiratory fitness test ($\dot{V}O_2$peak)

The incremental cardiopulmonary exercise test was performed on a cycle ergometer (Monark 839E, Monark Exercise AB, Sweden) and different protocols were applied to each of the four subgroups (Supplementary Table 2). The gas analysers were calibrated before each CPET with a compressed gas mixture of 5% CO_2 and 16% O_2 and the digital flowmeter was calibrated using a 3-L calibration syringe (Cosmed, Italy). The measurement error of the Quark CPET gas analyser is 0.02% for CO_2 and 0.1% for O_2 and 2% for the flowmeter (Cosmed, Italy). Unfortunately, due to a measurement error, data from the third CPET of two participants were excluded. These two CPET were performed on the same day in the laboratory. Data from all CPET from the above two participants are presented in Supplementary Figure 2. The difference between measured fractions of inspired (FIO_2) and expired oxygen (FEO_2) was higher during the test on test day three compared with test day one and test day two for both participants (C and D in Supplementary Figure 2). As the ventilation during the test from all three test days was similar (E and F in Supplementary Figure 2), this resulted in an incorrectly high oxygen consumption during test day three for both participants (G and H in Supplementary Figure 2). This is the explanation for the exclusion of test day three from the two participants. When the measurement error was discovered, it was too late to conduct a new test day that would be within a reasonable timeframe.

Every CPET was controlled for the achievement of a $\dot{V}O_2$ plateau. As mentioned in the article a plateau in $\dot{V}O_2$ was defined as less than 2.1 $ml \cdot min^{-1} \cdot kg^{-1}$ change in $\dot{V}O_2$ with increasing workload. In 50 out of the 58 included CPET, a $\dot{V}O_2$ plateau was achieved. Six of

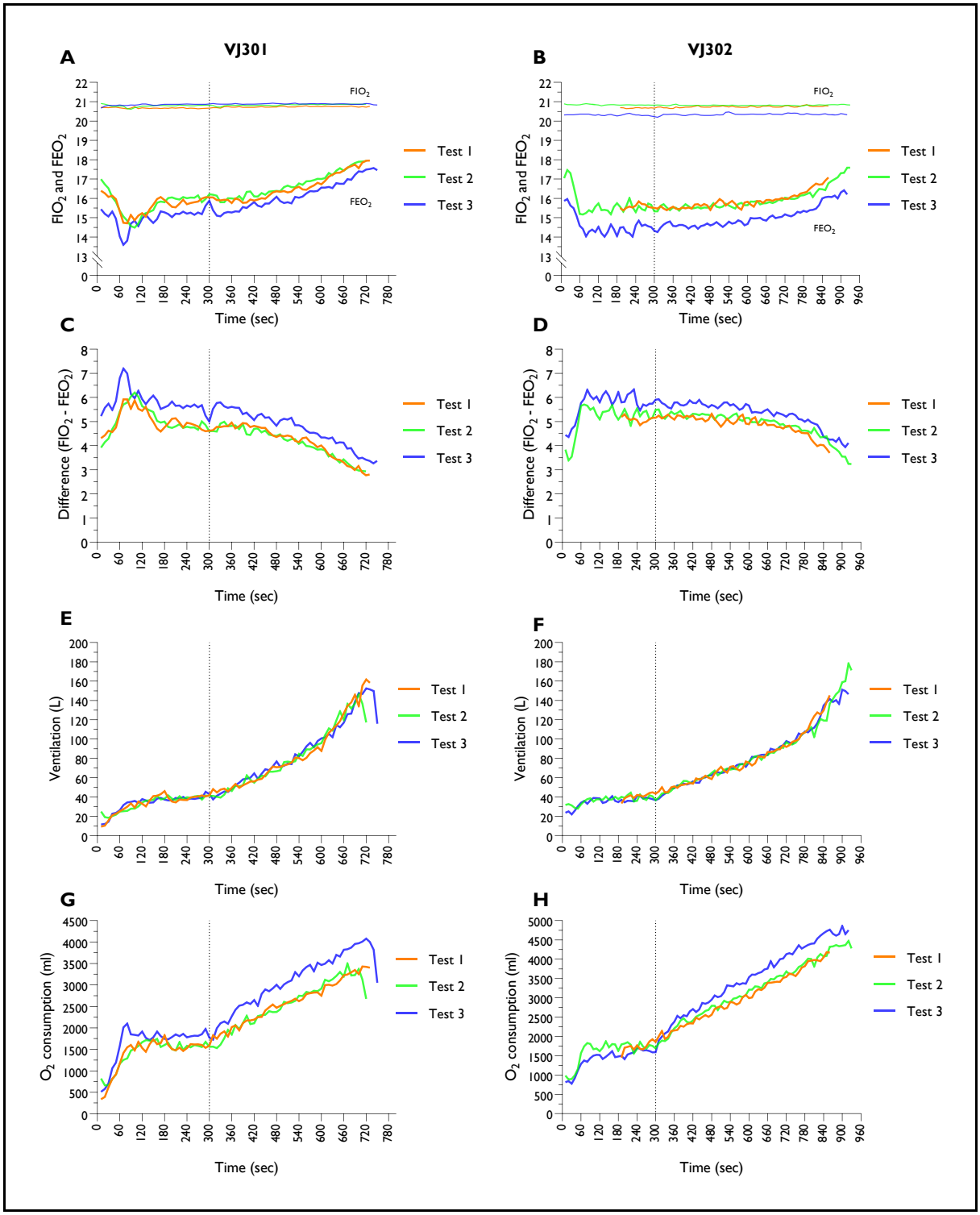
the eight CPET not achieving a $\dot{V}O_2$ plateau were on test day 1 and the remaining two on test day 3. All participants achieved a $\dot{V}O_2$ plateau on the second test day. The eight CPET that did not achieve a $\dot{V}O_2$ plateau fulfilled at least two out of three secondary criteria (a respiratory exchange ratio > 1.10, a maximal heart rate within 5 bpm of the highest measured value on the three test days and ≥ 18 on Borg 6-20 scale).
Therefore, data from 58 CPET is included in the analysis. Relevant individual values from the CPET are presented in Supplementary Figure 3.

Supplementary Table 1: Recruitment strategy

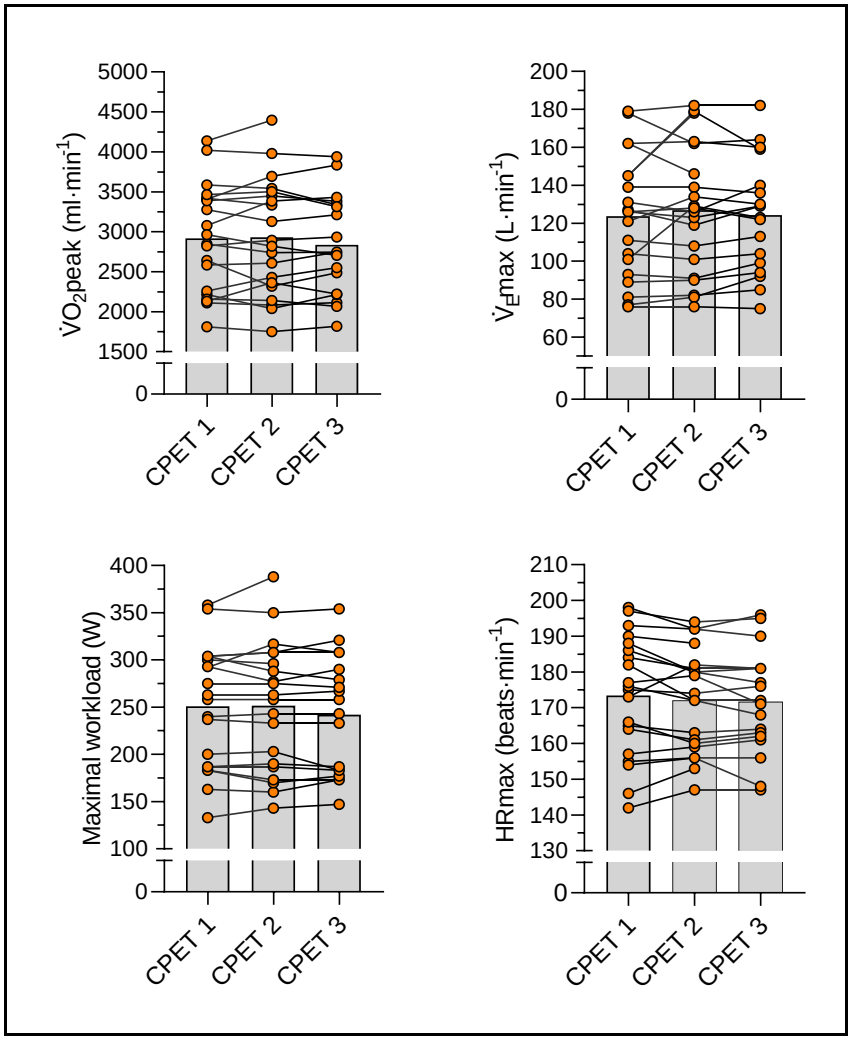
	Age: 20 - 40 yrs.		**Age: 40 - 75 yrs.**		Total
	n =	ml/min/kg	n =	ml/min/kg	n =
Trained group:	**4**		**6**		**10**
- males	2	> 50	3	> 40	5
- females	2	> 42	3	> 38	5
Untrained group:	**4**		**6**		**10**
- males	2	< 40	3	< 35	5
- females	2	< 35	3	< 30	5
Total, n =	**8**		**12**		**20**

Supplementary Table 2: CPET protocol for trained and untrained men and women

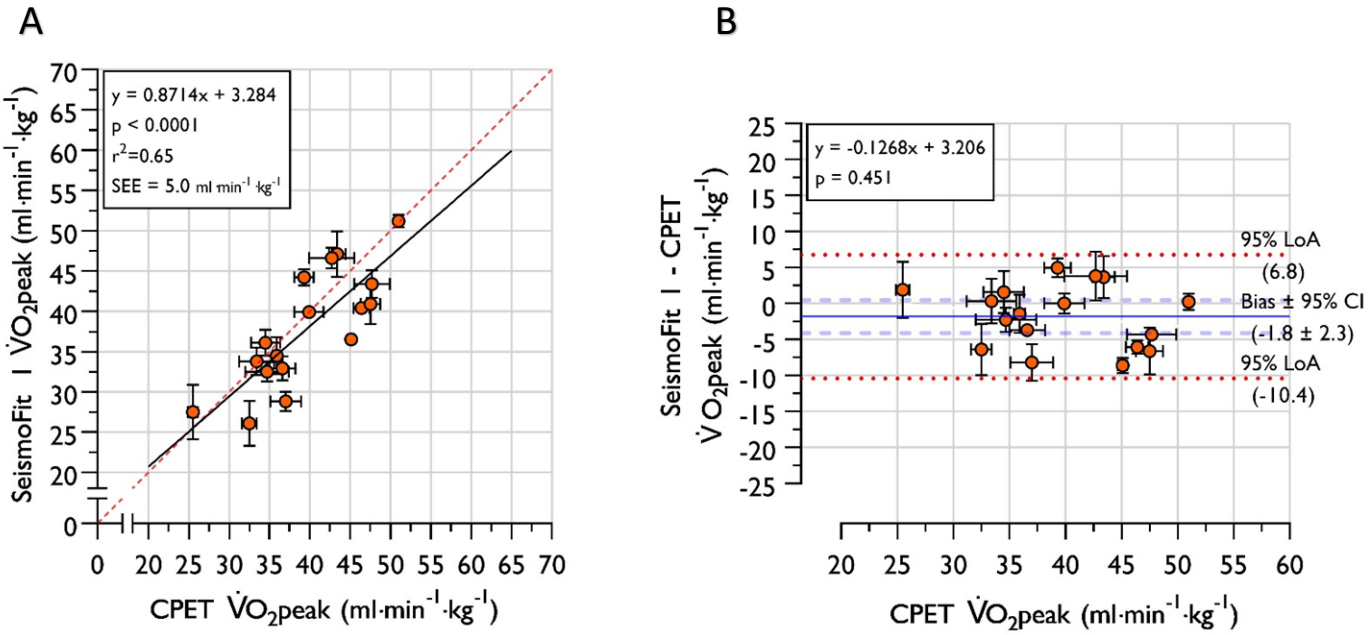
	Warm-up workload (Watt)	**Initial test workload (Watt)**	**Increase in workload per minute (Watt)**
Men			
Trained	100	150	25
Untrained		125	
Women			
Trained	70	100	20
Untrained		80	



Supplementary Figure 2. Pulmonary gas exchange data was measured during three graded exercise tests performed on a cycle ergometer from two participants (VJ301 and VJ302). Figure A and B show the fraction of inspired oxygen (FIO_2) and the fraction of expired oxygen (FEO_2) during the tests. Figure C and D show the difference between FIO_2 and FEO_2 during the tests. Figure E and F show the ventilation during the test and figure G and H show the oxygen consumption during the test. The dotted line represents the beginning of workload increments after warm-up.



Supplementary Figure 3. The figure is showing the individual data from the three CPET conducted (n=20). The bars represent the group mean for each of the three CPET. VO_2 peak; peak oxygen consumption, $V_E$max; maximal ventilation measured over 10 seconds, HRmax; maximal heart rate. Maximal workload is calculated using the last completed Watt stage + (Seconds / 60 seconds * watt increments in the respective protocol).



Supplementary Figure 4. Data (n=17) are mean ± 95% CI of three separate tests for each participant with an age under 70 years. A) A Scatter plot with linear regression between VO_2peak estimated with a non-exercise model using seismocardiography (SeismoFit 1) and directly measured during a graded exercise test with pulmonary gas exchange measurements (CPET). The red dotted line represents the line of identity (r=1.0). B) A Bland-Altman plot of the agreement between SeismoFit 1 and CPET on the right. LoA; limits of agreement. The Blue line represents the bias and the blue dotted line is the 95% CI of the bias. The red dotted line represents the 95% LoA.

Supplementary Table 3. Individual values of estimated and measured VO_2peak (ml/min/kg)

	CPET			SeismoFit 1			SeismoFit 2			Polar Fitness Test		
Subject	**Test 1**	**Test 2**	**Test 3**	**Test 1**	**Test 2**	**Test 3**	**Test 1**	**Test 2**	**Test 3**	**Test 1**	**Test 2**	**Test 3**
1	43,9	42,9	-	49,1	45,1	49,9	47,7	46,4	50,0	60	62	60
2	46,3	49,1	-	42,2	44,6	43,1	43,9	43,5	42,5	66	66	65
3	46,9	45,4	46,9	40,0	40,1	41,0	39,2	40,7	40,4	52	51	52
4	36,3	35,4	36,1	32,2	35,4	36,0	29,9	34,1	33,0	38	41	39
5	40,1	43,1	45,0	46,4	47,8	45,5	46,4	46,6	47,4	55	58	57
6	38,2	35,1	37,7	29,5	29,4	27,6	31,2	30,4	29,9	41	39	40
7	25,7	24,9	26,0	29,1	29,3	24,0	28,0	30,0	25,8	27	28	29
8	37,2	32,5	34,5	33,2	31,2	33,0	33,7	31,8	33,0	29	30	29
9	32,6	31,3	31,0	25,6	28,7	28,8	30,3	29,6	27,5	31	32	32
10	31,5	33,4	35,4	35,0	32,1	34,2	33,5	32,6	33,7	41	44	39
11	40,1	39,6	38,1	45,1	43,4	44,2	43,9	45,3	44,9	46	45	46
12	50,7	51,3	50,9	51,9	50,5	51,2	52,8	50,7	52,2	56	59	57
13	45,3	45,3	44,7	36,0	36,3	37,2	37,5	36,7	36,6	54	54	54
14	43,4	46,9	47,2	33,0	31,3	32,5	31,3	32,3	30,9	42	42	42
15	46,2	48,2	48,0	42,1	42,2	38,3	42,2	40,8	38,7	46	45	41
16	33,0	32,8	31,6	23,5	26,4	28,4	24,7	25,5	28,7	33	36	36
17	41,3	45,8	42,6	29,2	31,0	25,4	29,1	30,0	24,4	38	50	41
18	35,8	35,8	38,3	32,2	32,1	34,5	31,8	32,9	34,7	45	45	47
19	36,0	34,6	32,9	36,1	34,7	37,5	35,9	33,7	36,5	34	35	35
20	40,5	41,1	38,1	39,6	40,6	39,5	39,4	39,8	38,5	36	36	36

Performance of algorithm version 4.5

The Seismofit algorithm version 4.3 reported in the result section of the current study was the newest algorithm at the time of the study. Algorithm version 4.3 was developed using the recordings from 123 subjects from two previous studies [1, 2] and was developed without access to the current study data. Features were selected based on cross-validation. As discussed in a previous paper [3] the algorithm version 4.3 might be overfitted due to a high number of model features. Therefore algorithm version 4.5 was developed, immediately after the current study was finalized. Algorithm version 4.5 was trained in a larger dataset which in addition to the previous dataset included a 50% split (n=48) of the subjects in a cross-sectional study [3]. The remaining 50% split of the subjects and the current study was used as a test set. Features were selected based on cross-validation in the training set.

Algorithm version 4.5 is a simplified version of algorithm version 4.3 with fewer SCG features. In addition, the algorithm version 4.5 does not include the demographic prediction model from the FRIENDS study, but included the demographical variables Sex, Age, Weight & Height directly.

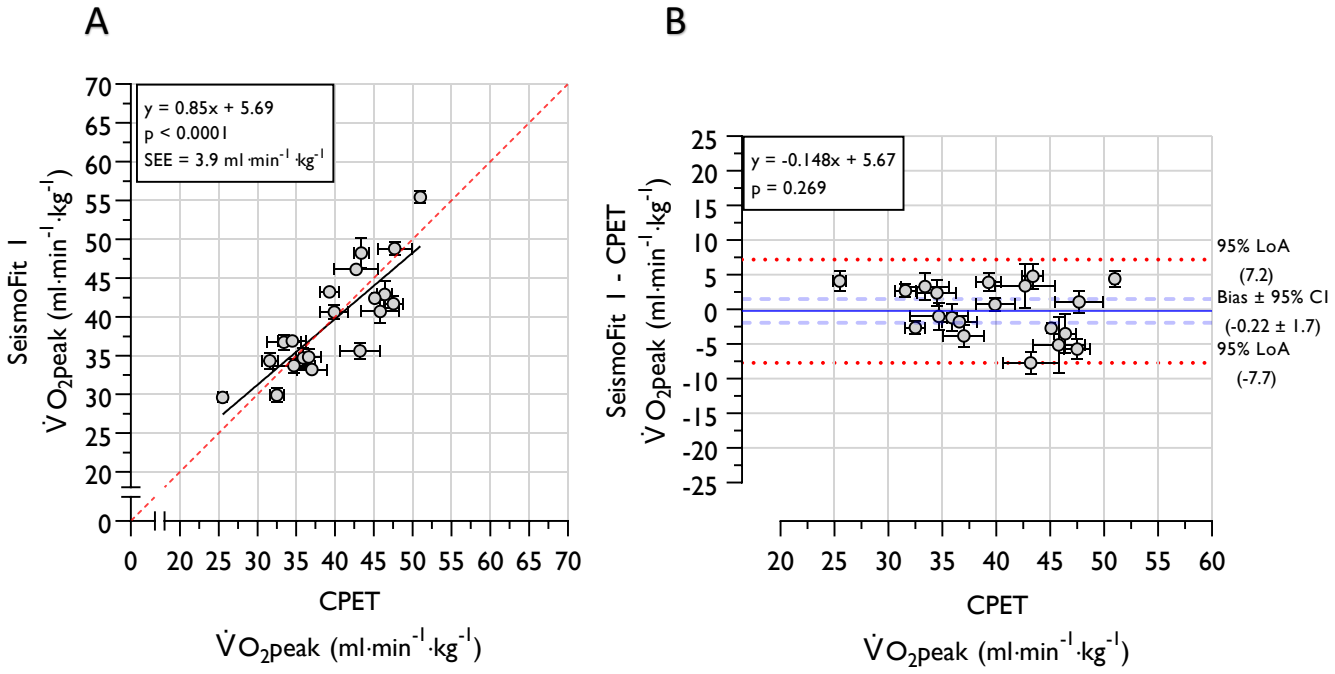
$$\dot{V}O2peak\ algo\ 4.5 = (7.63) + (8.41 \cdot Male\ Sex) + (-0.19 \cdot Age) + (-0.22 \cdot Weight) + (0.10 \cdot Height) + (0.002 \cdot RR) + (112.8 \cdot amp_{Dd} - amp_{Cd}) + (0.132 \cdot S2Morphology) + (0.42 \cdot S1FrequencySpec))$$

The results of the algorithm version 4.5 in the current study dataset is provided in **Supplementary Table 4** and **Supplementary Figure 5**. Algorithm version 4.5 was superior to the previous algorithm version 4.3. The reproducibility of algorithm 4.5 is shown in **Supplementary Table 5**. The reproducibility is improved when using algorithm version 4.5.

Supplementary Table 4. Accuracy between non-exercise VO_2peak estimations algorithms version 4.3 and 4.5 and a gold standard cardiopulmonary exercise test (CPET)

	Pearson r	**Bias** ml·min^{-1}·kg^{-1}	**SEE** ml·min^{-1}·kg^{-1}	**MAPE** %	**CoV** %
Seismofit I algorithm version 4.3	0.70	-3.1 ± 2.4*	6.6	12.0	10 ± 3
Seismofit I algorithm version 4.5	0.84	-0.2±1.7	3.9	8.4	6 ± 1

Data are presented as mean ± 95% CI. n=20; SEE, standard error of estimate; MAPE, mean absolute percentage error. CoV; coefficient of variation. *significant different from CPET (p<0.05).



Supplementary Figure 5. Data are mean ± 95% CI of three separate tests for n=18, and two separate tests for n=2. A) A Scatter plot with linear regression between $\dot{V}O_2$peak estimated with a non-exercise model using seismocardiography (SeismoFit 1) applying algorithm version 4.5, and directly measured during a graded exercise test with pulmonary gas exchange measurements (CPET). The red dotted line represents the line of identity (r=1.0). B) A Bland-Altman plot of the agreement between SeismoFit 1 applying algorithm version 4.5 and CPET. LoA; limits of agreement. The Blue line represents the bias and the blue dotted line is the 95% CI of the bias. The red dotted line represents the 95% LoA. n=20.

Supplementary Table 5. Variation across three separated test days of algorithm version 4.5

	Day 1	Day 2	Day 3	Within-subject SD	Within-subject CoV%	ICC	P-value
Seismofit 1 (ml·min^{-1}·kg^{-1})	39.6 ± 3.0	39.6 ± 3.0	39.6 ± 3.2	1.2	2.5 ± 0.4	0.97	0.99
Seismofit 2 (ml·min^{-1}·kg^{-1})	39.4 ± 3.1	39.6 ± 3.0	39.1 ± 3.0	1.1	2.5 ± 0.7	0.98	0.41

Data are presented as mean ± 95% CI. SD; standard deviation. CoV; coefficient of variation. ICC; interclass correlation coefficient.

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