Safety of the CO-Rebreathing Method in Patients with Coronary Artery Disease

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ABSTRACT

KARLSEN, T., I. M. LEINAN, I.-L. AAMOT, H. DALEN, and A. STØYLEN. Safety of the CO-Rebreathing Method in Patients with Coronary Artery Disease. *Med. Sci. Sports Exerc.*, Vol. 48, No. 1, pp. 33–38, 2016. **Purpose**: To address and study the safety concerns with the improved carbon monoxide (CO) rebreathing method for measuring total blood volume in patients with coronary artery disease to implement the use of the methodology in this patient group. **Methods**: Eighteen patients with stable coronary artery disease (age 62 ± 7 yr, 24 ± 5 months since diagnosis) were investigated using the improved CO-rebreathing test. Before, during, and up to 2 h after the test, ECG, blood pressure, arterial oxygen saturation, carbon monoxide bound to hemoglobin (HbCO%), and cardiac function were measured. At 24 h, HbCO% and troponin-T were measured. **Design**: Cross-over **Results**: Six minutes after the CO-rebreathing test, HbCO increased from 1.5% ± 0.4% to 6.0% ± 0.6%, with a subsequent decrease to 4.5% ± 0.4% and 1.4% ± 0.4% at 2 h and 24 h after the test, respectively. Resting heart rate, stroke volume, cardiac output, and ejection fraction were 64 ± 11 bpm, 93.9 ± 16.5 mL per beat, 5.84 ± 0.99 L, and 48.5% ± 5.7% and remained unchanged during and 10 min after the rebreathing. All patients were in sinus rhythm during the 2-h observation period, without ST- or T-wave changes, with low numbers of premature beats and normal rate variability. Systolic and diastolic blood pressure gradually decreased during the observation period. Troponin-T was below the 99th percentile for all the participants 24 h after the test. **Conclusion**: Cardiovascular function and safety indices remained unchanged after exposure to approximately 6% HbCO, indicating that the method is safe to perform in patients with stable coronary artery disease. **Key Words:** HEMOGLOBIN MASS, RCM, CARDIAC FUNCTION, CVD, HEART DISEASE, $\dot{V}O_{2max}$

Determining total blood volume (BV) and hemoglobin mass (Hb mass) has clinical value, particularly in heart disease, where anemic status, volume loading, and blood pressure regulation are important (1). Blood volume is positively associated with maximal oxygen uptake ($\dot{V}O_{2max}$) in healthy subjects (17). As $\dot{V}O_{2max}$ is a strong predictor of mortality and myocardial infarction (4,10), knowledge of BV and Hb mass in patients with known coronary artery disease is important, as they are determinants of oxygen supply and $\dot{V}O_{2max}$ size (14). In patients with heart failure, knowledge of BV and Hb mass may be even more vital, as volume overload and vascular volume regulation are major concerns, and anemic and hemoglobin status may be challenging to diagnose owing to hemodilution (1). The current best available and valid method for BV and Hb-mass identification is the improved carbon monoxide (CO)-rebreathing method (CO rebreathing) (16). As the method is based on a 2-min rebreathing period of a small bolus of 100% CO gas in mixture with 3 L of 100% oxygen aiming to increase HbCO from approximately 1% to approximately 6%, the methodology has not been recommended for use in patients with heart disease owing to the risk of added hypoxia and ischemia. Thus, we aimed to investigate the immediate safety of the CO-rebreathing method as applied in patients with stable coronary artery disease. We hypothesized the method to be safe, with no indication of ischemic events or arrhythmias in resting patients with stable coronary disease patients.

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METHODS

Patients. Two women and 16 men with stable coronary artery disease were recruited to this cross-sectional study from among patients who had completed phase II cardiac rehabilitation at the St. Olav's University Hospital in Trondheim between November 2011 and February 2012. All the participants signed the informed consent agreement, which was approved by the regional ethical committee for medical research.

Procedure. The participants met at the hospital in the morning for the investigation. All were in a fasting state.

Initially, their body height was recorded and their body composition was measured with a bio-impedance scale (OMRON-BF500, Body Composition Monitor, Omron Healthcare Co., Japan). After 30 min of supine rest, venous blood samples were drawn for analysis of hematology, cardiovascular risk parameters, and troponin-T. Subjects were then connected to a continuous monitoring system for 12-lead ECG and blood pressure (Philips IntelliVue MP50, Philips, Germany) and to a bioelectrical impedance device for measurement of cardiac function (PhysioFlow PF07 Enduro, Manatec Biomedical, Macheren, France) (5).

Blood volume. Total BV and Hb mass was measured by the improved CO-rebreathing technique (Blood Tec, Bayreuth, Germany). By measuring the change in CO bound to hemoglobin after inhaling a defined volume of CO gas and measuring Hb concentration and hematocrit, BV and plasma volume can be calculated (7,16). The participants inhaled one bolus of 99.9% CO (with a factor of 0.7 kg^{-1} body weight for untrained women, 0.8 kg^{-1} body weight for untrained men for calculating the volume of CO gas they would receive) and rebreathed the gas together with 100% oxygen for 2 min followed by 4 min of rest. Capillary blood samples were collected before the CO rebreathing and again at 6 and 8 min after the start of the rebreathing. These samples were analyzed for HbCO% on the blood gas analyser ABL800 Basic Analyser (Radiometer Medical ApS, Denmark). In addition, the end-tidal CO concentration was measured with a CO gas-tester (Draeger, Luebeck, Germany) before and 4 min after the CO inhalation, and the gas volume and CO concentration were measured in the spirometer after the procedure. Blood volume, plasma volume, erythrocyte volume, and Hb mass were calculated using the Spico Calculation Software 2.0 (Bloodtec, GbR, Bayreuth, Germany). This method has been found to be valid and reliable for estimating Hb mass with an error of measurement of less than 2.2% (8,16).

Safety monitoring. The participants were monitored continuously for 2 h, with measurements taken for ECG, blood pressure, hemoglobin oxygen saturation, and capillary blood gas. In addition, cardiac function—including cardiac output, stroke volume, ejection fraction, and end-diastolic volume through bio-impedance—was measured during the rebreathing procedure and for 10 min after the rebreathing. The subjects were resting in the supine position before the test and were sitting comfortably in the bed during the test and for 2 h after the test. Patients met in the laboratory 24 h after the procedure for a blood sample and to give a self-report on their health.

Maximal oxygen uptake. The participants performed a treadmill maximal oxygen uptake test within 1 month of the BV measurements. After a 10-min warm-up at a submaximal work load chosen by the patients, with an aim to break sweat and to be lightly out of breath and correspond to 60%–70% of maximal heart rate (HR_{max}), subjects received a facial mask and ECG electrodes, and the test was started with a submaximal work load corresponding to approximately 70% of HR_{max}. During the test, continuous cardiopulmonary measurements were performed with ergospirometry (Cortex MetaMax II, Cortex, Leipzig, Germany). An individualized ramp protocol was used and was based on the patients' training habits and fitness at the end of cardiac rehabilitation. During the test, workload was increased approximately every 1–1.5 min until the participants reached exhaustion. If participants were walking during the test, the workload was increased by increasing the inclination by 2%–3% at every increase in workload; if they were running, the speed was increased by 1 $km \cdot h^{-1}$ at every increase and the grade on the treadmill held constantly at 5%. None of the patients had to terminate the test prematurely owing to cardiac symptom limitation. $\dot{V}O_{2max}$ was defined as the mean of the 3 highest consecutive 10-s interval $\dot{V}O_2$ measurements, where $\dot{V}O_2$ leveled off despite a further increase in workload. In addition, $R \geq 1.1$ was used as a criterion for a peak test.

Statistics. IBM-SPSS 18 (SPSS Inc, Chicago, IL) was used for statistical analysis, and figures were made through Graph-pad 6.0 (GraphPad Prism, La Jolla, CA, USA). A 2-sided significant level was set to $P \leq 0.05$, and data are reported as mean ± standard deviation. Repeated-measures ANOVA was used to compare changes from the baseline and the test points in the follow-up period. When significant differences were detected, a Bonferroni post hoc analysis was performed. Bivariate correlation analysis was performed (Pearson rank correlation coefficient).

RESULTS

The age of the participants was 62 ± 7 yr, whereas body weight was 82 ± 11 kg, body height was 175 ± 6 cm, BMI was 26.7 ± 3.1, and percent muscle and fat mass were 32% ± 3% and 26% ± 6%, respectively.

The mean time since diagnosis of coronary artery disease was 24 ± 5 months. Of the 18 participants, 12 were diagnosed with myocardial infarction, 12 had a percutaneous coronary intervention, 6 had coronary artery bypass grafting, and 7 were currently diagnosed with hypertension and 2 had a diagnosis of type 2 diabetes. Through the ECG analyses, pathological Q-waves were revealed in 4 patients, T-wave inversions in 8 patients, and more unspecific changes were revealed in all others, except for one in whom the ECG was normal (Table 1). The participants' blood profiles were as follows: Hb, 15.1 ± 1.2 $g \cdot dL^{-1}$; hematocrit, 44.4% ± 2.4%; mean corpuscular volume, 90.7 ± 5.7 fL; mean corpuscular hemoglobin; 30.9 ± 2.7 pg; mean corpuscular hemoglobin concentration, 339.4 ± 12.7 $g \cdot L^{-1}$; leukocytes, 6.12 ± 1.33 × 10^9 L^{-1}; erythrocytes, 4.91 ± 0.36 × 10^{12} L^{-1}; thrombocytes, 212 ± 47 × 10^9 L^{-1}; total cholesterol, 4.3 ± 1.0 $mmol \cdot L^{-1}$; low-density lipoprotein cholesterol, 2.6 ± 0.8 $mmol \cdot L^{-1}$; high-density lipoprotein cholesterol, 1.5 ± 0.4 $mmol \cdot L^{-1}$; ferritin, 158 ± 145 $\mu g \cdot L^{-1}$; and CRP, <5 $mg \cdot L^{-1}$. Two patients had total cholesterol level greater than 5.0 $mmol \cdot L^{-1}$, one patient had triglyceride level greater than 1.7 $mmol \cdot L^{-1}$, and all patients had high-density lipoprotein cholesterol levels greater than 1.0 $mmol \cdot L^{-1}$.

TABLE 1. Individual baseline heart rhythm demographics and changes during the test.

Patient	Rhythm	QRS Duration (ms)	ST-segment Depression (mm)	Median Heart Rate (Interquartile Range) (bpm)	Heart Rate Variability (bpm)	Ventricular Premature Beats (bpm)
1	SR	nsQ 2,3,aVF	T-inv 2,3 aVF	61.5 (57–66)	9	0
2	SR	Q 2,3,aVF V1-V3, RBBB	T-inv 2,3,aVF (V1-V6)	62.0 (57–67)	10	18
3	SR	Low progression V1-V6	T-inv 2,3 aVF	69.5 (63–76)	13	6
4	SR	Ve axes (LVH?)	T-inv 3, ST-nonsp aVF	55.5 (52–59)	7	0
5	SR	Q 1 and aVL	ST-nonsp V1-V3	98.5 (94–103)	9	15
6	SR	R-loss V1-V3	STE-nonsp V1-V3	58.5 (55–62)	7	0
7	SR	Q V2-V3, ve axis	STE-nonsp V1-V3	65 (58–72)	14	6
8	SR	nsQ 3	T-inv 3	64 (59–69)	10	0
9	SR	Q V1-V3 (3)	STE-nonsp V1-V3	59.5 (53–66)	13	150
10	SR	nsQ 3, R-loss V1-V4		78.5 (73–94)	11	4
11	SR	R-loss V1-V3	STE-nonsp V1-V3, T-inv V1-V3 og aVL	54.0 (49–59)	10	24
12	SR	R-loss 3, aVF	T-inv 3, aVF	65 (64–66)	2	12
13	SR	nsQ 3	Inflat T-inv	71 (65–77)	12	9
14	SR		T-inv i 3	54.5 (51–58)	7	12
15	SR			60.5 (68–73)	5	18
16	SR		T-inv i 3	54 (49–59)	10	12
17	SR	nsQ 3	T-inv 3, VF, STE-nonsp V1-V3	71.5 (69–74)	5	12
18	SR	nsQ 3, aVF		76 (73–79)	6	9

aVF, augmented vector foot; min, minutes; mm, millimeter; ms, milliseconds; nsQ, nonsignificant Q complex; nonsp, nonspecific; Q, Q-complex; R-loss, loss of ECG signal in specific leads; RBBB, right bundle branch block; SR, sinus rhythm; T-inv, T inversion; V, specific ECG lead numbers; Ve-axis, left axis deviation.

Ten participants were ex-smokers and one was a current smoker. Nine were currently working, 6 were retired, and 2 were on medical leave. The following medications were used: aspirin (n = 15), clopidogrel (n = 2), statins (n = 11), beta-blockers (n = 9), ACE-inhibitors or A2 antagonists (n = 2), diuretics (n = 1), cholesterol absorption inhibitors (n = 1), thyroxine (n = 1), esomeprazole (n = 1), and tamsulosin (n = 1).

One of the subjects was unable to perform the CO-rebreathing procedure correctly. He was followed up along with the remaining participants, but owing to a lack of increase in capillary HbCO% after the breathing procedure, he was excluded from the data analysis.

There were no adverse events during the CO-rebreathing procedure, during the 2 h of close monitoring or by any self-reported incidences within 24 h of performing the method in any of the participants. The troponin-T values were at or below the 99th percentile in all participants 24 h after the CO-rebreathing test. Three participants had troponin-T levels of 11, 12, and 14 $ng \cdot L^{-1}$, respectively, whereas the remaining participants' levels were less than 10 $ng \cdot L^{-1}$. At baseline, one participant had increased troponin-T levels greater than the 99th percentile with 18 $ng \cdot L^{-1}$, but this was normalized at 24 h.

Compared to baseline, the immediate increase in HbCO% did not change heart rate, stroke volume, cardiac output, end-diastolic volume, or left ventricular ejection fraction during or 10 min after the rebreathing (Table 2). In the 2 h of rest after the rebreathing, there was a gradual decrease in systolic, diastolic, and mean arterial blood pressure, with a significant decrease after 60 min and through the remaining observation period ($P < 0.05$; Fig. 1), whereas resting heart rate remained unchanged (Tables 2 and 3). Arterial oxygen saturation remained normal and did not change during the test or in the 2-h observation period after the CO rebreathing; however, owing to a mean increase in HbCO% to approximately 6%, only approximately 92% of the hemoglobin now binds oxygen (Table 3).

The individual descriptions of baseline heart rhythm and variability in the 2 h of the supervised period are shown in Table 1. All patients were in sinus rhythm, and no changes in ST-segment depression, T-waves, or QRS morphology were detected during the 2-h observation period. Two patients had first-degree atrioventricular block at baseline. There were no significant changes in ventricular premature beats, PQ- or QT-time duration, or development of arrhythmias during the observation period. The median (interquartile range) heart rate, heart rate variability, and ventricular premature beats per hour were 63 (58–71), 9.5 (6.8–11.3), and 10.5 (3.0–15.8), respectively.

The capillary HbCO% increased as expected from 1.5% ± 0.4% at baseline to 6.0% ± 0.6% after rebreathing, and decreased thereafter with values of 4.5% ± 0.4% at 2 h after the rebreathing ($P < 0.05$; Fig. 2), giving a half-life of HbCO of 278 min. The HbCO% was equal to baseline, with values 1.4% ± 0.4% at 24 h after the rebreathing (Fig. 2). End expiratory CO concentration increased as expected after the

TABLE 2. Cardiac function before, during, and directly after CO rebreathing.

	Baseline Rest	During CO Rebreathing	CO + 2–6 min	CO + 6–10 min
HR, bpm	64 ± 11	66 ± 11	65 ± 11	63 ± 11
SV, mL per beat	93.9 ± 16.5	91.0 ± 14.8	91.7 ± 13.6	89.8 ± 12.9
QO, $L \cdot min^{-1}$	5.84 ± 0.99	5.96 ± 1.38	5.88 ± 1.11	5.62 ± 0.89
EDV, mL	192.4 ± 48.8	188.8 ± 45.0	192.1 ± 46.2	186.4 ± 48.6
EF, %	48.5 ± 5.7	49.0 ± 6.2	48.4 ± 5.99	48.2 ± 6.3

The table timeline describes the time from the start of CO rebreathing to each investigation: CO + 6 min = 6 min after start of rebreathing. CO + 10 min = 10 min after start of rebreathing. Baseline = mean of 3 min at rest; during rebreathing = mean of the 2-min rebreathing period; CO + 2–6 min = mean of values between 2 and 6 min in the test; CO + 6–10 min = mean of values between 6 and 10 min in the test.
Values are reported as mean ± SD.
EDV, end-diastolic volume; EF, ejection fraction; HR, heart rate; QO, cardiac output; SV, stroke volume.

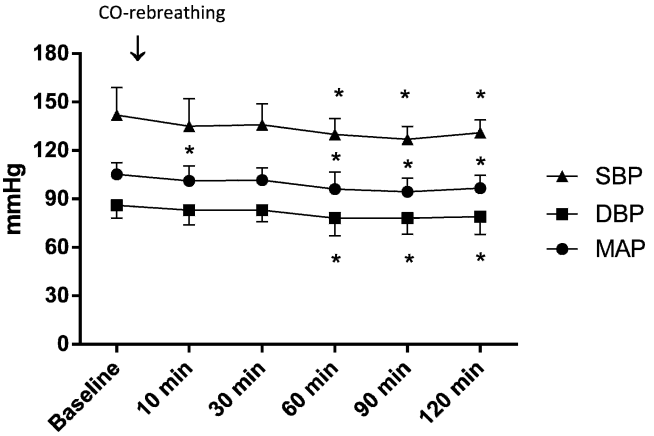

FIGURE 1—Change in systolic (SBP), diastolic (DBP), and mean arterial (MAP) blood pressure during the CO-rebreathing test and the 2-h follow-up period. *Significant reduction compared to baseline.

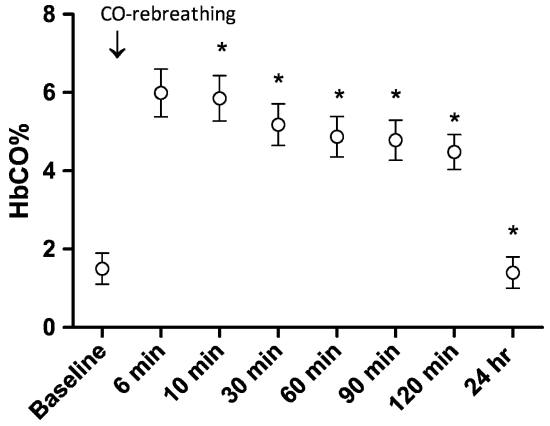

FIGURE 2—Change in percentage of Hb that binds to CO throughout the CO-rebreathing test, the 2-h follow-up phase, and 24 h after the test. *Significant reduction compared to 6 min after rebreathing (the highest HbCO%).

rebreathing and gradually declined from the 6-min observation point to the 2-h observation point ($P < 0.05$; Table 3) and was normal with a concentration of 16 ± 8 ppm at 24 h after the rebreathing.

Measurements of blood and plasma volume and Hb mass are displayed in Table 4. Maximal oxygen uptake and exercise test results are displayed in Table 4. Maximal oxygen uptake ($L \cdot min^{-1}$) was significantly correlated with total BV, plasma volume, and Hb mass with r values of 0.61, 0.59. and 0.55, respectively ($P < 0.02$).

DISCUSSION

The primary finding of the study is that the improved CO-rebreathing test for BV and Hb mass safely can be applied to patients with stable coronary artery disease when HbCO increases to 6%. Currently, the CO-rebreathing test is primarily used in healthy athletes. With the thorough demographic description of the patient in this study, a close clinical follow-up during, and up to 2 h after testing, and with no indication of adverse effects of an immediate increase in HbCO, this study provides data on the safety of the use of the CO-rebreathing test in patients with cardiovascular disease.

In this study, we show that performing the rebreathing test does not affect short-term cardiac function indices such as stroke volume, cardiac output, end-diastolic volume, ejection fraction, rhythm and heart rate, either during or immediately after the test. There was no ECG indication that the test induced cardiac ischemia or arrhythmias within the 2 h of intensive observation in any of the patients. In addition, observing no change in heart rate, PQ-, QRS-, or QT-duration and no change in ventricular premature beats indicates that the CO-rebreathing test does not influence the heart's electrical signaling system in patients with stable coronary artery disease. The test did not alter blood pressure or cardiac function indices negatively during the test or in the 2 h of observation after the test, indicating that the increase in HbCO to 6% did not influence vascular and cardiac function. However, in contrast, 1 h of rest decreased blood pressure, including systolic, diastolic, and mean arterial pressure, as the participants were sitting comfortably reading or watching TV.

As the troponin-T levels were at and below the 99th percentile for all subjects 24 h after the rebreathing, there is no indication of myocardial cell injury during or after the test. The finding of one subject with increased troponin-T levels at baseline, which then returned to normal at 24 h, might be related to chance or to other activities as well as normal daily fluctuation in troponin-T (9).

Hemoglobin and hematocrit values in the patients were normal, and there were no indications of anemia, with normal cardiovascular risk parameters. The absolute and relative blood, plasma, and erythrocyte volumes in the participants were slightly higher than in a previous study of healthy men in their 60s (4.75, 2.96 and 1.79 L, respectively [6]) and only slightly below young men in their 20s (6); however, plasma and erythrocyte volumes constituted approximately 60% and approximately 40% of the total BV for both the old participants (6) and our subjects. The reason for the slightly higher values in our study is unknown but could include the following: use of a different methodology, the Evans Blue Dye method by Davy et al. (1994) (6), higher degree of medication in our study, or

TABLE 3. Heart rate, oxygen saturation, and CO expiration at baseline and in the 2-h follow-up period.

	Baseline	CO + 6 min	10 min	30 min	60 min	90 min	120 min
HR, bpm	64 ± 11	65 ± 11	63 ± 11	66 ± 11	66 ± 12	67 ± 13	67 ± 13
SpO_2, %	98 ± 2	–	98 ± 2	98 ± 1	98 ± 2	99 ± 1	98 ± 2
End expiratory CO, ppm	11 ± 8	44 ± 9	–	35 ± 8*	34 ± 9*	33 ± 11*	29 ± 7*

The table timeline describes the time from the start of CO rebreathing to each investigation: CO + 6 min = 6 min after start of rebreathing.
*Significant reduction compared to CO + 6-min test time point. Values are reported as mean ± SD.
SpO_2, arterial oxygen saturation.

TABLE 4. Blood, plasma and erythrocyte volumes, hemoglobin mass absolute and relative to body mass, and $\dot{V}O_{2max}$ results.

Blood volume, L	5.97 ± 0.80 (2.97)
Plasma volume, L	3.50 ± 0.49 (2.14)
Erythrocyte volume, L	2.42 ± 0.44 (1.58)
Total Hb mass, g	825 ± 164 (547)
Relative blood volume, mL·kg^{-1}	73.7 ± 10.9 (35.7)
Relative plasma volume, mL·kg^{-1}	44.0 ± 6.1 (21.9)
Relative erythrocyte volume, mL·kg^{-1}	29.7 ± 5.3 (17.8)
Hb-mass relative, g·kg^{-1}	10.1 ± 1.9 (7.10)
$\dot{V}O_{2max}$, mL·kg·min^{-1}	36.2 ± 7.6 (23.85)
$\dot{V}O_{2max}$, L·min^{-1}	2.88 ± 0.61 (2.20)
$\dot{V}E$, L·min^{-1}	110.7 ± 21.5 (71.3)
R	1.12 ± 0.07 (0.24)

Values are reported as mean ± SD (range).
R, respiratory equivalent; $\dot{V}E$, ventilation.

be a reflection of training status as our participants had higher mean $\dot{V}O_{2max}$ values compared to the old men in the study of Davy et al. (1994) (compared to our data, the mean difference in $\dot{V}O_{2max}$ between the old subjects was 0.434 L·min^{-1}) (6). As expected, there was a positive correlation between $\dot{V}O_{2max}$ and BV, plasma volume, and Hb mass, as has previously been seen in healthy subjects (17). The strength of the correlation is comparable to other studies where Pearson *r* values of 0.50–0.73 have been reported (6) and somewhat lower than values reported by Stevenson et al. (1994) in highly trained women (17). The difference between studies could be due to the methodology used (CO rebreathing vs Evans Blue Dye method), the comparison of relative versus absolute $\dot{V}O_{2max}$ and volume values, and different populations measured. The $\dot{V}O_{2max}$ level in our study is also comparable to normal data from this age group in Norway (3) and might indicate that having coronary artery disease does not reduce BV and Hb mass as long as $\dot{V}O_{2max}$ is maintained at a normal age-expected level (or vice versa) (6). In this study, most of the patients had only minor sequelae after the myocardial infarctions, and most of the patients were revascularized.

As the patients were followed up for only a short time (2–24 h) and they remained in a resting condition during the observation period, we do not know if physical activity immediately after the rebreathing might induce arrhythmias or additional cardiac ischemia. It is known that the rebreathing method acutely decreases $\dot{V}O_{2max}$ by 3% in healthy subjects (16), and one should expect the same response in the patients with coronary artery disease, as the increase in HbCO% is the same. After 24 h, HbCO% returned to baseline levels as expected in healthy subjects. The calculated half-life of HbCO in this study is more than twice as long as the 132 min reported by Schmidt and Prommer (2005) in moderately trained young men and women (16), but slightly shorter than the 320 min reported by Peterson and Stewart (1970) in inactive young men (11). As described by others, the HbCO half-time is highly dependent on the degree of ventilation. The HbCO half-time is reduced after strenuous exercise testing, where high ventilation is present (16), whereas HbCO is increased in subjects with high airflow obstruction (18). Our data give indication to a normal exhalation of CO in the participants with coronary artery disease; however, if increasing half time compared to young moderately trained subjects are due to resting metabolism, reduced ventilation or airway obstruction remains unanswered. For future investigations on how this methodology might be used in patients with heart failure, the findings from using the methodology in patients with stable coronary artery disease give an indication of minimal influence on cardiac and vascular function when performed in resting conditions.

Limitations. As the subjects were patients with stable coronary artery disease who were fairly fit for their age, with well-preserved cardiac function during rest and with a short follow-up, the conclusions on how the test may influence individuals with more severe and unstable coronary artery disease, worse cardiac function, or lower levels of fitness is unknown. The sample size is relatively limited; however, the study gives an indication of what to expect in such patients, and documents that the rebreathing of CO follows the same pattern with increase and decrease in HbCO% as has previously been shown in healthy subjects (16). In previous studies of the methodology in healthy individuals (16), athletes at altitude (13,15), patients with polycythemia vera (2), and subjects recovering from blood donation (12), there have been no reports of serious adverse events, making a statistical power calculation challenging for the present study. However, based on the fact that we observed no influence on sensitive cardiac indices, we find that the present study seems to be adequately powered. However, the study has a relatively small sample size; therefore, additional studies over a range of disease severity are needed for generalizability of the results.

CONCLUSION

Cardiovascular function remained normal during exposure to approximately 6% HbCO, indicating that the method is safe to perform on patients with stable coronary artery disease.

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The authors have no conflicts of interests to declare.

The results of the study do not constitute endorsement by the American College of Sports Medicine.

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