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The reliability of noninvasive cardiac output measurement using the inert gas rebreathing method in patients with advanced heart failure

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Abstract

Background: *Impaired cardiac output (CO) is a key element of heart failure (HF). So far, there has been no simple, reliable, inexpensive and non-invasive CO measurement method feasible for clinical practice. Not a single diagnostic test has been elaborated to diagnose and monitor HF. The aim of the study was the evaluation of the reliability of a new, non-invasive CO measurement device utilizing an inert gas rebreathing technique and an infrared photoacoustic gas analyzer, in comparison with standard invasive methods.*

Methods: *In 21 patients with advanced HF (NYHA classes III and IV) undergoing cardiac catheterization as a routine hemodynamic evaluation before heart transplantation, CO measurements with the tested non-invasive method were carried out during invasive examination.*

Results: *CO measured by the inert gas rebreathing technique (CO_{RB}), according to the statistical Bland-Altman method, was, on average, 0.1 L/min higher than that determined by thermodilution (CO_{TD}) and 0.006 L/min higher than the CO determined by the Fick formula (CO_{Fick}). This magnitude of difference equals 2.8% of CO_{TD} and 0.15% of CO_{Fick} values. The limits of agreement between CO_{RB} and CO_{TD} were ± 1.4 L/min, and between CO_{RB} and CO_{Fick} ± 1.3 L/min. In the subgroup with atrial fibrillation, the mean difference between tested and reference methods (0.3 ± 1.0 L/min for both CO_{TD} and CO_{Fick}) was higher than in the sinus rhythm subgroup (0.06 ± 1.5 L/min for CO_{TD} and 0.08 ± 1.5 for CO_{Fick}).*

Conclusions: *CO measurement with the inert gas rebreathing method utilizing an infrared photoacoustic gas analyzer seems reliable enough to be employed in clinical practice. Being non-invasive, it may well be used for repeated determinations in patients with HF.* (Cardiol J 2008; 15: 63–70)

Key words: chronic heart failure, cardiac output, gas rebreathing

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Introduction

Depressed cardiac output (CO) below the demands of metabolizing tissues is a key element of heart failure (HF) definition, but, in practice, it is hardly ever used to support diagnosis [1]. Currently, CO is mainly measured invasively, predominantly in end-stage HF patients qualifying as heart transplant recipients [2]. Introducing a simple and reliable non-invasive CO measurement would make the parameter clinically more relevant. An estimation of CO could be useful during diagnosis verification in patients suspected of having HF, or in following-up disease progression and/or responses to treatment. Systematically repeated tests could reveal occult deterioration of cardiac function and give a rationale for pharmacological treatment intensification or for introducing non-pharmacological therapy with heart transplantation on the top. The severity of heart failure is currently estimated mainly on the basis of subjective exercise tolerance limitation (NYHA classification), but not only circulatory compromise can cause a patient to feel unable to exercise. Subjective exercise endurance depends both on organic disabilities (HF, chronic obstructive lung disease, anemia) and on emotional state [3]. In less advanced HF, CO can be normal at rest but fails to rise properly during exertion. In such a group of patients, CO measurements during exercise are more relevant. Maximal oxygen uptake (VO_2max), appreciated as a valuable prognostic factor in chronic HF, is in fact an indirect derivate of CO [4]. The prognostic value of exercise-induced CO change is indeed higher [5] but the invasiveness of current procedures makes these tests useless for wider clinical practice and encourages the use of an indirect derivate (VO_2max) instead of a primary parameter (CO) [6]. The prognostic significance of CO in HF patients can be enhanced by taking into consideration actual blood pressure. Cardiac power output is a product of CO and mean arterial blood pressure. The accuracy of this parameter was proved for hemodynamic data obtained invasively. If the same is true for CO measured non-invasively, we could obtain a valuable prognostic parameter for most heart failure patients, even those with less advanced disease [3]. In reality, a reliable, simple and non-invasive hemodynamic prognostic parameter in heart failure is still missing [6]. The clinical experience with the inert gas rebreathing method using an infrared photoacoustic gas analyzer in patients with heart failure is encouraging but still limited to a small number of patients mainly in NYHA classes II and III [7].

The aim of our study was to evaluate the accuracy of the inert gas rebreathing method in comparison with standard invasive methods in advanced chronic heart failure patients, NYHA class III and IV, who had qualified as potential heart transplant recipients.

Methods

Patients

The study population consisted of patients suffering from advanced HF despite optimal treatment after all other options of treatment had been exhausted. On the basis of symptoms and non-invasive tests, the patients had qualified as potential heart transplant recipients. Contraindications to cardiac transplantation or cardiac catheterization were exclusion criteria for our study. Right-heart catheterization was performed as a standard procedure to verify the existence of hemodynamic contraindications to transplantation. Local ethical committee approval for the study was obtained, and the study was carried out according to the tenets of the Declaration of Helsinki. Before the procedure, informed consent was obtained from each patient for participation in the study.

The performance of invasive tests was preceded by practice of the rebreathing technique to make the patient familiar with the tested equipment before the procedure (usually 2–3 attempts were sufficient). During this phase, foreign gases were not added to the gas mixture and CO was not calculated. In a cath-lab, a Swan-Ganz catheter was inserted, pressures in the appropriate vessels and chambers measured, and both arterial and mixed venous blood sampled for CO_{Fick} measurement. In the calculations, estimated oxygen consumption was used. CO_{TD} was repeated five times using in-line injections of 10 mL iced saline. Extreme values were rejected and from the remaining three closest measurements, the mean value was calculated. Immediately after thermodilution, inert gas rebreathing measurements were performed twice at 5-minute intervals. The mean value of the results was calculated. All CO measurements were performed with the patient in the supine position.

Cardiac output determination by the gas rebreathing method

Inert gas rebreathing determination was performed using an Innocor device (Innovision, Denmark) equipped with an infrared photoacoustic gas analyzer, instead of the mass-spectrometer used before. Two types of physiologically inert gases were used in the device: one being blood-soluble N_2O and the other blood-insoluble SF_6. Their initial concentrations in the gas mixture were 0.5% and 0.1% respectively. The rate of washout of the blood-soluble compound (N_2O) reflects effective pulmonary capillary blood flow, which equals CO until no significant intrapulmonary or intracardiac shunt is present. Blood-insoluble SF_6 was used to determine lung vital capacity, tightness of the system and the accuracy of gas mixing between the rebreathing bag and alveolar air. The initial volume of the gas mixture in the rebreathing bag was programmed as 30% of the predicted forced vital capacity, reduced by 10%. During the procedure, 4–5 breaths were performed in a closed system. The changes in gas concentrations recorded during two or three initial breaths were automatically excluded from the calculations due to insufficient gas mixing between the rebreathing bag and alveolar air.

Statistical analysis

Apart from the Pearson correlation coefficient, we used the Bland and Altman method for calculating the mean difference and the limits of agreement between the two diagnostic tests. The mean differences reflect the bias, i.e. systematic difference between methods, and the limits of agreement describe the random fluctuation around the mean. The value of the limits of agreement were calculated by adding and deducting from the mean difference the doubled standard deviation (SD) of the differences (more precisely 1.96 ± SD), which describe, with 95% probability, the maximal magnitude of difference between the results obtained with the tested method and the reference method. In our study, the differences between results obtained by each method according to this formula were presented as a mean difference 1.96 ± SD. The correlations were presented as a correlation coefficient — r and level of significance — p [2, 8].

Results

The characteristics of the enrolled patients are summarized in Table 1 (demographic and clinical data) and Table 2 (hemodynamic data). After the exclusion of one patient who was intolerant to the mouthpiece (due to a vomitory reflex), the study group consisted of 21 patients in NYHA classes III and IV. With this group, 27 series of measurements were performed using each method (three patients were catheterized twice and one underwent 48-hour hemodynamic monitoring with four sets of measurements). The mean CO was: 3.91 L/min if measured with the thermodilution method (CO_{TD}); 3.98 L/min with the Fick method (CO_{Fick}); and 3.99 L/min with the tested inert gas rebreathing method (CO_{RB}).

Table 1. Characteristics of the study group.

Variable	Value
Age	46.5 years
Gender	1 female, 20 male
Time after diagnosis of HF	4.9 years
Ischemic cardiomyopathy	5 (24%)
Dilated cardiomyopathy	16 (76%)
Sinus rhythm	16 (76%)
Atrial fibrillation	5 (24%)
NYHA class III	13 (62%)
NYHA class IV	8 (38%)
Ejection fraction	28 ± 8.4%
Left ventricle diameter diastole	7.1 ± 1.0 cm
Left ventricle diameter systole	5.6 ± 1.1 cm

Data expressed as mean ± SD, or number and percentage; NYHA — New York Heart Association; HF — heart failure

For the entire study group, the mean CO_{RB} was 0.1 ± 1.4 L/min higher than CO_{TD} (the magnitude of difference equals 2.8% of CO_{TD} value) (Fig. 1). In the case of atrial fibrillation, the mean CO_{RB} was 0.3 ± ± 1.0 L/min higher than CO_{TD} (7.4% CO_{TD}); whereas, in the subgroup with sinus rhythm, the mean CO_{RB} was 0.06 ± 1.5 L/min lower than CO_{TD} (1.4% CO_{TD}). Correlation coefficients between the results obtained by both methods were, respectively, r = 0.7529 ($p < 0.001$) for the entire study group, r = 0.7699 ($p < 0.001$) for patients with sinus rhythm, and r = 0.8909 (p = 0.003) for patients with atrial fibrillation (Table 3).

Values of CO_{RB} were slightly higher than values of CO_{Fick} in the entire population (0.006 ± 1.3 L/min, mean difference accounts for 0.2% of CO_{Fick} value) (Fig. 2) and in the subgroup with atrial fibrillation (0.258 ± 1.1 L/min, 6.7% of CO_{Fick} value); whereas, in patients with sinus rhythm, values of CO_{RB} were slightly lower than CO_{Fick} (0.081 ± 1.5 L/min = = 2% of CO_{Fick} value). Correlations between the methods were as follows: in the entire group, r = = 0.7835 ($p < 0.001$); in patients with atrial fibrillation, r = 0.8816 (p = 0.004); and r = 0.7769 ($p < 0.001$) in patients with sinus rhythm (Table 3).

Discussion

CO measured with the non-invasive gas rebreathing method equipped with the photoacoustic gas analyzer (CO_{RB}) differed by only –0.1 L/min (2.8% of CO_{TD} value) from CO measured by

Table 2. Hemodynamic characteristics.

Hemodynamic parameters	Measured values			Normal ranges [Units]
	Mean	Minimal	Maximal	
RAP m	14	8	31	2–6 [mm Hg]
PAP s	46	27	74	< 25 [mm Hg]
PAP d	25	12	44	< 10 [mm Hg]
PAP m	33	18	54	< 20 [mm Hg]
PAWP	23	12	41	8–12 [mm Hg]
PAP m – PAWP	10	1	24	2–10 [mm Hg]
Sat a O_2	96	89	99	> 95 (%)
Sat v O_2	64	51	77	60–75 (%)
CO_{TD}	3.9	2.3	5.4	
CO_{Fick}	4.0	2.2	6.3	4–8 [L/min]
CO_{RB}	4.0	2.2	6.4	
CI_{TD}	2.0	1.2	3.0	
CI_{Fick}	2.1	1.1	3.5	2.5–4 [L/min/m^2]
CI_{RB}	2.0	1.2	3.6	
SV_{TD}	54	24	105	
SV_{Fick}	55	30	95	50–100 [mL/beat]
SV_{RB}	55	23	107	
SI_{TD}	28	13	51	
SI_{Fick}	28	15	46	25–45 [mL/beat/m^2]
SI_{RB}	28	12	51	
PVR_{TD}	2.8	0.2	9.2	
PVR_{Fick}	2.8	0.3	10.8	1.5–2.5 [Wood Units]
PVR_{RB}	2.9	0.2	7.9	
$PVRI_{TD}$	5.4	0.4	17.7	
$PVRI_{Fick}$	5.3	0.6	20.7	1–3 [Wood Units × m^2]
$PVRI_{RB}$	5.5	0.4	15.1	
SVR_{TD}	18.9	11.9	28.4	
SVR_{Fick}	18.7	10.1	28.7	11.25–16.25 [Wood Units]
SVR_{RB}	19.0	10.8	37.0	
$SVRI_{TD}$	36.7	23.9	51.0	
$SVRI_{Fick}$	36.3	20.1	56.1	23.75–30 [Wood Units × m^2]
$SVRI_{RB}$	36.4	19.9	62.3	

RAP — right atrium pressure, PAP — pulmonary artery pressure, PAWP — pulmonary artery wedge pressure; $SatO_2$ — blood O_2 saturation; v — mixed venous; a — arterial; m — mean, s — systolic, d — diastolic; CO — cardiac output, CI — cardiac output index, SV — stroke volume, SI — stroke volume index, PVR and PVRI — pulmonary vascular resistance and its index, SVR and SVRI — systemic resistance and its index; TD — parameters measured by thermodilution, Fick — by Fick, RB — rebreathing method

thermodilution. Dispersion of the differences between the results obtained by the compared methods was, nevertheless, considerable (limits of agreement ± ± 1.5 L/min) (Fig. 1, Table 3). Taking into account the limits of agreement, the value of CO_{RB} can be from 1.6 L/min lower to 1.4 L/min higher than CO_{TD}. However, the difference between CO_{RB} and CO_{TD} (–0.1 ± 1.4 L/min) was comparable to that between CO_{Fick} and CO_{TD} (–0.07 ± 1.5 L/min) (Fig. 3, Table 3). In the entire study group, correlations between all used methods were statistically significant ($r > 0.5$ and $p < 0.05$) (Table 3).

Similar results were obtained by Gabrielsen and Videbaek, who evaluated an older model of the device equipped with a similar photoacoustic gas analyzer (AMIS2001). In a group of 21 patients, the mean difference between CO_{RB} and CO_{TD} (continuous thermodilution technique) was –1.0 ± 0.8 L/min [9].

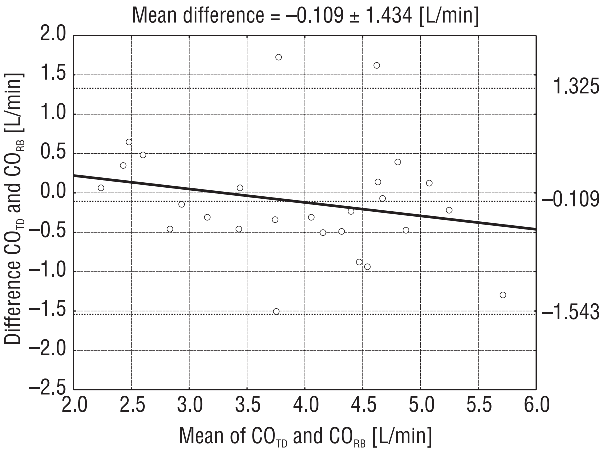

Figure 1. Accuracy of CO_{RB} against CO_{TD} in whole studied group — Bland Altman diagram; CO — cardiac output: TD — measured by thermodilution, RB — by rebreathing method.

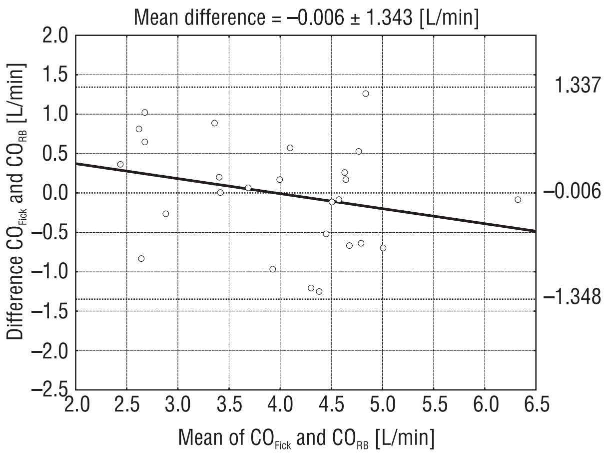

Figure 2. Accuracy of CO_{RB} against CO_{Fick} in whole studied group — Bland Altman diagram; CO — cardiac output: Fick — measured by Fick, RB — by rebreathing method.

Peyton and Thompson compared the accuracy of the Innocor in a group of nine patients with normal left ventricular systolic function during elective cardiosurgery. They carried out 20 series of measurements. The mean difference between CO_{RB} and CO_{TD} (with ambient temperature saline) was 0.01 ± 1.7 L/min with a correlation coefficient of r = 0.57. The mean difference between CO_{RB} and CO_{Fick} was 0.3 ± 2.5 L/min (r = 0.52) [1]. Agostoni compared CO_{RB} with traditional invasive measurements during cardiopulmonary exercise tests in 20 patients with chronic, systolic HF, predominantly in NYHA class II. The correlation coefficient r for CO_{RB} *vs*. CO_{TD} was 0.9382; CO_{RB} *vs*. CO_{Fick} 0.9482 and CO_{TD} *vs*. CO_{Fick} 0.9465 (p value not published). In Agostoni's study, the mean CO_{RB} exceeded both the mean for CO_{Fick} (by 0.1 L/min) and CO_{TD}

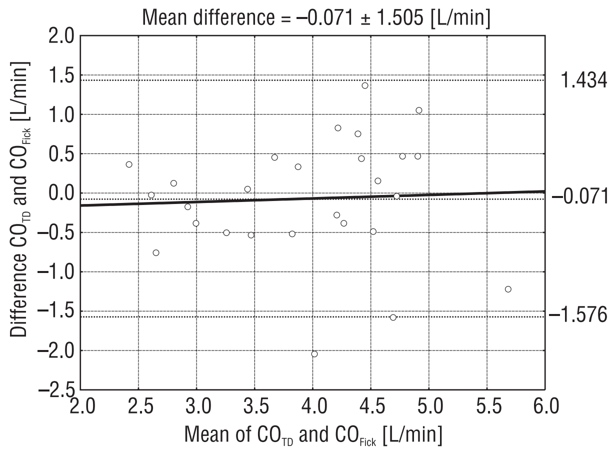

Figure 3. Accuracy of CO_{Fick} against CO_{TD} in whole studied group — Bland Altman diagram; CO — cardiac output: TD — measured by thermodilution, Fick — by Fick method.

Table 3. Comparison of cardiac output determined by different methods.

Reference method		CO_{TD}				CO_{Fick}			
		Accuracy [L/min]		Correlation		Accuracy [L/min]		Correlation	
Compared method		Mean difference	Limits of agreement ± 1.96 SD	r	p	Mean difference	Limits of agreement ± 1.96 SD	r	p
CO_{RB}	Whole group	–0.109	1.434	0.753	< 0.001	–0.006	1.343	0.784	< 0.001
	Sinus rhythm	+0.056	1.474	0.770	< 0.001	+0.081	1.453	0.777	< 0.001
	Atrial fibrillation	–0.285	0.963	0.891	< 0.001	–0.258	1.052	0.882	0.004
CO_{Fick}	Whole group	–0.071	1.505	0.656	< 0.001				
	Sinus rhythm	–0.025	1.532	0.692	0.002				
	Atrial fibrillation	+0.061	0.854	0.871	0.002				

CO — cardiac output measured by (CO_{Fick}) Fick, (CO_{TD}) thermodilution, or (CO_{RB}) rebreathing method (by 0.6 L/min; thermodilution with iced saline) [10]. The stronger correlation between the CO determination techniques obtained by Agostini than by other authors may result from the higher number of performed measurements (95) and/or from a homogeneity of the studied population.

The mean difference between the gas rebreathing method and invasive methods, both in the authors' own research and in quoted studies, was relatively small (from 0.01 L/min to maximal 1.0 L/min). The limits of agreement seem, nonetheless, quite wide (mean ± ± 1.5 L/min). Taking in the mean difference (0.1 L/min was assumed) and limits of agreement, the CO_{RB} may underestimate the actual CO value by a maximum of 1.4 L/min, or overestimate it by 1.6 L/min.

There are no obligatory criteria for the acceptable magnitude of the difference between CO estimation methods, allowing them to be used interchangeably. CO_{Fick} determined using measured versus calculated oxygen consumption differs by 0.04 ± ± 3.3 L/min [11]. The extent of the difference by no means eliminates from regular practice CO_{Fick} measurement using calculated oxygen consumption. Shoemaker studied the clinical significance of CO differences measured by impedance and thermodilution in a group of 680 circulatory instable patients. The mean difference (based on 2192 pairs of measurements) between cardiac index — CI measured by these methods was 0.12 ± 0.75 L/min/m^2 and did not result in a difference in accuracy of therapeutic decisions [12]. In our study, the mean difference between CI_{RB} and CI_{TD} was –0.04 ± 0.799 L/min/m^2. According to Shoemaker's conclusions, clinical decisions based on CO_{RB} and CO_{TD} should not differ.

CO_{RB} is calculated from the rate of nitrous oxide washout from the gas mixture as a result of its pulmonary blood absorption. For the sake of the calculations, it is assumed that the gas dissolves in circulating blood only. It has not been studied to what extent gas dissolving in the blood congested in the lungs may influence the concentration drop in the rebreathing air and, consequently, CO calculation [13]. The amount, insignificant in healthy humans, may prove important and responsible for a cardiac output overestimation in patients with pulmonary congestion. It is possible, however, that the gas dissolves in retained blood only during the initial breaths, which was automatically excluded from analysis. So far, the studies using nitrous oxide for CO determination in heart failure patients have been few and did not solve this problem [9, 10]. Gabrielsen et al. [9] compared CO determined by similar rebreathing equipment and a continuous thermodilution method in 10 patients (II and III NYHA classes) during cardiac catheterization at rest (probably in a supine position). The mean CO_{RB} was 1.0 ± ± 0.8 L/min lower than for CO_{TD}. In the second part of the study, gas rebreathing, thermodilution and Fick were compared. The mean CO_{RB} was 0.1 ± 0.9 L/min lower; whereas, CO_{TD} was 0.8 ± ± 1.3 L/min higher in comparison to CO_{Fick} [9]. In both parts of this study, the rebreathing method underestimated CO against thermodilution by c. 1.0 L/min. Agostoni et al. [10] measured cardiac output during an exercise test in the sitting position in a group of 20 patients, predominantly in NYHA class II. In this study, CO_{RB} was, on average, 0.6 L higher than CO_{TD} (measured with iced saline) and 0.1 L/min higher than CO_{Fick}. In both presented studies, patients differed with heart failure severity, body position during the test and thermodilution technique. It seems plausible that the shift of ventilation/perfusion ratio caused by the change of body position influences CO measurements by the rebreathing method, at least in patients with heart failure. Earlier studies, however, proved that CO_{RB} remains accurate after a change of body position, despite alteration in the ventilation/perfusion ratio [14]. The results of the ESCAPE study showed that the intensity of dyspnoea in heart failure correlates with capillary wedge pressure [15]. Therefore, more intense dyspnoea suggests greater pulmonary congestion. Patients in lower NYHA classes (in the aforementioned studies of classes I and II) are less likely to have substantial pulmonary congestion than patients with more advanced heart failure (classes III and IV in the present study). Such a mechanism might explain why, in Gabrielsen's study, CO_{RB} was lower, as opposed to our own study in which it was higher than CO measured invasively.

CO_{RB} is calculated as the sum of effective capillary pulmonary blood flow and functional pulmonary shunt. Ignoring existing shunt in calculations results in CO underestimation. In calculations, a drop in arterial blood saturation below 98% is assumed to be a sign of significant pulmonary shunt. However, shunt is not the sole factor lowering arterial blood saturation. In advanced HF, desaturation of mixed venous blood secondary to low CO may be so great that, despite the lack of shunt, arterial blood saturation remains reduced. If, under such circumstances, correction based on a drop in arterial blood saturation is performed, CO by rebreathing will overestimate the real one [9, 10]. In our study group, arterial blood saturation exceeded 98% only in 10 measurements. After correcting the value of effective pulmonary blood flow determined with the tested device by the value of the calculated pulmonary shunt, neither the mean error nor correlation coefficient improved. In Gabrielsen's study, taking into account the pulmonary shunt improved accuracy of the gas rebreathing method against CO_{Fick}, the limits of agreement changed from 0.6 ± 1.2 L/min to 0.3 ± 0.9 L/min [9].

In our study, the correlation between subsequent CO_{TD} measurements was high in the entire group (r = 0.96), in the subgroup with sinus rhythm (r = 0.96), and the group with atrial fibrillation (r = 0.95; for all the correlations $p < 0.001$). The Bland and Altman analysis revealed that the repeatability of subsequent CO_{TD} determinations was high (–0.03 L/min in the entire population, –0.02 L/min in the subgroup with sinus rhythm, and –0.03 L/min in patients with atrial fibrillation); whereas, the limits of agreement were nearly twice as high in the group with atrial fibrillation (± 0.44 L/min) as in the entire study group (± 0.27 L/min) and in patients with sinus rhythm (± 0.16 L/min). This is in accordance with reports by other authors, who point out the adverse influence of atrial fibrillation on the repeatability of thermodilution CO determinations [16]. This fact is of utmost importance for cardiac failure patients as atrial fibrillation and other arrhythmias are more frequent than in the general population. We analyzed the influence of atrial fibrillation on the accuracy of CO_{RB} measurements against CO_{TD}. In the sinus rhythm subgroup, the mean difference between CO_{RB} and CO_{TD} was smaller (+0.06 ± ± 1.5 L/min) than in the entire study group (–0.1 ± ± 1.4 L/min) and patients with atrial fibrillation (–0.29 ± 0.96 L/min). A similar relation was observed when comparing CO_{RB} and CO_{Fick} (–0.01 ± 1.3 L/min in the entire population, 0.08 ± 1.5 L/min in the subgroup with sinus rhythm and –0.26 ± 1.1 L/min in atrial fibrillation). The differences between particular methods may well be explained differently. The Fick method reflects the average cardiac output over the period of time necessary to cause gas concentration changes in arterial and venous blood (about 2–3 min), but both thermodilution and gas rebreathing methods express temporary values (reflecting 10–15 s) [17]. The difference between CO_{TD} and CO_{RB} is, thus, the difference between two temporary determinations separated by time. The differences between CO_{Fick} and CO_{RB} or CO_{TD} are differences between the mean and temporary values. These differences are of no importance at stable rhythm and stable stroke volume. If, however, significant changes of CO occur quickly, as in rhythm disturbances, the differences are reflected as a wider distribution of values — both within one method and between methods. In atrial fibrillation, the changes are especially vivid, where the stroke volume of each myocardial contraction has a random value (with some contractions hemodynamically ineffective).

The ESCAPE study, evaluating hemodynamic monitoring in decompensated HF, revealed a slightly better functional improvement in invasively monitored patients. Nonetheless, an increase in survival or shortening of hospitalization was not observed [15]. If it emerges that non-invasive measurements are equally helpful in achieving greater functional improvement, the tests may well be performed more often. Non-invasive monitoring would then change the daily practice of cardiology departments treating patients with decompensated heart failure [18––20]. However, for the time being, literature is lacking in data concerning the gas rebreathing method in the monitoring of decompensated heart failure patients.

Limitations of the study

Calculated values were used instead of measured ones, due to the impossibility of determining oxygen consumption in the Fick formula. Thus, our CO_{Fick} values involve a degree of estimation error. The limited number of patients in the studied population did not allow us to conduct subgroup analyses. The low number of patients included in the study resulted from the fact that hemodynamic invasive tests in advanced stable heart failure are currently rarely performed.

Conclusions

1. Our study shows that the inert gas rebreathing method is a reliable technique for determining cardiac output in patients with advanced heart failure. Measurements are most accurate in patients with sinus rhythm.
2. It may be expected that the reliability of the method is sufficient to make proper clinical decisions. This comfortable, simple and noninvasive method means that measurements can be repeated frequently in patients with heart failure and, potentially, may be used in the monitoring of heart failure patients.

Acknowledgements

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