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Research article

Quantification of the impaired cardiac output response to exercise in heart failure: Application of a non-invasive device

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Abstract
An impaired cardiac output (CO) response to exercise is a hallmark of chronic heart failure (CHF), and the degree to which CO is impaired is related to the severity of CHF and prognosis. However, practical methods for obtaining cardiac output during exercise are lacking, and what constitutes and impaired response is unclear. Forty six CHF patients and 13 normal subjects underwent cardiopulmonary exercise testing (CPX) while CO and other hemodynamic measurements at rest and during exercise were obtained using a novel, non-invasive, bioreactance device based on assessment of relative phase shifts of electric currents injected across the thorax, heart rate and ventricular ejection time. An abnormal cardiac output response to exercise was defined as achieving ≤ 95% of the confidence limits of the slope of the relationship between CO and oxygen uptake (VO_2). An impaired CO slope identified patients with more severe CHF as evidenced by a lower peak VO_2, lower peak CO, heightened VE/VCO_2 slope, and lower oxygen uptake efficiency slope. CO can be estimated during exercise using a novel bioreactance technique; patients with an impaired response to exercise exhibit reduced exercise capacity and inefficient ventilation typical of more severe CHF. Non-invasive measurement of cardiac performance in response to exercise provides a simple method of identifying patients with more severe CHF and may complement the CPX in identifying CHF patients at high risk.

Key words: Heart failure, cardiac output, oxygen uptake, exercise testing.

Introduction
The cardiopulmonary exercise test (CPX) has been widely used over the last two decades in the management of patients with chronic heart failure (CHF). Its applications include classifying the severity of disease, evaluating the effects of therapy, estimating prognosis, and developing a safe and effective exercise prescription (Arena et al., 2007; Myers, 2005). In particular, a large number of studies have been published related to the prognostic applications of the CPX. Directly measured maximal oxygen uptake (peak VO_2) has been an important medium for estimating risk in patients with CHF because it closely parallels the cardiac output (CO) response to exercise (Pina et al., 2003). However, peak VO_2 can be difficult to determine in some patients (Myers, 1996; Noakes, 1998), can be difficult to define (Myers et al., 1989; Myers, 1996; Noakes, 1998), is influenced by motivation, and varies considerably in some patients with similar cardiac function (Myers et al., 2006; Wilson et al., 1995a; 1995b; 1999). For example, Wilson and colleagues (1995a; 1995b; 1999) reported dissociations between exertional symptoms, peak VO_2, and circulatory function in patients with CHF. Chomsky and colleagues (Chomsky et al., 1996) observed that the CO response to exercise was a stronger predictor of survival than peak VO_2 among cardiac transplant candidates. These and other investigations (Lang et al., 2007; Metra et al., 1999; Williams et al, 2001; 2005) have therefore suggested that the CO response to exercise should be quantified when assessing the degree of cardiac dysfunction or when estimating risk in patients with CHF.

However, drawbacks to the routine measurement of CO include the fact that it is invasive, time consuming, carries an inherent risk, is not always accurate, is expensive, and is particularly difficult to measure during exercise. Thus, it is impractical for routine clinical use. For these reasons, a non-invasive and easily applied method to quantify CO and other hemodynamic indices during exercise would have important applications for the routine clinical evaluation of CHF patients. While a number of non-invasive approaches have been proposed and acceptable agreement with the direct Fick, thermodilution or other techniques have been reported at rest (Leslien et al., 2004; Newman and Callister, 1999; Remmen et al., 2002; Thomas and Popovic, 2006), few previous studies have validated non-invasive estimates of cardiac output during exercise in patients with CHF. One novel approach that has recently undergone validation involves the analysis of blood flow-dependent changes in the phase shifts of electrical currents applied across the chest. This differs from the bioimpedance approach, which relies on detection of flow-dependent changes in electrical signal amplitude, which are inherently more difficult to detect and more subject to noise. Accordingly, this approach (termed "*bioreactance*") has an improved signal-to-noise ratio and is less susceptible to physical factors such as body habitus, body motion and ambient conditions (Keren et al., 2007). The accuracy and precision of this technique has been demonstrated previously in comparison to invasive measurements with thermodilution (Raval et al., 2008; Squara et al., 2007).

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The ability to easily identify CHF patients with an abnormal cardiac output response to exercise would be useful in order to better classify the degree of exercise impairment, the severity of disease, and to estimate risk. The purposes of the current study were: 1) to propose a measurement standard for using such a device when classifying the degree of hemodynamic impairment in CHF; and 2) to determine the association between this response and CHF severity based on other clinical and CPX responses.

Methods

Subjects

This was a retrospective analysis of data obtained from 59 consecutive subjects referred to a private cardiology clinic for CPX testing for evaluation of dyspnea. All subjects provided written consent for the use of their data in the analysis. Forty six of the subjects had heart failure (27 with low EF, 19 with normal EF) and 13 were ultimately diagnosed as normal (normal EF and peak VO_2, dyspnea based on noncardiac factors). Demographic and clinical characteristics of the subjects are summarized in Table 1. In the overall population there was a broad range of EFs, peak VO_2 and peak CO values. All subjects were limited during exercise by fatigue or dyspnea, and none had clinical evidence of pulmonary disease or ischemic changes on the ECG.

Exercise testing

Symptom limited maximal exercise tests were performed on a treadmill using a ramp protocol (Myers et al., 1991). All subjects were requested to abstain from eating or smoking at least 3 hours prior to the test. Ventilatory oxygen uptake was measured using a Medical Graphics Corporation system (CPX-D, St. Paul, MN). Gas exchange data were acquired breath-by-breath and expressed in ten second intervals of rolling 30 second averages. Oxygen uptake, carbon dioxide production, minute ventilation, and respiratory exchange ratio were calculated on-line. The percentage of age-predicted normal peak VO_2 was determined for each patient using the equation of Wasserman et al. (Wasserman et al., 2004). Estimated metabolic equivalents (METs) were determined from the American College of Sports Medicine equations (American College of Sports Medicine, 2009). A 12-lead electrocardiogram was monitored continuously and recorded every minute. Blood pressure was recorded manually every two minutes throughout the test. All subjects were encouraged to provide a maximal effort; among patients with CHF, the Borg 0 to 10 perceived exertion scale was used to quantify effort (Borg, 1998).

The ventilatory threshold was determined by two experienced, independent reviewers using the V-slope method (Beaver et al., 1986) and confirmed by ventilatory criteria. VE and VCO_2 responses, acquired from the initiation of exercise to peak, were used to calculate the VE/VCO_2 slope via least squares linear regression ($y = mx + b$, m = slope) (Arena et al., 2007). The oxygen uptake efficiency slope (OUES) was derived by the slope of a semi-log plot of minute ventilation versus VO_2 from rest to peak exercise. As such, the OUES is an estimation of the efficiency of ventilation with respect to VO_2, with greater slopes indicating greater ventilatory efficiency (Arena et al., 2007).

Cardiac output

The NICOM bioreactance-based system (Cheetah Medical, Wilmington, Delaware) is based on an analysis of relative phase shifts of an oscillating current that occur when traversing the thoracic cavity. This contrasts with the traditional bioimpedance-based systems which rely only on measured changes in signal amplitude. The NICOM system is comprised of a radiofrequency generator for creating a high frequency current that is injected across the thorax, 4 dual surface electrodes that are used to establish electrical contact with the body, a receiving amplifier for recording the transthoracic voltage in response to the injected current and circuitry for determining the relative phase shift between the injected current

Table 1. Demographic and clinical characteristics. Data are means (± SD).

Patient characteristics	Normals	CHF	p value
N	13	46	
Age (years)	51 (11)	63 (12)	.001
Height (m)	1.72 (.1)	1.73 (.1)	.81
Weight (kg)	76 (14)	89 (23)	.06
Ejection Fraction (%)	56.5 (9.0)	42.5 (17.0)	.007
Peak VO_2 ($ml \cdot kg^{-1} \cdot min^{-1}$)	24.8 (6.2)	15.9 (5.6)	<.001
CHF Etiology, # subjects (%)	-		-
Ischemic Cardiomyopathy	-	19 (41)	-
Idiopathic Dilated Cardiomyopathy	-	1 (2)	-
CHF with Normal EF*	-	18 (39)	-
NYHA Classification, # (%)			
Class I	-	11 (24)	-
Class II	-	5 (11)	-
Class III	-	24 (52)	-
Class IV	-	6 (13)	-
Medications, # subjects (%)			
Digoxin	-	3 (6)	-
Beta Blocker	6 (46)	35 (76)	.11
ACE/ARB	5 (38)	26 (57)	<.001

CHF=chronic heart failure; EF=ejection fraction; NYHA=New York Heart Association; ACE/ARB=ACE inhibitor/angiotensin receptor blocker *>45%

Table 2. Non-invasive cardiac output data at rest and during exercise. Data are means (±SD).

Rest	Normals	CHF and Normal CO Response	CHF and Abnormal CO Response	p value
Cardiac output (L·min^{-1})	5.4±1.7	4.5±1.4	5.7±1.4	0.03
Cardiac index (L·min^{-1}·M^{-2})	2.9±0.78	2.2±0/61*	3.0±0.81*†	0.003
Dx/dt (ohme·sec^{-1})	171.3±107	92.3±52	225.4±151	<0.001
VET (msec)	174.3±36	167.3±21	154.5±17	0.14
Ejection fraction	56.5±9	43.4±17	43.0±19	0.05
Peak Exercise				
Cardiac output (L·min^{-1})	20.0±10.0	19.7±6.5	11.1±4.4*†	0.002
Cardiac index (L·min^{-1}·M^{-2})	10.6±4.7	9.8±3.3	5.6±1.7*†	<0.001
Dx/dt (ohme·sec^{-1})	557.8±239	429.9±194	322.4±141†	0.01
VET (msec)	143.6±17	142.5±11	148.7±13	0.39

p value represents ANOVA main effect between groups. *p < 0.05 vs CHF patients with a normal cardiac output response. †p <0.05 vs normal subjects. VET = ventricular ejection time. Dx/dt = peak aortic flow.

and the recorded voltage. Within each of the dual electrodes, one electrode is used by the high frequency current generator, while the other is used by the input voltage amplifier. Signals are applied to and recorded from the left and right sides of the thorax; these signals are processed separately and averaged after digital processing. During exercise testing, the electrodes can be placed on the subject's back so that the cables do not interfere with upper body motion.

The signal processing unit of the system determines the relative phase shift (ΔΦ) between the input signal relative to the output signal. ΔΦ in turn is due to changes in blood flow in the aorta. It has been shown that stroke volume (SV) is estimated by:

$$SV = C \cdot VET \cdot d\Phi/dt_{max}$$

where C is a constant of proportionality and VET is ventricular ejection time which is determined from the NICOM and ECG signals. The value of C has been optimized in prior studies and accounts for patient age, gender and body size (Borg, 1998). CO is then calculated using the relation: CO = SV x HR, where HR is the heart rate. CO was expressed as minute-by-minute values from rest to peak exercise. The NICOM system has CE mark in Europe and 510(k) clearance from the US Food and Drug Administration and is available for clinical use in both Europe and United States.

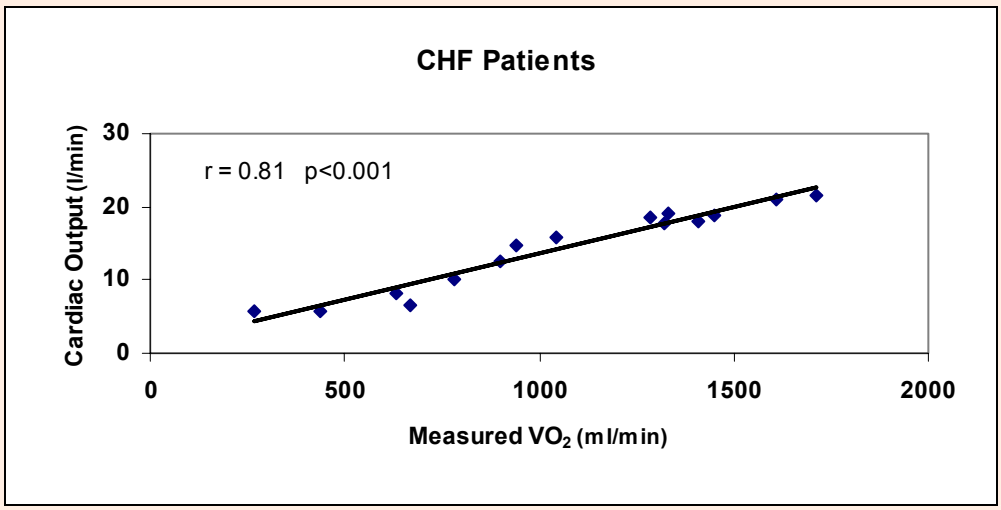
Statistical analysis

Descriptive statistics are presented as mean (±SD). The associations between non-invasive CO data, clinical variables, and other exercise test responses were assessed using linear regression. The adequacy of the cardiac output response to exercise was assessed by quantifying the minute-by-minute slope of the linear relation between CO and oxygen uptake. A patient achieving ≤ 95% of the confidence limits of the slope of this relationship (slope ≤0.09) was considered to have an abnormal CO response to exercise. Comparisons between normal subjects and CHF patients with normal and abnormal cardiac output responses to exercise were performed using one-way ANOVA. Post-hoc testing was performed using the Bonferroni method.

Table 3. Exercise test responses in normal subjects and CHF patients with normal and abnormal cardiac output response to exercise (mean ± SD).

	Normals	CHF and Normal CO Response	CHF and Abnormal CO Respons	p value
Rest				
Standing heart rate (beats·min^{-1})	75 (13)	74 (14)	77 (11)	.79
Systolic blood pressure (mmHg)	125 (9)	118 (9)	118 (9)	.05
Ventilatory Threshold				
Heart rate (beats·min^{-1})	130 (22)	105 (23) †	97 (18) †	.001
Systolic blood pressure (mmHg)	140 (7)	127 (11) †	126 (12) †	.008
Diastolic blood pressure (mmHg)	84 (7)	82 (7)	73 (13)	.07
Oxygen uptake (ml·min^{-1})	1487 (483)	1124 (419)	906 (460) †	.007
Oxygen uptake (ml·kg^{-1}·min^{-1})	19.8 (6.0)	11.4 (3.9) †	10.7 (4.2) †	<.001
Minute ventilation (L·min^{-1})	38.2 (15.0)	32.3 (12.0)	25.7 (8.0) †	.05
CO_2 production (ml·min^{-1})	1445 (580)	1027 (445) †	827 (428) †	.007
Perceived exertion	--	5.3 (2.9)	3.2 (1.3)	.21
Maximal Exercise				
Heart rate (beats·min^{-1})	139 (24)	116 (27) †	112 (18) †	.008
Systolic blood pressure (mmHg)	143 (12)	134 (12)	132 (19)	.09
Oxygen uptake (ml·min^{-1})	1857 (464)	1494 (518)	1169 (628) *†	.009
Oxygen uptake (ml·kg^{-1}·min^{-1})	24.8 (6.2)	16.8 (5.5) †	14.1 (5.8) †	<.001
Minute ventilation (L·min^{-1})	63.7 (16.0)	58.7 (20.0)†	43.7 (16.0)	.02
CO_2 production	2173 (577)	1678 (674)	1298 (694) †	.006
Respiratory exchange ratio	1.15 (.09)	1.12 (.10)	1.12 (.09)	.61
VE/VCO_2 Slope	.28 (.03)	.35 (.08) †	.37 (.09) †*	.007
OUES	2.1 (.59)	1.61 (.55)	1.39 (.68) †	.01
Perceived exertion	--	7.9 (1.8)	7.9 (2.5)	.94

p value represents ANOVA main effect between groups. *p <0.05 vs CHF patients with a normal cardiac output response. †p <0.05 vs normal subjects. CO - cardiac output. OUES - oxygen uptake efficiency slope.



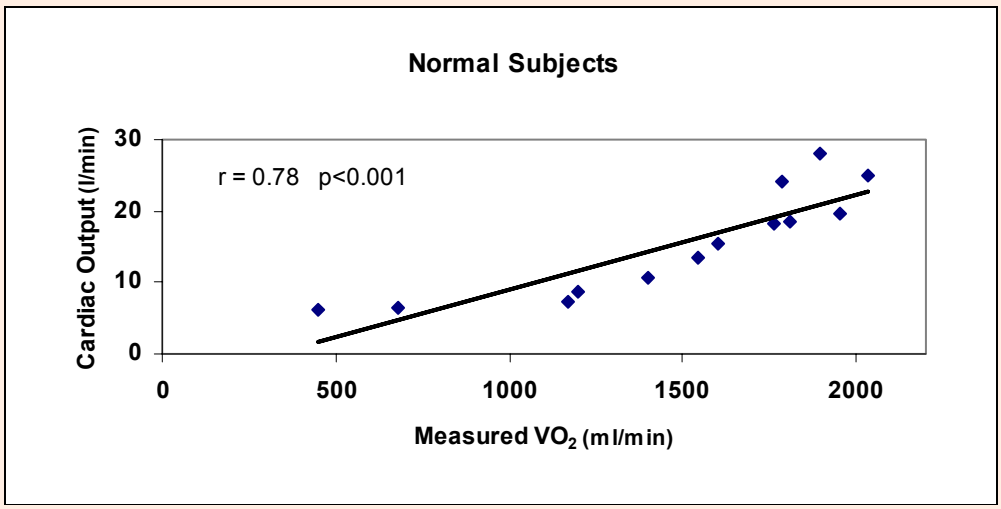


Figure 1. The relationships between cardiac output and oxygen uptake (VO_2) during exercise in patients with heart failure and normal subjects. Data points represent the group mean values for each minute during exercise.

Results

Eleven of the patients with CHF had an abnormal CO response to exercise. Table 2 shows resting and peak exercise CO, cardiac index, peak aortic flow (Dx/dt), and ventricular ejection time (VET) between normal subjects and CHF patients with normal and abnormal CO responses to exercise. Resting cardiac index was higher in CHF patients with an abnormal CO response to exercise vs. CHF patients with a normal response ($p < 0.05$). However, while peak exercise CO and cardiac index were similar between normal subjects and CHF patients with a normal CO response to exercise (peak CO 20.0 ± 10 and 19.7 ± 6.5 $l \cdot min^{-1}$, respectively), they were lower among patients with an abnormal CO response to exercise (peak CO 11.1 ± 4.4 $l \cdot min^{-1}$, $p < 0.001$ between groups). Arterio-venous (a-VO_2) oxygen difference at peak exercise was wider in patients with an abnormal CO response to exercise vs. those with a normal CO response (12.0 ± 3.8 vs. 8.7 ± 3.3 ml/100 ml, $p < 0.05$).

Exercise test responses among normal subjects, those with CHF and a normal CO response, and CHF patients with an impaired CO response are summarized in Table 3. For the overall group, the mean maximal perceived exertion was 7.8 ± 1.7 (range 5-10), and the mean peak respiratory exchange ratio was 1.12 ± 0.09 (range 0.87-1.28), suggesting that maximal effort was achieved by most patients. Normal subjects generally achieved higher exercise test responses than both groups of patients with CHF. Mean maximal oxygen uptake values for normal subjects and patients with a normal and abnormal CO response were 24.8 ± 6.0, 16.8 ± 6.0, and 14.1 ± 6.0 $ml \cdot kg^{-1} \cdot min^{-1}$, respectively ($p < 0.001$). Similarly, oxygen uptake at the ventilatory threshold was highest among normal subjects and lowest among CHF patients with an impaired CO response to exercise. Relative to both normal subjects and the subgroup of patients with a normal CO response, peak VO_2 expressed in $ml \cdot min^{-1}$ was lower among CHF patients with an abnormal CO response to exercise (1857 ± 464, 1494 ± 518, and 1169 ± 628 $ml \cdot min^{-1}$, respectively, $p < 0.001$). CHF patients with an abnormal CO response to exercise also had a higher VE/VCO_2 slope and tended to have a lower OUES vs. patients with a normal CO response.

Figure 1 illustrates the relationship between changes in CO and VO_2 during exercise in normal sub-

jects and patients with CHF, expressed as group means each minute. In both groups, these two responses were closely related (r = 0.81 for CHF and r = 0.78 for normal subjects, p < 0.001 for both). Table 4 presents correlation coefficients between CO slope, cardiac performance measures at peak exercise, and CPX responses in patients with CHF and normal subjects. The CO slope was significantly related to peak VO_2 in patients with CHF (r = 0.51, p < 0.001) and was significantly related to peak CO in both groups (r = 0.48, p < 0.001 and 0.79, p = 0.002 for CHF and normal subjects, respectively).

Discussion

In the present study we sought to better define a normal standard when using a novel non-invasive device for classifying the degree of exercise impairment and stratifying risk in patients with CHF. Because the measurement of cardiac performance has been suggested to be an important complement to peak VO_2 and other CPX responses when assessing circulatory dysfunction and stratifying risk in CHF (Chomsky et al., 1996, Lang et al., 2007, Metra et al., 1999, Williams et al., 2001, Williams et al., 2005, Wilson et al., 1995a), the ability to acquire such data easily and without the need for arterial or mixed venous blood sampling potentially has a great deal of value for both clinical and research applications in these patients.

Table 4. Correlation coefficients (r) between the slope of the relationship between cardiac output and oxygen uptake (CO slope) and hemodynamic and exercise variables.

CHF Subjects	CO Slope	p value
Peak VO_2	.51	<.001
Peak CO	.48	.001
Peak CI	.54	<.001
Peak VET	.22	.18
VE/VCO_2 Slope	-.08	.61
OUES	-.07	.66
NYHA Class	.05	.75
EF	-.02	.89
Normal Subjects	**CO Slope**	**p value**
Peak VO_2	.17	.59
Peak CO	.79	<.002
Peak CI	.81	.001
Peak VET	-.50	.10
VE/VCO_2 Slope	-.36	.25
OUES	.58	.05
EF	.28	.40

VO_2 = oxygen uptake; CO = cardiac output; CI = cardiac index; VET = ventricular ejection time; OUES = oxygen uptake efficiency slope; NYHA = New York Heart Association; EF = ejection fraction.

The accuracy of the NICOM device to measure cardiac output noninvasively as compared to thermodilution has been demonstrated in two prior studies (Raval et al., 2008; Squara et al., 2007). These studies compared invasive and NICOM-based measurements of CO over long periods of time (up to 24 hours), in varied clinical settings and spanning wide ranges of CO values. Results of two other studies (Maurer et al., 2009; Myers et al., 2007) have reported a tight relationship between VO_2 and CO during exercise using this method that are similar to those reported in earlier studies. Hemodynamic measurements derived from the device have also identified NYHA class-dependent abnormalities during exercise that are consistent with prior studies using invasive methods (Maurer et al., 2009). The validity of the NICOM device is further suggested by the present data showing a close relationship between the change in VO_2 and CO throughout exercise (r = 0.83, p < 0.001). This close association is well-established in the literature and is typical of previous studies using directly-measured CO (Damato et al., 1966, Lewis et al., 1983, Myers et al., 1991, Wilmore and Costill, 1999). In addition, the resting and peak exercise values for CO and other hemodynamic responses fell within the expected range for normal subjects and patients with CHF (Table 2).

We observed that patients with more severe disease, those with more inefficient ventilation, and those with a lower exercise capacity generally had worse ventricular performance during exercise (reduced slope of the relationship between VO_2 and CO, lower peak CO) as estimated by the bioreactance technology. Whereas CHF patients with a normal CO response to exercise had a peak CO that was similar to normal subjects (both approximately 20 $l \cdot min^{-1}$), subjects with an impaired CO slope during exercise had a peak CO that was reduced by nearly 50%. The importance of an impaired CO response to exercise emphasized by studies measuring CO directly has been based in part on the fact that resting cardiac function and even peak VO_2 can be similar among subjects who differ markedly in their cardiac performance during exercise (Chomsky et al., 1996; Lang et al., 2007; Metra et al., 1999; Wilson et al., 1995a; 1995b). Our observations confirm this in that patients with an impaired CO response to exercise actually had resting CO values that were higher than those in patients with a normal CO response to exercise. In addition, similar to the findings of Wilson et al. (1995), cardiac impairment in response to exercise was only modestly related to peak VO_2 (Table 4). This underscores the concept that identifying patients who have an impaired hemodynamic response to exercise is clinically relevant independent of resting cardiac function and peak VO_2 (Chomsky et al., 1996; Lang et al., 2007; Metra et al., 1999; Wilson et al., 1995a; 1995b).

There are a number of clinical implications related to a valid non-invasive measure of cardiac performance during exercise. First, guidelines on risk stratification in CHF have traditionally focused on resting hemodynamic measurements, but resting measures have tended to be inadequate predictors of risk (Chomsky et al., 1996; Metra et al., 1999; Myers and Gullestad, 1998; Myers et al., 1998). Thus, the addition of exercise hemodynamic responses to the risk paradigm in CHF, in addition to CPX responses, will likely increase the predictive value of risk models (Chomsky et al., 1996; Metra et al., 1999), although this has not been a universal finding (Aaronson et al., 1997; Myers and Gullestad, 1998). Second, the cardiac output response to exercise has been shown to be an even more powerful prognostic marker than peak VO_2, and estimates of risk appear to be optimized when these two responses are combined (Cotter et al., 2003; Metra et al., 1999; Williams et al., 2001; 2005). Third, despite the widely-recognized importance of ventilatory gas ex-

change techniques in patients with CHF (Arena et al., 2007; Myers, 2005), surveys have shown that the vast majority of clinical exercise testing is done without them (Myers et al., 2000). Thus, the use of non-invasive CO may be particularly useful when ventilatory gas exchange techniques are not available. Finally, the technique is non-invasive, inexpensive, and is not burdensome for the patient or user. Thus, the addition of non-invasive indices of cardiac performance to the standard exercise test has the potential to better quantify cardiac dysfunction and estimate risk in patients routinely evaluated for CHF.

An important consideration in our analysis was how best to establish what constitutes a normal and impaired response in order to classify patients appropriately, since there are few such data in the literature with which to compare. While there have been a number of efforts using invasive techniques to determine the appropriate CO response to upright exercise and its confidence limits (Damato al., 1966; Higginbotham et al., 1983; Julius et al., 1967; Rowell, 1986), these have generally been limited to normal subjects and it is unclear what an appropriate response and the variance of CO is among patients with CHF. We chose to use the slope of the relationship between CO and VO_2 since it reflects the capacity of CO to increase in accordance with physiologic work. We defined an impaired response as a slope that fell below the 95% confidence limits of normal. Similar approaches have been used to study O_2 kinetics in response to exercise (Myers et al., 1991; Porszasz et al., 2003; Tamesis et al., 1993), and it has been demonstrated that patients with CHF have a marked impairment in O_2 kinetics compared to normal subjects and those with coronary disease (Myers et al, 1991). Intuitively, patients with more severe CHF will have the most impaired increase in CO (a lower slope), and it is well-known that such patients compensate for an inadequate CO response to exercise by a widening of the a-VO_2 difference (Myers and Froelicher, 1991; Sullivan et al., 1989), as we observed in the current study. While the approach we employed was empirical, it provided a marked distinction between normal subjects and CHF patients with and without an impaired CO response to exercise. Further refinement of methods to define this response will likely need to consider age, type of heart failure, gender, and its association with risk for future adverse events.

Limitations

As mentioned above, the estimation we used to define the adequacy of the CO response to exercise was empirical; there may be other methods with which to express this response. In addition, there are other methods of estimating cardiac output, including CO_2 rebreathing and inert gas rebreathing methods (Lang et al., 2007); the adequacy of the CO response to exercise in CHF using these methods has not been fully explored. The application of the bioreactance device must be further validated by direct measurements of CO, and among populations of patients with varying degrees of CHF. Our approach focused on the central hemodynamic response to exercise, but peripheral factors also play an important role in determining exercise tolerance in CHF, and these must also be considered when using the exercise response to make clinical judgments in CHF.

Conclusion

An impairment in the CO response to exercise using a novel non-invasive technique identified CHF patients with more severe disease, lower exercise capacity and inefficient ventilation, and thus provided added insight into the cardiovascular status of patients with CHF. Non-invasive measurement of cardiac performance in response to exercise has potentially important applications for the functional and prognostic assessment of patients with CHF.

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Key points

- Non-invasive measurement of cardiac output during exercise is feasible in patients with heart failure.
- Impairment in the CO response to exercise identifies heart failure patients with more severe disease, lower exercise capacity and inefficient ventilation.
- Non-invasive measurement of cardiac performance during exercise has potentially important applications for the functional and prognostic assessment of patients with heart failure.

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