Cardiac Output and Cardiopulmonary Responses to Exercise in Heart Failure: Application of a New Bio-Reactance Device

JONATHAN MYERS, PhD,[1] PRADEEP GUJJA, MD,[2] SURESH NEELAGARU, MD,[3] AND DANIEL BURKHOFF, MD[4]

Palo Alto, California; Amarillo, Texas; New York, New York

ABSTRACT

Background: Cardiopulmonary exercise testing (CPX) is widely used to evaluate heart failure (HF) patients, but lacks information about ventricular performance. There is a need for a noninvasive cardiac output (CO) measurement.

Methods and Results: Twenty-three HF patients and 13 normals underwent CPX and CO measurements with a new, noninvasive, bioreactance technology based on assessment of relative phase shifts ($d\Phi/dt$) of electric currents injected across the thorax, heart rate, and ventricular ejection time. CO and oxygen uptake (VO_2) closely paralleled each another during exercise, and peak CO was strongly correlated with peak VO_2 ($r = 0.73$, $P < .001$). The relationships between peak VO_2 and peak cardiac index (CI) were similar for directly measured CI ($r = 0.61$) and noninvasive CI ($r = 0.61$). The CO-VO_2 relationship was also similar between the current study and previous studies from the literature, as evidenced by a similar line of best fit and 95% confidence limits. Maximal CO was significantly related to indices of ventilatory efficiency, including the VE/VCO_2 slope ($r = -0.47$, $P < .01$), and the oxygen uptake efficiency slope ($r = 0.67$, $P < .01$).

Conclusion: Noninvasive measurement of CO during exercise using a novel bioreactance-based device has potentially important applications as a simple, inexpensive tool to supplement the clinical evaluation of patients with HF. (*J Cardiac Fail 2007;13:629–636*)

Key Words: Heart failure, cardiac index, oxygen uptake, exercise testing.

The cardiopulmonary exercise test (CPX) is an important tool in the evaluation of patients with chronic heart failure (CHF) and has wide applications for assessing therapy and stratifying risk in these patients.[1–3] A fundamental characteristic of CHF is an impaired ability to increase cardiac output appropriately with exercise.[4,5] Because oxygen uptake (VO_2) is relatively easy to measure and generally parallels cardiac output during exercise, peak VO_2 has historically been considered a surrogate for maximal cardiac output. However, cardiac output cannot be accurately estimated from CPX, largely because VO_2 is influenced by numerous central and peripheral factors in addition to cardiac input.[4,6] Numerous investigators over the last decade have reported a dissociation between peak VO_2 and the degree of cardiac dysfunction in patients with CHF,[7,8] which has the potential to lead to inappropriate medical management decisions, including transplantation.

Thus more precise estimates of cardiac output during exercise, along with CPX responses, are advantageous. The direct measurement of cardiac output by thermodilution (generally considered the ''gold standard'') however, is cumbersome, invasive, not always accurate, and carries an added expense and degree of risk. As a result, numerous methods to acquire cardiac output responses noninvasively have been proposed. Techniques such as bioimpedance, echocardiography, and CO_2 rebreathing have been employed, but limitations of these methods, including reliability and reproducibility, particularly during exercise, have been well-documented.[9–13] An entirely new and novel approach to analyzing changes in transthoracic electrical

From the [1]Cardiology Division, Veterans Affairs Palo Alto Health Care System and Stanford University, Palo Alto, California; [2]Texas Tech University of Health Sciences, Amarillo, Texas; [3]Lonestar Arrhythmia and Heart Failure Center, Amarillo, Texas; and [4]Colombia University, New York, New York.

Manuscript received February 15, 2007; revised manuscript received April 9, 2007; revised manuscript accepted May 23, 2007.

Reprint requests: Jonathan Myers, PhD, VA Palo Alto Health Care System, Cardiology Division - 111C, 3801 Miranda Avenue, Palo Alto, CA 94304.

Supported in part by a grant from Cheetah Medical Inc, Wilmington, DE.

1071-9164/$ - see front matter

doi:10.1016/j.cardfail.2007.05.009

properties has been developed that offers the possibility of accurate, easy to perform, noninvasive measurement of cardiac output during exercise testing.[14] This new approach is based on analysis of blood flow—dependent changes in the phase shift of electrical currents applied across the chest. In contrast to the bioimpedance approach, which relies on detection of flow-dependent changes in electrical signal amplitude, phase shifts are inherently more accurately detectable and less 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. This system was recently reported to have acceptable precision and responsiveness for monitoring cardiac output in the intensive care unit among patients with a wide range of circulatory dysfunction.[15] The utility of this system during exercise, however, has not been reported.

In the current study, we addressed the practicality and potential clinical utility of this technique in a retrospective analysis of tests performed on a clinical basis in patients being evaluated for dyspnea. The specific aims of the study were to 1) summarize initial clinical experience using this new technology for measuring cardiac output at rest and during exercise, 2) characterize cardiac output and other measures of cardiac performance in response to exercise among patients with CHF to illustrate the potential clinical utility of the device, and 3) explore the interactions between CPX and cardiac output responses to exercise in patients with CHF.

Methods

Subjects

This was a retrospective analysis of clinical data obtained from 36 consecutive subjects referred to a private cardiology clinic for CPX testing for evaluation of dyspnea. All patients provided consent for the use of their data in the analysis. Twenty-three of the subjects had heart failure (18 with low ejection fraction [EF], 5 with normal EF) and 13 were ultimately diagnosed as normal (normal EF, 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 values, and peak cardiac outputs. All subjects were limited during exercise by fatigue or dyspnea, and none had clinical evidence of pulmonary disease or ischemic changes on the electrocardiogram.

Exercise Testing

Symptom-limited maximal exercise tests were performed on a treadmill using a ramp protocol.[16] All subjects were requested to abstain from eating or smoking at least 3 hours before the test. Ventilatory oxygen uptake was measured using a Medical Graphics Corporation (CPX-D, St. Paul, MN). Gas exchange data were acquired breath-by-breath and expressed in 10-second intervals of rolling 30-second averages. Oxygen uptake, carbon dioxide production, minute ventilation, and respiratory exchange ratio were calculated online. The percentage of age-predicted normal peak VO_2 was determined for each patient using the equation of Wasserman et al.[17] Estimated peak VO_2 was determined from the American College of Sports Medicine equations.[18] A 12-lead electrocardiogram was monitored continuously and recorded every minute. Blood pressure was recorded manually every 2 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.[19]

Table 1. Demographic and Clinical Characteristics

Patient Characteristics	CHF	Normals	*P*
N	23	13	
Age (y)	66.6 ± 10	51.0 ± 11	<.001
Height (cm)	176 ± 10	172 ± 10	.20
Weight (kg)	87.0 ± 15	76.1 ± 15	.04
Ejection fraction (%)	35.2 ± 12	58.2 ± 6.4	<.001
Peak VO_2 (mL·kg·min)	14.7 ± 5.4	24.8 ± 6.2	<.001
CHF etiology, number of subjects (%)			
Ischemic cardiomyopathy	17 (74)	—	—
Idiopathic dilated cardiomyopathy	1 (4)	—	—
CHF with normal EF*	4 (17)	—	—
NYHA classification, number (%)		—	
Class I	1 (5)	—	—
Class II	3 (15)	—	—
Class III	13 (65)	—	—
Class IV	3 (15)	—	—
Medications, number of subjects (%)			
Digoxin	3 (13)	0 (0)	—
β-blocker	22 (96)	6 (46)	.05
ACE/ARB	17 (74)	5 (38)	.05

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

The ventilatory threshold was determined by 2 experienced, independent reviewers using the V-slope method[20] and confirmed by ventilatory criteria. Ventelation and carbon dioxide uptake (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).[1,21] The oxygen uptake efficiency slope (OUES) was derived by the slope of a semi—log plot of minute ventilation versus VO_2. As such, the OUES is an estimation of the efficiency of ventilation with respect to VO_2, with greater slopes indicating greater ventilatory efficiency.[1,21]

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 that rely only on measured changes in signal amplitude. The NICOM system comprises 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 and the recorded voltage. Within each of the dual electrodes, 1 electrode is used by the high-frequency current generator, whereas 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