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Gas Exchange Efficiency in Congestive Heart Failure II

Robert L. Johnson, Jr, MD

It has become increasingly apparent that congestive heart failure (CHF) affects not only the cardiovascular system, but every organ system involved with oxygen transport, including the respiratory system, skeletal muscles, and the hormonal and neural feedback control systems for breathing, cardiac output, blood pressure, blood volume, and distribution of blood flow. One segment of this transport system cannot be isolated from the rest. The ventilatory response to exercise in patients with CHF is augmented despite normal arterial O2 saturation and a normal or low end-tidal Pco2.1-6 The augmented ventilatory response is measured as a steep slope of the increase in ventilation with respect to CO2 output (ΔVe/ΔVco2) or as a high Ve/Vco2 ratio at peak exercise. The source of this ventilatory augmentation has been controversial, but its pathophysiological significance is clear. A high slope at submaximal exercise or a high Ve/Vco2 ratio at peak exercise is a powerful index of poor prognosis in patients with CHF.4,7 As indicated by Ponikowski et al8 in the current issue of Circulation, this prognostic power is retained in patients with CHF, even when the maximal O2 uptake (Vo2 max) is near the normal range.

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A high Ve/Vco2 ratio has 2 possible sources: (1) increased ventilation, which is required to overcome a large dead space to maintain a normal arterial CO2 tension (Paco2), or (2) increased central drive to ventilation, which drives the Paco2 below what is normally expected. Ponikowski et al8 present convincing evidence that the augmented ventilatory response to exercise in CHF is significantly correlated with other markers of abnormal cardiorespiratory reflex control (ie, central and peripheral chemoreceptor control of ventilation, ergoreceptor drive to ventilation, and both autonomic and baroreceptor control of the circulation). Thus, the high Ve/Vco2 seems related to altered chemoreceptor gain and ergoreceptor drive to ventilation, as well as to impaired reflex control of the heart and circulation. Impaired autonomic and baroreceptor control become manifest in severe heart failure by an abnormally reduced variability in heart rate and an increased variability in blood pressure, with predisposition to arrhythmias and sudden death.9,10 These observations provide a major link between augmented exercise ventilation in CHF and poor prognosis.

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Is the augmented ventilation during exercise an integral part of the deranged cardiorespiratory reflex controls in CHF or a manifestation of structural changes in the lung that impair ventilation/perfusion matching, as I suggested in a previous editorial?11 Ponikowski et al8 and others6,12 from the same laboratory provide indirect support for a high ventilatory drive related to increased chemoreceptor gain and ergoreceptor drive in skeletal muscle. However, if present, such an increased ventilatory drive should force the Paco2 below expected levels during exercise and generate a negative correlation between Paco2 and Ve/Vco2 at peak exercise. No convincing data from arterial blood gases indicate that this occurs. Wasserman et al5 provided comprehensive data on alveolar arterial blood gas exchange in 130 patients with CHF and 52 normal controls. They concluded that “the increase in ventilatory response in CHF is due primarily to 2 mechanisms: (1) the increased CO2 output relative to VO2, owing to bicarbonate buffering of accumulating lactic acid, and (2) the increase in Vd/Vt ratio due to reduced perfusion of ventilated lung.” Arterial Paco2 was not depressed from rest to heavy exercise, although end-tidal Paco2 was depressed because of a high alveolar dead space. There was no evidence for increased central or peripheral drive to ventilation.

Franciosa et al2 reported both arterial blood gas and hemodynamic data at rest and peak exercise in 28 patients with CHF. They concluded that “exercise intolerance in patients with severe CHF is associated with marked elevation of pulmonary capillary wedge pressure and anaerobic metabolism without hypoxemia or altered carbon dioxide tension.” The mean Paco2 (35±7 mm Hg) was the same at rest and peak exercise; hence, similar to the data from Wasserman et al,3 there was no evidence suggesting a high ventilatory drive. Fortunately, however, Franciosa et al2 provided the blood gas and hemodynamic data on each subject in a table, which allowed a more comprehensive analysis. Both the Ve/Vco2 and dead-space gas volume to tidal gas volume (Vd/Vt) ratios can be calculated at peak exercise from the tabulated data and plotted with respect to Paco2. (Figure 1). This yields a highly significant inverse correlation between Ve/Vco2 and Paco2 (Figure 1A) that supports Ponikowski et al’s8 hypothesis. There is also a highly significant, direct correlation between Vt/Vco2 and the Vd/Vt ratio (Figure 1B), confirming an uneven distribution of ventilation with respect to perfusion in the lung. Thus, the Paco2 is driven to low levels during peak exercise in CHF, despite inefficient gas exchange from a high Vd/Vt ratio.

From whence might this increased drive arise? Ponikowski et al8 show high chemoreceptor gains for Po2 and Pco2 in CHF that positively correlate with a high Ve/Vco2 slope. Normal individuals who have high chemoreceptor gain also have an augmented ventilatory response to exercise.13-15 In Figure 2, I compare the relationship between Ve/Vco2 and
Franciosa et al, with that in normal subjects studied by their respective set points. This is like the gain of et al, who also showed a positive correlation between chemoreceptor gains and a lower PaCO2. The normal subjects had different chemoreceptor gains for PO2 and PCO2 at rest, which were augmented at exercise; those normal subjects with high chemoreceptor gains had higher ratios of VE/VECO2 and a lower PaCO2. The point of the graph is to illustrate from the regression lines that that ventilation had to be about twice that in the normal subjects to achieve the same PaCO2 because of the inefficient gas exchange (ie, the high Vd/Vt ratio). This means that ventilatory drive had to be, on average, twice as high in the CHF patients than in the normal subjects studied by Martin et al. It is hard to explain this increased drive by a simple increase in chemoreceptor gain, however, because chemoreceptor gain does not represent a unidirectional drive; rather, it represents the strength of feedback control to minimize any deviation of arterial PO2 and PCO2 in either direction from their respective set points. This is like the gain of the thermostat in a home air-conditioning system. Exercise must alter the set point of the control system, perhaps by increased sympathetic stimulation or from increased stimulation from skeletal muscle ergoreceptors, both of which are augmented in CHF. A high chemoreceptor gain would then tighten the control and ensure a smaller error signal at full response. It would be of interest to know whether normal subjects who have a high chemoreceptor gain and a high ventilatory response to exercise also have a high ergoreceptor drive from skeletal muscle.

The augmented ventilatory response to exercise in CHF correlates with control and reflex abnormalities and with hemodynamic alterations. The latter relationships can also be illustrated from the data of Franciosa et al (Figure 3). There is a strong inverse correlation of VE/VECO2 with cardiac index (Figure 3A) and with pulmonary artery pressure (Figure 3B). Hence, there are multiple reasons why this simple ratio of VE/VECO2, or the slope of the increase in VE with respect to VCO2 during exercise, provides a powerful prognostic index in heart failure. It seems to reflect the severity of derangement in almost all aspects of CHF; it is also an objective measurement that can be made easily.

Figure 1. Relationship of augmented ventilation with respect to CO2 output (VE/VECO2) to arterial CO2 tension (PaCO2) and to dead-space ventilation (Vd/Vt) at peak exercise in patients with CHF, derived from data of Franciosa et al. Averaged data from Clark et al fall within same range. Results indicate that augmented ventilatory response in patients with heart failure is a consequence of both an increase in ventilatory drive and a corresponding increase in dead-space ventilation.

Paco2 at peak exercise in the CHF patients studied by Franciosa et al with that in the normal subjects studied by Martin et al. The normal subjects had different chemoreceptor gains for PO2 and PCO2 at rest, which were augmented at exercise; those normal subjects with high chemoreceptor gains had higher ratios of VE/VECO2 and a lower PaCO2. The point of the graph is to illustrate from the regression lines that that ventilation had to be about twice that in the normal subjects to achieve the same PaCO2 because of the inefficient gas exchange (ie, the high Vd/Vt ratio). This means that ventilatory drive had to be, on average, twice as high in the CHF patients than in the normal subjects studied by Martin et al. It is hard to explain this increased drive by a simple increase in chemoreceptor gain, however, because chemoreceptor gain does not represent a unidirectional drive; rather, it represents the strength of feedback control to minimize any deviation of arterial PO2 and PCO2 in either direction from their respective set points. This is like the gain of the thermostat in a home air-conditioning system. Exercise must alter the set point of the control system, perhaps by increased sympathetic stimulation or from increased stimulation from skeletal muscle ergoreceptors, both of which are augmented in CHF. A high chemoreceptor gain would then tighten the control and ensure a smaller error signal at full response. It would be of interest to know whether normal subjects who have a high chemoreceptor gain and a high ventilatory response to exercise also have a high ergoreceptor drive from skeletal muscle.

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Figure 2. Data from Franciosa et al plotted in Figure 1A is compared with similar data in normal subjects studied by Martin et al, who also showed a positive correlation between chemosensitivity to hypoxia and hypercapnia similar to that in patients with CHF. Normal subjects with high chemosensitivity had a lower PaCO2 and higher VE/VECO2 than subjects with low chemosensitivity, but ventilation at same CO2 output in patients must be, on average, twice that in normal subjects to achieve same PaCO2 as a consequence of inefficient gas exchange.

Figure 3. High VE/VCO2 ratio in CHF also correlates significantly with hemodynamic abnormalities, as demonstrated here using data of Franciosa et al for cardiac index at peak exercise and for resting pulmonary artery (PA) pressure.


**Key Words:** Editorials ■ heart failure ■ ventilation