Published in final edited form as:

Int J Cardiol. 2010 September 24; 144(1): 101–102. doi:10.1016/j.ijcard.2008.12.143.

The Oxygen Uptake Efficiency Slope is Reduced in Older Patients with Heart Failure and a Normal Ejection Fraction

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Abstract

The oxygen uptake efficiency slope (OUES) response has not been characterized in heart failure (HF) patients with a normal ejection fraction (NEF). Fifty-nine subjects with systolic HF, 59 with HF-NEF and 28 healthy age-matched controls participated in this analysis. The OUES (systolic HF: 1.23 ± 0.41 vs. HF-NEF: 1.22 ± 0.30 vs. controls: 1.51 ± 0.49) was significantly reduced in both HF groups compared to controls ($p < 0.001$). Compared to healthy controls, the OUES is reduced in HF-NEF patients to a similar degree as those with systolic HF. Thus, as in systolic HF, the OUES may provide clinically useful information in patients with HF-NEF.

Keywords

Diastolic; Exercise Testing; Ventilatory Efficiency

Introduction

The diagnostic and prognostic value of cardiopulmonary exercise testing (CPX) in patients with systolic heart failure (HF) is supported by a robust body of evidence.(1) There is, however, a paucity of information regarding the clinical utility of CPX in patients diagnosed with HF but presenting with a normal ejection fraction (NEF). One investigation has found the minute ventilation/carbon dioxide production (VE/VCO_2) slope, but not peak oxygen consumption (VO_2), retains prognostic value in patients with HF-NEF in a multivariate regression analysis.(2) While the VE/VCO_2 slope and peak VO_2 are the most prominent CPX variables in present day research investigations and clinical practice, other measures have demonstrated potential value. The oxygen uptake efficiency slope (OUES) is one such measure, which is purported to reflect the integration of pulmonary, cardiovascular, and skeletal muscle function during exercise.(3) Previous research examining the prognostic value of the OUES is presently equivocal. Davies et al.(4) found the OUES was prognostically superior to both peak VO_2 and the VE/VCO_2 slope. Arena et al.(5) conversely reported the VE/VCO_2 slope was the superior prognostic marker compared to the OUES. Both of these investigations included cohorts that were exclusively(4) or predominantly(5) diagnosed with systolic HF.

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Similar to Guazzi et al.(2), our group has found the VE/VCO₂ slope is significantly lower in patients with HF-NEF compared to those with systolic HF.(6) Conversely, peak VO₂ was similarly diminished, and significantly lower in both HF-NEF and systolic HF groups compared to apparently healthy controls.

Because little is known about OUES in the key population of older persons with HF-NEF, the primary purpose of this analysis was to compare the characteristics of the OUES in older HF subjects and specifically in those with HF-NEF as compared to systolic HF and healthy age-matched subjects.

Methods

General methodology for CPX testing in this cohort have been previously reported.(6) Briefly, a total of 146 subjects (mean age: 72 ±6 years, 59% women) participated in the study. Fifty-nine subjects were diagnosed with systolic HF (mean ejection fraction: 31 ±10%), 59 with HF-NEF (mean ejection fraction: 60 ±7%) and 28 were healthy age-matched controls. All subjects underwent CPX on an electronically braked lower extremity ergometer using an incremental staged protocol. In the previous investigation, it was found that the VE/VCO₂ slope was significantly lower in healthy controls and HF-NEF subjects compared to those with systolic HF, with no differences between the two former groups.(6) Peak VO₂ was comparably reduced in NEF and systolic HF subgroups compared to healthy controls. Lastly, peak respiratory exchange ratio was >1.05 in all three groups, indicating maximal effort at a comparable level.

For the present investigation, the OUES was retrospectively calculated with a computer software package (Microsoft Excel, Seattle, WA) by the following equation: $VO_2 = a \log_{10} VE + b$; where a = slope and units = L/min.(3) One way ANOVA compared the OUES amongst HF-NEF, systolic HF and healthy control subgroups. Tukey's honestly significant difference was used to determine groups that were significantly different when the one-way ANOVA p-value was <0.05. Pearson product moment correlation assessed the relationship between the OUES and both peak VO₂ and the VE/VCO₂ slope in each group. All statistical tests with a p-value <0.05 were considered significant.

Results

The OUES was significantly lower in both HF groups compared to controls (systolic HF: 1.23 ±0.41 vs. HF-NEF: 1.22 ±0.30 vs. controls: 1.51 ±0.49, $p<0.01$), which is illustrated in Figure 1.

Pearson product moment correlation results are listed in Table 1. The OUES was significantly correlated with peak VO₂ in all three groups, but weakest in patients with HF-NEF. The correlation between the OUES and the VE/VCO₂ slope was only significant in the HF groups. Although reaching statistical significance, this relationship was again weaker in the HF-NEF group.

Discussion

The results of the present study expand upon our previous findings that compare the CPX response between patients with HF-NEF and systolic HF.(6) Unlike the VE/VCO₂ slope, a more established marker of ventilatory efficiency in HF, the OUES was strikingly similar in HF subgroups. Moreover, unlike the VE/VCO₂ slope(6), the OUES was significantly correlated with peak VO₂ in HF-NEF patients. This relationship was, however, weaker than that found in systolic HF and healthy control groups.

Several studies have examined the pathophysiologic mechanism(s) accounting for an elevated VE/VCO₂ slope in systolic HF, finding ventilation/perfusion mismatch(7), pulmonary vasoconstriction(8) and hyperactive chemo/ergoreceptors(9,10) all being linked to this abnormal response. However, this type of analysis has, to our knowledge, not been performed in patients with HF-NEF. Moreover, the analysis of the pathophysiologic mechanism(s) helping to explain a decreased OUES is lacking in any HF cohort. Future research should focus on discerning the pathophysiologic implications of the OUES in both patients with HF-NEF and systolic HF. Lastly, given the VE/VCO₂ slope differs according to HF type while the OUES is similar, future prognostic investigations should assess each variable's role in determining increased risk for adverse events, particularly in patients with HF-NEF, where this type of research is presently limited.

In conclusion, research examining this assessment tool in patients with HF-NEF is just beginning to emerge with initial promising results.(2) Our previous(6) and present findings indicate certain CPX measures of ventilatory efficiency differ (the VE/VCO₂ slope) according to HF type (NEF vs. systolic) while others appear to be similar (OUES). Future research should focus on determining the unique clinical importance of different representations of ventilatory efficiency in patients with HF-NEF.

Acknowledgments

Supported by NIH grants R37AG18915 and P60AG10484

Reference List

1. Arena R, Myers J, Guazzi M. The clinical and research applications of aerobic capacity and ventilatory efficiency in heart failure: an evidence-based review. *Heart Fail Rev.* 2008; 13:245–69. [PubMed: 17987381]
2. Guazzi M, Myers J, Arena R. Cardiopulmonary Exercise Testing in the Clinical and Prognostic Assessment of Diastolic Heart Failure. *Journal of the American College of Cardiology.* 2005; 46:1883–90. [PubMed: 16286176]
3. Baba R, Nagashima M, Goto M, et al. Oxygen intake efficiency slope: a new index of cardiorespiratory functional reserve derived from the relationship between oxygen consumption and minute ventilation during incremental exercise. *Nagoya J Med Sci.* 1996; 59:55–62. [PubMed: 8725489]
4. Davies LC, Wensel R, Georgiadou P, et al. Enhanced prognostic value from cardiopulmonary exercise testing in chronic heart failure by non-linear analysis: oxygen uptake efficiency slope. *Eur Heart J.* 2006; 27:684–90. [PubMed: 16338939]
5. Arena R, Myers J, Hsu L, et al. The minute ventilation/carbon dioxide production slope is prognostically superior to the oxygen uptake efficiency slope. *J Card Fail.* 2007; 13:462–9. [PubMed: 17675060]
6. Moore B, Brubaker PH, Stewart KP, Kitzman DW. VE/VCO₂ Slope in Older Heart Failure Patients With Normal Versus Reduced Ejection Fraction Compared With Age-Matched Healthy Controls. *Journal of Cardiac Failure.* 2007; 13:259–62. [PubMed: 17517344]
7. Wada O, Asanoi H, Miyagi K, et al. Importance of abnormal lung perfusion in excessive exercise ventilation in chronic heart failure. *Am Heart J.* 1993; 125:790–8. [PubMed: 8438708]
8. Reindl I, Wernecke KD, Opitz C, et al. Impaired ventilatory efficiency in chronic heart failure: possible role of pulmonary vasoconstriction. *Am Heart J.* 1998; 136:778–85. [PubMed: 9812071]
9. Ponikowski PP, Chua TP, Francis DP, Capucci A, Coats AJS, Piepoli MF. Muscle Ergoreceptor Overactivity Reflects Deterioration in Clinical Status and Cardiorespiratory Reflex Control in Chronic Heart Failure. *Circulation.* 2001; 104:2324–30. [PubMed: 11696473]
10. Ponikowski P, Banasiak W. Chemosensitivity in chronic heart failure. *Heart Fail Monitor.* 2001; 1:126–31.

Figure 1. Difference in the OUES amongst patients with HF-NEF, Systolic HF and Healthy Controls

* $p < 0.01$; HF-NEF and Systolic HF vs. Control

Table 1

Pearson Product Moment Correlation Analysis

	Peak VO ₂	VE/VCO ₂ Slope
OUES: HF-NEF	0.28 p=0.04 *	-0.42 p=0.001 *
OUES: Systolic HF	0.67 p<0.001 *	-0.58 p<0.001 *
OUES: Healthy Controls	0.64 p<0.001 *	-0.17 p=0.39

* Statistically significant