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Prognostic Significance of the Oxygen Uptake Efficiency Slope: Percent-Predicted versus Actual Value

Ross Arena, PhD,
Richmond, VA

Jonathan Myers, PhD,
Palo Alto, CA

Joshua Abella, MD,
Palo Alto, CA

Sherry Pinkstaff, DPT,
Richmond VA

Peter Brubaker, PhD,
Winston-Salem, NC

Dalane Kitzman, MD,
Winston-Salem, NC

Mary Ann Peberdy, MD,
Richmond, VA

Daniel Bensimhon, MD,
Greensboro, NC

Paul Chase, MD, and
Greensboro, NC

Marco Guazzi, MD, PhD
Milano, Italy

The oxygen uptake efficiency slope (OUES) is a marker of ventilatory efficiency with potential prognostic value in patients with heart failure (HF).¹ Like peak oxygen consumption (VO₂), the OUES is modulated by age, sex and body habitus, creating the potential for the utility of a percent-predicted expression.² Our group has recently demonstrated a percent-predicted expression of peak VO₂, using the equations proposed by Wasserman and Hansen, prognostically outperforms the actual value in a large HF cohort.³ No previous investigation has compared the prognostic characteristics of actual and percent-predicted OUES expressions in patients with HF. As such, the purpose of the present investigation was to test the hypothesis that a percent-predicted expression of the OUES will provide better prognostic resolution compared to the actual value in a group of patients with HF.

Seven hundred and twenty-one patients with HF (Age: 62.4 ± 13.8 years, ejection fraction: 37.2 ± 16.1%, 82% male, 45% ischemic HF) underwent cardiopulmonary exercise testing (CPX) to

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determine peak oxygen consumption (VO_2) and ventilatory efficiency (VE/VCO_2 slope and OUES). The oxygen uptake efficiency slope (OUES) was determined via least squares linear regression ($\text{VO}_2 = a \log_{10} \text{VE} + b$; both CPX measures expressed in L/min)⁴ by spreadsheet software (Microsoft Excel, Seattle, Washington) using all of the exercise data. Percent-predicted peak VO_2 was determined by the equations proposed by Wasserman and Hansen.⁵ ⁶ Percent-predicted OUES values were calculated using the only male/female equations that are currently available.² The CPX laboratories involved in the current analysis and testing procedures have been previously described.³ All subjects completed a written informed consent and institutional review board approval was obtained by each participating institution. Subjects were subsequently tracked for major cardiac events for three years following CPX. The prognostic characteristics of the actual and percent-predicted OUES expressions were assessed by receiver operating characteristic curve analysis. Multivariate Cox regression analysis assessed the combined prognostic value of CPX variables.

Mean values for peak VO_2 , percent-predicted peak VO_2 , the VE/VCO_2 slope, the OUES and percent-predicted OUES were $18.3 \pm 7.3 \text{ mL O}_2 \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$, $84.6 \pm 44.5\%$, 32.2 ± 8.4 , 1.9 ± 0.87 and $79.3 \pm 29.4\%$, respectively. There were 96 (85 deaths, 9 transplants and 2 LVAD implantations) major cardiac events over the three year tracking period. Receiver operating characteristic curve analysis, illustrated in Figure 1, revealed that the area under the curve was slightly greater for the percent-predicted OUES expression (area: 0.74, 95% CI: 0.69-0.79, $p < 0.001$) compared to the actual value (area: 0.73, 95% CI: 0.68-0.78, $p < 0.001$). Two separate multivariate Cox regression analyses demonstrated the VE/VCO_2 slope (Chi-square: 67.9, $p < 0.001$) was the strongest prognostic maker in both instances. Both expressions of the OUES were retained in the separate regressions with the percent-predicted OUES adding slightly better prognostic information compared to the actual value (Residual chi-square: 24.5 vs. 19.9, $p < 0.001$). Moreover, in multivariate analyses including percent-predicted OUES, neither the actual or percent-predicted peak VO_2 value added prognostic information (Residual chi-square: ≤ 2.7 , $p > 0.10$).

The VE/VCO_2 slope is less influenced by age, sex and body habitus^{7, 8}, lending support to its robust prognostic power when expressed as an actual value. Conversely, the percent-predicted expression of the OUES is strongly influenced by these baseline characteristics², but nevertheless supplements the prognostic power of CPX in HF patients undergoing this procedure.

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References

1. Davies LC, Wensel R, Georgiadou P, Cicoira M, Coats AJ, Piepoli MF, Francis DP. Enhanced prognostic value from cardiopulmonary exercise testing in chronic heart failure by non-linear analysis: oxygen uptake efficiency slope. *Eur Heart J* 2006;27:684–690. [PubMed: 16338939]
2. Hollenberg M, Tager IB. Oxygen uptake efficiency slope: an index of exercise performance and cardiopulmonary reserve requiring only submaximal exercise. *Journal of the American College of Cardiology* 2000;36:194–201. [PubMed: 10898434]
3. Arena R, Myers J, Abella J, Pinkstaff S, Brubaker P, Moore B, Kitzman D, Peberdy MA, Bensimhon D, Chase P, Forman D, West E, Guazzi M. Determining the Preferred Percent-Predicted Equation for Peak Oxygen Consumption in Patients With Heart Failure. *Circ Heart Fail* 2009;2:113–120. [PubMed: 19808326]
4. Baba R, Nagashima M, Goto M, Nagano Y, Yokota M, Tauchi N, Nishibata K. 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]
5. Hansen JE, Sue DY, Wasserman K. Predicted values for clinical exercise testing. *Am Rev Respir Dis* 1984;129:S49–S55. [PubMed: 6421218]
6. Wasserman, K.; Hansen, JE.; Sue, DY.; Stringer, W.; Whipp, BJ. Normal Values.. In: Weinberg, R., editor. *Principles of Exercise Testing and Interpretation*. 4th ed. Lippincott Williams and Wilkins; Philadelphia: 2005. p. 160-182.
7. Habedank D, Reindl I, Vietzke G, Bauer U, Sperfeld A, Glaser S, Wernecke KD, Kleber FX. Ventilatory efficiency and exercise tolerance in 101 healthy volunteers. *Eur J Appl Physiol Occup Physiol* 1998;77:421–426. [PubMed: 9562292]
8. Sun XG, Hansen JE, Garatachea N, Storer TW, Wasserman K. Ventilatory efficiency during exercise in healthy subjects. *Am J Respir Crit Care Med* 2002;166:1443–1448. [PubMed: 12450934]

Figure 1.
Receiver Operating Characteristic Curve Analysis for Actual and Percent-Predicted OUES