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Exercise oscillatory ventilation reflects diminished quality of life and perceived functional capacity in patients with heart failure

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A significant number of patients with heart failure (HF) present with both diminished self-reported quality of life and perceived functional capacity. The Minnesota Living with HF Questionnaire (MLWHFQ) and the Duke Activity Status Index (DASI) are two validated and reliable tools that have been frequently used to quantify quality of life and functional capacity in this chronic disease population [1,2]. Previous research by our group has demonstrated that peak oxygen consumption (VO_2) is significantly correlated with both the MLWHFQ and DASI in HF patients [3,4]. Conversely, the VE/VCO_2 slope, an established marker of ventilatory efficiency in HF patients, is not associated with quality of life [4] and seemingly no information is available on its relationship to perceived functional capacity. Exercise oscillatory ventilation (EOV) has garnered great attention in recent years, demonstrating a robust ability to predict increased risk for adverse events and reflect disease severity [5,6]. To our knowledge, we are unaware of any previous investigation that has assessed the relationship between EOV and self-reported quality of life or perceived functional capacity, which is the purpose of the present study.

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Forty-six patients (33 males; mean age=50±14 years, mean left ventricular ejection fraction=26.6±10.7%) underwent cardiopulmonary exercise testing (CPX) using a conservative treadmill protocol. The ventilatory expired gas analysis system (SensorMedics Vmax29, Yorba Linda, CA) was calibrated before each test according to manufacturer specifications. Ten-second averaged minute ventilation data during rest and the entire exercise test was plotted using Microsoft Excel software (Microsoft, Seattle, WA). Exercise oscillatory ventilation was defined as an oscillatory pattern at rest that persisted for 60% of the exercise test at an amplitude of 15% of the average resting value [5]. Peak VO_2 was defined as the highest 10-second averaged value during CPX. Minute ventilation and VCO_2 values, acquired from the initiation of exercise to peak, were input into spreadsheet software (Microsoft Excel, Microsoft Corp., Seattle, WA) to calculate the VE/VCO_2 slope via least squares linear regression ($y=mx+b$, $m=\text{slope}$). Immediately prior to testing, all subjects completed the MLWHFQ and DASI. For the MLWHFQ, the overall, physical sub-score (sum of questions 2,3,6,7,11,12, and 13), and psychosocial/symptomatology sub-score (sum of remaining questions) were determined. The DASI score was expressed in $\text{mLO}_2 \text{ kg}^{-1} \text{ min}^{-1}$. Institutional board approval was obtained and all subjects signed a written informed consent.

Statistical analysis was performed using SPSS 19.0 (SPSS, Chicago, IL). Unpaired t-testing assessed differences in MLWHFQ and DASI scores according to the presence or absence of EOv. Unpaired t-testing was also used to assess differences in age, peak VO_2 and the VE/VCO_2 slope according to EOv status. Receiver operating characteristic (ROC) curve analysis assessed the ability of MLWHFQ and DASI scores to predict EOv during the exercise test. Pearson product moment correlation was used to assess the relationship between the completed questionnaires and both peak VO_2 and the VE/VCO_2 slope. All statistical tests with a p value ≤ 0.05 were considered significant.

Fourteen of the 46 subjects met the pre-defined EOv criteria during CPX. Age (51 ± 10 vs. 50 ± 15) and the VE/VCO_2 slope (32.6 ± 6.0 vs. 30.3 ± 6.0) were not significantly different ($p = 0.20$) according to EOv (mean values for EOv subjects reported first). Peak VO_2 was, however, significantly lower ($p < 0.01$) in subjects presenting with EOv (14.5 ± 2.4 vs. $18.4 \pm 5.0 \text{ mL O}_2 \text{ kg}^{-1} \text{ min}^{-1}$). Peak VO_2 was significantly correlated with the overall MLWHFQ score ($r = -0.54$, $p < 0.001$), the physical sub-score ($r = -0.47$, $p < 0.01$), the psychosocial/symptomatology sub-score ($r = -0.51$, $p < 0.001$), and the DASI score ($r = 0.50$, $p < 0.001$). The VE/VCO_2 slope was not correlated with the overall MLWHFQ score or subscores ($r = 0.25$, $p = 0.90$) and was only weakly correlated with the DASI score ($r = -0.29$, $p = 0.048$). The overall MLWHFQ score (60.4 ± 29.6 vs. 31.4 ± 24.1) as well as physical (22.9 ± 12.3 vs. 11.9 ± 9.8) and psychosocial/symptomatology (37.9 ± 18.8 vs. 20.2 ± 15.2) sub-scores were all significantly higher ($p < 0.01$) in subjects presenting with EOv. Conversely, the DASI score (18.5 ± 6.2 vs. $24.3 \pm 6.3 \text{ mL O}_2 \text{ kg}^{-1} \text{ min}^{-1}$) was significantly lower ($p < 0.01$) when EOv was present. Differences in the overall MLWHFQ score, MLWHFQ sub-scores and DASI score according to EOv status are illustrated in Fig. 1.

Receiver operating characteristic curve analysis revealed the MLWHFQ and DASI scores were able to significantly identify subjects with EOv during CPX. The optimally identified

threshold value for each score produced a sensitivity and specificity above 70%. Results from the ROC curve analysis are listed in Table 1.

Previous research has demonstrated a correlation between aerobic capacity and both self-reported quality of life and perceived functional capacity in patients with HF [3,4], a finding confirmed by the current analysis. The relationship between ventilatory efficiency, assessed through the VE/VCO₂ slope and these same subjective assessments does not appear to be as robust in this or previous reports [4]. To our knowledge, this is the first study to report on the relationship between EOV and both self-reported quality of life and perceived functional capacity. These findings indicate patients with EOV have a significantly poorer perception of quality of life and functional capacity, which may be explained by the fact that EOV represents an advanced state of HF that is likely to impact a patient's daily life in a substantive way.

There also appears to be threshold values for both the MLWHFQ and DASI that predict likelihood of EOV during CPX. This may be clinically relevant since it suggests a potential application of questionnaires to identify patients at greater prognostic risk who would be most likely to benefit from further assessment using CPX to refine risk profile and related management priorities. Given the fact that CPX referral for the entire HF population is neither feasible nor economical, the use of questionnaires to identify patients who would be most likely to benefit from CPX may be a reasonable approach if supported by future research.

The authors of this manuscript have certified that they comply with the Principles of Ethical Publishing in the International Journal of Cardiology (Shewan and Coats 2010;144:1–2).

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Fig. 1. Differences in MLWHFQ and DASI scores according to the presence or absence of EO. MLWHFQ: Minnesota Living With Heart Failure Questionnaire. EO: Exercise Oscillatory Ventilation. *, Overall scores significantly different ($p < 0.01$). #, Physical sub-scores significantly different ($p < 0.01$). ^, Psychosocial sub-scores significantly different ($p < 0.01$). DASI: Duke Activity Status Index. EO: Exercise Oscillatory Ventilation. *, DASI scores significantly different ($p < 0.01$).

Table 1

Receiver operating characteristic curve analysis: MLWHFQ and DASI score effectiveness in predicting EOV.

	Area under the curve (95% confidence interval)	p value	Optimal threshold value	Sensitivity/ specificity (%)
MLWHFQ overall score	0.78 (0.61–0.94)	0.003	</ 42	72/79
MLWHFQ physical sub-score	0.77 (0.60–0.94)	0.004	</ 19	75/78
MLWHFQ psychosocial/ symptomatology sub-score	0.76 (0.60–0.92)	0.006	</ 28	75/71
DASI score	0.76 (0.59–0.92)	0.006	/>20	72/71

EOV: Exercise Oscillatory Ventilation.

MLWHFQ: Minnesota Living with Heart Failure Questionnaire.

DASI: Duke Activity Status Index