

Diastolic blood pressure is predictive of an elevated ventilatory efficiency slope in at-risk middle-aged obese adults that are asymptomatic for cardiovascular disease

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ABSTRACT

Background: Cardiopulmonary exercise tests (CPET) assess oxygen uptake (VO_2) and ventilatory efficiency ($V_E/V\text{CO}_2$ slope) as both are predictive measures of cardiovascular disease (CVD) severity in symptomatic adults. Specifically, the $V_E/V\text{CO}_2$ slope is a powerful prognostic tool for assessing CVD severity and prognosis as it is effectively independent of a patient's capacity to reach volitional fatigue. In asymptomatic adults, several clinical risk factors for CVD have been established for use in health assessments, and as a method for early CVD detection and prevention. Therefore, we evaluated the relationship between the $V_E/V\text{CO}_2$ slope and several clinical CVD risk factors in at-risk but asymptomatic middle-aged obese adults. **Methods:** 29 obese adults (Mean \pm SE; Age 46.5 ± 2.6 years; BMI 35.9 ± 1.1 kg/m²) were stratified into low (LR < 2 risk factor) or moderate risk (MR ≥ 2 risk factors) from self-reported health history questionnaires and quantitative assessments and performed a treadmill CPET. **Results:** No differences in $V_E/V\text{CO}_2$ slope between risk groups (LR 30.1 ± 1.8 , MR 29.2 ± 0.9 $V_E/V\text{CO}_2$ slope). The $V_E/V\text{CO}_2$ slope positively associated with age and diastolic blood pressure (DBP) and not with the CVD risk factors BMI, HDL-C, LDL-C, fasting blood glucose, systolic blood pressure, or total risk factors; further DBP was the only predictor ($r=0.429$, $r^2=0.184$, $p=0.037$). **Conclusion:** DBP predicted a steeper ventilatory efficiency ($V_E/V\text{CO}_2$ slope) in at-risk but asymptomatic for CVD middle-aged obese adults. Our findings indicate that the ventilatory efficiency slopes CVD risk and prognosis assessment extends to clinically at-risk middle-aged asymptomatic obese adults, and may function as an additional measure for long-term health monitoring.

Keywords: body weight, exercise test, heart disease, obesity, & risk factors

INTRODUCTION

Cardiovascular disease (CVD) related deaths are the leading cause of mortality worldwide. According to the World Health Organization in 2008, the mortality rate due to CVD was 214–455 deaths per 100,000 varying by globally¹. In the United States, heart disease currently rep-

resents the leading cause of death, accounting for 27% of total deaths in people age 65 and over². The development of CVD can be attributed to both modifiable risk factors such as obesity, blood pressure, physical activity status, cholesterol, pre-diabetes and smoking; as well as non-modifiable risk factors such as age, gender, family history and genetic predisposition^{3,4}. The primary mechanism by which risk factors contribute to the development of CVD is their role in the development of atherosclerotic plaque deposition⁵. Coronary heart disease (CHD) due to atherosclerosis represents the largest proportion of CVD related deaths resulting from acute myocardial infarction (MI)⁶. The high incidence and mortality rates of CVD demonstrate a need to continuously improve current detection methods for severity and progression

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of CVD and the associated risk factors. Presently, CVD prevention is focused on methods of early detection of at-risk individuals and the subsequent identification and management of specific CVD risk factors. Clear relationships have been established between the presence of single and multiple risk factors and the development of CHD⁷. Moreover, 90% of all CHD related events can be attributed to the identification of known risk factors⁵. In addition, several functional cardiovascular fitness assessments, specifically oxygen uptake capacity, are employed to categorize an individual's functional capacity and population based risk for developing CVD⁴.

The early identification of CVD and associated risk factors has several positive outcomes including reduced patient re-hospitalization and lower incidences of mortality⁸⁻¹⁰. Exercise tolerance which is commonly assessed via cardiopulmonary exercise testing (CPET) is a valuable tool for the detection of cardiac impairment in patients with diagnosed heart failure¹¹⁻¹³. Respiratory gas analysis during CPET provides clinicians and exercise physiologists with measures for a differential diagnosis which often clarified severity of cardiac impairment. The CPET is a non-invasive diagnostic tool that has multiple outcome measures to determine the underlying causes contributing to a patient's pain, dyspnea, and or fatigue during physical activity^{8,14}. Two common measures used to diagnose and grade the severity of CVD are the CPET derived variables peak or highest achieved oxygen uptake (VO_2) and recently the ventilatory efficiency slope (V_E/VCO_2 slope)¹⁵.

As an independent measure, peak VO_2 has been strongly correlated with rates of hospitalization and incidence of mortality in heart failure patients and is strong measure of overall health status in un-diagnosed adults¹⁶⁻¹⁸. However, as an independent measure, VO_2 prognostic precision is partially limited in patients unable to provide a maximal effort to volitional fatigue. In contrast, the ventilatory efficiency slope (V_E/VCO_2 : rise in minute ventilation plotted against the rate of ventilated carbon dioxide), has been shown to be a similar predictor of CHD patient outcomes as peak VO_2 alone^{9,10,16-18}. Specifically, the ventilatory efficiency slope's prognostic capacity has been shown to not be limited by patient effort or capacity to reach volitional exhaustion during a CPET¹⁵. Therefore, as a clinical measure the ventilatory efficiency slope retains the capacity to be an effective evaluator of prognosis and severity within a wide range of symptomatic heart disease patients exercise capacities. Normative ranges for V_E/VCO_2 slopes for adults aged 41-50 years of age reported to be 25.2 ± 2.9 ¹⁹. Although no established

clinical parameters exist for ventilatory efficiency, a V_E/VCO_2 slope of 30 or greater, has indicated a CVD patient with increased risk for cardiac event reoccurrence and or mortality, while a slope of 34 or greater is associated with an even poorer prognosis with a greater risk for mortality^{10,14}. Further, as a longitudinal measure a progressive rise in V_E/VCO_2 slope over a CVD patients treatment duration may indicate an advancing decline in cardiovascular function and is associated with higher rates of re-hospitalization and mortality^{9,10,16}. There is presently no clear indication if the predictive capacity of the V_E/VCO_2 slope is retained in adults that are clinically at-risk but asymptomatic for cardiovascular disease. In asymptomatic but clinically at-risk adults, the ventilatory efficiency slope could prove to be a valuable tool in addition to common CVD risk factors in further describing cardiovascular health and aid in early identification of CVD. Therefore, the purpose of this study is to determine the relationship between clinically relevant CVD risk factors and the CPET derived measure of ventilatory efficiency (V_E/VCO_2 slope), in a sample of asymptomatic obese middle-aged adults free of diagnosed heart disease.

Materials and Methods

Subjects

Subjects for this study were prospectively recruited from a university weight loss program, where data was collected prior to any weight loss interventions. Exercise testing was completed on a single visit for all subjects included in the study. Approval from the university institutional review board and a written informed consent was obtained prior to exercise testing and administered to each study subject. Prior to exercise testing, subjects were stratified into one of two risk categories based on responses to a self-guided health history questionnaire citing cardiovascular disease risk factors. In addition to self-report, we measured total cholesterol and fasting blood glucose from a fasted blood sample, resting heart rate, and resting blood pressure the day prior to CPET testing. Risk stratification was in accordance to the logic model provided by the American College of Sports Medicine (ACSM)⁴. Testing was performed on low and moderate risk subjects that reported no signs, symptoms or diagnosis of CVD.

Inclusion Criteria

Study inclusion criteria consisted of subjects having a body mass index ($\text{BMI} = \text{kg}/\text{m}^2$) of 30 or greater and being designated as either low (≤ 1 CVD Risk Factor) or moderate risk (≥ 2 CVD Risk Factor) according to the ACSM

logic model for risk stratification⁴. Subjects that reported smoking within the previous 12-months, expressed the presence of signs and symptoms and or were diagnosed with cardio-metabolic disease were excluded from the study. In addition, subjects were required to complete a health history questionnaire with physician approval for maximal exercise.

Anthropometric Measures

All subjects underwent a preliminary screening one day prior to CPET testing between the hours of 7am and 9am. Height was measured three times and averaged to the nearest tenth of a centimeter. Subject weight was measured using a digital scale. Weight was measured twice and averaged to the nearest tenth of a kilogram. The average height and weight values were used to compute the body mass index (kg/m^2) for each participant. Resting blood pressure and resting heart rate were measured twice on two separate days and averaged for each subject. All measurements were performed after each subject rested in a chair for five minutes in order to more accurately reflect true resting values.

Risk Stratification

Subjects were stratified into one of two risk categories (low vs. moderate) according to the self-reported and quantified number of CVD risk factors and following the logic model provided by the ACSM⁴. Specifically, subjects with ≤ 1 risk factor for CVD were designated as low risk and those with ≥ 2 risk factors for CVD were designated as moderate risk. The presence of physician diagnosed vascular disease, obstructive or restrictive lung disease, heart disease, metabolic disease, or major signs and/or symptoms of the aforementioned conditions was grounds for designation as a high risk subject and resulted in exclusion from exercise testing⁴. Determination of the presence of CVD risk factors were based on established thresholds set forth by the ACSM in accordance with their risk stratification logic model⁴. The positive risk factors include, age, family history of CVD, tobacco smoking, sedentary lifestyle, obesity, hypertension, dyslipidemia, and pre-diabetes with one negative risk factor for HDL.

Fasted blood samples were obtained via a venipuncture from all subjects on their first day in the laboratory between the hours of 7am and 11am. Samples were stored at subzero temperatures (-80°C) until the time of analysis. Analysis consisted of standard colorimetric assays to quantify total cholesterol (TCHOL) (Thermo Fisher Scientific, Pittsburgh, PA), total triglycerides (TRIG)

(Thermo Fisher Scientific, Pittsburgh, PA) and fasting plasma glucose (IFG) (Wako Chemicals, Richmond, VA). High density lipoprotein-cholesterol (HDL-C) was measured by the precipitation of apolipoprotein B (apo-B) containing lipoproteins with a heparin sodium (1.63% w/v) and $\text{MnCl}_2 \cdot 4\text{H}_2\text{O}$ (1 M) solution followed by enzymatic measurement of the supernatant for the remaining cholesterol. Low density lipoprotein-cholesterol (LDL-C) was determined using the Friedewald Equation for estimating LDL-C.

Respiratory Gas Analysis

Ventilatory expired gas was analyzed using a ParvoMedics metabolic cart and linear pneumotachometer (ParvoMedics MMS-2400, Salt Lake City, UT). The O_2 and CO_2 gas analyzing sensors were calibrated prior to testing using gases with known values for O_2 and CO_2 (16% O_2 , 4% CO_2) and according to recommended ranges ($< 3\%$ change from known calibration gas value for O_2 and CO_2). The flow sensor was calibrated using a standard three liter syringe, also according to recommended ranges for metabolic testing ($< 3\%$ change for both high and low volumes obtained).

Cardiopulmonary Exercise Testing

Exercise testing with ventilatory expired gas analysis was conducted on a motorized treadmill (Trackmaster TMX55, Newton, KS). Following a 4 minute warm-up at 3 mph and 0% grade (to allow familiarity with treadmill and head gear apparatus), each subject performed a graded exercise test at a constant speed of 3.5 miles per hour with a 2.5% grade increase at two minute intervals. Low risk subjects performed the test to volitional fatigue or until test termination was requested. Moderate risk individuals performed the exercise test until 76% of maximal predicted heart rate ($220 - \text{age}$) or until a work rate of 6 METS (Metabolic Equivalent, 1 MET = $3.5 \text{ ml} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$) was achieved. The ranges for percent predicted heart rate and MET level are consistent with ACSM recommended ranges for exercise testing of moderate risk persons in the absence of a physician⁴. Procedures for testing low and moderate risk patients were held constant throughout the data set. Monitoring of subjects consisted of continuous heart rate recordings at every stage of exercise as well as rating of perceived exertion (Borg 6–20 scale) at each stage.

The following variables were collected continuously throughout the duration of the exercise test: ventilated oxygen ($\text{VO}_2 \text{ ml} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$), ventilated carbon dioxide

Ventilatory Slope and CVD Risk

($\text{VCO}_2 \text{L} \cdot \text{min}^{-1}$), and minute ventilation ($\text{V}_E \text{L} \cdot \text{min}^{-1}$). Highest achieved VO_2 was expressed as the highest 15-second average value obtained during the last stage of the exercise test. It should be noted that values of peak VO_2 (for the moderate risk group) are not, by definition, representative of true peak VO_2 or VO_2 max as test duration was limited by the aforementioned termination protocol and a plateau in the rate of oxygen consumption was not observed for all subjects. However, values for both risk groups will subsequently be referred to as VO_2 throughout the remainder of the results and discussion. The slope of V_E/VCO_2 was obtained using the proprietary software provided on the Parvo Medics metabolic cart and was defined as the rise in V_E ($\text{L} \cdot \text{min}^{-1}$ BTPS (body temperature and pressure saturated)) to the increase in VCO_2 ($\text{L} \cdot \text{min}^{-1}$ STPD (standard temperature and pressure dry)) throughout the entire exercise session.

Statistical Analysis

Results were expressed as mean plus or minus the standard error of the mean ($\text{mean} \pm \text{SE}$) with significance set at an alpha level of less than 0.05 ($p \leq 0.05$). All statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) version 18 (IBM, Wontauk, NY). Subjects were initially divided into two groups (low risk vs. moderate risk) based on the number of risk factors present and according to the ACSM logic model for risk stratification. Group differences between total number of risk factors, age, BMI, systolic and diastolic

blood pressure, total cholesterol, HDL-C, LDL-C, fasting glucose, and V_E/VCO_2 slope were analyzed with an independent T-test. Pearson product moment correlation was used to determine which risk factors were associated with the ventilator efficiency slope.

Groups were then combined into one “asymptomatic at-risk” group for analysis. Stepwise linear regression modeling was used to determine which CVD risk factors were constant predictor variables for the ventilatory efficiency slope. All quantified risk factors were included, independent of significant Pearson correlation, in the predictive modeling. Following analysis, the predictive model was assessed for co-linearity with the excluded variables of the linear regression in the model using beta coefficients.

Results

Low and Moderate Risk Participant Groups

Subjects were divided into low (LR $n=7$) and moderate risk (MR $n=22$) categories based on the total number of clinically relevant ACSM CVD risk factors obtained via direct measurement and a self-report questionnaire in accordance with the logic model provided by the ACSM⁴. Data was analyzed for normal distribution and determined to be acceptable for parametric analysis. Group differences were analyzed with a 2-tailed independent samples t-test and reported in Table 1. There were no significant differences in group characteristics of age

Table 1 Low vs. Moderate Risk Group Characteristic Comparisons with an Independent samples T-test.

Variable	Low Risk (n=7)	Moderate Risk (n=22)	Significance (p=)
Age (years)	40.6±4.2	48.6±2.1	0.079
Male	n=3	n=6	
Female	n=4	n=16	
BMI (kg/m^2) [†]	31.7±1.4	37.3±1.7	0.080
Systolic Blood Pressure(mmHg) [†]	126.9±3.3	133.3±2.4	0.176
Diastolic Blood Pressure(mmHg) [†]	82.3±3.6	89.6±1.4*	0.028*
Total Cholesterol ($\text{mg} \cdot \text{dL}^{-1}$) [†]	170.7 ±8.9	164.6±8.0	0.678
HDL-C ($\text{mg} \cdot \text{dL}^{-1}$)	49.4±4.0	45.7±2.2	0.435
LDL-C ($\text{mg} \cdot \text{dL}^{-1}$) [†]	106.0±10.2	91.7±8.1	0.378
Fasting Glucose ($\text{mg} \cdot \text{dL}^{-1}$) [†]	75.6±2.4	99.3±4.3*	0.004*
Total Risk Factors [†]	1.0 ±0.0	3.9±0.3*	0.001*
Peak VO_2 ($\text{ml} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$)	37.2±3.9	20.7±1.2*	0.001**
V_E/VCO_2 Slope [‡]	30.1±1.8	29.2±0.9	0.636

Data presented as Mean ± Standard Error, Significance $p \leq 0.05$. Body mass index (BMI), High density lipoprotein-cholesterol (HDL-C), low density lipoprotein-cholesterol, peak maximal oxygen uptake (Peak VO_2), ventilatory efficiency slope (V_E/VCO_2 Slope).

*Difference between Low and Moderate Risk Groups

**Different CPET termination criteria

[†]Independent variable in regression model

[‡]Dependent variable in regression model

Ventilatory Slope and CVD Risk

($p=0.079$) or BMI ($p=0.080$) between either group. There were group difference in the positive risk factors of diastolic blood pressure ($p=0.028$), fasting glucose ($p=0.004$), and total number of risk factors ($p=0.001$). In contrast, both groups had similar systolic blood pressure ($p=0.176$), total cholesterol ($p=0.678$), HDL-C ($p=0.435$), LDL-C ($p=0.378$), and ventilatory efficiency slope ($p=0.636$). As we controlled for exercise intensity termination as a factor of risk category we did not analyze for statistical differences in highest achieved VO_2 .

Relationships amongst the dependent variable and independent variables were determined through the Pearson Product Moment correlation statistic. There were no significant relationships between the ventilatory efficiency slope and BMI, HDL-C, LDL-C, total cholesterol, total number of risk factors, fasting blood glucose, and sys-

tolic blood pressure. There were significant relationships between the ventilatory efficiency slope and diastolic blood pressure ($r=0.429$, $p=0.01$) and age ($r=0.403$, $p=0.02$).

Prediction modeling was performed using quantified clinically relevant risk factors, which included age, total number of risk factors, systolic blood pressure, diastolic blood pressure, BMI, LDL-C, HDL-C, and fasting glucose as independent variables of interest to predict the variance in the dependent variable (the V_E/VCO_2 slope). With V_E/VCO_2 as the dependent variable, diastolic blood pressure was the only independent variable able to predict the dependent variable ($r=0.429$, $r^2=0.184$, $p=0.037$) (Figure 1). Co-linearity was assessed with the excluded independent variables within the prediction model using beta coefficients, and no significant effect size was present (Table 2).

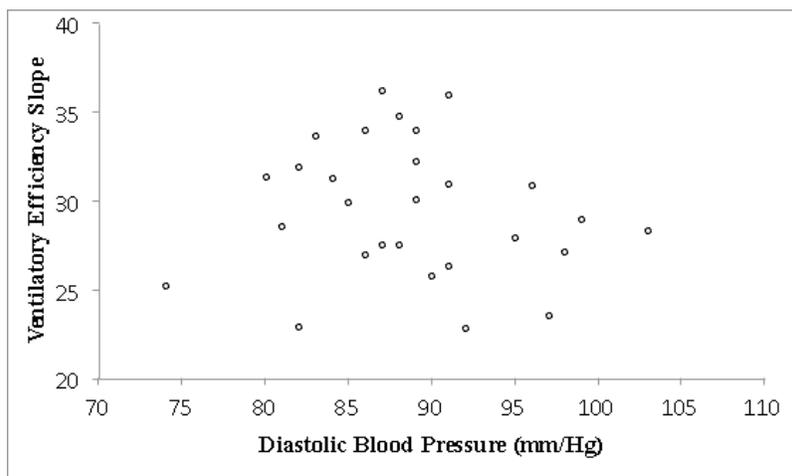


Figure 1: Data spread of the predictive variable resting diastolic blood pressure (mmHg) and ventilatory efficiency slope (V_E/VCO_2).

Table 2 Regression model Beta Coefficients testing for co-linearity with the excluded independent variables and the dependent variable ventilatory efficiency (V_E/VCO_2 Slope).

Independent Variables**	Beta Coefficient	Significance ($p =$)
Diastolic Blood Pressure (mmHg)*	0.429	0.037*
Systolic Blood Pressure (mmHg)	0.082	0.696
HDL-C (mg·dL ⁻¹)	-0.203	0.308
LDL-C (mg·dL ⁻¹)	0.168	0.395
Fasting Blood Glucose (mg·dL ⁻¹)	-0.089	0.657
Body Mass Index (kg/m ²)	0.055	0.801
Age (years)	-0.075	0.736
Total Risk Factors	-0.147	0.494

Body mass index (BMI), High density lipoprotein-c (HDL-C), low density lipoprotein-C

*Significant predictor for the dependent variable

**Dependent variable is the ventilatory efficiency slope (V_E/VCO_2 Slope).

Model Summary ($R=0.429$, $r^2=0.184$, $p=0.037$)

Discussion

This study compared the relationship between the cardiopulmonary exercise test (CPET) derived ventilatory efficiency slope and quantified clinically relevant cardiovascular disease (CVD) risk factors in asymptomatic middle-aged obese adults. We found that the ventilatory efficiency slope was highest in older patients with elevated diastolic blood pressure suggesting the potential for the measure to differentiate CVD risk in obese middle-aged adults that are at-risk but asymptomatic for cardiovascular disease. In addition, no other single or any combination of clinically relevant risk factors was predictive of the ventilatory efficiency slope values in our study. Our findings are significant, as the ventilatory efficiency slope is an independent measure that may be used for further determination of CVD prognosis and risk severity in symptomatic adults and its usefulness may extend further in identifying risk in middle-aged at-risk but asymptomatic obese adults.

Use of the CPET derived ventilatory efficiency slope is increasing in clinical practice as both a prognostic and diagnostic tool in heart disease patients. Despite formally established clinical parameters a clear threshold appears to exist as CVD patients with slope values of 30 or greater are at a significant risk for experiencing a cardiac event and slope values of 34 or greater are associated with a worsening prognosis, re-hospitalization, and sudden death^{9,10,16}. In addition, 10 year normative age ranges for adults 21 to over 60 years of age were from 22.9 to 27.5 respectively, with our population's age range of 41–50 years old at 25.2¹⁹. However, in adults that are undiagnosed with CVD, but who are still at-risk as a result of the presence of clinically relevant characteristics, such as our middle-aged obese population in this study, the ventilatory efficiency slope may still retain clinical significance for clarifying CVD risk progression. Elevated diastolic blood pressure alongside with age has been shown to be the strongest predictive measure of CHD in adults below 50 years¹⁹ as represented in this sample (LR 40.6±4.2 years and MR 48.6±2.1 years). In addition, elevated diastolic blood pressure and age appear to increase risk for CVD²⁰. According to The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure, for individuals 40 to 70 years of age each increment of 10mmHg in diastolic blood pressure doubles the risk of CVD across the diastolic blood pressure range of 75mmHg-115mmHg²¹. In addition, hypertension has long been linked to vascular trauma and damage to the intima of systemic blood vessels^{5,6}, often resulting in the progression of atherosclerosis, increased

vascular resistance, and ultimately heart disease^{3,22–24}. The predictive relationship between the ventilatory efficiency slope and diastolic blood pressure underscores its use as a measure of CVD risk and may provide insight to underlying health of the cardiovascular system in patients absent of signs and symptoms of heart disease.

One possible explanation of the predictive relationship between ventilatory efficiency slope and diastolic blood pressure may be attributed to increased pulmonary ventilation-perfusion mismatch as a result of increased vascular pressure in the lung^{9,16}. The increased pulmonary pressure affects gas exchange dynamics by altering partial pressures of oxygen and carbon dioxide in the lung^{25,26}. In addition, research on ventilatory changes in obese populations have documented shifts in the regional distribution of pulmonary ventilation from upper to lower lung regions²⁷ and significant decreases in pulmonary gas exchange as a result of added fat-mass in the morbidly obese²⁸. Since ventilation-perfusion mismatching is the primary proposed mechanism in the production of a steep ventilatory efficiency slope, and shifts in pulmonary ventilation and decreases in pulmonary gas exchange efficiency have been documented in the obese and attributed to increased vascular resistance in the lung, it is reasonable to theorize that the elevated vascular resistance as assessed with diastolic blood pressure in addition to ventilatory adaptations in obesity have significantly contributed to the steeper slope values exhibited in both the low and moderate risk groups analyzed in this study (30.1±1.8 and 29.2±0.9, respectively). The use of the ventilatory efficiency slope to grade the severity of cardiovascular impairment in diseased populations^{9,10,16} and an increased risk of CVD attributable to diastolic hypertension (≥90 mmHg)²⁰ provide evidence that the existing relationship between diastolic blood pressure is an accurate depiction of risk for CVD in asymptomatic obese adults.

Presently, peak or highest achieved relative VO₂ derived from CPET is the most commonly used measure in clinical practice to determine functional capacity, grade the risk severity for CVD, and to stratify patients overall health to population based norms⁸. The strength of peak VO₂ as a measure of the severity of heart disease and cardiac function arises primarily from the Fick equation and the contribution of cardiac output to peak VO₂. Outside of heart disease patients, peak VO₂ has been evaluated primarily as an index of cardiorespiratory fitness and aerobic capacity and the relationship between cardiorespiratory fitness and health has been enumerated and is reflected in the recommendations and guidelines for daily physical activity and the promotion of health and longevity exhibited by

nearly all governing health organizations⁴. Low levels of functional capacity (cardiorespiratory fitness) are associated with an increased risk of premature death from all causes, specifically CVD^{29–31}. However, as an independent measure in classifying adult health and disease risk, VO_2 is susceptible to the individual capacity to complete a CPET to near maximal capacity and the inability to reach volitional exhaustion do to conditions outside of functional capacity may erroneously effect result interpretation. In contrast, the $V_E/V\text{CO}_2$ slopes predictive capacity in CVD patients is protected from individual effort and may serve as a more consistent measure of risk over a period of time. The $V_E/V\text{CO}_2$ slope may not be as precise a measure of cardiac output as VO_2 , as it is potentially moderated by pulmonary ventilation-perfusion mismatching and chemoreceptor sensitivity in addition to cardiac stroke volume²⁶. Regardless, as an independent CPET derived measure the $V_E/V\text{CO}_2$ slope may add additional insight into the underlying health of the cardiopulmonary system and particularly in at-risk asymptomatic adults may be beneficial for long term health monitoring. From our evidence, and in accordance with work in the CVD population, regular CPET testing and measurement of the $V_E/V\text{CO}_2$ slope in addition to VO_2 in at-risk asymptomatic adults may provide an early indication of potential health risks and aid in early detection. Further investigation into the efficacy of the $V_E/V\text{CO}_2$ slope as a potential indicator of cardiovascular health in at-risk asymptomatic obese adults is warranted.

There are a few study limitations that should be considered in regard to our work. First, although we screened and excluded subjects with any form of cardiopulmonary disease, there is the chance that a subject has undiagnosed lung disease which would elevate the ventilatory efficiency slope independent of cardiac output. Second, the generalizability of our findings are limited by our small homogenous sample size, and although we report significant relationships between ventilatory efficiency and diastolic blood pressure in obese middle-age adults, such a relationships may not be valid in every sub-population of adults. Therefore, larger scale studies are warranted to extend on our preliminary findings and confirm the use of the ventilatory efficiency slope as an indicator of heart disease risk in at-risk asymptomatic adults.

In conclusion, we report a significant predictive relationship between the CPET derived ventilatory efficiency slope and diastolic blood pressure in at-risk asymptomatic middle-aged obese adults. In addition to diastolic blood pressure, age was the only other potential risk factor that was positively associated with the ventilatory efficiency

slope in our study. Our findings may suggest that sub-maximal or maximal CPET derived ventilatory efficiency slopes may contribute to the early detection of advanced risk for CVD in asymptomatic middle-aged obese adults and provide a potential measure for long term health monitoring. Further, the capacity of the ventilatory efficiency slope to retain predictive capacity in un-diagnosed adults that are at-risk for CVD provides clinicians and exercise professionals with a valuable tool to further understand a patients risk and track their health over a course of care.

Disclosure

The authors of this manuscript report no real or perceived conflicts of interest in regard to the findings or methods employed within this project.

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Ventilatory Slope and CVD Risk

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