Calculating Ventilatory Threshold in Patients after Stroke

A thesis submitted to the University of Arizona College Of Medicine – Phoenix
in partial fulfillment of the requirements for the degree of Doctor of Medicine

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Class of 2018

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ABSTRACT

BACKGROUND: Aerobic training intensity is commonly determined from heart rate reserve (HRR) or a percentage of maximal heart rate measured during a graded exercise stress test. This method has limitations in people after stroke, who may not reach maximal heart rate. Ventilatory Threshold (VT) is an alternate method of establishing aerobic training intensity. VT indicates the exercise intensity above which ventilation increases disproportionately compared to whole-body oxygen uptake, theoretically representing the optimal intensity for sustaining aerobic exercise.

METHODS: This study assessed the most effective ways of calculating VT from gas-exchange data from patients after stroke. We used retrospective analyses of gas-exchange data collected during submaximal and maximal stress tests with post-stroke individuals. Data were graphed using 3 different methods to determine if they provide similar information.

RESULTS: Mean (standard deviation) VT time was 3.355 (1.349) minutes using the Ventilation Curve method; 3.383 (1.372) minutes using the V-Slope Method; and 2.725 (1.118) minutes using the Ventilatory Equivalents method. ANOVA results indicate that the Ventilation Curve method and the V-slope methods yield equivalent VT values ($p=0.83$), but VT was achieved earlier using the Ventilatory Equivalents method ($p=0.04$).

CONCLUSION: Ventilatory Threshold in stroke patients undergoing treadmill testing can be effectively calculated from gas exchange data using the Venilation Curve and the V-slope methods. More research is needed to assess other factors that may affect VT measurements, such as medications or diseases impacting respiratory and cardiac function in patients with stroke to determine the most optimal and effective means of establishing training intensity after stroke.

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INTRODUCTION

Each year 800, 000 people are affected by stroke[1], causing long-term disability and serious medical sequelae. Stroke, by and large, affects patients with already pre-morbidly low levels of physical fitness[1], and the consequences of stroke further impede mobility and participation in activities of daily living (ADLs)[2].Aerobic Capacity is strongly associated with mortality among healthy individuals, and also among those with cardiac comorbidities and/or a previous history of stroke[1]. Consequently, reduction of mortality risk has been seen with improvement of aerobic capacity, as well as reduction in the risk for a subsequent stroke[3]. However, aerobic training in post-stroke patients is complicated by the sequelae that accompany stroke that may impair the ability to effectively engage in exercises. Functional and neurological deficits, such as balance issues, hemiparesis, discoordination, as well as comorbid cardiac and BP issues, that follow stroke can lead to difficulties with regards to properly and effectively engaging in and tolerating exercise protocols. The addition of these factors may lead to an inappropriate or suboptimal exercise training intensity[4].

Exercise training intensity is commonly estimated by using VO2R (Ventilatory Reserve) and HRR (Heart Rate Reserve) measures during cardiorespiratory exercise[5]. Ventilatory Threshold (VT) is an alternate method of establishing aerobic training intensity and indicates the exercise intensity above which ventilation increases disproportionately compared to whole-body oxygen uptake – representing the optimal intensity for sustaining aerobic exercise[6]. This may provide a more effective training stimulus than HRR to improve aerobic capacity in individuals with stroke thereby reducing mortality risk[1]. This study aims to determine the most effective ways of analyzing gas-exchange data to determine VT, which may be of use in determining target training intensity in patients with a history of stroke engaging in aerobic training protocols.

Ventilatory Threshold

Ventilatory Threshold is a method of establishing aerobic training intensity that is independent of heart rate response and may provide a more effective means of determining training intensity[8] for post-stroke patients. VT reflects the anaerobic or lactate threshold – the exercise intensity at which anaerobic respiration and lactate accumulation occur – by comparing VO2 to VCO2, determining the point at which lactate accumulation occurs, inciting an increase in VCO2 due to the compensatory buffering of the decreased pH in the blood. This provides a measure of cardiopulmonary performance that can help determine training intensity of sufficient magnitude to provide more of an improvement in aerobic capacity.

Training just below the anaerobic threshold has been shown to be an effective and efficient means of raising aerobic fitness and provides a useful measure in determining appropriate training stimulus for exercise prescription.[5]

VT and Anaerobic threshold

Beaver et al[9] demonstrated that Ventilatory Threshold is closely correlated to the point at which aerobic respiration is supplemented by anaerobic respiration in the body, indicating that the subject is exercising at a sufficient intensity to be able to achieve an effective training stimulus for a cardiorespiratory training effect[10]. The point at which the switch from aerobic to anaerobic respiration occurs varies from person to person depending on their level of cardiorespiratory fitness, age, comorbidities and other factors[5]. VT is measured by gas exchange analysis wherein there is a non-linear increase in VE (minute ventilation) that is not matched by oxygen consumption (VO2). This change is related to the increased lactate in blood serum levels and the subsequent increase in CO2 output generated by the buffering of [H+] ions by the HCO3- buffer system which is expelled through the respiratory system.

Directly measuring anaerobic threshold by taking blood samples to determine increased lactate levels and decreased bicarbonate concentrations has been used as an effective measure of physical fitness in both healthy individuals and patients with cardiorespiratory diseases. This is done by taking arterial lactate levels during periods of increasing work rate and determining the point at which it increases. This method, is, however cost inefficient, invasive[9] and is impractical for routine clinical purposes.

In a study by Beckers et al comparing the determination of anaerobic threshold by measuring heart rate turning point (change in the rate of increase/decrease of HR during exercise), blood lactate levels and respiratory compensation point (VT: VE vs VCO2 inflection point). They found that there was a significant correlation between the second lactate threshold (LTP2) and respiratory compensation point (RCP).[6]

The determination of anaerobic threshold by measuring gas exchange data is a less invasive, more practical approach to determining appropriate exercise intensity, lending credence to the use of VT in patients undergoing aerobic exercise training. Its correlation with changes in blood lactate levels indicating a switch from aerobic to anaerobic metabolism has been shown to be useful in optimizing the intensity of exercise prescription and assessing risks in patients with cardiovascular disease[11] and may prove to be effective for patients who have had stroke as well.

Utility of Ventilatory Threshold in Research and Clinical Applications

Ventilatory threshold has been used clinically and in research for the determination of the optimal levels of aerobic training intensity to elicit gains in endurance[10]. Measurements of VT have been used extensively in cardiopulmonary exercise testing, particularly with heart failure patients, as a noninvasive means of measuring cardiac performance in heart failure patients[12] and in type II diabetic patients[13].

The comorbidities of stroke can have an effect on the cardiovascular response of patients, such as heart rate and blood pressure changes, during aerobic exercise. There is may also be a decreased capacity for effectively executing exercise modalities at a high enough level to elicit an appropriate aerobic intensity because of functional deficits[14].

The traditional methods used for determining the intensity of aerobic conditioning may be affected by the above mentioned factors. Maximum heart rate response in these patients may not be an accurate reflection of the patient's aerobic workload, due to the presence of anti-hypertensive medications that may have inotropic or chronotropic effects on HR as well as considerations regarding increased effort necessitated by compensatory mechanisms for movement and balance deficits, rendering the intensity of training programs inadequate to optimize improvements in aerobic capacity in this patient population.

For this patient population, basing training intensity on heart rate response may lead to an underestimation of the target intensity required to make significant improvements in aerobic capacity. Patients on anti-hypertensive medications such as beta-blockers, which is common for stroke patients, that can blunt heart rate response, may lead to inaccurate determinations of proper exercise intensity. This might explain the lack of significant increase in aerobic capacity in Askim et al's study on high-intensity aerobic interval training with stroke patients[4]. While the patients in their study showed significant increases in functional walking capacity, peak oxygen uptake (VO2max), an indicator of aerobic physical fitness, were not significantly improved.

Background of Stroke, Aerobic capacity and Conditioning

Stroke causes long-term disability and serious medical sequelae[1]. Stroke, by and large, affects patients with already pre-morbidly low levels of physical fitness[1], and the consequences of stroke further impede mobility and participation in activities of daily living (ADLs)[2]. Decreased Aerobic Capacity is strongly associated with mortality among healthy individuals, and also among those with cardiac comorbidities and/or a previous history of stroke[1]. Consequently, reduction of mortality risk has been seen with improvement of aerobic capacity, as well as reduction in the risk for a subsequent stroke[3].

Gallanagh et al opined that for patients with a history of stroke, one of the ways that their risk for subsequent strokes can be lowered is by improving their aerobic capacity[3]. Marfu et al showed that aerobic exercise can be used to complement antihypertensive drugs to achieve blood pressure control[15] which is another factor that can help reduce risk of subsequent stroke.

Aerobic training in post-stroke patients, however, is complicated by a number of considerations not limited to: functional deficits that may limit options for safe participation in aerobic exercise activities such as gait deficits, hemiparesis and impaired balance, coordination, an issue which was attempted to be addressed by using Body-weight supported treadmill training in a study by Jorgensen et al[16]. This points to the need to modify and adapt current protocols for exercise training for post-stroke patients in order to achieve adequate gains. The increased work needed to overcome these functional deficits need to be taken into account in exercise prescription for this patient population

Tang et al examined the feasibility of adapting cardiac rehabilitation protocols for stroke patients[17] with promising results that indicated an increase in aerobic capacity as well as a need for further research. Calmels et al demonstrated the feasibility of using cycloergometer training in stroke patients[7], while Globas et al showed that the use of treadmill exercises was also feasible in chronic stroke survivors, leading to improvements in cardiovascular fitness and gait[18]. Both Calmels and Globas used VO2max as initial measures of aerobic capacity, while the study by Tang et al determined initial training intensity using a comparison between heart rate reserve and VT.

There is, however, a paucity of information regarding the application of VT in the aerobic exercise training protocols and exercise prescription for patients with a history of cerebrovascular accidents. There is a need to be able to more accurately provide analysis and data to determine the most effective and efficient means of calculating VT as a measure of training intensity in stroke populations.

METHODOLOGY

Study Population and Design

This study is a retrospective analysis of the data gathered from VT trials in patients with a history of chronic stroke undergoing sub-maximal and maximal exercise testing from previous studies.

De-identified data consisting of gas-exchange readings including VO2, VCO2 and VE from post-stroke subjects participating in treadmill walking obtained from previous studies which have undergone previous IRB approval.

In total, there were 15 participants, 12 male and 3 female subjects. Average age of the participants was 50 years old. Average BMI was 27.8 kg/m2 (Table 1). Gas exchange data was collected over the course of 39 instances of gait training on a treadmill with ventilatory data being collected.

Age		*Height (cm)*		*weight (kg)*		*BMI*	
Mean	**49.93**	**Mean**	**176.57**	**Mean**	**86.68**	**Mean**	**27.71**
Median	51.00	Median	177.80	Median	85.00	Median	27.37
SD	**12.31**	**SD**	**9.83**	**SD**	**17.00**	**SD**	**4.32**
Range	41.00	Range	36.98	Range	67.00	Range	17.44
Minimum	26.00	Minimum	156.01	Minimum	54.00	Minimum	18.68
Maximum	67.00	Maximum	192.99	Maximum	121.00	Maximum	36.13
Count	15	Count	15	Count	15	Count	15

***Table 1**: Participant Demographics*

Measurement and Calculation of VT

There are three methods that we examined in this study in calculating the Ventilatory Threshold: the Ventilation Curve, the V-Slope Method and the Ventilatory Equivalents method.

Ventilation Curve

The Ventilation Curve involves plotting the minute ventilation (VE) against oxygen consumption (VO2) with the point at which linear rise in VE with regards to VO2 begins to become non-linear. This reflects the increasing ventilatory rate in compensation for rising lactate levels[6].

The slopes of the data points were compared and the largest increase was determined by both computational analysis in Excel and visual verification the trend line of the graph of VE vs VO2. (Fig 1)

V-Slope

The V-Slope Method[9], first proposed by Beaver et al, requires that VO2 be plotted against CO2 consumption (VCO2). Here, the VT is determined to be at the VO2 measurement that corresponds with an increase in the slope of the VO2 to VCO2 plot.

The slopes of the data points were compared and the largest increase was determined by both computational analysis in excel and visual verification of the graph of VO vs VCO2. Trend lines were compared from the points prior to and after the highest increase in slope and the intersection of the 2 trend lines. (Fig. 2)

Ventilatory Equivalents

Using the Ventilatory Equivalents Method involves plotting ventilatory equivalent of O2 (VE/VO2) and ventilatory equivalent of CO2 (VE/VCO2) with the anaerobic threshold corresponding to the point at which there is a rise in VE/VO2 without a concomitant rise in VE/VCO2.

The slopes of the 2 ventilatory equivalents were graphed and visual verification of the point of divergence between VE/VO2 and VE/VCO2 were compared to computation of the largest difference of the slopes of each point of the graph (Fig.3).

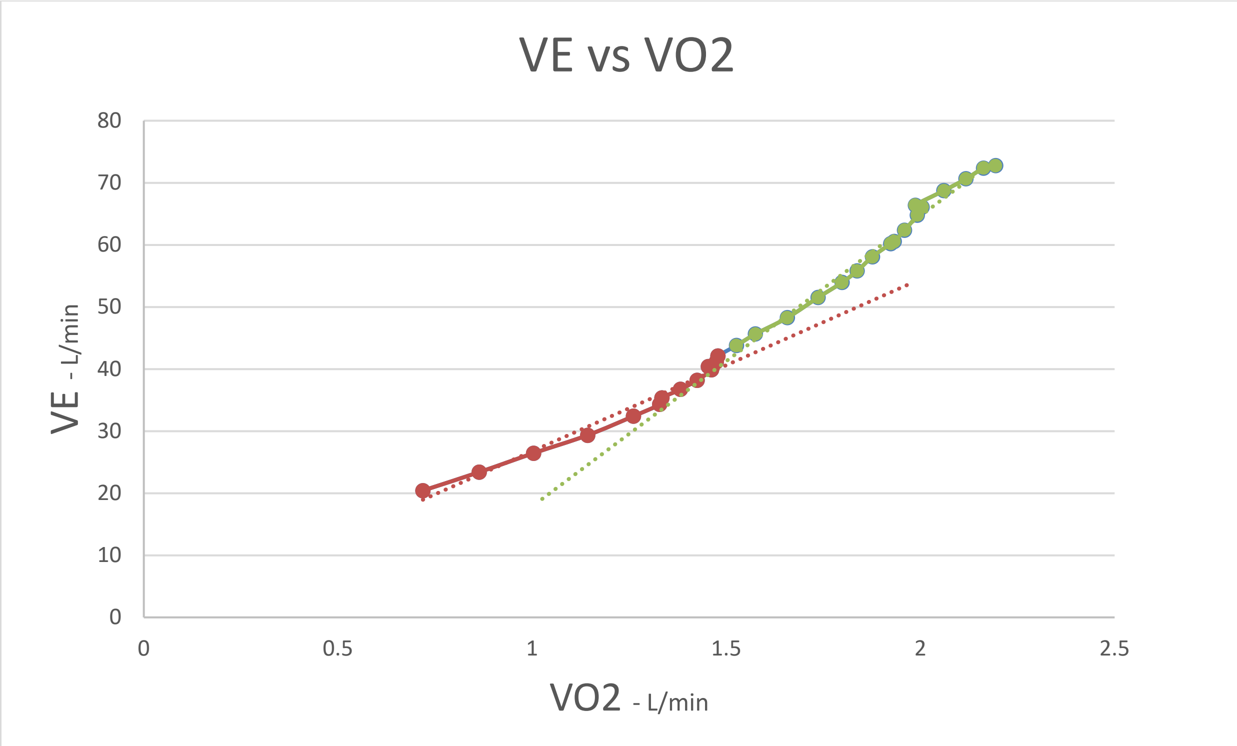

Figure 1*: Ventilation Curve - The Ventilation curve involves plotting the minute ventilation (VE) against oxygen consumption (VO2) with the point at which linear rise in VE with regards to VO2 begins to become non-linear. This reflects the increasing ventilatory rate in compensation for rising lactate levels*

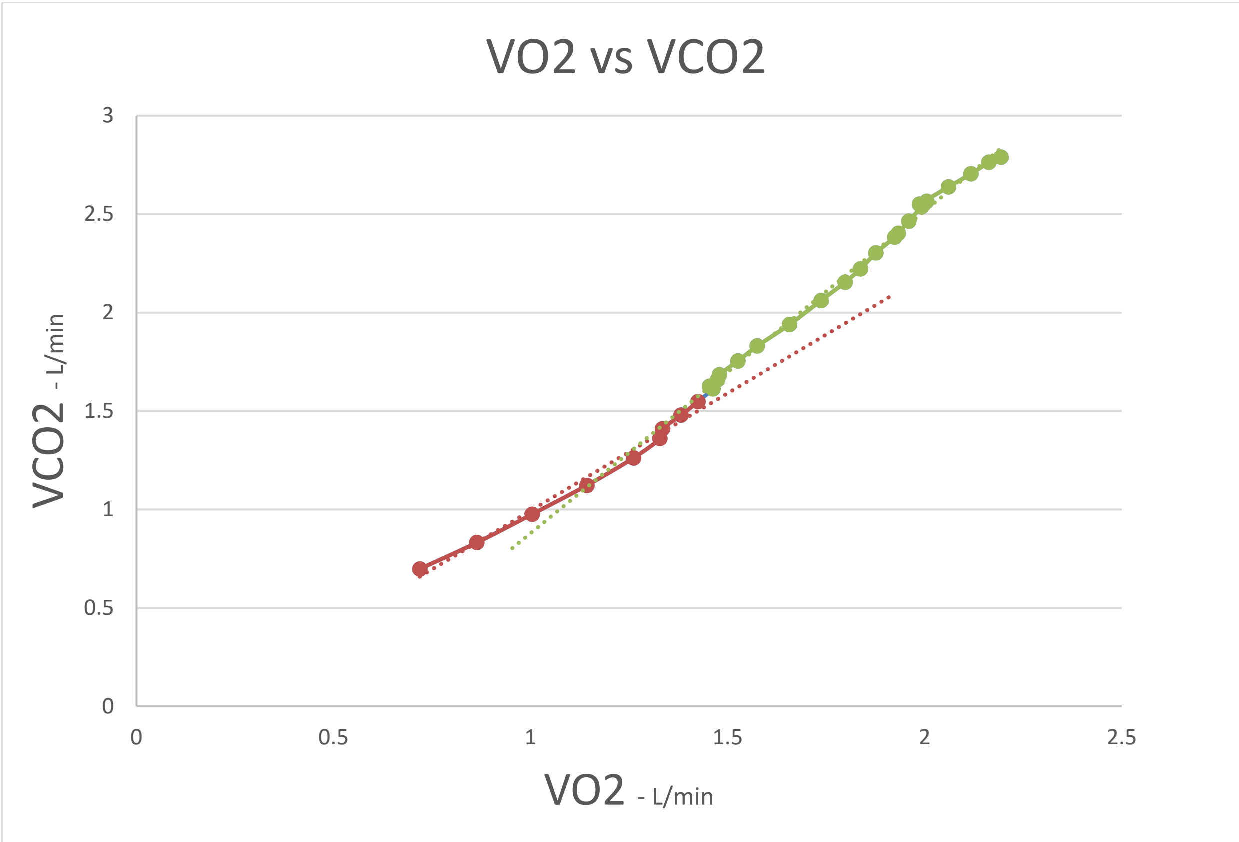

***Figure 2**: V-Slope - The V-Slope Method, first proposed by Beaver et al, requires that VO2 be plotted against CO2 consumption (VCO2). Here, the VT is determined to be at the VO2 measurement that corresponds with an increase in the slope of the VO2 to VCO2 plot.*

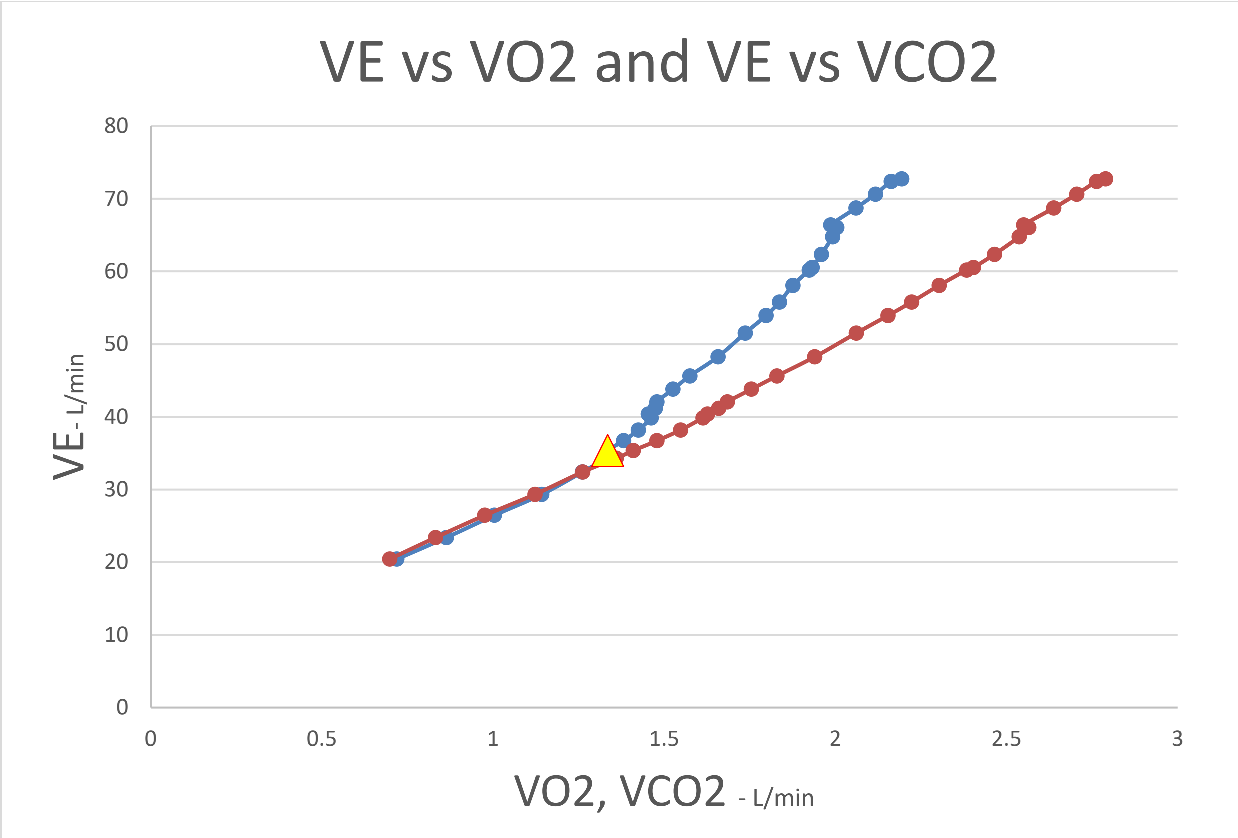

***Figure 3**: Ventilatory Equivalents - The Ventilatory Equivalents Method involves plotting ventilatory equivalent of O2 (VE/VO2) and ventilatory equivalent of CO2 (VE/VCO2) with the anaerobic threshold corresponding to the point at which there is a rise in VE/VO2 without a concomitant rise in VE/VCO2.*

RESULTS

The average value for the time at which the Ventilatory Threshold was achieved for the Ventilation Curve was 3.355 minutes with a standard deviation of 1.349. For the V-Slope Method it was 3.383 minutes and a standard deviation of 1.372. The Ventilatory Equivalents method averaged at 2.725, significantly lower than the other 2 methods of calculating VT, with a standard deviation of 1.118. (Table 2)

An analysis of variance showed that when comparing VT determination using the time stamps at which the participants start to show signs of anaerobic respiration based on their gas exchange data, with the Ventilatory Equivalents method showing an earlier time compared to the other 2 methods, $p = 0.04$. (Fig. 4, Table 3)

The same analysis using heart rate measurements as a possible indicator for achieving VT showed that there was no significant difference between the 3 methods, $p = 0.83$. (Fig. 5, Table 4)

Some of the participants for whom we had data were engaged in a 10-week treadmill training program. Since we had pre- and post-intervention VT values for these individuals, we compared changes in VT. In comparing the relative increase in performance from the initial measurement of VT to the second measurement of VT after 2 months of gait training, our data showed an increase of 30-40 seconds before VT was achieved, indicating an increase in time before anaerobic metabolism needed to be activated (Table 5). This was shown in both the Ventilation Curve and the V-Slope calculation, but was not apparent in the calculations for Ventilatory Equivalents (Table 6, Table 7).

Time and HR to achieve VT				
	Mean Time (sec)	SD	Mean HR (bpm)	SD
VE/VO2	201.285	80.944	113.893	21.550
VCO2/VO2	203.000	82.310	114.143	21.597
VE/VCO2/VO2	163.522	67.056	111.018	21.096

Table 2*: Mean time in seconds and HR in beats/min at which VT was achieved*

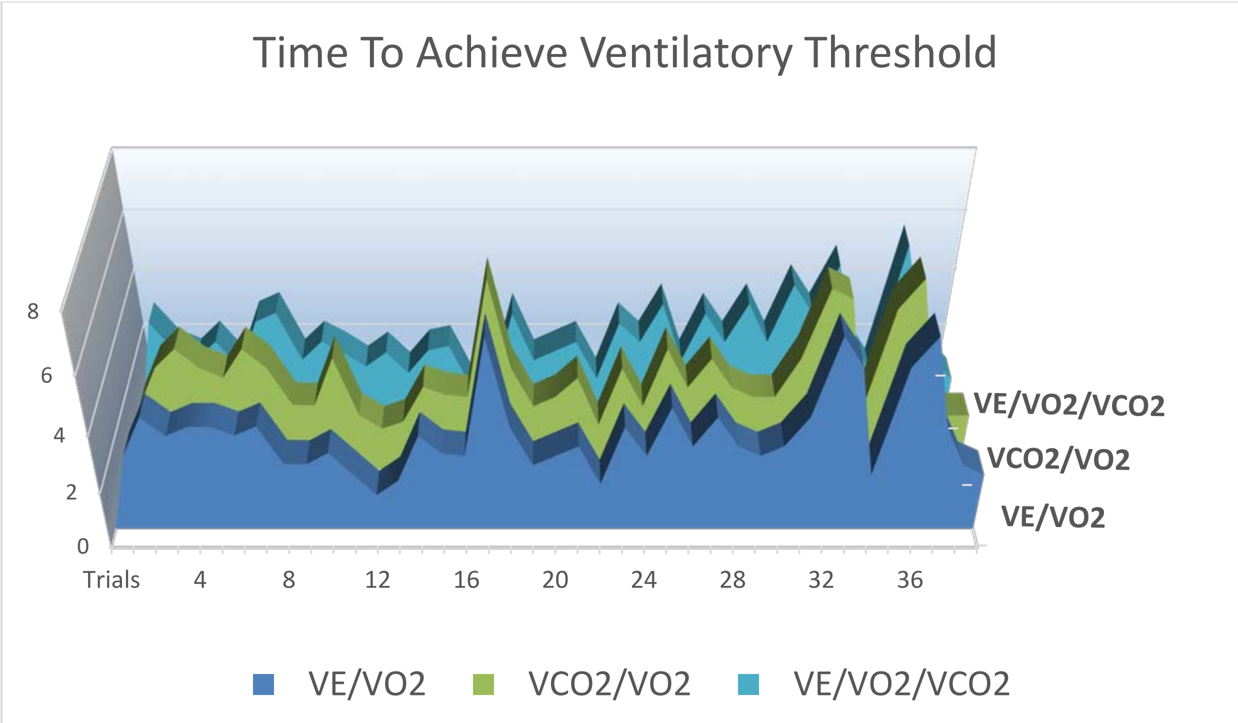

Figure 4*: Comparison of calculated time to achieve VT in minutes*

ANOVA for Time to Achieve VT						
Source of Variation	*SS*	*df*	*MS*	*F*	*P-value*	*F crit*
Between Groups	10.78841	2	5.394206	3.268604	0.041656	3.075853
Within Groups	188.1352	114	1.650309			
Total	198.9237	116				

Table 3*: Analysis of variance between the 3 methods of calculation of time to achieve VT*

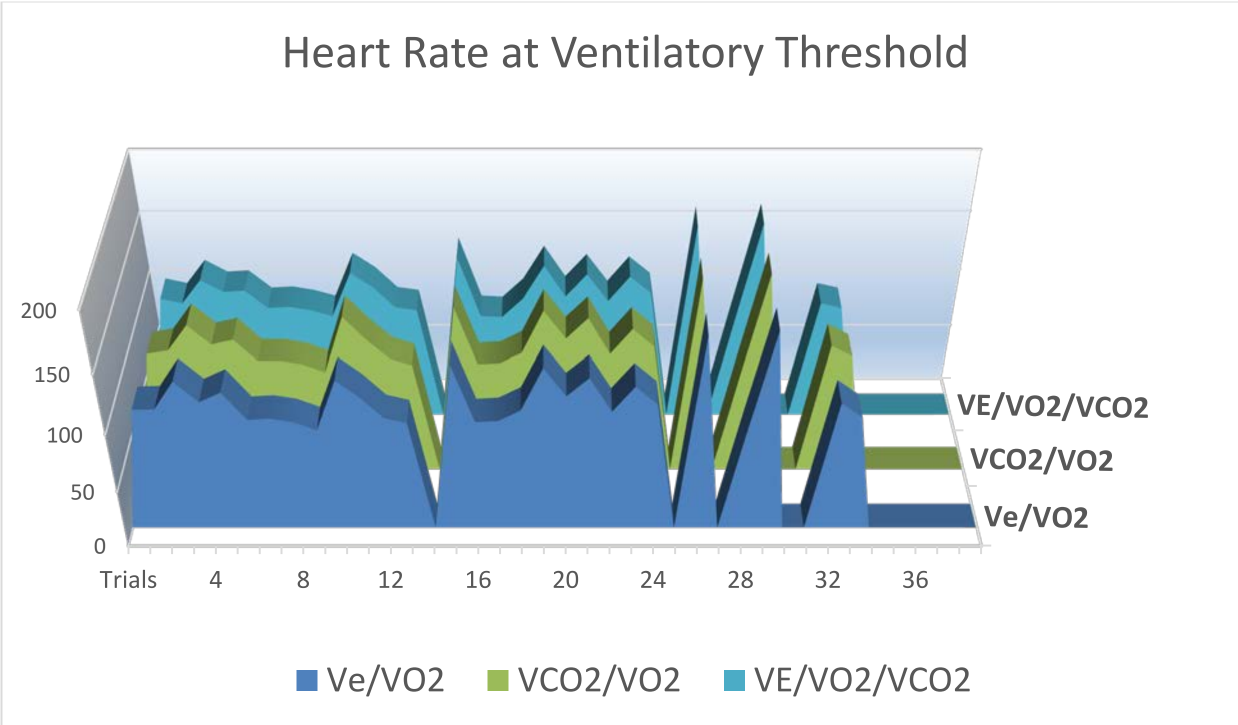

***Figure 5**: Comparison of subject heart rate once ventilatory threshold was achieved.*

ANOVA for HR at VT						
Source of Variation	*SS*	*df*	*MS*	*F*	*P-value*	*F crit*
Between Groups	168.875	2	84.4375	0.184109	0.832192	3.109311
Within Groups	37148.85	81	458.6278			
Total	37317.72	83				

***Table 4**: Analysis of variance between the 3 methods of calculation of HR at which VT is achieved*

Time improvement and HR change at VT after training				
	Mean Improvement (sec)	SD	Mean HR Change	SD
VE/VO2	42.955	170.471	2.733	593.102
VCO2/VO2	29.417	196.901	2.467	605.695
VE/VCO2/VO2	-8.552	68.975	2.967	583.374

***Table 5**: Change in the HR and time in seconds at which VT was achieved after a 10-week treadmill training program.*

ANOVA for Change in Time to Achieve VT						
Source of Variation	*SS*	*df*	*MS*	*F*	*P-value*	*F crit*
Between Groups	5.941479291	2	2.970739646	1.225476072	0.303901378	3.219942293
Within Groups	101.8143626	42	2.424151489			
Total	107.7558418	44				

Table 6: Analysis of variance for the 3 calculations with regards to change in time to achieve VT before and after a 10-wk treadmill training program.

ANOVA for HR change						
Source of Variation	*SS*	*df*	*MS*	*F*	*P-value*	*F crit*
Between Groups	1.877777778	2	0.938888889	0.001580469	0.998420839	3.219942293
Within Groups	24950.4	42	594.0571429			
Total	24952.27778	44				

Table 7: Analysis of variance for the 3 calculations with regards to change in HR at VT before and after a 10-wk treadmill training program.

DISCUSSION

In comparing different methods of calculating anaerobic threshold by determining the ventilatory threshold based on gas exchange data, our results indicate that using the Ventilation Curve method and the V-Slope methods are virtually equal. The Ventilatory Equivalents method showed compartively earlier time points at which ventilatory threshold was achieved in comparison. This may indicate that the Ventilatory Equivalents method might be more in line with the first lactate threshold than the second lactate threshold that has been found in previous studies. However, blood samples need to be drawn during testing to verify this.

In addition, the data on heart rate was found to have no significant differences in all three of the methods analyzed. A previous study measuring VT in CHF patients showed comparable results for HR at VT to our own results[6]. This might be related to other factors in this population of stroke patients relating to cardiac function, such as medications that may affect heart rate or autonomic responses in patients such as blood pressure medications. This indicates that HR at VT could be another way to calculate exercise intensity after stroke.

In some of the cases, there was significant difficulty obtaining both computational and visual graphical verification of inflection points of the data, some plots being erratic with no clear delineation between changes in the overall progression of the changes going in in the gas exchange data. Deconditioning may play a role in this, as patients with significant debility, respiratory issues or an inability to effectively and consistently maintain the required level of exertion can affect this aspect of the data.

Limitations of this study include that in some cases, there was difficulty obtaining either computational or visual verification of VT from the data. These plots were erratic with no clear delineation to indicate metabolic changes. Deconditioning may play a role in this, as patients with stroke tend to have significant disability. Respiratory issues or an inability to effectively and consistently maintain the required level of exertion could also have affected the data. Finally, all tests were conducted on a treadmill. Cycle ergometry[7] testing may result in less noise in the data and more clear evidence of metabolic shift with increasing workloads.

CONCLUSION

Ventilatory Threshold in stroke patients undergoing treadmill gait training can be effectively calculated using gas exchange data. Using the Venilation Curve and the V-Slope method appear to be most consistent with each other and the Ventilatory Equivalents method appears to deviate to an earlier threshold. While more research is needed in order to determine more accurate and more feasible means of determining optimal aerobic intensity for patients with stroke, this study shows the relative utility of using gas exchange data in setting more appropriate and adequate exercise intensity for patients with stroke. The use of ventilatory threshold calculations allows the establishment of a more effective and appropriate training stimulus for attaining gains in aerobic capacity that takes into account the functional difficulties and concerns that are inherent to stroke populations, thereby allowing a more effective reduction in risk for subsequent strokes.

As such, more research needs to be done on other confounding factors that may affect ventilatory threshold measurements, ranging from medications or diseases affecting respiratory and cardiac function in patients with stroke, in order to determine the most optimal and effective means of arriving at an appripriate training intensity that will provide stroke patients with both functional utility and increased aerobic gains.

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