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**THRESHOLD CHANGES IN BLOOD LACTATE, BEAT-TO-CARDIOVASCULAR
FUNCTION, AND BREATH-BY-BREATH VO₂ DURING INCREMENTAL EXERCISE**

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ABSTRACT

THRESHOLD CHANGES IN BLOOD LACTATE, BEAT-TO-CARDIOVASCULAR FUNCTION, AND BREATH-BY-BREATH VO₂ DURING INCREMENTAL EXERCISE. **Melissa Knight-Maloney, Robert A. Robergs, Ann Gibson, Farzenah Ghasvand. JEPonline.** 2002;5(3):39-53. The relationships between the systolic blood pressure threshold (ST), heart rate (HR) threshold (HT), rate pressure product threshold (RT), lactate threshold (LT) and ventilatory threshold (VT) were studied in 14 subjects (10 males, 4 females). All subjects performed an incremental cycle ergometer test to volitional exhaustion. HR data was collected via ECG. SBP was determined beat by beat by tonometry. The LT and VT were determined through standard methods. The threshold or breakpoint for SBP, HR and RPP, as a function of VO₂, was determined as the deviation from linearity when the data were analyzed with non-linear regression analysis. When the pre and post threshold slopes for SBP, HR and RPP were analyzed it was found that most subjects demonstrated either an increased or decreased response post-threshold. The threshold responses were analyzed using two-way ANOVA. For SBP, it was found there was no significant difference in pre and post-threshold SBP in subjects that demonstrated an increase in SBP slope post-threshold (p=0.36). In contrast, there was a significant difference between the pre and post-threshold slopes for the subjects that exhibited a decreased post-threshold SBP response (p=0.000). The analysis of the HR data pre and post HT revealed differences in pre and post-threshold slopes for those subjects that demonstrated an increase HR response post-threshold (p=0.003) and those that exhibited a decreased post-threshold HR response (p=0.001). There was no significant difference in the pre and post-threshold RPP responses for either the group that demonstrated an increased post-threshold response or the group that demonstrated a decreased RPP response post-threshold. Two-way ANOVA revealed significant differences between the VO₂ at the RT (2.17±0.26 L/min) and LT (1.84±0.13 L/min) (p=0.011) and the RT and VT (1.87±0.11 L/min) (p=0.011). There were also significant differences between HT (2.24±0.14 L/min) and LT (p=0.0019) and HT and VT (p=0.0025), indicating that the RT occurs at a significantly different VO₂ than either the LT or VT. In summary, differences were noted in the pre and post threshold responses for SBP and HR. The RPP slopes were inconsistent between subjects due to both positive and negative changes in

the SBP and HR curves after the threshold. The intensities at the HT and RT did not coincide with either the LT or VT.

Key Words: Metabolism, Heart Rate, Blood Pressure, Vascular Resistance.

INTRODUCTION

Although measurements of blood pressure and heart rate are traditionally performed during incremental exercise testing, the frequencies of these recordings are slow and typically occur every 3 min. With the recent introduction of more sophisticated electronic equipment, the frequency at which heart rate and blood pressure signals can be acquired during exercise testing has increased to beat-by-beat capabilities. Similarly, the measurements and calculations involved in indirect expired gas analysis calorimetry can be done on a breath-by-breath basis. These advancements in the temporal resolution of cardiovascular and metabolic signal acquisitions have not been extensively researched together in a single study.

Tanaka et. al. (38) determined the rate pressure product (RPP) every 15 s during incremental exercise. Blood lactate was measured every 30 s. Data revealed differences in the slopes of RPP above and below the LT. Although Tanaka et al. (38) did not measure changes in blood catecholamines, the threshold changes in SBP and the RPP were theorized to be dependent on the exponential increases in sympathetic activation and circulating catecholamines during incremental exercise.

Despite the unique findings of Tanaka et. al. (38), these researchers only reported the relationship between the threshold change in the RPP (RT) and LT, and did not assess whether these thresholds occurred at the same exercise intensity, or how the data compared to the ventilatory threshold (VT). Also, the relationships between the variables' non-linear changes with increasing exercise intensity were not elucidated. These shortcomings are problematic for a number of reasons. 1) The VT is more commonly and easily quantified during clinical graded exercise testing, but can deviate from the LT (7, 12) and may differ to the RT. 2) The known sinusoidal changes in SBP (13) that can only be adequately detected from beat-to-beat measurements make time averages of blood pressure difficult to interpret (13). 3) It remains unclear if the changes in RPP are due more to SBP increases rather than HR increases. 4) Finally, it also remains unclear how the changes in beat-to-beat measurements of cardiovascular function during incremental exercise compare to changes in breath-by-breath data of oxygen consumption and ventilation.

Although the literature examining the occurrence of the heart rate threshold (HT) and its relationship to the LT is extensive, there are no studies that examined the occurrence of a SBP threshold (ST) or RT, and at what exercise intensity these thresholds occur. There are also no studies that determined if this ST and RT occur at an exercise intensity similar to the exercise intensity at the VT. A study needs to be done that uses beat-to-beat blood pressure technology to better assess the changes in HR, SBP, RPP, and also simultaneously uses procedures suited to rapid measurement of VO_2 , ventilation, and blood lactate during incremental exercise.

The purpose of this study was to examine the changes in SBP, HR, RPP, blood lactate and ventilatory and metabolic parameters during incremental exercise. These relationships were further assessed by comparisons of the pre and post-threshold changes in HR, SBP, and RPP. The VO_2 at each of the thresholds of SBP, RPP, blood lactate, ventilation and HR were analyzed to determine if these phenomena occur at the same exercise intensity. The hypotheses for the study were as follows; 1) There will be no significant differences in the pre- and post-threshold responses for HR, SBP and RPP. 2) There will be no significant differences in the exercise intensity (VO_2 or % VO_2max) for the occurrence of each threshold.

METHODS

Subjects

This study and informed consent were approved by the Human Subjects Research Review Committee of the sponsoring institution. Fourteen subjects (10 males and 4 females) were recruited from university student and faculty populations, as well as the surrounding community. All potential subjects read and signed a comprehensive and IRB-approved human subject consent form prior to participation in any testing. Each subject was required to complete a comprehensive medical history questionnaire to identify individuals at risk for cardiovascular disease, or who had medical conditions that precluded their participation, as described and recommended by the American College of Sports Medicine (1).

Subjects were not allowed to consume any medications that affect heart rate, stroke volume or total peripheral resistance in the week prior to the study. In order to be considered a subject in the study, each volunteer generated an acceptable signal with the Colin tonometry unit. Acceptable signals were defined as generating a roughly symmetrical tonogram, sustaining a hold down pressure between 60 and 140 and signal strength between 60 and 150 throughout the incremental exercise test (manufacturer's guidelines and terminology). Gravid females were not used as subjects in the study due to the effect of pregnancy on the cardiovascular system, especially blood pressure.

Protocol

The subjects were familiarized with the cycle ergometer (Cybex MET 2000) and the Colin® tonometry unit (Colin Pilot, Belmont, Texas) prior to beginning the exercise session. Cycling seat position and height was determined at this time. The subjects were informed and familiarized with the MedGraphics® (MedGraphics Corp., Minnesota) gas analysis system and the discomforts of exercising with a mouthpiece and nose clip.

Prior to the exercise testing, a Teflon® catheter was placed in an antecubital vein of the contralateral arm for tonometry. A 3-way stopcock was attached, a 1 mL blood sample was obtained, and 3 mL of sterile saline was infused to keep the catheter patent until the start of the exercise test. Additional infusions of 3 mL of saline occurred every 10 min until the start of exercise. Blood samples were dispensed into borosilicate tubes, and 250 µL of whole blood was dispensed into 0.5 mL of 7% perchloric acid.

After the initial blood sample, the subjects, while standing, straddled the cycle ergometer. The tonometry unit was placed on the subject's right radial artery, according to manufacturer's guidelines (Colin Pilot, Belmont, Texas). The oscillometric calibration cuff was placed on the right arm. The cuff for manual sphygmomanometry was placed on the left arm.

Once the tonometric equipment was placed, a minimum 10 min automatic calibration commenced. The 10 min calibration was needed to prevent oscillometric re-calibration during the exercise test, and was conducted according to the manufacturers guidelines. During the 10 min calibration the subjects were required to stand while straddling the cycle ergometer in order to hold the tonometric unit still and improve subject comfort. The tonometer calibration was considered successful if after two oscillometric cuff measurements the tonometric signal remained constant. If the unit could not be calibrated on a subject, that subject was excluded from the trial. Once a successful calibration was completed the automatic calibration was turned off and there was no automatic re-calibration during the trial.

After the successful 10-minute calibration, the subjects were prepared for incremental exercise to VO_2max . The subjects were fitted with a mouthpiece for expired gas analysis. Oxygen consumption was determined in a breath-by-breath manner throughout the test using a Medical Graphics CPX/D System® (Medical Graphics Corp,

Minnesota). Heart rate was recorded continuously with beat-to-beat resolution by electrocardiography (Biopac, Goleta, CA).

After equipment calibration, the subjects was seated on the cycle ergometer and following 2 minutes of resting data collection (VO_2 , VE, SBP, HR) began cycling at 50 Watts and 80 rev/min. Power output then increased stepwise by 20, 25, or 30 Watts/min, depending upon the pre-determined (verbal interview) cardiorespiratory endurance and training status of the subjects. Test termination occurred when the subjects could no longer continue at a cadence equal to or greater than 50 rev/min, after which subjects “cooled down” with an active recovery of cycling at 50 Watts for 10 min.

Tonometric beat-by-beat blood pressures were determined continuously throughout exercise and recovery. Blood samples were obtained every 60 s during the exercise test.

Analog signals of the blood pressure and ECG waveforms were integrated electronically through the use of data acquisition hardware (BIOPAC, Goleta, CA), and later processed using Acknowledge III® software (BIOPAC, Goleta, CA). VO_2max was determined according to the criteria set forth by the ACSM (1), where: (a) RER must exceed 1.1, (b) heart rate must be within 10 beats/min of the age-predicted maximal heart rate ($220-\text{age}$), and (c) the difference between two consecutive VO_2 values corresponding to maximal exertion should not exceed 100 mL/min. All of these criteria were met in all subjects, and the average of the two highest VO_2 values was denoted VO_2max .

Data Processing

Cardiovascular and Calorimetry Variables

After each test, the blood pressure and ECG waveforms were saved on computer disk for latter processing and analysis. Heart rate (HR) was calculated from the ECG waveform based on the R-R interval of each cardiac cycle. The data were then converted to numerical text in beats/min based on the time interval between R waves. This data set was then saved in a text-based journal. The journal was then examined for anomalous HR output and the waveforms scan for missed R waves. Were anomalies from peak detection occurred, R-R intervals and heart rates were manually determined for this section of data and entered into the data file. HR numerical text data was then converted to text files for additional processing in spreadsheet format (Excel®, Microsoft Corporation, WA). Systolic blood pressure (SBP) was determined as described for HR, except peak values from each cardiac cycle were denoted as systolic blood pressure.

In order to align the data, the HR and SBP spreadsheets were then examined for temporal continuity of the electrical and contractile portions of the cardiac cycle, meaning that the data set was examined to ensure the electrical activity occurred prior to the contractile phase. Each set of data (HR and SBP) was transferred from text file to the Excel file with the time each data point was collected. The HR and SBP data were aligned to the closest 0.001 s. The rate pressure product (RPP) was then calculated as, $(\text{HR} \times \text{SBP})/1000$.

Oxygen consumption and ventilatory values were also transformed into text form and then again converted to an Excel® spreadsheet. A seven function smoothing process was performed on all relevant beat-by-beat and breath-by-breath data (HR, SBP, RPP, VE and VO_2). The VO_2 data were aligned temporally with the HR and SBP data to the closest 0.001 s, in a procedure similar to that previously described for aligning the HR and SBP. This process was repeated for each subject.

The shape of the SBP, RPP and HR vs. VO_2 curves was detected by curve fitting for each individual and each variable set (SBP- VO_2 , HR- VO_2 , RPP- VO_2). Linear and quadratic equations were then examined to determine which model best explains the data using the mean squared error (MSE).

Metabolic Thresholds

Blood lactate was assayed in duplicated using enzymatic spectrophotometry. Blood lactate data were converted to logarithmic values and graphed against VO_2 according to Beaver et al. (2). In summary, two-component linear regression fitting was performed to result in two linear regression lines being fit to the data with minimal error. The intersection of these lines was denoted as the lactate threshold.

For detection of the VT, the point of a consistent increase in the ventilatory equivalent for oxygen (VE/VO_2) was used as described by Caizzeo et al. (6). The heart rate threshold (HT) was detected by applying a quadratic regression equation to the heart rate data. The linear component of the heart rate curve was visually detected, a straight line was fitted to these data, and the point of deviation between the linear and quadratic regression lines was identified. This technique has been the traditional method used to detect the HT (5,14,15, 32). The same procedure was used to detect SBP and RPP thresholds.

Calculations and Statistics

The shape of the curve for SBP, HR, RPP, blood lactate and VE was determined for each individual with the use of trend analysis. The linear and quadratic proportion of the error associated with each model (MSE) was compared with a Student's t-test. The significant p value for all statistical analysis was set at 0.05.

The slopes of the SBP, RPP and heart rate curves above and below their respective thresholds were determined by the use of linear regression analysis. The slopes (pre and post threshold) for each variable were then compared through the use of two-way ANOVA with repeated measures. One independent variable was a grouping variable. The subjects were grouped according to their post-threshold response (increased post-threshold slope or decreased post-threshold slope) for each variable: HR, SBP and RPP. The second independent variable was the threshold point (pre or post-threshold). The interaction between post-threshold response and threshold was also determined. A Tukey's Post Hoc analysis determined significant differences between specific means.

The exercise intensity (VO_2) at each threshold (LT, VT, HT, ST, and RT) was assessed by one-way analysis of variance with repeated measures. The percent VO_2max at which each threshold occurred was also tested using one-way analysis of variance with repeated measures. Significant differences between means were determined by a Tukey-Kramer Post Hoc analysis for unequal cell size.

Based on past research statistical power was calculated for the relationship between the LT and RT. At the 0.05 level the statistical power was estimated to be 1.0. Statistical power was also calculated for the difference between the pre and post threshold HR, SBP and RPP slopes. At the 0.05 level of significance, power was estimated to be 0.98, 1.0 and 1.0 respectively.

RESULTS

Subject Characteristics

Table 1 contains descriptive data for 14 subjects. Twenty-nine percent of the subjects were female ($n=4$), and 71% of the subjects were males ($n=10$). All subjects indicated that they were free from medications and were in good health.

Table 1. Subject characteristics

<i>Characteristic</i>	<i>Mean\pmSD</i>
<i>Height (cm)</i>	186.64 \pm 7.56
<i>Weight (kg)</i>	73.48 \pm 10.98
<i>VO₂ Max (L/min)</i>	3.5 \pm 6.70
<i>Age (y)</i>	30.62 \pm 5.78

The raw data for selected subjects, representative of the subjects who demonstrated a clear threshold for most variables, is presented in Figure 1a-f. These figures show the beat-by-beat and breath-by-breath data for pertinent variables, as well as the blood lactate data. The lines added to the figures reveal the similarities and differences between each of the thresholds.

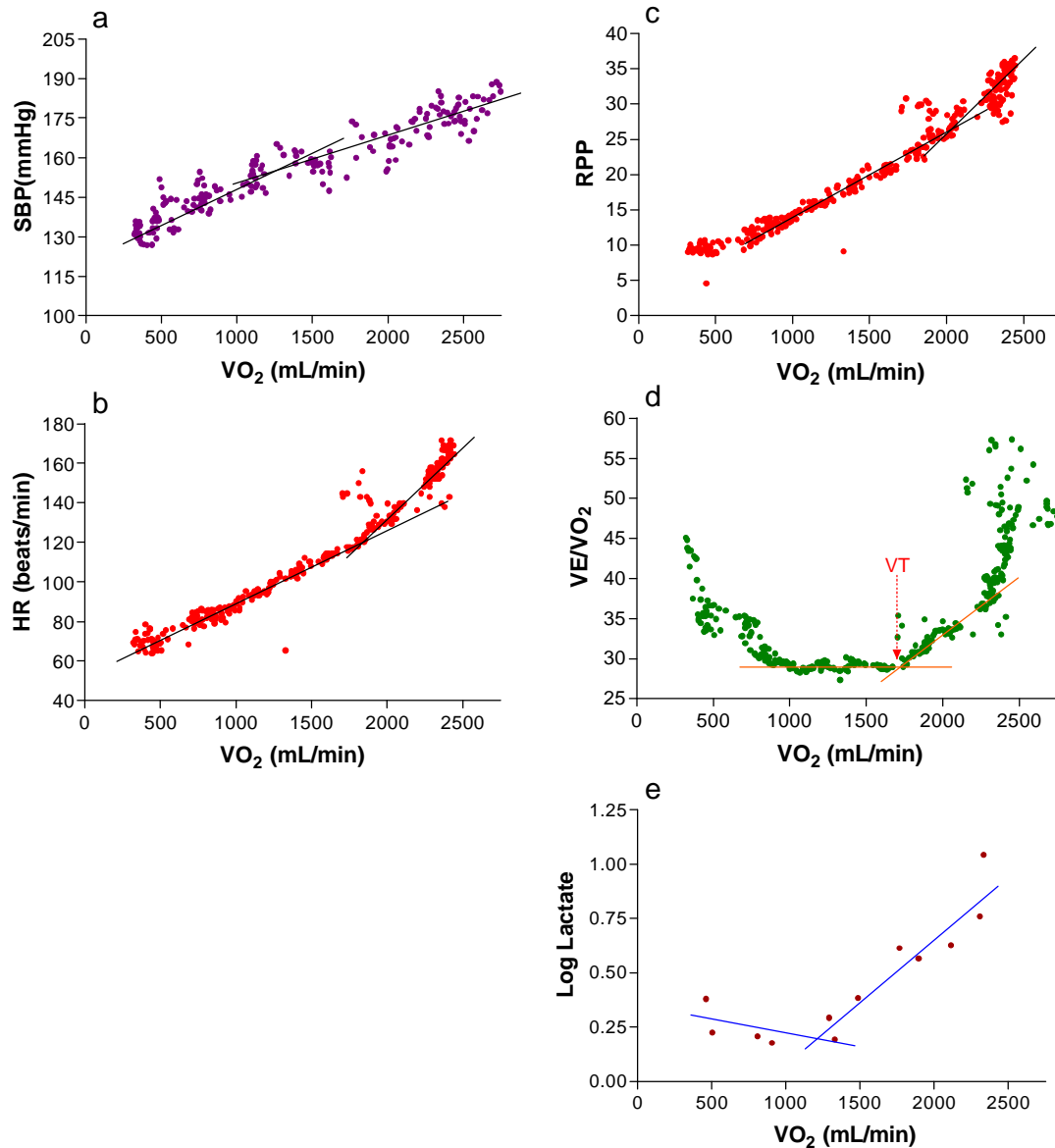


Figure 1: The responses to incremental exercise from a single subject for a) SBP, b) HR, c) RPP, d) VE/VO₂, and e) log blood lactate.

Threshold Comparisons

There was a significant main effect for differences between the ST, HT, RT and LT variables ($p=0.018$), as illustrated in Figure 2.

Tukey-Kramer Post Hoc analysis for unequal cell size showed that RT was significantly different from LT and VT ($p=0.011$ for both comparisons). HT was also significantly different from the LT and VT ($p=0.0019$, $p=0.0025$ respectively). There were no significant differences between the other threshold variables.

The ST, although it demonstrated a higher mean than either the RT or HT and is moved further from the LT and VT than either the RT or HT, was not significantly different from any of the means. This was due to the amount of variance associated with the ST values.

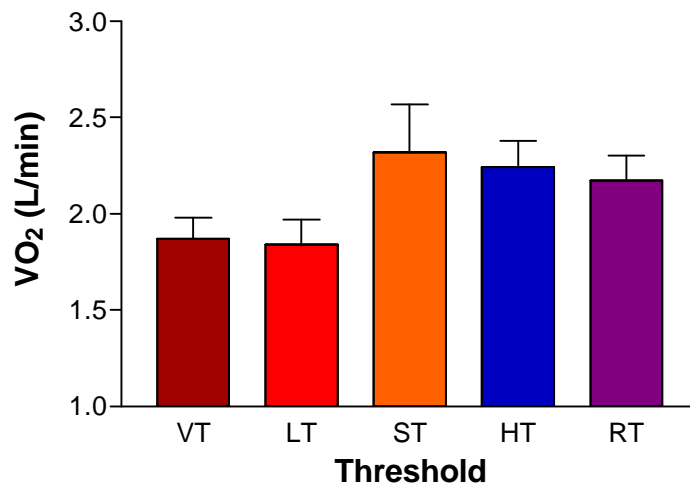


Figure 2: Comparison of the Mean \pm SD data for each threshold variable. Each of HT and RT were significantly different from VT and LT.

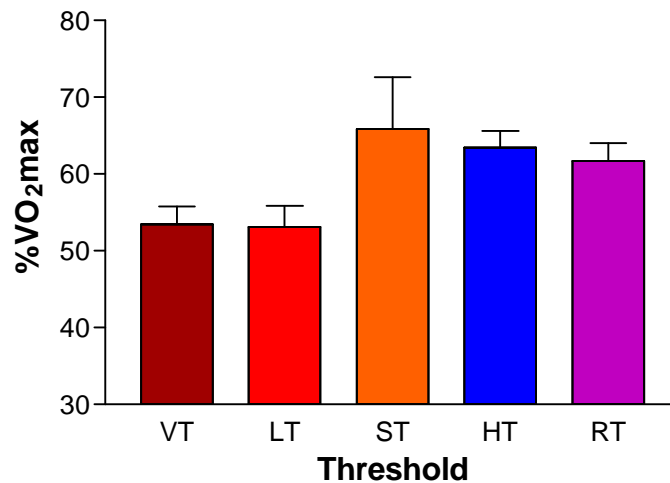


Figure 3: Comparison of the Mean \pm SD data for each threshold variable. Each of HT and RT were significantly different from VT and LT.

A second one-way (5 level) ANOVA was then performed examining the relationship between % VO_2 max of threshold occurrence and the threshold variables (Figure 3). A significant main effect for the threshold intensity variable ($p=0.047$) was demonstrated. Tukey-Kramer Post Hoc analysis for unequal cell size showed that RT was significantly different from LT and VT ($p=0.023$ and $p=0.05$ respectively). HT was also significantly different from LT and VT ($p=0.04$, $p=0.048$ respectively). There were no significant differences between the other variables.

Slope Comparisons

The mean slope for the SBP curve below the threshold was 32.0 ± 4.22 , and the mean slope above the threshold was 14.32 ± 4.61 (Table 3). The slope data represent the mean \pm SD of the slopes for the individual regression line as determined for each subject.

Table 3. Comparisons of the Main Effect Slopes of the Linear Regression Lines Related to the SBP, HR and RPP to VO_2 pre and post-threshold.

<i>Variable</i>	<i>Below Threshold</i>	<i>Above Threshold</i>	<i>Significance</i>
<i>SBP mmHg/L</i>	32.00 ± 15.79	14.32 ± 17.25	0.000
<i>HR beats.l</i>	35.02 ± 7.03	33.04 ± 19.16	0.945
<i>RPP</i>	8.30 ± 1.42	3.94 ± 22.34	0.251

Systolic Blood Pressure Slope Comparisons

Two-way (response x pre/post threshold) ANOVA was used to examine the difference between the SBP slopes. Eight of the 14 subjects demonstrated a decreased post-threshold slope, while 6 subjects demonstrated definitive increased post-threshold responses.

The results of the ANOVA showed a significant interaction between the slope pre and post-threshold and subject response ($p=0.000$). Simple effects analysis showed that there was no significant difference between the slopes of the subjects who demonstrated increased slopes post threshold ($p=0.365$). When simple effects analysis was performed, there was a significant difference noted between the pre and post threshold slopes of the subjects who exhibited a decreased post threshold response ($p=0.000$). These data are presented in Table 4.

Table 4. Comparison of the SBP slopes of the linear regression lines for individuals with increased or decreased slopes post-threshold.

<i>Variable</i>	<i>Below ST (N=6)</i>	<i>Above ST (increase slope)</i>	<i>p-value</i>	<i>Below ST (N=8)</i>	<i>Above ST (decrease slope)</i>	<i>p-value</i>
<i>SBP (mmHg/L)</i>	19.76 ± 15.15	22.89 ± 17.25	0.364	41.18 ± 23.54	7.89 ± 17.25	0.000

The slope data represent the Mean \pm SD of the slopes for the individual regression line as determined for each subject.

Heart Rate Threshold Slope Comparisons

Table 4 exhibits the comparison between the pre and post-threshold values for HR. There was no significant difference between the slopes for the main effect of HR response. However, eight subjects had a decreased HR response slope post-threshold. Consequently, the slope responses were analyzed using a two-way (response x pre/post threshold) ANOVA. The results of the ANOVA showed a significant interaction between slope response pre and post threshold ($p=0.00012$). Simple effects analysis showed a significant difference in the slopes pre and post threshold for those subjects who demonstrated an increased HR response post threshold ($p=0.0028$). The simple effects analysis also showed a significant difference between the slopes of the subjects that demonstrated a decreased HR response post-threshold ($p=0.0012$) (Table 5).

Table 5. Comparison of the HR slopes of the linear regression lines for individuals with increased or decreased slopes post-threshold.

<i>Variable</i>	<i>Below HT (N=6)</i>	<i>Above HT (increase slope)</i>	<i>p-value</i>	<i>Below HT (N=8)</i>	<i>Above HT (decrease slope)</i>	<i>p-value</i>
HR beats/L	34.35±9.73	49.45±24.36	0.0028	35.52±10.4	20.80±13.96	0.0012

The slope was the Mean±SD of the slopes for the individual regression line as determined for each subject.

Rate Pressure Product Slope Comparisons

All subjects exhibited a RPP threshold. In this analysis, eight of the subjects exhibited an increased RPP response post-threshold and six of the subjects exhibited a decreased RPP response post-threshold. The difference between RPP response pre and post threshold was examined using a two-way (response x pre/post threshold) ANOVA (Table 6). There was no significant difference between the pre and post-threshold slopes for the pooled data ($p=0.251$).

There was a significant interaction between post-threshold response and the pre/post-threshold difference ($p=0.042$). Simple effects analysis showed that there was a significant difference between the pre-threshold slope and the post-threshold slope for those individuals with an accelerated RPP response post-threshold ($p=0.000$). There was no significant difference between the pre and post-threshold slopes for the decelerated response ($p=0.493$). The means±SD can be seen in Table 6.

Table 6. Comparison of the RPP slopes of the linear regression lines for individuals with increased or decreased slopes post-threshold.

<i>Variable</i>	<i>Below RT (N=8)</i>	<i>Above RT (increase slope)</i>	<i>p-value</i>	<i>Below RT (N=6)</i>	<i>Above RT (decrease slope)</i>	<i>p-value</i>
RPP	9.42±3.29	14.10±3.70	0.000	7.8±2.24	-9.5±20.02	0.493

The slope data represent the Mean±SD of the slopes for the individual regression line as determined for each subject.

DISCUSSION

Systolic Blood Pressure Response to Incremental Exercise

Through analysis of individual subject data, it was found that subjects exhibited either an accelerated or decelerated SBP response after the SBP threshold. Many textbooks have stated that SBP demonstrates a linear response to increases in exercise intensity (27,33,44). These statements are true in clinical exercise testing situations where blood pressure is generally obtained every 3 minutes, or at the end of every exercise stage. This study collected SBP beat-by-beat, resulting in a much more discrete examination of the SBP response and the finding that the SBP exhibits a quadratic, non-linear response to incremental exercise.

Although SBP continued to increase with increases in exercise intensity, meeting ACSM guidelines for exercise testing (1), the rate of this increase did not continue to change in four subjects and eventually decreased in 8 subjects. These results are in contrast to the results presented by Spence et.al. (3) and Tanaka et.al. (38). Both of these studies reported an increase in SBP response after the LT, as both authors found only an increased post-

LT response. Although the purpose of either study was not to examine the SBP response before and after the LT, the ST occurred after the LT and it can be assumed that similar dynamics occurred in each study.

There are many possible explanations for the SBP response noted in this study. The first, most simple explanation for the decelerated SBP response during incremental exercise could be due to the SV reaching maximal output at approximately 40-50% VO_2max (33,34,39). In these individuals, HR might not increase enough to compensate and cause an increase in cardiac output ($\text{HR} \times \text{SV}$) at a rate great enough to increase the SBP response. This could have resulted in a blunted increase in SBP ($\text{cardiac output} \times \text{TPR}$).

A second possible explanation for the blunted post-threshold SBP response could be due to increased peripheral vasodilation. The eight individuals that had a blunted SBP response to graded cycle exercise could have had an increased vasodilation of the arterioles that supply the skeletal muscle. This action would decrease TPR and allow the SBP response to be blunted post-threshold. This response is one mechanism responsible for the post-exercise hypotension observed after dynamic leg exercise (19).

These conclusions are supported by Martin et.al. (25) who found a blunted SBP response to isoproterenol after high intensity exercise. The decelerated post-threshold SBP response could be a complex interaction of reduced stroke volume, increased skeletal muscle vasodilation due to β_2 mediated vasodilation, vasodilation due to local factors, and β_1 receptor down regulation.

Heart Rate Response to Incremental Exercise

In this study, it was found that eight of the subjects demonstrated a decelerated, post-threshold HR response to incremental exercise, while six of the subjects showed an accelerated, post-threshold HR response. Consequently, ninety-three percent of the subjects exhibited a HT. Nevertheless, there were no differences in the pre-threshold responses of either group. These findings are similar to most of the literature pertaining to the HT (5,8,14,15). However, the existence of this phenomenon is still controversial in the literature since not all studies show a significant number of subjects exhibiting a HT (17,24). However, Hoffman et al. (15) noted that the majority of their subjects exhibited a HT. They also found that the subjects exhibit either an accelerated or decelerated HR deflection in response to incremental exercise.

The majority of the studies regarding the HT and the HR response to graded exercise were concerned with determining the relationship of the HT to the LT (3,30). Few studies concerned with the HT and HR response to exercise have specifically addressed the pre and post-threshold response to incremental exercise. In this study, both the accelerated and decelerated post-threshold HR responses were significantly different from their respective pre-threshold responses. Again, when examining the HR response, it is important to note that although eight subjects exhibited a blunted post-threshold response to graded exercise, the overall HR response revealed an accelerated increase with increasing exercise intensity.

The differences between an accelerated or decelerated HR response post-threshold could be associated with a change in the myocardial β_1 -adrenergic receptors in certain individuals (11). Eysmann et al. (11) demonstrated that a possible down-regulation of the β_1 -adrenergic receptors can occur during exercise. Pokan et al. (30) also suggested this as a mechanism for a flattening of the HR curve after the HT in certain individuals.

As determined in this study, the HR response to exercise is very individualized. Pokan et al. (29) examined the left ventricular ejection fraction (LVEF) during cycle ergometry. It was found that when the LVEF remains constant in individuals during increasing exercise intensity, there is a decelerated HR response. When the LVEF decreases at higher exercise intensities, the reduced SV is usually compensated for by an increased HR response. In these individuals there was either no decrease in the HR curve or actually a positive inflection in the HR curve.

In conclusion, the post-threshold HR response to incremental exercise is very individualized and any conclusions drawn from HR data must account for this individuality.

Rate pressure product response to incremental exercise

The RPP responded as predicted, with a curvilinear response to incremental exercise to exhaustion. All subjects had a threshold response. There is little research pertaining to the shape of the RPP curve during incremental exercise. Both Tanaka et.al. (38) and Riley et.al. (32) examined the RPP response and found a breakpoint, or threshold, response. Both authors then examined that relationship between the RPP breakpoint and the LT and found a strong relationship (32,38).

Tanaka et al. (38) also examined the post-threshold RPP response. It was found that the RPP response was accelerated in all subjects after the LT. In the present study, it was found that there was a significant interaction between the group (post-threshold response) and pre- and post-thresholds. The post-threshold RPP response significantly increased from pre-threshold in 8 of the subjects, with 6 of the subjects showing non-significant, decelerated post-threshold responses. It should be noted that although there is a seemingly large difference in the means between the pre and post-threshold response in the group showing post-threshold RPP deceleration, the post-threshold response is associated with a high amount of variability. At this time, there is no explanation for this variability.

The RPP acceleration after the LT was explained by Tanaka et al. (38) to result from the increasing influence of the catecholamines on HR and SBP, causing increased myocardial oxygen demands. The acceleration of the post-threshold RPP response in the six individuals may be due to similar factors, including a catecholamine-induced increase in HR, SV, and cardiac output. It has been shown previously that the influence of the catecholamines can increase HR, SV and cardiac output (11,18,36,37,39) and SBP (18,37). All of these factors can also affect the RPP. An increase in HR would increase the RPP, assuming that the SBP remains unchanged. Likewise, an increase in SV, cardiac output, or TPR would increase SBP and increase RPP.

The HR, SBP and RPP responses found in this study demonstrate the individuality of the cardiovascular response to dynamic incremental exercise. Although curvilinear responses were found in the majority of the subjects, the post-threshold responses were extremely varied. More research needs to be conducted using beat-by-beat technology examining the suggested factors that can influence HR, SBP, and RPP response to exercise.

The Relationships between the Cardiovascular and Metabolic Thresholds as a Function of Oxygen Consumption

The hypothesis that all threshold values would occur at similar exercise intensities (VO_2 , % $\text{VO}_{2\text{max}}$) was not supported. One-way ANOVA showed that significant differences were observed between the HT and the LT, VT (VO_2 , % $\text{VO}_{2\text{max}}$) and RT, and the LT and VT (VO_2 , % $\text{VO}_{2\text{max}}$). These results are in contradiction to much of the research on the HT, as this research suggests that the HT and LT occur at similar power outputs (14,15) and exercise intensities (5). Bunc et.al. (5) also showed that there was no significant difference between the HT and LT.

Kuipers et.al. (24) showed that the HR deflection does not coincide with the LT during incremental exercise. Jones and Doust (17) questioned the reliability of the HT due to the fact that only 40% of the subjects tested demonstrated a repeated HT. These authors suggested that the HT does not occur consistently and that it does not occur at the same exercise intensity in consecutive exercise tests.

The literature studying the HT does not develop any consensus about the HT and its existence. In the present study, the HT was evident in the majority of the subjects and occurred at a significantly higher exercise intensity

(VO_2 , % $\text{VO}_{2\text{max}}$) than either the LT or VT (Figures 2, 3). This result could be due to the fact that although the LT, VT and HT have been theorized to occur in response to an increase in catecholamine concentration (5), the threshold phenomenon are due to different mechanisms. The LT occurs in response to catecholamine-induced stimulation of glycogenolysis and the mass action effect on glycolytic metabolism (26,28,31). The VT is a response to by-products of glycolytic metabolism (9,22,41). There are other factors that contribute to the occurrence of the LT. These factors include an increased fast-twitch fiber activation (16), a decreased ability to clear blood lactate, or a decrease in cytosolic redox (42). The changes in the HR response to exercise are due, not only to increased catecholamine secretion (23,27,40), but also to chemoreceptor and baroreceptor influences (10,20,35). Although the autonomic nervous system is the major regulatory system influencing HR, there are other factors independent of the autonomic nervous system that influence HR. Likewise, there are other factors independent of catecholamine secretion that influence blood lactate concentrations during incremental exercise.

Pokan et.al. (30) studied the relationship between catecholamine concentrations and the HT. They found that there was a low correlation between the LT and HT ($r=0.30$), and they also reported low correlations between the HT and the norepinephrine (NE) and epinephrine (EP) thresholds ($r=0.118$, $r=0.192$). In the present study, it was found that there are high and significant correlations between the HT and each of the LT and VT ($r=0.838$, $p=0.000$ and $r=0.836$, $p=0.000$). These results show that there are significant relationships between the HT and the LT and VT, but conclusions drawn from correlational data must be interpreted with caution (4). The correlations in this study show, for example, that when a subject has a high VO_2 value at the HT, that subject also has a high VO_2 at the LT value. This results in a high r -value, but this test does not determine if the VO_2 values for each threshold occur at similar exercise intensities. Correlational studies show the relationship of the data points to each other, but it is not appropriate to use these results to suggest that the thresholds occur at similar or dissimilar exercise intensities.

There are no studies that have attempted to compare the RT and LT/VT as a function of oxygen consumption. Tanaka et.al. (38) reported that there was a high correlation between the VO_2 at the occurrence of the RT and LT ($r=0.900$); however, they did not further investigate this relationship. Similarly, Riley et.al.(32) reported a high correlation between the LT and RT ($r=0.865$).

In the present study it was found that the RT occurred at significantly higher exercise intensities (VO_2 and % $\text{VO}_{2\text{max}}$) than either the LT or VT. As with the HT, there are factors other than catecholamine secretion that could influence the LT and, therefore, the VT. There are also other factors that could influence the RT than catecholamine secretion. HR can be influenced by chemoreceptor and baroreceptor influences (10,20,35). SBP can be influenced by increases or decreases in SV due to changes in venous return (3) or decreases in left ventricular function independent of catecholamine concentration (29). These other factors could influence the occurrence of the HT, LT, and VT independent of the catecholamine influence. This suggests that the catecholamines can influence the response to incremental exercise, but there are also other influences that could affect the exercise intensity at which the thresholds occur. This study is unique in the fact that it is the only study to compare the occurrence of the LT, VT, ST, HT and RT as a function of oxygen consumption.

When the relationship between the RT and the LT/VT was compared, it was found that there was a significant relationship between the RT and LT ($r=0.664$, $p=0.018$). There was also a significant relationship between the RT and VT ($r=0.711$, $p=0.004$). Again, this result cannot be used to state that the thresholds occur at similar exercise intensities, but that when a subject has a high VO_2 value for the LT that subject can also have high VO_2 value for the RT.

One interesting observation pertains to the ST. The ST demonstrated the highest mean threshold value for absolute oxygen consumption and % $\text{VO}_{2\text{max}}$, but there was no significant difference between the ST and any of

the other threshold values (Tables 6, 7). If the standard deviation is examined (Table 6,7) then the most likely explanation for the lack of a significant difference between the ST and the other threshold variables is due to the individual variability of the VO_2 values at the ST. Williamson et al. have shown inter-individual variation in the blood pressure response to exercise (43). When the relationships between the ST and LT/VT are examined this variation in the ST value becomes more apparent. There is a non-significant relationship between the ST and LT ($r=0.371$, $p=0.213$) and the VT ($r=0.379$, $p=0.182$). When a subject has a high VO_2 value for the LT, that subject does not necessarily have a high ST value. Given a VO_2 value for the ST, the VO_2 at the occurrence of the LT could not be predicted with any degree of accuracy. But again this test could not be used to suggest that the VO_2 values for the LT and ST occur at significantly different exercise intensities. These findings show the need for further research to determine the factors that contribute to the variability of the ST.

A final major finding of this study was that the RT and the HT occur at significantly higher exercise intensities (VO_2 , % $\text{VO}_{2\text{max}}$) than either the LT or VT. Using either the RT or HT as a non-invasive indicator of a shift in metabolism is not valid based on the findings of this study. However, the finding that a majority of the subjects exhibited a HT and RT, and by inference a threshold in the MVO_2 , this finding could be used in exercise prescription, especially for those individuals concerned about the cardiac response to exercise. In fact, using these threshold values to prescribe exercise routines could be more applicable for these individuals due to the exercise intensity being more related to myocardial work than to increased glycolytic metabolism.

Recommendations

Based on the data obtained in this project the following recommendations were developed:

1. Additional research should be conducted, using beat-by-beat technology, to determine the factors that influence the post-threshold HR, SBP and RPP responses to incremental exercise.
2. The role, or lack thereof, of the catecholamines and the adrenergic receptors could be elucidated by using different pharmacological interventions.
3. The β -receptor contribution to SBP and RPP can also be examined by blocking the receptors with β -receptor antagonists.
4. The HR, SV, LVEF and cardiac output contributions to the HR, SBP and RPP responses could be physically examined by using echocardiography or radionuclide imagery during incremental exercise.
5. It is also recommended that the manufacturers of the tonometric system develop an integrated system to determine the HT, ST and RT in one unit that could be used in cardiac rehabilitation settings. The major factor hindering the development of this type of system is the lack of an objective method to determine the threshold point.
6. It is strongly recommended that further research be conducted to develop a more precise and objective method to determine various physiological thresholds regions.

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