



Original Article

## Double product break point estimates ventilatory threshold in individuals with type 2 diabetes

CAIO VICTOR DE SOUSA<sup>1)a\*</sup>, MARCELO MAGALHÃES SALES<sup>1,2)a</sup>, SAMUEL DA SILVA AGUIAR<sup>1)</sup>, DANIEL ALEXANDRE BOULLOSA<sup>1)</sup>, THIAGO DOS SANTOS ROSA<sup>1)</sup>, VILMAR BALDISSERA<sup>3)</sup>, HERBERT GUSTAVO SIMÕES<sup>1)</sup>

<sup>1)</sup> Graduate Program on Physical Education, Universidade Católica de Brasília-UCB: Brasília DF, Brazil, EPTC, QS07, LTI s/n. Bloco G Sala 15, CEP 72030-170 Águas Claras, Taguatinga/DF, Brazil

<sup>2)</sup> Health School, UDF – Centro Universitário, Brazil

<sup>3)</sup> Faculty of Physical Education, Universidade Federal de São Carlos, Brazil

**Abstract.** [Purpose] To verify the identification of the anaerobic threshold through the double product breakpoint (DPBP) method for individuals with type 2 diabetes. [Subjects and Methods] Nine individuals with T2D (7 females; age=63.2 ± 8.9 y) and 10 non-diabetic (ND) (7 females; age=58.3 ± 7.8 y) performed an incremental exercise test on a cycle ergometer. Heart rate (HR), blood pressure (BP) and expired gas were measured at the end of each stage. The ventilatory threshold (VT) and DPBP were considered as the exercise intensities above which an over proportional increases in VE and DP were observed in relation to increasing workload. [Results] No differences were observed between the workloads, HR and VO<sub>2</sub> corresponding to the AT identified respectively by VT and DPBP. For the T2D, strong correlations between VT and DBPB workloads ( $r=0.853$ ), HR ( $r=0.714$ ), and VO<sub>2</sub> ( $r=0.863$ ) were found. These relationships were similar to those found for the control group ( $r=0.923$ ;  $r=0.881$ ; and  $r=0.863$ , respectively). [Conclusion] These results demonstrate that the DPBP enables for the prediction of AT and correlated well the VT in both the T2D and ND participants.

**Key words:** Anaerobic threshold, Systolic pressure, Heart rate

(This article was submitted Jan. 19, 2016, and was accepted Feb. 28, 2016)

### INTRODUCTION

The anaerobic threshold (AT) is a hallmark of the aerobic fitness of athletes<sup>1)</sup>, physically active individuals<sup>3)</sup> and on a minor scale for special populations, such as individuals with type 2 diabetes (T2D)<sup>2, 4, 5)</sup>. AT has been considered the gold standard along with maximum oxygen consumption (VO<sub>2</sub>max) for the evaluation of aerobic fitness and the subsequent prescription of aerobic exercise<sup>6-9)</sup>. Moreover, monitoring of aerobic training adaptations through AT determination may be especially interesting because no maximal effort is needed, and could be safer for individuals with pathologies such as hypertension and diabetes<sup>10, 11)</sup>.

The AT can be identified using several markers representing different physiological systems. For instance, the AT has been determined through the analysis of heart rate variability (HRV)<sup>2)</sup>, blood catecholamines<sup>12)</sup>, blood glucose and lactate<sup>3)</sup>, ventilation and respiratory equivalents<sup>13, 14)</sup>, and the double product (DP)<sup>15-22)</sup>.

Identification of AT through different indices, such as the double product (DP), has been widely utilized for healthy individuals<sup>16, 17, 19)</sup>, athletes<sup>20)</sup> and individuals with cardiovascular diseases<sup>15, 16, 18)</sup>. However, few studies have identified the AT of individuals with T2D through different methods<sup>2, 23)</sup>, while the exercise recommendations for T2D<sup>24)</sup> indicate that these patients should be encouraged to undertake an exercise test before being submitted to physical training. For instance, the AT

\*Corresponding author. Caio Victor de Sousa (E-mail: cvsousa89@gmail.com)

<sup>a</sup>These authors have contributed equally to this work.

©2016 The Society of Physical Therapy Science. Published by IPEC Inc.

This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial No Derivatives (by-nc-nd) License <<http://creativecommons.org/licenses/by-nc-nd/4.0/>>.

of T2D individuals is often observed to be between 60–70% of  $VO_{2max}$ <sup>6, 8, 25</sup>), which is an exercise intensity that has been widely recommended for this population for better blood glucose and cardiovascular control<sup>24</sup>).

Further, previous studies have shown that aerobic exercises performed around AT intensities significantly reduced the blood pressure (BP) of individuals with T2D in the post-exercise period<sup>6–8, 25, 26</sup>), and none of these previous studies reported complications during the experimental sessions, suggesting the desirability of AT identification for this population, since inadequate physical exertion can be a powerful triggering factor of myocardial infarction<sup>27</sup>).

Individuals with T2D often present autonomic dysfunction<sup>28–30</sup>). Compared to healthy individuals, it is therefore likely that they would show a different hemodynamic reaction [heart rate (HR) and BP, and in turn DP] during exercise, such as an exaggerated exercise blood pressure response<sup>31</sup>). This would make AT identification through cardiovascular responses difficult or even impossible. In addition, hypertension and T2D very frequently coexist, since 20% of hypertensive patients have T2D, and 80% of people with T2D are hypertensive<sup>32</sup>). Hypertensiveness, could also affect the hemodynamic responses during exercise, which may in turn complicate AT detection through cardiovascular responses. Sales et al. have presented the feasibility of AT identification for T2D individuals through HRV analyses<sup>2</sup>) and Kumagai et al. identified the double product breakpoint (DPBP) in T2D individuals, but did not compared with any other anaerobic threshold identification method<sup>23</sup>). Thus, we hypothesized that AT could be predicted through the DPBP during exercise performed by T2D individuals, similar to healthy individuals<sup>16</sup>). Moreover, identification of AT through the DPBP would be relevant since the DP can provide information that correlates with myocardial oxygen consumption, which is recognized as a non-invasive indicator of cardiac overload<sup>33, 34</sup>) as well as cardiac ischemic events including acute myocardial infarction<sup>35</sup>). Further, the determination of AT through the DPBP is a simple method that does not depend on the use of complex equipment such as gas analyzers, which are expensive and require the use of specialized technicians to operate them.

The validity of the DPBP in estimating the AT using a sphygmomanometer and stethoscope has not been investigated yet. Experiments have used either automated blood pressure monitor<sup>15–17, 19, 20, 23</sup>) or a cannula inserted into the brachial artery<sup>18</sup>). These procedures are not accessible to most practioners because they require costly equipment as well as highly invasive procedures. In addition, to the best of our knowledge, no study has examined the DPBP as an estimate of the AT in individuals with T2D.

Thus, the purpose of this study was to verify whether or not the AT of T2D individuals can be predicted through the DP method, and to analyze the relationships between the workload (Watts), oxygen consumption ( $VO_2$ ) and HR obtained by the DPBP and the ventilatory threshold (VT) methods.

## SUBJECTS AND METHODS

After approval from the local human research ethics committee (*Universidade Católica de Brasília*: 011/2011), and obtaining the written informed consent of the volunteers, 11 T2D individuals (8 females), and 10 controls (7 females) were initially selected to participate in this study. Exclusion criteria for participation in this study included previous diagnosis of peripheral neuropathy or retinopathy, as well as diabetic foot ulcerations osteomioarticular complications, the endogenous use of insulin, and/or use of medicines that could have directly affected HR or BP. All the individuals were recruited at a public hospital, and all had been previously assessed using standard tests conducted by endocrinologists and cardiologists. Two participants with T2D were excluded from the analysis because it was not possible to detect their VT and/or DPBP (*Table 1*). Therefore, the statistical power a priori conferred on this sample (n=19) was 82% (power=0.82). The T2D individuals were receiving medical treatments of oral hypoglycemics (*Metformin*, *Metformin + Glibenclamide*). The general characteristics of the volunteers are presented in *Table 2*.

All experimental sessions were carried out at the Laboratory of Physical Evaluation and Training (LAFIT) of the *Universidade Católica de Brasília* 2 h after volunteers eaten a standardized breakfast of a moderate glycemic index meal without any substances that could have directly affected the HR and/or the BP. The participants were given a physical evaluation including anthropometric measurements (body mass, height and body fat percentage) and then performed an incremental

**Table 1.** The number of cases in which the ventilatory threshold (VT) and the double product breakpoint (DPBP) were detected by all observers

Parameter	T2D (n)	ND (n)	TOTAL
Participants initially screened	11	10	21
VT detected	10	10	20
DPBP detected	9	10	19
HR primarily responsible for DPBP	1	1	2
SBP responsible for DPBP	5	4	9
Participants included in the analysis	9	10	19

T2D: individuals with type 2 diabetes; ND: individuals without T2D; VT: ventilatory threshold; DPBP: double product breakpoint; HR: heart rate; SBP: systolic blood pressure

exercise test (IT). During the IT, measurements of HR, BP and ventilatory variables were continuously monitored. To carry out the measurement of body fat percentage by bipolar bioimpedance, the individuals were told to: avoid caffeine and alcohol for 24 hours before the test; not perform physical activity or eat a heavy meal for at least 4 hours before the test; and suspend diuretic medication 24 hours before the test<sup>36</sup>.

The IT was performed on a cycle ergometer (Monark, 828 E, Valburg/Sweden) at 60 rpm, and began one minute at zero Watt (W) load, followed by increments of 15 W every 3 minutes until voluntary exhaustion. The cardiologist of the laboratory monitored the electrocardiogram (ECG) of the volunteers throughout the test in order to identify any abnormality.

During the period before the exercise, as well as during the last 30 seconds of each stage, blood pressure (BP) was measured non-invasively by the auscultatory method using a mercury column sphygmomanometer (Tycos Instrumentos Hospitalares, São Paulo, Brazil). Expired gases were measured during the IT through a gas analyzer (Metalyzer 3B, Cortex Biophysik, Leipzig, Germany) that was previously calibrated with a 3-L syringe (flow calibration) and a standard mixed gas containing 4.9% CO<sub>2</sub> and 17% O<sub>2</sub> (gas calibration). The values of ventilation (VE) and oxygen uptake (VO<sub>2</sub>) were recorded breath-by-breath, but, they only were analyzed every 20 s in each 3-min stage.

The ventilation (VE) kinetics during the IT stages were used to identify the occurrence of VT by two experienced researchers. This was considered to be the exercise intensity above which an over proportional increase in VE was observed in relation to increasing workload<sup>37</sup>.

Systolic blood pressure (SBP) and HR were collected in the final minute of each stage. The DPBP was considered to be the exercise intensity at which an over proportional increase in DP was observed in relation to increasing workload. Two experienced researchers determined DPBP, and when a discrepancy between them occurred, a third researcher was consulted. All the plots were blinded, therefore the researchers did not know the identity of the subjects or the conditions of the test. It is noteworthy that the same evaluator, which did not participated in the determination of DPBP and VT, carried out all collections of BP and HR. These procedures were carried out to ensure that researchers remained 'blinded' to the analysis.

After assessing the normality and homogeneity of data through the Shapiro-Wilk and Levene's test, respectively, the data were presented as means ( $\pm$ ) standard deviation. In order to compare the characteristics of the groups, the Student's t-test for independent samples was conducted. Between and within groups comparisons were carried out using Split-Plot ANOVA (Mixed ANOVA). When any of the dependent variables did not show sphericity in Mauchly's test, the epsilon of Greenhouse-Geisser was used to analyze the *F* statistic. Since there were only two groups, the post hoc is unable to locate the differences, therefore, it was necessary to apply parallel test, named: pairwise comparisons. Thus, the paired Student's t-test was used to compare the anaerobic threshold identification methods within groups (VT and DPBP). The Effect size within (VT and DPBP) and between groups (T2D and ND) was evaluated using Cohen's *d*<sup>38</sup>. Pearson's correlation coefficients were used to verify the relationships between the studied methods used to determine anaerobic threshold. For the sample size calculation, the statistical power (1- $\beta$ ) was used a priori, using comparison analysis applied (ANOVA for repeated measures), an effect size of *f*=0.35 and an alpha of 5%. Furthermore, the Bland and Altman technique was used to verify the level of agreement between the different methods<sup>39</sup>. A significance level of 5% (*p*<0.05) was used. All the procedures were carried out using the Statistical Package for the Social Sciences (SPSS 20.0) and G\*Power (version 3.1.9.2).

## RESULTS

The DPBP was identified in all 11 ND individuals and in 9 from 11 T2D individuals (81.8%), with SBP being primarily responsible for the DPBP in almost half of all cases (Table 1).

The results presented in Table 3 show no there were no significant differences between the workloads (watts), HR (bpm)

**Table 2.** Characteristics of the individuals with type 2 diabetes (T2D) and non-diabetic (ND) controls

	T2D (n=9)	ND (n=10)
Age (yrs)	63.2 $\pm$ 8.9	58.3 $\pm$ 7.8
Body mass (kg)	70.2 $\pm$ 14.1	72.5 $\pm$ 19.2
Height (m)	1.59 $\pm$ 0.1	1.61 $\pm$ 0.11
BMI (kg·m <sup>-2</sup> )	26.3 $\pm$ 5.0	27.1 $\pm$ 4.1
Body Fat (%)	37.4 $\pm$ 5.6	34.5 $\pm$ 7.0
HbA <sub>1c</sub> (%)	6.8 $\pm$ 1.3	5.2 $\pm$ 0.2*
VO <sub>2peak</sub> (ml·kg <sup>-1</sup> ·min <sup>-1</sup> )	21.4 $\pm$ 3.5	22.6 $\pm$ 5.1
Maximal heart rate (bpm)	150.2 $\pm$ 24.6	155.2 $\pm$ 12.6

Data expressed as mean  $\pm$  standard deviation.

T2D: individuals with type 2 diabetes; ND: individuals without T2D; BMI: body mass index; HbA<sub>1c</sub>: glycated hemoglobin; \*significant difference (*p*<0.05)

**Table 3.** Workload (watts), heart rate (bpm) and oxygen uptake (ml·kg<sup>-1</sup>·min<sup>-1</sup>) measurements at VT and DBBP of the T2D and ND groups

Parameter		T2D (n=9)	ND (n=10)
Workload (watts)	DPBP	45 $\pm$ 21.2	60 $\pm$ 29.2
	VT	40 $\pm$ 24.9	63 $\pm$ 30.6
Heart rate (bpm)	DPBP	124.7 $\pm$ 13.6	119.1 $\pm$ 17.4
	VT	122.1 $\pm$ 14.6	121.4 $\pm$ 19.1
VO <sub>2</sub> (mL·kg <sup>-1</sup> ·min <sup>-1</sup> )	DPBP	14.6 $\pm$ 2.4	15.1 $\pm$ 2.9
	VT	14.1 $\pm$ 3.4	15.3 $\pm$ 3.6

Data expressed as mean  $\pm$  standard deviation.

T2D: individuals with type 2 diabetes; ND: individuals without T2D; DPBP: double product breakpoint; VT: ventilatory threshold

and  $\text{VO}_2$  corresponding to the AT identified by the VT and DPBP methods. Further, for the T2D group, strong and significant correlations ( $p < 0.01$ ) between workloads at VT and DPBP ( $r = 0.853$ ), HR ( $r = 0.714$ ), and  $\text{VO}_2$  ( $r = 0.863$ ) were found. Strong and significant correlations ( $p < 0.001$ ) were also found in the ND group for all parameters investigated; they were  $r = 0.923$  for the workload at VT and DPBP,  $r = 0.881$  for HR, and  $r = 0.863$  for  $\text{VO}_2$ .

The Bland and Altman analyses indicate there was good agreement for the  $\text{VO}_2$  ( $\text{L} \cdot \text{min}^{-1}$ ) corresponding to VT and DPBP based on the low bias and narrow limits of agreement [Bias ( $\pm 95\%$  of confidence interval)] for VT and DPBP [0.03 (0.11)  $\text{LO}_2 \cdot \text{min}^{-1}$ ] for the T2D group, and VT and DPBP [-0.02 (0.13)  $\text{LO}_2 \cdot \text{min}^{-1}$ ] for the ND group.

## DISCUSSION

The main finding of this research is that the DPBP can be used to estimate the AT of T2D and ND individuals, since there were no significant ( $p < 0.05$ ) differences between the workloads (Watts), HR and  $\text{VO}_2$  of the VT and DPBP methods. Furthermore, the effect size analyses also demonstrated that the visual differences of the variables mentioned above, had little (small) or no effect, according to Cohen's  $d^{38}$ .

From a physiological point of view, it is presumed that the DP could be a marker of AT determination, to the extent that, when performing an incremental exercise test, there is a gradual reduction in the vagal activity and consequent increase in sympathetic nervous activity. However, at a certain intensity, a complete vagal withdrawal is expected and this presents as a persistent depression of the autonomic nervous system until the end of the tests, featuring the HRV threshold<sup>2, 40, 41</sup>. Accordingly, there is a marked increase in sympathetic nerve activity, which results in a significant elevation of catecholamines, which is known as the catecholamines threshold<sup>12</sup>. The increased levels of catecholamines, in turn, result in a marked increase in BP and HR, and thus on DP, and as a result the DPBP<sup>15-19</sup>. Furthermore, increased levels of catecholamines also produce a significant increase in glycolytic activity<sup>42</sup>, enabling for the identification of the glycemic and lactate thresholds<sup>3</sup>. This increased glycolysis also contributes to a sharp increase in  $\text{CO}_2$  production which causes hyperventilation and results in the appearance of the VT<sup>43</sup>.

Consequently, it is reasonable to infer that, similar to other markers (HRV, catecholamines, glucose, lactate and ventilation), the DP can also be used to determine the AT, with the advantage of it being a non-invasive and low cost method. Exercise tests involving blood collection and biochemical measures, and the use of expensive apparatus for expired gases analysis, as well as trained professionals who know protocols are high-priced, and thus inaccessible to a major portion of the T2D population.

Interestingly, although there was no significant difference of the workloads (Watts) between the groups (T2D and ND), the effect size of the difference was considered medium ( $d = 0.588$ ) for DPBP and large ( $d = 0.824$ ) for VT. From a practical point of view, it is noteworthy that the effect size is considered the main finding of a quantitative study, with the statistical significance ( $p$ ) being the least important<sup>44, 45</sup>, since the relevant point is the magnitude of differences<sup>45</sup>.

With regard to the internal load variables (HR and  $\text{VO}_2$ ), these did not present significant differences ( $p > 0.05$ ) between the groups (T2D and ND), while the effect sizes of the differences were small or even null. Additionally, intra-group differences were always null. Moreover, the fact that significant differences ( $p > 0.05$ ) were not observed between the internal load variables (HR and  $\text{VO}_2$ ) of T2D and ND groups, may be partly explained by the higher cardiorespiratory capacity of the healthy individuals, as they reached an absolute external load (Watts), but with a similar cardiorespiratory responses (HR and  $\text{VO}_2$ ). Additionally, another aspect that should be considered regarding the absence of significant differences between the T2D and ND groups, is that they presented quite similar characteristics (Table 2), since the only variable that was different between the groups was glycated hemoglobin ( $\text{HbA}_{1c}$ ).

It is noteworthy that the statistics reveal there were strong and significant correlations between workloads (Watts), HR and  $\text{VO}_2$ , and also a good agreement in both the T2D and ND groups. This is in agreement with the study of Riley et al., who reported a strong and significant correlation between  $\text{VO}_2$  at the lactate threshold (LT) and DPBP ( $r = 0.86$ ;  $p < 0.01$ )<sup>16</sup>. Likewise Tanaka et al. also observed a strong and significant correlation between the DPBP and the LT ( $r = 0.90$ ;  $p < 0.01$ ) in a sample of 90 patients<sup>17</sup>. Additionally, Kumagai et al. identified the DPBP in 63 T2D individuals in a submaximal ramp test (rating of perceived exertion of 15) performed on a cycle ergometer<sup>23</sup>. However, it is noteworthy that in that study the DPBP was not compared with any other AT identification method.

Regarding the comparison of DPBP and VT, Brubaker et al. previously demonstrated a strong and significant correlation between the methods ( $r = 0.81$ ,  $p < 0.01$ ) in a progressive test on a treadmill, and suggested that DPBP could be a valid alternative to VT for individuals with coronary artery disease<sup>15</sup>. Also Omiya et al. reported a high and significant association between workloads (Watts) ( $r = 0.95$ ;  $p = 0.01$ ) of both the DPBP and VT of 15 patients with cardiovascular diseases<sup>18</sup>.

Similarly, Hargens et al. conducted an elegant longitudinal study in order to evaluate the effect of eight weeks of aerobic training at vigorous intensity on DPBP and VT. They evaluated 7 men and 11 sedentary women, using a ramp protocol on a cycle ergometer, and observed that HR and  $\text{VO}_2$  at baseline and at the end of the training period were similar ( $p > 0.05$ ) and showed good agreement<sup>19</sup>. The fact that this previous study reported an increase of DPBP after training, confirms it is a reliable and sensitive method of identifying AT adaptations to training.

One limitation of the present study was that the intensity of the maximum lactate steady state (MLSS) was not determined for comparison with the investigated protocols of DPBP and VT. The determination of MLSS is considered the gold standard

among the exercise assessment methods<sup>1)</sup>. Nevertheless, Denadai et al. and van Schuylenbergh indicate that this parameter is not different from the lactate threshold and VT<sup>46–48)</sup>. Thus, it is reasonable to infer that the methods investigated in this study, DPBP and VT, which did not differ between themselves, may also represent the MLSS intensity.

The present study demonstrated that the DPBP can be easily determined during incremental exercise in both T2D and ND controls. Additionally, the DPBP happened at exercise intensities related to the VT in both the populations studied, suggesting that DPBP can be a useful marker of exercise intensity associated with AT.

## ACKNOWLEDGEMENTS

The authors are thankful to the *Conselho Nacional de Desenvolvimento Científico e Tecnológico* (CNPq), *Coordenação de Aperfeiçoamento de Pessoal de Nível Superior* (CAPES) and *Fundação de Apoio a Pesquisa do Distrito Federal* (FAP/DF) for the financial support.

## REFERENCES

- 1) Svedahl K, MacIntosh BR: Anaerobic threshold: the concept and methods of measurement. *Can J Appl Physiol*, 2003, 28: 299–323. [[Medline](#)] [[CrossRef](#)]
- 2) Sales MM, Campbell CS, Morais PK, et al.: Noninvasive method to estimate anaerobic threshold in individuals with type 2 diabetes. *Diabetol Metab Syndr*, 2011, 3: 1. [[Medline](#)] [[CrossRef](#)]
- 3) Simões HG, Campbell CS, Kushnick MR, et al.: Blood glucose threshold and the metabolic responses to incremental exercise tests with and without prior lactic acidosis induction. *Eur J Appl Physiol*, 2003, 89: 603–611. [[Medline](#)] [[CrossRef](#)]
- 4) Simões HG, Hiyane WC, Benford RE, et al.: Lactate threshold prediction by blood glucose and rating of perceived exertion in people with type 2 diabetes. *Percept Mot Skills*, 2010, 111: 365–378. [[Medline](#)] [[CrossRef](#)]
- 5) Katoh J, Hirayama M, Murakami M, et al.: Physical fitness and exercise endurance measured by oxygen uptake kinetics in patients with type 2 diabetes mellitus. *J Phys Ther Sci*, 2001, 13: 83–85. [[CrossRef](#)]
- 6) Motta DF, Lima LC, Arsa G, et al.: Effect of type 2 diabetes on plasma kallikrein activity after physical exercise and its relationship to post-exercise hypotension. *Diabetes Metab*, 2010, 36: 363–368. [[Medline](#)] [[CrossRef](#)]
- 7) Morais PK, Campbell CS, Sales MM, et al.: Acute resistance exercise is more effective than aerobic exercise for 24h blood pressure control in type 2 diabetics. *Diabetes Metab*, 2011, 37: 112–117. [[Medline](#)] [[CrossRef](#)]
- 8) Karoline de Morais P, Sales MM, Alves de Almeida J, et al.: Effects of aerobic exercise intensity on 24-h ambulatory blood pressure in individuals with type 2 diabetes and prehypertension. *J Phys Ther Sci*, 2015, 27: 51–56. [[Medline](#)] [[CrossRef](#)]
- 9) Mynarski W, Cholewa J, Rozpara M, et al.: Recommendations for health-enhancing physical activities in type 2 diabetes patients. *J Phys Ther Sci*, 2015, 27: 2419–2422. [[Medline](#)] [[CrossRef](#)]
- 10) Zanuso S, Jimenez A, Pugliese G, et al.: Exercise for the management of type 2 diabetes: a review of the evidence. *Acta Diabetol*, 2010, 47: 15–22. [[Medline](#)] [[CrossRef](#)]
- 11) Al Saif A, Alesnany S: Aerobic and anaerobic exercise training in obese adults. *J Phys Ther Sci*, 2015, 27: 1697–1700. [[Medline](#)] [[CrossRef](#)]
- 12) Mazzeo RS, Marshall P: Influence of plasma catecholamines on the lactate threshold during graded exercise. *J Appl Physiol* 1985, 1989, 67: 1319–1322. [[Medline](#)]
- 13) Wasserman K: Determinants and detection of anaerobic threshold and consequences of exercise above it. *Circulation*, 1987, 76: VI29–VI39. [[Medline](#)]
- 14) Whipp BJ: Physiological mechanisms dissociating pulmonary CO<sub>2</sub> and O<sub>2</sub> exchange dynamics during exercise in humans. *Exp Physiol*, 2007, 92: 347–355. [[Medline](#)] [[CrossRef](#)]
- 15) Brubaker PH, Kiyonaga A, Matrazzo BA, et al.: Identification of the anaerobic threshold using double product in patients with coronary artery disease. *Am J Cardiol*, 1997, 79: 360–362. [[Medline](#)] [[CrossRef](#)]
- 16) Riley M, Maehara K, Pórszász J, et al.: Association between the anaerobic threshold and the break-point in the double product/work rate relationship. *Eur J Appl Physiol Occup Physiol*, 1997, 75: 14–21. [[Medline](#)] [[CrossRef](#)]
- 17) Tanaka H, Kiyonaga A, Terao Y, et al.: Double product response is accelerated above the blood lactate threshold. *Med Sci Sports Exerc*, 1997, 29: 503–508. [[Medline](#)] [[CrossRef](#)]
- 18) Omiya K, Itoh H, Harada N, et al.: Relationship between double product break point, lactate threshold, and ventilatory threshold in cardiac patients. *Eur J Appl Physiol*, 2004, 91: 224–229. [[Medline](#)] [[CrossRef](#)]
- 19) Hargens TA, Griffin DC, Kaminsky LA, et al.: The influence of aerobic exercise training on the double product break point in low-to-moderate risk adults. *Eur J Appl Physiol*, 2011, 111: 313–318. [[Medline](#)] [[CrossRef](#)]
- 20) Silva NM, Pereira LN, Tucher G: Relação entre o limiar de lactato e o break point do duplo produto em jogadores de futebol. *Bra J Biomotricity*, 2011, 5: 9.
- 21) Ohtsuki K, Watanabe S: Effect of incremental load of circulatory response on double product break point detection. *J Phys Ther Sci*, 2007, 19: 293–298. [[CrossRef](#)]
- 22) Ohtsuki K, Watanabe S: The double-product-break-point derived from measurements with a digital automatic sphygmomanometer. *J Phys Ther Sci*, 2008, 20: 1–5. [[CrossRef](#)]
- 23) Kumagai S, Kai Y, Hanada H, et al.: Relationships of the systolic blood pressure response during exercise with insulin resistance, obesity, and endurance fitness in men with type 2 diabetes mellitus. *Metabolism*, 2002, 51: 1247–1252. [[Medline](#)] [[CrossRef](#)]
- 24) Colberg SR, Sigal RJ, Fernhall B, et al. American College of Sports Medicine American Diabetes Association: Exercise and type 2 diabetes: the American College of Sports Medicine and the American Diabetes Association: joint position statement executive summary. *Diabetes Care*, 2010, 33: 2692–2696. [[Medline](#)] [[CrossRef](#)]



- 25) Lima LC, Assis GV, Hiyane W, et al.: Hypotensive effects of exercise performed around anaerobic threshold in type 2 diabetic patients. *Diabetes Res Clin Pract*, 2008, 81: 216–222. [[Medline](#)] [[CrossRef](#)]
- 26) Noh JW, Park JE, Jung JH, et al.: Exercise is associated with metabolism regulation and complications in Korean patients with type 2 diabetes. *J Phys Ther Sci*, 2015, 27: 2189–2193. [[Medline](#)] [[CrossRef](#)]
- 27) Nawrot TS, Perez L, Künzli N, et al.: Public health importance of triggers of myocardial infarction: a comparative risk assessment. *Lancet*, 2011, 377: 732–740. [[Medline](#)] [[CrossRef](#)]
- 28) Jermendy G: Clinical consequences of cardiovascular autonomic neuropathy in diabetic patients. *Acta Diabetol*, 2003, 40: S370–S374. [[Medline](#)] [[CrossRef](#)]
- 29) Carnethon MR, Jacobs DR Jr, Sidney S, et al. CARDIA study: Influence of autonomic nervous system dysfunction on the development of type 2 diabetes: the CARDIA study. *Diabetes Care*, 2003, 26: 3035–3041. [[Medline](#)] [[CrossRef](#)]
- 30) Tentolouris N, Argyrakopoulou G, Katsilambros N: Perturbed autonomic nervous system function in metabolic syndrome. *Neuromolecular Med*, 2008, 10: 169–178. [[Medline](#)] [[CrossRef](#)]
- 31) Weston KS, Sacre JW, Jellis CL, et al.: Contribution of autonomic dysfunction to abnormal exercise blood pressure in type 2 diabetes mellitus. *J Sci Med Sport*, 2013, 16: 8–12. [[Medline](#)] [[CrossRef](#)]
- 32) Contreras F, Rivera M, Vasquez J, et al.: Diabetes and hypertension physiopathology and therapeutics. *J Hum Hypertens*, 2000, 14: S26–S31. [[Medline](#)] [[CrossRef](#)]
- 33) Kitamura K, Jorgensen CR, Gobel FL, et al.: Hemodynamic correlates of myocardial oxygen consumption during upright exercise. *J Appl Physiol*, 1972, 32: 516–522. [[Medline](#)]
- 34) Nelson RR, Gobel FL, Jorgensen CR, et al.: Hemodynamic predictors of myocardial oxygen consumption during static and dynamic exercise. *Circulation*, 1974, 50: 1179–1189. [[Medline](#)] [[CrossRef](#)]
- 35) Hoberg E, Schuler G, Kunze B, et al.: Silent myocardial ischemia as a potential link between lack of premonitoring symptoms and increased risk of cardiac arrest during physical stress. *Am J Cardiol*, 1990, 65: 583–589. [[Medline](#)] [[CrossRef](#)]
- 36) Ellis KJ, Bell SJ, Chertow GM, et al.: Bioelectrical impedance methods in clinical research: a follow-up to the NIH Technology Assessment Conference. *Nutrition*, 1999, 15: 874–880. [[Medline](#)] [[CrossRef](#)]
- 37) Wasserman K, McIlroy MB: Detecting the threshold of anaerobic metabolism in cardiac patients during exercise. *Am J Cardiol*, 1964, 14: 844–852. [[Medline](#)] [[CrossRef](#)]
- 38) Cohen J: *Statistical power analysis for the behavioral sciences*. Academic Press, 2013.
- 39) Bland JM, Altman DG: Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet*, 1986, 1: 307–310. [[Medline](#)] [[CrossRef](#)]
- 40) Karapetian GK, Engels HJ, Gretebeck RJ: Use of heart rate variability to estimate LT and VT. *Int J Sports Med*, 2008, 29: 652–657. [[Medline](#)] [[CrossRef](#)]
- 41) Karapetian GK, Engels HJ, Gretebeck KA, et al.: Effect of caffeine on LT, VT and HRVT. *Int J Sports Med*, 2012, 33: 507–513. [[Medline](#)] [[CrossRef](#)]
- 42) Schneider DA, McLellan TM, Gass GC: Plasma catecholamine and blood lactate responses to incremental arm and leg exercise. *Med Sci Sports Exerc*, 2000, 32: 608–613. [[Medline](#)] [[CrossRef](#)]
- 43) Koyal SN, Whipp BJ, Huntsman D, et al.: Ventilatory responses to the metabolic acidosis of treadmill and cycle ergometry. *J Appl Physiol*, 1976, 40: 864–867. [[Medline](#)]
- 44) Cohen J: Things I have learned (so far). *Am Psychol*, 1990, 45: 1304. [[CrossRef](#)]
- 45) Sullivan GM, Feinn R: Using effect size-or why the P value is not enough. *J Grad Med Educ*, 2012, 4: 279–282. [[Medline](#)] [[CrossRef](#)]
- 46) Denadai BS, Figueira TR, Favaro OR, et al.: Effect of the aerobic capacity on the validity of the anaerobic threshold for determination of the maximal lactate steady state in cycling. *Braz J Med Biol Res*, 2004, 37: 1551–1556. [[Medline](#)] [[CrossRef](#)]
- 47) Van Schuylenbergh R, Vanden Eynde B, Hespel P: Correlations between lactate and ventilatory thresholds and the maximal lactate steady state in elite cyclists. *Int J Sports Med*, 2004, 25: 403–408. [[Medline](#)] [[CrossRef](#)]
- 48) Yamamoto J, Harada T, Okada A, et al.: Difference in physiological components of VO<sub>2</sub> max during incremental and constant exercise protocols for the cardiopulmonary exercise test. *J Phys Ther Sci*, 2014, 26: 1283–1286. [[Medline](#)] [[CrossRef](#)]