

Ventilatory efficiency response is unaffected by fitness level, ergometer type, age or body mass index in male athletes

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ABSTRACT: The aim of this study was to evaluate the ventilatory efficiency (V_E/VCO_2 slope) and the respiratory control (V_t/Ti slope) in a wide range of athletes and describe the influence of fitness level, age, ergometer type or BMI on these parameters. Ninety-one males (30.4 ± 10.53 years; 175.52 ± 7.45 cm; 71.99 ± 9.35 kg) were analysed retrospectively for the study. Ventilatory efficiency reacted similarly in athletes independently of the fitness level, age, BMI or the ergometer used for testing. No significant differences were found in V_E/VCO_2 slope and the V_t/Ti slope between variables analyzed ($P > 0.05$). The slope of the predictive equations was similar in all cases studied in V_E/VCO_2 slope and the V_t/Ti slope. Moreover, the central control impulse of respiration was not affected by the variables studied. These observations suggest that ventilatory efficiency (V_E/VCO_2 slope) could be a variable fixed by the respiratory system which tends to respond similarly in athletes.

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INTRODUCTION

Ventilatory efficiency can be defined as the relationship between carbon dioxide production (VCO_2) and ventilation (V_E) during an incremental exercise test [1]. Several ways for measuring ventilator efficiency have been reported [2, 3]. However, using the slope of the relationship between VCO_2 and V_E (V_E/VCO_2 slope) has been suggested as the best way for achieving a correct evaluation of the ventilatory efficiency during an incremental exercise test [4]. It adds information about the global ventilatory efficiency throughout entire test and not only at one metabolic rate as it happens with the equivalent of CO_2 (V_E/VCO_2) [5].

Ventilatory efficiency has been widely studied in patients suffering congestive heart failure (CHF) or cardio-respiratory weakness [6-9]. Values exceeding 34 are considered abnormal [1, 10] or indicative of the inefficiency of the respiratory system [2]. In healthy subjects, there has been reported variability in the values of the V_E/VCO_2 slope (from 19 to 32) [3].

The role and importance of ventilatory efficiency in human sport performance remains controversial. The matching of ventilation and perfusion in the lungs is the primary determinant of ventilatory efficiency [4]. Conditions in which the CO_2 production is elevated, such as exercise, seem to play an essential role in the ventilatory control [11]. In this regard, it could be possible that greater efficiency of CO_2 elimination during exercise might allow a higher sport performance. However, in elite juvenile cyclists, no relationship has

been found between maximal oxygen uptake (VO_{2max}) and V_E/VCO_2 slope [2]. Similarly, it was reported that changes in sport performance in world class-cyclists over three competitive seasons were not related to changes in V_E/VCO_2 slope [5]. In synchronized swimmers, ventilatory efficiency remained unchanged by working conditions during apnoeic episodes [12]. Data from our research group revealed that submaximal cycling performance was not related to the ventilatory efficiency response [13]. We hypothesized that increments in CO_2 production are linked to proportional increments in ventilation regardless of the fitness level.

Physiologic dead space (V_D/V_T) has been suggested as a variable that could modify the ventilatory efficiency response [3]. Age and anthropometric characteristics might influence V_D/V_T [14]. However, in children, ventilatory efficiency was not affected by sex despite differences in anthropometric characteristics [15]. Similar results were found in adults: no age or sex differences were found for ventilatory efficiency in healthy participants [3]. However, according to our knowledge there have been no studies evaluating ventilatory efficiency in athletes with different characteristics. Thus, measuring the influence of age and BMI on ventilatory efficiency is necessary in order to better clarify whether there are differences between athletes with different characteristics.

Regarding type of ergometer, a test dependency has been reported in healthy women, but not in males [16]. The authors explained

these results in terms of the low level of arterial hypoxemia coupled with a low level of arterial hypercapnia in women [16]. However, to our knowledge this is the only study mainly focused on this analysis. Thus, further evaluation in athletes is necessary in order to evaluate the influence of type of ergometer on ventilatory efficiency response.

Although ventilatory efficiency has already been studied in healthy people, this variable has not been widely studied in athletes. Contrary to ventilatory efficiency, breathing pattern has been widely studied in athletes [17-19]. V_E can be decomposed into the product of two components: (a) central inspiratory activity, known as “driving” and expressed as the relationship between V_t and inspiratory time (V_t/T_i); and (b) the inspiration-expiration alternation, known as “timing”, and expressed by the relationship between T_i and the total duration of the breathing cycle (T_i/T_{tot}) [20, 21]. V_t/T_i and T_i/T_{tot} responses during incremental exercise appear to be stable and independent of fitness level [12, 17]. By studying the relationship between V_E , V_t/T_i and VCO_2 we could determine whether the central control of respiration makes ventilatory efficiency (V_E/VCO_2 slope) behave similar in athletes independently of their characteristics.

Thus, the aim of this study was to evaluate ventilatory efficiency and respiratory control in a wide range of athletes and describe the influence of fitness level, age, ergometer type or BMI on these parameters. In this regard, we hypothesize that ventilatory efficiency could be an inborn characteristic with similar responses in athletes independently of fitness level, age, ergometer or BMI.

MATERIALS AND METHODS

Subjects

From a large amount of incremental exercise tests carried out in our laboratory, we selected those which were carried out by healthy sportspersons from different endurance sport disciplines (running, cycling, triathlon) and with different fitness levels (amateur, semi-professional). Ninety-one active, healthy males (30.4 ± 10.53 years; 175.52 ± 7.45 cm; 71.99 ± 9.35 kg) were analysed retrospectively for the study. Participants were classified in different groups depending on the ergometer used for testing, BMI, age and VO_{2max} (treadmill ($n=37$); cycle ergometer ($n=54$); BMI: 18-25 ($n=70$); 25-30 ($n=21$); age: 16-25 ($n=40$); 25-35 ($n=16$); 35-45 ($n=23$); >45 ($n=12$); VO_{2max} : <45 VO_{2max} (37.8 ± 7.4 $ml \cdot kg^{-1} \cdot min^{-1}$; $n=43$);

>45 VO_{2max} 51.9 ± 5.1 $ml \cdot kg^{-1} \cdot min^{-1}$; ($n=48$)). Fitness level classification was according to Paap and Takken [22]. Cardio-respiratory variables are shown in Table 1.

Participants were tested in our laboratory for different previous proposes. All previous studies were approved by the ethical committee of Pablo Olavide University and conformed to standards of treatment of human participants in research as outlined in the Fifth Declaration of Helsinki. Participants were informed (both in writing and orally) about all testing and training procedures and gave their written informed consent to participate prior to entering the study.

Procedures

From the tests carried out in our laboratory we selected those performed with the same protocol on a cycle ergometer (Ergoselek 200, Ergoline, Germany) or on a treadmill (Ergorun 8, Down electronics, Germany). Each participant performed a maximum incremental exercise tests with gas analysis. During each test, oxygen uptake (VO_2), carbon dioxide output (VCO_2), respiratory exchange ratio (RER), ventilation (V_E), breathing frequency (f_R), tidal volume (VT), oxygen equivalent ($EqVO_2$), carbon dioxide equivalent ($EqCO_2$), driving (V_t/T_i) and timing (T_i/T_{tot}) were recorded every 5 seconds breath by breath with a gas analyser (MedGraphics CPX Ultima, USA). The system was calibrated prior to each test with gas mixtures of known concentration. After 4 min of warming up, participants started the test at 50 W and then the load was increased by 25 W each minute until volitional exhaustion on the cycle ergometer. On the treadmill, after 4 min of warming up the participants started the test at 7 km/h and the velocity was increased by 1 km/h each minute until volitional exhaustion. Tests were carried out under similar and controlled environmental conditions (20-25°C; 45-55% relative humidity). Achievement of maximal oxygen uptake (VO_{2max}) was accepted when a plateau was found in the relationship between VO_2 and power output or when three of the four criteria for maximal VO_{2max} were obtained [23].

Ventilatory efficiency and breathing pattern

The ventilatory efficiency of each subject was calculated from the slope of the relationship between VCO_2 and V_E during each test. To exclude the influence due to respiratory compensation for acidosis

TABLE 1. Maximum cardio-respiratory values during the incremental exercise test ($n=91$).

	VO_2 ($ml \cdot min^{-1}$)	VCO_2 ($ml \cdot min^{-1}$)	f_R ($br \cdot min^{-1}$)	VT (ml)	V_E ($l \cdot min^{-1}$)	T_i/T_{tot}	V_t/T_i ($ml \cdot sec^{-1}$)	PETCO ₂ (mmHg)
Mean	3219.8	4051.9	51.2	2240.4	112.8	0.41	4823.1	43.6
SD	571.1	808.2	11.6	424.6	26.2	0.05	962.6	6.6

SD, standard deviation; VO_2 , oxygen uptake; VCO_2 , carbon dioxide output; f_R , breathing frequency; V_t , tidal volume; V_E , ventilation; T_i/T_{tot} , timing; V_t/T_i , driving; PETCO₂, end tidal pressure of carbon dioxide.

during highly intensive exercise, the V_E/V_{CO_2} slope was determined from the beginning of the test until the second ventilatory threshold (VT_2). VT_2 was identified using the criteria of increase in both ventilatory equivalents – EqO_2 and $EqCO_2$ – and end tidal partial pressure of oxygen ($PETO_2$) with no concomitant increase in end tidal partial pressure of carbon dioxide ($PETCO_2$) or decrease in $PETCO_2$ [24, 25]. The value of the slope representing the relationship between V_E and Vt/Ti during each test (Vt/Ti slope) was used to test the central component of respiration.

Statistical analysis

Data are expressed as mean \pm SD and with Cohen's d effect size (ES) for each variable. Subjects were included in different groups depend on fitness level, ergometer used for testing, BMI and age. The normal distribution of the data in each group was checked by means of the Shapiro–Wilk test. The homogeneity of variance was evaluated by Levene's test. To compare the mean values obtained for V_E/V_{CO_2} slope and Vt/Ti slope in each group the following statistical tests were carried out. Student's t-test for independent samples was used to compare fitness level groups and type of ergometer groups. The Kruskal–Wallis H-test was carried out to compare mean values between BMI groups. The one-way ANOVA test was used to compare mean values between age groups. The Bonferroni test was selected as a post hoc test. Linear regression analysis was performed for each group between V_E (dependent variable) and V_{CO_2} (independent variable) and Vt/Ti (dependent variable) with data from each subject. Effect sizes (ES) were also calculated using Cohen's d. The level of significance was set at $P < 0.05$ for each statistical analysis. An ES of $d < 0.2$ was considered small, 0.5 medium and $d > 0.8$ large [26].

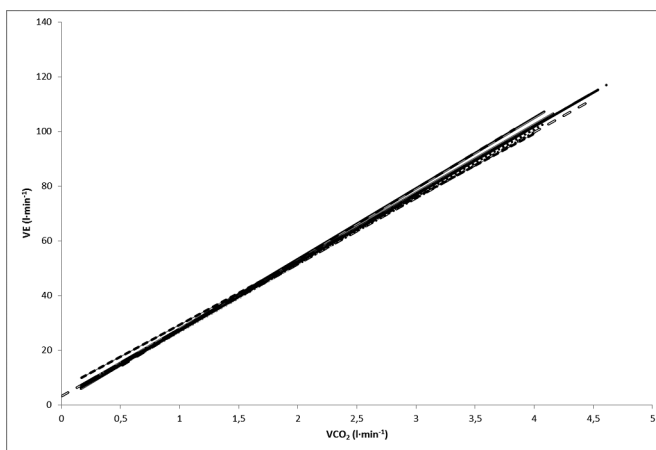


FIG. 1. Evaluation of ventilatory efficiency (V_E/V_{CO_2} slope) showing regression lines measured in each group (treadmill (n=37); cycle ergometer (n=54); BMI: 18-25 (n=70); 25-30 (n=21); age: 16-25 (n=40); 25-35 (n=16); 35-45 (n=23); >45 (n=12); VO_{2max} : <45 VO_{2max} (n=43); >45 VO_{2max} (n=48)). All groups showed a similar linear adjustment.

RESULTS

Data on the ventilatory efficiency and ventilatory control evaluation are shown in Table 2. The statistical analysis revealed non-significant differences ($P > 0.05$) both for the V_E/V_{CO_2} slope and Vt/Ti slope for all the variables included in the analysis (ergometer, BMI, age, and fitness level). Effect size analysis showed a low ES between cycle-ergometer and treadmill testing on V_E/V_{CO_2} slope and Vt/Ti slope (0.29 and 0.09 respectively). Regarding BMI, a low-medium ES was

TABLE 2. Comparison of mean \pm SD values of the V_E/V_{CO_2} slope and Vt/Ti slope for the treadmill and cycle ergometer cardiopulmonary exercise tests, the body mass index (BMI) ranges (18-25; 25-30), age ranges (16-25; 25-35; 35-45; >45) and fitness level (<45 VO_{2max} ; >45 VO_{2max}) in athletes.

	ERGOMETER				Effect size	BMI ($kg \cdot m^{-2}$)				Effect size
	Cycle (n=37)	Treadmill (n=54)	p-value			18-25 (n=70)	25-30 (n=21)	p-value		
V_E/V_{CO_2} slope	23.6 \pm 3.8	24.8 \pm 4.4	0.146		0.29	24.5 \pm 4.1	22.6 \pm 4	0.067		0.46
Vt/Ti slope	38.7 \pm 6.5	39.4 \pm 6.3	0.592		0.09	38.8 \pm 6.3	40.4 \pm 7.1	0.336		0.26

	AGE (years)					Effect size	FITNESS LEVEL: VO_{2max} ($ml \cdot kg^{-1} \cdot min^{-1}$)					Effect size
	16-25 (n=40)	25-35 (n=16)	35-45 (n=23)	>45 (n=12)	p-value		<45 VO_{2max} (n=43)	>45 VO_{2max} (n=48)	p-value			
V_E/V_{CO_2} slope	24.3 \pm 3.8	22.9 \pm 4.5	24.1 \pm 4.6	25.6 \pm 3.7	0.146	0.16	23.4 \pm 4.2	24.8 \pm 4.1	0.111		0.33	
Vt/Ti slope	38.8 \pm 6.4	38.4 \pm 6.2	40.7 \pm 6.6	38.1 \pm 6.7	0.416	0.15	40.5 \pm 6.3	38.3 \pm 6.3	0.100		0.33	

*Significantly different between groups ($p < 0.05$).

§ Large effect size ($ES \geq 0.8$).

TABLE 3. Predictive equations for the ventilatory efficiency response.

	Predictive equations					
	a	b	r ²	r	Standard error	p-value
Ergometer						
Cycle	25.81	0.964	0.929	0.964	0.07	<0.001
Treadmill	24.11	0.913	0.834	0.913	0.106	<0.001
BMI (kg·m⁻²)						
18-25	24.70	0.948	0.899	0.948	0.064	<0.001
25-30	24.66	0.950	0.903	0.950	0.125	<0.001
AGE (years)						
16-25 (n=48)	24.91	0.963	0.927	0.963	0.072	<0.001
25-35 (n=28)	24.49	0.936	0.875	0.936	0.137	<0.001
35-45 (n=23)	23.28	0.890	0.793	0.890	0.177	<0.001
>45 (n=12)	26.03	0.986	0.973	0.986	0.088	<0.001
FITNESS LEVEL: VO_{2max} (ml·kg⁻¹·min⁻¹)						
<45 VO _{2max} (n=43)	24.12	0.945	0.893	0.945	0.094	<0.001
>45 VO _{2max} (n=62)	24.88	0.941	0.885	0.941	0.081	<0.001

* Level of significance ($p < 0.05$).

$y = a \cdot x + b$ ($y=V_E$ (ventilation); $x=VCO_2$ (carbon dioxide output); $a=V_E/VCO_2$ slope; $b=$ y-intercept).

found between groups in V_E/VCO_2 slope and Vt/Ti slope (0.46 and 0.24 respectively). No age effect was found in V_E/VCO_2 slope and in Vt/Ti slope (0.16 and 0.15 respectively). Fitness level showed a low ES for differences between groups in V_E/VCO_2 slope (0.33) and Vt/Ti slope (0.33). Table 3 shows the predictive equations for V_E/VCO_2 slope after regression and statistical analysis. The slope of the predictive equations was similar in all cases studied (Table 3). Figure 1 shows the regression lines for each variable studied.

DISCUSSION

To the best of our knowledge, this is the first study to evaluate the influence of ergometer type, age, BMI and fitness level on ventilatory efficiency in athletes. We hypothesized that ventilatory efficiency could behave independently of the aforementioned variables in athletes. The main finding of this study was that ventilatory efficiency is not influenced by the ergometer used for testing, the athlete's age, BMI or fitness level. These findings support the hypothesis that ventilatory efficiency could be an inborn characteristic which reacts independently of fitness level, anthropometric profile, age or the ergometer used for testing.

Ventilatory efficiency has been proposed as an effective method to detect cardiorespiratory weakness and healthy problems [6, 7, 9]. Values exceeding 34 indicate the inefficiency of the cardiorespiratory system [1, 27]. However, it is not as clear that athletes with better ventilatory efficiency are those who demonstrate high sport performance. In our study, no differences were found in V_E/VCO_2

slope between athletes with a low VO_{2max} and those with a high VO_{2max} (23.4 ± 4.2 and 24.8 ± 4.1 , respectively). The slope of the predictive equations was also similar in both cases (24.12 and 24.88, respectively) (Table 3) (Figure 1). Similar mean values of efficiency were found in world-class cyclists over a 3-year period (24.6 ± 3.1 ; 23.6 ± 2.7 ; 24.8 ± 2.6) [5]. Even though these cyclists were tested with a totally different protocol (50W each 4 min) and gas analyzer and they had a higher VO_{2max} (77.5 ± 6.2 ml·kg⁻¹·min⁻¹), they showed similar values of ventilatory efficiency to our subjects. Thus, changes in sport performance (peak power output) were not related to changes in V_E/VCO_2 slope or VO_{2max} in world-class cyclists [5]. In juvenile cyclists, no relationship was found between VO_{2max} and V_E/VCO_2 slope [2]. No correlation was found between V_E/VCO_2 slope and VO_{2max} in sport students before and after inspiratory muscle training, either in normoxia or in hypoxia [13]. Thus, our results and the evidence reported before help us to confirm the hypothesis that V_E/VCO_2 slope could not be a variable related to sport performance. In this regard, it has been suggested that if an athlete has poor cardio-respiratory efficiency (high V_E/VCO_2 slope) it has no bearing on their maximal ability to use oxygen [2] or achieve high performance [5]. Therefore, V_E/VCO_2 slope is not efficacious in quantifying the performance of the physiological systems which support an athlete's ability to perform at high oxygen uptakes [2].

In terms of age and BMI, controversial data about ventilatory efficiency has been reported. On the one hand, Sun and Hansen [3] carried out an evaluation of ventilatory efficiency on healthy people

without significant difference between sexes and ages. On the other hand, ventilatory efficiency showed sex and age dependence in healthy subjects [4]. In children, ventilatory efficiency response was not affected by sex [15]. In our study, we could not compare ventilatory efficiency between sexes due to the small sample size in females. Regarding age analysis, no differences were found between age groups in V_E/VCO_2 slope (Table 2). These results are in concordance with previous studies [3, 15]. Physiologic dead space (V_D/V_T) has been proposed as a variable that could modify ventilatory efficiency in healthy subjects [3]. Maturation and age could modify the V_D/V_T [14] and as a consequence ventilatory efficiency. In our subjects, the mean values obtained in age groups were similar to values measured in children [15] (Table 2). Thus, ventilatory efficiency might be a variable not affected by age or anthropometric characteristics in healthy athletes.

With reference to type of ergometer, we did not find a difference between subjects tested on a treadmill or a cycle ergometer in ventilatory efficiency response (Table 2). We compared ventilatory efficiency data from world-class cyclists [5], who were tested with a different gas analyzer and with a different protocol (50 W/4 min), with our subjects (25 W/min). The mean values obtained were similar in both cases (~24). The same results were obtained in men but not in women, suggesting independence of test mode evaluation [16] and independence of speed used in the test from ventilatory efficiency response [28]. In the first study [16], the protocol used (4 min of walking at $72 \text{ m}\cdot\text{min}^{-1}$ and 0% grade; at the end of minutes 4, 7 and 10, the speed was increased by $10 \text{ m}\cdot\text{min}^{-1}$) was totally different to ours. In the second [28], they did not find a difference between the fast (25 W/min) and the slow protocol (five work rate increments of equal size each 4 min). But one more time, the slope values reported (24.19 and 23.23 respectively) were in concordance with our results. Similarly, Sun and Hansen [3] found no effect of laboratory site or ergometer in ventilatory efficiency evaluation, with a greater reproducibility for V_E/VCO_2 slope (online data supplement). The slope of the predictive equations was similar in all cases studied (Table 3). According to these results, the type of ergometer or protocol used might not modify the ventilatory efficiency response in healthy athletes.

In addition to ventilatory efficiency analysis, we carried out an analysis of driving component of respiration (V_t/T_i slope). As it occurs with V_E/VCO_2 slope, the increment in the driving impulse was similar in all our subjects and it was independent of age, fitness level, BMI or ergometer type (Table 2). In all these cases, the increment in driving impulse was close to ~40. This indicates that the increases in V_E during progressive exercise are associated with a proportional increase in the inspiratory driving activity without any alteration in the relationship between inspiration and expiration, even at the highest working intensities (Figure 3) [5]. Thus, the linear relationship of V_E with V_t/T_i and VCO_2 suggests that the main factor conditioning the stability of ventilatory efficiency (as V_E/VCO_2 slope) could be the central impulse of respiration (V_t/T_i).

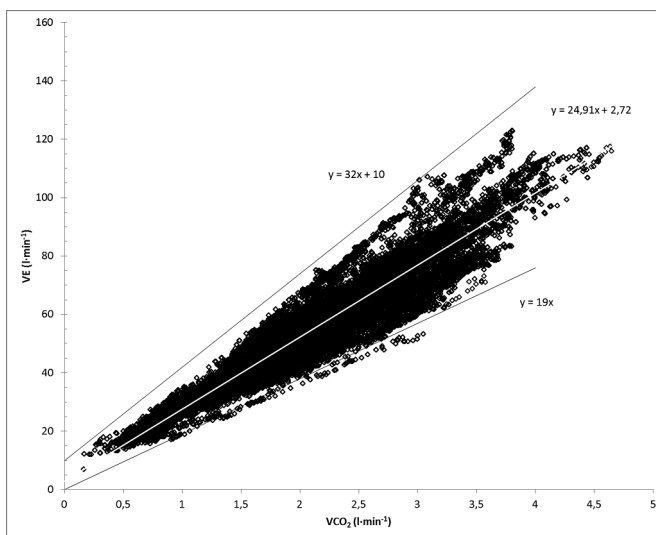


FIG. 2. Graph showing the linear relation between carbon dioxide output (VCO_2) and ventilation (V_E) with data from whole sample ($n=91$). This can be used as a nomogram for assessing ventilatory efficiency in healthy athletes during exercise regardless of the ergometer type, fitness level, age or body mass index.

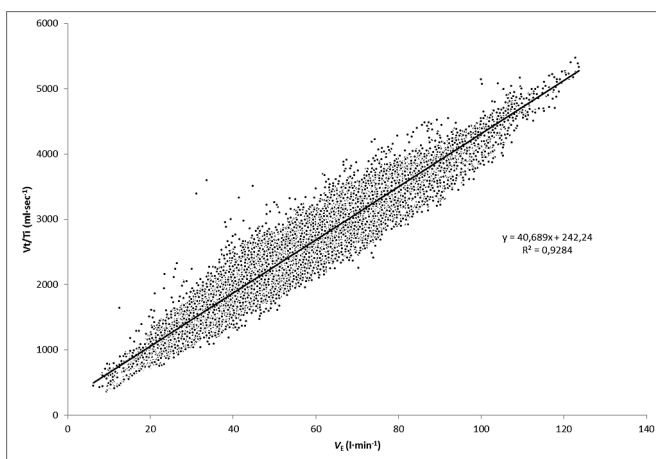


FIG. 3. Graph showing the linear relation between ventilation (V_E) and driving impulse (V_t/T_i) with data from whole sample ($n=91$). Central impulse of respiration responded similarly in all participants regardless of the ergometer type, fitness level, age or body mass index.

Some limitations have to be addressed. First, this study was retrospective and we could not measure body composition variables in our subjects. Further investigations taking into account body composition variables are necessary in order to better clarify whether body composition could influence ventilatory efficiency response. Lastly, we could not include females in our study due to the low sample size. New research to evaluate the influence of gender on ventilatory efficiency is necessary in order to better clarify the involvement of this variable on ventilatory efficiency response.

Based on the previous evidence reported and in our results, we propose a nomogram for assessing ventilatory efficiency (V_E/VCO_2 slope) (Figure 2). This nomogram might help to carry out a better evaluation of ventilatory efficiency in athletes completing the proposal of Naranjo and Centeno [12]. In addition, it could help to easily detect cardio-respiratory problems or deficiencies in respiration control when an incremental test is carried out in athletes.

In summary, ventilatory efficiency reacted similarly in athletes independently of the fitness level, age, BMI or the ergometer used for testing. Moreover, the central control impulse of respiration was not affected by the variables studied (Figure 3). These observations

suggest that ventilatory efficiency (V_E/VCO_2 slope) could be a variable fixed by the respiratory system which tends to respond similarly in athletes. Finally, ventilatory efficiency could be assessed easily during an incremental test in athletes using the nomogram proposed.

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Conflict of interest

No potential conflict of interest was reported by the authors.

REFERENCES

- Arena R, J Myers, L Hsu, MA Peberdy, S Pinkstaff, D Bensimhon, et al. The minute ventilation/carbon dioxide production slope is prognostically superior to the oxygen uptake efficiency slope. *J Card Fail.* 2007;13(6):462-9.
- Brown SJ, Raman A, Schlader Z, Stannard SR. Ventilatory efficiency in juvenile elite cyclists. *J Sci Med Sport.* 2013;16(3):266-70.
- Sun X-G, JE Hansen, N Garatachea, TW Storer, K Wasserman. Ventilatory efficiency during exercise in healthy subjects. *Am J Respir Crit Care Med.* 2002;166(11):1443-8.
- Habedank D, Reindl I, Vietzke G, Bauer U, Sperfeld A, Gläser S, et al. Ventilatory efficiency and exercise tolerance in 101 healthy volunteers. *Eur J Appl Physiol Occup Physiol.* 1998;77(5):421-6.
- Salazar-Martínez E, Terrados N, Burtscher M, Santalla A, Naranjo Orellana J. Ventilatory efficiency and breathing pattern in world-class cyclists: A three-year observational study. *Respir Physiol Neurobiol.* 2016; 229:17-23.
- Arena R, Myers J, Guazzi M. The clinical and research applications of aerobic capacity and ventilatory efficiency in heart failure: an evidence-based review. *Heart Fail Rev.* 2008;13(2):245-69.
- Ingle L, Goode K, Carroll S, Sloan R, Boyes C, Cleland JG, et al. Prognostic value of the VE/VCO_2 slope calculated from different time intervals in patients with suspected heart failure. *Int J Cardiol.* 2007;118(3):350-5.
- Laveneziana P, Agostoni P, Mignatti A, Mushtaq S, Colombo P, Sims D, et al. Effect of Acute β -blocker Withholding on Ventilatory Efficiency in Patients With Advanced Chronic Heart Failure. *J Card Fail.* 2010; 16(7):548-55.
- Magri D, Limongelli G, Re F, Agostoni P, Zachara E, Correale M, et al. Cardiopulmonary exercise test and sudden cardiac death risk in hypertrophic cardiomyopathy. *Heart.* 2016;heartjnl-2015-308453.
- Arena R, M Guazzi, J Myers. Prognostic value of end-tidal carbon dioxide during exercise testing in heart failure. *Int J Cardiol.* 2007;117(1):103-8.
- Milsom WK, Abe AS, Andradeb DV, Tattersall GJ. Evolutionary trends in airway $CO_2/H+$ chemoreception. *Respiratory physiology & neurobiology.* 2004; 144(2):191-202.
- Naranjo J, Centeno RA, Carranza MD, Cayetano M. A test for evaluation of exercise with apneic episodes in synchronized swimming. *Int J Sports Med.* 2006;27(12):1000-4.
- Salazar-Martínez E, Gatterer H, Burtscher M, Naranjo Orellana J, Santalla A. Influence of inspiratory muscle training on ventilatory efficiency and cycling performance in normoxia and hypoxia. *Front Physiol.* 2017; 8:133.
- Mummery HJ, Stolp BW, deL Dear G, Doar PO, Natoli MJ, Boso AE, et al. Effects of age and exercise on physiological dead space during simulated dives at 2.8 ATA. *J Appl Physiol.* 2003;94(2):507-17.
- Guerrero L, Naranjo J, Carranza MD. Influence of gender on ventilatory efficiency during exercise in young children. *J Sports Sci.* 2008; 26(13):1455-7.
- Davis JA, Tyminski TA, Soriano AC, Dorado S, Costello KB, Sorrentino KM, et al. Exercise test mode dependency for ventilatory efficiency in women but not men. *Clin Physiol Funct Imaging.* 2006;26(2):72-8.
- Lucía A, Carvajal A, Calderon FJ, Alfonso A, Chicharro JL. Breathing pattern in highly competitive cyclists during incremental exercise. *Eur J Appl Physiol Occup Physiol.* 1999; 79(6):512-21.
- Lucía A, Hoyos J, Pardo J, Chicharro JL. Effects of endurance training on the breathing pattern of professional cyclists. *Jpn J Physiol.* 2001;51(2):133-41.
- Scheuermann BW, Kowalchuk JM. Breathing patterns during slow and fast ramp exercise in man. *Exp Physiol.* 1999;84(1):109-20.
- Milic-Emili J. Recent advances in clinical assessment of control of breathing. *Lung.* 1982;160(1):1-17.
- Milic-Emili J, Grunstein MM. Drive and timing components of ventilation. *Chest.* 1976;70(1 Suppl):131-3.
- Paap D, Takken T. Reference values for cardiopulmonary exercise testing in healthy adults: a systematic review. *Expert Rev Cardiovasc Ther.* 2014; 12(12):1439-53.
- Howley ET, Bassett DR, Welch HG. Criteria for maximal oxygen uptake: review and commentary. *Med Sci Sports Exerc.* 1995;27(9):1292-301.
- Lucía A, Hoyos J, Pérez M, Chicharro JL. Heart rate and performance parameters in elite cyclists: a longitudinal study. *Med Sci Sports Exerc.* 2000;32(10):1777-82.
- Skinner JS, McLellan TH. The transition from aerobic to anaerobic metabolism. *Res Q Exerc Sport.* 1980; 51(1):234-48.
- Cohen J. *Statistical power analysis.* 1988.
- Chase P, Arena R, Myers J, Abella J, Peberdy MA, Guazzi M, et al. Relation of the prognostic value of ventilatory efficiency to body mass index in patients with heart failure. *Am J Cardiol.* 2008;101(3):348-52.
- Davis JA, Sorrentino KM, Soriano AC, Pham PH, Dorado S. Is ventilatory efficiency dependent on the speed of the exercise test protocol in healthy men and women? *Clin Physiol Funct Imaging.* 2006;26(2):67-71.