ORIGINAL ARTICLE

The Physiological Society · american physiological society · **PHYSIOLOGICAL REPORTS**

Exercise ventilatory efficiency in elite athletes assessed for the Paris 2024 Olympic Games: The effect of sex and sport categories

Maria Rosaria Squeo[1] | **Ilaria Menichini[1]** | **Matteo Morviducci[2]** | **Alessandro Spinelli[1]** | **Giuseppe Di Gioia[1,3]** | **Viviana Maestrini[1,4]** | **J. Alberto Neder[5]** | **Paolo Palange[1,2]** (ORCID)

[1]National Italian Olympic Committee (CONI), Institute of Sport and Science Medicine, Rome, Italy

[2]Department of Public Health and Infectious Disease, Respiratory and Critical Care Division, Sapienza University of Rome, Rome, Italy

[3]Department of Cardiovascular Sciences, Campus Bio-Medico University, Rome, Italy

[4]Department of Clinical, Internal, Anesthesiological and Cardiovascular Sciences, Sapienza University of Rome, Rome, Italy

[5]Respiratory Investigation Unit, Division of Respirology, Department of Medicine, Queen's University and Kingston Health Science Center, Kingston, Canada

Correspondence

Paolo Palange, Department of Public Health and Infectious Disease, Respiratory and Critical Care Division, Sapienza University of Rome, Rome, Italy.
Email: paolo.palange@uniroma1.it

Abstract

Ventilatory efficiency during cardiopulmonary exercise testing (CPET) is obtained by relating minute ventilation (V'_E) to CO_2 output ($V'CO_2$). Limited information is available regarding exercise ventilatory efficiency in young elite athletes. We assessed ventilatory efficiency in elite athletes; evaluating the influence of sex and/ or ESC sport categories; evaluating the agreement between the $V'_E/V'CO_2$ slope and nadir in measuring ventilatory efficiency; evaluating differences between subgroups of athletes stratified by ventilatory efficiency. A cohort of 443 elite athletes prospectively underwent CPET. The slope (s_1) and the intercept of the linear region of the $V'_E/V'CO_2$ relationship, the $V'_E/V'CO_2$ value at the lactate threshold and the $V'_E/V'CO_2$ nadir were used to assess ventilatory efficiency. Male athletes and endurance athletes, both males and females, had higher exercise ventilatory efficiency ($p < 0.001$). A strong positive correlation was observed between $V'_E/V'CO_2$ s_1 and nadir ($p < 0.001$). Of note, both high ($V'_E/V'CO_2$ $s_1 < 24$) and very high ($V'_E/V'CO_2$ $s_1 < 22$) levels of ventilatory efficiency were associated with greater exercise tolerance (i.e., peak oxygen uptake, maximal power; $p < 0.001$). The results of our study emphasize the need to include the measurement of ventilatory efficiency in the evaluation of elite athletes, potentially refining their training strategies.

KEYWORDS

CPET, elite athletes, exercise, ventilatory efficiency

1 | INTRODUCTION

Cardiopulmonary Exercise Testing (CPET) is the gold standard for the assessment of aerobic fitness, allowing the evaluation of the integrated cardiovascular, respiratory, and metabolic response to incremental exercise (American Physical Therapy Association, 2001; ERS Task Force et al., 2007). Currently, the most widely used parameter in sports-related research regarding athletes' fitness is peak oxygen uptake ($V'O_2$ peak) (Petek

et al., 2022). On the contrary, there is limited information available concerning the impact of exercise ventilatory response and ventilatory efficiency on exercise performance in elite athletes (Petek et al., 2021, 2023; Salazar-Martínez et al., 2018). This is a subject of particular importance for this population where even modest uncomfortable exertional sensations—such as breathlessness caused by excessive ventilation (Neder et al., 2022)—may negatively impact maximal performance.

In this context, it is well known that the rate of the increase in minute ventilation (V'_E) over carbon dioxide output ($V'CO_2$) reflects the subject's "ventilatory efficiency" (Di Paolo et al., 2019; Neder et al., 2017; Ramos et al., 2013). Specifically, each exercise level of minute ventilation (V'_E) corresponding to a particular $V'CO_2$ is inversely related to the "set point" at which arterial CO_2 partial pressure (P_aCO_2) is controlled and influenced by the physiological dead space fraction of tidal volume (V_D/V_T) according to the following equation (Ramos et al., 2013):

$$\frac{V'E}{V'CO_2} = \frac{1}{PaCO_2\left(1 - \left(\frac{V_D}{V_T}\right)\right)}$$

At very low exercise intensity, a slight decrease in arterial CO_2 pressure ($PaCO_2$) due to hyperventilation may be observed. At high exercise intensity, V'_E increases disproportionately to $V'CO_2$, due to high levels of metabolic acidosis leading to a decrease in $PaCO_2$ (Ramos et al., 2013; Sun et al., 2002). Individuals who chronically hyperventilate or have an elevated V_D typically exhibit higher $V'_E/V'CO_2$ values (Di Paolo et al., 2019; Neder et al., 2017; Ramos et al., 2013). In healthy sedentary individuals, the expected normal value for the $V'_E/V'CO_2$ slope, from unloaded pedaling to the ventilatory compensation point (VCP), is approximately 25, with 30 representing the upper limit of normal (Arena et al., 2008; Neder et al., 2001; Sun et al., 2002).

Conversely, lower $V'_E/V'CO_2$ slope values indicate a more efficient elimination of CO_2 during exercise, suggesting a potential advantage to sports performance (Salazar-Martínez et al., 2018). It is object of debate whether $V'_E/V'CO_2$ slope values may be predictive of exercise tolerance (Di Paco et al., 2017; Salazar-Martínez et al., 2016) or fitness level (Salazar-Martínez et al., 2018); while it does not seem to correlate with $V'O_2$ max (Brown et al., 2012), BMI, or age (Salazar-Martínez et al., 2018). Regarding the effect of sex differences, it has been shown that female athletes have higher slope values of $V'_E/V'CO_2$ compared to males (Collins et al., 2021; Guenette et al., 2007; Harms et al., 1998; Petek et al., 2023); these studies, however, have involved only a small number of young elite athletes, and they all focus primarily on endurance athletes and not on other sport categories.

The principal objective of our study was to prospectively analyze exercise ventilatory efficiency in a large cohort of elite athletes. We were specifically interested in establishing a frame of reference for this important variable, exposing the underlying factors that may modulate exertional ventilatory efficiency. We aimed to answer the following original research questions: (a) are there differences in ventilatory efficiency between male and female elite athletes? (b) is ventilatory efficiency modulated by ESC category? (Pelliccia et al., 2021); (c) can the different metrics of ventilatory efficiency ($V'_E/V'CO_2$ slope and the nadir value of $V'_E/V'CO_2$ ratio) be used interchangeably in elite athletes? and (d) are there physiological differences between subgroups of athletes stratified by ventilatory efficiency?

2 | MATERIALS AND METHODS

2.1 | Participants

Our study included a cohort of 443 Italian elite athletes (229 males and 214 females), selected for the 2023 European Games in Cracow (Poland) and potential candidates for the Paris 2024 Olympic Games. The study was conducted at the Institute of Sports Medicine and Science-CONI, in Rome, Italy, between January and June 2023. This study received approval from the ethics committee ("Comitato Etico Territoriale Lazio Area 1", approval number 0851/2024). Written informed consent was obtained from each participant. Patients or the public were not involved in the design, conduct or evaluation of the study.

2.2 | Procedure

The athletes were stratified based on their predominant component of the ESC categories, as described by the 2020 ESC guidelines for exercise prescription (Pelliccia et al., 2021): (A) skill-based (e.g., golf, sailing), (B) power-based (e.g., weightlifting, boxing), (C) mixed (e.g., basketball, rugby, fencing), and (D) endurance-focused activities (e.g., long distance running, cycling, rowing, triathlons). Pulmonary function tests, including spirometry and maximal voluntary ventilation (MVV) were obtained in each athlete. These measurements were obtained by using a pulmonary function testing system (Quark PFT, Cosmed, Pavona, Italy). The procedures followed the standards recommended by the American Thoracic Society (ATS) and the European Respiratory Society (ERS) (Graham et al., 2019). All measured variables were presented as absolute and

percentage of the predicted values (adjusted for age, sex, BMI, and ethnicity) (Cooper et al., 2017). Each participant underwent a maximal incremental exercise test on an electronically braked cycle ergometer (Cosmed bike, Ergoselect 100, Ergoline, Bitz, Germany). The exercise protocol adhered to international recommendations (Radke et al., 2019; Weisman et al., 2001) and incorporated predicted normal values as outlined by Wasserman et al. (Radke et al., 2019; Sietsema et al., 2020; Weisman et al., 2001). The exercise phase involved incremental increases in work rate, ranging from 15 to 40 watts/min. These increments were tailored to the athletes' physical performance and the predicted $V'O_2$ peak, aiming to achieve maximal exertion within the 8- to 12-min timeframe. Electrocardiogram (ECG) data were continuously monitored throughout both maximal exercise and the subsequent 5-min recovery period. A metabolic cart was utilized for gas exchange analysis (Quark CPET, Cosmed, Pavona, Italy). The following variables were measured breath-by-breath and then averaged every 20 s: $V'O_2$, $V'CO_2$, tidal volume, breathing frequency, V'_E, end tidal O_2 (PetO$_2$), and end tidal CO_2 (PetCO$_2$). The oxygen pulse was calculated using the ratio $V'O_2$ over heart rate HR ($V'O_2$/HR). The lactate threshold (LT) was identified using both the V-slope and ventilatory equivalents methods (Sietsema et al., 2020). The VCP was determined by analysing the relationship between V'_E and $V'CO_2$ over time, following established standard criteria (Sietsema et al., 2020). Ventilatory efficiency was assessed by using: (a) the $V'_E/V'CO_2$ slope ($V'_E/V'CO_2$ s$_1$) and the intercept ($V'_E/V'CO_2$ I), with the exclusion of the data above the VCP; (b) $V'_E/V'CO_2$ value at the LT ($V'_E/V'CO_2$@LT); (c) the $V'_E/V'CO_2$ value at the nadir ($V'_E/V'CO_2$ nadir); (d) the $V'_E/V'CO_2$ slope above the VCP ($V'_E/V'CO_2$ s$_2$).

2.3 | Statistical analysis

Descriptive statistics, such as means and standard deviations, were computed for essential CPET parameters to provide a summary of central tendency and variability within the dataset. To assess differences in CPET results between males and females, as well as across sport categories, the unpaired Student's t-test was employed. Additionally, group comparisons were conducted using ANOVA. Linear regression and the Bland–Altman plot were employed to assess the agreement between $V'_E/V'CO_2$ s$_1$ and nadir in evaluating ventilatory efficiency. A significance level of $p < 0.05$ was set as the threshold for determining statistical significance. All statistical analyses were carried out using Microsoft Excel and GraphPad Prism.

3 | RESULTS

Baseline and spirometric characteristics of all the participants are shown in Table 1. The average age of the population was 25 ± 5 years, with a similar distribution between males and females. In contrast, males exhibited higher values of height and BMI compared to females. As expected, spirometric absolute values forced vital capacity (FVC), forced expiratory volume in the first second (FEV$_1$), forced mid-expiratory flow (FEF$_{25-75}$) and MVV were higher in males than in females, while the percentage of predicted values was similar and higher than normal for both genders (Graham et al., 2019).

3.1 | Physiological variables at CPET

Compared to males, females exhibited lower exercise tolerance, as evidenced by significantly lower values in $V'O_2$ peak ($p < 0.001$), $V'O_2$/kg peak ($p < 0.001$), and maximal power ($p < 0.001$) (Table 2). Conversely, the ratio of increase of $V'O_2$ work rate relationship ($V'O_2$/WR) appeared to be independent of sex or ESC category. Furthermore, at peak exercise, males showed lower HR values, higher $V'O_2$/HR, and higher V'_E. As shown in Table 3, endurance athletes (ESC D) had a significantly higher $V'O_2$ peak,

TABLE 1 Baseline and spirometric characteristics.

	Total	Males	Females
Number of subjects	443	229	214
Age, years	25 ± 5	26 ± 6	25 ± 5
Height, cm	175 ± 10	182 ± 9	169 ± 7
BMI, kg/m^2	23.4 ± 2.9	24.3 ± 3.0	22.5 ± 2.6
ESC classification			
A	115 (26)	55 (24)	60 (28)
B	76 (17)	40 (17)	36 (17)
C	190 (43)	100 (44)	190 (42)
D	62 (14)	34 (15)	28 (13)
Hb, mg/dL	14.1 ± 1.4	14.9 ± 1.3	13.3 ± 1.0
FVC, l (%)	5.1 ± 1.1 (103 ± 14)	5.8 ± 0.9 (102 ± 11)	4.4 ± 0.7 (105 ± 16)
FEV$_1$, l (%)	4.2 ± 0.8 (102 ± 12)	4.8 ± 0.7 (101 ± 11)	3.7 ± 0.5 (103 ± 13)
FEV$_1$/FVC, %	83 ± 7	82 ± 7	84 ± 6
FEF$_{25-75}$, l (%)	4.4 ± 1.2 (99 ± 22)	4.9 ± 1.3 (99 ± 25)	3.9 ± 0.8 (98 ± 20)
MVV, l	145.6 ± 33.0	169.3 ± 26.7	122.9 ± 19.9

Note: Data are presented as mean ± standard deviation.

Abbreviations: BMI, Body Mass Index; FEF$_{25-75}$, Forced Expiratory Flow at 25%–75%; FEV$_1$, Forced Expiratory Volume in the first second; FVC, Forced Vital Capacity; Hb, Hemoglobin; MVV, Maximum Voluntary Ventilation.

	Total (443)	Males (229)	Females (215)	*p* Value
Maximal power, watt	242 ± 68	283 ± 61	199 ± 45	<0.001
V'O$_2$ peak, mL/min	2970 ± 743	3438 ± 630	2472 ± 486	<0.001
V'O$_2$/Kg peak, mL/min/kg	41.4 ± 9.1	43.6 ± 10.0	39.1 ± 7.4	<0.001
V'O$_2$ peak, % predicted	118.4 ± 23.5	108.3 ± 18.4	129.2 ± 23.6	<0.001
V'CO$_2$ peak, mL/min	3282 ± 830	3836 ± 659	2689 ± 532	<0.001
RER	1.12 ± 0.08	1.14 ± 0.08	1.11 ± 0.07	<0.001
V'O$_2$/WR, mL/watt	10.1 ± 0.9	10.1 ± 0.8	10.1 ± 0.9	NS
HR peak, bpm	167 ± 11	165 ± 11	169 ± 10	<0.001
V'O$_2$/HR, mL/bpm	17.9 ± 4.7	20.9 ± 4.1	14.7 ± 3.0	<0.001
V'$_E$ peak, L/min	100.5 ± 26.0	116.2 ± 24.1	83.9 ± 16.4	<0.001
BR, L/min	30.6 ± 25.0	30.8 ± 30.4	30.4 ± 17.7	NS
V'$_E$/V'CO$_2$ s$_1$	25.5 ± 2.9	24.7 ± 2.6	26.3 ± 2.9	<0.001
V'$_E$/V'CO$_2$@LT	25.8 ± 2.7	25.0 ± 2.6	26.7 ± 2.5	<0.001
V'$_E$/V'CO$_2$ nadir	25.0 ± 2.4	24.3 ± 2.1	25.8 ± 2.4	<0.001
V'$_E$/V'CO$_2$ i	3.2 ± 2.1	3.4 ± 2.2	2.9 ± 2.0	<0.05
V'$_E$/V'CO$_2$ s$_2$	45.8 ± 19.5	46.8 ± 25.2	44.6 ± 8.7	NS
Power @LT, watt	125 ± 50	146 ± 52	103 ± 38	<0.001
VO$_2$@LT, mL/min	1775 ± 555	2011 ± 550	2967 ± 653	<0.001
Power @RCP, watt	206 ± 64	241 ± 59	165 ± 42	<0.001
VO$_2$@VCP, mL/min	2583 ± 710	1525 ± 439	2132 ± 469	<0.001

TABLE 2   Physiologic variables at CPET.

Note: Data are presented as mean $\pm$ standard deviation.

Abbreviations: BR, Breathing Reserve; i, intercept; LT, lactate threshold; RER, Respiratory Exchange Ratio; V'CO$_2$, carbon dioxide output; V'O$_2$, oxygen uptake; VCP, Ventilatory Compensation Point; V'$_E$, minute ventilation; WR, Work Rate.

V'O$_2$/kg peak and maximal power, compared to other ESC categories. In addition, ESC D athletes had a better cardiovascular performance (i.e., V'O$_2$/HR and HR peak), and higher V'$_E$ peak; this was particularly evident when compared to skill athletes (ESC A).

3.2 | Ventilatory efficiency

As shown in Table 2 and Figure 1, female athletes showed lower ventilatory efficiency, with higher values of V'$_E$/V'CO$_2$ s$_1$ ($p < 0.001$), V'$_E$/V'CO$_2$ nadir ($p < 0.001$), V'$_E$/V'CO$_2$@AT ($p < 0.001$), and V'$_E$/V'CO$_2$ i ($p < 0.05$). Both males and females of the subgroup of endurance athletes (ESC D) exhibited higher ventilatory efficiency, with lower values for V'$_E$/V'CO$_2$ s$_1$ ($p < 0.001$), V'$_E$/V'CO$_2$ nadir ($p < 0.001$), V'$_E$/V'CO$_2$@LT ($p < 0.001$), and V'$_E$/V'CO$_2$ i ($p < 0.001$), compared to skill athletes (ESC A) (Table 3).

A strong positive correlation (Figure 2a) was observed between V'$_E$/V'CO$_2$ s$_1$ and V'$_E$/V'CO$_2$ nadir for all athletes ($r = 0.91$; $p < 0.001$). By using the Bland–Altman test, we found a good agreement between V'$_E$/V'CO$_2$ s$_1$ and V'$_E$/V'CO$_2$ nadir in determining ventilatory

efficiency (Figure 2b). A minimal deviation from the line of equality was observed and, on average, the difference between the nadir values minus the s$_1$ values was only 0.46. The mean bias of the two measurements, defined as ± 1.96 standard deviations, were -1.94 and 2.85. A total of 420 measurements out of 443 (99.5%) fell within this interval.

3.3 | Ventilatory efficiency below and above limits of normality

Two subgroups of athletes were identified based on their V'$_E$/V'CO$_2$ s$_1$ values: one with high values and another with low values. The cutoff values were chosen in accordance with the upper limit of normality (V'$_E$/V'CO$_2$ s$_1 > 32$) (Radke et al., 2019; Sietsema et al., 2020; Weisman et al., 2001) and -1 standard deviation from the mean value of the entire population (V'$_E$/V'CO$_2$ s$_1 < 22$).

Fifty-one athletes (11.7%) had a V'$_E$/V'CO$_2$ s$_1$ lower than 22 while eight athletes (1.8%) had a V'$_E$/V'CO$_2$ s$_1$ higher than 32 (Table 4). In the two subgroups, V'$_E$/V'CO$_2$ s$_2$ ($p < 0.05$), V'$_E$/V'CO$_2$ nadir ($p < 0.001$), V'$_E$/V'CO$_2$@LT ($p < 0.001$), and V'$_E$/V'CO$_2$ i ($p < 0.001$) were also

TABLE 3 Physiologic variables at CPET—sport categories.

	Total	ESC A (115)	ESC B (76)	ESC C (190)	ESC D (62)	*p* Value
Sex						
Males (%)	229 (52)	55 (48)	40 (53)	100 (53)	34 (55)	
Females (%)	214 (48)	60 (52)	36 (47)	90 (47)	28 (45)	
Maximal power, watt	242 ± 68	195 ± 49	238 ± 59*	255 ± 57*†	297 ± 83*†‡	<0.001
V'O_2 peak, mL/min	2970 ± 743	2445 ± 570	2986 ± 676*	3112 ± 637*	3496 ± 843*†‡	<0.001
V'O_2/Kg peak, mL/min/kg	41.4 ± 9.1	36.4 ± 7.2	42.0 ± 6.5*	40.8 ± 5.4*	51.0 ± 11.8*†‡	<0.001
V'O_2 peak, % predicted	118.4 ± 23.5	103.3 ± 17.9	119.0 ± 17.8*	120.3 ± 20.0*	139.9 ± 29.7*†‡	<0.001
V'CO_2 peak, mL/min	3282 ± 830	2763 ± 636	3332 ± 782*	3402 ± 761*	3830 ± 921*†‡	<0.001
RER	1.12 ± 0.08	1.15 ± 0.09	1.13 ± 0.08	1.11 ± 0.07*	1.11 ± 0.08*	NS
V'O_2/WR, mL/watt	10.1 ± 0.9	10.1 ± 1.0	10.4 ± 0.9	10.0 ± 0.8†	10.0 ± 0.7†	<0.05
HR peak, bpm	167 ± 11	170 ± 11	163 ± 11*	166 ± 10*	166 ± 11*	<0.001
V'O_2/HR, mL/bpm	17.9 ± 4.7	14.4 ± 3.4	18.5 ± 5.2*	18.8 ± 4.0*	20.8 ± 4.9*†‡	<0.001
V'$_E$ peak, L/min	100.5 ± 26.0	87.0 ± 19.3	101.6 ± 29.5*	104.6 ± 24.9*	112.2 ± 28.0*†‡	<0.001
BR, L/min	30.6 ± 25.0	36.9 ± 13.9	28.8 ± 26.5*	30.7 ± 16.6*	21.0 ± 48.0*	<0.001
V'$_E$/V'CO_2 s_1	25.5 ± 2.9	25.9 ± 3.1	25.2 ± 3.0	25.5 ± 2.7	25.0 ± 2.5*	NS
V'$_E$/V'CO_2 LT	25.8 ± 2.7	26.4 ± 2.8	25.3 ± 2.3*	25.9 ± 2.9	25.1 ± 2.1*‡	<0.05
V'$_E$/V'CO_2 nadir	25.0 ± 2.4	25.4 ± 2.6	24.7 ± 2.3	25.1 ± 2.3	24.5 ± 2.1*	NS
V'$_E$/V'CO_2 interc.	3.2 ± 2.1	2.8 ± 2.0	3.0 ± 2.1	3.4 ± 2.3*	3.1 ± 1.8	NS
V'$_E$/V'CO_2 s_2	45.8 ± 19.5	44.6 ± 8.5	50.8 ± 42.8*	45.1 ± 9.4	44.4 ± 8.4	NS
Power @LT, watt	125 ± 50	92 ± 27	121 ± 36*	131 ± 40*	171 ± 79*†‡	<0.001
V'O_2 @LT, mL/min	1775 ± 555	1428 ± 321	1750 ± 429*	1846 ± 489*	2239 ± 784*†‡	<0.001
Power @RCP, watt	206 ± 64	161 ± 46	206 ± 53*	218 ± 55*	257 ± 80*†‡	<0.001
V'O_2 @RCP, mL/min	2583 ± 710	2094 ± 545	2620 ± 637*	2715 ± 608*	3078 ± 837*†‡	<0.001

*$p < 0.05$ versus ESC A, using post hoc test. †$p < 0.05$ versus ESC B, using post hoc test. ‡$p < 0.05$ versus ESC C, using post hoc test.

Note: Data are presented as mean ± standard deviation.

Abbreviations: BR, Breathing Reserve; I, intercept; LT, lactate threshold; RER, Respiratory Exchange Ratio; V'CO_2, carbon dioxide output; V'O_2, oxygen uptake; VCP, Ventilatory Compensation Point; V'$_E$, minute ventilation; WR, Work Rate.

statistically different. Furthermore, in athletes with V'$_E$/V'CO_2 $s_1 < 22$, PetCO2 was significantly higher at rest ($p < 0.001$), LT ($p < 0.001$), nadir ($p < 0.001$), and at peak work rate ($p < 0.001$) compared to those athletes with V'$_E$/V'CO_2 $s_1 > 32$. Of note, the group of athletes exhibiting V'$_E$/V'CO_2 $s_1 < 22$ showed significantly higher V'O_2 peak, V'O_2/kg peak, and maximal power compared to the group with V'$_E$/V'CO_2 s_1 higher than 32. Watt max of the high ventilatory efficiency group was also significantly higher compared to all athletes studied (see Table 2; $p < 0.05$).

3.4 | Ventilatory efficiency as a continuum

To further investigate the potential link between ventilatory efficiency and exercise tolerance, the athletes were also divided into tertiles based on their V'$_E$/V'CO_2 s_1. The three subgroups were defined as follows: V'$_E$/V'CO_2 $s_1 < 24$, between 24 and 27, and >27. A total of 132 athletes (29.8%)

were classified in the first group, 186 athletes (42.0%) in the second group, and 125 athletes in the third group (28.2%). Importantly, progressively higher ventilatory efficiency was associated with higher V'O_2 peak ($p < 0.001$), V'O_2/kg peak ($p < 0.001$), maximal power ($p < 0.001$), and V'O_2/HR ($p < 0.05$) (Table 5).

4 | DISCUSSION

This is the largest study to assess ventilatory efficiency as related to exercise performance in elite athletes evaluated by CPET. It provides a comprehensive analysis of maximal exercise tolerance and, more importantly, the ventilatory and pulmonary gas exchange adaptations to maximal incremental exercise. Notably, ventilatory efficiency emerged as a potentially critical correlate of athletic performance, highlighting its practical importance beyond conventional cardiopulmonary fitness parameters.
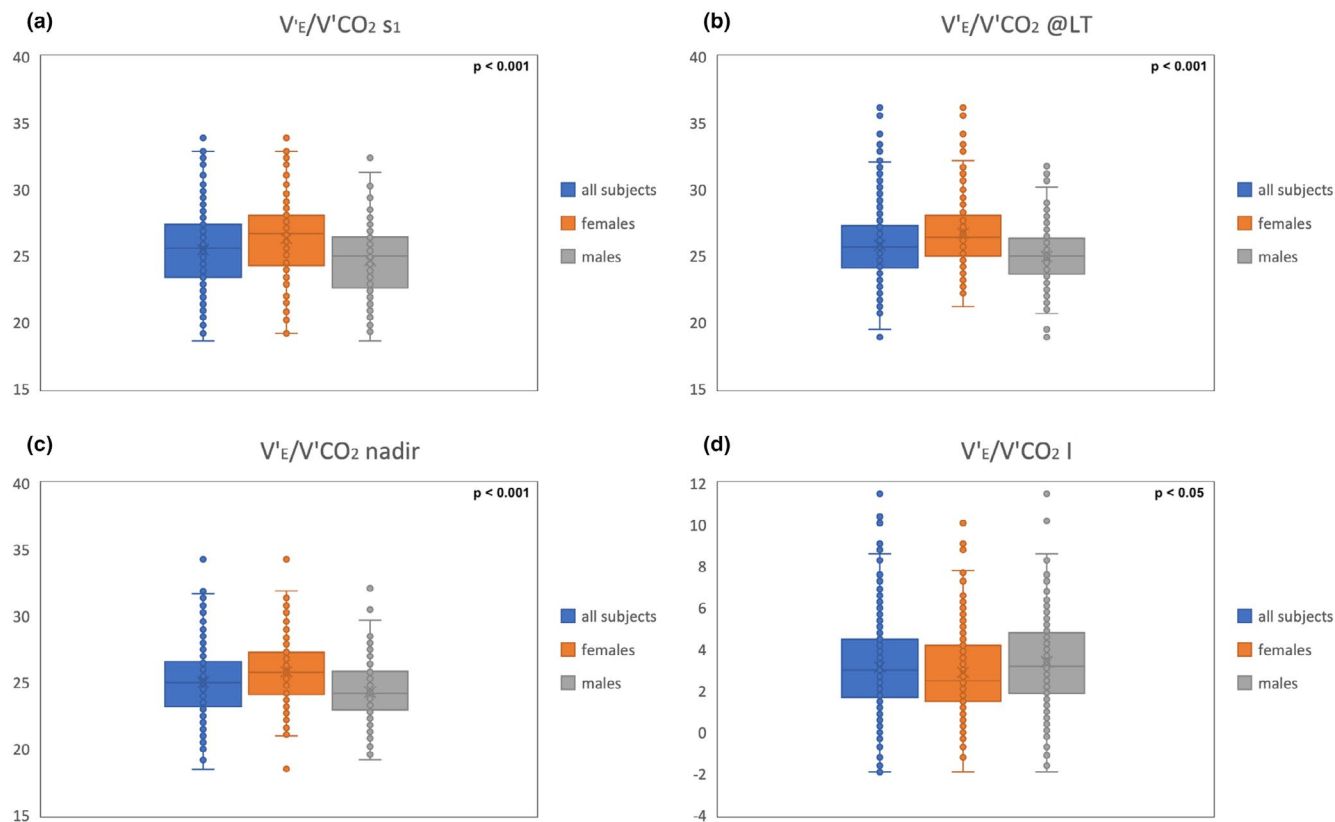
FIGURE 1 Comparison of $V'_E/V'CO_2$ slope (a), at the lactate threshold (b), nadir (c) and intercept (d) between females and males. The y-axis reports the values of $V'_E/V'CO_2$. $V'CO_2$, carbon dioxide output; V'_E, minute ventilation; S_1, slope before the ventilatory compensation point; LT, lactate threshold; I, intercept.

4.1 | Sex differences

One of the main results of our study was the observed difference in ventilatory efficiency between male and female athletes. Females exhibited higher exercise $V'_E/V'CO_2$ values, indicating less efficient CO_2 elimination compared to males. These results are in accordance with previous data from literature in non-athletic populations (Collins et al., 2021; Neder et al., 2001; Sietsema et al., 2020). Several studies have suggested that this difference arises from the mechanical disadvantage that females face during exercise, due to narrower airways and smaller lung volumes (Collins et al., 2021; Dominelli et al., 2013; Guenette et al., 2009; Kilbride et al., 2003; Neder et al., 2001; Sietsema et al., 2020). These physiological factors lead to a higher resistive work of breathing and an increased dead space ventilation tidal volume ratio (V_d/V_t) during exercise; females tend to adopt a more tachypneic breathing pattern, characterized by lower tidal volumes and higher breathing frequency (Collins et al., 2021; Dominelli et al., 2013; Guenette et al., 2009; Kilbride et al., 2003; Neder et al., 2001; Sietsema et al., 2020). Additionally, a lower CO_2 set point in females compared to males has been proposed

as another potential factor contributing to the reduced ventilatory efficiency (Collins et al., 2021; Dominelli et al., 2013; Kilbride et al., 2003; Neder et al., 2001; Sietsema et al., 2020).

4.2 | Athletes stratified by ESC categories

Importantly, we also observed differences in ventilatory efficiency among different ESC sport categories. Notably, endurance athletes (ESC D) exhibited higher ventilatory efficiency compared to athletes engaged in skill-based sports (ESC A). It is possible to hypothesize that a more efficient pulmonary gas exchange during exercise is needed to accomplish the high aerobic demands of endurance sport activities. Future studies, however, are needed to understand whether high ventilatory efficiency in these athletes is genetically based (e.g., neural control of breathing) and/or could be influenced by specific training programs.

We also found that peak $V'O_2$, $V'O_2/kg$, and $V'O_2/HR$ (O_2 pulse) values are markedly increased in the ESC D category compared to the other categories. Research data on this topic are limited. Our findings, however, are in agreement with previous literature, which shows the enhanced
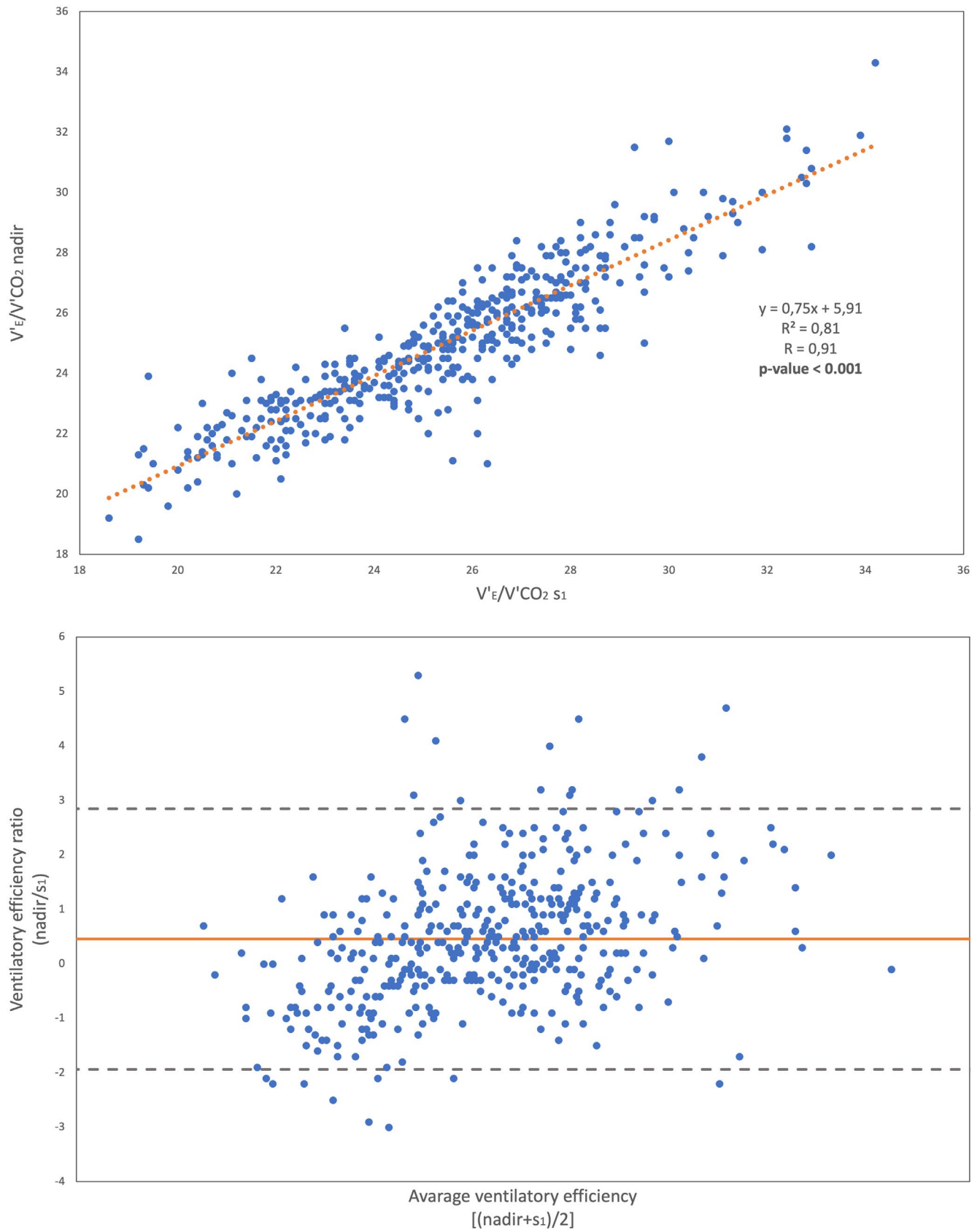
FIGURE 2 Upper panel: Linear regression, comparison between $V'_E/V'CO_2$ nadir versus $V'_E/V'CO_2$ s_1 values. Lower panel: Bland–Altman plot, comparison between $V'_E/V'CO_2$ nadir versus $V'_E/V'CO_2$ s_1 values; $V'CO_2$, carbon dioxide output; V'_E, minute ventilation; S_1, slope before the ventilatory compensation point.

TABLE 4 Ventilatory efficiency below and over limits of normality.

	VE/ VCO2 < 22	VE/ VCO2 > 32	p Value
Number of subjects (%)	51 (11.7)	8 (1.8)	
Age, years	24.8 ± 5.5	25.0 ± 7.2	
Sex			
Males (%)	14 (26.9)	1 (12.5)	
Females (%)	37 (71.1)	7 (87.5)	
Height, cm	178 ± 10	173 ± 6	
Weight, kg	70.8 ± 9.3	72.9 ± 13.9	
Comorbidities			
Asthma	1 (2%)	1 (13%)	NS
Smoking history	0 (0%)	2 (33%)	NS
Hypertension	0 (0%)	0 (0%)	NS
Diabetes	0 (0%)	1 (13%)	NS
Dyslipidemia	1 (2%)	0 (0%)	NS
Estroprogestinic therapy	6 (12%)	3 (38%)	**<0.05**
Maximal power, watt	260 ± 60	205 ± 48	**<0.05**
$V'O_2$ peak, mL/min	3064 ± 723	2526 ± 423	**<0.05**
$V'O_2/Kg$ peak, mL/min/kg	42.8 ± 8.7	35.8 ± 5.0	**<0.05**
$V'O_2$ peak, % predicted	111.5 ± 8.7	122.5 ± 24.0	NS
$V'_E/V'CO_2 s_1$	20.7 ± 0.9	33.0 ± 0.7	**<0.001**
Intercept	5.9 ± 1.9	1.0 ± 1.6	**<0.001**
$V'_E/V'CO_2$ LT	23.3 ± 1.8	32.0 ± 2.3	**<0.001**
$V'_E/V'CO_2$ nadir	21.8 ± 1.2	31.0 ± 1.7	**<0.001**
$V'_E/V'CO_2 s_2$	42.0 ± 10.6	53.0 ± 7.0	**<0.05**
$PetCO_2$ rest, mmHg	34.3 ± 2.7	30.0 ± 4.3	**<0.001**
$PetCO_2$ LT, mmHg	46.8 ± 3.3	35.0 ± 2.6	**<0.001**
$PetCO_2$ nadir, mmHg	50.5 ± 3.0	35.0 ± 2.2	**<0.001**
$PetCO_2$ peak of exercise, mmHg	44.3 ± 4.3	32.0 ± 2.2	**<0.001**
Delta $PetCO_2$, mmHg	16.2 ± 3.8	2.0 ± 5.0	**<0.001**

Note: Data are represented as mean ± standard deviation.

Abbreviations: Delta, $PetCO_2$@nadir – $PetCO_2$@rest; I, intercept; LT, lactate threshold; $V'CO_2$, carbon dioxide output; $V'O_2$, oxygen uptake; V'_E, minute ventilation.

cardiovascular and oxygen-carrying ability and/or oxygen extraction capacity observed in athletes who perform aerobic training (Adami et al., 2022; Degens et al., 2019).

Moreover, in our study, the $V'O_2$/WR relationship was found to be independent of both sex and ESC categories. This confirms data from the literature describing mechanical efficiency ($V'O_2$/WR relationship) to be independent of age, sex, and height (Barron et al., 2015; Sietsema et al., 2020), while the role of fitness level or training in changing this relationship is still debated. Some studies showed higher slopes in trained cyclists (Sietsema et al., 2020) and lower ones in less fit subjects (Neder et al., 2001). On the other hand, it has been stated that lower $V'O_2$/WR values could represent a potential advantage for endurance athletes, resulting in a lower percentage of $V'O_2$ max utilization per work rate (Mazaheri et al., 2021).

4.3 | Athletes stratified by ventilatory efficiency

Another important finding of our study is that we were able to identify a significant subset of athletes, 51 out of 444 athletes (11.7%), showing particularly high ventilatory efficiency (i.e., $V'_E/V'CO_2$ s1 < 22), which is indicative of a different strategy in eliminating CO_2 during exercise. This level of efficiency seemed to be advantageous, as it was associated with greater exercise performance; in fact, when all athletes were divided into three tertiles, according to the levels of ventilatory efficiency, this finding was also confirmed. However, the direct correlation between high ventilatory efficiency and sports performance outcomes remains underexplored and forms a critical avenue for future research.

Our results are in agreement with the work of Bussotti and colleagues that described (Bussotti et al., 2008), in healthy young individuals, a higher exercise tolerance and maximal aerobic capacity in those subjects with a blunted ventilatory response to exercise associated with higher end-tidal CO_2. As shown in Table 3, athletes of ESC D category had higher $V'O_2$ peak associated with higher ventilatory efficiency, that is, lower $V'_E/V'CO_2$@LT. In addition, as shown in Table 3, subjects with very high ventilatory efficiency ($V'_E/V'CO_2$ s_1 < 22) had a higher $V'O_2$ peak compared with those with low ventilatory efficiency ($V'_E/V'CO_2$ s_1 > 32). These findings support the hypothesis, originally proposed by Harms and colleagues (Harms et al., 1997; Harms & Stager, 2005), that a blunted ventilatory response to exercise, with associated lower respiratory muscle work, has a favorable effect on muscle leg blood flow of exercising muscles.

4.4 | Clinical implications

Looking forward, the potential implications of these findings are vast. Establishing a link between ventilatory efficiency and performance could change training strategies and athlete assessment protocols. Moreover, comparing

TABLE 5 Ventilatory efficiency as a continuum.

	$V'_E/V'CO_2 < 24$	$V'_E/V'CO_2$ 24–27	$V'_E/V'CO_2 > 27$	p Value
Number of subjects (%)	132 (29.8)	186 (42.0)	125 (28.2)	
Sex				
Males (%)	84 (64)	105 (56)	40 (32)	
Female (%)	48 (36)	81 (44)	85 (68)	
ESC classification (%)				
A	33 (23)	46 (25)	38 (30)	
B	27 (20)	27 (15)	22 (18)	
C	57 (43)	80 (43)	53 (42)	
D	17 (13)	33 (18)	12 (10)	
Age, years	25 ± 5	25 ± 5	25 ± 6	NS
Height, cm	177 ± 10	176 ± 10	173 ± 10	**<0.05**
BMI, kg/m^2	23.3 ± 2.5	23.6 ± 2.8	23.4 ± 3.7	NS
Maximal power, watt	257 ± 62	246 ± 71	$221 \pm 64^{*\dagger}$	**<0.001**
V'O$_2$ peak, mL/min	3090 ± 696	3038 ± 781	$2746 \pm 686^{*\dagger}$	**<0.001**
V'O$_2$/Kg peak, mL/min/kg	42.7 ± 8.6	41.6 ± 8.5	$39.4 \pm 7.9^*$	**<0.001**
V'O$_2$ peak, % predicted	117.4 ± 25.6	117.6 ± 22.3	120.6 ± 22.9	NS
V'CO$_2$ peak, mL/min	3505 ± 762	3358 ± 834	$2959 \pm 747^*$	**<0.001**
RER	1.15 ± 0.08	$1.12 \pm 0.07^*$	$1.09 \pm 0.07^{*\dagger}$	**<0.05**
V'O$_2$/WR, mL/watt	10.1 ± 0.9	10.1 ± 0.8	10.2 ± 0.9	NS
HR peak, bpm	167 ± 10	167 ± 11	166 ± 12	NS
V'O$_2$/HR, mL/bpm	18.5 ± 4.3	18.2 ± 4.9	$16.7 \pm 4.5^{*\dagger}$	**<0.05**
VE peak, L/min	97.9 ± 24.2	102.6 ± 26.0	100.3 ± 28.6	NS
BR, L/min	33.5 ± 34.7	30.5 ± 19.9	27.0 ± 17.8	NS
V'$_E$/V'CO$_2$ s$_2$	44.9 ± 32.7	44.3 ± 8.2	49.3 ± 8.8	NS

$^*p < 0.05$ versus V'$_E$/V'CO$_2 < 24$, using post hoc test. $^\dagger p < 0.05$ versus V'$_E$/V'CO$_2$ 24–28, using post hoc test.

Note: Data are presented as mean ± standard deviation.

Abbreviations: BR, Breathing Reserve; I, intercept; LT, lactate threshold; RER, Respiratory Exchange Ratio; V'CO$_2$, carbon dioxide output; V'O$_2$, oxygen uptake; VCP, Ventilatory Compensation Point; V'$_E$, minute ventilation; WR, Work Rate.

these CPET-derived parameters across various disciplines could provide deeper insights into how athletes can optimize performance through targeted interventions (e.g., training, diet, etc). Such studies could also stress the use of CPET as a routine part of athletic physical performance evaluation and monitoring, not just for clinical assessments.

5 | CONCLUSIONS

In conclusion, our study not only contributes to the current understanding of cardiopulmonary responses in elite athletes but also opens new insights for the analysis of ventilatory efficiency in sports medicine.

AUTHOR CONTRIBUTIONS

FUNDING INFORMATION

CONFLICT OF INTEREST STATEMENT
We confirm that none of the authors has any conflict of interest.

DATA AVAILABILITY STATEMENT
The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy.

ETHICS STATEMENT
This study received approval from the ethics committee ("Comitato Etico Territoriale Lazio Area 1", approval number 0851/2024). Written informed consent was obtained from each participant.

ORCID
Paolo Palange https://orcid.org/0000-0002-5824-6455

REFERENCES

Adami, P. E., Rocchi, J. E., Melke, N., De Vito, G., Bernardi, M., & Macaluso, A. (2022). Physiological profile comparison between high intensity functional training, endurance and power athletes. *European Journal of Applied Physiology*, *122*, 531–539.

American Physical Therapy Association. (2001). Guide to Physical Therapist Practice Association, American physical therapy. *Physical Therapy*, *81*, 1913.

Arena, R., Myers, J., & Guazzi, M. (2008). The clinical and research applications of aerobic capacity and ventilatory efficiency in heart failure: An evidence-based review. *Heart Failure Reviews*, *13*, 245–269.

Barron, A. J., Dhutia, N. M., Gläser, S., Beate Koch, B., Ewert, R., Obst, A., Dörr, M., Völzke, H., Francis, D. P., & Wensel, R. (2015). Physiology of oxygen uptake kinetics: Insights from incremental cardiopulmonary exercise testing in the study of health in Pomerania. *IJC Metabolic & Endocrine*, *7*, 3–9.

Brown, S. J., Raman, A., Schlader, Z., & Stannard, S. R. (2012). Ventilatory efficiency in juvenile elite cyclists. *Journal of Science and Medicine in Sport*, *16*, 266–270.

Bussotti, M., Magrì, D., Previtali, E., Farina, S., Torri, A., Matturri, M., & Agostoni, P. (2008). End-tidal pressure of CO_2 and exercise performance in healthy subjects. *European Journal of Applied Physiology*, *103*, 727–732.

Collins, S. É., Phillips, D. B., Brotto, A. R., Rampuri, Z. H., & Stickland, M. K. (2021). Ventilatory efficiency in athletes, asthma and obesity. *European Respiratory Review*, *30*, 200206.

Cooper, B. G., Stocks, J., Hall, G. L., Culver, B., Steenbruggen, I., Carter, K. W., Thompson, B. R., Graham, B. L., Miller, M. R., Ruppel, G., Henderson, J., Vaz Fragoso, C. A., & Stanojevic, S. (2017). The global lung function initiative (GLI) network: Bringing the world's respiratory reference values together. *Breathe*, *13*, e56–e64.

Degens, H., Stasiulis, A., Skurvydas, A., Statkeviciene, B., & Venckunas, T. (2019). Physiological comparison between non-athletes, endurance, power and team athletes. *European Journal of Applied Physiology*, *119*, 1377–1386.

Di Paco, A., Dubé, B. P., & Laveneziana, P. (2017). Changes in ventilatory response to exercise in trained athletes: Respiratory physiological benefits beyond cardiovascular performance. *Archivos de Bronconeumología*, *53*, 237–244.

Di Paolo, M., Teopompi, E., Savi, D., Crisafulli, E., Longo, C., Tzani, P., Longo, F., Ielpo, A., Pisi, G., Cimino, G., Simmonds, N. J., Neder, J. A., Chetta, A., & Palange, P. (2019). Reduced exercise ventilatory efficiency in adults with cystic fibrosis and normal to moderately impaired lung function. *Journal of Applied Physiology*, *127*, 501–512.

Dominelli, P. B., Foster, G. E., Dominelli, G. S., Henderson, W. R., Koehle, M. S., McKenzie, D. C., & Sheel, A. W. (2013). Exercise-induced arterial hypoxaemia and the mechanics of breathing in healthy young women. *The Journal of Physiology*, *591*, 3017–3034.

ERS Task Force, Palange, P., Ward, S. A., Carlsen, K.-H., Casaburi, R., Gallagher, C. G., Gosselinke, R., O'Donnell, D. E., Puente-Maestu, L., Schols, A. M., Singh, S., & Whipp, B. J. (2007). Recommendations on the use of exercise testing in clinical practice. *The European Respiratory Journal*, *29*, 185–209.

Graham, B. L., Steenbruggen, I., Miller, M. R., Barjaktarevic, I. Z., Cooper, B. G., Hall, G. L., Hallstrand, T. S., Kaminsky, D. A., McCarthy, K., McCormack, M. C., Oropez, C. E., Rosenfeld, M., Stanojevic, S., Swanney, M. P., & Thompson, B. R. (2019). Standardization of spirometry 2019 update. An official American Thoracic Society and European Respiratory Society technical statement. *American Journal of Respiratory and Critical Care Medicine*, *200*, e70–e88.

Guenette, J. A., Querido, J. S., Eves, N. D., Chua, R., & Sheel, A. W. (2009). Sex differences in the resistive and elastic work of breathing during exercise in endurance-trained athletes. *American Journal of Physiology. Regulatory, Integrative and Comparative Physiology*, *297*, R166–R175.

Guenette, J. A., Witt, J. D., McKenzie, D. C., Road, J. D., & Sheel, A. W. (2007). Respiratory mechanics during exercise in endurance-trained men and women. *The Journal of Physiology*, *581*, 1309–1322.

Harms, C. A., Babcock, M. A., McClaran, S. R., Pegelow, D. F., Nickele, G. A., Nelson, W. B., & Dempsey, J. A. (1997). Respiratory muscle work compromises leg blood flow during maximal exercise. *Journal of Applied Physiology*, *82*, 1573–1583.

Harms, C. A., McClaran, S. R., Nickele, G. A., Pegelow, D. F., Nelson, W. B., & Dempsey, J. A. (1998). Exercise-induced arterial hypoxaemia in healthy young women. *The Journal of Physiology*, *507*, 619–628.

Harms, C. A., & Stager, J. M. (2005). Low chemoresponsiveness and inadequate hyperventilation contribute to exercise-induced hypoxemia. *Journal of Applied Physiology*, *79*, 575–580.

Kilbride, E., McLoughlin, P., Gallagher, C. G., & Harty, H. R. (2003). Do gender differences exist in the ventilatory response to progressive exercise in males and females of average fitness? *European Journal of Applied Physiology*, *89*(6), 595–602. https://doi.org/10.1007/s00421-003-0853-z

Mazaheri, R., Schmied, C., Niederseer, D., & Guazzi, M. (2021). Cardiopulmonary exercise test parameters in AthleticPopulation: A review. *Journal of Clinical Medicine*, *10*, 5073.

Neder, J. A., Berton, D. C., Arbex, F. F., Alencar, M. C., Rocha, A., Sperandio, P. A., Palange, P., & O'Donnell, D. E. (2017). Physiological and clinical relevance of exercise ventilatory

efficiency in COPD. *The European Respiratory Journal*, *49*, 1602036.

Neder, J. A., Nery, L. E., Peres, C., & Whipp, B. J. (2001). Reference values for dynamic responses to incremental cycle ergometry in males and females aged 20 to 80. *American Journal of Respiratory and Critical Care Medicine*, *164*, 1481–1486.

Neder, J. A., Phillips, D. B., O'Donnell, D. E., & Dempsey, J. A. (2022). Excess ventilation and exertional dyspnoea in heart failure and pulmonary hypertension. *European Respiratory Journal*, *60*, 2200144.

Pelliccia, A., Sharma, S., Gati, S., Bäck, M., Börjesson, M., Caselli, S., Collet, J. P., Corrado, D., Drezner, J. A., Halle, M., Hansen, D., Heidbuchel, H., Myers, J., Niebauer, J., Papadakis, M., Piepoli, M. F., Prescott, E., Roos-Hesselink, J. W., Graham Stuart, A., ... ESC Scientific Document Group. (2021). 2020 ESC guidelines on sports cardiology and exercise in patients with cardiovascular disease. *European Heart Journal*, *42*, 17–96.

Petek, B. J., Churchill, T. W., Gustus, S. K., Schoenike, M. W., Nayor, M., Moulson, N., Guseh, J. S., Van Atta, C., Blodgett, J. B., Contursi, M., Lewis, G. D., Baggish, A. L., & Wasfy, M. M. (2023). Characterization of ventilatory efficiency during cardiopulmonary exercise testing in healthy athletes. *European Journal of Preventive Cardiology*, *30*, e21–e24.

Petek, B. J., Gustus, S. K., & Wasfy, M. M. (2021). Cardiopulmonary exercise testing in athletes: Expect the unexpected. *Current Treatment Options in Cardiovascular Medicine*, *23*, 49.

Petek, B. J., Tso, J. V., Churchill, T. W., Guseh, J. S., Loomer, G., Di Carli, M., Lewis, G. D., Weiner, R. B., Kim, J. H., Wasfy, M. M., & Baggish, A. L. (2022). Normative cardiopulmonary exercise data for endurance athletes: the Cardiopulmonary Health and Endurance Exercise Registry (CHEER). *European Journal of Preventive Cardiology*, *29*, 536–544.

Radke, T., Crook, S., Kaltsakas, G., Louvaris, Z., Berton, D., Urquhart, D. S., Kampouras, A., Rabinovich, R. A., Verges, S., Kontopidis, D., & Boyd, J. (2019). ERS statement on standardisation of cardiopulmonary exercise testing in chronic lung diseases. *European Respiratory Review*, *28*, 180101.

Ramos, R. P., Alencar, M. C. N., Treptow, E., Arbex, F., Ferreira, E. M. V., & Neder, J. A. (2013). Clinical usefulness of response profiles to rapidly incremental cardiopulmonary exercise testing. *Pulmonary Medicine*, *2013*, 359021.

Salazar-Martínez, E., de Matos, T. R., Arrans, P., Santalla, A., & Orellana, J. N. (2018). Ventilatory efficiency response is unaffected by fitness level, ergometer type, age or body mass index in male athletes. *Biology of Sport*, *35*, 393–398.

Salazar-Martínez, E., Terrados, N., Burtscher, M., Santalla, A., & Orellana, J. N. (2016). Ventilatory efficiency and breathing pattern in world-class cyclists: A three-year observational study. *Respiratory Physiology & Neurobiology*, *229*, 17–23.

Sietsema, K. E., Stringer, W. W., Sue, D. Y., & Ward, S. (2020). *Wasserman & Whipp's principles of exercise testing and interpretation*. Lippincott Williams & Wilkins (LWW). Wolters Kluwer Health.

Sun, X. G., Hansen, J. E., Garatachea, N., Storer, T. W., & Wasserman, K. (2002). Ventilatory efficiency during exercise in healthy subjects. *American Journal of Respiratory and Critical Care Medicine*, *166*, 1443–1448.

Weisman, I. M., et al. (2001). ATS/ACCP statement on cardiopulmonary exercise testing. Chapter III (Methodology) and Chapter V (Reference Values), *American Journal of Respiratory and Critical Care Medicine*, *167*.