Pathophysiology of exertional dyspnoea in athletes and its impact on ventilatory efficiency

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Summary

Introduction: During lengthy, high-intensity exercise it is not unusual for healthy athletes to complain of breathlessness. Therefore, the main objectives of this study were to elucidate the pathophysiology of this exertional dyspnea and to test its impact on ventilatory efficiency.

Material and method: Observational, retrospective, analytical study, conducted on 252 healthy recreational athletes (59 women) who performed a maximal, incremental-stepped cardiopulmonary exercise test (CPET) on a treadmill with breath-by-breath gas-exchange analysis and continuous ECG recording. Test were divided into 3 phases in relation to ventilatory thresholds (VT1 and VT2). The collected data were compared with reference values and analyzed using either the analysis of variance (ANOVA) or the normal distribution test.

Results: The results obtained at the end of the CPET showed in both sexes: 1) a difference between inspiratory and expiratory minute volume (V_{Eins}-V_{Eexp}) at peak exercise ≥73% of vital capacity (VC), 2) a critical decrease in inspiratory reserve volume (IRV<500 ml), 3) a tidal volume to inspiratory capacity ratio (V_T/IC) >88%, 4) a decrease in inspiratory capacity (IC) as of its peak (near VT2) with an increase in end-expiratory lung volume (EELV) >360 ml, 5) a decrease in expiratory time (T_E) of 74%, 6) signs of dynamic airway compression in >57% of the subjects, and 7) a nadir V_E/VCO_2<34.

Conclusion: Exertional dyspnea was caused by both inspiratory mechanical constraint and pulmonary hyperinflation secondary to expiratory flow limitation, both induced, in turn, by the ventilatory response to metabolic acidosis resulting from high-intensity exertion; however, these restrictions did not affect ventilatory efficiency.

Key words:
Exertional dyspnea.
Ventilatory threshold.
Metabolic acidosis. Mechanical restriction. Hyperinflation.
Efficiency ventilatory.

Fisiopatología de la disnea de esfuerzo en deportistas y su impacto sobre la eficiencia ventilatoria

Resumen

Introducción: Durante el ejercicio prolongado de alta intensidad no es inusual que deportistas sanos se quejen de dificultad respiratoria al llegar al esfuerzo máximo, por lo que planteamos el presente estudio con el objetivo de dilucidar la fisiopatología de esta disnea de esfuerzo y evaluar su impacto sobre la eficiencia ventilatoria.

Material y método: Estudio observacional, retrospectivo y analítico, realizado sobre 252 deportistas recreativos sanos (59 mujeres) que realizaron una prueba de esfuerzo (CPET) incremental y máxima con análisis de gases respiración a respiración y registro continuo ECG en una cinta ergométrica. La CPET se dividió en 3 fases en relación con los umbrales ventilatorios 1 y 2 (VT1 y VT2). Los datos recopilados se compararon con valores de referencia y se analizaron mediante los test análisis de varianza (ANOVA) y distribución normal.

Resultados: Los resultados obtenidos mostraron en ambos sexos: 1) una diferencia entre el volumen minuto inspiratorio y espiratorio (V_{Eins}-V_{Eexp}) al final del ejercicio ≥73% de la capacidad vital (VC), 2) una disminución crítica del volumen inspiratorio de reserva (IRV<500 ml), 3) una relación volumen corriente/capacidad inspiratoria (V_T/IC) >88%, 4) una disminución de la capacidad inspiratoria (IC) a partir de su pico (cerca de VT2) con un aumento del volumen pulmonar al final de la espiración (EELV) >360 ml, 5) una disminución del tiempo espiratorio (T_E) del 74%, 6) signos de compresión dinámica de la vía aérea en >57% de los sujetos, y 7) un nadir V_E/VCO_2<34.

Conclusión: La disnea de esfuerzo fue causada tanto por la restricción mecánica inspiratoria como por la hiperinsuflación pulmonar secundaria a la limitación del flujo espiratorio, ambas inducidas, a su vez, por la respuesta ventilatoria a la acidosis metabólica resultante del esfuerzo de alta intensidad; sin embargo, estas restricciones no afectaron la eficiencia ventilatoria.

Palabras clave:
Disnea de esfuerzo.
Umbral ventilatorio.
Acidosis metabólica. Restricción mecánica. Hiperinsuflación.
Eficiencia ventilatoria.

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Introduction

During a cardiopulmonary exercise test (CPET), it is not unusual for athletes to complain of shortness of breath on reaching their maximal exercise level, saying that the mask to which the mass flow sensor is connected does not allow them to take in enough air. This sensation of dyspnoea also appears during competition and high-intensity training; however, it does not appear during sub-maximal exertion, in relation to expiration, nor is it a reason for bringing tests to an end. Exertional dyspnoea has been studied widely in different chronic cardiopulmonary diseases (asthma, chronic obstructive pulmonary disease, interstitial lung disease, cystic fibrosis, pre-capillary pulmonary hypertension, congestive heart failure, etc.)[1-6] but not so much, at least recently, in healthy recreational athletes. Consequently, we put forward this study to help explain the pathophysiology of this dyspnoea and its impact on ventilatory efficiency.

Materials and methods

Subjects

Observational, retrospective, analytical study, carried out on a linear sample of 193 men (41.3 ± 11.2 years of age) and 59 women (39.8 ± 12.6 years of age), all healthy recreational athletes, mostly mountain runners, who voluntarily performed a CPET in the Sports Medicine Unit at Consorcio Hospitalario Provincial de Castellón to determine their sports fitness and level of aerobic endurance.

Methodology

After signing the informed consent, their anamneses were taken and a physical examination was performed while at rest which included: collection of personal and family medical history, anthropometric study (height, weight and body mass index [BMI]), 12-lead electrocardiogram (ECG) (Cardiosoft®), pre- and post-exercise cardiopulmonary auscultation, peripheral pulse reading, bilateral manual blood pressure (BP) measurement (Riester®) and slow and forced vital capacity spirometry tests (Vyntus ® CPX). The exclusion criteria for the study were: 1) clinical history of exercise-induced asthma, 2) abnormal resting spirometry, according to reference values[7]; and 3) sub-maximal CPET for any reason.

The subjects then performed a maximal CPET following a continuous, incremental-step protocol (warm-up: 5 km/5 min; exercise: 8 km/h/2 min + Δ2 km/h/2 min.; recovery: 5 km/h/5 min; 1% incline) on treadmill (HP Cosmos Quasar®) with breath-by-breath gas analysis (Vyntus ® CPX) and continuous ECG recording (Cardiosoft®). A 12-lead ECG was printed on paper and BP was recorded manually in the second minute of each phase, at the end of the test and after 10 minutes of recovery, and arterialised right-earlobe blood lactate (Lactate Pro 2®) was measured in the first minute of recovery. Exercise tidal flow-volume loops (extFVL) were placed in the maximal flow-volume loop (MFVL) at rest and during the first 30 s of the last minute of each phase following the indications of Vyntus® CPX. The maximal test criteria were: reaching a plateau at VO_2 (VO_{2max}), predicted maximum heart rate (HR) (220-age), respiratory exchange ratio (RER) >1.1 and/or signs of exhaustion. All the tests were performed between 8:30 a.m. and 1 p.m. in controlled environmental conditions (temperature: 22 – 24ºC; humidity: 40 – 70%, at sea level) and after the subjects had consumed only a standard breakfast or similar meal at least 2 hours beforehand. After the completion of the test, the mean per minute of the data recorded were calculated and printed in tabular form for clinical and physiological assessment according to the reference values[8-10], determining the ventilatory thresholds 1 (VT1 or isocapnic buffering point) and 2 (VT2 or respiratory compensation point) according to Skinner & McLellan's three-phase model[11]. This allowed us to divide the test into 3 phases: phase 1, between rest and VT1 (aerobic phase); phase 2, between VT1 and VT2 (aerobic-anaerobic transition zone); and phase 3, between VT2 and the end of the test (anaerobic phase).

Statistical method

The following were considered independent variables: minute (min) and running speed (km/h) at rest, VT1, VT2 and maximal exercise; and dependent variables: minute ventilatory volume (V_E), inspiratory tidal volume (V_{Ti}), expiratory tidal volume (V_{Te}), inspiratory time (T_I), expiratory time (T_E), breathing rate (B_R), inspiratory capacity (IC), end-expiratory lung volume (EELV) and the ratio of dead space volume to tidal volume (VD/VT). From these parameters and those of resting spirometry [vital capacity (VC) and expiratory flow in the 1st second of forced vital capacity (FEV_1)], the following parameters were calculated: Inspiratory V_E ($MV_i = V_{Ti} \times B_R$), expiratory VE ($MV_e = V_{Te} \times B_R$), the V_{Ti}/IC, V_{Te}/IC, V_{Ti}/T_I, V_{Te}/T_E, T_I/T_{TOT} and IC/EELV ratios, total breath time ($T_{TOT} = T_I+T_E$), inspiratory reserve volume ($IRV = IC-V_{Ti}$), expiratory reserve volume (ERV = VC-IC), maximal voluntary ventilation ($MVV_1 = FEV_1 \times 35$ and $MVV_2 = FEV_1 \times 40$), ventilatory equivalent of O_2 (V_E/VO_2), ventilatory equivalent of CO_2 (V_E/VCO_2) and ventilatory reserve [$V_{r(1\text{-}2)} = 100-(VE \times 100/MVV_{(1\text{-}2)})$]. The other metabolic and haemodynamic parameters recorded, although shown in the Results section, were not analysed because they were beyond the scope of this study.

For the statistical study (Microsoft Excel 2010®), the analysis of variance (ANOVA) test and the normal distribution test were used. Previously, we applied the Kolmogorov-Smirnov test to compare the normal distribution of the variables. To analyse whether the distribution and percent change (%Δ) for paired samples was the same throughout the test (e.g. MVi at rest, during and at maximal exercise), the analysis of variance (ANOVA) test was used for repeated measures. When multivariate analysis detected statistically significant differences, multiple comparisons were performed using Scheffé's method, which determined between which variables such differences existed. The normal distribution test was used to analyse whether the distribution of the variables was the same for two independent samples at a given time (e.g. MVi vs MVe in maximal exercise). The results were presented as the mean ± standard deviation (SD). The statistical significance level was set at $P < 0.05$ and expressed in the text.

This study was carried out in accordance with the code of ethics of the World Medical Association (Declaration of Helsinki) for experiments on human subjects, with the informed consent of the patients, and was approved by the Research Committee of Consorcio Hospitalario Provincial de Castellón.

Results

Study conducted on 252 healthy recreational athletes, 193 men (41.3 ± 11.2 years of age; 7.7 ± 3.1 hours of training/week) and 59 women (39.8 ± 12.6 years of age; 7.0 ± 3.1 hours of training/week), mostly mountain runners, whose anthropometric study showed:

Men:
- height: 174.7 ± 6.8 cm
- weight: 74.4 ± 9.5 kg
- BMI: 24.4 ± 2.6 kg/m^2

Women
- height: 163.1 ± 5.6 cm
- weight: 57.0 ± 6.1 kg
- BMI: 21.5 ± 2.1 kg/m^2

The results obtained from anamnesis and clinical examination at rest showed no contraindications for CPET or reasons for exclusion from the study (Table 1). During CPET, the haemodynamic, metabolic and respiratory adaptations to exertion were normal (Tables 2, 3, 4 and 5), with all tests being maximal and ending with exhaustion.

In relation to the respiratory system, V_E, MV_i and MV_e increased progressively from rest to peak exercise in both sexes ($P < 0.0001$) (Tables 4 and 5). The largest increases were recorded in phase 1 ($P < 0.0001$), with no differences between the increases in VE, MVi and MV_e ($P > 0.05$) (Tables 4 and 5). The MV_i values were always greater than those of MV_e with a final difference of 3.74 ± 2.53 l mi^{n-1} ($P = 0.038$) (73.8% VC) in men and 2.94 ± 1.79 ($P > 0.05$) (81.7% VC) in women. The MVVs calculated were $MVV_1 = 139.3 \pm 21.2$ l min^{-1} and $MVV_2 = 159.1 \pm 24.3$ l min^{-1} in men, and $MVV_1 = 99.0 \pm 15.6$ l min^{-1} and $MVV_2 = 113.1 \pm 17.9$ l min^{-1} in women; therefore $V_{r1} = 6.3 \pm 12.5\%$ and $V_{r2} = 18.0 \pm 11.0\%$ in men, and $V_{r1} = 9.4 \pm 17.1\%$ and $V_{r2} = 22.4 \pm 9.9\%$ in women.

Table 2. Haemodynamic adaptations to exertion.

		At rest	VT1	VT2	Maximum
Time (min)	M	0	6.0 ± 1.7	8.8 ± 1.6	15.1 ± 2.0
	W	0	5.2 ± 2.2	8.3 ± 1.5	12.7 ± 2.0
Speed (km/h)	M	0	7.6 ± 1.4	10.0 ± 1.6	16.5 ± 2.1
	W	0	7.0 ± 1.6	9.4 ± 1.5	14.2 ± 2.0
HR (bpm)	M	56.6 ± 9.4	122.4 ± 17.9	146.1 ± 15.3	179.2 ± 11.9
	W	57.0 ± 8.8	125.9 ± 19.8	153.3 ± 13.5	177.7 ± 11.6
TMHR (bpm)	M				178.7 ± 11.2
	W				180.2 ± 12.6
% CI	M				100.4 ± 5.8
	W				98.7 ± 5.1
% H_{RR}	M				101.0 ± 8.9
	W				98.4 ± 7.4
% SpO_2	M	97.8 ± 1.1	97.8 ± 1.8	97.7 ± 2.0	97.6 ± 1.2
	W	98.1 ± 0.9	98.0 ± 1.1	97.9 ± 1.1	97.9 ± 1.2
O_2 pulse (ml beat^{-1})	M	6.9 ± 1.8	15.4 ± 3.1	17.5 ± 2.8	19.8 ± 3.0
	W	5.0 ± 1.3	11.1 ± 2.4	12.6 ± 2.2	13.9 ± 2.3
T O_2 pulse (ml beat^{-1})	M				14.8 ± 1.8
	W				9.5 ± 1.6
% T O_2 pulse	M				133.8 ± 17.5
	W				148.8 ± 27.0
SBP (mmHg)	M	114.1 ± 11.4	143.5 ± 15.3	158.8 ± 19.6	186.3 ± 7.4
	W	104.7 ± 12.2	127.7 ± 16.7	141.7 ± 18.1	160.6 ± 17.2
DBP (mmHg)	M	70.2 ± 7.6	69.8 ± 8.1	70.5 ± 8.3	71.2 ± 8.3
	W	65.4 ± 7.0	65.3 ± 6.9	65.6 ± 6.9	65.8 ± 7.9
HR x SBP	M	6472 ± 1330	17613 ± 3423	23217 ± 3960	33973 ± 3942
	W	5965 ± 1165	16063 ± 3184	21676 ± 2988	28502 ± 3264

The values are expressed as mean±SD. Statistical study not performed. M: men (n = 193). W: women (n = 59). VT1: ventilatory threshold 1. VT2: ventilatory threshold 2. T: theoretical. HR: heart rate CI: chronotropic index. HRR: reserve heart rate. SpO_2: oxygen saturation; SBP: systolic blood pressure. DBP: diastolic blood pressure; HR x SBP: rate-pressure product.

Table 1. Results of simple and forced spirometry.

SS:	VC (l)	VT (l)	IRV (l)	ERV (l)	
M	5.07 ± 0.75	1.00 ± 0.39	2.78 ± 0.67	1.34 ± 0.58	
W	3.60 ± 0.51	0.74 ± 0.30	2.02 ± 0.47	0.84 ± 0.38	
FS	**%FVC**	**%FEV_1**	**%FEV_1/FVC**	**%MMEF**	**%PEF**
M	97.8 ± 10.5	99.2 ± 12.3	82.5 ± 6.4	94.9 ± 25.4	105.9 ± 17.8
W	93.7 ± 10.7	95.4 ± 10.4	84.5 ± 5.4	85.1 ± 20.3	95.6 ± 18.0
% Normal	>80%	>80%	>70%	>60%	80 – 120%

The values are expressed as mean±SD. SS: simple spirometry. FS: forced spirometry. M: men (n = 193). W: women (n = 59). VC: vital capacity. VT: tidal volume. IRV: inspiratory reserve volume. ERV: expiratory reserve volume. FVC: forced vital capacity. FEV_1: expiratory flow in the 1st second of forced vital capacity. FEV_1/FVC ratio; MMEF: maximum expiratory flow at 25-75% of FVC. PEF: peak expiratory flow. % Normal[7].

In the men, V_{Ti} and V_{Te} increased gradually from rest to the minute 13.8 ± 2.1 (14 km h^{-1}), at which point they reached their highest values ($V_{Ti} = 2.725 \pm 0.400$ l= 53.8 ± 5.8%VC; $V_{Te} = 2.648 \pm 0.392$ l = 52.3 ± 5.7% VC) ($P < 0.0001$), to then decrease from there until the end of exercise (P (VT_i)= 0.0055; $P(V_{Te}) = 0.0064$) (Table 4). The women, on the other hand, reached their maximum value in the minute 11.7 ± 1.9 (12 km/h) ($V_{Ti} = 1.848 \pm 0.258$ l = 51.7 ± 5.3% VC; $V_{Te} = 1.790 \pm 0.260$ l = 50.0 ± 5.4% VC) ($P < 0.0001$), then decreased until the end of exercise (P (V_{Ti}) >0.05; P (V_{Te}) >0.05) (Table 5). The greatest increases in both sexes were recorded in phase 1 ($P < 0.0001$), with no differences between the increases in

Table 3. Metabolic adaptations to exertion.

		At rest	VT1	VT2	Maximum
Time (min)	M	0	6.0 ± 1.7	8.8 ± 1.5	15.1 ± 2.0
	W	0	5.2 ± 2.2	8.3 ± 1.5	12.7 ± 2.0
Speed (Km h^{-1})	M	0	7.6 ± 1.4	10.0 ± 1.6	16.5 ± 2.1
	W	0	7.0 ± 1.6	9.4 ± 1.5	14.2 ± 2.0
VO_2 (ml min^{-1})	M	382.5 ± 51.2	1886.7 ± 454.0	2542.2 ± 411.1	3532.9 ± 518.1
	W	281.3 ± 65.3	1398.0 ± 381.1	1922.1 ± 328.8	2460.6 ± 396.6
VO_2 (ml kg^{-1} min^{-1})	M	5.2 ± 1.1	25.5 ± 5.9	34.4 ± 5.2	47.8 ± 6.5
	W	5.0 ± 1.2	24.7 ± 6.6	33.9 ± 5.4	43.3 ± 6.0
%VO_{2max}	M	10.9 ± 2.6	53.1 ± 10.5	72.0 ± 9.6	99.9 ± 5.8
	W	11.6 ± 2.9	56.6 ± 12.1	78.5 ± 9.6	99.9 ± 0.4
T VO_{2max} (ml min^{-1})	M				2661.0 ± 420.9
	W				1711.5 ± 335.3
T %VO_{2max}	M	14.7 ± 3.5	71.7 ± 16.8	97.1 ± 18.0	134.0 ± 16.9
	W	16.9 ± 4.6	83.9 ± 25.6	115.6 ± 25.8	146.8 ± 26.6
VCO_2 (ml min^{-1})	M	315.1 ± 77.4	1554.4 ± 425.2	2319.9 ± 402.5	4041.2 ± 553.3
	W	235.6 ± 67.5	1121.4 ± 370.1	1762.8 ± 328.8	2751.1 ± 427.6
RER	M	0.82 ± 0.08	0.82 ± 0.06	0.91 ± 0.05	1.15 ± 0.06
	W	0.83 ± 0.09	0.79 ± 0.07	0.93 ± 0.06	1.12 ± 0.07

The values are expressed as mean±SD. Statistical study not performed. M: men (n = 193). W: women (n = 59). VT1: ventilatory threshold 1. VT2: ventilatory threshold 2. T: theoretical. VO_2: O_2 consumption; VO_{2max}: maximum O_2 consumption; VCO_2: CO_2 volume eliminated; RER: respiratory exchange ratio.

Table 4. Respiratory adaptations to exertion in men.

	At rest	VT1	VT2	Maximum
Time	0	6.0 ± 1.7	8.8 ± 1.6	15.1 ± 2.0
Speed (Km h^{-1})	0	7.6 ± 1.4	10.0 ± 1.6	16.5 ± 2.1
V_E (l min^{-1})	12.3 ± 2.9	45.1 ± 12.4	65.8 ± 12.9	129.4 ± 20.2
M_{Vi} (l min^{-1})	12.7 ± 2.8	46.5 ± 13.1	67.9 ± 13.3	133.1 ± 20.9
M_{Ve} (l min^{-1})	12.4 ± 2.9	45.2 ± 12.4	65.9 ± 12.8	129.4 ± 20.3
V_{Ti} (l)	0.823 ± 0.256	1.801 ± 0.444	2.273 ± 0.420	2.623 ± 0.390
V_{Te} (l)	0.799 ± 0.252	1.750 ± 0.423	2.208 ± 0.409	2.550 ± 0.382
IRV (l)	2.107 ± 0.127	1.225 ± 0.649	0.778 ± 0.598	0.378 ± 0.383
ERV (l)	2.161 ± 0.371	2.062 ± 0.566	2.036 ± 0.612	2.147 ± 0.531
IC (l)	2.93 ± 0.48	3.03 ± 0.57	3.05 ± 0.62	2.94 ± 0.53
EELV (l)	4.11 ± 0.46	4.02 ± 0.62	3.99 ± 0.65	4.10 ± 0.59
% IC/EELV	71.6 ± 11.9	77.4 ± 16.8	79.3 ± 22.4	73.6 ± 18.6
% V_{Ti}/IC	28.3 ± 7.6	61.2 ± 17.4	76.9 ± 18.0	90.3 ± 11.4
B_R (bpm)	16.0 ± 3.3	26.2 ± 6.1	30.5 ± 6.4	51.4 ± 8.5
T_{TOT} (s)	3.93 ± 0.90	2.44 ± 0.67	2.06 ± 0.48	1.20 ± 0.20
T_I (s)	1.55 ± 0.46	1.15 ± 0.36	1.00 ± 0.26	0.58 ± 0.10
T_E (s)	2.38 ± 0.68	1.29 ± 0.34	1.07 ± 0.24	0.62 ± 0.11
T_I/T_{TOT} (%)	39.8 ± 7.1	47.0 ± 3.4	48.1 ± 3.3	48.5 ± 2.5
V_{Tins}/T_I (l s^{-1})	0.56 ± 0.20	1.65 ± 0.46	2.36 ± 0.48	4.58 ± 0.73
V_{Tesp}/T_E (l s^{-1})	0.35 ± 0.09	1.43 ± 0.42	2.13 ± 0.44	4.20 ± 0.72
V_D/V_T	13.1 ± 4.1	10.7 ± 3.1	9.3 ± 3.0	9.6 ± 2.8
V_E/VO_2	32.5 ± 4.9	23.9 ± 2.9	25.9 ± 3.2	36.4 ± 5.0
V_E/VCO_2	39.6 ± 4.8	29.2 ± 3.0	28.4 ± 3.0	32.1 ± 3.5
$P_{ET}O_2$ (mmHg)	117.0 ± 3.8	102.8 ± 4.5	105.8 ± 4.5	117.0 ± 3.8
$P_{ET}CO_2$ (mmHg)	36.0 ± 3.0	39.8 ± 3.0	40.5 ± 3.8	36.8 ± 3.0

The values are expressed as mean±SD. n= 193. ANOVA and normal distribution tests."p"value in the text. VT1: ventilatory threshold 1. VT2: ventilatory threshold 2. V_E: minute ventilation volume. MV_i: inspiratory minute ventilation volume. MV_e: expiratory minute ventilation volume. V_{Ti}: inspiratory tidal volume. V_{Te}: expiratory tidal volume. IRV: inspiratory reserve volume. ERV: expiratory reserve volume. IC: inspiratory capacity. EELV: end-expiratory lung volume. B_R: breathing rate. T_{TOT}: total breath time. T_I: inspiratory time. T_E: expiratory time. T_I/T_{TOT}: ratio of inspiratory time to total time. V_D/V_T: ratio of dead space volume to tidal volume. V_{Ti}/T_I: inspiratory flow. V_{Te}/T_E: expiratory flow; V_E/VO_2: ventilatory equivalent of O_2. V_E/VCO_2: ventilatory equivalent of CO_2. $P_{ET}O_2$: partial pressure of end-tidal O_2; $P_{ET}CO_2$: partial pressure of end-tidal CO_2.

V_{Ti} and V_{Te} (P >0.05) (Table 6). V_{Ti} increased at the expense of decreased IRV throughout the trial (P <0.0001) and of decreased ERV only to VT2 ($P_{(men)} = 0.0075$; $P_{(women)}$ >0.05), after which ERV increased to values similar to those at rest ($P_{(men)}$ >0.05; $P_{(women)}$ >0.05). The V_{Ti} values were always greater than those of V_{Te}, with a final difference of 0.071 ± 0.050 l in men ($P = 0.0314$) and 0.060 ± 0.030 l in women (P >0.05).

In the men, IC increased significantly up to minute 8.3 ± 3.0 (10 km h^{-1}) (IC = 3.43 ± 0.49 l) (P <0.0001) and then decreased to values similar to those at rest (P <0.0001). Logically, EELV behaved conversely to IC, reaching a minimum value of 3.61 ± 0.49 l (Table 4). The IC/EELV ratio reached a maximum value of 96.3 ± 17.3 (P <0.0001). The V_{Ti}/IC ratio progressively increased from rest to maximal exercise, reaching a value of 90.3 ± 11.4% (P <0.0001). In the women, IC increased significantly up to minute 7.4 ± 2.9 (8 km h^{-1}) (IC = 2.42 ± 0.35 l) (P <0.0001) and then decreased to values similar to those at rest (P <0.0001). EELV reached a minimum value of 2.77 ± 0.35 l (Table 5). The IC/EELV ratio reached a maximum value of 88.1 ± 14.6% (P <0.0001), and the V_{Ti}/IC ratio gradually increased from rest to maximal exercise to reach a value of 88.1 ± 9.5% (P <0.0001).

B_R increased progressively from rest to maximal exercise in both sexes (P <0.0001) (Tables 4 and 5), the smallest increases being in phase 2 (P <0.0001) (Table 6). B_R increased due to the decrease in T_{TOT} (P <0.0001), which occurred at the expense of both T_I and T_E. The largest decreases in T_I occurred in phase 3 ($P_{(men)}$ <0.0001; $P_{(women)}$ <0.005), while the largest in T_E were in phases 1 and 3 ($P_{(men)}$ <0.0001; $P_{(women)}$ <0.005) (Table 6). The T_E values were always greater than those of T_I (P <0.0001) although the differences decreased according to the evolution of the T_I/T_{TOT} ratio.

V_{Ti}/T_I and V_{Te}/T_E increased progressively from rest to maximal exercise in both sexes (P <0.0001). V_{Ti}/T_I was always greater than V_{Te}/T_E ($P_{(men)}$ <0.0001; P(women) <0.01) (Tables 4 and 5). The greatest increases occurred in phase 1 (P <0.0001), with the increase in V_{Te}/T_E being greater than in V_{Ti}/T_I ($P_{(men)}$ <0.0001; $P_{(women)}$ <0.001); however, the increases in phases 2 and 3 no longer showed significant differences between them (P >0.05) (Table 6).

Table 5. Respiratory adaptations to exertion in women.

n = 59	At rest	VT1	VT2	Maximum
Time	0.0	5.2 ± 2.2	8.3 ± 1.5	12.7 ± 2.0
Speed (km h^{-1})	0.0	7.0 ± 1.6	9.4 ± 1.5	14.2 ± 2.0
V_E (l min^{-1})	9.5 ± 2.5	34.4 ± 10.9	52.6 ± 9.7	88.6 ± 15.9
MV_i (l min^{-1})	10.1 ± 2.1	35.2 ± 11.5	54.4 ± 10.1	90.1 ± 13.0
MV_e (l min^{-1})	9.6 ± 2.5	34.4 ± 11.0	52.6 ± 9.8	87.2 ± 12.9
V_{Ti} (l)	0.642 ± 0.283	1.280 ± 0.333	1.621 ± 0.268	1.792 ± 0.254
V_{Te} (l)	0.601 ± 0.229	1.254 ± 0.322	1.569 ± 0.267	1.734 ± 0.257
IRV (l)	1.398 ± 0.439	0.875 ± 0.459	0.529 ± 0.420	0.308 ± 0.271
ERV (l)	1.556 ± 0.390	1.440 ± 0.346	1.445 ± 0.381	1.495 ± 0.402
IC (l)	2.04 ± 0.45	2.16 ± 0.38	2.15 ± 0.43	2.10 ± 0.35
EELV (l)	3.15 ± 0.47	3.03 ± 0.44	3.04 ± 0.43	3.09 ± 0.46
% IC/EELV	66.4 ± 17.9	72.7 ± 16.8	72.4 ± 18.7	69.6 ± 17.1
% V_{Ti}/IC	33.3 ± 17.6	60.8 ± 18.0	77.7 ± 17.0	88.1 + 9.5
B_R (bpm)	16.8 ± 4.0	27.6 ± 6.1	34.0 ± 6.0	50.8 ± 7.6
T_{TOT} (s)	3.86 ± 1.30	2.29 ± 0.57	1.83 ± 0.33	1.21 ± 0.18
T_I (s)	1.48 ± 0.55	1.05 ± 0.26	0.87 ± 0.16	0.59 ± 0.09
T_E (s)	2.39 ± 0.93	1.24 ± 0.33	0.96 ± 0.20	0.62 ± 0.10
T_I/T_{TOT} (%)	38.7 ± 7.4	46.1 ± 2.8	47.7 ± 3.5	49.1 ± 2.8
V_{Ti}/T_I (l s^{-1})	0.47 ± 0.25	1.28 ± 0.43	1.90 ± 0.39	3.06 ± 0.47
V_{Te}/T_E (l s^{-1})	0.26 ± 0.07	1.07 ± 0.34	1.68 ± 0.34	2.85 ± 0.45
V_D/V_T	10.5 ± 1.9	10.4 ± 2.5	10.2 ± 2.1	11.2 ± 1.9
V_E/VO_2	34.1 ± 5.0	24.5 ± 3.2	27.5 ± 3.3	36.4 ± 6.6
V_E/VCO_2	41.1 ± 5.5	31.1 ± 3.6	30.1 ± 3.6	32.6 ± 6.8
P_ETO_2 (mmHg)	114.0 ± 4.5	104.3 ± 5.3	108.8 ± 3.8	116.3 ± 3.8
$P_{ET}CO_2$ (mmHg)	32.3 ± 3.0	37.5 ± 4.5	39.0 ± 3.8	36.8 ± 3.8

The values are expressed as mean±SD. n= 59. ANOVA and normal distribution tests. "*P*" value in the text. VT1: ventilatory threshold 1. VT2: ventilatory threshold 2. V_E: minute ventilation volume. MV_i: inspiratory minute ventilation volume. MV_e: expiratory minute ventilation volume. V_{Ti}: inspiratory tidal volume. V_{Te}: expiratory tidal volume. IRV: inspiratory reserve volume. ERV: expiratory reserve volume. IC: inspiratory capacity. EELV: end-expiratory lung volume. B_R: breathing rate. T_{TOT}: total breath time. T_I: inspiratory time. T_E: expiratory time. T_I/T_{TOT}: ratio of inspiratory time to total time. V_D/V_T: ratio of dead space volume to tidal volume. V_{Ti}/T_I: inspiratory flow. V_{Te}/T_E: expiratory flow; V_E/VO_2: ventilatory equivalent of O_2. V_E/VCO_2: ventilatory equivalent of CO_2. $P_{ET}O_2$: partial pressure of end-tidal O_2; $P_{ET}CO_2$: partial pressure of end-tidal CO_2.

Table 6. Changes (Δ) between phases.

		Phase 1.	Phase 2.	Phase 3.
Δ% V_{Eins}	M	70.6 ± 10.4	31.1 ± 16.2	48.0 ± 11.9
	W	68.7 ± 10.6	36.0 ± 14.7	38.7 ± 12.0
Δ% V_{Eesp}	M	70.6 ± 10.9	30.9 ± 15.7	48.2 ± 11.9
	W	70.2 ± 10.1	35.2 ± 14.2	39.4 ± 12.5
Δ% V_{Tins}	M	52.4 ± 16.5	20.0 ± 17.3	13.0 ± 12.0
	W	49.0 ± 15.6	21.5 ± 13.1	9.3 ± 9.7
Δ% V_{Tesp}	M	52.6 ± 10.6	19.8 ± 17.0	13.1 ± 12.2
	W	51.1 ± 14.5	20.4 ± 12.9	9.3 ± 9.7
Δ IRV (l)	M	-0.88 ± 0.71	-0.45 ± 0.71	-0.46 ± 0.63
	W	-0.52 ± 0.49	-0.35 ± 0.38	-0.22 ± 0.45
Δ ERV (l)	M	-0.10 ± 0.60	-0.03 ± 0.67	0.11 ± 0.59
	W	-0.12 ± 0.44	0.00 ± 0.31	0.05 ± 0.37
Δ% V_{Tins}/IC	M	32.9 ± 17.9	15.7 ± 21.4	13.4 ± 19.4
	W	27.4 ± 20.1	16.9 ± 16.4	8.7 ± 18.7
Δ% B_R	M	36.1 ± 17.7	13.1 ± 16.1	39.7 ± 12.8
	W	37.4 ± 10.5	18.6 ± 12.8	32.5 ± 11.1
Δ% T_I	M	-21.3 ± 31.2	-11.0 ± 17.5	-39.1 ± 13.5
	W	-21.2 ± 43.8	-15.3 ± 12.7	-39.9 ± 10.9
Δ% T_E	M	-42.8 ± 18.0	-14.8 ± 17.0	-40.0 ± 13.5
	W	-43.9 ± 18.8	-20.3 ± 14.4	-34.2 ± 12.2
Δ% T_I/T_{TOT}	M	15.3 ± 15.3	2.0 ± 6.6	0.5 ± 7.4
	W	15.3 ± 16.3	4.0 ± 5.1	2.2 ± 5.7
Δ% V_{Tins}/T_I	M	63.7 ± 16.5	29.8 ± 15.7	47.6 ± 11.8
	W	61.7 ± 15.3	33.5 ± 14.2	37.3 ± 11.9
Δ% V_{Tesp}/T_E	M	73.5 ± 11.5	32.1 ± 17.3	48.2 ± 13.1
	W	73.0 ± 10.8	36.6 ± 14.6	40.3 ± 12.7

The values are expressed as mean ± SD. M: men (n = 193). W: women (n = 59). ANOVA test. "*P*" value in the text. MV_i: inspiratory minute ventilation volume. MV_e: expiratory minute ventilation volume. V_{Ti}: inspiratory tidal volume. V_{Te}: expiratory tidal volume. IRV: inspiratory reserve volume. ERV: expiratory reserve volume. V_{Ti}/IC: ratio of inspiratory tidal volume to inspiratory capacity. BR: breathing rate. T_I: inspiratory time. T_E: expiratory time. T_I/T_{TOT}: ratio of inspiratory time to total time. V_{Ti}/T_I: inspiratory flow. V_{Te}/T_I: expiratory flow.

The V_D/V_T ratio progressively decreased to VT2 ($P_{(men)}$ <0.0001; $P_{(women)}$ >0.05). From this point on, a non-significant rise was observed in men (*P* >0.05), while a significant one was observed in women (*P* = 0.0034) (Tables 4 and 5).

The lowest point of V_E/VO_2 was recorded in VT1, while that of VE/VCO_2 was in VT2 in both sexes (Tables 4 and 5).

Meanwhile, plotting the extFVLs in the MFVLs showed that, towards the end of exercise, 57% of men and 68% of women displayed airflow limitation due to dynamic airway compression with medium or low lung volumes (>20% encroachment of extFVL on MFVLs).

Finally, a comparison of male and female respiratory parameters at the end of exercise showed significant differences (*P* <0.0001) in MV_i, MV_e, V_{Ti}, V_{Te}, ERV, IC, EELV, V_{Ti}/T_I, V_{Te}/T_E and V_D/V_T, while the differences in IRV, %IC/EELV, %V_T/IC, B_R, T_{TOT}, T_I, T_E, T_I/T_{TOT}, V_E/VO_2 and V_E/VCO_2 were not statistically significant (*P* >0.05).

Discussion

As a consequence of the increase in the metabolic demand for O_2 and the production of CO_2 and H^+, physical exercise always leads to an increase in V_E. The ventilatory response to exercise is proportional to the metabolic rate and aims to maintain arterial pH, PaO_2 and $PaCO_2$[12-14]. According to the three-phase model described by Skinner & McLellan[11], during incremental exercise, two inflection points can be identified on the V_E-workload graph. Initially (phase 1 or aerobic phase) V_E, VO_2 and

VCO_2 increase linearly to a point from which a first inflection point (VT1) can be observed (start of phase 2 or aerobic-anaerobic transition phase), after which V_E and VCO_2 increase disproportionately with respect to VO_2. This is due to the additional CO_2 generated after the buffering of H^+ from the dissociation of lactic acid by HCO_3-, which stimulates the central and peripheral chemoreceptors[14,15]. Initially, this increase in V_E is sufficient to compensate for metabolic acidosis[9] and VE maintains a linear relationship with VCO_2, so the V_E/VCO_2 ratio remains stable or decreases (isocapnic buffering), while the V_E/VO_2 ratio begins to increase. If the intensity of exercise continues to increase, another inflection point (VT2) is reached (beginning of phase 3 or anaerobic phase) in which the V_E slope increases further and its relationship with VCO_2 ceases to be linear, increasing the V_E/VCO_2 ratio. This reflects a respiratory compensation of metabolic acidosis[9,10], which is usually overcome with time, so plasma pH decreases to 7.25-7.35[9].

Basically, and coinciding with the literature [9,16,17], the increase in V_E occurred at the expense of both V_T and B_R; however, the relative contribution of each parameter was different according to the phase of the test. In phases 1 and 2, V_E increased mainly at the expense of V_T, while in phase 3 it did so at the expense of B_R, even though V_T continued to increase up to workloads close to maximum, as occurs in subjects with very high ventilatory demands[9]. At its maximum value, V_T tripled the at-rest value and accounted for more than 50% of VC, which agrees with what other authors describe[9,18-20].

Up to approximately VT2, VT increased due to both the decrease of IRV and, to a lesser extent, that of ERV, due to the recruitment of the expiratory muscles[21] (increase in IC and decrease in EELV); from this point, IRV continued to decrease while ERV began to increase (decrease in IC and increase in EELV) in such a way that by the end of the exercise, IC and EELV had values similar to those at rest. At that point, IRV had a critical value <500 ml[22-24] and the V_T/IC ratio was > 88%[19,21,25,26], both important dyspnoea-producing factors[27] due to the increase in inspiratory elastic load with decreased compliance, represented by the V_T/IC ratio[4,9,21], and the permanent contraction of the inspiratory muscles, which shorten and need to generate high pulmonary pressure to overcome the elastic recoil forces of the lung[28]. Mechanical inspiratory restriction, therefore, occurred[6,19]. On the other hand, the resulting increase in inspiratory neural drive required to maintain V_E, although not measured, must have contributed to the sensation of dyspnoea due to the neuromechanical dissociation at play[2,24,27,29]. Assuming that total lung capacity (TLC) does not change with exertion[30], measurement of IC at rest and during CPET (with subsequent calculation of EELV, IRV, ERV, and V_T/IC) is the best physiological and clinical approach to identifying mechanical ventilatory restriction during exercise and investigate the mechanisms involved in and quantify the intensity of exertional dyspnoea[3,13]. In this respect, a decrease in IC during exercise, accompanied by a corresponding increase in EELV, is the typical finding of dynamic hyperinflation[3,6,13,27,30-32].

As of VT2, there was a change in respiratory pattern and V_E increased mainly at the expense of B_R. During exercise, $_{BR}$ can increase up to 6-7 times in highly trained athletes[9]. The increase in B_R reflected a decrease in both T_I and T_E, said decrease being greater in the latter, as reflected in the literature[9]. The drop in T_E is caused by the early interruption of expiration, which leads to incomplete emptying of the lungs[3] and, consequently, an increase in EELV[33], and to increases in V_{Ti} needing to be carried out purely at the expense of IRV, which implies breathing with ever-growing lung volumes. The increase in B_R also implies more breathing in and out per unit of time, with the consequent increase in the work of the respiratory musculature to overcome both elastic resistance (decreased compliance) and viscous resistance (turbulent airflow)[5,18,20,34]. A shorter T_E also causes forced expiration and higher expiratory flow rates (V_{Te}/T_E), which increases the likelihood of dynamic airway compression and expiratory flow limitation (EFL), thus contributing to the development of dynamic hyperinflation[6,20,21]. Indeed, the extFVLs of 57% of the male and 68% of the female subjects showed signs of dynamic airway compression. Such compression has been described in normal trained adults[21,34] and is not necessary for the development of dynamic hyperinflation[33]. EFL also has an inhibitory effect on the ventilatory response to exercise[20] as subjects tend to stop expiration prematurely at a volume at which EFL does not yet exist or is minimal[33]. The intensity of dyspnoea, however, seems to correlate more with the degree of hyperinflation than with airflow limitation[31], highlighting the importance of neuromechanical dissociation in the development of dyspnoea[2]. Finally, an increase in B_R leads to an increase in V_D, which is initially compensated by a greater increase in VT, so V_D/V_T decreases[20]. In our study, this compensation occurred up to VT2, given that, thereafter, V_D/V_T increased slightly in both sexes.

Dynamic hyperinflation, meanwhile, is a consequence of trapped air as a result of an imbalance between the volume of inspired and expired air[31,32]. Our outcomes showed gradually increasing differences between V_{Ti} and V_{Te}. These differences have been explained by arguing that the VO_2 from inspired air is greater than the VCO_2 exhaled[18]; however, it does not explain the differences when RER ≥1. Translated into VE, the differences between MV_i and MV_e at the end of exercise accounted for more than 73% of VC.

Despite the mechanical restrictions and airflow limitations found, the respiratory musculature showed no obvious signs of fatigue, given the evolution of the ratios V_{Ti}/T_I and V_{Te}/T_E, with V_{Ti}/T_I being greater than V_{Te}/T_E throughout the entire test. The V_{Ti}/T_I ratio has been used as an index of muscle shortening speed and inspiratory drive[35].

V_r, on the other hand, has traditionally been used to determine the existence and degree of ventilatory restriction, in such a way that a V_r <15% is considered pathological[9,21]; however, its use entails important limitations[9,34] since, in addition to it being possible that there is ventilatory restriction with a normal V_r[6,36], trained athletes can reach and even exceed their theoretical MVV[10], which implies a V_r with negative values. In our study, we obtained V_{r1} <15% and V_{r2} >15% in both sexes. In all events, a V_r <15% in trained people is always associated with a VO_{2max} higher than the reference value[9,37], as our results show.

In relation to ventilatory efficiency, defined by the amount of ventilation necessary to remove metabolically produced CO_2[38], a nadir of

V_E/VCO_2 <349 is considered normal. A higher value during exercise reflects: 1) a low $PaCO_2$, as a result of metabolic acidosis, 2) a high VD/V_T ratio due to a ventilation-perfusion mismatch or right-left shunt[13], or 3) very shallow breathing[9]. Furthermore, a high V_E/VCO_2 results in abnormally high inspiratory neural drive and earlier mechanical limitations, which increase dyspnoea[39]. The subjects in our study presented mechanical inspiratory restriction and expiratory flow limitation, but not ventilatory inefficiency, given the V_E/VCO_2 and $P_{ET}CO_2$ values recorded in both sexes.

Finally, the men and women showed significant differences in those respiratory parameters highly dependent on lung size (V_E, V_T, etc.)[20]; however, the parameters indicative of mechanical restriction (IRV, $\%V_T/IC$) and those dependent mainly on neural drive[16] (B_R, T_{TOT}, T_I, T_E) did not show significant differences, so the two sexes share the pathophysiology of exertional dyspnoea.

In summary, unlike in patients with chronic lung diseases[1-6], mechanical pulmonary limitations do not seem to be a primary limiting factor of exercise in healthy recreational athletes because ventilatory efficiency (V_E/VCO_2 and $P_{ET}CO_2$), O_2 saturation (SpO_2), O_2 supply (O_2 pulse) and O_2 consumption (VO_2) remain normal, as our results show. Exertional dyspnoea is, therefore, most probably a consequence of pulmonary restrictions derived from respiratory compensation of metabolic acidosis because they only appear after passing VT2. Acidosis likely acts as a limiting trigger for lung function in a manner analogous to how it limits muscle contraction by inhibiting the enzymatic activity of energy metabolism and altering the release of Ca^{+2} from the sarcoplasmic reticulum and its interaction with troponin C[40].

The study has various limitations. The degree of muscle fatigue and of neuromechanical dissociation was not measured. Similarly, arterial blood gases were not measured, so changes in acid-base balance were deduced from the ventilatory response (VT1, VT2) and descriptions in the literature[9-11]. Finally, post-exertional spirometry was not performed, so hypothetical bronchial hyperresponsiveness to exertion was only ruled out by pulmonary auscultation at the end of recovery.

Conclusion

Exertional dyspnoea was caused by both mechanical inspiratory restriction and pulmonary hyperinflation secondary to expiratory flow limitation, both induced, in turn, by the ventilatory response to metabolic acidosis resulting from high-intensity exertion. However, these pulmonary restrictions did not affect ventilatory efficiency.

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Conflict of interest

The authors declare no conflict of interest.

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