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Intercostal muscle oxygenation during expiratory load breathing at rest

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ABSTRACT

Background: During acute bronchial obstruction, despite a higher work of breathing, blood supply and oxygen availability may be reduced in intercostal muscles because of mechanical constraints. This hypothesis was assessed in healthy subjects breathing with and without expiratory load (ETL).

Methods: Eleven men (24 ± 2 years) breathed at rest for 5 min in unloaded condition and for 20 min through a 20-cmH_2O ETL. Tissue saturation index (TSI) and changes (Δ) in concentration of total and oxy-haemoglobin ([tHb] and [O_2Hb]) were measured in the seventh intercostal space by near-infrared spectroscopy.

Results: [tHb] and [O_2Hb] decreased with ETL (-5.16 μM and -3.54 μM; $p < 0.05$). TSI did not vary. Negative correlations were observed between Δ[O_2Hb] and changes in expiratory flow rate (ΔVt/Te) and between ΔTSI and Δ $\dot{V}$E (r = -0.78 and -0.74; $p \leq 0.01$).

Conclusion: Despite decreases in Hb concentrations, saturation in oxygen was not reduced with ETL in intercostal muscles, suggesting a satisfactory ventilatory and/or hemodynamic arrangement.

1. Introduction

Obstructive lung diseases are characterized by airway narrowing. In asthma, the bronchoconstriction induced by different factors such as allergens, environmental conditions or exercise is sudden and reversible. In chronic obstructive pulmonary diseases (COPD), obstruction is not fully reversible and is associated with airway wall damage and reduced elastic lung recoil due to inflammation and long duration of the disease. Whatever the cause, bronchial obstruction induces an increase in expiratory resistance. As a result, expiratory muscles are recruited to maintain expiratory flow by increasing driving pressure (Gorini et al., 1999). Active expiration renders it possible to exhale until reaching static equilibrium volume before a new inspiration. However, pulmonary hyperinflation due to a progressive rise in end-expiratory lung volume is commonly observed and contributes to dyspnea. As ventilatory requirements are higher, hyperinflation occurs more frequently during exercise than at rest (Gagnon et al., 2014; Mediano et al., 2017).

During pulmonary hyperinflation, in order to preserve ventilation, a shift in tidal volume to a less compliant part of the respiratory pressure-volume curve occurs and inspiratory muscle load increases (O'Donnell, 2006). However, muscle stretch and higher strength can lead to a compression of capillary vessels in the muscle (Leenaerts and Decramer, 1990; Supinski et al., 1990; Järvholm et al., 1991; McCully, 2010). Hence, blood perfusion may be decreased during contraction, at a time when needs are increased. Furthermore, during hyperinflation, inspiratory muscle activity seems to be maintained during expiration, thereby reducing their relaxation period (Martin et al., 1980; Muller et al., 1980; Gorini et al., 1999). In this condition, the decreased blood perfusion occurring during muscle contraction may not be sufficiently compensated for during the relaxation period, inducing inadequacy between oxygen demand and availability.

Respiratory alkalosis is a common acid-base disturbance reported during acute severe asthma in patients with better preservation of forced expiratory flows (Raimondi et al., 2013), which increases haemoglobin-oxygen affinity. Therefore, oxygen extraction impairment could worsen the difficulties in meeting the expected oxygen demand in respiratory muscles.

To summarize, during acute severe obstruction, paradoxical events may occur simultaneously in the respiratory muscles, affecting their oxygenation.

Acute obstruction can be simulated in healthy subjects by applying expiratory resistance at the mouth, thereby shedding light on adaptive responses and, more precisely, on ventilatory muscle adaptations in case of increased work of breathing. The aim of this study was to evaluate, in healthy subjects at rest, the effect of a 20-cmH_2O expiratory load on intercostal muscle oxygenation. Investigation was targeted at the intercostal muscles because we supposed that their functional position and their length might be modified during loaded breathing due to lung hyperinflation and changes in thoracic pressure or even by a

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Table 1
Anthropometric and respiratory characteristics.

	Absolute values			Predicted values (%)		
BMI (kg/m^2)	25	±	3		–	
Body fat mass (%)	13	±	6		–	
Right 7th IS ATT (mm)	4.2	±	2.1		–	
ERV (L)	1.7	±	0.4		–	
IRV (L)	2.7	±	0.5		–	
IC (L)	3.6	±	0.5		–	
SVC (L)	5.3	±	0.8	105	±	15
FEV1 (L)	4.3	±	0.6	104	±	14
FVC (L)	5.2	±	0.8	107	±	15
FEV1/FVC (%)	83	±	4	101	±	5
MMEF 25-75% (L/sec)	4.5	±	0.7	90	±	15

Values are mean ± SD. BMI; body mass index, IS; intercostal space, ATT; adipose tissue thickness, ERV; expiratory reserve volume, IRV; inspiratory reserve volume, IC; inspiratory capacity, SVC; slow vital capacity, FEV1; forced expiratory volume during the first second, FVC; forced vital capacity, MMEF; mean median expiratory flow between 25% and 75% of FVC.

change in respiratory pattern. Intercostal muscles were investigated noninvasively using near-infrared spectroscopy (NIRS) to assess oxygenation-dependent chromophores during loaded expiration. We postulate that decreased intercostal muscle oxygenation may be involved in dyspnea and possibly linked to a vascular compression due to a stretch and/or high muscle strength.

2. Methods

2.1. Subjects

Eleven healthy active men (24 ± 2 years, 1.70 ± 0.10 m, 71 ± 8 kg) were included in this study. Anthropometric and pulmonary function characteristics are summarized in Table 1. All subjects had a skinfold inferior to 20 mm at the seventh right intercostal space. For each participant, FEV1 was higher than 80% of the predicted value (Quanjer et al., 1993) and FEV1/FVC ratio was superior to 70%. No history of cardio-respiratory disease or disturbance was reported. All subjects tolerated the expiratory resistance applied during the experimentation. The protocol was fully and explicitly presented, and the signed consent form was returned prior to the beginning of the study, which was approved by the CERSTAPS ethical committee (2018-25-01-22).

2.2. Study protocol

2.2.1. Experimental protocol

The protocol is shown in Fig. 1. First, subjects breathed as naturally as possible for 5 min (control period). Five minutes later, a 20-cmH_2O expiratory threshold load (ETL, Threshold PEP, Respironics Inc., Murrysville, PA, USA) was applied at the mouth for 20 min (ETL period). No instruction was given concerning the respiratory behaviour to adopt when ETL was imposed. During the control and ETL periods, subjects were seated on a chair and breathed with a nose clip. A placebo tube was used during the control condition to produce the same dead space as the ETL device. To avoid any effects due to trunk movements, subjects were required to maintain their posture to the greatest possible extent.

2.2.2. Measurements and materials

Anthropometry. A skinfold caliper (Harpenden, British Indicators Ltd., St. Albans, England) was used to assess skinfold at the seventh right intercostal space. Body fat mass was assessed with a whole-body bioelectrical impedance analysis (Tanita BC-418 MA, Tanita Corporation, Tokyo, Japon).

Pulmonary function tests. A computerised spirometer (Hyp'Air Compact+, Medisoft, Dinant, Belgium) was used following calibration to perform pulmonary function tests. Each maneuver was conducted according to the ATS/ERS Task Force recommendations (Miller et al., 2005). During respiratory functional exploration, three acceptable slow and forced vital capacities (SVC and FVC, respectively) were obtained and represented conventional pulmonary volumes and flows. During the protocol, a set of two acceptable SVC maneuvers was carried out during the last minute of the control condition, with the pneumotach connected to the placebo tube. Two other sets were carried out at 10 min and at the end of the 20 min ETL period (10' and 20'ETL), with the pneumotach connected to the resistance. Inspiratory and expiratory reserve volumes (IRV and ERV, respectively), SVC and inspiratory capacity (IC) were measured. The data retained for analysis were selected according to the ATS criteria (American Thoracic Society, 1995).

Respiratory muscle oxygenation. Near-infrared spectroscopy (NIRS) (Oxymon Mk III, Artinis Medical Systems, Zetten, The Netherlands) was used to continuously and non-invasively assess concentration changes in (Δ) oxygenated and deoxygenated haemoglobin (Δ [O_2Hb] and Δ [HHb], respectively) in the respiratory muscles (Athanasopoulos et al., 2010; de Bisschop et al., 2014). Concentration change in total haemoglobin (Δ [tHb]) was calculated as the sum of Δ [O_2Hb] and Δ [HHb]. The changes for the relative NIRS variables were based on the zero rendered by the device at the beginning of the recording. The tissue saturation index (TSI) was likewise recorded. The optode was placed in the seventh intercostal space, on the right side of the subject, between the midclavicular and the anterior axillary lines. The inter-optode distance was adjusted between 3.3 and 4.8 mm according to adipose tissue thickness. A differential pathlength factor of 4 was used.

Concentration changes in oxygenated and deoxygenated haemoglobin were assessed using wavelengths of 859 and 763 nm, respectively. Data were recorded at 10 Hz and exported at 1 Hz after a running average filtering.

Respiratory pattern and gas exchanges. Inspiratory and expiratory times (Ti and Te, respectively) and tidal volume (Vt) were measured breath-by-breath using a Metamax 3B device (Cortex Biophysik GmbH, Leipzig, Germany). In this setting, total respiratory time (Ttot), inspiratory duty cycle (Ti/Ttot), breathing frequency (BF) and ventilaory flow ($\dot{V}E$) were calculated, as mean inspiratory and expiratory flow rates (Vt/Ti and Vt/Te). Oxygen consumption ($\dot{V}O_2$), carbon dioxide production ($\dot{V}CO_2$) and end-tidal CO_2 pressure ($PetCO_2$) were likewise recorded. Respiratory exchange ratio (RER) and respiratory equivalents in oxygen ($\dot{V}E/\dot{V}O_2$) and carbon dioxide ($\dot{V}E/\dot{V}CO_2$) were calculated. A switch from the Metamax 3B to the Hyp'Air Compact + was performed during the ETL period for the first set of SVC. The pneumotach of the Metamax 3B was reconnected to the ETL immediately afterwards. Flow and gas calibrations were performed before each experimentation.

Dyspnea. Perception of dyspnea was assessed using the modified 0–10 Borg-scale, one minute before each set of pulmonary function tests (Kendrick et al., 2000).

Pulse oximetry. Peripheral haemoglobin oxygen saturation (SpO_2)

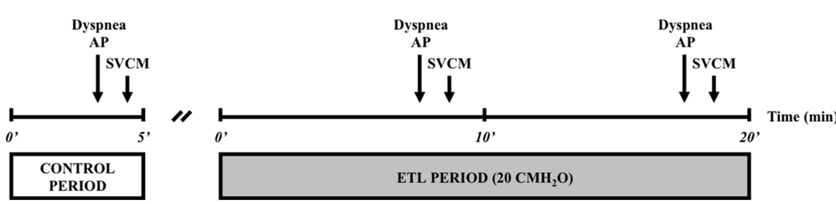

Fig. 1. Protocol and time measurements. AP; arterial pressures, SVCM; slow vital capacity maneuver, ETL; expiratory threshold load.

was recorded continuously at the right index using a pulse oximeter (Wrist Ox2 3150, Nonin Medical Inc., Plymouth, MN, USA).

Cardiovascular parameters. After calibration, stroke volume (SV) and heart rate (HR) were measured non-invasively and beat-by-beat (PhysioFlow PF-05, Manatec Medical, Poissy, France) using a bio-impedance technique and an ECG derivation (Charloux et al., 2000). Cardiac output ($\dot{Q}c$) was calculated as the product of SV and HR. Systolic and diastolic blood pressures (SBP and DBP, respectively) were measured using an automatic sphygmomanometer (Mobil-O-Graph 24 h ABP, IEM GmbH, Stolberg, Germany), one minute before each set of pulmonary function tests. Mean arterial pressure (MAP) was calculated as follows: MAP = DBP + 1/3 (SBP - DBP).

2.3. Statistical analysis

Statistical analysis was performed with Statistica (StatSoft Inc., Tulsa, OK, USA). Data spontaneously obtained at the end of the control period (Ctrl) and at 10' and 20'ETL were included in the analysis. For variables recorded continuously, means were calculated from the last 30 s preceding each round of spirometry. As soon as any data (or mean) was missing, the subject was removed from analysis of the corresponding variable. A repeated one-way ANOVA with 3 levels was performed, followed by a Tuckey post-hoc analysis when ANOVA was significant. Gaussian distribution and the sphericity were assessed with Shapiro-Wilk and Mauchly tests, respectively. The correlation coefficient between the variables was assessed using the Pearson or Spearman test, according to Gaussian distribution, and was based on the changes in variables (Δ = 20'ETL - Ctrl). Values were expressed as mean ± standard deviation (SD) and results were considered as significant for a p-value < 0.05.

3. Results

3.1. Ventilation

Ventilatory variables are displayed in Fig. 2 and Table 2. Tidal volume and $\dot{V}E$ increased with ETL as compared to Ctrl (20'ETL: +0.6 L and +7 L/min; $p \leq 0.001$). Conversely, BF decreased with ETL (10'ETL: -4.1 c/min; $p < 0.001$ and 20'ETL: -2.3 c/min; $p < 0.05$). Inspiratory time, Ttot, Ti/Ttot and Vt/Te were significantly greater with ETL than during Ctrl, while Te and Vt/Ti did not vary (Fig. 2). Dyspnea occurred with ETL (Borg score, 20'ETL: 3.4 ± 2.1 vs. Ctrl: 0.4 ± 0.4; $p < 0.001$).

ERV and SVC were lower with ETL than during Ctrl ($p < 0.01$), whereas IRV and IC did not change.

Data were not significantly different between 10' and 20'ETL for any of the previous variables.

3.2. Intercostal muscle oxygenation

NIRS values are shown in Fig. 3. [tHb] and [O_2Hb] was lower at 20'ETL as compared to Ctrl (-5.16 μM and -3.54 μM, respectively; $p < 0.05$) while [HHb] did not change. Tissue saturation index was 68 ± 8% during Ctrl and did not vary significantly with ETL.

3.3. Gas exchanges

As compared to Ctrl, RER increased at 20'ETL (+0.2, $p < 0.001$), as well as $\dot{V}E/\dot{V}CO_2$ (+14.6, $p < 0.001$) and SpO_2 (+2%, $p < 0.001$). Conversely, $PetCO_2$ decreased at 20'ETL (-12 mmHg; $p < 0.001$) (Table 2).

$\dot{V}O_2$ and $\dot{V}CO_2$ were not significantly changed by breathing with ETL. During Ctrl, $\dot{V}O_2$ was 4.6 ± 0.7 ml/min/kg and $\dot{V}CO_2$ was 3.9 ± 0.6 ml/min/kg. At 20'ETL, $\dot{V}O_2$ was 4.4 ± 0.7 ml/min/kg and $\dot{V}CO_2$ was 4.6 ± 1.3 ml/min/kg.

3.4. Cardiovascular variables

Cardiac variables are displayed in Table 2. As compared to Ctrl, HR increased with ETL while SV decreased (+6 bpm and -7 ml at 20'ETL; $p < 0.05$). Data were not significantly different between 10' and 20'ETL. Cardiac output and arterial pressures (systolic, diastolic and mean) did not significantly change with ETL. Mean arterial pressure was 100 ± 9 mmHg during Ctrl. With ETL, MAP was 104 ± 11 mmHg at 20 min.

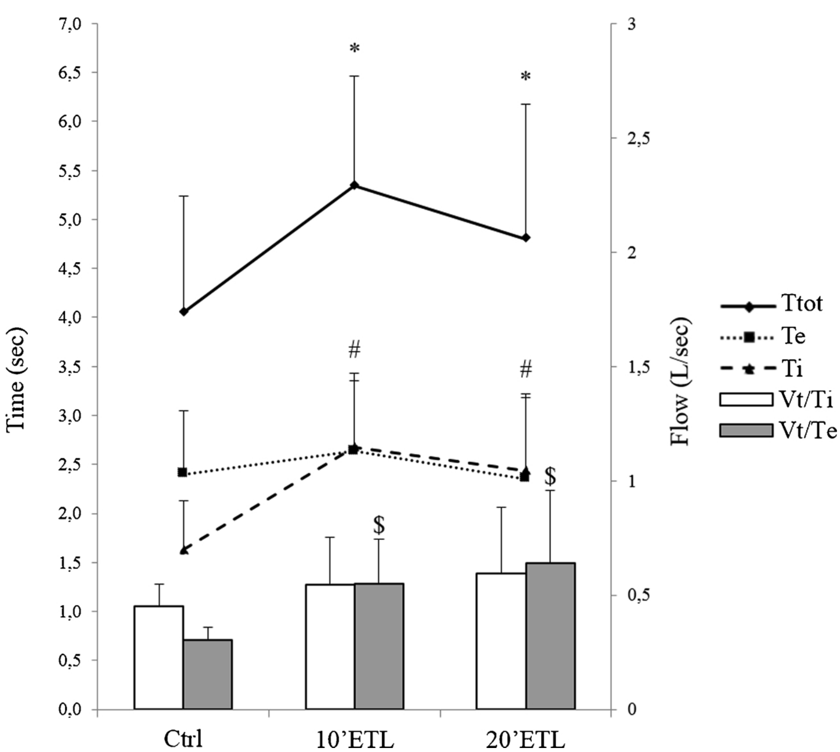

Fig. 2. Ventilatory variables. Values are mean ± SD. Total respiratory time (Ttot), expiratory time (Te), inspiratory time (Ti), mean inspiratory flow rate (Vt/Ti) and mean expiratory flow rate (Vt/Te) during control (Ctrl) and expiratory threshold load condition (ETL), at the 10th and the 20th minute (10' and 20'ETL). *, significantly different from Ctrl ($p < 0.05$) for Ttot, Ti and Vt/Te.

Table 2
Cardiorespiratory and pulmonary variables during control (Ctrl) and expiratory threshold load (ETL) conditions.

	n	Ctrl			10'ETL				20'ETL			
Ventilatory pattern												
Vt (L)	11	0.7	±	0.2	1.4	±	0.4	***	1.3	±	0.4	***
BF (c/min)	11	15.8	±	3.8	11.8	±	2.4	***	13.5	±	4.3	*
$\dot{V}E$ (L/min)	11	10.8	±	2.0	15.8	±	4.5	*	17.8	±	8.3	***
Ti/Ttot (%)	11	40	±	3	50	±	9	***	51	±	9	***
Gas exchanges												
RER	11	0.8	±	0.1	1.1	±	0.1	***	1.1	±	0.2	***
$\dot{V}E/\dot{V}CO_2$	11	34.9	±	3.6	44.4	±	7.7	**	49.5	±	11.3	***
$PetCO_2$ (mmHg)	11	39.6	±	2.4	28.6	±	6.7	***	27.6	±	8.7	***
SpO_2 (%)	11	95.4	±	1.2	97.2	±	1.0	***	97.4	±	1.1	***
Pulmonary volumes and capacities												
ERV (L)	9	1.6	±	0.3	1.2	±	0.5	**	1.3	±	0.5	**
IRV (L)	9	2.6	±	0.5	2.5	±	0.5		2.5	±	0.6	
IC (L)	9	3.5	±	0.6	3.7	±	0.6		3.7	±	0.6	
SVC (L)	9	5.1	±	0.9	4.9	±	0.7	**	5.0	±	0.8	*
Cardiac variables												
HR (bpm)	11	65.4	±	10.1	73.3	±	11.2	**	71.7	±	8.2	*
SV (ml)	11	100.4	±	12.7	91.6	±	14.0	**	93.4	±	14.0	*
$\dot{Q}c$	11	6.5	±	1.0	6.7	±	1.3		6.7	±	1.2	

Values are mean ± SD. 10'ETL and 20'ETL, 10th and 20th minute of the ETL condition; Vt, tidal volume; BF, breathing frequency; $\dot{V}E$, ventilatory flow; Ti/Ttot, inspiratory duty cycle; RER, respiratory exchange ratio; $\dot{V}E/\dot{V}CO_2$, ventilatory equivalent for CO_2; $PetCO_2$, end-tidal CO_2 pressure; SpO_2, pulse haemoglobin oxygen saturation; ERV, expiratory reserve volume; IRV, inspiratory reserve volume; IC, inspiratory capacity; SVC, slow vital capacity; HR, heart rate; SV, stroke volume; $\dot{Q}c$, cardiac output. Value was significantly different from Ctrl: *, $p < 0.05$; **, $p < 0.01$; ***, $p < 0.001$.

3.5. Correlations

Correlations, based on the differences between 20'ETL and Ctrl values, are displayed in Fig. 4. Changes in TSI (Δ TSI) were negatively correlated with changes in $\dot{V}E$ (Δ $\dot{V}E$) ($r = -0.74$, $p = 0.01$, panel A), as well as Δ $[O_2Hb]$ versus Δ Vt/Te ($r = -0.78$, $p = 0.004$, panel B). In other words, the more the $\dot{V}E$ increased the more the TSI decreased, and the more the Vt/Te increased the more the $[O_2Hb]$ decreased. Changes in Borg score were correlated with Δ Vt/Ti ($r = 0.72$, $p = 0.01$, panel C) but not with Δ Vt/Te.

4. Discussion

During acute bronchial obstruction inducing high respiratory muscle load and dyspnea, oxygenation of intercostal muscles may be altered due to vascular compression and inadequacy between oxygen demand and availability. To test this hypothesis, tissue oxygenation of the intercostal muscles was assessed by NIRS in resting subjects breathing against an ETL. Despite decreased Hb muscle concentration, oxygen saturation in the intercostal muscles was not reduced during acute airway obstruction, thereby suggesting a successful adaptation to

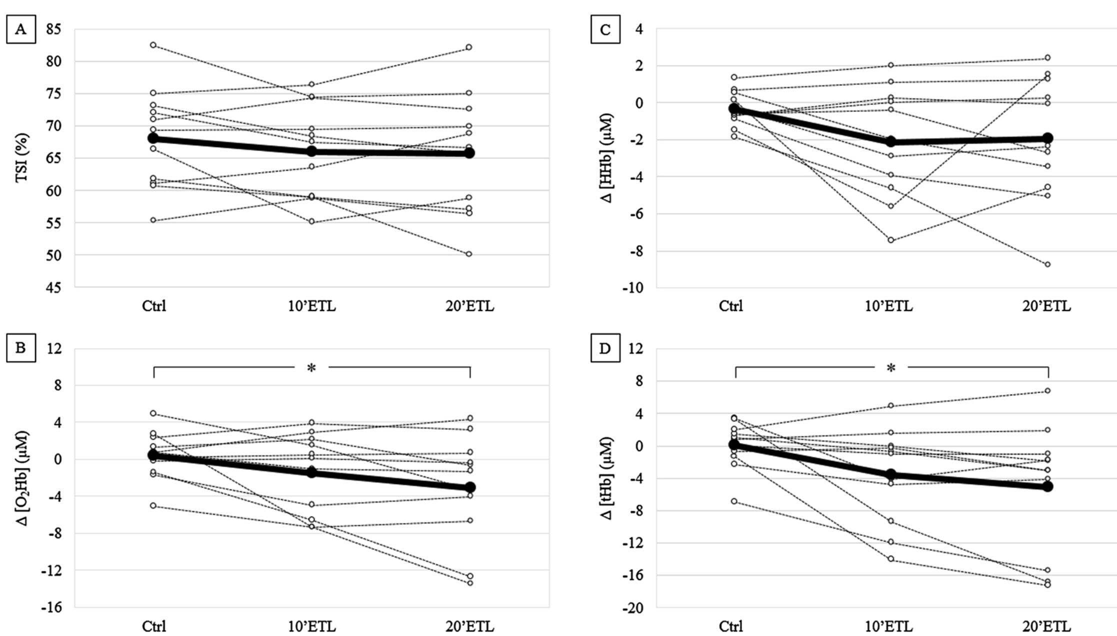

Fig. 3. Intercostal muscle oxygenation. Individual (O) and mean (•) values are shown. Tissue saturation index (TSI, panel A) and concentration changes in oxyhaemoglobin (Δ $[O_2Hb]$, panel B), deoxyhaemoglobin (Δ [HHb], panel C), and total haemoglobin (Δ [tHb], panel D) during control (Ctrl) and expiratory threshold load condition (ETL), at the 10th and the 20th minute (10' and 20'ETL). *, significantly different between Ctrl and 20'ETL, $p < 0.05$.

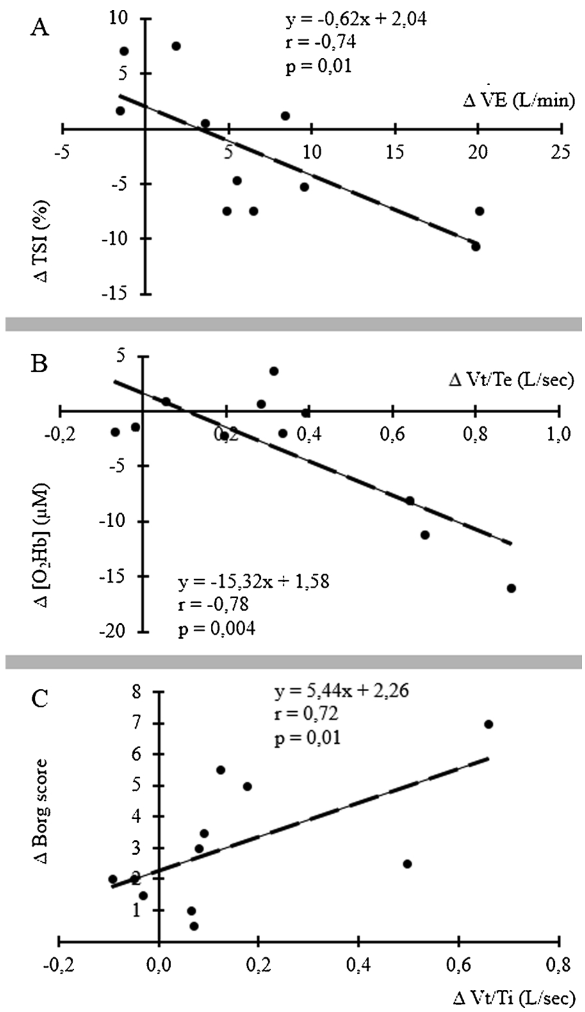

Fig. 4. Correlations based on the responses to expiratory load. Correlation between changes in tissue saturation index (Δ TSI) and in ventilatory flow (Δ $\dot{V}$E) (panel A), changes in oxyhaemoglobin concentration (Δ [O_2Hb]) and in mean expiratory flow rate (Δ Vt/Te) (panel B), changes in dyspnea (Δ Borg score) and in mean inspiratory flow rate (Δ Vt/Ti) (panel C).

expiratory load most likely involving a favorable arrangement in hemodynamic and/or in respiratory biomechanics.

4.1. Intercostal muscle blood volume

Change in [tHb] measured by NIRS has been shown to result from variations in blood volume induced by a change in vascular diameter (Ogata et al., 2002). The decrease in [tHb] in intercostal muscles observed in this study could consequently be due to vasoconstriction or to compression of the vessel induced by ETL.

A compression of muscle vessel due to stretch has previously been reported in muscles such as the vastus lateralis or the diaphragm (Supinski et al., 1990; McCully, 2010). Respiration at a high pulmonary volume as occurs in pulmonary hyperinflation and modified pulmonary pressure may favour intercostal vessel compression. In this study performed at rest, Vt, Vt/Te and $\dot{V}$E increased with ETL, but pulmonary hyperinflation failed to occur (Guenette et al., 2013). A lack of hyperinflation at rest in response to ETL has likewise been reported in other studies (Barrett et al., 1994; Stark-Leyva et al., 2004; Xiao et al., 2012). As a result, the drop in [tHb] in intercostal muscles observed here probably cannot be ascribed to compression of the vessel by hyperinflation. Conversely, the two-fold increase in Vt may be related to a stretch of intercostal muscles occurring at the end of the inspiration.

In an obstructive context, the lack of pulmonary hyperinflation is congruent with the hypothesis of intercostal muscle recruitment to potentiate expiration. Activation of the intercostal muscles has been electromyographically demonstrated in animals (Dimarco et al., 1984) as well as humans breathing against ETL (Sears and Davis, 1968; Chonan et al., 1990). In agreement, our results suggest a recruitment in intercostal muscles. However, the decrease in [tHb] we observed could be due to increased pressure around the capillaries during contraction. Indeed, when a 20-cmH_2O ETL is applied at the mouth, the pressure on capillaries resulting from active expiration may be heightened, especially in the intercostal muscles (Leenaerts and Decramer, 1990). In addition, this pressure shall most likely be maintained around the capillaries for a longer duration insofar as expiration is lengthened (Barrett et al., 1994; Xiao et al., 2012; Morawiec et al., 2015). In this study, if Te was not modified with ETL, it was probably in order to avoid or at least not exacerbate the expiratory muscle fatigue associated with prolonged ischemia (Taylor and Romer, 2009). Usually, muscle perfusion takes place during the relaxation period. However, a massive reduction in blood perfusion during muscle contraction may be insufficiently counteracted during the relaxation period, in particular when the latter is of short duration.

4.2. Intercostal muscle oxygenation

Despite the increase in $\dot{V}$E with ETL, TSI in intercostal muscles was not significantly altered in healthy subjects at rest. Our results agree with those reported by Vogiatzis et al. (2010) in COPD patients as TSI in intercostal muscles did not vary while patients increased their $\dot{V}$E up to approximately 35 L/min.

A lack of change in TSI implies a conservation of oxygenated to total haemoglobin concentration ratio in intercostal muscles (McManus et al., 2018). In the study by Athanasopoulos et al. (2010), TSI and [HHb] in intercostal and vastus lateralis muscles were not significantly different from rest to exercise in healthy subjects. The authors explained these results by an increase in local blood flow adequate to satisfy the metabolic demand, the lack of change in TSI reflecting a balance between oxygen need and supply (De Backer et al., 2010; Vogiatzis et al., 2010; McManus et al., 2018). In our study, [O_2Hb] and [tHb] seemed to be reduced proportionally in intercostal muscles in response to ETL and TSI was not significantly disturbed despite the increase in work of breathing. Then, the lack of change in TSI in intercostal muscles with ETL could be explained by a hemodynamic adaptation adequate to meet metabolic needs (Athansopoulos et al. 2010; Vogiatzis et al., 2010). In the hypothesis of increased local blood flow, as capillaries were likely compressed, we can speculate that the successful hemodynamic adaptation may have resulted from an increase in blood velocity.

As TSI was not significantly altered with ETL while our subjects were breathing freely, we assume that most of them found a satisfactory ventilatory arrangement allowing them to overcome ETL without significantly disturbing oxygen saturation in respiratory muscles. However, the negative correlations observed between delta $\dot{V}$E (20'ETL - Ctrl values) and delta TSI and between delta Vt/Te and delta [O_2Hb] show that the more the respiratory pattern was modified with ETL (ie increase in $\dot{V}$E and Vt/Te) the more the TSI and [O_2Hb] decreased. This means that the changes in ventilation in response to ETL may have consequences on muscle oxygenation and shows that some subjects are able to develop better respiratory adaptation than others.

4.3. Dyspnea

Dyspnea took place while subjects were breathing with ETL (+2-3 on Borg scale), which is not surprising because of the disturbance in ventilation. Dyspnea may result from changes in respiratory efferent and/or respiratory afferent or from a conflict between the two (Parshall et al., 2012). In this study, dyspnea could be induced by an increased respiratory load due to ETL or perhaps by displacement of Vt toward high pulmonary volume along with hyperinflation (O'Donnell, 2006). As IC was not modified with ETL, we can postulate that Vt was not shifted toward the nonlinear part of the pressure-volume relationship and that pulmonary hyperinflation was most likely not involved in dyspnea.

Breathing with ETL induced changes in most of the ventilatory variables in response to the expiratory load. Increases in Ti, Ttot, Vt, $\dot{V}E$, and Vt/Te were recorded without any change in $\dot{V}O_2$. All of these increases probably facilitate thoracic and muscle adjustments or elastic recoil, thereby improving ventilation efficiency and minimizing the disorder due to ETL. The Vt/Te increase recorded with ETL indicates that expiration was particularly vigorous (Barrett et al., 1994; Morawiec et al., 2015) while Ti, which was lengthened, may be considered as a relatively restful period (even if inspiration is always active). In previous works, Vt/Ti ratio has been used as an index of inspiratory neural drive and inspiratory muscle activity (Milic-Emili and Grunstein, 1976; O'Donnell, 2006). In the present study, while Vt/Ti non-significantly increased with ETL, a correlation was observed between the changes in Vt/Ti and dyspnea. In agreement, García-Rio et al. (1996) showed that pregnant women with dyspnea had a greater Vt/Ti at rest, than those who were non-dyspneic. It is not impossible that during ETL breathing, inspiration does not allow subjects to experience relative rest from powerful expiration. As a result, respiratory discomfort might be heightened, thereby inducing dyspnea.

4.4. Limits

All of the subjects included in the study were physically fit male students. This could explain their being able to increase their expiratory power in response to ETL without change in the length of expiration or pulmonary hyperinflation. This response might not be transferable to patients.

The effect of ETL on respiratory muscle oxygenation was investigated in intercostal muscles due to their accessibility via NIRS. While the exact thickness of the intercostal muscles was unknown, that of the external muscle has been estimated by De Troyer et al. (2003) at 7–10 mm. NIRS depth measurement also took adipose tissue thickness into account.

The activity of the intercostal muscles was not measured electromyographically during this study. Their activation has previously been demonstrated under similar conditions in humans (Sears and Davis, 1968; de Bisschop et al., 2017). In the present study, increases in Vt, Vt/Te and $\dot{V}E$ showed that expiration was more vigorous and that intercostal muscles were likely to be recruited (Dimarco et al., 1984; Stark-Leyva et al., 2004).

Based on NIRS results, a compression of the vessels was suggested as occurring in intercostal muscles during ETL breathing because of reduction in blood volume ([tHb]). Assessment of vessel calibre and blood flow is feasible with echo-Doppler (de Bisschop et al., 2017) and this technique would have been interesting to apply, in addition to NIRS. However, intercostal artery has a small internal diameter approximating 1 mm and a flow of a few ml/min, which means that implementation of this method requires a highly skilled experimenter. Other limits consist in the fact that measurements are restricted to the last intercostal spaces in the mid-dorsal portion of the thorax, in subjects with thin skin and subcutaneous tissues. Intercostal muscle blood flow may also be measured using the dye dilution method. With this technique, NIRS is used in combination with indocyanine green dye, a light-absorbing tracer (Guenette et al., 2008). However, the main limitation of this method stems from its invasiveness as it requires perfusion of the tracer.

Cardiac values were measured with a Physioflow device, of which the accuracy has been criticized, particularly in airway obstructive context (Bougault et al., 2005). In our study however, cardiac parameters were measured only at rest, and in view of carrying out a general survey of cardiac adjustments beside intercostal activity during breathing with ETL.

4.5. Clinical implications and perspectives

This study may be of interest in respiratory diseases in which acute obstruction or exacerbation may occur. Muscle oxygenation investigation may provide insight on intercostal muscle adaptation and dyspnea in a severe obstructive context that lasts, and in which overstrain of the respiratory muscle may arise. In cases of increased expiratory resistance, intercostal muscle oxygenation seems to depend on respiratory response and is most likely impaired when the expiratory flow rate is strongly increased. It also seems that changes in inspiratory flow rate could exacerbate dyspnea. Thereby, workshops based on breath control in obstructive patients may be interesting as means of decreasing dyspnea and preventing respiratory muscle fatigue. It would also be relevant to perform investigations on patients specifically in view of validating and enacting recommendations.

Intercostal muscles, which we chose to explore, present an anatomical location between the ribs rendering their investigation relevant due to the fact that their functional position may be modified by a change in thoracic volume, spacing of the ribs or by changes in thoracic pressure. In future studies, it would be interesting to closely study pulmonary hyperinflation that might more pronouncedly disturb intercostal muscle running and to assess the changes that occur in the course of the switch.

5. Conclusion

In conclusion, decreases in total haemoglobin and oxyhaemoglobin concentrations were observed in the intercostal muscles of healthy subjects breathing against an expiratory load at rest. They were probably due to a compression of the vessel resulting from vigorous expiration. Despite a decrease in tissue Hb concentration, intercostal muscle O_2 saturation was not impaired with ETL, at rest, suggesting satisfactory ventilatory and/or hemodynamic arrangements. However, intercostal muscle oxygenation appears to depend on respiratory response.

Declaration of interest

None.

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