Novel Correlations between Exhaled Breath VOCs and Lung Function in Ultramarathon Runners: Insights from the 2019 Ultra-Trail du Mont Blanc

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Aim

This study aims to investigate the relationship between exhaustive exercise, lung function, and breath VOCs in ultramarathon runners, and assess the potential of breath analysis as a non-invasive tool for monitoring physiological responses to extreme endurance.

Introduction

Ultramarathon running induces significant physiological stress, particularly in the lungs and metabolic systems[1]. While blood-based biomarkers have been used to monitor these changes, repeated blood sampling can be invasive, uncomfortable, and impractical in the field.

Volatile organic compounds (VOCs) in exhaled breath offer a non-invasive alternative for assessing systemic metabolic and physiological responses. Previous studies have demonstrated alterations in breath VOC profiles following ultramarathon events[2], suggesting their potential as biomarkers of exercise-induced stress and adaptation.

To explore this, we investigated associations between breath VOCs and changes in lung function in a cohort of elite athletes participating in the 2019 Ultra-Trail du Mont Blanc (UTMB®).

Method

Thirty-two healthy participants in the 2019 UTMB ultra-marathon (171km, ~10,000m ascent) underwent assessments 24–72h before and 1–4h after the race. Tests included blood sampling, spirometry, exhaled nitric oxide, transthoracic ultrasound, breath VOC collection (ReCIVA®, Owlstone Medical – Figure 1), and submaximal cycling to assess lung diffusion (DLco/DLno, Dmco, Vc). Clinical and respiratory parameters were measured using portable devices following ATS/ERS guidelines. Breath samples (n=48 from 24 subjects) were analyzed pre- and post-race without fasting requirements. Data were analyzed in Python using Wilcoxon Signed-Rank and Spearman's correlation; coefficients >0.7 were considered strong, 0.5–0.7 moderate.

Figure 1: The Owlstone breath collection system includes; CASPER – a filtered air supply unit, which provides air scrubbed of background VOCs to patients via the ReCIVA, ReCIVA – a reliable and reproducible non-invasive breath sample collection unit, which prefentially collects alveolar breath fraction identified using pressure tracing and selected for with two pumps, and lastly Breath Biopsy Collect – which connects to and operates the ReCIVA enabling collection of specific breath fractions and monitoring patient breathing in real-time.

Results

Respiratory function and correlation analysis

Post-race clinical data revealed a modest decline in pulmonary function, with significant reductions in vital capacity (VC), forced expiratory volume in one second (FEV1), and maximal expiratory pressure (MEP), as expected following exhaustive exercise[3]

Correlation and network analyses highlighted a strengthening of associations between respiratory parameters post-race (Table 1). Given the close relationship between respiratory muscle strength and lung function, correlations between MEP and spirometric measures like FVC and FEV1 are expected. However, the post-race strengthening of these associations, despite declines in absolute values, suggests that exhaustive exercise enhances the coupling between expiratory effort and lung function.

Correlations which emerge only in post-race measurements (Figure 2) demonstrate a) that muscle strength may become a dominant determinant of expiratory flow (given the FEV1-MEPS correlation) and b) the tight integration of systemic metabolic responses, including correlations between BUN and lactate, glucose and FEV1 and cTnI with CK-MB.

	Variable	Variable	Coefficient (r), pre-race	Coefficient (r), post-race
Variables correlate (r > 0.5) but no change between pre- and post-race	FV	V	0.78	0.88
	FV	FEV1	0.95	0.87
	MIPS	FV	0.53	0.63
	MIPS	V	0.65	0.52
Variables correlate (r > 0.5) and strengthened (r > 0.7) in post-race	V	FEV1	0.67	0.84
	FV	MEPS	0.57	0.75
Variables correlate (r > 0.5) only in post-race	BUN	Lactate		0.51
	Glu	FEV1		0.52
	cTnI	CK-M		0.62
	FEV1	MEPS		0.73

Table 1: Correlation analysis between clinical variables in pre- and post-race samples. All variables here are at least moderately correlated (r >0.5) with each other. FVC – Forced Vital Capacity, VC – Vital Capacity, FEV1 – Forced Expiratory Volume in one second, MIPS – Maximal Inspiratory Pressures, MEPS – Maximal Expiratory Pressure, BUN – Blood Urea Nitrogen, Glu – Blood glucose, cTnI – Cardiac Troponin I, CK-MB – Creatine Kinase-MB isoform.

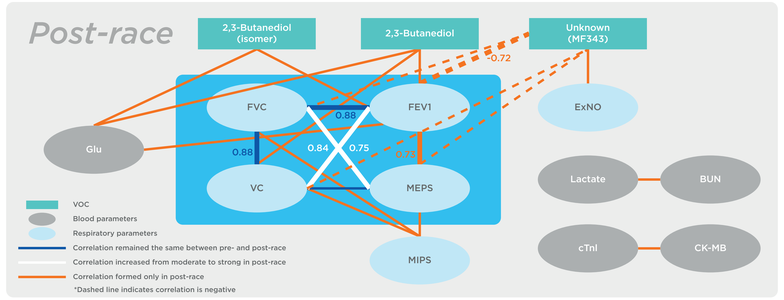

Figure 2: Correlation with clinical metadata and VOCs in post-race samples. Clinical metadata and VOCs presented include only those which reached statistical significance between pre- and post-race comparisons. Clinical data within the turquoise box suggests clustering. Unless indicated within a correlation coefficient, all correlations presented are moderate (0.5-0.7).

VOC Alterations

Given the increased post-race correlations between respiratory function and metabolic parameters, we further investigated associations between volatile organic compounds (VOCs) and respiratory measures. A total of 63 VOCs were found to change significantly ($p < 0.05$) between pre- and post-race samples. Several of these were gut-derived, including 2,3-butanediol, which showed a significant increase in post-race samples.

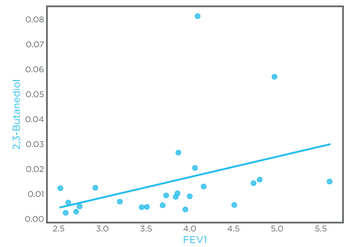

Figure 3: Correlation with clinical metadata between FEV1 and VOC 2,3-butanediol in post-race samples.

Notably, 2,3-butanediol demonstrated a further positive correlation with both VC (r = 0.53) and FEV_1 (r = 0.63), but only in post-race samples (see figure 3). As a product of anaerobic glucose fermentation by gut microbiota, this compound's emergent association with respiratory parameters may reflect increased gut–lung axis activity following exhaustive exercise.

While the mechanisms underlying this correlation remain to be fully elucidated, previous work has suggested that altered gut barrier integrity[4] or shifts in microbial fermentation activity during exercise[5] could be contributing factors. The potential of breath VOCs, like 2,3-butanediol, to inform our understanding of physiological adaptation to exercise warrants further investigation.

Conclusions

Our findings reveal that exhaustive exercise not only alters lung function but may also influence microbial metabolism, as indicated by the emergence of post-race correlations between respiratory parameters and gut-derived VOCs such as 2,3-butanediol. This study is the first to demonstrate correlations between exhaled breath VOCs and clinical respiratory variables in the context of an ultramarathon.

Taken together, our data underscores the potential of breath-based biomarkers for tracking physiological strain and recovery, with implications for performance optimization and athlete health monitoring.

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