# THE ROLE OF IMPULSE OSCILLOMETRY IN DETECTING AIRWAY DYSFUNCTION IN ATHLETES

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**ABSTRACT**

**Background:** Impulse oscillometry (IOS) has previously been proposed to provide greater sensitivity than spirometry when employed with indirect bronchoprovocation testing for the diagnosis of airway dysfunction in athletes. However, this recommendation is based on a highly selected population of symptomatic patients. **Objective:** To compare IOS, spirometry and respiratory symptoms following indirect bronchoprovocation in a screened cohort of athletes. **Methods:** One hundred and one recreational athletes were recruited. Respiratory symptoms were assessed via the Dyspnoea-12 questionnaire. Spirometry and IOS were performed pre-and post- a eucapnic voluntary hyperpnoea (EVH) challenge. **Results:** Ninety-four athletes completed the study. Sixteen athletes (17%) were positive for airway dysfunction based on spirometry (i.e. ≥10% fall in $FEV_1$) and seventeen athletes (18%) based on IOS (i.e. ≥50% increase in $R_5$). Only nine athletes (10%) met both diagnostic thresholds. A poor relationship was observed between respiratory symptoms (i.e. Dyspnoea-12 score) and all spirometry and IOS variables. A direct relationship was observed between percentage change in $R_5$ ($r = 0.65$), $Z_5$ ($r = 0.68$), $R_F$ ($r = 0.65$), $A_X$ ($r = 0.69$) and the maximum fall in $FEV_1$ ($\Delta FEV_1max$) ($P< 0.001$). A weak relationship was observed between $R_{20}$ ($r = 0.27$), $X_5$ ($r = 0.37$) and $\Delta FEV_1max$ ($P<0.01$). **Conclusion:** Impulse oscillometry and spirometry do not concur precisely following indirect bronchoprovocation. However IOS detects additional cases of airway dysfunction in athletes and therefore may provide diagnostic value in this population. Further work is required to establish diagnostic thresholds and fully determine the place of IOS in screening athletes for airway dysfunction.

## INTRODUCTION

Airway dysfunction is prevalent in endurance athletes of all abilities (1, 2) and its detection is important in order to optimise respiratory health and athletic performance (3). In athletes, a variety of bronchoprovocation challenge tests have been recommended for the detection of airway dysfunction and/or to infer the presence of exercise-induced bronchoconstriction (4). However, regardless of the specific provocation methodology, the criteria employed to determine a 'positive result' is typically based on a change in airway function established by forced spirometry e.g. ≥10% reduction in forced expiratory volume in one second ($FEV_1$) (5, 6) .

It is now accepted that a spirometric-based measurement can fail to detect the complex perturbations in airway function that can arise following a bronchoprovocation challenge (7) and in addition may be prone to influence from poor technique and respiratory muscle fatigue (8). Moreover, there appears to be a poor relationship between change in $FEV_1$ following airway challenge and the presence of exertional symptoms in athletes (9). Therefore, the study and evaluation of other methods for assessing airway calibre and dynamic alterations in pulmonary function in this setting is required.

Impulse oscillometry (IOS) is a non-effort dependent method of assessing airway function. Impulses generated by IOS are superimposed on tidal breathing and respiratory impedance is calculated by pressure and volume changes caused by impulses during the measurement. Respiratory impedance values are expressed over a range of impulse frequencies which can subsequently allow detection of the site of airway obstruction more precisely (10). In addition, IOS provides information regarding the elastic properties of the respiratory system.

Impulse oscillometry has previously been utilised in athletic individuals to evaluate their airway function following bronchoprovocation (11, 12). Evans et al. (11) observed a change in airway

function following room temperature and cold air exercise challenges that would have otherwise remained undetected by spirometry. The conclusion from a series of studies (11-13) was that IOS yields greater sensitivity for detecting changes in airway function in athletes. These studies established diagnostic thresholds with one specific IOS parameter (i.e. ≥50% increase in respiratory resistance at 5 Hz) recommended as the most appropriate cut-off value when employed in conjunction with a EVH challenge (90% sensitivity; 80% specificity) to detect post-challenge airway obstruction (13).

To date, the studies utilising IOS in athletes have been conducted in a highly selected population of symptomatic patients with a high pre-test probability of airway dysfunction. We therefore undertook this study with the aim of establishing the utility of IOS following indirect bronchoprovocation in a large cohort of recreational athletes screened for airway dysfunction. We compared the relationship between IOS and spirometry and utilised the described cut-offs to determine the prevalence of airway dysfunction. In addition, IOS and spirometry parameters were compared with respiratory symptoms. We selected eucapnic voluntary hyperpnoea (EVH) as the bronchoprovocation challenge since it is the test currently favoured by the International Olympic Committee-Medical Commission (IOC-MC) for diagnosing airway dysfunction in athletes (14).

## METHODS

### Study population

One hundred and one (male: $n$ = 69) recreational athletes (mean ± SD: 6 ± 1 hours training/week) were recruited for this study. A variety of sporting disciplines were represented (endurance: $n$ = 88; intermittent high-intensity: $n$ = 9; strength: $n$ = 4). All subjects were non-smokers, and were free from respiratory, cardiovascular, metabolic and psychiatric disease, or any other significant medical condition except mild asthma. Twenty subjects had a prior physician diagnosis of clinical asthma; all were stable at time of study entry (i.e. no respiratory tract infection or change in medication for two weeks prior to inclusion) and all were prescribed short acting beta-2 agonist (SABA) with fourteen prescribed maintenance inhaled corticosteroid.

### Experimental design

Subjects attended the laboratory on a single occasion to complete clinical assessment, pulmonary function measurements and a EVH challenge. Subjects were asked to refrain from strenuous exercise, caffeine and alcohol consumption on the day of testing. Subjects with asthma were asked to abstain from using short-acting inhaled beta-2 agonist and inhaled corticosteroids for 24 and 72 hrs, respectively, prior to the study. The study was approved by Northumbria University research ethics committee (Ethics ID: RE20-01-12590) and all subjects provided written informed consent for experimentation with human subjects.

### Clinical assessment

Respiratory symptoms were determined via completion of the Dyspnoea-12 questionnaire (15). A sum of responses was calculated to determine the total score (scale range, 0 – 36; a high score indicating worse dyspnoea - mild: 1-12, moderate: 13-24, severe: 25-36). Subjects were classified as either asymptomatic (score: 0) or symptomatic (score: 1-36).

## Pulmonary function measurement

### *Spirometry*

Lung function was assessed by maximal forced flow-volume spirometry (MicroLoop ML3535; Cardinal Health, Basingstoke, UK) according to international guidelines (8), with established reference ranges employed (8).

### *Impulse oscillometry*

Measures of respiratory impedance were obtained by impulse oscillometry (IOS) (MasterLab IOS System, Erich Jaeger Co., Wurzburg, Germany). In accordance with international recommendations (10) subjects performed 30 s of tidal breathing prior to maximal inspiration followed by passive expiration.

## Eucapnic voluntary hyperpnoea challenge

A modified version of EVH was performed based on the protocol described previously (17, 22). Briefly, subjects breathed a dry compressed gas mixture (21% $O_2$, 5% $CO_2$, balance $N_2$) at a target ventilation rate equivalent to 85% (baseline $FEV_1$ * 30) of their predicted maximal voluntary ventilation (MVV) for 6 min. Spirometry was performed at baseline and in duplicate at 3, 5, 7, 10 and 15-min post EVH. Spirometric values within 5% were considered acceptable (8). Impulse oscillometry was performed pre and immediately post EVH. A positive diagnosis of airway dysfunction was defined as a fall in $FEV_1$ of ≥10% at two consecutive time points or ≥50% increase in $R_5$ post provocation. The maximum fall in $FEV_1$ ($\Delta FEV_1max$) was used for analysis.

## Statistical analysis

Pulmonary function variables for airway dysfunction positive and negative subjects were compared using a two-way unpaired *t*-test. The relationship between spirometry and IOS

parameters were assessed using Pearson's product-moment correlation coefficient (normally distributed data) (mean ± SD). A Spearman's rank correlation was used to assess relationships between respiratory symptoms (i.e. Dyspnoea-12 score) and pulmonary function variables (median and range). Data was analysed using PASW Statistics 21 statistical software package (SPSS Inc., Version 21, Chicago, IL) and GraphPad Prism Version 5.0 (GraphPad Software, San Diego, California, USA). $P<0.05$ was considered statistically significant.

## RESULTS

### Study population

One hundred and one athletes consented to take part in the study. Seven athletes were excluded ($n$ = 3; baseline airway obstruction and $n$ = 4; unable to complete the EVH challenge). Consequently, ninety-four athletes (male: $n$ = 64) completed the assessment (Table 1).

### Baseline pulmonary function

All baseline pulmonary function measures were within normal predicted limits (Table 2). A direct relationship was observed between baseline $FEV_1$, FVC and all IOS variables ($P$<0.05), with the exception of $X_5$ ($P$>0.05). Baseline $FEV_1$/FVC displayed no relationship with any IOS parameter.

Neither spirometry nor IOS parameters at baseline were predictive of the $\Delta FEV_1max$ ($P$>0.05). Likewise baseline spirometry did not differentiate between airway dysfunction positive and negative athletes, however resting $X_5$ was lower (P<0.01) and $A_X$ was higher (P<0.05) in airway dysfunction positive (i.e. ≥10% fall in $FEV_1$) compared to negative athletes respectively.

### Clinical assessment

Exercise associated respiratory symptoms (e.g. cough, wheeze, dyspnoea etc.) were reported by forty-five athletes (48%) (mild: 91%; moderate: 9%). Nineteen athletes (95%) with a prior diagnosis of asthma were symptomatic (mild: 85%; moderate: 15%).

A poor relationship was observed between respiratory symptoms (i.e. Dyspnoea-12 score) and $\Delta FEV_1max$ (r = 0.12) and all post challenge IOS parameters; $R_{20}$ (r = 0.18), $X_5$ (r = 0.08), $R_F$ (r = 0.18), $A_X$ (r = 0.14) ($P$>0.05), $R_5$ (r = 0.26), $Z_5$ (r = 0.25) ($P$<0.05) (Figure 1). However, those with a positive diagnosis of airway dysfunction based on $\Delta FEV_1max$ were more likely to be symptomatic (75%) in comparison to IOS cut-off values (65%) (Figure 2).

**Airway response to eucapnic voluntary hyperpnoea**

The EVH target ventilation was calculated as 121.0 ± 23.9 $L.min^{-1}$. The achieved ventilation rate was 101.0 ± 27.8 $L.min^{-1}$ (range: 42.9 – 155.1 $L.min^{-1}$) (predicted: 83.2 ± 35.4%). Eighty-seven athletes (93%) met their target ventilation (i.e. minute ventilation ≥60% MVV) thus achieving test validation (16). When the athletes who failed to achieve their target ventilation were excluded from the analysis ($n$ = 7), the relationship between $\Delta FEV_1 max$ and IOS variables remained similar (data not shown).

Sixteen athletes (17%) were positive for airway dysfunction based on spirometric assessment ($\Delta FEV_1$ max = -18.9 ± 10.7%). Only seven athletes with a prior diagnosis of asthma had a positive EVH result (i.e. ≥10% fall in $FEV_1$). When based on an IOS cut-off (i.e. ≥50% increase in $R_5$), seventeen athletes (18%) had evidence of airway dysfunction. Therefore when based on either $FEV_1$ or $R_5$ cut-off values, twenty-four athletes (26%) had evidence of airway dysfunction. However, only nine athletes (10%) were diagnosed with airway dysfunction based on both diagnostic thresholds (i.e. $FEV_1$ and $R_5$ cut-off values did not identify the same patients). Post-EVH values for all IOS values were higher for athletes with airway dysfunction ($P<0.01$) (Table 3).

**Spirometry vs. Impulse oscillometry**

A direct relationship was observed between percentage change in $R_5$ (r = 0.65), $Z_5$ (r = 0.68), $R_F$ (r = 0.65), $A_X$ (r = 0.69) and $\Delta FEV_1 max$ ($P<0.001$). A weak relationship was observed between change in $R_{20}$ (r = 0.27), $X_5$ (r = 0.37) and $\Delta FEV_1 max$, respectively ($P<0.01$) (Figure 3). When the athletes whose $\Delta FEV_1 max$ ≥25% were excluded from the analysis ($n$ = 2), the relationship between $\Delta FEV_1 max$ and IOS variable remained similar (data not shown). Moreover, in athletes who were not previously prescribed ICS ($n$ = 80), the relationships

remained unchanged; $R_5$ (r = 0.67), $Z_5$ (r = 0.68), $R_F$ (r = 0.69), $A_X$ (r = 0.68) and $\Delta FEV_1max$, respectively (P<0.001) and $R_{20}$ (r = 0.34), $X_5$ (r = 0.31) and $\Delta FEV_1max$ (*P*<0.01).

## DISCUSSION

The accurate detection of airway dysfunction is important in order to optimise the health and performance of athletes. The present study indicates that the application of IOS in conjunction with an indirect bronchoprovocation challenge identifies abnormalities in airway function that would otherwise have remained undetected if only spirometry was performed. This finding has important implications for the utility of IOS in clinical practice and its potential application as a non-volitional means for identifying bronchoconstriction in athletes.

The prevalence of airway dysfunction in our cohort of recreational athletes when utilising a spirometric cut-off value (i.e. ≥10% fall in $FEV_1$) was 17% and similar to previous work in a comparable population (>13%) (17). Similarly, when employing a previously published IOS cut-off value (i.e. ≥50% increase in $R_5$) (13) a prevalence of 18% was observed. However importantly, only 10% of athletes met both diagnostic thresholds. Indeed only moderate correlations were observed between change in $R_5$, $Z_5$, $R_F$ and $A_X$ and weak correlations between $R_{20}$ and $X_5$ and $\Delta FEV_1max$ respectively. This discrepancy in diagnostic methodologies highlights a potential for misdiagnosis of both athletes with and without airway dysfunction. Indeed the implications of over and under-diagnosis of airway dysfunction have previously been raised in elite level athletes (18).

In agreement with previous findings (11, 12), neither resting spirometry nor IOS correlated with $\Delta FEV_1max$; supporting the recommendation that bronchoprovocation testing is required to confirm a diagnosis of airway dysfunction in athletes (19). However, interestingly we found significantly lower resting $X_5$ and higher resting $A_X$ values in athletes with airway dysfunction. Whilst speculative, this may imply that patients with airway dysfunction have more rigid airways which might contribute to low-grade airway remodelling as a consequence of airway injury (20).

The present study highlights a similar relationship between IOS and spirometry following indirect bronchoprovocation as described previously (11, 12). However a number of important differences between studies should be acknowledged. In contrast to our screened cohort of athletes, Evans and colleagues (11, 12) only recruited subjects with "probable EIB" as determined by a "maximal fall of ≥7% in $FEV_1$" following EVH, with variability in severity of bronchoconstriction not considered. Indeed 64% of their cohort had a previous physician diagnosis of asthma, with all subjects reporting symptoms suggestive of airway dysfunction during and post exercise. In addition, peak percentage change in $FEF_{50}$ was the principal variable shown to correlate with resistance of the airways determined by IOS. However, the use of mid-expiratory flow has been previously highlighted as insufficiently sensitive to diagnose airway dysfunction reliably in athletic populations (21).

Although Rundell et al. (13) reported strong correlations between IOS variables (resistance and reactance) and $\Delta FEV_1$max following EVH, the study consisted of only twenty subjects with ($n$ = 10) and without ($n$ = 10) a previous diagnosis of airway hyper-responsiveness (AHR). In addition, the average reduction in lung function following EVH for individuals with a positive diagnosis was significantly greater (30.6%) i.e. moderate severity in contrast to only mild severity (18.9%) in the present study. More specifically, 30% of athletes in the study by Rundell et al. were classified as having moderate to severe airway dysfunction whereas the majority of positive athletes (88%) in the current study were classified as only mild airway dysfunction (i.e. ≥10 - <25% $FEV_1$). In addition, a mean fall of 4.5% in $FEV_1$ for negative athletes was observed which is comparable with prior literature (22).

The diagnostic threshold recommended by the IOC-MC when employing EVH in athletes is currently ≥10% reduction in $FEV_1$ post challenge (14). However, it has been argued that this cut-off value may not provide optimum diagnostic accuracy (5) with poor short-term test re-test reproducibility recently observed (23). Interestingly, when employing a 15% reduction in

$FEV_1$ as the diagnostic cut-off in the present study, IOS detected 88% of positive athletes. Moreover, when a 20% reduction in $FEV_1$ was employed IOS detected 100% of positive athletes (i.e. spirometry and IOS detected the same patients). The possibility that the relationship between IOS and spirometry improves as the severity of airway dysfunction increases is therefore consistent with our findings and previous research (13). In addition, this observation suggests that performing a solitary IOS measure immediately post provocation in athletes with greater severity bronchoconstriction (i.e. ≥15% fall in $FEV_1$) accurately detects airway dysfunction. This finding supports the concept that IOS may provide greater sensitivity when employed with an indirect bronchoprovocation challenge (11, 12).

Although we have shown that IOS does not concur precisely with spirometry in identifying athletes with mild airway dysfunction, the application of IOS appears to identify additional individuals with an underlying airway abnormality. Therefore whilst our findings do not support the sole use of IOS in diagnosing airway dysfunction, they do provide a strong argument for IOS as an adjunctive tool. In addition, the utility of IOS in populations unable to perform forced breathing manoeuvres (i.e. paediatric populations) (24, 25) or in providing a common differential diagnosis, such as exercise-induced laryngeal obstruction, should not be overlooked (26).

No clear relationship was found between respiratory symptoms and presence of airway dysfunction as detected by changes in either spirometry or IOS. Although this is a common observation in studies that have employed spirometry to objectively assess airway dysfunction (27), this is the first study to evaluate respiratory symptoms against changes in IOS in athletes. The discrepancy observed may be in part explained by the general perception of breathing discomfort when approaching maximal exercise (5). This finding provides further evidence for the poor prognostic value of respiratory symptoms in athletes (27).

In order to differentiate between 'normal' exertional breathlessness associated with increasing exercise intensity and abnormal respiratory symptoms suggestive of airway dysfunction, recent studies have focussed on the 'perception' of symptoms in athletes and non-athletes following indirect bronchoprovocation (i.e. EVH and methacholine). However only minor differences in perception of bronchoconstriction-related symptoms were observed between groups (9). The explanation between the presence of classic airway-centric symptoms (i.e. chest tightness) suggestive of airway dysfunction and physiological airway changes (i.e. increased work of breathing) in athletic populations therefore remains to be determined and warrants further work.

**Methodological considerations/future research**

At present there is no specific guidance in the relevant Respiratory Society statements (4) regarding the optimum protocol when utilising IOS for the diagnosis of airway dysfunction in athletes. Our findings highlight that IOS may detect airway dysfunction from a solitary measurement post challenge in athletes with moderate to severe airway dysfunction. Therefore whilst future studies may wish to provide a direct comparison between IOS and spirometry at several time points post EVH, it is more appropriate to establish diagnostic thresholds based on the mean plus two or three standard deviations of the response in healthy subjects (28). Future studies should therefore apply this principle to IOS in conjunction with the traditional indirect bronchoprovocation measures in order to be able to establish cut-off values to be employed in clinical practice.

**Conclusion**

In conclusion, in a large screened cohort of athletes, we have demonstrated that although IOS does not concur precisely with spirometry, it does detect additional athletes with evidence of airway dysfunction. This highlights the potential utility of IOS as a supplementary measure in detecting airway dysfunction in athletes. Furthermore our findings emphasise the poor

relationship between respiratory symptoms and objective testing. Future work is required to establish diagnostic thresholds in order to determine the role and overall utility of IOS in detecting athletes for airway dysfunction.

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Nil relevant.

## DECLARATION OF INTEREST

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

## CONTRIBUTION STATEMENT

OP was involved in the conception and design of the study, acquisition, interpretation of data, drafting and critical revision of manuscript and final approval of the version to be published.

LA was involved in the conception and design of the study, interpretation of data, drafting and critical revision of manuscript and final approval of the version to be published

AB was involved in the drafting and critical revision of manuscript and final approval of the version to be published

JH was involved in the conception and design of the study, interpretation of data, drafting and critical revision of manuscript and final approval of the version to be published

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**TABLE HEADINGS**

**Table 1.** Subject clinical characteristics.

**Definitions of abbreviations: BMI**, body mass index.

**Table 2.** Baseline pulmonary function.

**Definitions of abbreviations: $FEV_1$**, Forced expiratory volume in $1^{-s}$; **FVC**, Forced vital capacity; $\mathbf{R_5}$, Resistance at 5 Hz; $\mathbf{R_{20}}$, Resistance at 20 Hz; $\mathbf{X_5}$, Reactance at 5Hz; $\mathbf{Z_5}$, Magnitude of impedance at 5 Hz; $\mathbf{R_F}$, Resonance frequency, $\mathbf{A_X}$, Area of reactance (area integrated from 5Hz to $R_F$).

**Table 3.** Impulse oscillometry values post eucapnic voluntary hyperpnoea.

**Definitions of abbreviations**: $\mathbf{R_5}$, Resistance at 5 Hz; $\mathbf{R_{20}}$, Resistance at 20 Hz; $\mathbf{X_5}$, Reactance at 5Hz; $\mathbf{Z_5}$, Magnitude of impedance at 5 Hz; $\mathbf{R_F}$, Resonance frequency, $\mathbf{A_X}$, Area of reactance (area integrated from 5Hz to $R_F$).

**Table 1.**

| **Variables** | |
|---|---|
| Sex (M:F) | 64 : 30 |
| Age (years) | 32 ± 9 |
| Height (cm) | 174.2 ± 8.8 |
| Weight (kg) | 73.7 ± 12.6 |
| BMI ($kg \bullet m^{-2}$) | 24.2 ± 3.0 |
| Training ($hrs \bullet wk^{-1}$) | 6 ± 1 |

Data presented as Mean ± SD

**Table 2.**

| Variables | Airway dysfunction | |
|---|---|---|
| | **Negative** | **Positive** |
| $FEV_1$ (L) | 4.02 ± 0.81 | 4.12 ± 0.74 |
| $FEV_1$ (% predicted) | 105.1 ± 9.5 | 101.0 ± 9.5 |
| FVC (L) | 4.89 ± 0.95 | 5.19 ± 0.85 |
| FVC (% predicted) | 108.3 ± 11.1 | 106.7 ± 10.2 |
| $FEV_1$/FVC (%) | 82.2 ± 5.6 | 79.5 ± 7.5 |
| $R_5$ ($kPa \bullet L^{-1} \bullet s^{-1}$) | 0.24 ± 0.06 | 0.27 ± 0.07 |
| $R_{20}$ ($kPa \bullet L^{-1} \bullet s^{-1}$) | 0.22 ± 0.06 | 0.24 ± 0.05 |
| $X_5$ ($kPa \bullet L^{-1} \bullet s^{-1}$) | -0.08 ± 0.05 | -0.14 ± 0.12** |
| $Z_5$ ($kPa \bullet L^{-1} \bullet s^{-1}$) | 0.26 ± 0.06 | 0.29 ± 0.08 |
| $R_F$ (Hz) | 10.57 ± 2.76 | 11.62 ± 3.16 |
| $A_X$ (Hz. $kPa \bullet L^{-1} \bullet s^{-1}$) | 0.21 ± 0.14 | 0.34 ± 0.32* |

Data presented as Mean ± SD. *$P$<0.05; ** (P<0.01) denotes difference between airway dysfunction negative and positive athletes. Note: positive athletes determined based on current guidelines (i.e. $\Delta FEV_1$max).

**Table 3.**

| Variables | Airway dysfunction | |
|---|---|---|
| | **Negative** | **Positive** |
| $R_5$ ($kPa \bullet L^{-1} \bullet s^{-1}$) | 0.30 ± 0.09 | 0.43 ± 0.14** |
| $R_{20}$ ($kPa \bullet L^{-1} \bullet s^{-1}$) | 0.25 ± 0.06 | 0.30 ± 0.07** |
| $X_5$ ($kPa \bullet L^{-1} \bullet s^{-1}$) | -0.09 ± 0.04 | -0.14 ± 0.10** |
| $Z_5$ ($kPa \bullet L^{-1} \bullet s^{-1}$) | 0.32 ± 0.09 | 0.46 ± 0.16** |
| $R_F$ (Hz) | 13.20 ± 3.86 | 20.36 ± 6.94** |
| $A_X$ (Hz. $kPa \bullet L^{-1} \bullet s^{-1}$) | 0.37 ± 0.31 | 1.32 ± 1.09** |

Data presented as Mean ± SD. ** ($P<0.01$) denotes difference between airway dysfunction negative and positive athletes.

## FIGURE LEGENDS

**Figure 1.** Relationship between Dyspnoea-12 score and (a) maximum fall in $FEV_1$; (b) resistance at 5Hz post eucapnic voluntary hyperpnoea.

**Figure 2.** Venn diagram depicting the association between respiratory symptoms and objective evidence of airway dysfunction.

**Figure 3.** Resistance at 5 Hz (a); Resistance at 20 Hz (b); Reactance at 5Hz (c); Magnitude of impedance at 5 Hz (d); Resonance frequency (e), Area of reactance (f) vs. maximum fall in $FEV_1$ post eucapnic voluntary hyperpnoea. Broken vertical line represents abnormal lung function (i.e. ≥10% fall in $FEV_1$).

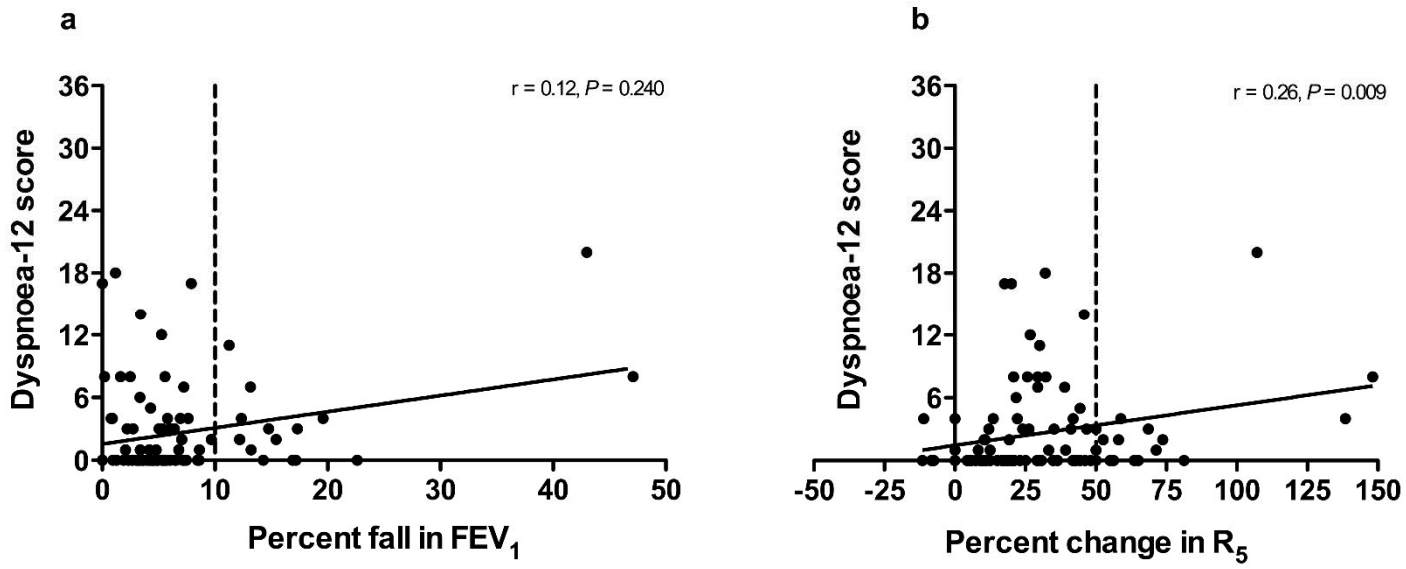
a
r = 0.12, P = 0.240
Dyspnoea-12 score
36
30
24
18
12
6
0
0
10
20
30
40
50
Percent fall in FEV1
b
r = 0.26, P = 0.009
Dyspnoea-12 score
36
30
24
18
12
6
-50
-25
0
25
50
75
100
125
150
Percent change in R5

**Figure 1.**

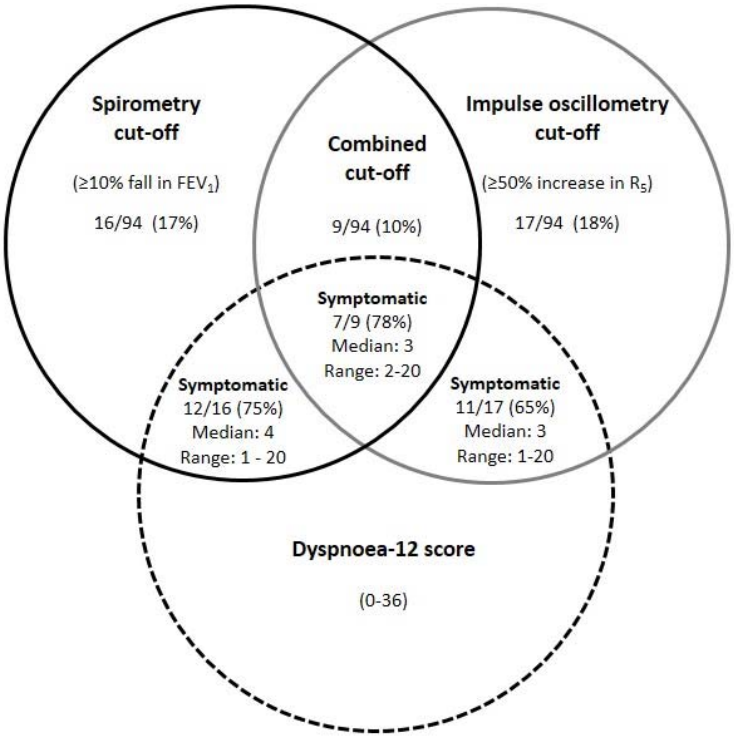
Spirometry cut-off
(≥10% fall in FEV1)
16/94 (17%)
Combined cut-off
9/94 (10%)
Impulse oscillometry cut-off
(≥50% increase in RS)
17/94 (18%)
Symptomatic
7/9 (78%)
Median: 3
Range: 2-20
Symptomatic
12/16 (75%)
Median: 4
Range: 1 - 20
Symptomatic
11/17 (65%)
Median: 3
Range: 1-20
Dyspnoea-12 score
(0-36)

**Figure 2.**

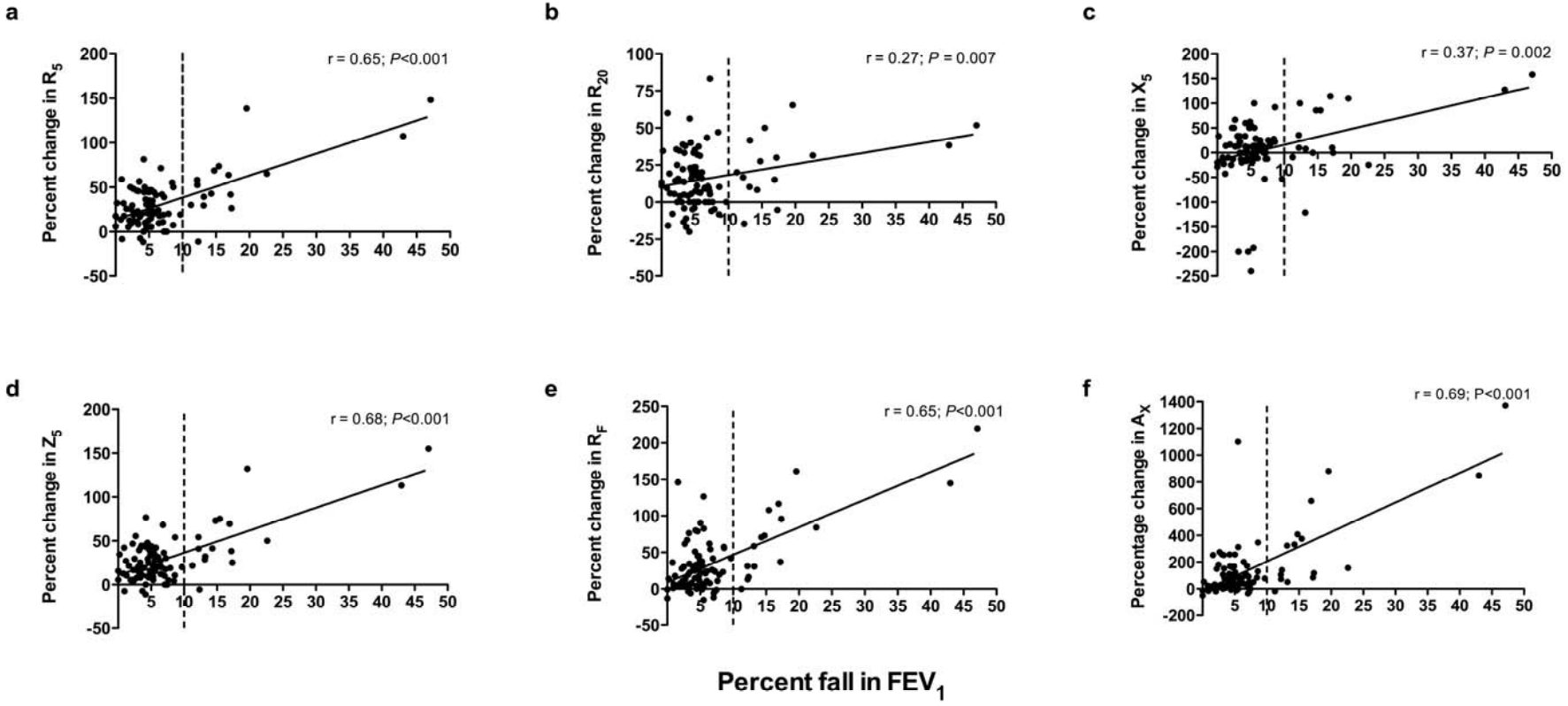
a
Percent change in $R_5$
r = 0.65; P<0.001
b
Percent change in $R_{20}$
r = 0.27; P = 0.007
c
Percent change in $X_5$
r = 0.37; P = 0.002
d
Percent change in $Z_5$
r = 0.68; P<0.001
e
Percent change in $R_F$
r = 0.65; P<0.001
f
Percentage change in $A_X$
r = 0.69; P<0.001
Percent fall in $FEV_1$

**Figure 3.**