Airway Narrowing Measured by Spirometry and Impulse Oscillometry Following Room Temperature and Cold Temperature Exercise*

Tina M. Evans, PhD, ATC; Kenneth W. Rundell, PhD; Kenneth C. Beck, PhD; Alan M. Levine, PhD; and Jennifer M. Baumann, MS, RD, LDN

Study objective: The efficacy of using impulse oscillometry (IOS) as an indirect measure of airflow obstruction compared to spirometry after exercise challenges in the evaluation of exercise-induced bronchoconstriction (EIB) has not been fully appreciated. The objective was to compare airway responses following room temperature and cold temperature exercise challenges, and to compare whether IOS variables relate to spirometry variables.

Design: Spirometry and IOS were performed at baseline and for 20 min after challenge at 5-min intervals.

Setting: Two 6-min exercise challenges, inhaling either room temperature (22.0°C) or cold temperature (4°C) dry medical-grade bottled air. At least 48 h was observed between these randomly assigned challenges.

Participants: Twenty-two physically active individuals (12 women and 10 men) with probable EIB.

Interventions: Subjects performed 6 min of stationary cycle ergometry while breathing either cold or room temperature medical-grade dry bottled air. Subjects were instructed to exercise at the highest intensity sustainable for the duration of the challenge. Heart rate and kilojoules of work performed were documented to verify exercise intensity.

Measurements and results: Strong correlations were observed within testing modalities for post-room temperature and post-cold temperature exercise spirometry and IOS values. Spirometry revealed no differences in postexercise peak falls in lung function between conditions; however, IOS identified significant differences in respiratory resistance (p < 0.05), with room temperature-inspired air being more potent than cold temperature-inspired air.

Conclusions: Correlations were found between spirometric and IOS measures of change in airway function for both exercise challenges, indicating close equivalency of the methods. The challenges appeared to elicit the EIB response by a similar mechanism of water loss, and cold temperature did not have an additive effect. IOS detected a difference in degree of response between the temperatures, whereas spirometry indicated no difference, suggesting that IOS is a more sensitive measure of change in airway function. (CHEST 2005; 128:2412–2419)

Key words: bronchoconstriction; dry air; eucapnic voluntary hyperventilation; exercise; impulse oscillometry; spirometry; temperature

Abbreviations: AX = low-frequency reactance area; CTEX = cold temperature exercise; EIB = exercise-induced bronchoconstriction; EVH = eucapnic voluntary hyperventilation; FEF_{50} = isovolume forced expiratory flow at 50% of vital capacity; Fves = resonant frequency; IOS = impulse oscillometry system; kJ = kilojoules; PFT = pulmonary function test; Raw = airway resistance; RTEX = room temperature exercise; Ve = minute ventilation; X = reactance at 5 Hz

The knowledge that respiratory symptoms alone do not predict the presence of exercise-induced bronchoconstriction (EIB) justifies the need for objective testing methods for diagnosis.¹ EIB, a transient narrowing of the airways during or (most often) shortly following the termination of exercise in sus-

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ceptible individuals, exceeds the estimated 10 to 12% prevalence of asthma in both the general population (4 to 20%) and in the elite athlete population (11 to 50%). The symptoms and observable signs of EIB are varied and disparate in nature, commonly including cough, wheeze, dyspnea, chest tightness, and/or excess mucus.1

Although the precise pathophysiology of EIB is not certain, theories have been proposed that link the condition with hyperosmolarity of the bronchial epithelia, release of chemical mediators, and exchange of water and heat (reactive hyperemia) in the airway. Inspired air is warmed to body temperature and saturated with water from the airway surface liquid prior to reaching the terminal alveoli membranes. The osmotic theory holds that airway drying occurs as a consequence of exercise hyperventilation. If airway surface liquid is not replenished, resident airway cells increase in osmolarity. The reestablishment of intracellular osmolarity on cessation of exercise is proposed to cause the release of chemical mediators4 that result in smooth muscle contraction and increased mucus production, leading to the EIB response.5

EIB is most often documented by a 10% baseline to postchallenge fall in FEV1, regardless of the mode of challenge utilized to elicit the EIB response.6 Spirometry is highly dependent on correct technique, as the maneuver is effort dependent and requires active cooperation by the patient, which may present clinical difficulties with children and the elderly, or with cognitively impaired individuals. Impulse oscillometry (IOS) is effort independent, as brief random pressure pulses of 5 to 35 Hz (generated by a small loudspeaker mounted in series with a pneumotach) are applied during tidal breathing. The pressure-flow oscillations are superimposed on the subject’s tidal breaths, and real-time recordings are used to provide an estimate of total respiratory system impedance and its two components, resistance and reactance.7 IOS has been used to measure short-term changes in bronchial tone in bronchodilator testing8 and has been shown to correlate with FEV1,9–15 as well as airway resistance (Raw) determined by body plethysmography.16–17 The IOS maneuver provides the advantages of requiring only passive cooperation during tidal breathing and does not cause respiratory fatigue.7

Although the clinical efficacy of measuring respiratory impedance using IOS as an indirect measure of airflow obstruction after methacholine challenge has been demonstrated,10–14 its usefulness in measuring changes in airway caliber brought on by exercise challenges has not been established. In light of this, the purpose of this study was to compare airway responses following room temperature exercise (BTEX) and cold temperature exercise (CTEX) challenges, and to compare whether IOS variables relate to spirometry variables. To accomplish this, exercise challenges were performed at both room temperature and cold temperature in an attempt to provoke the EIB response, with baseline and postchallenge lung function being measured by both spirometry and IOS. Since IOS and spirometry measure two different outcome variables, we evaluated whether temperature affected IOS differently than spirometry. We hypothesized that the water content of the air and not temperature is a trigger for EIB, and that we would be able to identify the EIB response using IOS.

METHODS AND MATERIALS

Subjects

Twenty-two physically active individuals with probable EIB were recruited to participate in this study (mean age ± SD, 25.2 ± 5.4 years; height, 1.71 ± 0.08 m; weight, 74.7 ± 15 kg; 10 men and 12 women). The Institutional Review Board of Marywood University approved the study protocol, and subjects provided written informed consent for participation. Eight subjects reported using an inhaled β2-agonist prior to exercise, one subject was receiving salmeterol, one subject was receiving fluticasone in combination with salmeterol, and one subject was receiving montelukast.

Demographic/Medical History Screening Procedure

Subjects completed a demographic and medical history questionnaire prior to the study. Questionnaires were reviewed for possible safety concerns and to ensure the absence of specific exclusion criteria for this study, which included the following: participants who smoke; had an active upper respiratory tract infection within 6 weeks of testing; had an exacerbation of asthma requiring hospitalization in his or her lifetime; had received systemic steroids within 6 weeks of testing; had received the influenza vaccination within 6 weeks prior to the start of testing; had cardiovascular disease; and/or were pregnant during the time of the study.19 Participants who regularly or sporadically used asthma medications were asked to temporarily abstain from taking them prior to any testing. The specific medications and the time frames at which their use was suspended were as follows: short-acting bronchodilators, 4 h prior to any testing; long-acting or sustained-release bronchodilators; antihistamine medications; 48 h prior to any testing; leukotriene antagonists and combined long-acting bronchodilators 4 days prior to any testing.19 No physical activity or caffeine consumption was permitted for at least 8 h prior to testing. Subjects had no pulmonary complaints or evidence of upper respiratory tract or other infection during the course of the study.

Eucapnic Voluntary Hyperventilation Screening Procedure

Eucapnic voluntary hyperventilation (EVH) required subjects to breathe compressed dry gas mixture (21% O2, 5% CO2, balance N2) at a predetermined rate of 30 × baseline FEV1 (85% maximal voluntary ventilation).19,20 EVH gas flowed from a cylinder through a calibrated rotameter (1110 Series Flowmeter;
Subjects completed 6 min of stationary cycle ergometry on an electronically braked cycle ergometer (Lode Excalibur Sport; Lode; Groningen, the Netherlands) while breathing medical-grade dry bottled air. Subjects were instructed to exercise at the highest intensity sustainable for the duration of the challenge and were verbally encouraged to give a maximal effort at all times. All subjects wore wireless heart rate monitors to verify exercise intensity (Polar Vantage XL; Polar Electro; Oy, Finland), and Ve was continuously monitored (Vmax Spectra Respiratory Analysis System Model 229D; SensorMedics; Yorba Linda, CA). Inhaled gas during the EVH challenge was at approximately 22°C, with minimal water content as compressed air from a tank containing < 3 mg H2O × L of air. Those subjects identified as EIB probable by a maximal fall of ≥ 7% in FEV1,21,22 were asked to return for a RTEX challenge and a CTEx challenge (as described below), assigned to the subjects in random order no less than 48 h but no more than 1 week later. This liberal 7% cutoff value was used to account for those subjects who may be more responsive to exercise than EVH.21

Exercise Challenges

Subjects completed 6 min of stationary cycle ergometry on an electronically braked cycle ergometer (Lode Excalibur Sport; Lode; Groningen, the Netherlands) while breathing medical-grade dry bottled air. Subjects were instructed to exercise at the highest intensity sustainable for the duration of the challenge and were verbally encouraged to give a maximal effort at all times. All subjects wore wireless heart rate monitors to verify exercise intensity (Polar Vantage XL; Polar Electro; Oy, Finland), and Ve was continuously monitored (Vmax Spectra Respiratory Analysis System Model 229D; SensorMedics) throughout the challenges. Total work accumulated was recorded on completion of the challenges. Inhaled air (measured at the mouth) during the RTEX challenge and CTEx challenge was at approximately 22°C and –1°C, respectively, with minimal water content (< 3 mg H2O × L of air). Bottled air for the CTEx challenge and gas and inhalation lines were chilled in a climate-controlled chamber of the Human Performance Laboratory for a minimum of 24 h prior to use. Inhalation air temperature was monitored at the inhalation port of the two-way nonbreathing valve (Hans Rudolf).

Pulmonary Function Test Procedures

Raw and airway reactance in response to EVH and exercise were determined by IOS (Jaeger MS-IOS; Hoechberg, Germany; LAB Manager Software version 4.53.2, 2002) using the recommended techniques of the manufacturer. Real-time recordings of mouth pressure and flow signals pulsed through 5- to 35-Hz spectrum were superimposed over tracings of tidal breathing and displayed on a computer screen. Measurements of Raw, resonant frequency (Fres), reactance at 5 Hz (X5), and low-frequency reactance area (AX; area of reactance integrated from 5 Hz up to Fres) were recorded at 5, 10, 15, and 20 min after challenge.

Pulmonary function response to EVH and exercise was determined using spirometry (immediately following the IOS maneuver) using a calibrated computerized pneumotachograph spirometer (Jaeger Masterscope PC; Hoechberg, Germany; LAB Manager Software version 4.53.2, 2002). Standard measures of pulmonary function were collected, including FVC, FEV1, and isovolume forced expiratory flow at 50% of vital capacity (FEF50) calculated from baseline FVC. FEV1/FVC ratio was calculated. The procedure for all pulmonary function tests (PFTs) included the following: (1) three normal tidal volume breaths, followed by (2) inhalation to total lung capacity, and (3) forced maximal exhalation lasting at least 6 s, terminating with (4) a final maximal inhalation. All tests were performed according to current American Thoracic Society spirometry standards.21 Resting baseline pulmonary function was established prior to each challenge by selecting the best-of-three resting PFT results based on the highest sum of FVC and FEV1. Postchallenge pulmonary function was measured at 5, 10, 15, and 20 minutes. One maneuver was performed at each postchallenge time point in an effort to minimize subject fatigue and guard against potential effects of deep inhalation.24 However, if any baseline or postchallenge time point measurement was technically unacceptably, the PFT maneuver was repeated immediately.

Statistical Analysis

Descriptive statistics for resting lung function were calculated for IOS and spirometry lung function measurements. Airway responses were analyzed by analysis of variance, followed by post hoc paired t tests when significant F values were obtained. Pearson product-moment correlations were used to evaluate relationships between resting measurements and between postchallenge falls in FVC, FEV1, FEF50, as well as Raw and airway reactance measurements determined by IOS. Analysis was performed using statistical software (Statistical Package for the Social Sciences, Version 12.0; SPSS; Chicago, IL). An α of p ≤ 0.05 was considered significant.

RESULTS

Baseline Lung Function

Individual and mean resting lung function values from IOS and spirometry are presented in Table 1. Resting FVC values were normal, ranging from 81.67 to 135.59% of predicted values. One subject demonstrated below-normal resting FEV1 (78.6% of predicted value). Five of 22 subjects (22.7%) demonstrated < 70% of predicted FEF50 suggestive of mild airflow limitation and small-airway involvement. Significant correlations were identified between resting spirometry and IOS values (p < 0.05): V˙E and FEV1 correlated to Raw (r = −0.52 and r = −0.50, respectively), and FEV1 percentage of predicted correlated to Fres and AX (r = −0.57 and r = −0.44, respectively). No resting spirometric or IOS measures related to post-EVH or postexercise falls in FEV1. Resting Raw was significantly correlated to post-RTEX peak fall in FEF50 (r = −0.46, p < 0.05). Baseline spirometry and IOS measurements were not different between the two challenges.

Airway Response to EVH and Exercise

No significant differences in Ve during RTEX and CTEx were apparent (121.3 ± 27.3 L/min and 124.7 ± 24.1 L/min, respectively; Fig 1), nor was the area under the curve for Ve during exercise different between the challenges (677.7 ± 152.6 and 676.7 ± 131.7 for RTEX and CTEx, respectively). Peak heart rate during the RTEX and CTEx challenges was not different: 179.6 ± 15.1 beats/min and 181.9 ± 13.7 beats/min. Likewise, kilojoules (kJ) of

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work performed during the 6-min challenges were not different (68.1 ± 22.5 kJ and 68.1 ± 24.6 kJ for RTEX and CTEX, respectively).

No differences were observed between RTEX and CTEX in postchallenge peak percentage falls for FVC, FEV₁, or FEF₅₀ (Fig 2, top). Figure 2, bottom, presents changes in FEV₁ for 20 min after challenge in 5-min intervals. Only the 5-min postchallenge time point was significantly different, with RTEX demonstrating a greater fall in FEV₁ than CTEX. RTEX also resulted in a small but statistically greater increase in Raw (p < 0.05); Fres, X, and AX were not different between challenges (Fig 3).

Figure 4 illustrates percentage changes in IOS values for 20 min after challenge in 5-min increments. Raw was significantly greater for RTEX at 5 min after challenge (p < 0.05). This finding was consistent with the postchallenge percentage change in FEV₁ (as shown in Fig 2, bottom).

**Relationship Between Spirometry and IOS**

Strong correlations were observed within testing conditions among the postexercise percentage change values for spirometric and IOS parameters. The percentage of peak fall in FEV₁ was significantly correlated to the percentage of peak fall in FVC (RTEX, r = 0.44; CTEX, r = 0.64; p < 0.05) and FEF₅₀ (RTEX, r = 0.56; p < 0.05). Peak increase in Raw was significantly correlated to peak increases in Fres, X, and AX (RTEX, r = 0.79, r = −0.87, and r = 0.86, respectively; CTEX, r = 0.78, r = −0.82, and r = 0.87, respectively; p < 0.05). Peak increase

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### Table 1—Spirometry and IOS Values at Baseline*

<table>
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<tr>
<th>Patient No.</th>
<th>FVC, L</th>
<th>FEV₁, L</th>
<th>FEV₁/FVC</th>
<th>FEF₅₀, L × s</th>
<th>Raw, cm H₂O/L/s</th>
<th>Fres, Hz</th>
<th>X, cm H₂O/L/s</th>
<th>AX, cm H₂O/L</th>
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<td>7 to &gt; 10%</td>
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<td>1</td>
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<td>3.81 (92.70)</td>
<td>76.51</td>
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<td>80.95</td>
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<td>0.73 (13.81)</td>
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<td>23.71</td>
<td>1.20</td>
<td>2.87</td>
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<td>3.13</td>
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*Data are presented as mean (percentage of predicted) or mean.
in \( F_{res} \) was significantly correlated to peak increase in \( X \) and \( AX \) (RTEX, \( r = -0.76 \) and \( r = 0.94 \), respectively; CTEX, \( r = -0.62 \) and \( r = 0.91 \), respectively; \( p < 0.05 \)). Peak increase in \( X \) was significant.
postchallenge FEV1 from baseline are considered a sensitive measure of change in airway function. 

For RTEX, postchallenge peak percentage change in FEF_{50} was significantly correlated to peak percentage change in X (r = −0.54). For CTEX, postchallenge peak percentage change in FEV1 was significantly correlated to peak percentage change in X (r = 0.43, p < 0.05), and postchallenge peak percentage change in FEF_{50} was significantly correlated to peak percentage change in Raw and peak percentage change in X (r = −0.50 and r = 0.52, respectively; p < 0.05).

**Discussion**

In this study, we compared airway responses following randomly assigned RTEX and CTEX challenges and examined whether resting and postchallenge spirometry variables correlated with resting and postchallenge IOS variables. Six minutes of exercise while breathing dry medical-grade bottled air was a suitable challenge for inducing the EIB response. Heart rate during exercise and the amount of work performed indicated that the challenges were at an intensity sufficient to provoke EIB, and comparable Ve and total amount of air ventilated during RTEX and CTEX verified that the challenges were similar except for the inspired air temperature; no greater EIB response was obtained by chilling the inspired dry air.

We found a high correlation between spirometric measures of change in airway function and IOS measures of change for both exercise challenges, indicating close equivalency of the two testing methods. Interestingly, IOS detected a difference in the degree of peak response to RTEX compared to CTEX, whereas spirometry only indicated a difference at the 5-min postchallenge time point but no peak differences, suggesting that IOS is a more sensitive measure of change in airway function.

Postchallenge spirometric measurements from maximal expiratory flow volume maneuvers were compared to measurements of postchallenge airway impedance from IOS during tidal breathing. Falls in postchallenge FEV1 from baseline are considered the “gold standard” indirect measure of changes in airway caliber, as they are representative of approximately 90% of the entire flow volume curve, and are the most widely used index of EIB. Our results of postchallenge change in IOS variables demonstrate that IOS is an accurate and reliable measure of lung function.

In asthmatics, EIB is commonly associated with abnormalities in baseline lung function. In this group of subjects, resting lung function was within normal expectations, as the mean percentages of predicted values were 109.07%, 106.90%, and 96.60% for FVC, FEV1, and FEF_{50}, respectively. Likewise, IOS values were within the normal range. As indexes of change in airway obstruction, midexpiratory flows have been reported to be valid only when vital capacity is unaltered. We calculated FEF_{50} using baseline FVC in order to allow accurate comparisons of FEF_{50} to IOS values.

Both the RTEX and CTEX challenges were potent stimuli of EIB. Significant intermodality correlations were identified between resting spirometry and IOS values; however, no resting spirometry or IOS indexes correlated with the postchallenge peak fall in FEV1. This is not unexpected, as Bundell et al found no relationship between EIB status and baseline lung function or symptoms in elite female ice hockey players. In this study, postchallenge spirometry indexes were not significantly different between RTEX and CTEX; however, peak postchallenge Raw was significantly different between RTEX and CTEX (p < 0.05), suggesting that RTEX may be more potent than CTEX and that IOS is more sensitive to changes in airway caliber than spirometry.

Previous studies have suggested that IOS measurements are frequency dependent, with the more pronounced changes occurring at the lower frequencies. Bisgaard and Klug found X at 5 Hz to be significantly more sensitive than FEV1, with several IOS indexes revealing subclinical bronchial obstruction. Buhr et al found X to be more discriminative than Raw in detecting impaired lung function. Goldman et al found that Raw and reactance over the range of low frequencies below FVC (AX) provide evidence of airflow obstruction beyond the sensitivity of spirometry. Our results indicate that peak Raw is the most sensitive of the IOS indexes, although AX demonstrated a significantly greater value for RTEX (p < 0.05) at the 5-min postchallenge time point.

Of the 22 EIB-probable subjects, 14 subjects (64%) had a fall of ≥ 10% in FEV1 after RTEX, and 12 subjects (55%) had a fall of ≥ 10% in FEV1 after CTEX. Nine of the 13 patients who were EIB positive by RTEX were positive by CTEX, and 9 of the 11 patients who were positive by CTEX were positive by RTEX. All subjects demonstrated a postchallenge increase of at least 100% from baseline Raw for both challenges, including the six subjects that had a fall in FEV1 of < 10%. Although these subjects did not meet the ≥ 10% cutoff value in FEV1 for EIB, they demonstrated elevated Raw after exercise consistent with airway obstruction, suggesting that the forced expiratory maneuver may mask changes in airway tone. Similar results were observed in measurements of Fres, X, and AX. This
was not unexpected, as Assena et al. found that deep inspiration by children and adults resulted in a similar effect of bronchodilation in healthy persons and mild asthmatics, and bronchoconstriction in patients with moderate-to-severe asthma. Others have documented similar airway responses in patients with airway hyperresponsiveness and asthma.

Although airway cooling as a mechanism of EIB holds popularity in light of the common observation that EIB worsens in cold temperatures and is more prevalent in winter sport athletes, our results suggest that water content of the air rather than temperature is essential to the EIB response, as the cold temperature inhalation challenge did not have an additive effect. Because only the inspired air was chilled and not the subjects’ faces or entire bodies, the possibility of a thermally sensitive somatic-afferent vagal-efferent reflex playing a role in airway narrowing was unlikely. A similar mechanism of water loss for the provocation of EIB during the exercise challenges is in agreement with Zeitoun et al. who noted that the airway surface liquid was maintained during low ventilation but not during high ventilation.

Strong correlations were observed within testing modalities for post-RTEX and post-CTEX values; baseline FVC and FEV\textsubscript{1} correlated to baseline Raw, and baseline FEV\textsubscript{1} percentage of predicted correlated to Fres and AX. No resting spirometric measures were related to post-RTEX or post-CTEX falls in FEV\textsubscript{1}. No significant relationships were identified between resting Raw, Fres, X, and AX and peak fall in FEV\textsubscript{1}, although resting Raw was significantly correlated to post-RTEX peak fall in FEF\textsubscript{50}. Spirometry did not identify any differences in the potency of the two challenges; however, changes in airway caliber as measured by IOS identified RTEX more potent than CTEX.

This study produced two findings that are noteworthy for clinicians. Our results indicate that IOS is indeed sensitive to changes in airway caliber following RTEX and CTEX and can be used as a surrogate to spirometry in evaluating EIB. IOS provides the advantages of requiring only passive cooperation during tidal breathing, which is well suited for the evaluation of the elderly, cognitively impaired, and children, while also not causing respiratory fatigue. In addition, IOS is capable of assessing both central and peripheral Raw as well as pulmonary reactivity. Since X is a function of lung compliance and inertia, it can be used to evaluate the elastic properties of the lung.

Both challenges appeared to provoke EIB by a similar mechanism of water loss, as cold temperature did not have an additive effect to the response. Based on our findings, we suggest that the potential role of IOS in the evaluation of EIB is deserving of further study, and that water content of the inspired air and not temperature is critical to the EIB response.

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