Letter to the Editor

Utility of impulse oscillometry in patients with moderate to severe persistent asthma

To the Editor:

We have previously shown in a cohort of patients with asthma that impulse oscillometry (IOS) and spirometry are equally useful in predicting asthma control as assessed by prescriptions of oral corticosteroid and inhaled albuterol using health informatics.[1] These were patients referred from primary care for screening into clinical trials. We wanted to know how IOS and spirometry were related to the asthma control questionnaire (ACQ) in a real-life secondary care clinic setting. In particular, we were interested in finding out whether IOS outcomes reflecting the frequency-dependent heterogeneity in smaller airways,[2] namely, the difference in resistance between 5 Hz and 20 Hz (R5-R20) and the area under the reactance curve (AX), were more closely related to asthma control, as has previously been described in children with asthma.[3]

We evaluated a separate series of 108 unselected patients attending a National Health Service asthma secondary care clinic, who completed the ACQ-5[4] in addition to having spirometry and IOS as part of their usual care. Their current asthma therapy at the time of the clinic visit was also documented. We routinely perform IOS and spirometry and administer the ACQ in our clinic; hence, this audit of usual clinical care did not require ethics approval, although Caldicott guardian approval was obtained to allow appropriate access to the patient identifiable National Health Service data. IOS (Jaeger Masterscreen, Hochberg, Germany) and spirometry (Micromedical, Chatham, United Kingdom) were performed in triplicate according to European Respiratory Society guidelines.

We analyzed the IOS and spirometry data according to both ACQ-5 score and current salbutamol use comparing predefined cutoff values for each measurement as follows: FEV_1 less than 80% versus 80% predicted or more; forced expiratory flow at 25% to 75% of forced vital capacity (FVC) (FEF_{25-75}) less than 50% versus 50% predicted or more; FEV_1/FVC ratio less than 0.70 versus 0.70 or more; R5 less than 150% versus 150% predicted or more; R20 less than 150% versus 150% predicted or more; R5-R20 less than 0.1 versus 0.1 kPa/L·s or more (ie, 1 cmH_2O/L/s); AX less than 0.8 versus 0.8 kPa/L or more (ie, 8 cmH_2O/L), resonant frequency less than 15 versus 15 Hz or more. Comparisons for each outcome were made by unpaired Student *t* tests with alpha error set at 0.05 (2-tailed).

The patients (n = 108) had an overall mean age of 42 years, FEV_1 of 81% predicted, FEV_1/FVC of 0.68, R5 of 178% predicted, R5-R20 of 0.16 kPa/L·s, and ACQ-5 score of 2.37. All patients were receiving inhaled corticosteroids in a median beclomethasone equivalent dose of 800 µg/d, 80% were taking long-acting beta-agonists, and 36% were taking leukotriene receptor antagonists.

The results showed that IOS measurements of R5-R20, AX, and resonant frequency, but none of the spirometry measurements, were significantly different in terms of worse control as ACQ-5 score (Table I and Fig 1) whereas only R5-R20 was significantly different for increased salbutamol use: 5 versus 8 puffs/d (*P* = .006). Furthermore, when the data were analyzed using lower cutoff values for FEV_1/FVC ratio (<0.6 and <0.5) and FEF_{25-75} (<40% and <30% predicted), there were no significant differences in ACQ-5 scores.

Our data would therefore suggest that in a real-life clinic setting IOS rather than spirometry is more closely related to asthma control on the basis of the ACQ-5 score. Overall, our patients had moderate to severe persistent asthma in keeping with a high total airway resistance (R5) of 178% and mean ACQ score of 2.37.[5] Indeed, the lower bound of the 95% CI for ACQ was higher than the cutoff value of 1.5 for poorly controlled asthma for variables, even in those patients with a preserved FEV_1 of 80% or more (Fig 1). Pointedly, the ACQ score has been shown to be a

TABLE I. Pulmonary function measures in relation to ACQ-5 score

Measure	ACQ-5 score		n	ACQ-5 score		n	*P* value
IOS							
R5-R20 (kPa/L·s)		<0.1			≥0.1		.01
	2.03 ± 0.17		46	2.62 ± 0.15		62	
R5 (% predicted)		<150%			≥150%		.18
	2.18 ± 0.17		42	2.49 ± 0.15		66	
R20 (% predicted)		<150%			≥150%		.30
	2.50 ± 0.15		51	2.26 ± 0.17		57	
AX (kPa/L)		<0.8			≥0.8		.02
	2.08 ± 0.17		38	2.74 ± 0.21		41	
RF (Hz)		<15			≥15		.04
	2.06 ± 0.20		31	2.65 ± 0.19		48	
Spirometry							
FEV_1 (% predicted)		<80%			≥80%		.09
	2.59 ± 0.19		47	2.20 ± 0.14		61	
FEV_1/FVC (ratio)		<0.7			≥0.7		.49
	2.29 ± 0.17		55	2.45 ± 0.16		53	
FEF_{25-75} (% predicted)		<50%			≥50%		.57
	2.43 ± 0.17		59	2.30 ± 0.15		49	

Data for AX and RF were available only in a subgroup of 79 patients, whereas all other variables were on the full data set of n = 108. Values for ACQ-5 score are means ± SEM.
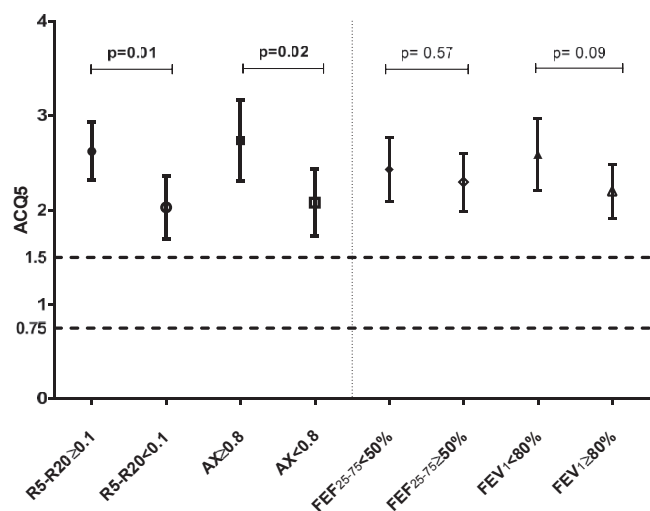*RF*, Resonant frequency.

FIG 1. Mean and 95% CI for ACQ-5 score when stratified for both IOS and spirometry cutoff values. Interrupted lines denote cutoff values for the ACQ score for well-controlled (<0.75) and poorly controlled asthma (≥1.50). Values for R5-R20 are in kPa/L·s, for AX are in kPa/L, and for FEV_1 and FEF_{25-75} are % predicted.

highly predictive proxy for the future risk of asthma exacerbations.[6]

The R5-R20 and AX are indicative of frequency-dependent heterogeneity for respiratory resistance and reactance, respectively, throughout the lung.[2] We were not able to measure resistance or reactance at frequencies of less than 5 Hz, which might better reflect smaller airways. Our patients had evidence of large airway obstruction as reflected by a mean FEV_1/FVC ratio of 0.68 and a mean FEV_1 of 81% predicted. As such our data would suggest that IOS is a more sensitive index of airway obstruction than spirometry irrespective of the site of obstruction at least in patients with mild to moderate persistent asthma. Nonetheless, we observed that neither R5 (reflecting total airway resistance) nor R20 (reflecting central airway resistance) was associated with a significant difference in the ACQ score, in contrast to the significant difference seen with R5-R20. Our data are similar to those of Shi et al[3] where the heterogeneity of resistance (R5-20) or reactance (AX) was more predictive of asthma control than either R5 or X5 in children with asthma.[3] However, in a cohort of patients with no evidence of large airway obstruction who had a preserved FEV_1 of more than 80%, an abnormal R5-R20 was associated with increased use of oral corticosteroid and albuterol.[7]

We did not however observe a significant difference with the ACQ score in relation to FEF_{25-75}, which is a rather variable volume-dependent measurement of flow rate.[8] Indeed, even when using a lower cutoff value of less than 30% predicted for FEF_{25-75}, there was still no significant difference in the ACQ score. IOS is considered to be more physiological than spirometry because it is performed during normal quiet breathing and therefore not affected by forced expiratory changes that occur during spirometry.[2] The present data differ from our previous observations[1] where we found that IOS and spirometry measures were equally useful as markers of asthma control using prescribing data for oral corticosteroid and inhaled albuterol use. This may be explained by the patients actually recording their ACQ score in the clinic at the same time as having their pulmonary function performed, perhaps resulting in a greater degree of concordance between physiology and symptoms. We elected to use the abbreviated ACQ-5 score because we did not want to confound the results by including FEV_1% or albuterol use. Moreover, it has been shown that the abbreviated ACQ-5 score is as sensitive as ACQ-7 score.[4]

In conclusion, IOS outcomes reflecting frequency-dependent heterogeneity appear to be more closely related to asthma control than spirometry in patients with moderate to severe persistent asthma. Further prospective trials are indicated to assess whether serial long-term IOS measurements may help guide decision making for patients with persistent asthma with disproportionate small airways disease, especially because health economics studies have suggested that using extrafine particle inhalers containing ICS inhalers may confer better long-term outcomes.[9]

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