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Published in:
Journal of Allergy and Clinical Immunology

DOI:
10.1016/j.jaci.2015.12.1336

Publication date:
2016

Document Version
Accepted author manuscript

Elsevier Editorial System(tm) for Journal of Allergy and Clinical Immunology
Manuscript Draft

Manuscript Number: JACI-D-15-01438R1

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

Article Type: Letter to the Editor

Section/Category: Asthma and Lower Airway Disease

Keywords: impulse oscillometry; asthma; control

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Manuscript Region of Origin: UNITED KINGDOM

Abstract: Outcomes measured with impulse oscillometry are more closely related to asthma control than spirometry in moderate to severe asthma.

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Declaration of funding: Funded by University departmental funds

Capsule Summary: Outcomes measured with impulse oscillometry are more closely related to asthma control than spirometry in moderate to severe asthma.

Key Words: Impulse oscillometry, asthma, control

Word Count =1056

To the Editor:

We have previously shown in a cohort of asthmatic patients 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 to see if IOS outcomes reflecting frequency dependent heterogeneity [2], namely the difference in resistance at 5Hz and 20Hz (R5-R20) and the reactance area (AX) between 5Hz and the resonant frequency (RF), are more closely associated with worse asthma control ,as has previously been described in children with asthma[3].

We have evaluated a separate series of 108 unselected patients attending a National Health Service (NHS) asthma secondary care clinic, who completed an ACQ-5 score [8] 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, spirometry and ACQ in our clinic, hence this audit of usual clinical care did not require ethics approval, although Caldicott guardian approval was obtained in order to allow appropriate access to the patient identifiable NHS data .IOS (Jaeger Masterscreen, Hochberg Germany) and spirometry (Micromedical Chatham Kent, UK) were performed in triplicate according to European Respiratory Society guidelines.

We analysed the IOS and spirometry data according to both ACQ-5 and current salbutamol use comparing predefined cut-off values for each measurement as follows: FEV_1 <80 % versus ≥80 % predicted; $FEF_{25–75}$ <50 % versus ≥50% predicted; FEV_1/FVC ratio <0.70 versus ≥0.70; R5 < 150 % versus ≥150 % predicted; R20 <150% versus ≥150% predicted, R5–R20 < 0.1 versus ≥0.1 kPa/l.s (i.e. 1 cmH_2O/l.s); AX <0.8 versus ≥ 0.8 kPa/l (i.e. 8 cmH_2O/l), RF (resonant frequency) <15 versus ≥ 15Hz. Comparisons for each outcome were made by unpaired Students t tests with alpha error set at 0.05 (two 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 (ICS) in a median beclomethasone equivalent dose of 800 µg/day, 80% were taking long acting beta-agonists (LABA) and 36% were taking leukotriene receptor antagonists.

The results showed that IOS measurements of R5-R20, AX and RF, but none of the spirometry measurements were significantly different in terms of worse control as ACQ-5 (Table and Figure), while only R5-R20 was significantly different for increased salbutamol use: 5 vs 8 puffs /day (P=0.006). Furthermore when the data were analyzed using lower cut-off values for FEV_1/FVC ratio (<0.6 and <0.5) and FEF_{25-75} (<40% and <30% predicted) there were also no significant differences in ACQ-5 .

Our data would therefore suggest that in a real life clinic setting IOS rather than spirometry is more closely related to asthma control based on 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[4]. Indeed the lower bound of the 95%CI for ACQ was higher than the cut off value of 1.5 for poorly controlled asthma for variables, even in those patients with a preserved FEV_1 ≥ 80% (Figure). Pointedly the ACQ score has been shown to be a highly predictive proxy for the future risk of asthma exacerbations[5].

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 <5Hz 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) were associated with a significant difference in ACQ, in contrast to the significant difference seen with R5-R20 . Our data are similar to those of Shi et al. where the heterogeneity of resistance (R5-20) or reactance (AX) were more predictive of asthma control than either R5 or X5 in asthmatic children[3] . However in a cohort of patients with no evidence of large airway obstruction who had a preserved FEV_1>80% ,an abnormal R5-R20 was associated with increased use of oral corticosteroid and albuterol [6].

We did not however observe a significant difference with ACQ in relation to FEF_{25-75} which is a rather variable volume dependent measurement of flow

rate [7]. Indeed even when using a lower cut off value <30 % predicted for FEF_{25-75} there was still no significant difference in ACQ score. IOS is considered to be more physiological than spirometry as it is performed during normal quiet breathing and therefore not affected by forced expiratory changes which 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 the ACQ-7 score[8].

In conclusion impulse oscillometry 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 since health economics studies have suggested that using extra fine particle inhalers containing ICS inhalers may confer better long term outcomes[9].

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Figure 1.

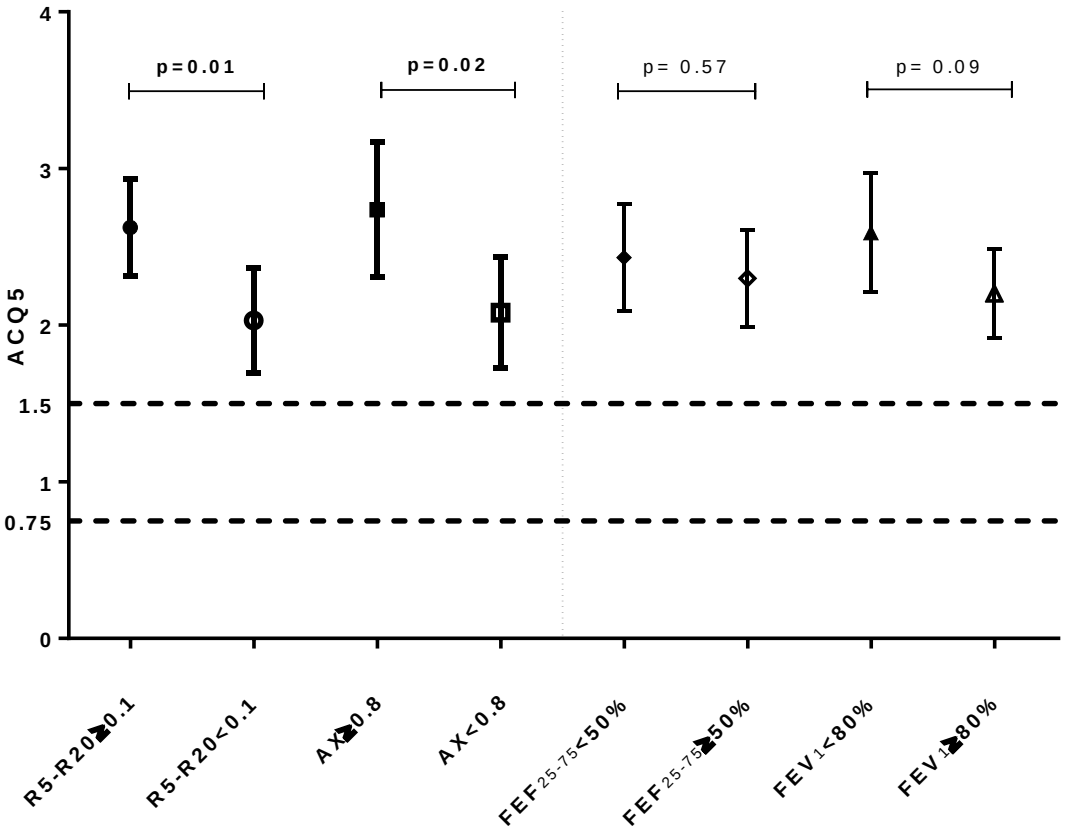

Figure Legend

Mean and 95% CI for ACQ5 score when stratified for both IOS and spirometry cut off values .Interrupted lines denote cut off values for ACQ score for well controlled (<0.75) and poorly controlled asthma (≥1.50).Values for R5-R20 are kPa/l.s and AX are kPa/l , FEV_1 and FEF_{25-75} are % predicted

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Table 1. Pulmonary function measures in relation to ACQ5 score

	ACQ5	n	ACQ5	n	p value
Impulse oscillometry					
R5-R20 (kPa/L.s)	**<0.1**		**≥0.1**		0.01
	2.03 (0.17)	46	2.62 (0.15)	62	
R5 (% pred)	**<150%**		**≥150%**		0.18
	2.18 (0.17)	42	2.49 (0.15)	66	
R20 (% pred)	**<150%**		**≥150%**		0.30
	2.50 (0.15)	51	2.26 (0.17)	57	
AX (kPa/L)	**<0.8**		**≥0.8**		0.02
	2.08 (0.17)	38	2.74 (0.21)	41	
RF (Hz)	**<15**		**≥15**		0.04
	2.06 (0.20)	31	2.65 (0.19)	48	
Spirometry					
FEV_1 (% pred)	**<80%**		**≥80%**		0.09
	2.59 (0.19)	47	2.20 (0.14)	61	
FEV_1/FVC (Ratio)	**<0.7**		**≥0.7**		0.49
	2.29 (0.17)	55	2.45 (0.16)	53	
FEF_{25-75} (% pred)	**<50%**		**≥50%**		0.57
	2.43 (0.17)	59	2.30 (0.15)	49	

Data for AX and RF were only available in a subgroup of n=79 patients, while all other variables were on the full dataset of n=108 .Values for ACQ-5 are means (SEM).