Airflow Obstruction (AFO) in mild, moderate, and severe asthma: associations with small airway disease, clinical characteristics and Type2 biomarkers

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BACKGROUND

Airflow obstruction (AFO) and preserved ratio impaired spirometry phenotype in asthma have been associated with more exacerbations, poorer symptoms, use of ICS, and small airway dysfunction (SAD) [Cottini et al,2025]. Here we present analysis of AFO across severities of asthma in a cross-sectional asthma cohort prior to enrolment in the MAPLE-UK longitudinal study.

CROSS SECTIONAL COHORT

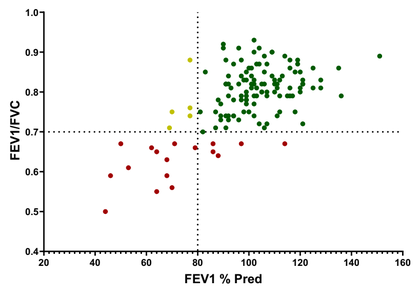
Approximately 200 GINA 1 to 5 patients with asthma attended hVIVO's clinical trial site. All patients had a range of clinical assessments to characterise their asthma for enrolment in clinical trials.

Asthma assessments

- Exacerbations, medical and medications
- AHR: Methacholine challenge
- SABA responsiveness
- Atopy: Skin Prick
- Lung function: FOT, spirometry
- T2 markers: FENO & BECs
- Asthma PROS/Control: ACQ, AIRQ
- Blood and nasal sampling

Of this cohort, 133 had complete FOT and T2 marker (FENO / blood epithelial cells [BECs]) data. Patients were grouped according to pre-bronchodilator spirometry as AFO (FEV1/FVC <0.7), PRISm (FEV1/FVC ratio ≥0.7 and FEV1<80% predicted), or NORMAL (FEV1≥80% and FEV1/FVC≥0.7) lung function (**Figure 1** red, yellow and green respectively). Pre- and post-bronchodilator results were also assessed (**Figure 2**).

Figure 1: FEV1% pred and FEV1/FVC for AFO (red), PRISM (yellow) & NORMAL (green)



AFO & LUNG FUNCTION

As shown in **Table 1**, among the 133 patients (median age 29, BMI 26, 41% female, 74% white Caucasian, no current smokers), 16% had poor control (ACQ-6≥1.5). 71% (n=95) were GINA step 1-3 and 29% (n=38) were GINA steps 4&5.

Pre-bronchodilator (Figure 2 left, & Figure 3)

- *AFO* was present in 17 (13%): 14 from GINA 1-3 (82%) and 3 from GINA 4&5 (18%).
- *PRISm* was present in 5 (4%): 4 from GINA 1-3 (80%) and 1 from GINA 4&5 (20%).
- *NORMAL* was present in 110 (83%): 76 (57%) from GINA 1-3 and 34 from GINA 4&5 (26%)

Pre-bronchodilator (Figure 2 right, & Figure 3)

- Overall, 17 of the 77 (22%) that performed SABA responsiveness were shown responsive.
- AFO: All 5 showed SABA responsiveness, however 2 retained an FEV1/FEV <0.7.
- PRISm: 1 showed SABA responsiveness and retained an FEV1% pred <80%.

Table 1: Cohort characteristics

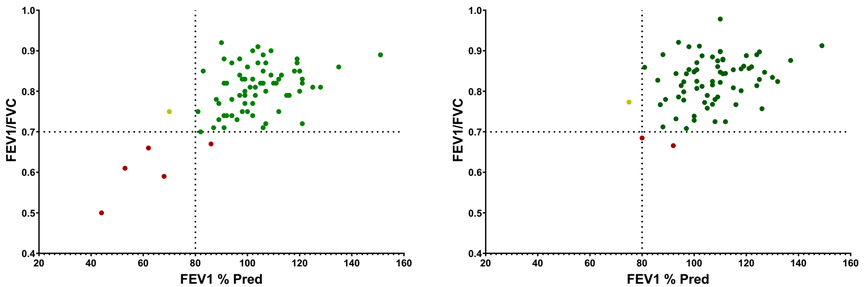
		N = 133
Age		32 (11) 29 [23, 39]
Weight		80 (17) 78 [69, 88]
Height		171 (9) 170 [164, 177]
BMI		27.3 (5.5) 25.9 [23.9, 30.1]
Sex		
	Female	41% (55 /133)
	Male	59% (78 /133)
Race		
	White	74% (98 /133)
	Black	7.5% (10 /133)
	Asian	4.5% (6 /133)
	Other	14% (19 /133)
Smoking.Cat		
	Never	83% (110 /133)
	Previous	17% (23 /133)
	Current	0% (0 /133)
GINA.classification		
	1	20% (26 /133)
	2	17% (23 /133)
	3	35% (46 /133)
	4	25% (33 /133)
	5	3.8% (5 /133)
ACQ6 Poor.Control		16% (21 /133)
AIRQ.Cat Poor Control		26.8% (36/133)
Skin.prick.test.positive		99% (132 /133)
T2.High (BEC ≥300µL or FeNO ≥ 50ppb)		38% (49 /130)
SAD R5-R20>0.07 kPa/L		34% (45 /133)
SAD R5-R20>0.10 + AX>=1kPa/L		20% (27 /133)

Group Comparisons and correlations

AFO, PRISm and NORMAL groups were compared for demographics, GINA step, flares/exacerbation history, medications, spirometry and FOT, SABA responsiveness, methacholine responsiveness (AHR), AIRQ, ACQ, FeNO, and blood eosinophils (BECs). Significant results are shown in **Figure 3**. Within AFO and NORMAL groups, FOT parameters were assessed for non-parametric Spearman correlations.

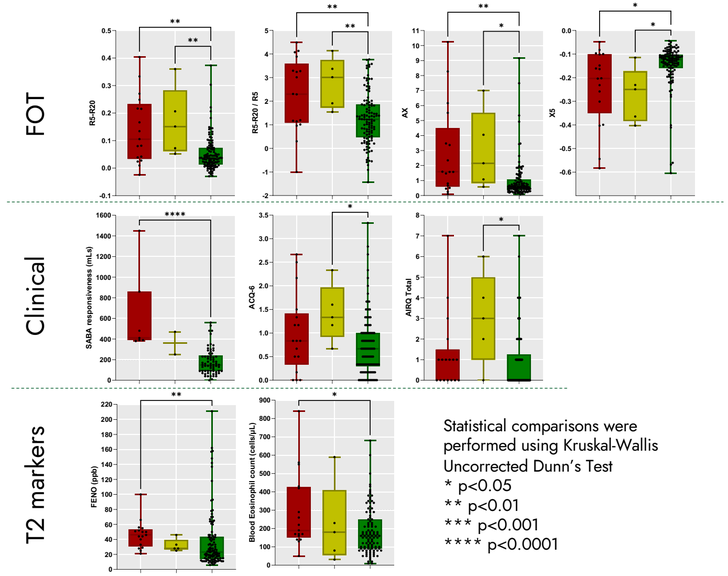
- AFO group: R5-R20 and AX had moderate associations with ACQ (r=0.52, p<0.05; and r=0.54, p<0.05 respectively).
- NORMAL group there were weak associations with Age, BMI, BECs and the number of exacerbations in 3 years.

Figure 2: Pre- (left) and Post- (right) bronchodilator FEV1% pred and FEV1/FVC: AFO (red), PRISm (yellow) & NORMAL (green)



AFO, SABA, SAD, CLINICAL, T2 MARKERS

Figure 3: FOT, clinical, & T2 markers by group: AFO (red), PRISm (yellow) & NORMAL (green)



Statistical comparisons were performed using Kruskal-Wallis Uncorrected Dunn's Test

* p<0.05
** p<0.01
*** p<0.001
**** p<0.0001

SUMMARY

- **Both AFO and PRISm showed evidence of peripheral airway dysfunction as**
  - abnormal R5-R20, R5-R20/R5, AX and X5 compared with normal spirometry.
- **AFO was associated with higher FeNO and BECs, and greater SABA responsiveness**
  - Consistent with a more conventional inflammatory and reversible, airflow-limitation phenotype. Within AFO, greater R5-R20 and AX were associated with poorer asthma control (ACQ-6).
- **PRISm patients had higher ACQ-6 and AIRQ scores despite preserved FEV1/FVC**
  - This suggests a potentially clinically relevant phenotype associated with peripheral airway dysfunction.
  - *Given the small PRISm sample (n=5), these findings are hypothesis-generating and require confirmation in the longitudinal MAPLE-UK cohort.*

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