Identification of plasma fibrinogen-high asthma phenotype

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INTRODUCTION

Asthma is a heterogeneous condition classifiable into different phenotypes.

Asthma exacerbation is an episodic worsening of symptoms and lung function, often leading to impaired quality of life and, occasionally, even to fatal events.

For this reason, it is essential to find biomarkers that could identify the frequent exacerbator phenotype (FE, characterized by ≥ 2 exacerbation per year).

Recently, it has been shown that, in subjects with severe asthma, high plasmatic levels of fibrinogen (above 361mg/dL) positively correlate with frequent exacerbations (JACIp;8:2392-2395.e7).

AIMS AND OBJECTIVE

We aim to identify the main clinical and functional characteristics and comorbidities of mild-to-severe asthmatics with high plasma fibrinogen (PFH).

METHODS

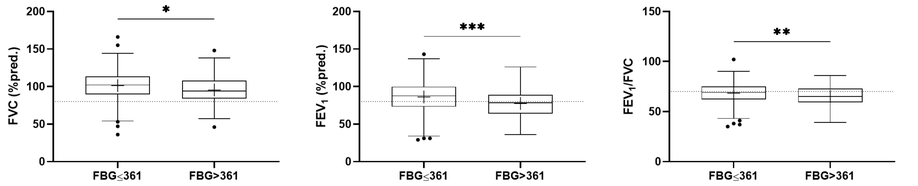
Demographic, clinical, and functional characteristics of 335 asthmatics were extracted from chart data and stratified according to plasmatic fibrinogen concentrations (PFH cut-off >361mg/dL).

RESULTS

The analyses revealed that high plasma fibrinogen asthmatics:

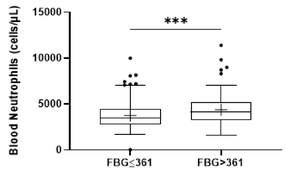
- are prevalently female ($p<0.05$), old ($p<0.01$), obese ($p<0.01$) and have a longer asthma duration ($p<0.05$, Table 1);
- are functionally characterized by:
  - airflow limitation (Figure 1): reduced FEV_1 ($p<0.001$) and FEV_1/FVC ($p<0.01$);
  - air trapping (Figure 1 and 2 and Table 1): lower FVC ($p<0.05$), increased RV ($p<0.05$) and RV/TLC ($p<0.0001$), resulting in reduction in SpO_2 ($p<0.05$);
- have a severe asthma (GINA step 5, $p<0.0001$) with frequent exacerbations ($p<0.05$), for which they receive higher doses of ICS ($p<0.01$) and make greater LAMA use ($p<0.0001$, Table 1);
- have a higher incidence of cardiovascular comorbidities such as hypertension ($p<0.05$), heart failure ($p<0.05$) and arrhythmia ($p<0.001$, Table 2);
- have higher levels of blood neutrophils ($p<0.001$, Figure 2).

FIGURE 1



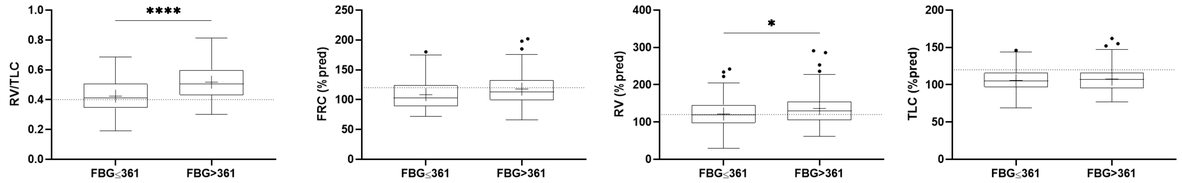
*= p<0,05 **=p<0,01; ***=p<0,001 vs FBG ≤361mg/dL

FIGURE 3



***=p<0,001 vs FBG ≤361mg/dL

FIGURE 2



*= p<0,05; ****=p<0,0001 vs FBG ≤361mg/dL

TABLE 1

CLINICAL PARAMETERS	Fibrinogen ≤361mg/dL (N=227)	Fibrinogen >361mg/dL (N=108)
Age (years)	57.2±15.3	63.0±11.3**
Sex (M/F)	100/127	33/75*
BMI (Kg/m^2)	26.8±4.9	29.1±5.9**
Asthma onset (mean±SD)	34.8±19.1	35.5±18.5
Asthma duration (years)	22.5±16.0	27.7±16.0*
Atopy	122/227 (53.7%)	57/108 (52.8%)
Current smokers	9/227 (4.0%)	6/108 (5.6%)
Past smokers	49/227 (21.6%)	28/108 (25.9%)
IgE (KUI/L)	118.0±119.3	148.2±156.5
FeNO (ppb)	33.1±22.6	29.1±21.9
Vitamin D (ng/mL)	32.7±35.1	30.2±36.5
SpO_2	96.6±1.5	96.1±1.5*
Exacerbation/year	1.2±2.3	1.1±1.5
Activity limitation	4.0±1.1	4.0±1.1
Asthma control	20.3±4.1	20.0±4.3
ICS/day	343.0±259.3	431.7±275.3
OCS use	15/227 (6.6%)	8/108 (7.4%)
LABA use	182/227 (80.2%)	92/108 (85.2%)
LAMA use	22/227 (9.7%)	30/108 (27.8%)***
Anti-leukotriene use	30/227 (13.2%)	19/108 (17.6%)
Nasal CS use	121/227 (53.3%)	56/108 (51.8%)
Omalizumab (yes/no)	13/227 (5.7%)	14/108 (13.0%)*
Mepolizumab (yes/no)	9/227 (4.0%)	10/108 (9.3%)
Benralizumab (yes/no)	4/227 (1.8%)	1/108 (1.0%)

*= p<0,05 **=p<0,01; ***=p<0,001 vs FBG ≤361mg/dL

TABLE 2

Comorbidties	Fibrinogen ≤361mg/dL (N=227)	Fibrinogen >361mg/dL (N=108)
Rhinitis	146/227 (64.3%)	71/108 (65.7%)
CRSwNP	48/227 (21.1%)	17/108 (15.7%)
CRSsNP	35/227 (15.4%)	28/108 (25.9%)*
Aspirin intolerance	33/227 (14.5%)	16/108 (14.8%)
Bronchiectasis	25/227 (11.0%)	18/108 (16.7%)
Emphysema	9/227 (4.0%)	8/108 (7.4%)
Pneumonia history	31/227 (13.6%)	18/108 (16.7%)
OSAS	15/227 (6.6%)	8/108 (7.4%)
GERD	45/227 (19.8%)	22/108 (20.4%)
Obesity	41/227 (18.1%)	34/108 (31.5%)**
Diabetes	11/227 (4.8%)	6/108 (5.6%)
Arterial Hypertension	62/227 (27.3%)	44/108 (40.7%)*
Acute myocardial infarction	9/227 (4.0%)	8/108 (7.4%)
Heart failure	0/227 (0.%)	3/108 (2.8%)*
Arrhythmia	7/227 (3.1%)	14/108 (13.0%)***
Anxiety-depression	27/227 (11.9%)	16/108 (14.8%)
Osteoporosis	17/227 (7.5%)	11/108 (10.2%)
Chronic Pain	9/227 (4.0%)	8/108 (7.4%)
Arthropathy	15/227 (6.6%)	10/108 (9.3%)

*= p<0,05 **=p<0,01; ***=p<0,001 vs FBG ≤361mg/dL

All authors declare that they have no conflicts of interest

CONCLUSIONS

High plasma fibrinogen levels could be useful in clinical practice to identify a severe asthmatic population phenotype with frequent exacerbations and increased prevalence of cardiovascular comorbidities.