Are asthma symptom intensity scales better than biomarkers for diagnosing asthma ? A prospective observational study

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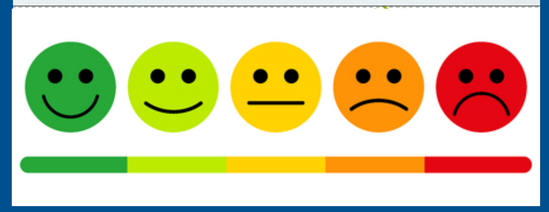
Introduction

Asthma is diagnosed on the basis of respiratory symptoms of wheeze, cough, chest tightness, secretion and/or dyspnea, accompanied by physiologic evidence of variable expiratory airflow limitation (GINA, 2018). A relatively high prevalence of misdiagnosis of asthma in primary care has been reported in the literature (Schneider et al, 2012 ; Aaron et al, 2018), producing adverse consequences to patients' health-related quality of life and to health care systems (e.g. costs of medication without potential for benefit).

A potential solution to reduce the incidence of underdetection of asthma is to increase patient reporting of respiratory symptoms, in particular, by developing validated diagnostic/screening tool (Gibson et al, 2000 ; Shawn et al, 2018). To the best of our knowledge no study has assessed the value of measuring the individual symptom intensity in making the diagnosis of asthma.

Objectives

As a consequence, we decided to explore the diagnostic power of each classical symptoms of asthma, as reported directly by the patient through visual analogue scales (VAS), and to compare them with classic biomarkers.



Main Finding

Our study shows that wheezing is the best symptom which discriminate between asthmatics and non-asthmatics in patients with recurrent or chronic respiratory symptoms and it performs better than classical biomarkers.

Combined to spirometry, it yields very good predictive value for correct diagnosis. It offers new windows of opportunity for primary care (PC) setting thanks to its quick and minimally invasive way to diagnose asthma. Our model should now be tested and validated in a PC setting in order to verify its sensitivity and specificity in a more heterogeneous population.

References:

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Methods

We conducted a prospective observational study between the beginning of March 2018 and the end of December 2019 including 177 patients without any maintenance treatment. These patients were referred to the University Asthma Clinic of Liège (Belgium), either on their own initiative or via primary care actors, because of chronic or episodic respiratory symptoms that may suggest asthma.

As soon as they entered the Asthma Clinic, they were asked to rate the intensity level of the 5 classic asthma symptoms (cough, chest tightness, secretion, dyspnea & wheezing) using VAS. These scales extend over 5 levels (from 0 to 4), where level 4 expresses the greatest intensity of the symptom concerned. Predicting values of symptom intensity, biomarkers and spirometric indices were assessed by ROC curves.

Results

- Among the 177 patients 107 had a confirmed asthma diagnosis in accordance with the GINA recommendations. Demographic, functional and inflammatory features of the studied population are given in table 1.

Table 1: Asthmatic (n=107) vs. Non-asthmatic (n=70) demographic, functional and inflammatory characteristics

	Asthmatic patients (n=107)	Non-Asthmatic patients (n=70)	All patients (n=177)
Variables	Median (IQR) / Percentage(n)	Median (IQR) / Percentage(n)	Median (IQR) / Percentage(n)
Age (years)	52 (39-65)	56 (41-63)	54 (40-64)
Gender (male)	40% (43)	37% (26)	39% (69)
BMI (kg/m2)	26 (23-29)	26 (22-29)	26 (23-29)
Non-Smoker	42% (45)	57% (40)	48% (85)
Ex-Smoker	35% (37)	27% (19)	32% (56)
Smoker	23% (25)	16% (11)	20% (36)
Atopy	48% (48)	43% (29)	46% (77)
FEV1 % pred.	91 (80-101)	104 (91-114)	95 (84-107)
FEV1/FVC %	77 (73-82)	83 (79-88)	80 (74-84)
FeNO (ppb)	19 (12-33)	19 (13-37)	19 (13-28)
Sputum eosinophils %	1 (0,2-4,6)	0,9 (0,15-2,1)	1 (0,2-3)
Blood eosinophils %	2,3 (1,3-3,2)	2 (1,2-3,2)	2,3 (1,3-3,2)
Total serum IgE (KU/L)	66 (21-214)	47 (20-130)	57 (21-175)

- The area under the curve (AUC) of the ROC curves showed that wheezing was the symptom, the intensity of which predicted the best the presence of asthma (AUC=0.64 ;95% CI: 0.56 - 0.72). None of the biomarkers had sufficient predictive value (e.g. FeNO AUC=0,48). FEV1/FVC ratio, and to a lesser extent FEV1, had significant predictive value, with an AUC equal to 0.75 (0.67-0.82) and 0.71 (0.64-0.79) respectively (Table 2).

Table 2: Performance of biomarkers, spirometry and symptoms VAS to diagnose asthma

	Treshold	AUC (95% CI)	Sensivity (95% CI)	Specificity (95% CI)
FeNO (ppb)	31	0.48 (0.40-0.57)	0.26 (0.13-0.34)	0.84 (0.54-0.93)
IgE (KU/L)	108.5	0.54 (0.46-0.63)	0.43 (0.28-0.54)	0.70 (0.51-0.82)
Sputum Eosinophils %	2.15	0.55 (0.45-0.65)	0.35 (0.19-0.47)	0.78 (0.54-0.90)
Blood Eosinophils %	4.25	0.54 (0.45-0.62)	0.19 (0-0.26)	0.91 (0.69-0.97)
FEV1 % pred.	102.5	0.71 (0.64-0.79)	0.79 (0.64-0.89)	0.54 (0.36-0.68)
FEV1/FVC %	77.5	0.75 (0.67-0.82)	0.52 (0.35-0.63)	0.86 (0.68-0.94)
Cough VAS	2.5	0.53 (0.44-0.61)	0.57 (0.42-0.69)	0.50 (0.36-0.63)
Secretion VAS	3.5	0.52 (0.44-0.61)	0.21 (0.11-0.31)	0.86 (0.74-0.93)
Chest tightness VAS	3.5	0.55 (0.47-0.64)	0.25 (0.12-0.36)	0.84 (0.71-0.92)
Dyspnea VAS	3.5	0.58 (0.49-0.66)	0.39 (0.23-0.52)	0.74 (0.62-0.84)
Wheezing VAS	1.5	0.64 (0.56-0.72)	0.72 (0.54-0.82)	0.56 (0.39-0.68)

- Combining wheezing with FEV1 and FEV1/FVC provided a good discriminative capacity with an AUC of 0.79 (0.72-0.85) ($p<0.001$) (Fig.1).

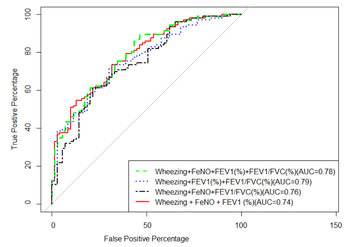

Figure 1. ROC curve for two and three combinations of variables