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RESEARCH ARTICLE

CAN FEV3 AND FEV6 REPLACE FEV1 IN THE FUNCTIONAL ASSESSMENT OF ASTHMATIC PATIENTS? A MULTICENTER CROSS-SECTIONAL STUDY

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ABSTRACT

Introduction: In asthma patients, reductions in FEV3 and FEV6 may reflect early bronchial obstruction and disease severity. This study aimed to evaluate FEV3 and FEV6 as complementary spirometric parameters to FEV1 for assessing asthma severity and control. ***Material and methods:*** Multicenter prospective cross-sectional study exhaustively including 221 adult asthma patients recruited from pulmonology departments at Oran University Hospital (EHU) and Bechar Hospital (EPH) from 04/01/2020 to 12/31/2023. Patients were classified according to GINA guidelines for asthma severity (intermittent, mild, moderate, severe) and control status (controlled, partially controlled, uncontrolled). Spirometric measurements (FEV1, FEV3, FEV6, FVC) were obtained using standardized procedures and expressed as percentages of predicted values. Statistical analyses included chi-square tests for categorical variables, Student t-tests and one-way ANOVA for continuous variables, and Pearson/Spearman correlations. Significance was set at $p<0.05$ using SPSS software. ***Results:*** A population of 221 asthma patients was collected. Mean age was 48.9±15.3 years with female predominance (sex ratio 0.27). Asthma was divided according to its severity into intermittent asthma in 2.7% of cases, mild in 46.2% of cases, moderate in 47.5% of cases, and severe in 3.6% of cases. Total control is present in 29.9% of cases while it is impaired (partially controlled and uncontrolled) in 70.1% of cases.FEV1<80% predicted in 50.5% of cases (women 52.9% vs men 42.6%) and <LLN in 42% (patients >60 years). Negative correlations between age and FEV1 ($r=-0.173$, $p=0.01$), FEV3, and FEV6. Mean FEV1/FEV3/FEV6 values decreased significantly with increasing asthma severity (ANOVA $p<0.001$) and worsening control ($p<0.001$). Higher FEV3/FEV6 values observed in physically active patients ($p=0.03$). ***Conclusion:*** FEV3 and FEV6 accurately reflect asthma severity and control, predicting FEV1 without replacing it as the reference parameter. Their systematic integration into spirometric protocols would optimize monitoring, particularly in patients with limited cooperation.

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INTRODUCTION

Asthma is a chronic inflammatory disease of the airways characterized by variable and usually reversible airflow obstruction. Lung function assessment is essential for diagnosis, grading severity, and monitoring response to treatment, with FEV1 and the FEV1/FVC ratio considered core spirometric outcomes in asthma guidelines [1,2,3]. However, performing a complete forced vital capacity (FVC) maneuver can be difficult for some patients, and may underestimate small airway involvement. Later expiratory volumes such as FEV3 and FEV6 are easier to obtain and have been proposed as surrogates for FVC and FEV1/FVC in detecting obstruction and restrictive patterns [4,5,6]. In chronic obstructive airway diseases, FEV3 and FEV1/FEV3 show comparable performance to FVC and FEV1/FVC for bronchodilator response and obstruction assessment[4,6]. Nevertheless, data in asthma populations remain limited, and it is unclear whether FEV3 and FEV6 could replace FEV1 in routine functional assessment. The objective of this study was to evaluate the role of FEV3 and FEV6, and their derived ratios, in the functional assessment of asthmatic patients and to explore whether they could serve as alternatives to FEV1 for evaluating disease severity and monitoring lung function.

MATERIAL AND METHOD

This was a multicenter, cross-sectional study with prospective data collection. Asthmatic patients were exhaustively recruited from the Pulmonology Departments of EHU Oran and EPH Bechar between 01/04/2020 and 31/12/2023. Inclusion criteria were: age ≥ 18 years, physician-diagnosed asthma according to international guidelines, and ability to perform acceptable spirometry. Patients with other chronic respiratory diseases (e.g. COPD, bronchiectasis) were excluded. For each participant, demographic data, smoking status, asthma duration, severity and control, and current treatment were recorded. Spirometry was performed according to ATS/ERS standards, before and after bronchodilator when indicated, measuring FEV1, FVC, FEV3, FEV6 and the ratios FEV1/FVC, FEV1/FEV3, FEV1/FEV6. The primary analysis compared FEV3 and FEV6 (and their ratios) with FEV1 and FEV1/FVC in relation to clinical severity and asthma control. Statistical analyses were performed using SPSS software. Quantitative variables were summarized as mean ± standard deviation, and qualitative variables as counts and percentages. Comparisons of proportions between categorical variables were carried out using the chi-square test (or Fisher's exact test when expected cell counts were small). Differences in means between two independent groups were assessed with the Student's t test, while comparisons among more than two groups were conducted using one-way analysis of variance (ANOVA). Associations between two quantitative variables were evaluated using Pearson's correlation coefficient (or Spearman's rank correlation in case of non-normal distributions). A p value < 0.05 was considered statistically significant for all two-sided tests

RESULTS

A population of 221 asthma patients was collected consisting of 47 (21.3%) males and 174 (78.7%) females with a sex ratio of 0.27. The average age of our population is 48.9±15.3 years. Asthma was divided according to its severity into intermittent asthma in 2.7% of cases, mild in 46.2% of cases, moderate in 47.5% of cases, and severe in 3.6% of cases. Total control is present in 29.9% of cases while it is impaired (partially controlled and uncontrolled) in 70.1% of cases. Metabolic factors were present in 75.3% of cases, of which 18.7% were diabetic, 26.2% of cases were hypertensive, 23.1% of cases were dyslipidemic of any type, 38.9% of cases had general obesity, 75.6% of cases had abdominal obesity, 73.3% had central obesity, and 28.5% of cases had multiple factors grouped under the metabolic syndrome framework.

Table 1. Distribution of cases by age and sex

Age (years)	Men		Women		Total	
	No.	%	No.	%	No.	%
<20	3	6,4	1	0,6	4	1,8
20 – 29	4	8,5	15	8,6	19	8,6
30 – 39	15	31,9	30	17,2	45	20,4
40 – 49	10	21,3	38	21,8	48	21,7
50 – 59	8	17,0	37	21,3	45	20,4
60 – 69	6	12,8	34	19,5	40	18,1
≥ 70	1	2,1	19	10,9	20	9,0
Total	47	100,0	174	100,0	221	100,0
Avg ± AND (years)	43,1±14,3		50,4±15,2		48,9±15,3	
Median (years)	42,0		50,5		48,0	
Min - Max	19-77		19-84		19-84	

The distribution of cases varies significantly according to age groups. The 30 and 59 age group accounts for 62.5% of asthma patients collected. The mean age of men (43.1±14.3 years) is significantly lower than that of women (50.4±15.2 years) with a statistically significant difference (p=0.003). The youngest subject is 19 years old and the oldest is 84 years old.

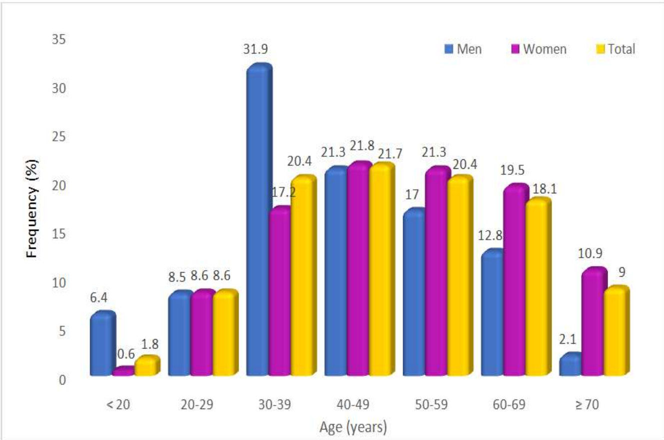
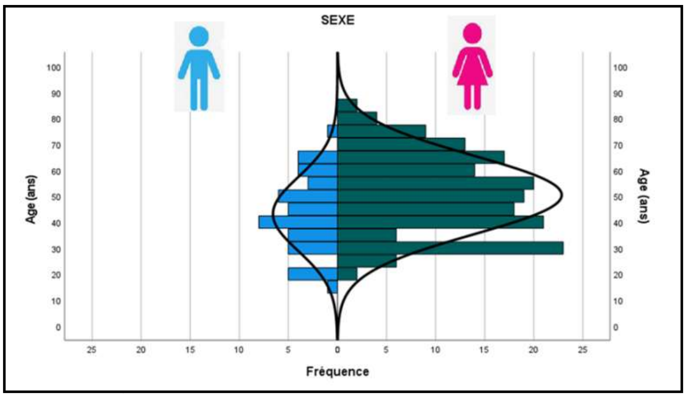


Fig. 1. Distribution of asthmatic cases by age



The most affected age group for men is between 40 and 45 years old, and that of women is between 30 and 35 years old.

Distribution of cases by profession: Table: Distribution of cases by occupational activity.

Profession	Men		Women		Total	
	No.	%	No.	%	No.	%
Active	33	70.2	27	15.5	60	27.1
In retirement	5	10.6	13	7.5	18	8.1
Unemployed	9	19.1	134	77.0	143	64.7
Total	47	100.0	174	100.0	221	100.0

P<0.001

The study of the profession of our cases shows that 64.7% of the subjects are unemployed while 27.1% are professionally active. There is a statistically significant difference between the two sexes (p<0.001) in terms of occupation. The majority of men are civil servants while the majority of women are housewives.

FEV1 and Sex:

Table: Distribution of cases by FEV1 and sex

		Men		Women		Total		
FEV1		No.	%	No.	%	No.	%	P
FEV1(%predicted)	≥80%	27	57.4	82	47.1	109	49.3	0.209
	<80%	20	42.6	92	52.9	112	50.7	
	Total	47	100.0	174	100.0	221	100.0	
	Mean±SD (%)	81.8±21.0		78.6±20.2		79.3±20.3		0.336
	Median (%)	84.0		78.0		79.2		
FEV1 vs LLN	FEV1 ≥ LLN	32	68.1	95	54.6	127	57.5	0.097
	FEV1<LLN	15	31.9	79	45.4	94	42.5	
	Total	47	100.0	174	100.0	221	100.0	
LLN<FEVS<80		5	10.6	14	8.0	19	8.6	0.574

50.7% of cases have a FEV1 rate of less than 80% compared to the predicted value, and the rest of the cases have a FEV1 greater than or equal to 80% (compared to the predicted value). 57.5% of cases have FEV1 rates above or below the lower limit of normal compared to 42.5% with FEV1 values below the lower limit of normal.

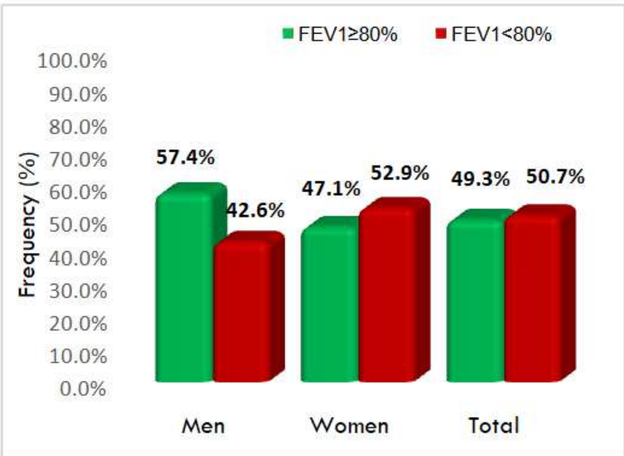


Fig: Distribution of asthmatic cases by theoretical FEV1 and sex

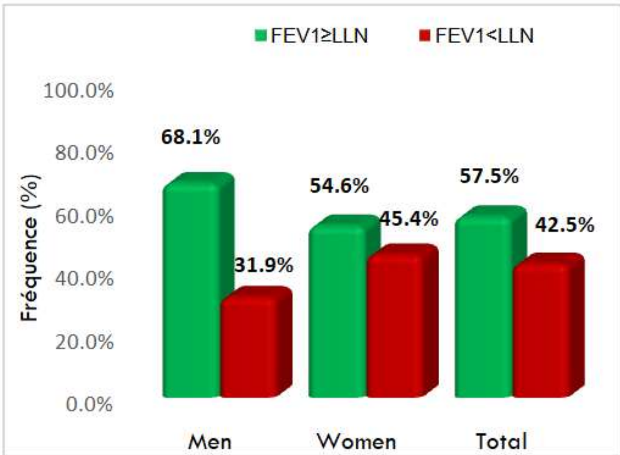
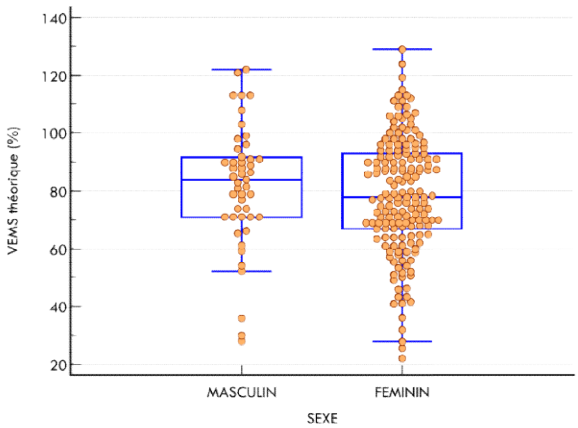
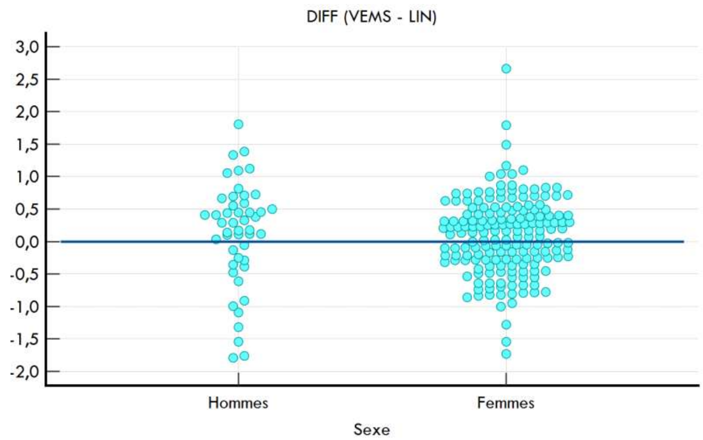


Fig: Distribution of asthmatic cases according to FEV1 vs LLN and Sex





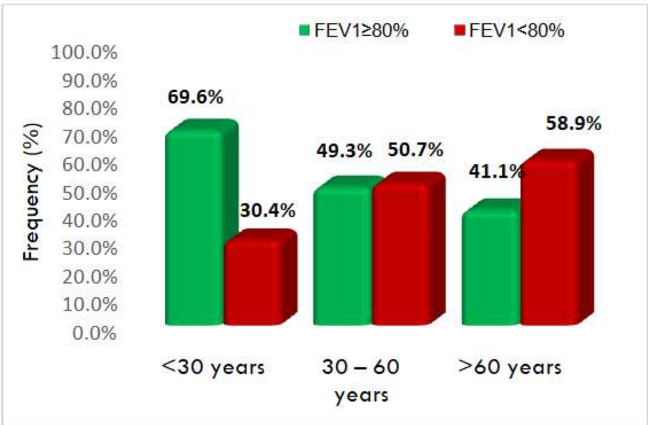
The FEV1 rate below 80% of the predicted value is more common in women (52.9%) than men (42.6%). Men with asthma more frequently have FEV1 values greater than or equal to the LLN (61.1%) compared to women with a frequency of 54.6%.

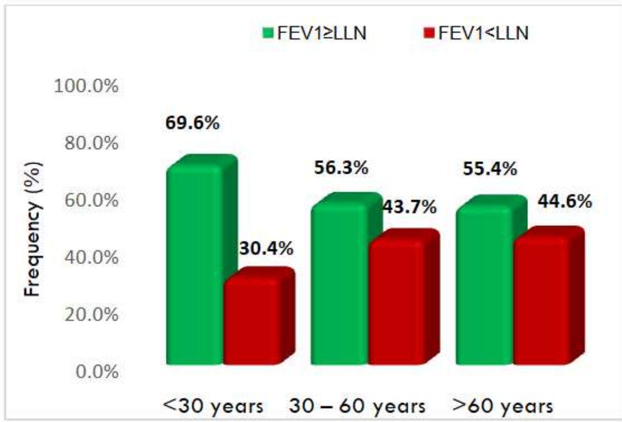
FEV1 by age

Table Distribution of cases by age and FEV1

	Theoretical FEV1				FEV1 vs LLN				LLN<FEV1<80			
Age(years)	≥80%		<80%		FEV1S≥LLN		FEV1<LLN				Total	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
<30	16	69.6	7	30.4	16	69.6	7	30.4	0	0.0	23	100.0
30 – 60	70	49.3	72	50.7	80	56.3	62	43.7	10	7.0	142	100.0
>60	23	41.1	33	58.9	31	55.4	25	44.6	9	16.1	56	100.0
Total	109	49.3	112	50.7	127	57.5	94	42.5	19	8.6	221	100.0
Mean ± SD	46.6±16.0		51.0±14.2		48.0±15.9		50.1±14.4		56.5±12.7		48.9±15.3	
Median	45.0		51.0		48.0		49.5		60.0		48.0	
Min – Max	15-84		20-83		15-84		20-78		30-83		15-84	
P	0.032				0.307				0.023			

Young subjects (less than 30 years of age) have FEV≥80% in 69.6% (of the predicted value). As age progresses, the frequency of patients with FEV1≥80% (of the predicted value) decreases and vice versa for FEV1<80% values (of the predicted value) which increase in frequency.





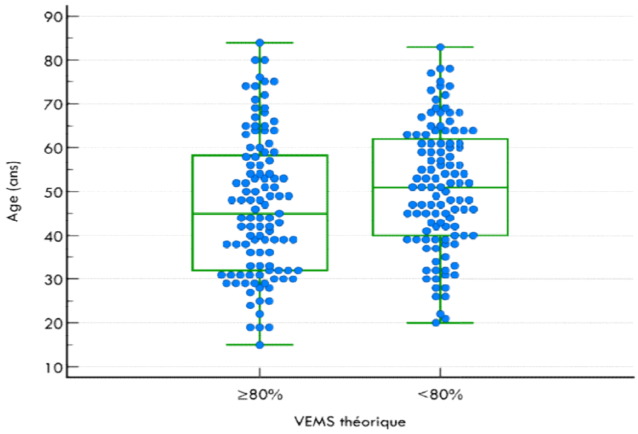


Fig: Box chart of age according to theoretical FEV1

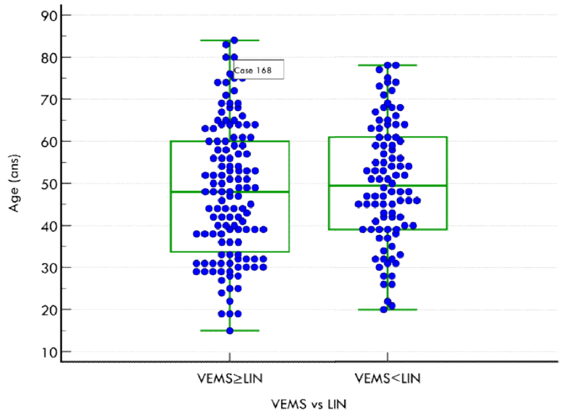


Fig: Box chart of age byFEV1 vs LLN

FEV1≥LLN values are frequently found in cases that are less than 30 years of age, while values below the LLN are frequently found in cases that are over 60 years of age.

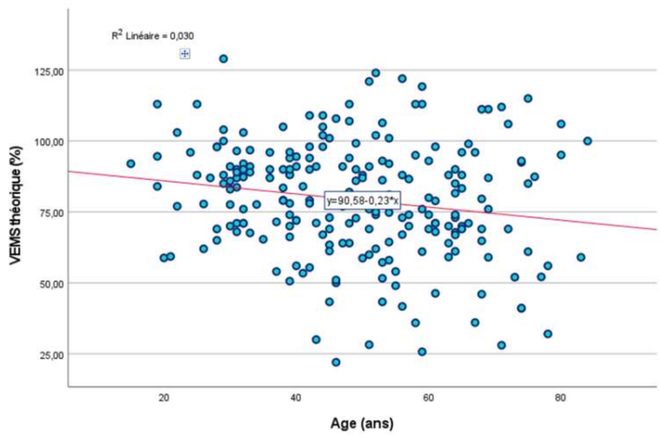


Fig. Scatter plot of theoretical FEV1 and age of asthmatics

R= -0.173 P=0.01

There is a negative (p=0.01) and weak (r=-0.173) correlation between age and theoretical FEV1. As age progresses, the FEV1 percentage (relative to the theoretical value) decreases slightly according to the formula:

FEV1 (%) = 90.58 – 0.23*age(years).

FEV3 and FEV6 volumes were found to be reduced in elderly subjects (similar results to FEV1).

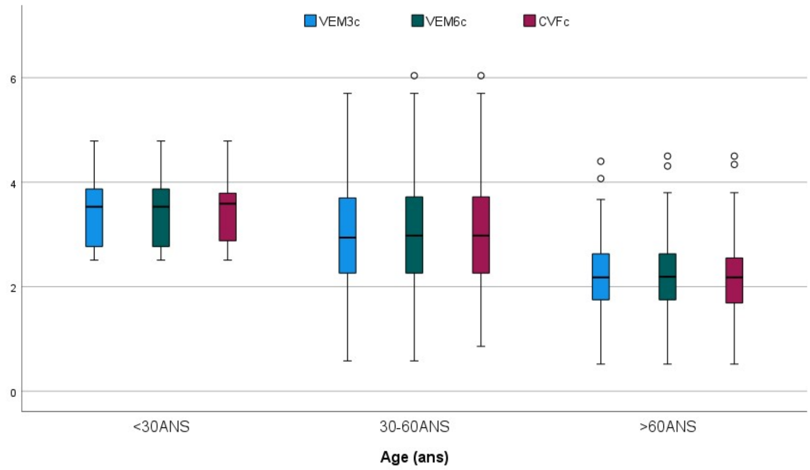


Fig: Box diagram of the calculated volumes (FEV3c, FEV6c and VFCc) by age

It has also been found that the numbers for these FEV3 and FEV6 volumes decrease with age (as with FEV1)

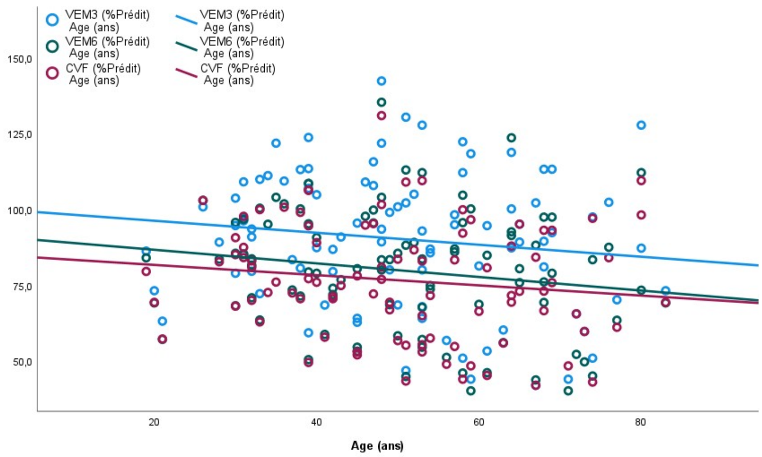


Fig: Scatter plot of FEV3(%Predicted) and FEV6(%Predicted) by case age

rFEV3(%Predicted) and Age (years)= -0.137 P = 0.194
rFEV6(%Predicted) and Age (years)= -0.171 P =0.102
rVCF(%Predicted) and Age (years)= -0.232P <0.001

The mean volumes of FEV3 and FEV6 differ significantly depending on the type of asthma of the cases. These averages decrease with worsening asthma and this finding was also seen with FEV1.

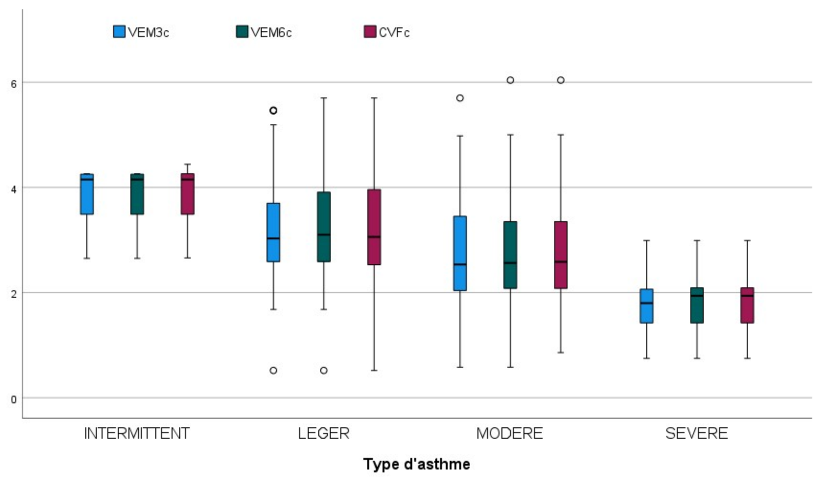


Fig. Box diagram of the calculated volumes (FEV3c, FEV6c and VFCc)by type of asthma

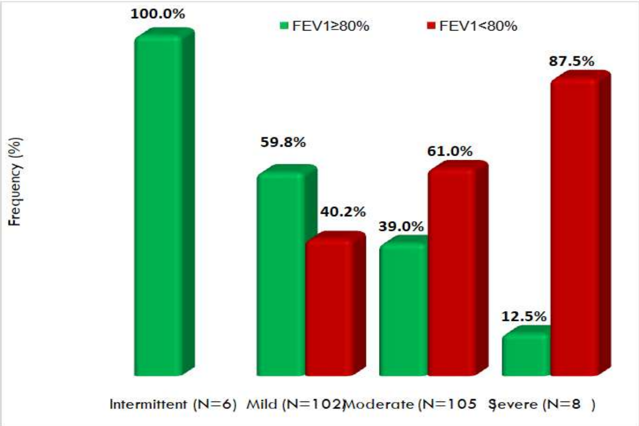


Fig: Distribution of asthmatic cases according to theoretical FEV1 and type of asthma

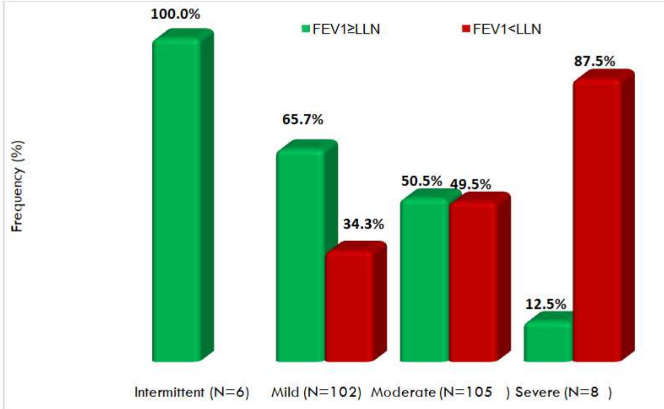


Fig: Distribution of asthmatic cases according to FEV1 vs LLN and the type of asthma

FEV1<80% (/predicted value) is frequently found in moderate to severe asthmatics. FEV<LLN is especially marked in severe cases.

There is a statistically significant difference between the mean FEV3 and FEV6 volumes and the asthma control type of the cases. These averages decrease as the disease loses control.

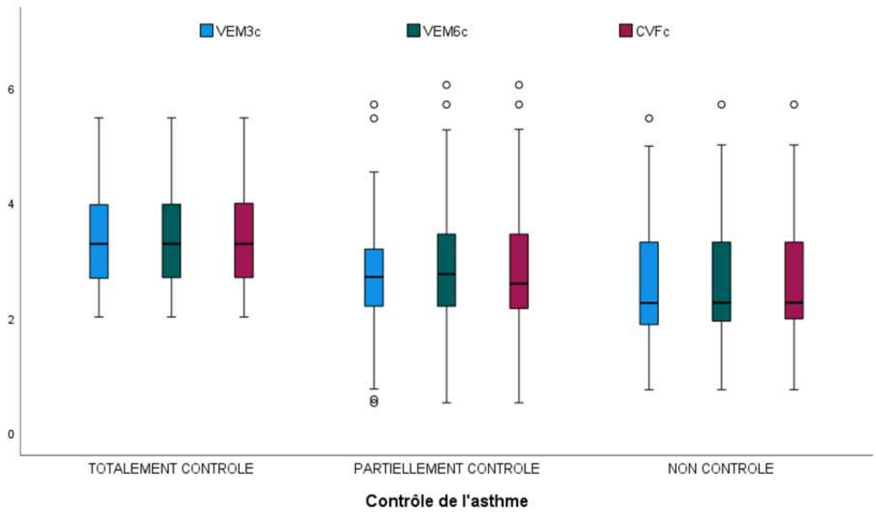


Fig: Box diagram of the calculated volumes (FEV3c, FEV6c and VFCc) according to asthma control

Accordingly, comparable findings were obtained for FEV_1, with FEV_1 values declining as the level of asthma control deteriorated.

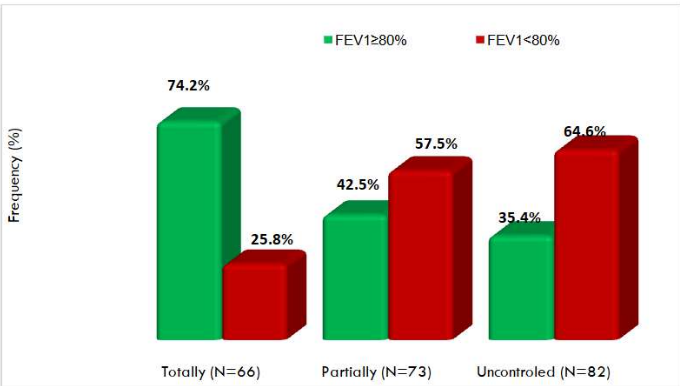


Fig: Distribution of asthmatic cases according to FEV1 theory and type of control

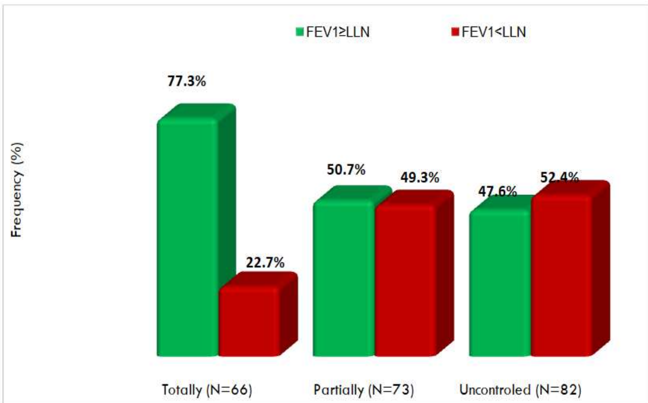


Fig: Distribution of asthmatic cases according to VEV1 vs LLN and the type of control

For patients with one or more metabolic factors, it has been noted that the volumes FEV3, FEV6 decrease slightly as blood glucose increases.

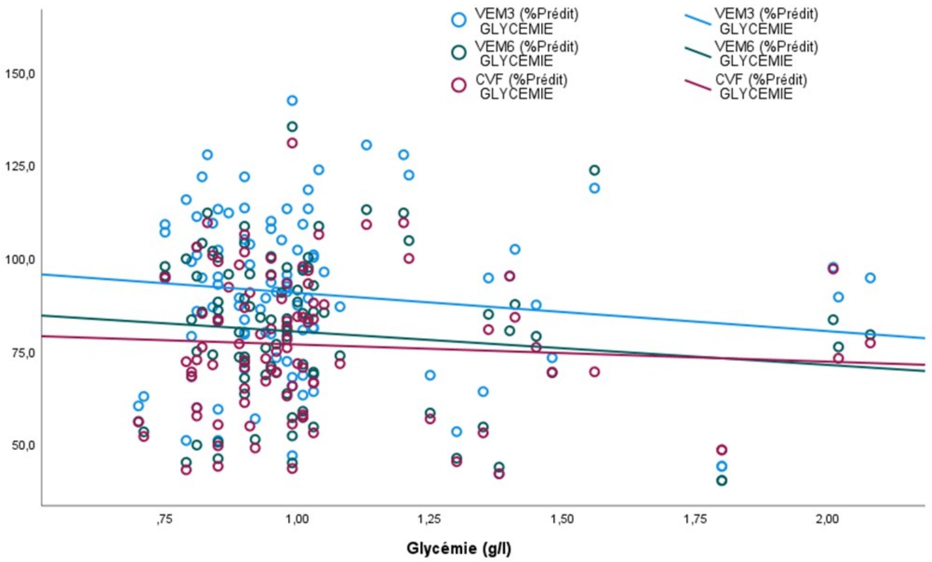
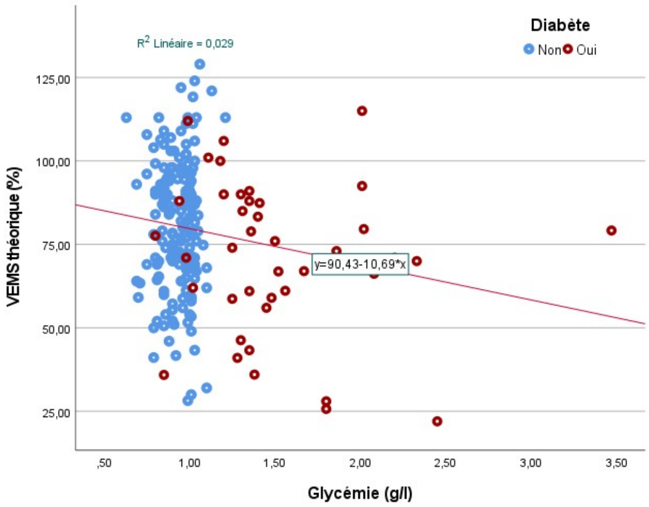


Fig: Scatter plot of FEV3 (%Predicted) and FEV6 (%Predicted) by blood glucose

rFEV3(%Predicted) and blood glucose= -0.131 P = 0.214
rFEV6(% predicted) and blood glucose = -0.122 P = 0.243
rFVC(% Predicted) and blood glucose = -0.143 P = 0.033

What was also found with FEV1: There is a significant negative linear correlation between FEV1 levels and glycemic counts, the higher the glycemic number the FEV1 rate decreases according to the formula: FEV1 (%) = 90.43 – 10.69*glycemia (g/L).



R= -0.171 P=0.011

Fig: Scatter plot of theoretical FEV1 and asthma blood glucose levels by diabetes

DISCUSSION

The study population is characterized by markedly altered spirometric values, as approximately half of the patients present FEV1 values below 80% of predicted and 42% have FEV1 values below the LLN, indicating a high frequency of ventilatory impairment in asthmatics who would generally be expected to have normal or near-normal FEV1. FEV1 is a key marker of airway obstruction, disease severity and control in asthma, and lower FEV1 values have been consistently associated with worse clinical outcomes and poorer asthma control [7,9,10]. In this context, the reduced FEV1 observed in our cohort can likely be explained by several contributing factors: a sedentary lifestyle in almost half of the patients, permanent contact with animals in about one third of cases, a very high prevalence of atopy (95.5%) that may promote clinical and spirometric instability, the presence of comorbidities known to impair ventilatory function in both asthmatic and non-asthmatic individuals, and a longer asthma duration, particularly beyond 20 years, which has been associated with cumulative structural and functional airway changes [7,8,10]. Moreover, more than two thirds (66.9%) of the patients do not engage in any sport activity, which may further exacerbate deconditioning and contribute to the decline in lung function. Consistent with previous observations indicating that FEV1 reflects the degree of asthma control and severity [7,10], our results demonstrate a strong association between lower FEV1 values and poor asthma control ($p < 0.001$), reinforcing the role of FEV1 as a robust indicator of disease control in routine practice. FEV3 and FEV6 were also slightly reduced, particularly among women and patients older than 60 years, and physical inactivity, poor asthma control and higher disease severity were associated with lower FEV3 and FEV6 values, both in absolute terms and as percentages of predicted. These findings are consistent with the concept that prolonged disease duration and more severe airway inflammation lead to progressive impairment of expiratory flows and volumes, especially beyond 10 years of asthma evolution, where a noticeable and progressive decline in FEV3 and FEV6 was observed [7,9]. In this regard, age and asthma duration emerged as important determinants of these volumes, supporting the hypothesis of cumulative functional damage over time, as previously reported in adult cohorts followed for several years [7,9]. Conversely, atopy and delay in treatment initiation did not appear to have a significant impact on FEV3 and FEV6 in our cohort, suggesting that these parameters may be more directly influenced by airway remodeling, physical inactivity and the level of asthma control than by allergic status alone [8,10]. Notably, sport activity was identified as a potentially protective factor, since approximately half of the physically active patients showed higher measured FEV3 and FEV6 values than inactive patients ($p < 0.010$ and $p = 0.03$, respectively), which is in agreement with previous work suggesting beneficial effects of regular physical exercise on lung function, symptom control and quality of life in asthma [10]. Several authors have demonstrated that FEV3 is useful for the early detection of airflow obstruction, particularly through the FEV3/FVC ratio, which may reveal early small airway dysfunction even when traditional indices such as FEV1/FVC remain within the normal range. In a large series, Morris et al.[11] reported that an isolated reduction in FEV3/FVC was associated with greater hyperinflation, air trapping and reduced diffusing capacity, suggesting that this abnormality may reflect early airflow limitation before more overt spirometric changes occur. Other studies have also suggested that FEV3/FEV6 can serve as a practical spirometric index for identifying early airway disease and for risk stratification in individuals at risk of chronic obstructive lung disease. In line with these observations, FEV3 and FEV6 have been reported to be accurate and reliable alternatives to FVC for assessing airway obstruction in obstructive diseases, including asthma, offering the advantage of shorter expiratory times and easier performance, particularly in those with advanced obstruction. In patients with obstructive ventilatory disorders, expiration may need to be prolonged to satisfy end-of-test criteria for FVC, which can be difficult and uncomfortable for both patients and technicians, whereas FEV3 and FEV6 maneuvers are simpler and less demanding while still providing clinically useful information. Previous research has shown that FEV3 and FEV6 exhibit similar diagnostic characteristics to FVC in the evaluation of ventilatory function and the detection of airflow obstruction. Our results extend these data by highlighting the interest of FEV3 and FEV6 as complementary indicators capable of predicting FEV1, without replacing FEV1 as the reference spirometric parameter in asthma. In our cohort, FEV1 values were significantly correlated with both FEV3 and FEV6, which corroborates previous studies reporting comparable performance of FEV1/FVC, FEV1/FEV3 and FEV1/FEV6 ratios in identifying obstructive patterns. Furthermore, FEV3 and FEV6 appeared to reflect disease severity and to capture dynamic changes in lung function, suggesting that these volumes may be useful for longitudinal monitoring of asthma progression and therapeutic response, particularly in more severe phenotypes [8,10]. Regular assessment of FEV3 and FEV6, alongside FEV1, could therefore help refine risk stratification, optimize follow-up and guide treatment adjustments in clinical practice, especially in patients for whom obtaining a reliable FVC is challenging [7-10].

CONCLUSION

In conclusion, while FEV3 and FEV6 effectively reflect asthma severity and serve as practical alternatives to FVC—offering shorter expiratory times and improved patient comfort—they do not supplant FEV1 as the cornerstone spirometric parameter for diagnosing and monitoring obstructive lung diseases (6,7-10). Integrating these volumes into routine functional assessment protocols could enhance data quality, particularly for patients with advanced obstruction or limited cooperation, while providing complementary insights into disease progression and treatment response. A multimodal spirometric approach combining FEV1, FEV3, and FEV6 would optimize respiratory monitoring in asthma by tailoring measurements to individual capacities and capturing nuanced changes in airway function. Prospective longitudinal studies are needed to establish standardized interpretation thresholds, validate their prognostic value across asthma phenotypes, and facilitate their broader clinical adoption alongside traditional indices.

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