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Variable expiratory airflow, and not airway obstruction, is the defining physiological feature of asthma

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Abstract

Asthma is usually diagnosed by history and presence of airway obstruction with a significant bronchodilator response on spirometry. However, airway obstruction may not always be present, or a bronchodilator response may not be significant. Contrary to wide perception, airway obstruction is not the defining functional feature of asthma. Definitions of asthma have never included the term 'airways obstruction'. According to the Global Initiative for Asthma, the diagnosis of asthma requires a history of typical variable symptoms and confirmation by variable expiratory airflow. It has emphasized that variable expiratory airflow is the key physiological feature of asthma. Airway obstruction is a manifestation of this variability and represents one end of the spectrum of this variation. When airways obstruction is observed, a positive bronchodilator response is the most convenient method to confirm the diagnosis. However, when airway obstruction or bronchodilator responsiveness is not demonstrable, there are other options to demonstrate variability in not demonstrable, there are other options to demonstrate variability of expiratory airflows and confirm the diagnosis.

Key words: spirometry, asthma, bronchodilator responsiveness, airway obstruction.

Introduction

Asthma is a chronic airways disease that is suspected from history and usually confirmed by the presence of airways obstruction and a significant bronchodilator response on spirometry. Airways obstruction is diagnosed by a ratio of forced expiratory volume in one second (FEV1)/forced expiratory capacity (FVC) less than the lower limit of normal (LLN) obtained from ethnically appropriate prediction equations [1]. A greater than 12% and 200ml increase in baseline FEV1 or FVC after inhalation of a bronchodilator, such as salbutamol, defines a positive bronchodilator response [1]. Previously called bronchoreversibility [2], this feature is now called bronchodilator responsiveness (BDR) [1]. Recently, it has been suggested that the change in FEV1 or FVC should be expressed as a percentage of predicted, a > 10% increase being labelled as positive [3]. The current Global Initiative for Asthma (GINA) guidelines have however recommended continued use of the “12% and 200ml” criteria [4].

Bronchial asthma has long epitomized “reversible” airways obstruction although it is now well-established that airway obstruction may not be fully reversible in asthma and patients with Chronic Obstructive Pulmonary Disease (COPD) may also have a good response to bronchodilators [5-7]. Response to bronchodilator has limited utility in differentiating asthma and COPD and should be interpreted in the clinical context. Given the utility of airways obstruction and a positive BDR in confirming a diagnosis of suspected asthma, it has been widely held down the ages that these are mandatory diagnostic requirements for asthma.

Nevertheless, both overdiagnosis and underdiagnosis of asthma are common [8]. Studies have shown that airways obstruction is not a constant feature of asthma. Prevalence of airways obstruction in cross-sectional population-based studies is lower than hospital-based cohorts and only up to a quarter of patients show airways obstruction [9]. In clinical practice too, airways obstruction may not always be present even though history is suggestive of asthma. Patients with well-controlled asthma, seasonal asthma, mild intermittent asthma and in remission may have a normal spirometry at one time point. Asthma may have atypical symptoms instead of a characteristic history and spirometry may be normal. A question therefore arises: How can a diagnosis of asthma be confirmed if there is no airways obstruction on spirometry? Further, even in the presence of airways obstruction, a BDR test may be negative. This is more likely in patients with persistent and more severe obstruction who may have undergone airways remodelling [5].

It is not often emphasized that though airways obstruction and positive BDR along with a typical history confirms a diagnosis of asthma, these are not the defining functional features

of asthma in contrast to COPD where it is a mandatory requirement for diagnosis. One or both of these features may not be observed at a given time point. Remarkably, definitions of asthma have never included the term 'airways obstruction'.

Definition of asthma

Scadding defined asthma as "a disease characterized by wide variations over short periods of time in resistance to flow in intrapulmonary airways" [10]. This emphasized the dynamic nature of airways function in asthma, that is wide variation in airflow. GINA's definition in 2026 phrases the functional component of asthma as "variable expiratory airflow" [4]. This retains the essence of Scadding's definition. The two definitions refer to the same physiological construct i.e. variations over time in airway calibre, expressed in terms of resistance to airflow in Scadding's definition and expiratory airflows in GINA's definition. This variability is central to asthma and manifests as variations in airway function over time. While overall airway resistance can be measured in a body plethysmograph, FEV1 on spirometry serves as a surrogate measure used much more widely at all levels of healthcare. Mathematically, FEV1 is also the result of integration of expiratory airflows in the first second. Thus, variations in FEV1 inform about variations in airways calibre. This variability is the functional abnormality that clinches the diagnosis coupled with history. According to GINA the diagnosis of asthma requires a history of typical variable symptoms and is confirmed by variable expiratory airflow [4].

If FEV1 is reduced disproportionately to FVC thereby reducing the FEV1/FVC ratio below the normal range, airways obstruction is said to be present. It varies with time, spontaneously or with treatment, and when the ratio is above the LLN, airways obstruction is ruled out. Airway obstruction therefore represents one end of the spectrum of variable expiratory airflows. The latter feature is the defining feature of asthma, of which airways obstruction is a manifestation [4]. This is illustrated in the following section.

Understanding variability of expiratory airflow

Figure 1 shows the variability of expiratory airflows resulting in variability of FEV1 [11]. On visit 1, the patient had an FEV1 of 2.15L at baseline (point A) that was below the LLN indicating airways obstruction. After bronchodilator, it increased by 19% and 410 ml to 2.56L (point B); BDR test was thus positive confirming the diagnosis. On subsequent visits,

serial spirometry showed variations in FEV1 including a fall below the LLN once during follow-up (visit 3).

Methods to demonstrate variability of expiratory airflow

Variable expiratory airflow can be demonstrated in several ways depending on the initial spirometry results. When airways obstruction is observed, a positive BDR is the best and the time-honoured method. It is also the most convenient and least time-consuming. This is illustrated in Figure 1 (point A to B, visit 1). However, in scenarios where airways obstruction is not demonstrable at baseline or when airways obstruction is present, but the BDR test is negative, there are other options to demonstrate variability of expiratory airflows. These are summarized in Table 1. One of these options, excessive variation in lung function between different visits, is illustrated in Figure 1. Points C and D represent FEV1 values on different visits and have a variability greater than 200ml and 12%.

In conclusion, variability of expiratory airflows is a universal feature and the defining physiological characteristic of asthma along with a typical history for diagnosing asthma. Airways obstruction and positive BDR are features to establish variability of expiratory airflows. In clinical scenarios where airways obstruction is not present or a BDR test is not positive, variability of expiratory airflows can be demonstrated by several other methods to confirm the diagnosis. Recognising variability of expiratory airflow as the defining physiological feature of asthma will improve diagnostic accuracy and reduce reliance on a single spirometric measurement and do away with trying to prove the presence of mandatory airflow obstruction to make a diagnosis of asthma.

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Table 1. Methods to demonstrate variability of expiratory airflows.

Status of Airways Obstruction	Methods to confirm variability
a) Airways obstruction is present at baseline	Positive BDR test
b) Airways obstruction is not present at baseline	Options: i. BDR test: may be positive in some patients with normal spirometry ii. Bronchial challenge test with methacholine or exercise iii. Excessive diurnal variation of peak expiratory flow rates over 2 weeks iv. Excessive variation in lung function between visits, comparing baseline spirometry on two separate visits (Points C and D, Fig 1)
c) Airways obstruction is present at baseline and BDR test is negative	Options: i. A repeat BDR test on another visit ii. Increase in baseline FEV1 after 4 weeks of inhaled corticosteroids-containing treatment iii. Increase in baseline FEV1 after a short course of oral corticosteroids

It should be ensured that the inhalational drug is correctly administered for the BDR test.

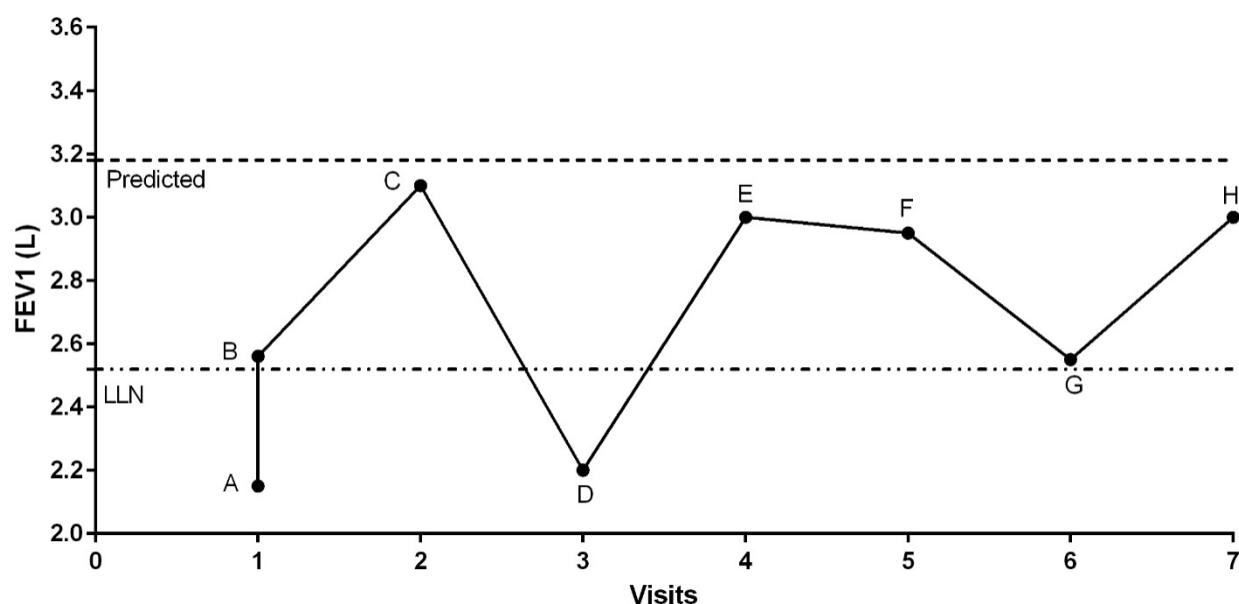


Figure 1. Illustration of variability of FEV1 over time on spirometry in a 40-year-old male patient with a history of asthma. The upper horizontal line (dashed) is the predicted value and the lower (dot-dashed) is the LLN [11]. Points A and B are pre- and post-bronchodilator values on the first visit showing greater than 200ml and 12% improvement from A to B. Points C to H are values on follow-up visits.