A Proposed Curvilinearity Index for Quantifying Airflow Obstruction

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BACKGROUND: Though forced expiratory volume in the first second (FEV_1) is the primary indicator of airway obstruction, curvilinearity in the expiratory flow-volume curve is used to support the quantitative assessment of obstruction via FEV_1. Currently there is no available index to quantify a pathological contour of curvilinearity. STUDY PURPOSE: We propose a "curvature" index (k_{max}) and compare FEV_1 values to the index with a sequential sample of spirometry data. METHODS: The hyperbolic function $b_0\dot{Q} + b_1\dot{Q}V + b_2V = 1$ (in which $\dot{Q}$ = flow rate, V = volume, and b_0, b_1, and b_2 are estimated from the patient's flow-volume data) is fit to a fixed segment of the descending phase of the expiratory flow-volume curve. A previously developed biomechanical interpretation of this relationship associates the coefficient b_1 with the rate of airway-resistance-increase as exhaled volume increases. A global curvature index $k_{max} = b_1/\sqrt{2(b_0b_2 + b_1)}$ is defined to quantify the curvilinearity phenomenon. We used statistics software to determine the k_{max} of spirometry data from 67 sequential patients, and to determine the relationship of k_{max} to FEV_1. RESULTS: Individual k_{max} estimates appeared to correspond well with the degree of curvilinearity observed and were related in an exponential manner to FEV_1. CONCLUSIONS: We defined a curvature index to quantify the curvilinearity phenomenon observed in the expiratory limb of flow-volume loops from patients with obstructive lung disease. This index uses data from a major segment of the flow-volume curve, and our preliminary data indicate an exponential relationship with FEV_1. This new index allows the putative association between curvilinearity and obstructive lung disease to be examined quantitatively in clinical practice and future studies. *Key words: flow-volume curve, forced expiratory volume, curvature index.* [Respir Care 2006;51(1):40–45. © 2006 Daedalus Enterprises]

Introduction

The measurement of vital capacity via spirometry has been employed since the mid-19th century to detect restrictive lung disease.[1] In the 20th century, however, the clinical emphasis in spirometry shifted to diagnosing and assessing the severity of obstructive lung disease.[1] Most clinicians and pulmonary specialists rely on forced expiratory volume in the first second (FEV_1) and its comparison to forced vital capacity (FVC) to quantify the degree of obstruction. If FEV_1 (with or without a comparison to FVC) is decreased, airflow obstruction is suspected. Sec-

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ondarily, a more pictorial qualitative method of interpreting spirometric tracings involves visual inspection of the descending phase of the expiratory flow-volume curve. If "bending" toward the volume axis (concavity of the curve) is noticed, obstructive lung disease may be inferred.[2]

Although direct visual inspection is simple, lacking a numerical index to quantify the extent of this geometric change has drawbacks. First, for patients with mild airflow obstruction, the transition from normal linearity to abnormal curvilinearity is very difficult to resolve. Second, escalation of a slight concavity is difficult to visualize during subsequent follow-up visits. Third, rigorous epidemiological studies of curvilinearity are not feasible without a quantitative assessment tool. For these reasons, even though most clinicians routinely look for curvilinearity and believe that the phenomenon is predictive of the development of obstructive pulmonary diseases, just exactly how effective this practice truly is remains unclear.

We here propose a curvature index to quantify the concavity of an expiratory flow-volume curve. The described algorithm is based on mathematical principle, easy to implement, and consistent with our intuitive perception.

Methodological Considerations

To standardize and quantify the geometric change of the expiratory flow-volume curve, we empirically selected the region of interest to start at 90% of the peak expiratory flow (the descending phase only) and end at 90% of FVC before flow ceases. This span of the curve is analyzed to avoid an initial highly-effort-dependent artifact and to ensure that most of the remaining data points are included (see Fig. 1).

Digital data from the selected range are then "least squares" fit to a curvilinear regression model.[3] Several mathematical equations were tested, including exponential, polynomial, and quadratic functions. Eventually we selected a hyperbolic function as the model of choice:

$$b_0\dot{Q} + b_1\dot{Q}V + b_2V = 1$$

Equivalently:

$$\dot{Q} = \dot{Q}(V) = \frac{1 - b_2V}{b_0 + b_1V}$$

where $\dot{Q} = \dot{Q}(V)$ airflow rate, V = expiratory lung volume (note that V is not the absolute lung volume as measured with a plethysmograph), b_0 is a volume-intercept parameter, b_1 (slope parameter normalized by FVC) measures how fast the airflow resistance ($R(V)$; see next section) increases with the expiratory lung volume V, and b_2 equates to the inverse of FVC. The primary basis for this model

selection is that the hyperbolic function appears robust to compute; that is, there is greater stability in the calculated index (it is minimally vulnerable to artifact), and it is flexible enough to correspond to the overall degree of curvilinearity. Also, this function is relatively simple and fits a previously reported biomechanical model, as described below. If, in this model, the coefficient b_1 is determined to be zero or near zero, the hyperbolic equation is reduced to a linear function (no curvilinearity):

$$b_0\dot{Q} + b_2V = 1$$

Equivalently:

$$\dot{Q}(V) = (1 - b_2V)/b_0$$

If the coefficient b_1 is substantially larger than zero, the hyperbolic equation predicts the presence of concavity (convexity if $b_1 < 0$).

Biomechanical Interpretation

The hyperbolic model we selected has a previously reported biomechanical interpretation, as described by Barnea and colleagues.[4] The key assumption introduced by Barnea is that the instantaneous transpulmonary pressure $P(t)$ changes linearly with expiratory lung volume $V(t)$:

$$P(t) \propto (FVC - V(t))$$

Furthermore, Barnea suggested that the airway resistance $R(t)$ could also be viewed as a function of volume $V(t)$. Assuming that $R(t)$ has a simple linear relationship to volume, $R(V) = a_0 + a_1V$, we have:

$$\dot{Q}(t) = \frac{P(t)}{R(t)} \propto \frac{FVC - V(t)}{a_0 + a_1V}$$

Equivalently:

$$\dot{Q}(V) = \frac{1 - b_2V}{b_0 + b_1V}$$

If the slope rate b_1 is small, the resistance increases only slightly with the expiratory volume. The resultant flow-volume curve would display a linear decline without cur-

vilinearity. On the other hand, a greater resistance increase would lead to curvilinearity.

Local Curvature

For a given planar curve $\dot{Q}(V)$ (hyperbolic or other function), the curvature of $\dot{Q}(V)$ at exhaled volume V can be mathematically defined as follows:[5]

$$k(V) = \frac{\dot{Q}''(V)}{(1 + (\dot{Q}'(V))2)^{3/2}} \tag{1}$$

Here, $\dot{Q}'(V)$ and $\dot{Q}''(V)$ are the first and second derivatives of $\dot{Q}(V)$ with respect to V. This definition has the desirable feature that it is invariant under Euclidean motions. Applying Equation 1 to evaluate the hyperbolic function:

$$\dot{Q}(V) = \frac{1 - b_2 V}{b_0 + b_1 V}$$

we have:

$$k(V) = \frac{\dot{Q}''(V)}{(1 + (\dot{Q}'(V))^2)^{3/2}}$$

$$= \frac{2b_1(b_0 b_2 + b_1)}{(b_0 + b_1 V)^3 \left(1 + \frac{(b_0 b_2 + b_1)^2}{(b_0 + b_1 V)^4}\right)^{3/2}} \tag{2}$$

Global Curvature

Because we are most interested in measuring the overall degree of curvilinearity, the maximum value of $k(V)$ is considered the representative global curvature. This summary index can be algebraically derived by taking the first derivative of $k(V)$ with respect to V, then solving the equation

$$\frac{d}{dV} k(V) = 0$$

for

$$V^* = \frac{-b_0 + \sqrt{b_0 b_2 + b_1}}{b_1}$$

in which V^* is lung volume at the point of greatest curvature.

Table 1. Frequency Distribution of Primary Pulmonary Function Test Interpretations of Study Patients

Primary Interpretation	Number ($n = 67$)	Percent of Total
Normal	12	18
Mild obstructive component	23	34
Moderate obstructive component	14	21
Severe obstructive component	10	15
Restrictive component	8	12

And, finally, we re-insert V^* back into Equation 2:

$$k_{max} = k(V^*) = \frac{b_1}{\sqrt{2(b_0 b_2 + b_1)}} \tag{3}$$

Data Analyses and Results

Flow-volume data from a flow-integrative-based spirometry system (V6200, SensorMedics, Yorba Linda, California) constitute the primary raw-data source for the current analysis. We downloaded instantaneous flow-volume data (t, $\dot{Q}(t)$, and $V(t)$) from 70 sequential patients who underwent pulmonary function tests (PFTs), for a range of clinical purposes, in January through March 2003. We found 3 records incomplete and consequently discarded those data. The "best curve" (greatest sum of FEV_1 and FVC) generated during 3–6 efforts was chosen for analysis. The tests were interpreted as normal or with restrictive or degrees of obstructive components (Table 1), but no group was large enough to justify further subset analysis. The flow-volume curves were sampled at 20 Hz and flagged at the starting and ending positions of each effort (points identified by commercial software). The 67 cases were then analyzed with statistics software (Systat, Systat Software, Point Richmond, California).

We used a nonlinear regression module in the statistics software to estimate b_0, b_1, and b_2 for each patient. The downloaded data file was transferred to another computer, and our statistical analysis was applied to the segment of interest, which consisted of approximately 100 data points.

The parameter estimation starts with the initial values $b_0 = 0.1$, $b_1 = 0$, and $b_2 = 0.25$, which were chosen, respectively, to assume a small basic resistance, no concavity, and an average FVC of 4 L, to start the iterative process. A Gauss-Newton method is then used to search in the parameter space and minimize the sum of residual squares (loss function). The convergence criteria for both the loss function and the parameter values are set at <0.00001. Once the regression coefficients (b_0, b_1, and b_2) are known, the curvature index k_{max} is computed using Equation 3.

Table 2. Descriptive Statistics of the Study Patients*

Age (mean ± SD y)	58.6 ± 15.1
Height (mean ± SD cm)	167 ± 10
Weight (mean ± SD kg)	86 ± 25
Gender (number and %)	
Female	40 (59.7)
Male	27 (40.4)
Race (number and percent)	
White	57 (85.1)
Nonwhite	10 (14.9)

*$n = 67$

The patients' ($n = 67$) demographic characteristics are summarized in Table 2. The mean ± standard deviation estimates of b_0, b_1, b_2, and k_{max} are 0.082 ± 0.227, 0.447 ± 1.352, 0.490 ± 0.428, and 0.292 ± 0.360, respectively. Because our study sample was obtained from patients with diverse disease conditions attending a pulmonary function laboratory of a mid-size hospital, the study subjects are not representative of the general population. Table 1 shows the frequency distribution of the basic PFT interpretations. The mean estimates of k_{max} (0.292) and b_1 (0.447) observed here are, therefore, likely to be higher, and the mean FEV$_1$ (2.04 L) lower, than healthy subjects from the general population. Three raw flow-volume curves are shown in Figure 1, to illustrate a comparison between the observed curvilinearity and our quantitative curvature estimates for a normal patient and patients with moderate and severe obstruction components (k_{max} = 0.031, 0.548, and 2.267, and FEV$_1$ = 3.57 L, 1.14 L, and 0.54 L, respectively). The scatter plot of FEV$_1$ versus k_{max} estimates suggests that the relationship is exponential in nature (Fig. 2).

Discussion

Evaluation of an obstructive component to chronic respiratory impairment is based on measurements that estimate the extent of underlying pathophysiology. Obstructive disease is characterized by expiratory flow limitation, which can lead to end-expiratory intrathoracic air-trapping. Indicators of air-trapping, such as elevation of residual volume, total lung capacity, or the ratio of residual volume to total lung capacity, are lung-volume measurements performed via methods that use helium dilution, nitrogen washout, or body plethysmography—techniques that are primarily available in complete pulmonary function laboratories.[1] As such, elevated lung volumes tend to indicate late-stage or severe disease. Office spirometry has become readily available for convenient, rapid assessment of lung disease, particularly

as an initial screen for the presence of an obstructive component. Spirometric tracings provide graphical evidence of airflow limitation, but airflow limitation is most frequently quantified by FEV$_1$. FEV$_1$ is a point estimate that is referenced to a predicted value based on age, height, race, and gender. FEV$_1$ is highly repeatable between maximal efforts and is quite useful in epidemiological and bronchodilator-effectiveness studies for tracking the development or resolution of disease. But as a measure derived from one part of an expiratory maneuver, FEV$_1$ does not account for surrounding curve information. And in the overall gradation of severity of obstruction, there is considerable disagreement between professional societies over key cutoff values for FEV$_1$. For example, the Global Initiative for Chronic Obstructive Lung Disease, American Thoracic Society, British Thoracic Society, and European Respiratory Society define severe obstruction as <30%, <35%, <40%, and <50% of predicted FEV$_1$, respectively.[6] Therefore FEV$_1$ is a consistent measure that is associated with epidemiological studies, but it is not specific for the severity of obstruction, and it neglects potentially useful curve information.

Several other variables that indicate airway obstruction have been examined and calculated from the flow-volume curve, including peak flow, forced expiratory flow at 25% of forced vital capacity, mid-flow, and forced expiratory flow at 75% of forced vital capacity.[1] Unfortunately, they lack the repeatability of FEV$_1$ and have not proved to be particularly valuable.[2] Therefore, the flow-volume loop is excellent as a qualitative assessment of maximum effort or as a repeatable tracing, but, otherwise, the contour of the flow-volume curve is underappreciated; yet practitioners agree that greater curvature of the expiratory tracing indicates an increasing degree of airflow limitation.[2] The usefulness of the expiratory limb is, however, limited by the lack of a quantitative assessment of the degree of curvature, as discussed in the introduction.

Several authors have proposed alternative methods to quantify the curvilinearity of flow-volume curves.[7–9] Mead[7] used a "slope-ratio" method to quantify curvilinearity and suggested that asynchronous emptying of diseased lungs underlies the pattern typical of obstructive disease. The slope-ratio method proposed by Mead is a local method that, like Equation 2, measures the degree of curvilinearity at a given expiratory volume *V*. Although a complete set of local measures can examine many curve details, Mead's approach can be very sensitive to rapid local fluctuations (noise). Furthermore, lacking a summary index also appears to render its use in a clinical setting cumbersome.

The proposals by Kapp et al[8] and O'Donnell and Rose[9] aimed to improve these deficiencies. Although both of the latter methods offer a usable single index, they are derived from 2 or 3 data points and their indices continue to re-
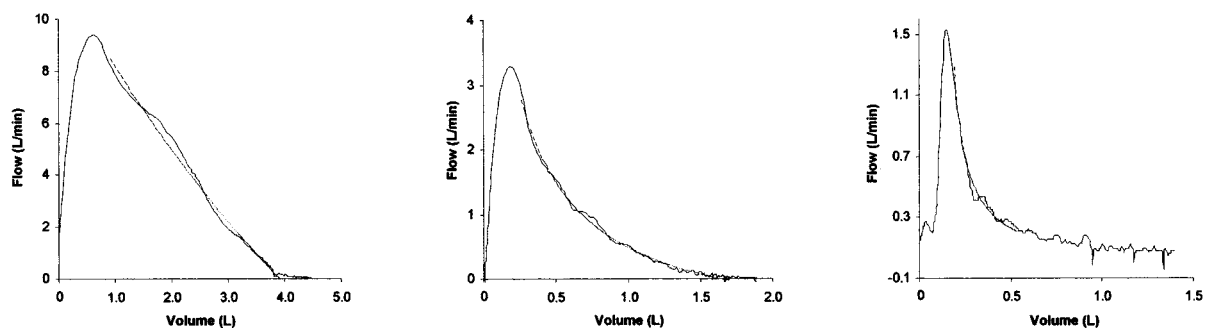
Fig. 1. Graphs of expiratory flow rate versus expiratory lung volume in normal (left panel), moderate obstructive (middle panel), and severely obstructive (right panel) conditions. Note that the Y axis scaling differs between the graphs, to allow a more direct comparison of curve differences. The descending phase is approximately a straight line for the normal-condition patient (left panel); the dotted line represents the result of a hyperbolic regression (b_1 = 0.008) and a computed curvature index (k_{max}) of 0.031 with FEV_1 of 3.57 L. The middle panel represents moderate obstruction; the descending phase bends toward the volume axis and the dotted line is a hyperbolic regression (b_1 = 0.671) with an estimated k_{max} of 0.548 and FEV_1 of 1.14 L. Severe airflow obstruction is displayed in the right panel; the estimated b_1 is 9.981, k_{max} is 2.267, and FEV_1 is 0.54 L. Note that the beginning of the flow-volume curve is irregular and difficult to define accurately. However, the estimate of k_{max} is unaffected by this artifact.
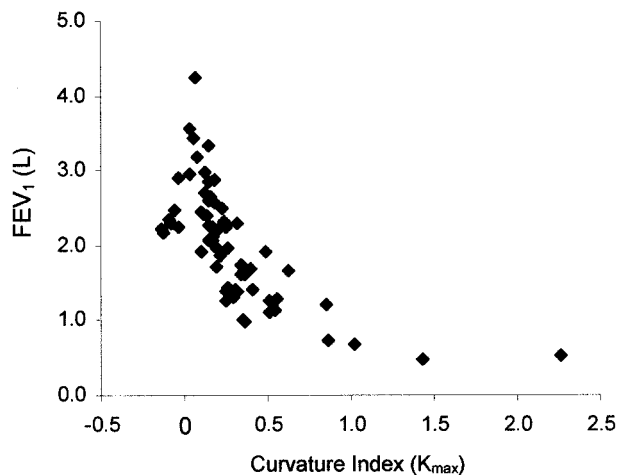

Fig. 2. Scatter plot of FEV_1 versus curvature index (k_{max}). The relationship is approximately exponential. As FEV_1 increases, k_{max} approaches 0. But as FEV_1 decreases to <1 L, k_{max} increases along an asymptote toward infinity.

main vulnerable to artifacts. The global curvature index we have proposed overcomes these deficiencies and, with the use of micro-processing spirometers, should be well suited for clinical application.

The slope parameter b_1 is an alternative index that could serve to quantify the phenomenon of curvilinearity. It has the advantage of possessing a biomechanical interpretation (ie, the velocity by which the airway resistance increases with the expiratory volume). But the disadvantage is that correct estimation of this parameter requires precise identification of the starting position V_0 (at which the flow rate $\dot{Q}(V_0) = 0$) of the expiratory volume, which is a continual problem in PFT testing (ie, the use of back-extrapolation to find a true start point). This pitfall can be illustrated by a simple algebraic substitution:

When $V_0 \neq 0$,

$$V \rightarrow V - V_0$$

$$\dot{Q}(V) \rightarrow \dot{Q}(V - V_0) = \frac{1 - b_2(V - V_0)}{b_0 + b_1(V - V_0)}$$

$$= \frac{1 - b_2{}^*V}{b_0{}^* + b_1{}^*V}$$

Here,

$$b_0{}^* = \frac{b_0 - b_1 V_0}{1 + b_2 V_0}$$

$$b_1{}^* = \frac{b_1}{1 + b_2 V_0}$$

$$b_2{}^* = \frac{b_2}{1 + b_2 V_0}$$

Although in theory the expiratory volume V should always return to its origin ($V_0 = 0$) as the respiratory system transitions from an inspiratory phase to an expiratory phase (the airflow rate should become zero at $V_0 = 0$), the true starting position is rarely known in practice. When a study subject performs the spirometry test, the instantaneous switch between inspiration and expiration is often very abrupt, erratic, or hesitant. Depending on how fast the computer samples the data series, a recorded V_0 ($\dot{Q}(V_0) \approx$ 0) is typically only an approximation and can deviate from the true origin. The V_0 thus identified will contain a certain

error and affect the estimates of the regression coefficients (b_0, b_1, and b_2). In contrast, the geometric measure k_{max} is invariant under Euclidian transformation. Its estimation is unaltered by the condition of:

$$V_0 \neq 0: k_{max} = \frac{b_1}{\sqrt{2(b_0 b_2 + b_1)}} = \frac{b_1*}{\sqrt{2(b_0*b_2* + b_1*)}}$$

For this reason, we feel that it is preferable to use k_{max} to quantify the curvilinearity phenomenon seen with airflow obstruction.

The hyperbolic function ($b_0\dot{Q} + b_1\dot{Q}V + b_2V = 1$) used in this study to model the descending phase of a flow-volume curve appears robust to compute. Using a nonlinear regression:

$$\dot{Q}(V) = \frac{1 - b_2 V}{b_0 + b_1 V}$$

to analyze the 67 spirometric records, we encountered no failure of convergence. Varying the initial values of b_0, b_1, and b_2 also had no effect on the final estimates. On the other hand, some empirical data-trimming algorithms (conducted before the modeling analysis) may be a potential source of discrepancy and will probably require further studies to standardize. For instance, we settled on a somewhat arbitrary definition of the region of curvilinearity, but other definitions of the area of interest might improve the index.

Conclusions

In summary, we report an analysis of a curvilinearity index to quantify the degree of obstruction, and we found that the index is associated exponentially with the currently used index, FEV_1. In comparison, FEV_1 provides a reproducible point estimate of flow limitation that is well established as an assessment tool but suffers from lack of agreement with degree of obstruction. Implications from this proposal are limited, as the index was evaluated with data from only 67 out-patients, who had a broad range of PFT interpretations. Future studies of this curvilinearity index should be directed toward (1) improving the algorithm, (2) determining correlation between the index and clinical signs and symptoms, (3) determining how well the index predicts clinical outcomes, and (4) determining how well the index tracks the degree of impairment.

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