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Maximum expiratory flow–volume curve: mathematical model and experimental results

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ABSTRACT

A mathematical simulation of the maximum expiratory flow–volume (MEFV) curve was developed using a lumped parameter model. The model uses a theoretical approximation of an activation function representing the lung's pressure–volume relationship during maximally forced expiration. The waveforms obtained by the model were compared to the flow–volume curves recorded from normal subjects and for patients with small airways disease, asthma, and emphysema. We were able to reproduce the flow–volume curves using the model and calculate new parameters that reflect the dependency of airways resistance on expired volume during FVC manoeuvre. These new parameters are based on the entire information presented in the flow–volume curve and on the reduction in flow at all lung volumes. We also calculated the mean slope of the resistance–expired volume curves $\bar{b}$ *obtained from the model by fitting a straight line to the curve. Using representative data for normal and COPD patients different mean slopes of 0.095, 0.13, 0.49 and 1.44 litre*$^{-1}$ *were obtained for normal subject, small airways disease, asthma and emphysema patients, respectively. The model-based parameters may be applicable to human studies. However, further studies in large groups of patients are required to better define the true predictive value of the new indices described for the diagnosis of COPD.*

Keywords: Maximum expiratory flow–volume, mathematical model

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INTRODUCTION

The maximal expiratory flow–volume (MEFV) curve depicts air flow rate as a function of forced expired vital capacity (FVC). The MEFV curve shows reduction in flow as a function of lung volumes. Indices of lung function such as FVC, forced expiratory volume in one second (FEV1), peak expiratory flow (PEF), and forced expiratory flows at 25%, 50%, and 75% of FVC (FEF25%, FEF50%, FEF75%) are obtained from this curve. The form of the flow–volume curve is a function of the mechanical characteristics of the lung and of the resistance of the airways. During normal quiet breathing the airway resistance is low. When the airways are obstructed the resistance increases, significantly changing the shape of the MEFV curve. A detailed review on the MEFV curve was presented by Hyatt and Black[1].

Mathematical models and computer simulations of respiratory mechanics were developed to study the behaviour of the bronchial tree, and the relationship between various types of airway obstructions and the shape of the flow–volume curve[2–11]. Fry[2] presented a theoretical hydrodynamic analysis of the MEFV curve and specified its important characteristics. In a further development of his model he presented a numerical method for modelling the nonlinear mechanical behaviour of the lung[5]. Other studies[3,9,11] were based on equations describing the pressure losses due to flow with elasticity and friction laws in order to predict maximum flow. Elad *et al.*[12] investigated various phenomena associated with flow limitations in a one dimensional model of the bronchial airways. These theoretical studies were not readily applicable to human studies, perhaps

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in part because the computations involved were too demanding.

In the present study a different approach is presented. A lumped parameter model was developed for the FVC manoeuvre. The model uses a theoretical approximation of an activating function representing the lung's pressure–volume relationship during maximally forced expiration. The waveforms obtained by the model were compared to the flow–volume curves recorded from normal subjects and for patients with small airways disease, asthma, and emphysema. We were able to reproduce the flow–volume curves using the model and calculate new parameters that reflect changes in airways resistance during FVC manoeuvre.

THE MODEL

The model is based on two elements: a volume-dependent pressure source and viscous resistance to air flow. The pressure source includes an activation function E that represents the lung's pressure–volume relationship in a similar manner to the model developed by Suga and Sagawa for cardiac contraction[13]. The ability to generate pressure during forced expiration depends on the lung's volume. The activation function (driving forces) varies with time and is assumed to reach a constant level. $E(t)$ is expressed as an exponential function:

$$E(t) = E_{max}(1 - e^{-t/\tau}) \quad (1)$$

where E_{max} is the maximum level of contraction expressed as a pressure–volume ratio in units of mmHg/ml, and the time constant of contraction, τ, is a parameter in units of second. *Figure 1* (top panel) shows the activation function ($E_{max} = 12$ and $\tau = 0.15$ s) as a function of time.

The pressure $P(t)$ developed in the lung is a function of the activating function and of the instantaneous lung volume $V(t)$:

$$P(t) = E(t)(V(t) - \mathrm{RV}) \quad (2)$$

where RV is the residual lung volume. The instantaneous volume in the lung can be expressed as the difference between total lung capacity (TLC) and expired volume $V_e(t)$:

$$V(t) = \mathrm{TLC} - V_e(t) \quad (3)$$

Substituting Equation (3) in Equation (2) yields:

$$P(t) = E(t)(\mathrm{TLC} - \mathrm{RV} - V_e(t))$$
$$= E(t)(\mathrm{FVC} - V_e(t)) \quad (4)$$

The airways resistance was represented by a volume-dependent piecewise-linear function with 10 segments (*Figure 2* top panel) having different coefficients a_j for each volume range limited by V_j.

$$R_1(V_e) = a_0 + a_1 V_e$$

$$R_n(V_e) = a_0 + \sum_{j=2}^{n} (a_{j-1} - a_j) V_{j-1} + a_n V_e \text{ for } n \geq 2$$

Following Poissieulle's law, the flow $Q(t)$ was cal-

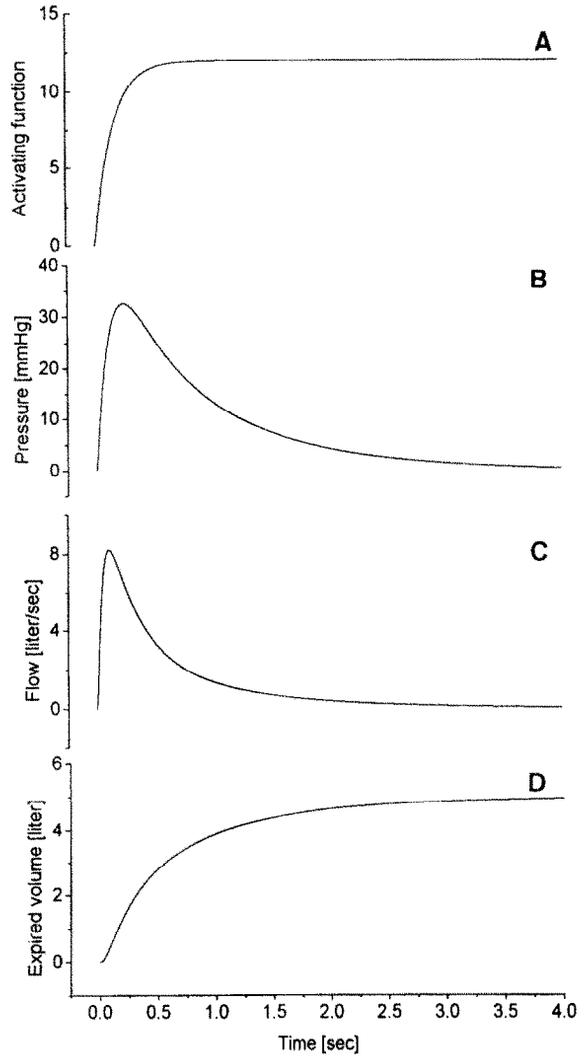


Figure 1 Model generated waveforms as functions of time: activation function (panel A), alveolar pressure (panel B), flow (panel C), and expired volume (panel D) ($E_{max} = 12$ mmHg/ml, $\tau = 0.15$ s, $a_0, \ldots, a_{10} = 2.0$, and FVC = 5.0 l)

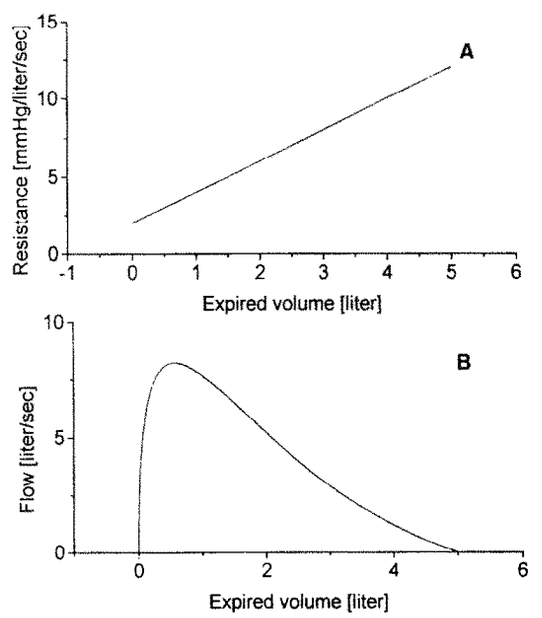


Figure 2 The model predicted normalized resistance as a function of volume and flow-volume curves for the same parameter as in *Figure 1*

culated as the ratio of the driving pressure and airways resistance:

$$Q(t) = \frac{E_{max}}{R(V_e)} (1 - e^{-t/\tau}) (FVC - V_e(t)) \quad (6)$$

Expired volume can be expressed as the flow integrated from the beginning of expiration to time t, and FVC can be expressed as the flow integrated from the beginning to the end of the forced expiration (t_e):

$$V_e(t) = \int_0^t Q(\xi) d\xi$$
$$FVC = \int_0^{t_e} Q(\xi) d\xi \quad (7)$$

Figures 1 and *2* show an example of the model predicted curves for the following parameter values: $E_{max} = 12$ mmHg/ml, $\tau = 0.15$ s, a_0 to a_{10} are all equal to 2.0, and FVC = 5.0 l. *Figure 1* shows the activation function (panel A), the alveolar pressure (panel B), the flow–time curve (panel C), the expired volume time curve (panel D). *Figure 2* shows the resistance–volume function (panel A) and the flow–volume curve (panel B).

DATA ACQUISITION AND ANALYSIS

Equation 6 describes the relationship between lung contraction, volume, and flow, based on the assumption that airways resistance is a function of expired volume. Before the parameters estimation process begins, FVC and $V_e(t)$ are obtained. FVC can be calculated from the flow (Equation 7) or obtained from body plethysmograph measurements. $V_e(t)$ is calculated from the measured flow. Equation 6 includes a ratio of E_{max} and $R(V_e)$. In the parameter estimation process, it is not possible to determine the magnitude of E_{max} and of $R(V_e)$ separately. Therefore, the resistance function is normalized with respect to E_{max} as follows:

$$\tilde{R}_1(V_e) = b_0 + b_1 V_e$$
$$\tilde{R}_n(V_e) = b_0 + \sum_{j=2}^{n} (b_{j-1} - b_j) V_{j-1} + b_n V_e$$
$$\text{for } n = 2,3,\ldots,10 \quad (8)$$

$$Q(t) = \frac{1}{\tilde{R}(V_e)} (1 - e^{-t/\tau}) (FVC - V_e(t)) \quad (9)$$

where

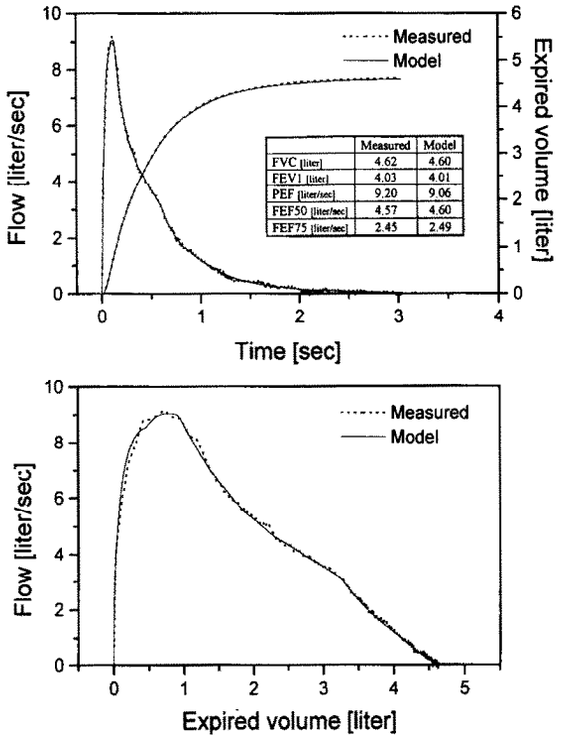
$$b_j = a_j / E_{max} \quad (10)$$

To test the model and explore its diagnostic value, flow–time curves were recorded during maximal forced expiration from a normal subject, a patient with emphysema, a patient with asthma, and a patient with small airways disease. The recordings were performed with a Jaeger Pneumotach (Transferscreen II, Erich Jaeger GmbH) and were digitized by a 12 bit analog to digital converter at a sampling rate of 200 Hz. The flow-time curves recorded from patients were used to estimate the parameters of the model: τ, $b_0,\ldots,b_{10}$ using an iterative optimization technique that minimized the square error between the recorded and the model-predicted curves. Both predicted and measured flow and expired volume were plotted as functions of time. Flow–volume curves were plotted for each case and the normalized resistances for all cases were plotted and compared. The mean slope of each resistance–volume curve, b, was obtained by fitting a straight line to the curve using linear regression analysis.

RESULTS

Figure 3 shows results obtained for a normal subject. The top panel presents the recorded forced expiratory flow–time and volume–time curves (dotted lines) as well as the curves obtained from the model (solid lines). The recorded (dotted lines) and the calculated (solid lines) flow–volume curves are shown in the bottom panel. The conventional lung function parameters, calculated from the recorded data and from the model curves are shown in the inset table. Similar results were obtained by the two methods. *Figures 4–6* show the curves and the conventional lung function parameters for patients with small airways disease, asthma, and emphysema, respectively. Very good agreement between measured and model predictions can be seen.

Figure 7 shows the model-based estimated resistance as a function of expired volume for all the above cases. The mean slope b of each curve was calculated. Mean slopes of 0.095, 0.13, 0.49 and



	Measured	Model
FVC [liter]	4.62	4.60
FEV1 [liter]	4.03	4.01
PEF [liter/sec]	9.20	9.06
FEF50 [liter/sec]	4.57	4.60
FEF75 [liter/sec]	2.45	2.49

Figure 3 The results obtained for a normal subject. The top panel presents the measured forced expiratory flow–time and volume–time curves (dotted lines) as well as the curves generated by the model (solid lines). The measured (dotted lines) and the calculated flow–volume curves (solid lines) are shown in the bottom panel. The conventional lung function parameters calculated from the measured data and from the model curves are shown in the table

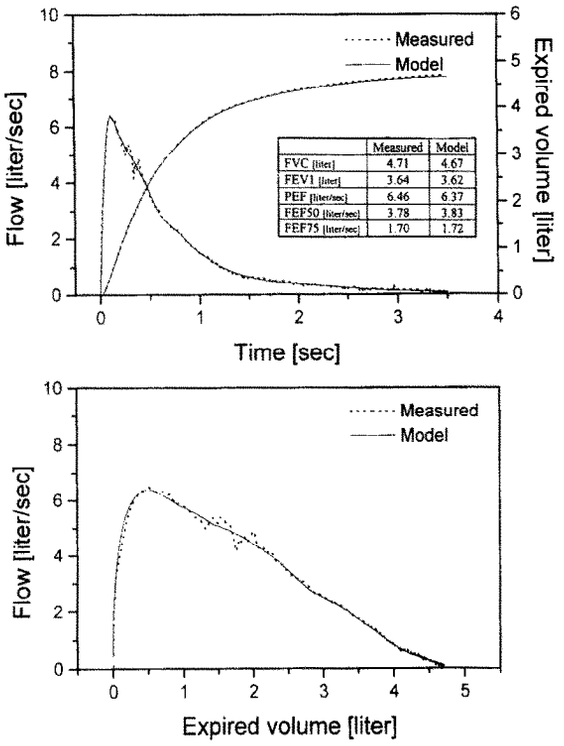


Figure 4 Results obtained for a patient with small airways disease

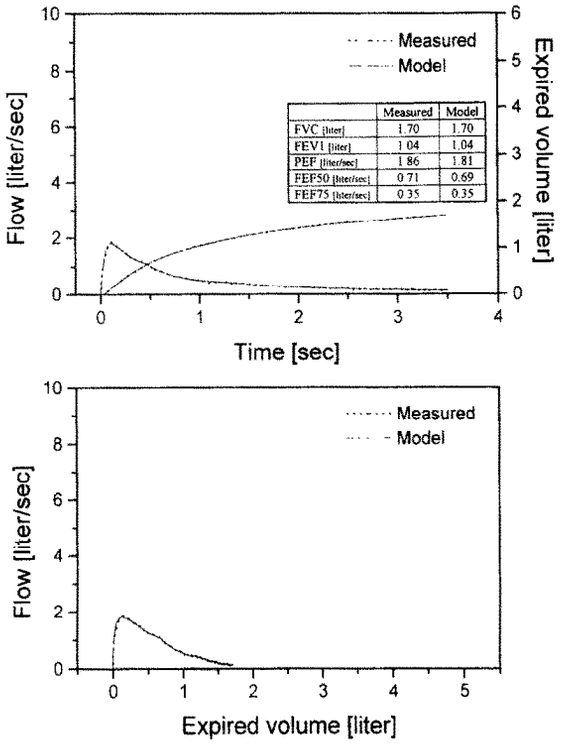


Figure 6 Results obtained for a patient with emphysema

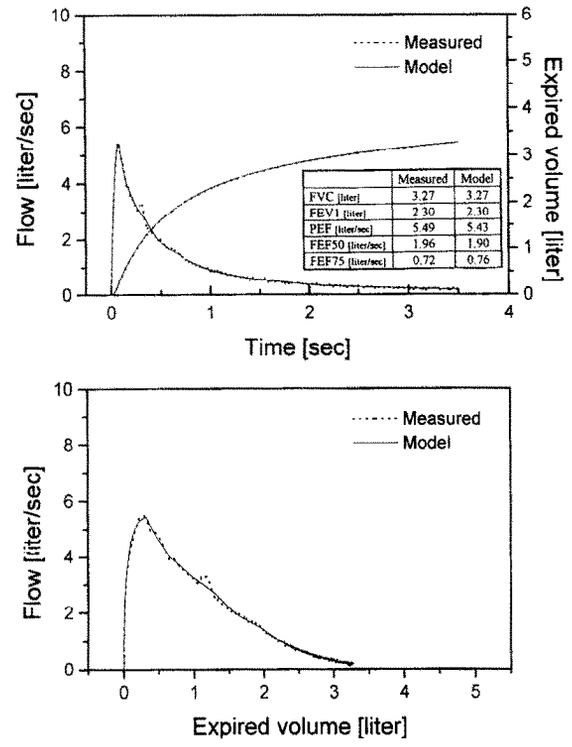


Figure 5 Results obtained for a patient with asthma

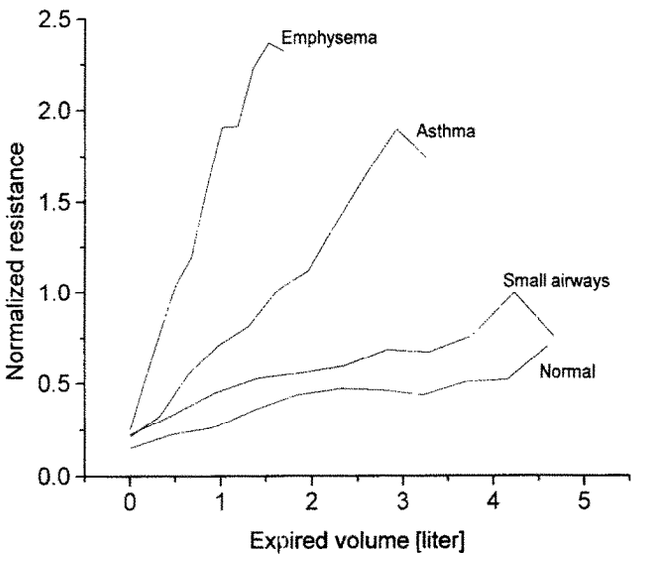


Figure 7 The normalized resistance as a function of expired volume predicted by the model for the normal subject and for the three patients with obstructive airways diseases

1.44 l^{-1} were obtained for normal subject, small airways disease, asthma and emphysema patients, respectively.

DISCUSSION

The maximal expiratory flow–volume (MEFV) curve has become a widely used noninvasive test of pulmonary function. It appears to be determined by the mechanical properties of the lung and the respiratory musculature. In the present study, a mathematical model of the MEFV curve was developed. The model was based on a time-dependent activation function representing a pressure–volume relationship of the lung. The developed pressure in the lung was, therefore, the product of that activating function and the instantaneous volume. Flow was calculated as the ratio of pressure and a nonlinear volume-dependent resistance. This paper presents the model and shows examples of its predictive capabilities.

The model is a lumped-parameter model that includes a number of elements that were con-

sidered important to simulate effects of lung disease. To keep the model simple and clinically useful, some underlying assumptions were made as a basis for the mode, such as the behaviour of the activation function with time and the behaviour of the airways resistance as a function of expired volume. These assumptions excluded several mechanisms that may be considered important when performing a detailed analysis of the respiratory system.

The waveforms obtained by the simulated model were compared to flow–volume curves recorded from a normal subject and from patients with chronic obstructive airways disease (COAD). We were able to satisfactorily reproduce the shape of the maximum expiratory flow–volume curves of normal and COAD subjects by tuning the model parameters. Representative forced flow–volume parametric waveforms were evaluated from the model for a normal subject, for a patient with emphysema, for a patient with asthma, and for a patient with small airways disease. As can be seen in *Figures 4–6*, similar conventional lung function indices were obtained from the recorded data and from the model curves. The model-based parameters for the healthy subject are characterized by low resistance to flow during the respiratory cycle. For small airways disease the flow at volumes close to TLC is almost normal with low resistance, and higher resistivity to flow for lower lung volumes. For emphysema, the resistivity to flow is high for volumes near TLC due to the compliance of the lungs, and increases to high values for lower volumes.

The behaviour of the normalized resistance as a function of expired volume predicted by the model (*Figure 7*) was very similar to experimental results reported by Pride *et al.*[4] For the normal subject there was a small change in the airways resistance in the lower range of the expired volume. For the patient with asthma the model predicted a much greater change in airways resistance throughout the FVC range. The patient with small airways disease did not show such a large rise in airways resistance. Pride *et al.*[4] observed that in patients with irreversible obstruction, the airways resistance is higher than for most normal subjects. The model predicted the same phenomena. Despite similar slopes in the normalized resistance curves in both normal and small airways disease patients, the normalized resistance in the latter was higher. The patient with emphysema exhibited a significantly more pronounced change in airways resistance throughout the FVC range.

In summary, a model of the forced expiratory manoeuvre is presented and new parameters related to airways resistance were obtained. Using this new formulation, parameter-dependent flow–volume waveforms with different shapes can be obtained and fitted to measured data. Based on the cases presented in the study clear differentiation between the different COPD patients was obtained. However, the different range of severity of the various diseases may overlap, especially when comparing small airways disease with asthma patients. It can be concluded that this model may be applicable to human study; however, further studies in large groups of patients are required to better define the true predictive value of the new indices described for the diagnosis of COPD.

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