Comparison of Maximal Midexpiratory Flow Rate and Forced Expiratory Flow at 50% of Vital Capacity in Children*

Ephraim Bar-Yishay, PhD; Israel Amirav, MD; and Shmuel Goldberg, MD

**Background:** The mid-portion of the maximal expiratory flow-volume (MEFV) curve is often described by values of the mean forced expired flow as lung volume decreases from 75% to 25% of vital capacity (ie, forced expiratory flow, midexpiratory phase [FEF25–75]). It is common practice to report also forced expired flow at 50% of vital capacity (FEF50).

**Study objective:** To investigate whether FEF50 and FEF25–75 are highly correlated or whether the difference between them reflects a degree of airways obstruction. Also, we wanted to investigate the correlation between the two in cases of irregularly shaped MEFV curves (ie, “saw-toothing”).

**Design:** Analysis of the correlation between FEF50 and FEF25–75 in a single determination. We assessed the relationship between the FEF50/FEF25–75 ratio and the degree of airways obstruction, as reflected by other traditional parameters such as FEV1, FEV1/FVC ratio, and specific airway conductance (SGaw).

**Patients:** There were 1,350 forced expiratory maneuvers performed by children with a broad range of pulmonary abnormalities.

**Results:** FEF50 correlated with FEF25–75 as follows: FEF50 (L/s) = 0.041 + 1.136*FEF25–75(L/s); r² = 0.956; standard error of the estimate = 0.013; p < 0.0001. The FEF50/FEF25–75 ratio remained stable and did not correlate with FEV1 (r = 0.12), FEV1/FVC ratio (r = 0.11), or SGaw (r = 0.02; difference not significant). The correlation between FEF25–75 and FEF50 was similar for both the smooth curve (r = 0.97) and the irregular curve (r = 0.96).

**Conclusions:** Although not identical, FEF25–75 and FEF50 are highly correlated, and the ratio of the two is fairly constant. Therefore, the practice of reporting both of them is unnecessary. We suggest that it is reasonable to prefer FEF50.

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Key words: forced expiratory flow at 50% of vital capacity; maximal expiratory flow-volume curve; maximal midexpiratory flow rate; modeling

Abbreviations: CI = confidence interval; FEF50 = forced expiratory flow at 50% of vital capacity; FEF25–75 = maximal midexpiratory flow rate; MEFV = maximal expiratory flow-volume curve; SGaw = specific airway conductance

Objective assessment of lung mechanics is an essential component in the care of patients with respiratory illnesses. Because of their simplicity and reproducibility, maximal expiratory flow volume (MEFV) maneuvers are very common in these patients. With the advent of computerized equipment, as many as 31 different forced expiratory flow variables can be measured from this maneuver. The values of FEV1, FVC, the FEV1/FVC ratio, and peak forced expiratory flow rate are well-established. It is also a common practice to report forced expiratory flow between 75% and 25% of vital capacity (ie, forced expiratory flow, midexpiratory phase [FEF25–75]), and/or forced expiratory flow at 50% of vital capacity (FEF50). Both are considered to be more sensitive in detecting small airway dysfunction.

In theory, a close agreement between these two parameters occurs when the lung empties monotonously with a single time constant. However, in this case the flow-volume relationship is always linear and its constant slope is inversely related to a single,
unchanging time constant of the respiratory system. In the presence of peripheral airways obstruction, the curvilinearity of MEFV increases, and, as the time constant increases, both parameters will fall in concert with no change in the ratio of the two. However, it is more commonly assumed that during the MEFV maneuver the lung empties nonhomogeneously, with more than a single time constant describing different lung zones.5,6 In this case, the difference between FEF 25–75 and FEF 50 may be related to the degree of nonhomogeneous emptying, and, since nonhomogeneous emptying increases with airway obstruction,6 the FEF 50/FEF 25–75 ratio should increase. If this is true, then it is important to report both FEF 25–75 and FEF 50. If, on the other hand, FEF 25–75 and FEF 50 are in agreement regardless of baseline lung function, then the difference between them may not reflect the degree of airways obstruction, and reporting both parameters is redundant.

In addition, whereas both parameters quantify flow during the middle portion of a forced expiration, FEF 25–75 is a time-weighted average and FEF 50 is an instantaneous value, and, as such, an increased ratio may not be accurate in cases of irregularly shaped MEFV curves (eg, “saw-toothed”).

If this ratio is not affected by airways obstruction or shape, then the difference between the measures may have no clinical significance, and, hence, there should be no value in reporting both.

Materials and Methods

A total of 1,350 recorded MEFV curves that had been obtained from patients < 18 years of age were retrieved for analysis. The characteristics of these patients are summarized in Table 1. All tests were performed using a body plethysmograph (model 6200; SensorMedics; Yorba Linda, CA). Flow was measured by a pneumotachograph while the plethysmograph door was open.

Statistical Analysis

The correlation between FEF 50 and FEF 25–75 was determined (Pearson correlation coefficient, r), and the assessment of the degree of agreement between FEF 25–75 and FEF 50 was carried out.7 The variances of the difference between the two and their ratios were tested for homoscedasticity. Also, since the differences were not normally distributed (the differences were proportional to the mean), various transformation models were investigated. To assess whether the relationship between the two measures was related to the degree of airways obstruction, individual FEF 50/FEF 25–75 ratios were plotted against FEF 50, FEV 1, FEV 1/FVC ratio, and SGaw values (% predicted) of the same subjects. A p value of < 0.05 was considered to be significant.

To evaluate whether the irregularity (ie, saw-tooth shape) of the

Table 1—Characteristics of the Study Population*

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<td>Patients</td>
<td>1,350</td>
</tr>
<tr>
<td>Male</td>
<td>733 (54.3)</td>
</tr>
<tr>
<td>White</td>
<td>1,100 (81.5)</td>
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<tr>
<td>Age, yr</td>
<td>10.8 ± 3.3</td>
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<td>Diagnosis</td>
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<td>Asthma</td>
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Figure 1. Examples of a normal MEFV curve (left, A) and an irregular MEFV curve (right, B). The normal-looking curve belongs to a 9-year-old girl, and the irregularly shaped curve belongs to an 8-year-old girl, both of whom have cystic fibrosis. The actual MEFV data are presented as thick lines, and the predicted curves are presented as thin lines.
MEFV curve influences the correlation between FEF<sub>25-75</sub> and FEF<sub>50</sub>. r values obtained from regular vs irregular curves were compared. A random sample of 100 curves was classified as regular, intermediate, or irregular, as judged by two independent observers (SG and IA). A regular curve was defined as one with a smooth shape without spikes or indentations in the general contour. An irregular curve was defined as one with multiple spikes and indentations (Fig 1). Agreement between observers was obtained in 91 of 100 curves. Of those, we found 31 regular curves (34%), 36 intermediate curves (40%), and 24 irregular curves (26%).

Results

The relationship between FEF<sub>25-75</sub> and FEF<sub>50</sub> values (L/s) for 1,349 tests is shown in Figure 2. The linear relationship can be described as follows:

$$\text{FEF}_{50} \text{ (liters per second)} = 1.1358 \times \text{FEF}_{25-75} \text{ (liters per second)} + 0.0417(\text{SEE}_y = 0.0115, \ r^2 = 0.956, \ p < 0.001),$$

where SEE<sub>y</sub> is standard error of the estimate. A nonlinear correlation did not yield better results ($r^2 = 0.949$). Assessing agreement between the two parameters, revealed that the differences were not normally distributed (difference = 0.1511 × mean – 0.0059; $r^2 = 0.340$). A log-transformation yielded a mean (± SD) log-difference of 0.160 ± 1.171 L/s (95% confidence interval [CI], 0.851 to 1.582; p < 0.001). The mean FEF<sub>50</sub>/FEF<sub>25-75</sub> ratio was 1.175 ± 0.201 (95% CI, 0.782 to 1.569) and did not correlate with the degree of small airways obstruction, as reflected by the FEF<sub>50</sub> (Fig 3), as follows: FEF<sub>50</sub>/FEF<sub>25-75</sub> = −5 × 10<sup>−5</sup> × FEF<sub>50</sub> + 1.179 ($r^2 = 0.00007; \ p = 0.77$). Neither the ratio nor the difference between FEF<sub>25-75</sub> and FEF<sub>50</sub> correlated with FEV<sub>1</sub>, FEV<sub>1</sub>/FVC, or sGaw (difference was not significant). The correlation between FEF<sub>25-75</sub> and FEF<sub>50</sub> was similar in both the smooth curve ($r = 0.97$) and the irregular curve ($r = 0.96$).

Discussion

In the era of computerized spirometry, as many as 31 variables can be measured from each recorded
While physiologic considerations justify the use of a variety of measures, the merit of using all measures remains unclear. The forced expiratory maneuver was measured originally by a spirometer inscribing a volume-time tracing, from which spirometric volume changes over time were derived. Alternatively, flow can be measured directly, and its integral yields volume changes. The MEFV represents essentially the same information as the volume-time tracings. While the FEF50 is the instantaneous flow, the FEF25–75 is an average value over the mid-vital capacity range. Both can be obtained by either technique. Furthermore, a very high correlation between the two parameters is to be expected as they are both determined by lung mechanics over the mid-vital capacity range, and it is unlikely that one index will provide information that is not contained by the other. Thus, the distinction between the two lies on historical and theoretical grounds, but not necessarily on physiologic grounds.

It is common practice to report both FEF25–75 and FEF50. If the two measures were independent unrelated measures, or if FEF25–75 may be thought to contain important information from events occurring at lower lung volumes, one could argue for their combined use. The results of this study demonstrate that there is a highly positive correlation between the two measurements. FEF50 is approximately 15% higher than FEF25–75, the difference between the two is fairly constant, is well-preserved in cases of irregularly shaped MEFV curves, and does not correlate with the degree of airways obstruction. Ligas et al compared FEF25–75 to FEF50 in 22 cystic fibrosis patients and 26 healthy patients, and they concluded that since the two were highly correlated there was no reason to use FEF50. However, no large-scale study has been previously conducted to compare the two measurements.

On theoretical grounds, if the lungs are considered as a simple resistor-capacitor circuit analog having a single time constant, one expects the FEF50/FEF25–75 ratio to increase as obstruction progresses. If that was the case, then presenting both parameters would be justified as the ratio can serve as an index of airways obstruction. However, we present evidence here (Fig 3) that this ratio is not affected by the degree of airways obstruction. Assuming the descending portion of the MEFV curve to be a straight line, and the volume to be a monoexponential decaying function of time, Douglas calculated the FEF50/FEF25–75 ratio to be 1.10. Our results, which were obtained from a very large sample of children, are in close agreement with the finding of Douglas even though our sample includes
MEFV curves with a wide spectrum of curvilinearity. The two measures are highly correlated, with a \( r^2 \) value of 0.96, which means that only 4% of the difference is not accounted for by the difference between related values. Considering the wide source of physiologic and nonphysiologic reasons for making the two parameters vary, it is quite surprising to find them in such close agreement. Such a small difference between two variables does not justify reporting both.

In theory, a close agreement between FEF\(_{50}\) and FEF\(_{25-75}\) must occur when the lung empties monotonically with a single time constant of the respiratory system, as follows: \( v = v_0 e^{-kt} \). However, the flow-volume relationship in this case is always linear (\( V' = -kV \)), and it does not allow for the curvilinearity that is the hallmark of the MEFV curves of patients with peripheral airways obstruction. In order to simulate curvilinear MEFV curves, a first-order equation will not suffice. The relationship \( F = dV/dt = kV e^n \) yields MEFV curves that may be curvilinear where \( n \) is a measure of curvilinearity, and the higher the curvilinearity (scoping in toward the volume axis), the slower the emptying of the lung. This model, however, is not realistic since the FEF\(_{50}/FEF_{25-75}\) ratio increases with \( n \), whereas we have shown here that the FEF\(_{50}/FEF_{25-75}\) ratio remains stable and does not increase with varying degrees of peripheral airways obstruction.

From the preceding description it is clear that the FEF\(_{50}/FEF_{25-75}\) ratio does not simply reflect the curvilinearity of the MEFV curve but rather depends on a function that describes lung emptying. Since we found this ratio to be unaffected by peripheral airways obstruction (Fig 3), other models (ie, a model with a changing time constant that increases as the lung empties) may possess all of the fundamental characteristics. Alternatively, it is possible that peripheral airways obstruction is simply only one of the parameters that influence the FEF\(_{50}/FEF_{25-75}\) ratio and that other variables, such as technical or commercially introduced aspects, may mask this phenomenon.

Which parameter, FEF\(_{25-75}\) or FEF\(_{50}\), should be preferred? Since we have shown that the two parameters are tightly correlated and are unaffected by severity of disease or by the shape of the MEFV curve, there is no reason to report both. It is our impression that while FEF\(_{50}\) is easily and directly determined, FEF\(_{25-75}\) is a calculated parameter that is affected by the manufacturers' choice of algorithms with which to determine it. Furthermore, in a literature search using PubMed for the years 1966 to 2001, 1,967 studies used the terms FEF\(_{25-75}\) and/or FEF\(_{50}\) (“maximal mid-expiratory flow” [MeSH] and other terms) in their abstract. Of these, 1,307 used only FEF\(_{25-75}\), 561 used only FEF\(_{50}\), and 81 used both. However, with the advent of sophisticated electronic equipment it was not surprising to find that the published ratio of FEF\(_{25-75}\) to FEF\(_{50}\) fell from 49.5 = 10 in the 1966 to 1975 decade to 253/124 = 2 in the last 5 years (ie, 1997 to 2002). We, therefore, suggest that it is reasonable to prefer FEF\(_{50}\).

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**REFERENCES**