FEV_6 Is an Acceptable Surrogate for FVC in the Spirometric Diagnosis of Airway Obstruction and Restriction

MAUREEN P. SWANNEY, ROBERT L. JENSEN, DAVID A. CRICHTON, LUTZ E. BECKERT, LAUREN A. CARDNO, and ROBERT O. CRAPO

Canterbury Health Ltd., Respiratory Physiology Laboratory, Clinical Services Block, Christchurch Hospital, Christchurch, New Zealand; and Pulmonary Division, and Department of Medicine, LDS Hospital and University of Utah School of Medicine, Salt Lake City, Utah

We analyzed the FEV_1/FEV_6 and FEV_1/FVC results of 502 consecutive patients in the spirometric diagnosis of airway obstruction. We also examined the agreement between FEV_6 and FVC in the spirometric diagnosis of restriction. Technically acceptable test results were obtained from 337 subjects (67%). The sensitivity of FEV_1/FEV_6 for diagnosing airway obstruction as defined by FEV_1/FVC was 95.0%; the specificity was 97.4%. When interpretations differed, the measured values were all close to the lower limits of the reference ranges. When analysis included ± 100-ml variability in FEV_1 and FEV_6, the sensitivity increased to 99.5% and the specificity to 100%. The reproducibility of FEV_6 was superior to that of FVC. These results suggest that FEV_6 is an accurate, reliable alternative to FVC for diagnosing airway obstruction and that FEV_6 is reasonably comparable to FVC for the spirometric diagnosis of restriction. FEV_6 is more reproducible and less physically demanding for patients.

Spirometry has become an essential tool in assessing respiratory disease (1). It is a test that will always require patient effort and cooperation; the effort to reach FVC is especially difficult for some patients. FVC is an essential element of the test, used to diagnose airway obstruction (reduced FEV_1/FVC) and to rule out a restrictive process (2, 3). The measurement of FVC requires the patient to empty his or her lungs completely, a process that may take up to 20 s and that can be physically exhausting for older or impaired individuals or those with severe respiratory diseases. The standard FVC also has the problem of being dependent on expiratory time in individuals with airway obstruction and in healthy individuals as they age. These problems have sparked an interest in identifying a surrogate for FVC, preferably one that requires a shorter exhalation and that offers a discrete end of test criterion. The National Lung Health Education Program (4) has proposed using forced expired volume in 6 s (FEV_6) and the FEV_1/FEV_6 ratio, but there are no data to support this proposal. Hankinson and coworkers have published reference values including predicted values for FEV_6 and FEV_1/FEV_6 (5). This makes it possible to compare FEV_6 with FVC.

Our primary question was as follows: In tests that meet American Thoracic Society (ATS) quality criteria, is FEV_1/FEV_6 equivalent to FEV_1/FVC in diagnosing airway obstruction? Secondary questions included the following: Is FEV_6 more reproducible than FVC? Is FEV_6 equivalent to FVC in the spirometric diagnosis of restriction?

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Correspondence and requests for reprints should be addressed to Maureen P. Swanney, M.Sc.(Hons.), Respiratory Physiology Laboratory, 2nd Floor, Clinical Services Block, Christchurch Hospital, Private Bag 4710, Christchurch 8001, New Zealand. E-mail: maureen@chhlth.govt.nz

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METHODS

The study was approved by the Canterbury Ethics Committee. Informed consent was not required because no additional tests were done and individuals were not identified. We analyzed data from consecutive adult patients referred to our laboratory for routine spirometry over a 6-wk period in early 1999. Patients were referred from respiratory clinics, general practice, and the medical and surgical services of Christchurch Hospital in Christchurch, New Zealand. This laboratory is the only respiratory function laboratory serving a population of 350,000. Spirometry was performed with one of two SensorMedics model 2130 dry rolling seal spirometers (SensorMedics Corporation, Yorba Linda, CA) in standard use in our laboratory. SensorMedics Corporation provided new software to measure and report FEV_6 and FEV_1/FEV_6 along with all other standard spirometric indices. Each spirometer was calibrated daily with a 3-L syringe. Subjects were tested while seated, and procedures detailed in the ATS guidelines were followed (6). Height was measured to the nearest centimeter without shoes, and weight was recorded to the nearest kilogram. Particular attention was made to ensure that maximal FEV_1 and FVC efforts were obtained. The reference equations published by Hankinson and coworkers were used in this study because they are the first to provide reference values and well-defined lower limits of normal for FEV_1, FEV_6, FVC, FEV_1/FVC, and FEV_1/FEV_6 in a large series of subjects (5).

Each study was screened for technical adequacy. We required at least three "acceptable trials," defined as (*1*) a good start of test (a well-defined early peak in flow and an extrapolated volume of less than 5% of FVC or 0.15 L, whichever was larger), (*2*) at least 6 s of expiration, and (*3*) no significant cough or other interruption in the test (6). As recommended by the ATS, data that did not meet reproducibility criteria were not excluded but subjects were asked to perform up to a maximum of eight trials in an attempt to obtain reproducible results (6). The computer report of expiratory time was verified from the volume/time tracings. The highest prebronchodilator FEV_1, FEV_6, and FVC from tests of acceptable quality were used for analysis.

Each subject was categorized as having "airway obstruction" or "no airway obstruction" by comparing both FEV_1/FVC and FEV_1/FEV_6 with the respective lower limits of normal defined by Hankinson and coworkers (5). We used FEV_1/FVC as the "gold standard" for diagnosing airway obstruction (2). The severity of airway obstruction was graded into one of four categories: possible normal variant (FEV_1 > 100% predicted), mild (FEV_1 70–100% predicted), moderate (FEV_1 50–70% predicted), and severe (FEV_1 < 50% predicted) (2). Similarly, each subject was also categorized as having spirometrically diagnosed restriction defined as a reduced FVC in the presence of a normal FEV_1/FVC and by a reduced FEV_6 in the presence of a normal FEV_1/FEV_6 (2).

Statistical Analyses

Sensitivity and specificity of FEV_1/FEV_6 in predicting obstruction defined by FEV_1/FVC were calculated using 2×2 tables. To simulate the known variability in within-subject day-to-day spirometric measurements (widely accepted as about ± 5%) and in estimates of lower limits of normal (reported to be about ± 2% [7, 8]), we also analyzed the data after adding and subtracting 100 ml from FEV_1 and FEV_6 (e.g., half the variability allowed by the ATS in a single test session). A range for the FEV_1/FEV_6 of each individual was defined by calculating an upper limit (adding 100 ml to FEV_1 and subtracting 100 ml from FEV_6) and a lower

TABLE 1

SUBJECT DEMOGRAPHICS AND SEVERITY OF AIRWAY OBSTRUCTION

				Severity of Airway Obstruction*					
				Not Obstructed†		Obstructed			
	n	Age Median, yr (*range*)	Height Median, cm (*range*)	Normal	Restricted	Normal Variant	Mild	Moderate	Severe
Males	209	65 (20–86)	171 (150–190)	53	14	1	26	41	74
Females	128	62 (26–89)	160 (144–180)	36	13	1	15	19	44

* *See text* for definitions of severity.
† Normal and restrictive spirometric patterns.

limit (subtracting 100 ml from FEV_1 and adding 100 ml to FEV_6). If the lower limit of normal taken from Hankinson and coworkers was within this range, the two measurements were within the confidence limits of the test and we called them "equivalent."

RESULTS

Tests on 502 subjects were evaluated. All were white. We found technically acceptable tests for 337 (67%) subjects. One hundred and sixty-five subjects (33%) were excluded from analysis, most often because the expiration time was less than 6 s. Of the tests excluded, 52 subjects had normal lung function and were less than 30 yr of age (persons in this age group are often unable to exhale for 6 s). Thirteen were more than 40 yr of age and had normal lung function but were unable to exhale for 6 s, and 38 subjects had restrictive patterns and short exhalation times. Other tests were excluded for submaximal effort, usually on account of illness (n = 35), coughs (n = 13), poor test starts (n = 10), and glottic closure during testing (n = 4).

Subject demographics and severity of obstruction are shown in Table 1. Table 2A contains the unadjusted comparison of FEV_1/FEV_6 with FEV_1/FVC for diagnosing airway obstruction. The sensitivity of FEV_1/FEV_6 was 95.0% and the specificity was 97.4%. In this group of patients, 66% had obstruction based on FEV_1/FVC, and the positive predictive value of FEV_1/FEV_6 for obstruction was 98.6%. The negative predictive value was 91.1%.

Table 3 shows the spirometric findings in subjects whose categorizations on the basis of FEV_1/FVC were different from those made on the basis of FEV_1/FEV_6. Three subjects with a normal FEV_1/FVC were categorized on the basis of FEV_1/FEV_6 as having airway obstruction. Eleven patients categorized as having airway obstruction by FEV_1/FVC were defined as normal by FEV_1/FEV_6. The discordant values in Table 3 were all relatively close to the lower limit of the reference range. When data were reanalyzed after allowing for ± 100-ml variability, only one subject still had a discordant classification (Tables 2B and 3). Sensitivity and specificity were 99.5% (95% confidence interval [CI] = 97.1–100%) and 100% (95% CI = 96.0–100%), respectively (Table 2B).

Table 4 shows the performance of FVC and FEV_6 as indicators of restriction when the FEV_1/FVC ratio is normal. Sensitivity was 92.6%; specificity was 100%.The intrasubject coefficient of variation for FEV_6 (3.4%) was 24% lower than the coefficient of variation for FVC (4.5%). Similarly, the coefficient of variation for FEV_1/FEV_6 (2.9%) was 30% lower than that for FEV_1/FVC (4.2%). The intersubject coefficient of variation for FEV_1/FVC was 28% compared with 22% for FEV_1/FEV_6, a 21% reduction.

DISCUSSION

With an overall accuracy approaching 100%, FEV_1/FEV_6 is an acceptable alternative to FEV_1/FVC for diagnosing airway ob-

TABLE 2

DIAGNOSIS OF AIRWAY OBSTRUCTION VERSUS NO AIRWAY OBSTRUCTION

A. Using precise lower limits of normal FEV_1/FVC and FEV_1/FEV_6*

	FEV_1/FVC		
	Obstruction	No Obstruction	Totals
FEV_1/FEV_6, obstruction	210	3	213
FEV_1/FEV_6, no obstruction	11	113	124
Totals	221	116	337

* Predicted values and lower limit of normal values based on Hankinson and coworkers (5).

Sensitivity:	95.0%	95% CI = 91.0–97.4%
Specificity:	97.4%	95% CI = 92.1–99.3%
Positive predictive value:	98.6%	95% CI = 95.6–99.6%
Negative predictive value:	91.1%	95% CI = 84.3–95.3%

B. After allowing for an error† of ± 100 ml in FEV_1 and FEV_6

FEV_1/FEV_6, obstruction	220	0	220
FEV_1/FEV_6, no obstruction	1	116	117
Totals	221	116	337

Definition of abbreviation: CI = confidence interval.
† *See text*. The error adjustment was applied only to FEV_1/FEV_6.

Sensitivity:	99.5%	95% CI = 97.1–100%
Specificity:	100%	95% CI = 96.0–100%
Positive predictive value:	100%	95% CI = 97.9–100%
Negative predictive value:	99.1%	95% CI = 94.6–100%

TABLE 3

FINDINGS IN THE FOURTEEN DISCORDANT CASES*

Categorization			Age	FEV_1/FVC†	FEV_1/FEV_6†	Expiratory time
FEV_1/FVC	FEV_1/FEV_6	Sex	(*yr*)	(%)	(%)	(*s*)
Normal	Obstruction	M	69	0.88	−2.59	7.55
Normal	Obstruction	M	65	0.04	−1.39	9.9
Normal	Obstruction	F	39	0.27	−1.21	7.96
Obstruction‡	Normal	M	72	−0.20	4.71	12.1
Obstruction	Normal	M	45	−2.85	1.10	15.2
Obstruction	Normal	M	68	−0.44	2.36	11.0
Obstruction	Normal	M	56	−1.36	2.04	17.9
Obstruction	Normal	M	72	−1.69	0.56	16.1
Obstruction	Normal	M	72	−1.11	1.22	16.5
Obstruction	Normal	M	65	−3.96	0.61	18.5
Obstruction	Normal	M	68	−1.34	1.02	11.0
Obstruction	Normal	F	76	−0.47	0.24	10.9
Obstruction	Normal	F	61	−1.10	4.12	13.6
Obstruction	Normal	F	71	0.93	1.79	13.4

Definition of abbreviations: F = female; M = male.
* Those whose FEV_1/FVC and FEV_1/FEV_6 categorizations differed. The measured value minus the lower limit of normal gives an index of closeness to the lower limit of normal. For example, a value of 0.88 indicates that the measured value was 0.88% above the lower limit of normal.
† Measured value minus lower limit of normal.
‡ After allowing for ± 100-ml variability in the measurement of FEV_1 and FEV_6, only this case remains discordant, with a 4.91% difference between the two measurements.

TABLE 4

COMPARISON OF FEV_6 WITH FVC IN CASES WITH A NORMAL FEV_1/FVC*

	FVC		
	Reduced	Normal	Totals
FEV_6, reduced	25	0	25
FEV_6, normal	2	90	92
Totals	27	90	117

Definition of abbreviation: CI = confidence interval.

* Sensitivity:	92.6%	95% CI = 74.2–98.7%
Specificity:	100%	95% CI = 94.9–100%
Positive predictive value:	100%	95% CI = 83.4–100%
Negative predictive value:	97.8%	95% CI = 91.6–99.6%

struction. When the diagnosis based on FEV_1/FEV_6 was different from that based on FEV_1/FVC, the measured values were close to the lower limit of their respective reference ranges. The ATS already recommends caution when interpreting test results that lie close to the lower limits of a reference range (2) because both test results and estimations of the thresholds could shift across the limit on another testing occasion. Interpretation of such results should include clinical information to assess the prior probability of disease (2). The difficulty of making a definitive diagnosis close to the lower limit of normal is confirmed in our study. When we allowed for some variability (± 100 ml) in the analysis, only one case was interpreted differently when using FEV_1/FEV_6 compared with FEV_1/FVC (Table 3). Examination of the flow volume and volume time tracings did not allow us to reach definitive categorization based on the waveform patterns for this case.

Although the number of subjects in our analysis is relatively small, we found the performance of FEV_6 in diagnosing a restrictive pattern to be similar to FVC (Table 4). We did not make an independent assessment of restrictive disease using total lung capacity (TLC). One study demonstrated that a restrictive spirometry pattern was a poor predictor of a low TLC (the positive predictive value was 58%) (3). However, the absence of a restrictive pattern had a negative predictive value of 95.4% (3).

As expected, both FEV_6 and FEV_1/FEV_6 were more reproducible than FVC and FEV_1/FVC. The excellent performance of FEV_6 and FEV_1/FEV_6 and their reduced variability suggest they may have a statistical advantage in diagnosing airway obstruction. Using FEV_6 as a surrogate for FVC has several practical advantages: (*1*) Spirometry may be less demanding because patients would never have to be pushed to a 15- to 20-s exhalation. This may be especially important in older and impaired patients; (*2*) shorter expiratory times require less data storage space, an important issue for smaller, portable spirometers; and (*3*) the end of a test is more easily and explicitly defined. An explicitly defined end of test will allow a better correspondence between measured and reference values. Reference values are valid only when they are technically and biologically appropriate to the population being studied (2). For example, suppose a middle-aged patient who exhaled for only 7 s was compared with a patient whose reference values were based on an average expiratory time of 15 s. The FEV_1/FVC of the middle-aged patient would, on average, be falsely elevated because measured FVC would be underestimated. The result would be more false-negative results.

Two-thirds of the patients in our study had spirometry with an airway obstruction pattern. The findings of our study may not apply to populations with a different prevalence of obstruction. They would also directly apply only to an adult population able to exhale for 6 s. The 6-s exhalation criterion is an even larger problem for children who are frequently unable to exhale for 6 s but usually reach an expiratory plateau. One approach might be to consider FVC and FEV_6 equivalent when expiratory time is less than 6 s. In fact, this definition was used in the NHANES III spirometry reference value study although exhalation times of less than 6 s were uncommon in adults ([5], and J. Hankinson, personal communication). Valid reference comparisons for FEV_6, and FEV_1/FEV_6 are possible for adults and children as long as this definition is used. When expiratory time is less than 6 s and no plateau is reached, it may also be possible to predict a reasonably accurate FEV_6 by projecting the slope of the spirometric curve to 6 s.

Summary

This study demonstrates that FEV_6 is an acceptable surrogate for FVC in the diagnosis of airway obstruction in adults. FEV_6 may also be an acceptable surrogate for the spirometric diagnosis of restriction. In addition, FEV_6 has the practical advantages of simplifying testing procedures, reducing test variability, and possibly improving accuracy in the diagnosis of airway obstruction. If other laboratories confirm our observations, FEV_6 and FEV_1/FEV_6 may replace FVC and FEV_1/FVC in interpreting spirometry.

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