

Inspiratory Flow-Volume Curve Evaluation for Detecting Upper Airway Disease

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BACKGROUND: The 2005 American Thoracic Society/European Respiratory Society guidelines on spirometry emphasize examination of the inspiratory curve of the flow-volume loop for evidence of intrathoracic or extrathoracic upper airway obstruction. We sought to determine how frequently evaluations are performed for abnormal inspiratory curves. **METHODS:** We retrospectively reviewed all examinations performed in our pulmonary function testing laboratory over a 12-month period ($n = 2,662$). In patients with normal spirometry or a mild restrictive defect, we inspected the inspiratory curves for truncation, flattening, or absent loop. With patients who had an abnormal inspiratory curve, we examined 3 flow-volume loops to determine if more than one loop showed an inspiratory abnormality, and to assess changes in the mid-flow ratio (ratio of forced expiratory flow at 50% of the forced expiratory volume to forced inspiratory flow at 50% of the forced inspiratory volume), and we used the loop that had the best inspiratory and expiratory curves. We reviewed the medical records for underlying disease processes and evidence of upper airway evaluation. **RESULTS:** One hundred twenty-three patients (4.6%) had an abnormal inspiratory curve. Sixty-nine (56%) of those 123 patients had inspiratory abnormalities on > 2 flow-volume loops. Evaluation of the inspiratory abnormality was undertaken in only 17% of all patients, and 30% of patients who had consistently abnormal inspiratory curves. A specific etiology was identified in 52% of the evaluated patients. Vocal cord dysfunction was the most frequent diagnosis. Utilizing the loop that had the combination of the best inspiratory and expiratory curves decreased the mid-flow ratio from 3.07 ± 1.63 to 1.77 ± 1.15 . **CONCLUSIONS:** An abnormal inspiratory curve in the presence of otherwise normal spirometry should prompt an evaluation for the etiology. If one of the flow-volume inspiratory curves shows an abnormality, all the inspiratory curves from that PFT session should be reviewed, and if more than one inspiratory curves is abnormal, both anatomical and functional evaluation should be undertaken for intrathoracic and extrathoracic upper airway obstruction. *Key words:* inspiratory curve, upper airway obstruction, pulmonary function testing. [Respir Care 2009;54(4):461–466]

Introduction

The 2005 American Thoracic Society (ATS)/European Respiratory Society (ERS) guidelines on spirometry em-

phasize the flow-volume loop as a possible indicator of intrathoracic or extrathoracic upper airway obstruction.¹ Use of the flow-volume loop for detection of obstructing lesions of the upper and central airways (defined as the airway from the glottis to the main carina) was first re-

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ported in 1973 by Miller and Hyatt,² who described 3 distinct patterns. Flattening of the expiratory limb suggested variable intrathoracic obstruction; flattening of the inspiratory limb suggested variable extrathoracic obstruc-

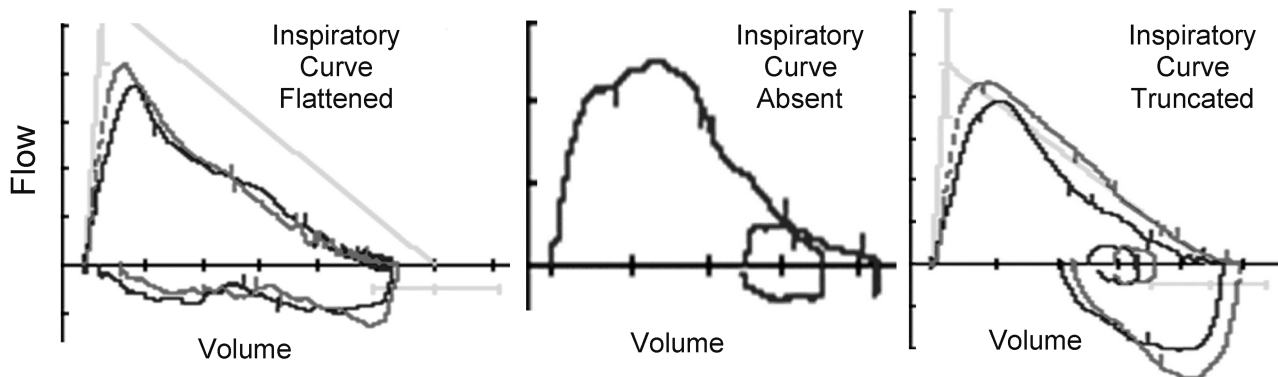


Fig. 1. Flow-volume loops with characteristic abnormalities of the inspiratory curve: flattened, absent, and truncated.

tion; and flattening of both limbs suggested a fixed airway obstruction.² However, the flow-volume loop is an insensitive indicator of central and upper airway obstruction. Early studies suggested that a lesion must narrow the tracheal lumen to < 8 mm (a $\geq 80\%$ tracheal narrowing) before abnormalities can be detected.³ The flow-volume loop indicates the functional (rather than anatomic) severity of the obstruction. Despite this limitation, spirometry is simple and readily available, so the flow-volume loop is useful if an upper airway lesion is suspected.^{4,5}

A wide variety of conditions have been reported to be associated with an abnormal inspiratory flow-volume curve.⁶⁻⁸ Anatomical abnormalities include tracheal stenosis, tumor, goiter, chronic infection, obstructive lung disease, and anastomoses in lung-transplant recipients.^{9,10} Functional abnormalities include vocal cord paralysis, sleep disorders, neuromuscular disorders, and vocal cord dysfunction.¹¹⁻¹⁴ However, few systematic studies have evaluated the clinical utility of the inspiratory flow-volume curve to detect airway lesions.^{4,15} Though studies have examined a single etiology (eg, goiter) for inspiratory-curve changes, there have been few studies of abnormal inspiratory curve as an indicator of disease. We reviewed pulmonary function test (PFT) results that had one or more abnormal inspiratory curves, to determine if upper airway evaluation was performed and whether a functional or anatomical airway obstruction was present.

Methods

This protocol was reviewed and approved by our hospital's institutional review board. In October 2005 to Sep-

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tember 2006, we reviewed PFT results from the electronic database that contains all PFT studies. All spirometry (Vmax22, Viasys Health Care/Cardinal Health, Dublin, Ohio) was in accordance with ATS standards, and included a standard forced maximal exhalation, followed by a forced maximal inhalation. The best expiratory effort was selected by the spirometry system's software. All the PFT results had been previously interpreted by a staff pulmonologist, with the National Health and Nutrition Examination Survey (NHANES) III reference values, with calculated 95% confidence intervals based on recommended ATS standards. Each report contained one flow-volume loop that had been chosen for interpretation based on the best expiratory effort. PFTs that had evidence of obstruction or restriction (suggested by a forced vital capacity of $< 70\%$ of predicted, based on the NHANES III reference values) were excluded from the analysis.

We selected PFTs on the appearance of the inspiratory curve. We looked for 3 types of inspiratory-curve abnormality: absent, truncated (early termination of the curve), or flattened (lack of normal concavity) (Fig. 1). Each inspiratory curve was reviewed by 2 investigators, to reach agreement on lack of concavity or truncation. No other variables were considered. When their interpretations differed, the reviewers discussed the curve and reached a consensus agreement. From the PFT results we recorded the forced expiratory volume in the first second, forced vital capacity, and mid-flow ratio (ie, the ratio of forced expiratory flow at 50% of the forced expiratory volume to forced inspiratory flow at 50% of the forced inspiratory volume). We also noted whether the official original interpretation of the PFT specifically commented on the appearance of the inspiratory curve.

With each PFT that had an abnormal inspiratory curve, we reviewed 3 flow-volume loops from that PFT session to determine how many of those loops showed an inspiratory abnormality.

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Table 1. Patient Demographics

	Entire Study Sample	All 3 Inspiratory Curves Abnormal	2 of 3 Inspiratory Curves Abnormal	1 of 3 Inspiratory Curves Abnormal	<i>P</i>
Patients (<i>n</i>)	123*	47	22	54	NA
Male (<i>n</i>)	65	29	12	24	NA
Female (<i>n</i>)	58	18	10	30	NA
Age (mean ± SD y)	48.8 ± 16.5	45.8 ± 16.2	44.7 ± 19.6	53.0 ± 14.7	.04
Body mass index (mean ± SD kg/m ²)	28.6 ± 5.3	28.1 ± 5.3	26.9 ± 4.6	29.7 ± 5.3	.08

* Patients who had ≥ 1 abnormal inspiratory flow-volume curve.
 NA = not applicable because not important in this context

To determine whether flow-volume loop selection affected the mid-flow ratio value, all PFTs were reanalyzed based on the loop that had both the best inspiratory and the best expiratory effort (based on the appearance of the 3 loops in that PFT).

We then reviewed the medical records to determine the extent of clinical evaluation for the abnormal inspiratory curve. We documented: indication for initial spirometry; repeat PFTs; chest and neck imaging (radiograph and computed tomogram [CT]); clinical and functional evaluation of the upper airway by pulmonary, otolaryngology, and/or speech pathology services; clinical diagnosis after evaluation; and associated conditions (eg, gastroesophageal reflux disease, seasonal allergic rhinitis, asthma, and obstructive sleep apnea [OSA]).

Analysis was performed with statistics software (SPSS 11.5, SPSS, Chicago, Illinois). We used a paired-sample *t*-test to compare the mean mid-flow-ratio value from the initial PFT interpretations to that from our reinterpretation based on the best inspiratory/expiratory flow-volume curve. We used 1-way analysis of variance with Bonferroni correction to compare the mean values for age, body mass index, and spirometry in 3 subgroups: those who had only 1 abnormal inspiratory curve; those who had 2 abnormal inspiratory curves; and those who had 3 abnormal inspiratory curves. *P* values < .05 were considered significant.

Results

We reviewed 2,662 PFTs. If a patient had multiple PFTs, we considered only the first of those PFTs. One hundred twenty-three patients (4.6%) had an abnormal inspiratory curve without indications of obstruction or greater than mild restriction (Table 1). Among those 123 patients, 54 patients had only one abnormal inspiratory curve (which suggests one poor inspiratory effort rather than an a functional or anatomical pathology); 22 patients had an abnormal

inspiratory curve on 2 of 3 loops; and 47 patients had an abnormal inspiratory curve on all 3 loops.

Physicians from the pulmonary clinic ordered 69% (85/123) of the PFTs that included an abnormal inspiratory curve. Nonpulmonary providers requested the other 31% (38/123). Only 37% of the initial interpretations included a comment about the inspiratory curve.

Table 2 summarizes the PFT results. Per our laboratory protocol, the initial interpretation used the loop with the best expiratory curve. Using the loop with the best overall inspiratory and expiratory curves significantly changed the mean mid-flow-ratio value. As expected, with the use of the loop that had the best inspiratory curve there was a significant decrease in mid-flow ratio, from 3.07 ± 1.63 to 1.77 ± 1.15 in the total group (*P* < .001), and in each subgroup (*P* < .001). The number of PFTs with mid-flow ratio > 2.2 decreased from 75 (65.8%) to 29 (23.8%).

Table 3 describes the clinical evaluations and diagnoses relative to the subgroups that had 1, 2, or 3 inspiratory-curve abnormalities. As documented in their medical records, only 21 of the patients (17%) underwent evaluation of the upper airway. If only patients who had more than one inspiratory-curve abnormality (*n* = 69) are included, the percentage evaluated increases to 30%. However, the clinical evaluation pertained specifically to the inspiratory-curve abnormality in only 16 of those 21 patients (13% of the total group). Many of the patients were evaluated in the pulmonary clinic for reasons other than dyspnea, and consequently underwent chest CT. Thyroid function testing was commonly performed in those patients, but unrelated to the flow-volume loop abnormality. Fifty-two percent, or 11/21, had a specific diagnosis, and 48% (10/21) did not. Overall, these 21 patients predominantly had vocal cord disorders: 8 with vocal cord dysfunction, 2 with vocal cord paralysis, and 1 with multiple sclerosis. The other 10 patients did not have a specific abnormality identified but had associated conditions that

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Table 2. Pulmonary Function Test Results

	Entire Study Sample (n = 123)	All 3 Inspiratory Curves Abnormal (n = 47)	2 of 3 Inspiratory Curves Abnormal (n = 22)	1 of 3 Inspiratory Curves Abnormal (n = 54)	P
Initial PFT values					
FEV ₁ (mean ± SD % predicted)	89.7 ± 12.5	90.8 ± 12.1	89.5 ± 8.5	88.8 ± 14.3	.71
FVC (mean ± SD % predicted)	90.1 ± 12.8	91.9 ± 12.6	89.1 ± 10.9	89.0 ± 13.7	.50
FEV ₁ /FVC (mean ± SD %)	99.7 ± 6.1	99.1 ± 6.8	100.9 ± 5.5	99.8 ± 5.7	.20
Mid-flow ratio (mean ± SD)	3.07 ± 1.63	3.39 ± 1.65	3.04 ± 1.23	2.78 ± 1.75	.19
Mid-flow ratio ≥ 2.2 (% of PFTs)	65.8	61.0	66.7	69.2	—
Best overall flow-volume loop					
Mid-flow ratio (mean ± SD)	1.77 ± 1.15	2.52 ± 1.54	1.78 ± 0.58	1.12 ± 0.49	< .001
Mid-flow ratio ≥ 2.2 (% of PFTs)	23.8	28.3	31.8	16.7	—

FEV₁ = forced expiratory volume in the first second
 FVC = forced vital capacity
 Mid-flow ratio = ratio of forced expiratory flow at 50% of the forced expiratory volume to forced inspiratory flow at 50% of the forced inspiratory volume
 PFT = pulmonary function test

Table 3. Clinical Evaluation and Diagnoses

	Entire Study Sample	All 3 Inspiratory Curves Abnormal	2 of 3 Inspiratory Curves Abnormal	1 of 3 Inspiratory Curves Abnormal
Patients (n)	123	47	22	54
Diagnostic studies (n and %)				
Upper-airway evaluation	21 (17)	8 (17)	8 (36)	5 (9)
Pulmonary evaluation	81 (66)	35 (74)	14 (64)	32 (59)
Otolaryngology evaluation	10 (9)	4 (9)	3 (14)	3 (6)
Chest computed tomogram	50 (41)	15 (32)	11 (50)	24 (44)
Neck imaging	6 (5)	2 (4)	1 (5)	3 (6)
Upper-airway endoscopy	18 (15)	6 (13)	7 (32)	5 (9)
Thyroid function testing	74 (60)	25 (53)	12 (55)	37 (69)
Diagnoses (n)				
Vocal-cord dysfunction	8	0	6	2
Neuromuscular	3	0	0	3
Reflux disease	5	4	0	1
Obstructive lung disease	3	1	2	0
Allergic rhinitis or sleep apnea	2	0	0	2

might have contributed to an abnormal inspiratory curve: 5 had gastroesophageal reflux disease, 3 had obstructive lung disease, 1 had OSA, and 1 had seasonal allergic rhinitis. Associated conditions in the entire cohort included gastroesophageal reflux disease (40%), OSA (19%), asthma (13%), and seasonal allergic rhinitis (8%).

Discussion

The inspiratory flow-volume curve is important and may help interpret pulmonary symptoms or upper airway disease. The most recent joint ATS/ERS guidelines emphasize the flow-volume loop as one indicator of possible

central and upper airway obstruction.¹ However, in the loops that were chosen on the basis of best expiratory effort, nearly 50% of the abnormal inspiratory curves were probably due to one poor inspiratory effort, rather than a pathology, because in those PFT sessions only one of the 3 loops had an abnormal inspiratory curve. Among the patients who had more than one abnormal inspiratory curve, only 20% underwent an evaluation for central or upper airway obstruction, and their diagnoses were primarily functional airway diseases, such as vocal cord dysfunction, not anatomical obstruction.

Though the ATS/ERS guidelines specifically state that “special attention should be paid by the technicians to

obtain maximal and repeatable PEFs [peak expiratory flows] and forced inspiratory maneuvers if there is a clinical or spirometric reason to suspect upper airway obstruction," that practice is seldom followed.¹ In accordance with ATS standards, the spirometry system software selects the loop with best expiratory effort for interpretation. In our laboratory we rarely perform a separate forced inspiratory maneuver. Our data suggest that in nearly 50% of PFTs in which the best expiratory effort is chosen by the software, there is an isolated abnormal inspiratory curve that suggests one poor effort, not central or upper airway obstruction. The clinician should routinely study the flow-volume loops from all the inspiratory and expiratory maneuvers to see how many of the loops show similar abnormalities, and should comment on a repeatable inspiratory-curve abnormality.

Early case series described inspiratory-curve abnormalities and reduced flow in patients with various causes of intrathoracic and extrathoracic upper airway obstruction, including tracheal stenosis, airway tumors, and bilateral vocal cord paralysis.¹⁶⁻¹⁸ Those authors asserted that reduced inspiratory flow is a "sensitive" indicator of central and upper airway obstruction, and that a reduced mid-flow ratio was diagnostic. The inspiratory curve has since been reported to be abnormal in many causes of chronic upper-airway obstruction, including laryngeal abnormalities, neuromuscular disease, airway burns, vocal cord dysfunction, obstructive sleep apnea, goiter, mediastinal disease, and bronchial anastomosis. For example, Miller et al found that 31% of patients with known goiter had an abnormal flow-volume loop that suggested central or upper airway obstruction.¹⁹

Though the classic description of flow-volume loop abnormalities has been well-reported in those diseases, there have been few studies of the utility of the flow-volume loop for diagnosing upper airway disease. Vincken and Cosio evaluated 40 patients with flow oscillations (reported to be indicative of OSA) and found that 16 of 31 patients had a structural disorder of the upper airway.²⁰ The only prospective study on flow-volume loop analysis evaluated 37 self-selected veterans of the 1991 Persian Gulf war, and compared them to 38 control subjects.¹⁵ They were found to have a higher mid-flow ratio (1.37 ± 0.44) than the control group (0.88 ± 0.33), and the mid-flow ratio was > 1.0 in 32 of 37 patients. Bronchoscopy revealed chronic laryngeal and tracheal inflammation in the 17 patients who underwent bronchoscopy, but did not reveal other causes of central or upper airway obstruction. The flow-volume loop has also been useful in monitoring response to treatment in various settings, such as goiter, laryngeal reconstruction, and mediastinal disease.^{19,21,22}

Of particular note in the present study is the frequency of functional abnormalities that cause upper airway obstruction, including vocal cord paralysis, OSA, neuromus-

cular disorders, and vocal cord dysfunction, which were more common than anatomical abnormalities. The largest percentage of our patients had vocal cord dysfunction, which has been a commonly reported cause of inspiratory curve truncation since the first series of 5 patients was described in 1983.²³

In patients with refractory asthma symptoms and upper-airway stridor, inspiratory curve truncation is commonly reported to be extremely helpful in suggesting vocal cord dysfunction. However, flow-volume loop abnormalities have been described in only 28% of all vocal cord dysfunction patients.²⁴ Vocal cord dysfunction can be intermittently symptomatic, and the flow-volume loop is very often normal in the absence of active vocal cord dysfunction symptoms such as wheezing, stridor, dyspnea, chest pain, or voice loss. The utility of the flow-volume loop for predicting vocal cord dysfunction has not been prospectively evaluated, but several studies confirmed its low predictive value. In a study of vocal cord dysfunction in young military personnel with exertional dyspnea, 20% of the patients had an abnormal flow-volume loop at rest, and 80% had exacerbation of vocal cord dysfunction during exercise.²⁵ Newman et al reported on the largest series of 95 patients with vocal cord dysfunction; the incidence of abnormal flow-volume loop in asymptomatic patients was 23%, whereas others reported that 25% of their patients with irritant-induced vocal cord dysfunction had abnormal flow-volume loops at baseline.^{14,26}

An early clinical study of 9 patients with central and upper airway obstruction found decreased ratio of mid-inspiratory flow to mid-expiratory flow.¹⁷ In their landmark study of 43 patients with known central and upper airway obstruction, Miller and Hyatt used the ratio of mid-inspiratory flow to mid-expiratory flow to group airway obstruction into fixed airway lesions (ratio 0.85), variable extrathoracic obstruction (ratio 2.20), and variable intrathoracic obstruction (ratio 0.32).² Other flow ratios, such as the ratio of forced expiratory volume in the first second to peak expiratory flow, have also been advocated.²⁷⁻²⁹

Couriel et al established normal values for the mid-flow ratio in a large pediatric population, but compared those 514 children to only 10 patients with known diagnoses of central and upper airway obstruction.³⁰ There are no other studies of a large population with central and upper airway obstruction to validate the mid-flow ratio as predictive. In our study, in which the majority of loops suggested variable extrathoracic obstruction, a mid-flow ratio > 2.2 was a poor predictor of airway obstruction: only 60% of patients with reproducible inspiratory-curve abnormalities had a mid-flow ratio > 2.2 at baseline, and this decreased to 28% when the best inspiratory curve was chosen. This suggests that the mid-flow ratio can be highly variable, based on the loop chosen for interpretation, and is not predictive of central or upper airway obstruction.

The applicability of the present study is limited, given its retrospective nature. Only 13% of the patients underwent an upper airway evaluation. We were unable to determine the true prevalence of either functional or anatomical airway abnormalities in our population. Given the intermittent nature of some functional upper airway-obstruction diseases (eg, vocal cord dysfunction), a single PFT may not find any abnormalities. Furthermore, we excluded patients who had any airway obstruction or greater than mild restriction, because of the difficulty of evaluating the inspiratory curve with concomitant decreases in inspiratory and expiratory flow.

Conclusions

An abnormal inspiratory curve is a common finding on routine spirometry. If the PFT results include one abnormal inspiratory curve, all the flow-volume loops from that PFT should be carefully reviewed. Nearly 50% of our patients had one poor inspiratory effort, which rarely indicated upper airway disease. However, even when the inspiratory curves were consistently abnormal, upper-airway evaluation was infrequent. Functional causes of central or upper airway obstruction are more likely than anatomical causes. A prospective evaluation of abnormal inspiratory curves is needed to determine their clinical importance.

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