Comparison of Expiratory Isovolume Pressure-Flow Curves With the Stop-Flow Versus the Esophageal-Balloon Method

Derya C Coursey PhD, Steven M Scharf MD PhD, and Arthur T Johnson PhD

BACKGROUND: Expiratory isovolume pressure-flow curves allow determination of flow limitation and airway resistance, but obtaining an isovolume pressure-flow curve requires placing an esophageal balloon. The stop-flow method of obtaining isovolume pressure-flow curves is easy and noninvasive. OBJECTIVE: To compare the stop-flow and esophageal-balloon methods by measuring the differences between the pressures and flows at which flow limitation first occurs. METHODS: In 5 healthy subjects we used the esophageal-balloon method and the stop-flow method at 25%, 50%, and 75% of vital capacity (VC), and constructed isovolume pressure-flow curves showing the pressure at which the flow became limited during forced expiration. RESULTS: The mean calculated pleural pressure at flow limitation with the stop-flow method was 2.7 times and 1.6 times that via the esophageal-balloon method at 25% of VC and 50% of VC, respectively. The maximum flow at flow-limitation with the stop-flow technique was 0.7 times and 0.6 times that via the esophageal-balloon method at 25% of VC and 50% of VC, respectively. We also calculated the resistance (the inverse of the slope of the line to the point of flow limitation), but there were large variations in the resistance values, so there was no statistically significant relationship between the stop-flow and esophageal-balloon methods. CONCLUSION: The stop-flow method showed potential to noninvasively obtain isovolume pressure-flow curves. *Key words: flow limitation; isovolume pressure-flow curve; stop-flow method; pulmonary function; esophageal balloon; expiratory flow.* [Respir Care 2011;56(7):969–975.

Introduction

Maximum expiratory flow-volume curves were first constructed[1,2] to demonstrate effort independence of maximum expiratory flow at lower lung volumes. It was determined that there was an upper limit to expiratory flow at low lung volumes.[1] In order to understand the mechanisms of flow limitation, isovolume pressure-flow curves were constructed,[2] in which, at any given lung volume, at increasing efforts, flow was plotted as a function of esophageal pressure. From these curves it was observed that at lower efforts, flow increased as pressure increased, but reached a plateau, such that further increases in pressure (effort) were not associated with increased flow.[1,2] Further, it was demonstrated that the pressure at which the maximum flow is reached depends on the volume, being higher at higher lung volumes.[1,2]

At a given lung volume, once the maximum flow was reached, flow was dependent on the difference between the driving alveolar pressure, alveolar pressure, and surrounding pressure (pleural pressure measured via esophageal balloon) (ie, transpulmonary pressure), and independent of the total pressure drop from alveolus to atmosphere.[3,4] Flow limitation was later explained according to the relationship between the speed of transmission of the impulse wave and the speed of sound (wave-speed) in the fluid.[5]

Early and accurate diagnosis requires a clear understanding of respiratory mechanics. In a diseased lung that

Drs Coursey and Johnson are affiliated with the Fischell Department of Bioengineering, University of Maryland, College Park, Maryland. Dr Scharf is affiliated with the Division of Pulmonary and Critical Care Medicine, University of Maryland, School of Medicine, Baltimore, Maryland.

Dr Johnson has a patent on the air-flow perturbation device required for the stop-flow method. The other authors have disclosed no conflicts of interest.

Correspondence: Derya C Coursey PhD, Fischell Department of Bioengineering, Jeong H Kim Engineering Building, University of Maryland, College Park MD 20742. E-mail: deryacalhan@yahoo.com.

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Table 1. Subjects

Subject	Age (y)	Height (cm)	Weight (kg)	FVC (L)	FVC (%)*	FEV_1 (L)	FEV_1 (%)*	FEV_1/FVC (%)
1	22	185	88	5.95	98	4.24	84	71
2	21	183	68	5.07	86	3.78	77	75
3	29	183	91	4.57	79	3.98	84	87
4	20	168	104	5.53	112	4.51	108	82
5	21	188	91	5.57	89	4.86	94	87

* Percent of predicted, per Hankinson et al.[13]
FVC = forced vital capacity

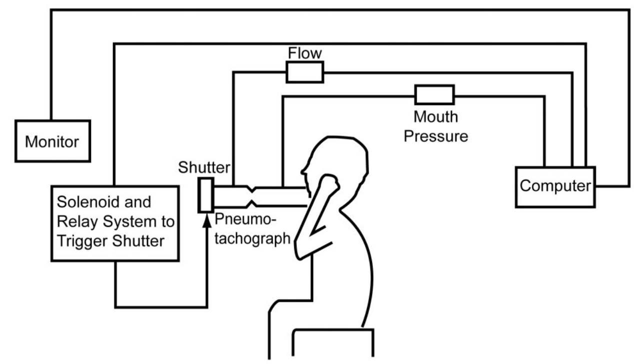

Fig. 1. Stop-flow experimental setup.

is not diagnosed at an early stage, the tissue changes in such a way that it cannot be repaired. In order to understand how diseases cause pathophysiological changes, it is important to understand the pressure-flow relationship of a healthy lung. Isovolume pressure-flow curves allow determination of both flow limitation and airway resistance and the effect of disease or treatment on these. Classically, obtaining pressure-flow curves requires rather complicated techniques, including placing an esophageal balloon.[6] Research on obstructive airways disease progression or regression with treatment might be facilitated by an easy, noninvasive technique for obtaining pressure-flow curves. An alternative method[4] for measuring pressure-flow curves is a modification of the classic flow-interruption technique.[7-12] This technique is based on the idea that during brief airway occlusion alveolar pressure equilibrates with mouth pressure.

In the present study we used a method similar to the flow-interruption technique[4] to obtain pressure-flow curves, and we compared them to pressure-flow curves obtained with the esophageal-balloon method. The focus was the predictability of pressure at which flow limitation occurs with the stop-flow method. We hypothesized that the stop-flow method and the esophageal-balloon method would yield the same pressure and flow at which flow becomes limited at any given lung volume.

Methods

Subjects

From our laboratory personnel we recruited 5 male subjects who had no history of respiratory disease (Table 1). All subjects gave written informed consent and filled out a medical history questionnaire. The study was approved by the University of Maryland institutional review board.

Stop-Flow Method

Figure 1 shows the stop-flow setup. The shutter positioned behind the pneumotachograph was built to control the mouth pressure at a desired lung volume, and was controlled by 2 solenoids: one to open the shutter, and the other to close it. There was a monitor in front of the subject so he could see his mouth pressure signal and maintain the desired mouth pressure.

We measured air flow with a pneumotachograph that was originally used in a 1993 model constant-volume body plethysmograph (Collins, Ferraris Respiratory, Louisville, Colorado). We tested the pneumotachograph for linear response[14] and daily calibrated it with a 3-L syringe. We used a differential pressure transducer (5-inch D-4V, All Sensors, Morgan Hill, California) with a range of ± 12.7 cm H_2O to correlate the pressure differential from the pneumotachograph to flow. We also measured the mouth pressure with a differential pressure transducer (ASCX05DN, Honeywell, Morristown, New Jersey, ± 350 cm H_2O). Data acquisition was with a 14-bit data-acquisition device (NI USB-6009, National Instruments, Austin, Texas), with a sampling rate of 1,000 Hz during the stop-flow experiments and 100 Hz during the esophageal-balloon experiments. We used graphics software (Labview 7, National Instruments, Austin, Texas) to manipulate and graph the data.

The shutter was triggered with a solenoid relay assembly (Fig. 2). We connected 2 push/pull-type solenoids (7110-2A, Dormeyer, Vandalia, Ohio) to a 3.8-cm knife gate valve that was used as the shutter. The digital output signal came from the data-acquisition card. Since the signal did not have enough power to trigger the relays, we used voltage followers. This signal fed into 2 solid state relays (SSRL240, Omega, Stamford, Connecticut) that eventually controlled the solenoid movement. Via analysis of high-speed video, we found that the valve closed in 27 ms and opened in 19 ms.

The subject was seated during the experiments, and held a round cardboard mouthpiece in his mouth, while wearing a nose clip. The subject was instructed to inhale to total lung capacity and then signal the technician. During forced expiration, at a preselected percent of vital capacity (VC), the shutter closed and the subject made a steadily increas-

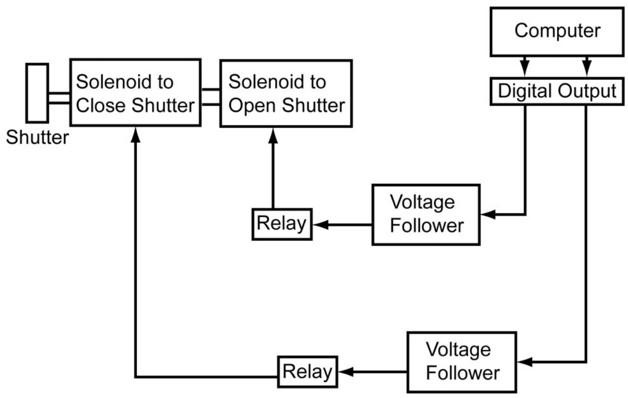

Fig. 2. Solenoid relay assembly that controls the shutter in the stop-flow method.

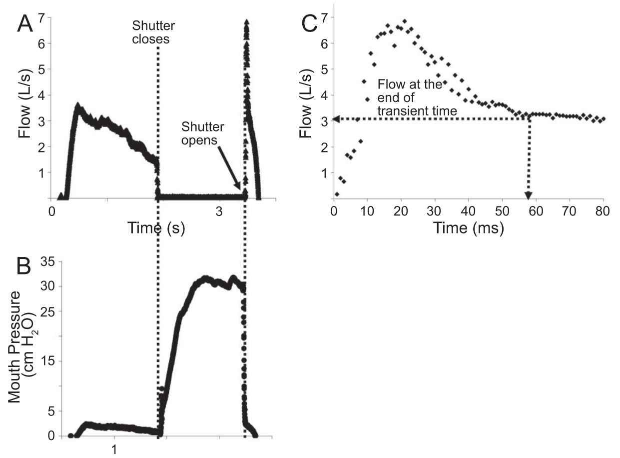

Fig. 3. Flow and pressure curves from the stop-flow method. A: Initial forced expiration. B: Mouth pressure recording. C: Transient flow after shutter opening.

ing effort to increase the pressure against the closed shutter, until the pressure reached a preset value, at which point the shutter opened again. The pressure just before the shutter opened was correlated with the flow at the end of the transient time of shutter opening. At each lung volume we obtained pressure measurements in 10-cm H_2O increments, up to 80 cm H_2O. Not all subjects were capable of generating mouth pressure as high as 80 cm H_2O. With those subjects we ended the experiment at the highest achievable mouth pressure.

During the stop-flow experiments the flow after shutter opening had a transient time of 30–70 ms after achievement of maximum flow (Fig. 3). The transient time was relatively constant for each subject but varied from one subject to another. The transient time was determined via visual inspection, to determine the flow at the end of the transient time and to correlate it with the mouth pressure before shutter opening.

Esophageal-Balloon Method

In the esophageal-balloon-method experiments we used the same experimental setup as in the stop-flow experiments, except that, instead of using the shutter assembly, we placed an esophageal balloon catheter (86-cm closed-end catheter with a 9.5-cm balloon, Cooper Surgical, Trumbull, Connecticut),[6] connected to a differential pressure transducer (143PC03D, Honeywell, Morristown, New Jersey, pressure test range ± 2.5 psi). A minimum volume of air has to be used in the balloon and catheter to transmit pleural pressure at the level of the balloon to the pressure transducer. We measured the pressure-volume characteristics of the balloon to determine how much air to inject into the system without affecting the measured pressure. The esophageal balloon-catheter had a flat pressure response up to a volume of 3 mL, so we injected 1 mL of air into the balloon in all the trials.

We instructed the subject to breathe out from total lung capacity to residual volume, with different effort levels, and we obtained correlated pleural pressure and flow values at each effort level and each lung volume. By testing the subject many times with different effort levels we obtained enough data points to construct the pressure-flow curves at 25%, 50%, and 75% of VC.

Pressure-Volume Relationship of the Lung

We constructed standard static pressure-volume curves by having the subject breath up to total lung capacity from residual volume. As the subject exhaled, we interrupted the flow for approximately 2 seconds, over a range of lung volumes. We plotted lung volume as a function of transpulmonary pressure (mouth pressure at zero flow minus esophageal pressure).

Constructing the Pressure-Flow Curves

An expiratory pressure-flow curve plots flow against driving pressure at a given lung volume. Driving pressure is changed at any given lung volume by changing the expiratory effort. We constructed pressure-flow curves for 25%, 50%, and 75% of the VC. Driving pressure is expressed as the esophageal pressure, which we assumed was equal to the pleural pressure. Thus, for the esophageal-balloon studies, we constructed pressure-flow curves with the directly measured esophageal-balloon pressure on the abscissa and the measured flow on the ordinate. In the stop-flow studies we calculated the esophageal pressure by subtracting the transpulmonary or elastic recoil pressure (obtained from the static pressure-volume curves described above) from the directly measured mouth pressure at the given lung volumes.

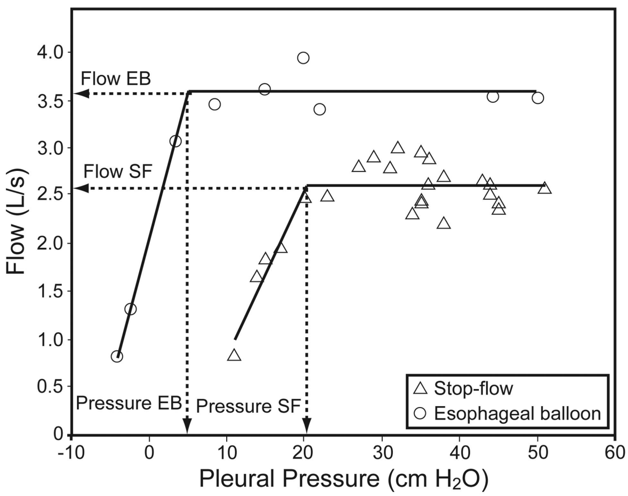

Fig. 4. Isovolume pressure-flow values from subject 2, at 25% of vital capacity. The horizontal dashed lines indicate the flows at the point of flow limitation. The vertical dashed lines indicate the pressure at the point of flow limitation (mouth pressure with the stop-flow method, and esophageal pressure with the esophageal-balloon method).

When there is flow limitation, a pressure-flow curve has 2 lines that intersect at the point where the flow becomes limited (Fig. 4). The line drawn through points after the limited flow has a slope of zero. To identify the pressure and flow at the limited-flow condition, we wrote a program (with MatLab, MathWorks, Natick, Massachusetts) to find the best-fit least-squares straight lines that could be drawn through the points. Figure 4 shows an example of fitted lines for the 2 methods, and the limited flows and the pressures at the onset of flow limitation.

Resistance Calculations

Another important piece of information to calculate with a pressure-flow curve is the resistance at which flow becomes limited. We calculated the resistance by finding the inverse of the slope of the line drawn to the point of flow limitation for each pressure-flow curve. This gave us additional means to investigate the relationship between the 2 methods. The goal was to observe whether the 2 methods gave the same resistance at flow limitation. If the resistances were the same, it would be another convincing step toward the use of the stop-flow method for obtaining pressure-flow curves. We tested the association between the resistances with linear regression, with the least-squares technique.

Statistical Analysis

We used the unpaired *t* test for unequal variances to compare the difference between the pressure and flow at which flow became limited for the stop-flow and esophageal-balloon methods. The null hypothesis was tested for rejection at the 5% level, and we report differences between the 2 measurements as mean ± SD.

Table 2. Mouth Pressure, Pleural Pressure, and Flow at the Point of Flow Limitation During the Stop-Flow Experiments

Subject	Lung Volume (% of VC)	Mouth Pressure (cm H_2O)	Pleural Pressure (cm H_2O)	Flow (L/s)
1	25	18.1	9.6	2.2
	50	28.7	15.0	4.2
	75	35.1	18.6	6.1
2	25	25.4	20.4	2.6
	50	41.8	33.0	4.5
	75	No flow limitation		
3	25	19.9	15.4	1.8
	50	35.0	25.0	4.1
	75	36.3	21.3	4.8
4	25	12.7	5.9	1.3
	50	19.8	9.6	2.2
	75	30.0	14.5	3.9
5	25	32.7	27.8	3.4
	50	No flow limitation		
	75	No flow limitation		

VC = vital capacity

Results

Stop-Flow Pressure-Flow Curves

We obtained mouth pressure and pleural pressure versus flow curves for all the subjects, at 25%, 50%, and 75% of VC (Table 2). All subjects reached flow limitation at 25% of VC. However, flow limitation was reached by only 4 subjects at 50% of VC, and by only 3 subjects at 75% of VC.

Esophageal-Balloon Pressure-Flow Curves

For each subject we plotted the pleural pressure (measured via esophageal balloon) versus flow curves at 25%, 50%, and 75% of VC (Table 3). At 25% and 50% of VC all the subjects had flow limitation, but at 75% of VC only one subject had flow limitation.

Comparison of the Pressure-Flow Curves

Both methods demonstrated expected features of flow limitation (see Tables 2 and 3). First, as lung volume increased, the pressure at which flow became limited also increased. Second, as lung volume increased, higher flows were measured at flow limitation, with both methods.

Table 3. Pressure and Flow at the Point of Flow Limitation During the Esophageal-Balloon Experiments

Subject	Lung Volume (% of VC)	Pressure (cm H_2O)	Flow (L/s)
1	25	–1.6	2.6
	50	9.4	6.5
	75	No flow limitation	
2	25	5.1	3.6
	50	11.7	6.7
	75	No flow limitation	
3	25	13.2	3.0
	50	19.5	6.0
	75	25.1	8.7
4	25	0.8	2.9
	50	11.9	6.7
	75	No flow limitation	
5	25	11.3	4.6
	50	16.8	9.3
	75	No flow limitation	

VC = vital capacity

We compared the pressure-flow curves from the 2 methods at 25% and 50% of VC, because flow limitations could be observed accurately with both methods at low lung volumes. Tables 4 and 5 show the pressure and flow values and the means and standard deviations at the onset of flow limitation at 25% and 50% of VC. From Tables 4 and 5 we make 2 observations. First, with the stop-flow method the calculated pleural pressure at flow limitation was greater than the pressure measured with the esophageal-balloon method, in all the subjects except subject 4, who had a slightly lower calculated pleural pressure with the stop-flow method at 50% of VC. Second, with the stop-flow method the measured flow at flow-limitation was always lower than with the esophageal balloons. The differences between the pleural pressures at flow limitation with the 2 methods were 10.1 ± 6.3 cm H_2O at 25% of VC and 7.5 ± 9.9 cm H_2O at 50% of VC. There was no statistically significant difference between the means of the calculated pleural pressure at flow limitation with the stop-flow method and the esophageal-balloon pressure at flow limitation at 25% of VC ($P = .08$) or at 50% of VC ($P = .25$).

The differences between the flows were −1.1 ± 0.4 L/s at 25% of VC and −2.7 ± 1.2 L/s at 50% of VC. The flows were significantly different at 50% of VC ($P = .01$), but not at 25% of VC ($P = .06$).

Resistance

The inverse of the slope of the line, resistance, which was drawn from zero flow to the point of flow limitation with the stop-flow and esophageal-balloon methods, was calculated for each subject when flow-limitation was demonstrated on the pleural pressure versus flow curve. At 50% of VC, resistance measured with the stop-flow method (stop-flow resistance) was higher than with the esophageal-balloon method (esophageal-balloon resistance) in all the subjects. At 25% of VC, stop-flow resistance was higher than esophageal-balloon resistance in 4 subjects (Fig. 5). There was no statistically significant correlation between stop-flow resistance and esophageal-balloon resistance, due to the high variation in the calculated resistances.

Discussion

Maximum expiratory flow is used to diagnose various respiratory diseases.[1,2] Isovolume pressure-flow curves might also be useful for diagnosing and following obstructive lung diseases, if they were as easy to obtain as maximum expiratory flow-volume curves. Since the pressure-flow curve shows the pressure-flow relationship, it could be possible to observe the change in lung mechanics and how fast that change is occurring. This might help to take preventive measures before those changes become irreversible. Another use of pressure-flow curves could be to observe the effect of various treatments on lung mechanics, which could help individualize treatment for each patient.

The classic method of obtaining a pressure-flow curve is invasive because it requires an esophageal balloon. In this study we obtained pressure-flow curves with the classic method and the stop-flow method. Though the behavior of pressures and flows at the points of flow limitation was that expected with changes in lung volume with both methods, there were substantial differences between the values measured with the 2 methods. On average, the calculated pleural pressure at flow limitation with the stop-flow method was 2.7 times and 1.6 times the esophageal-balloon pressure at flow limitation at 25% and 50% of VC, respectively. The stop-flow limited flow was 0.7 times and 0.6 times the esophageal balloon limited flow at 25% and 50% of VC, respectively.

The main assumption of the stop-flow method is that when the shutter is opened the alveolar pressure remains the same during the transient time of flow settlement. Most likely, the alveolar pressure decreases during that time. During the stop-flow experiments, the pressure before the shutter was closed correlated with the flow after shutter opening. If the alveolar pressure was changing after shutter opening, the flow after shutter opening might not correlate with the pressure before the shutter opening, so the pressure would be overestimated, which would result in higher pressure at flow limitation. This effect was demonstrated previously,[5] by measuring (with an esophageal balloon) the change in alveolar pressure after shutter open-

Table 4. Pressure and Flow at the Onset of Flow Limitation at 25% of Vital Capacity

Subject	Stop-Flow Method			Esophageal-Balloon Method	
	Mouth Pressure ($cm\ H_2O$)	Pleural Pressure ($cm\ H_2O$)	Flow (L/s)	Pleural Pressure ($cm\ H_2O$)	Flow (L/s)
1	18.1	9.6	2.2	–1.6	2.6
2	25.4	20.4	2.6	5.1	3.6
3	19.9	15.4	1.8	13.2	3.0
4	12.7	5.9	1.3	0.8	2.9
5	32.7	27.8	3.4	11.3	4.6
Mean ± SD	21.8 ± 7.6	15.8 ± 8.7	2.3 ± 0.8	5.8 ± 6.4	3.3 ± 0.8

Table 5. Pressure and Flow at the Onset of Flow Limitation at 50% of Vital Capacity

Subject	Stop-Flow Method			Esophageal-Balloon Method	
	Mouth Pressure ($cm\ H_2O$)	Pleural Pressure ($cm\ H_2O$)	Flow (L/s)	Pleural Pressure ($cm\ H_2O$)	Flow (L/s)
1	28.7	15.0	4.2	9.4	6.5
2	41.8	33.0	4.5	11.7	6.7
3	34.9	25.0	4.1	19.5	6.0
4	19.8	9.6	2.2	11.9	6.7
Mean ± SD	31.3 ± 9.3	20.7 ± 10.4	3.8 ± 1.0	13.1 ± 4.4	6.5 ± 0.3

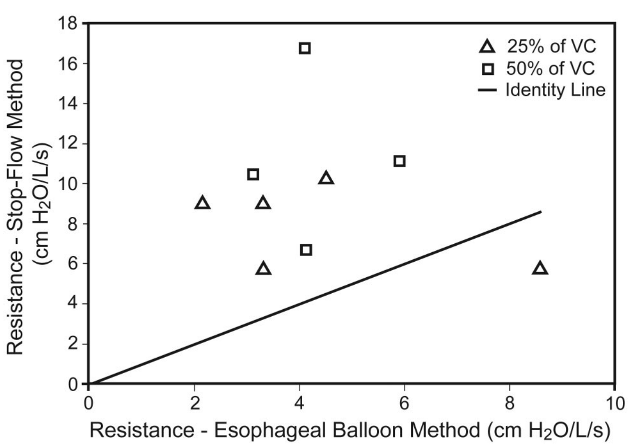

Fig. 5. Resistance with the esophageal-balloon method versus the stop-flow method, at 25% and 50% of vital capacity (VC). The identity line is the same at 25% and 50% of VC.

ing. During the 30 ms of transient time, the alveolar pressure fell 17% and 19% in the 2 subjects tested. Pride et al[4] assumed the transient time was constant for all the subjects tested, and it was 30 ms. They did not test what happens to the alveolar pressure if the transient time is longer. Most likely, the alveolar pressure decrease would be larger with a longer transient time. In the present study the transient time range was 30–70 ms and differed between subjects.

Another important observation was that the measured flow at flow limitation was lower with the stop-flow method, possibly because of the change in lung volume after shutter opening. In the stop-flow method the shutter closes at a specified lung volume. When the shutter opens, it is assumed that the lung volume does not change during the transient time. We tested this assumption by calculating the change in lung volume during the transient time, in 15 trials with one subject. The average change in VC (about 4,900 mL) was 170 ± 51 mL (approximately 4%) at 70% of VC. We concluded that the change in lung volume was not large enough to cause a big difference between the stop-flow limited flow and the esophageal-balloon limited flow. This change could be attributed to the high gas pressure in the lung during flow measurement, and gas flowing out of the lung during the transient time.[4]

One drawback of the stop-flow method is that it could be time-consuming; some of the subjects we tested had difficulty keeping their mouth pressure constant. However, when these subjects observed their mouth pressure on a monitor, they could relate their effort level to a pressure value, which helped to obtain more consistent values.

Another limitation of the stop-flow method is the subjectivity of determining the flow at the end of the transient time. However, the flow is relatively constant at the end of the transient time (see Fig. 3). Future studies should use blinded multiple observers to account for inter-observer and intra-observer variability

Conclusions

Though there were differences in the pressures and flows at flow limitation between the 2 methods, the stop-flow method shows the potential to noninvasively obtain useful pressure-flow curves, as long as one is aware of the differences between the methods.

REFERENCES

1. Hyatt RE, Schilder DP, Fry DL. Relationship between maximum expiratory flow and degree of lung inflation. J Appl Physiol 1958; 13(3):331-336.
2. Fry DL, Hyatt RE. Pulmonary mechanics: a unified analysis of the relationship between pressure, volume and gasflow in the lungs of normal and diseased human subjects. Am J Med 1960;29(4):672-689.
3. Mead J, Turner JM, Macklem PT, Little JB. Significance of the relationship between lung recoil and maximum expiratory flow. J Appl Physiol 1967;22(1):95-108.
4. Pride NB, Permutt S, Riley RL, Bromberger B. Determinants of maximal expiratory flow from the lungs. J Appl Physiol 1967;23(5): 646-662.
5. Dawson SV, Elliott E. A Wave-speed limitation on expiratory flow —a unifying concept. J Appl Physiol 1977;43(3):498-515.
6. Milic-Emili J, Mead J, Turner JM, Glauser EM. Improved technique for estimating pleural pressure from esophageal balloons. J Appl Physiol 1964;19(2):207-211.
7. Mead J, Whittenberger JL. Evaluation of airway interruption technique as a method for measuring pulmonary air-flow resistance. J Appl Physiol 1954;6(7):408-416.
8. Shephard RJ. Mechanical characteristics of the human airway in relation to use of the interrupter valve. Clin Sci 1963;25:253-280.
9. Jackson AC, Milhorn HT,Norman JR. A reevaluation of the interrupter technique for airway resistance measurement. J Appl Physiol 1974;36(2):264-268.
10. Ohya N, Huang J, Fukunaga T, Toga H. Airway pressure-volume curve estimated by flow interruption during forced expiration. J Appl Physiol 1989;67(6):2631-2638.
11. Clements JA, Sharp JT, Johnson RP, Elam JO. Estimation of pulmonary resistance by repetitive interruption of airflow. J of Clin Invest 1959;38(7):1262-1270.
12. Miyamoto Y, Nakabayashi T, Mikami T. Electronic device for the recording of isopressure flow-volume (i.p.f.v.) curves. Med Biol Eng Comp 1978;16(1):83-89.
13. Hankinson JL, Odencrantz JR, Fedan KB. Spirometric reference values from a sample of the general us population. Am J Respir Crit Care Med 1999;159(1):179-187.
14. Coursey D. Respiratory mechanics of flow limitation and characterization of resistance measurements with a non-invasive device. PhD Dissertation. College Park, MD: University of Maryland; 2009. http://drum.lib.umd.edu/handle/1903/9272. *Accessed May 10, 2011.*