

Detection of Expiratory Flow Limitation by Manual Compression of the Abdominal Wall

VINCENT NINANE, DMITRI LEDUC, SOPHIA ABDEL KAFI, MARWAN NASSER, MYRIAM HOUA, and ROGER SERGYSELS

Chest, Neurology, and Intensive Care Services, Saint-Pierre University Hospital, Brussels, Belgium

We have assessed a new method, manual compression of the abdominal wall (MCA) during expiration, in the detection of expiratory flow limitation. Twelve stable patients with chronic obstructive pulmonary disease (COPD) and five normal subjects were studied during spontaneous breathing in the supine and seated posture. MCA was performed during expiration with one hand at the umbilical level and we measured flow, volume, pleural (Ppl) and gastric (Pga) pressures and abdominal anteroposterior (AP) diameter at the umbilical level with magnetometers. No increase in expiratory flow during MCA relative to the preceding breath despite associated increases in pressures was considered as indicating expiratory flow limitation. In seven additional patients with increased upper airway collapsibility (obstructive sleep apnea syndrome [OSAS]), MCA was compared with negative expiratory pressure (NEP). In normal seated subjects, MCA was associated with a decrease in abdominal AP dimension (mean \pm SD: $-27 \pm 6\%$), an increase in Pga (14.7 ± 7.4 cm H₂O) and Ppl (6.2 ± 2.2 cm H₂O), and an increase in expiratory flow. MCA caused similar changes in abdominal AP dimension and pressures in seated patients with COPD but six of them (50%), including four patients with FEV₁ less than 1 L, had no increase in expiratory flow. In the supine posture, MCA always increased expiratory flow in normal subjects but four additional patients with COPD showed evidence of flow limitation. MCA invariably increased expiratory flow in patients with OSAS whereas the NEP method suggested flow limitation in some cases. We conclude that MCA is a very simple method that allows detection of flow limitation in different positions.

Patients with chronic obstructive pulmonary disease (COPD) often exhibit flow limitation that may cause dynamic pulmonary hyperinflation. This condition is associated in particular with an increased work of breathing at a time when the efficiency of inspiratory muscles is decreased (1, 2) and may also be an important determinant of dyspnea (3). These deleterious consequences as well as possible therapeutical implications (1) contribute to explain why efforts have been made to develop techniques that can detect flow limitation.

With expiratory flow limitation, increases in the driving pressure corresponding to the difference between alveolar and airway opening pressures fail to increase expiratory flow. Detection of expiratory flow limitation, then, requires comparisons of spontaneous breathing with forced expiratory flow-volume curves (4). There are, however, three potential limitations. The first is related to thoracic gas compression during forced expiration such that the registration of expired volume lags lung volume and the true maximal expiratory airflow is under-

estimated at any given lung volume. This gas compression artifact could in theory lead to a false-positive comparison (5). The second limitation relates to differences in the volume and time history that precede tidal expiration and forced expiratory maneuvers (6). Forced vital capacity maneuvers can record lower flows than forced expiratory maneuvers initiated from the usual end-inspiratory position. Implications are that comparisons of spontaneous breathing with forced vital capacity maneuvers may then also lead to false-positive results and overestimation of flow limitation. Third, a method that increases the alveolar-airway opening pressure difference by negative pressures applied at the airway opening during expiration by a special device (negative expiratory pressure [NEP]) (7–10) may cause upper airway collapse and again a false comparison with spontaneous expirations (11).

We were looking for a technique that would avoid these three potential false-positive comparisons, the first by employing a small gradient of pressure, the second by employing a maneuver that does not change the antecedent volume and time history, and the third by employing positive airway pressure rather than negative. We reasoned that manual compression of the abdominal wall (MCA), by roughly mimicking abdominal muscle contraction, may cause an inward displacement of the abdomen, as well as a rise in abdominal pressure that may result, provided the diaphragm is relaxed, into a cranial displacement of this muscle into the thorax and a rise in pleural pressure (Ppl). On a theoretical basis, this compression applied at the beginning of spontaneous expiration could then generate a very limited increase in alveolar gas pressure without changing the antecedent volume and time history. In addition, this method based on an increase in alveolar pressure rather than decreased airway opening pressure should not show artifact related to increased upper airway collapsibility. With this in mind, we have measured in normal subjects and patients with COPD, the effects of MCA on abdominal dimensions, gastric pressure (Pga) and Ppl as well as on flow and lung volume in different body positions. The potential limitation associated with upper airway problems was also assessed by comparing MCA and NEP in patients with obstructive sleep apnea syndrome (OSAS).

METHODS

Five normal subjects and 12 COPD patients without snoring or suspicion of OSAS as well as a third group of seven patients with OSAS were studied. The five normal subjects were males ranging in age from 26 to 43 yr (Subjects A through E; see Table E1: online-only supplement). They were recruited from hospital personnel and were aware of the purpose of the study. None had any history of cardiopulmonary or neuromuscular disease and their spirometry were within normal limits. The 12 patients with COPD (9 men, 3 women; see Table E1 in online data supplement) had a well-defined history of chronic airflow obstruction and no significant renal, hepatic, cardiovascular, or neuromuscular disease. They were all smokers or ex-smokers. FEV₁ was less than 1 L in four patients, and it ranged between 0.50 and 2.80 L. None of these patients had a history of asthma and they were in a medically stable condition for at least 4 wk when they were evaluated. Maximal inspiratory and expiratory flow-volume

(Received in original form April 13, 2000 and in revised form October 30, 2000)

D. Leduc was the recipient of a research fellowship from the Vésale Foundation, Brussels, Belgium.

Correspondence and requests for reprints should be addressed to Vincent Ninane, M.D., Chest Service, Saint-Pierre University Hospital, Rue Haute, 322, 1000 Brussels, Belgium. E-mail: Vincent_NINANE@stpierre-bru.be

This article has an online data supplement, which is accessible from this issue's table of contents online at www.atsjournals.org

Am J Respir Crit Care Med Vol 163, pp 1326–1330, 2001
Internet address: www.atsjournals.org

ume curves were also measured and compared with tidal breath; for this purpose, inspired and expired gas volumes were obtained by integration of flow at the mouth. The seven patients with OSAS (5 men, 2 women; Table E1) had an average apnea-hypopnea index of 61 ± 22 and were treated by nasal continuous positive airway pressure (nCPAP). They had no history of chronic airflow obstruction or asthma and their spirometers were within normal limits. All patients gave informed consent to the procedures as approved by the human studies committee of the institution.

MCA Maneuvers

The subjects were asked to breathe room air through a mouthpiece with the noseclip on and MCA tests were performed when they showed regular breathing. For this purpose, the investigator put one hand gently on the abdominal wall of the subject with the palm on the umbilicus oriented perpendicular to the axis between the xiphoid process and the pubis. Gentle palpation of the abdomen during two or three breathing cycles easily allowed recognition of the expiratory phase. The investigator then informed the subject that he was soon going to push on his abdominal wall. He subsequently exerted at the onset of expiration a firm compression in the anteroposterior (AP) direction that was maintained throughout expiration and afterwards, he removed his hand. MCA was performed in both the supine and seated position and the order of position was selected at random. In the supine position, the flap at the head end of the couch was in fact raised to an angle of approximately 20° and the head was supported on a pillow.

Measurements in Normal and COPD Patients

Airflow was measured with a heated Fleisch pneumotachograph connected to a Validyne differential pressure transducer (Validyne Corp., Northridge, CA) and volume was obtained by integration of the flow signal. Esophageal pressure (Pes) and Pga were measured with conventional balloon-catheter systems placed respectively in the midesophagus and in the stomach. The gastric balloon contained 2.0 ml of air and the esophageal balloon was filled with 0.5 ml of air. The respiratory changes in AP diameter of the abdomen were measured with a pair of linearized magnetometers (Van Herle, Brussels, Belgium) that were attached on the midline, 2 cm above the umbilicus. Between 6 and 10 MCA were performed in each subject, in each position and these maneuvers were separated by a period of regular breathing lasting at least 2 min. All the signals were registered on an eight-channel recorder (type WR3801; Graphtec Corp., Tokyo, Japan) and the flow-volume tracing was also continuously displayed on an X-Y recorder (Hewlett Packard 7046A; Palo Alto, CA) allowing comparison of the loops during MCA test with the previous control breath. Changes in abdominal AP diameter during MCA were expressed in centimeters as well as in percentage of the diameter measured during the preceding control end-expiration (diameter at end-expiration [DEE]). The associated increase

in Pga was measured as the increase in Pga relative to the pressure measured during the preceding control expiratory phase.

Measurements in OSAS Patients

Expiratory flow limitation was assessed with a computerized NEP technique (MICRO 5000+NEP; Medisoft, Dinant, Belgium). Flow-volume curve during application of 4 cm H₂O negative pressure at the mouth throughout expiration was compared with the flow-volume curve of the previous control expiration and the effect of MCA was measured with the same system. In each subject, five NEP and five MCA tests were performed in random order in each posture.

Unless otherwise specified, results are expressed as mean \pm SD. Wilcoxon test was used to assess the effect of position and Mann-Whitney U test to compare between normals and patients with COPD. The criterion for statistical significance was taken as $p < 0.05$.

RESULTS

Effect of MCA in Normal Subjects and in Patients with COPD

Figure 1 shows the effects of MCA in a normal subject (Subject E; see Table E1) breathing in the seated position: the decrease in abdominal AP diameter associated with MCA resulted in an increase in Pga and Ppl and an expiratory flow that increased more rapidly toward higher peak values than during the preceding control breath. Relative to the preceding control breath, the MCA flow-volume loop (Figure 1, right panel) showed an increased expiratory flow over the entire range of control tidal expiration. For the whole group of five seated normal subjects (Table 1), MCA was associated with a mean decrease in abdominal AP diameter of -7.7 ± 1.7 cm ($-27 \pm 6\%$ DEE) and a mean increase in Pga and Ppl of 14.7 ± 7.4 and 6.2 ± 2.2 cm H₂O, respectively. Flow-volume loop comparisons always revealed increased expiratory flow.

Figure 2 illustrates the effects of MCA in one representative patient with severe COPD (Patient 10): despite a major decrease in abdominal AP dimension and an increase in Pga and Ppl, no change in expiratory flow was observed as illustrated by the superimposed flow-volume loops in the right part of the figure. For the whole group of 12 seated patients with COPD, the decrease in abdominal AP dimension during MCA averaged -10.1 ± 5.3 cm (or $-26 \pm 10\%$ DEE) with an increase in Pga and Ppl averaging 17.2 ± 6.9 and 6.3 ± 4.0 cm H₂O, respectively. These results were not statistically different from the results observed in the normal seated subjects. MCA showed expiratory flow limitation over the entire range of

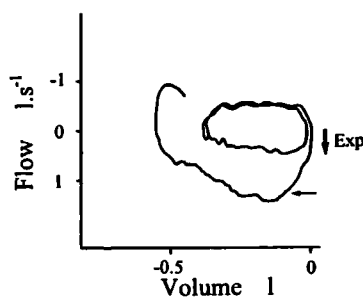
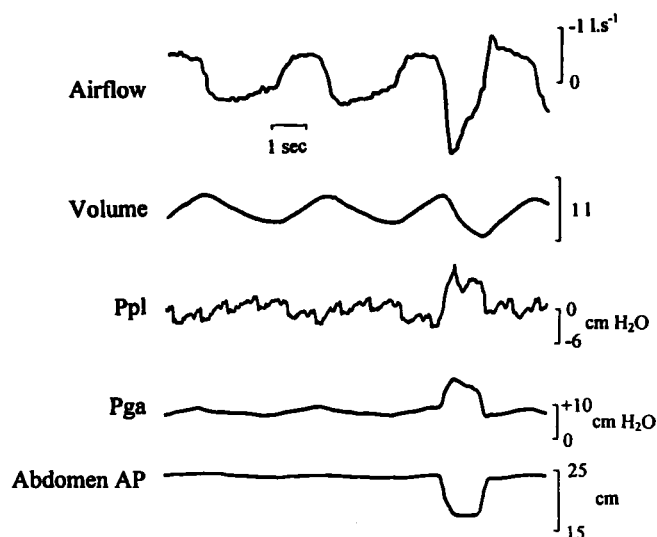


Figure 1. Left: record of airflow, volume, Ppl, and Pga and of abdominal AP diameter in a representative normal subject (Subject E) during resting breathing in the seated position and during MCA during expiration. Right: record of the flow-volume curves during this MCA test (arrow) and during the preceding control breath. Exp = expiration.

TABLE 1. EFFECTS OF MANUAL COMPRESSION OF THE ABDOMINAL WALL DURING EXPIRATION IN NORMAL SUBJECTS AND PATIENTS WITH COPD IN THE SEATED POSITION*

	Normal Subjects (n = 5)	COPD Patients (n = 12)
Δ AP abd, cm	-7.7 ± 1.7	-10.1 ± 5.3
Δ AP abd, %	-27 ± 6	-26 ± 10
Δ Pga, cm H ₂ O	14.7 ± 7.4	17.2 ± 6.9
Δ Ppl, cm H ₂ O	6.2 ± 2.2	6.3 ± 4.0
Flow limitation	0/5	6/12

Definition of abbreviations: Δ AP abd = changes in anteroposterior diameter of the abdomen; Δ Pga and Δ Ppl = changes in gastric and pleural pressures.

* Results are expressed as mean \pm SD.

control tidal expiration (Figure 2) in six seated patients with COPD, who in fact included all the four patients with a FEV₁ lower than 1 L. In the six other COPD patients in the seated posture, MCA did not reveal expiratory flow limitation.

Analysis of the superimposed flow-volume curve during resting breathing with the flow-volume curve obtained during forced expiratory vital capacity, however, suggested flow limitation in 10 of the 12 patients with COPD. These 10 patients included the six who were flow-limited on the basis of the MCA test but, clearly, the method based on the comparisons of spontaneous breathing with forced vital capacity maneuver led to false-positive results in four patients with COPD because MCA in these patients was associated with increased expiratory flow.

Changing position from seated to supine was associated with a decrease in end-expiratory abdominal AP diameter in both the normal subjects (28 ± 1 versus 25 ± 3 cm; $p < 0.05$) and the patients (37 ± 11 versus 31 ± 11 cm; $p < 0.05$). In the normal supine subjects, MCA was associated with similar changes in abdominal AP dimension and pressures and always caused an increase in expiratory flow. In the 12 supine COPD patients, MCA caused similar changes in abdominal AP diameter as in the seated position but the associated changes in Pga were higher (23 ± 7 versus 17 ± 7 cm H₂O; $p < 0.05$) despite similar changes in Ppl. The six patients who were flow-limited when seated showed similar results in the supine position. Four additional patients, however, showed evidence of flow limitation in the supine position. In one of them, flow limitation was present during the entire range of control tidal expiration whereas in the three other patients, it was only present during the lower part of this range (Figure 3).

Reproducibility and Tolerance of the MCA Test

As shown in Figure 4 illustrating the different MCA maneuvers performed in the same representative subject (4A) or COPD patient (4B), the comparison with the preceding control breath always allowed consistent interpretations with repeated tests in each subject. None of the normal subjects or patients with COPD reported abdominal pain associated with MCA. As illustrated in Figure 5, one COPD patient in the supine position (Patient 4) reacted to the MCA test by contracting the inspiratory muscles such that a paradoxical inspiratory flow was observed but this reflex contraction disappeared as soon as she was asked not to try to resist abdominal wall compression. As a consequence of MCA too, some patients (including the previous patient) also showed reflex glottic closure that was easily recognized by a rapid decrease of expiratory flow toward zero on the test flow-volume curve (Figure 5) but this reflex closure was only observed in four of the 12 patients and in eight of the total number of 197 MCA tests performed in the 12 patients in both positions.

MCA and NEP Tests in Patients with Increased Upper Airway Collapsibility

Figure 6 shows the superimposed flow-volume curves of MCA or NEP tests and of the preceding control breath in one patient with OSAS (Patient 6; see Table E1). Flow limitation was suggested by the NEP test during part of tidal volume in both seated and supine posture whereas MCA always caused clear-cut increase in expiratory flow. Two additional patients with OSAS (Patients 4 and 7) showed evidence of flow limitation when supine, on the basis of the NEP test only.

DISCUSSION

According to our initial hypothesis, compression of the abdominal wall with one hand, by grossly mimicking the mechanical action of the abdominal muscles, invariably caused an increase in Pga and Ppl and thereby, an increase in the pressure gradient between the alveolar and the airway opening. As a consequence, this test performed in the normal subject was systematically associated with an increase in expiratory flow (Figure 1). By contrast, we were unable to increase expiratory flow using this maneuver in some patients with COPD (Figure 2), including those with the most severe disease (FEV₁ < 1) despite clear-cut increases in gastric and pleural pressures. As previously reported (3, 9), we found that expiratory flow limi-

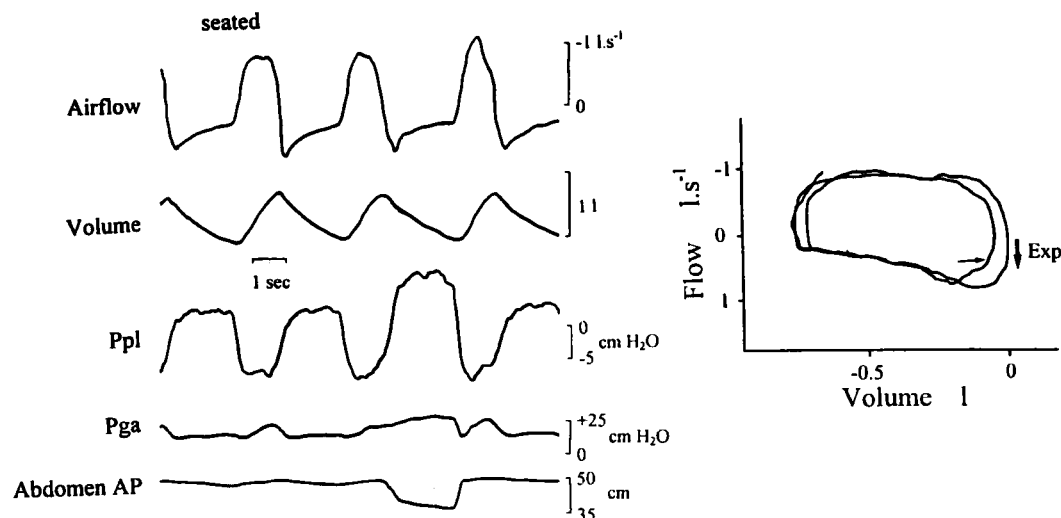


Figure 2. Left: record of airflow, volume, Ppl and Pga and of abdominal AP diameter in a representative patient with COPD (Patient 10) breathing at rest in the seated position and then, during MCA during expiration. Right: corresponding record of the flow-volume curves during the MCA test (horizontal arrow) and during the preceding control breath. In this patient, MCA does not increase expiratory flow despite a decrease in abdominal AP dimension, an increase in Pga and Ppl. Exp = expiration.

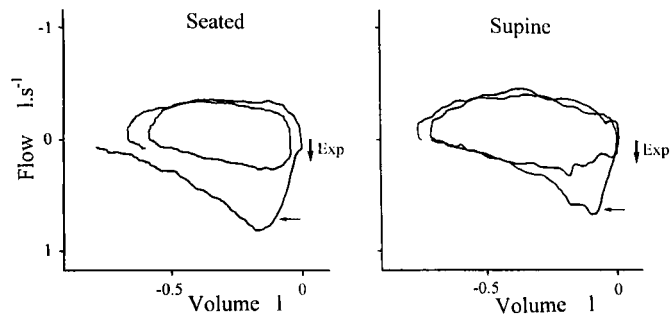


Figure 3. Record of flow–volume curves in a representative patient with COPD in the seated (left) or supine (right) position. The horizontal arrow indicates the test flow–volume curves. MCA failed to increase expiratory flow in this patient in the supine position only; this limitation was confined to the lower part of tidal breath.

tation at rest was more frequent in COPD in the supine than seated position, because of the associated decrease in FRC. The increase in Pga during MCA always exceeded that of Ppl (Figures 1 and 2, Table 1) and this finding may be related at least in part to the fact that pressure was exerted with the palm on a small part of the abdominal wall such that Pga increase may in fact cause a paradoxical increase in abdominal dimensions elsewhere. In infants, imposed compressions using inflatable vest around the chest and upper abdomen have also been used trying to infer the presence of flow limitation (12). One of the techniques used, the tidal volume rapid thoracoabdominal compression, shows some similarities with our method because imposed thoracoabdominal compression is used to generate expiratory flow–volume curves from end-tidal inspiration (12). The compression flow–volume curve and the preceding control breath are superimposed using end-

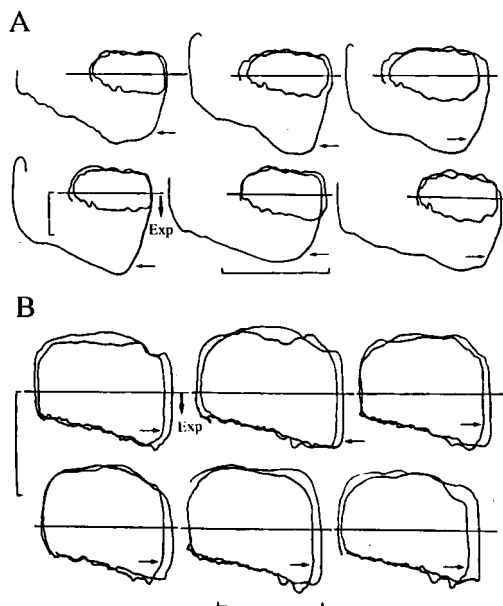


Figure 4. (A) Superimposed flow–volume curves during test (arrows) and during the preceding control breath obtained during six tests in a representative normal subject (Subject E) during resting breathing in the seated position. Horizontal lines represent the zero flow. Note that the MCA test was always associated with a clear-cut increase in expiratory flow. Flow scale: $1 \text{ L} \cdot \text{s}^{-1}$; volume scale: 1 L. (B) Superimposed flow–volume curves during six MCA tests in a patient with COPD (Patient 1). Same conventions and scale as in Figure 4, A.

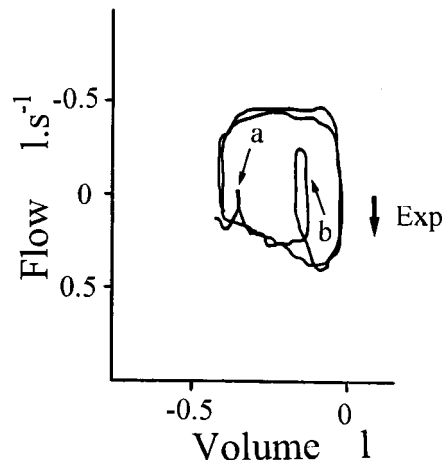


Figure 5. Record of flow–volume curves during MCA and during the preceding control breath in Patient 4 during resting breathing in the supine position. In this patient, this particular test was associated at the onset of expiration with an inspiratory effort resulting in an inspiratory flow (b) and at the end of the maneuver with a reflex glottic closure associated with a rapid decrease in expiratory flow toward zero (a).

inspiration as the anchor point and the maximal expiratory flow is measured at FRC. With this method, flow limitation is evidenced by the observation that, despite increase in jacket pressure, expiratory flow at FRC does not increase.

The magnitude of the pressure exerted by the investigator on the abdominal wall was not calibrated, and this factor certainly contributes to the variability of the mechanical effects between as well as within subjects. Indeed, even if the decrease in abdominal AP dimension during the MCA test averaged for the whole group of COPD patients in the seated position 26% DEE, this value ranged between 4% (Patient 3) and 37% (Patient 6) and changes in Ppl (mean value: 6.3 ± 4.0) ranged between 1.3 (Patient 5) and 12 cm H₂O (Patient 6). It is then possible that in some maneuvers associated with the largest changes in intrathoracic pressure, superimposition of the flow–volume curves of the control and test breaths may be related to gas compression rather than to “true” flow limitation. One might expect, however, if thoracic gas compression played a

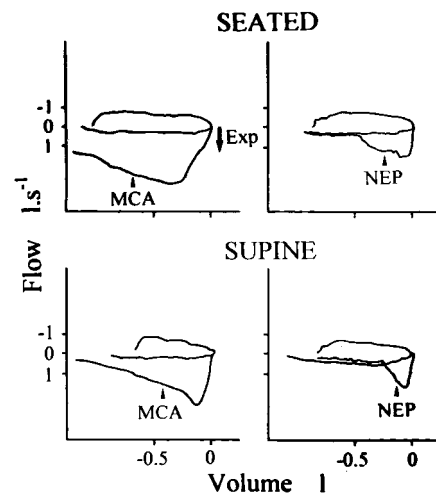


Figure 6. Comparison of control flow–volume curves with flow–volume loops during MCA or NEP in one patient with OSAS in both the supine and seated positions.

significant role, that the lack of standardization of the abdominal compression maneuver could lead to conflicting results in one given subject. In contrast, the comparison of MCA flow–volume loop with the preceding control breath always allowed qualitative reproducible interpretations in any given subject (Figure 4).

The repeated and unanticipated abdominal compression during a series of spontaneous breaths also ensures that differences in time and volume history between the preceding control breath and the MCA breath are negligible. By contrast, the method based on the comparison between the flow–volume curves during resting breathing and during forced expiratory vital capacity shows limitations related to gas compression and changes in time and volume history (5, 6), and this explains the discrepancy we observed between the results of the latter technique and the MCA method. Indeed, with the method based on comparisons between forced expiratory vital capacity and spontaneous expiration, 10 of our 12 patients with COPD showed flow limitation but in four of them (40%), MCA was able to increase expiratory flow. In a previous study (9), the NEP technique that shows no limitation related to gas compression and volume and time history, caused an increase in expiratory flow in a similar proportion (5 of 16, 31%) of patients classified as limited on the basis of the comparison of the resting flow–volume curves with the maximal expiratory flow–volume curves.

One major advantage of the MCA test is that it requires no special device. It also does not require the patient's collaboration and is well tolerated. In particular, abdominal pain was never encountered. The only artifact that was occasionally observed was a reflex glottic closure that was however easily suspected on the basis of flow–volume loop assessment. One may, however, suggest that increase in upper airway resistance without closure can occur during MCA in some individuals and limit expiratory flow, but the observation that expiratory flow in normal subjects was always clearly increased during MCA argues against this hypothesis. Occasional problems related to increased upper airway collapsibility have been described with the NEP technique. Indeed, pharyngeal structure is mainly constituted by muscles whose tone is lower during expiration than during inspiration (13) and Liistro and colleagues (11) have recently reported that snorers and patients with OSAS who have increased upper airway collapsibility, often showed when asleep flow limitation during application of -5 cm H_2O expiratory pressure. In some of them, flow limitation during NEP was present in the supine position only, presumably because upper airway resistance is affected by posture and is higher in the supine than seated position (14). We were able to reproduce Liistro's observations with the NEP technique in some patients with OSAS. In contrast, MCA in the latter patients was always associated with an increase in expiratory flow in both the supine and seated positions (Figure 6). If the theoretical advantages of the NEP technique are related to the fact that the level of pressure as well as the time when it is applied can be precisely chosen, on the other side, the MCA technique requires no special device and does not seem to be affected by increased upper airway collapsibility. With respect to this, these two techniques may in fact be complementary rather than exclusive: whenever one suspects upper airway problems, the MCA technique can be tried or vice versa.

Flow limitation is probably responsible for the highest degree of dynamic hyperinflation and intrinsic positive end-expiratory pressure (PEEPi) (1). To the extent that PEEPi represents a threshold load and is associated with an increased inspiratory work of breathing, several investigators have given external PEEP or continuous positive airway pressure (CPAP) in the belief that this would unload the inspiratory muscles and,

therefore, reduce the inspiratory work of breathing (15–17). In the spontaneously breathing patients with COPD or during assisted ventilation, however, PEEPi is difficult to measure and requires ideally the positioning of esophageal and gastric balloons (18, 19). With respect to this, MCA test would be very useful. Whenever this simple test that requires no special device confirms the absence of flow limitation, PEEPi measurement would probably not be required. Indeed, in cases of dynamic hyperinflation that are not related to flow limitation, application of external PEEP or CPAP may rather cause a further increase in hyperinflation and its deleterious consequences (20).

In conclusion, compression of the abdominal wall with one hand is a very simple method that allows the detection of flow limitation during spontaneous breathing in different body positions. This method requires neither the cooperation of the patient nor a body plethysmograph or any other special device and is not affected by upper airway collapsibility.

References

- Rossi A, Polese G, Brandi G, Conti G. Intrinsic positive end-expiratory pressure (PEEPi). *Intensive Care Med* 1995;21:522–536.
- Tzelepis G, McCool FD, Leith DE, Hoppin FG. Increased lung volume limits endurance of inspiratory muscles. *J Appl Physiol* 1988;64:1796–1802.
- Eltayara L, Becklade MR, Volta CA, Milic-Emili J. Relationship of chronic dyspnea and flow limitation in COPD patients. *Am J Respir Crit Care Med* 1996;154:1726–1734.
- Hyatt RE. The interrelationship of pressure, flow and volume during various respiratory maneuvers in normal and emphysematous patients. *Am Rev Respir Dis* 1961;83:676–683.
- Ingram RH, Schilder DP. Effect of gas compression on pulmonary pressure, flow and volume relationship. *J Appl Physiol* 1966;21:1821–1826.
- Milic-Emili J, Koulouris NG, D'Angelo E. Spirometry and flow-volume loops. *Eur Respir Mon* 1999;12:20–32.
- O'Donnell DE, Sani R, Anthonisen NR, Younes M. Effect of dynamic airway compression on breathing pattern and respiratory sensation in severe chronic obstructive pulmonary disease. *Am Rev Respir Dis* 1987;135:912–918.
- Valta P, Corbeil C, Lavoie A, Campodonico R, Koulouris NG, Chassé M, Braidly J, Milic-Emili J. Detection of expiratory flow limitation during mechanical ventilation. *Am J Respir Crit Care Med* 1994;150:1311–1317.
- Koulouris NG, Valta P, Lavoie A, Corbeil C, Chassé M, Braidly J, Milic-Emili J. A simple method to detect expiratory flow limitation during spontaneous breathing. *Eur Respir J* 1995;8:306–313.
- Koulouris NG, Dimopoulou I, Valta P, Finkelstein R, Cosio MG, Milic-Emili J. Detection of expiratory flow limitation during exercise in COPD patients. *J Appl Physiol* 1996;2:723–731.
- Liistro G, Veriter C, Dury M, Aubert G, Stancu D. Expiratory flow limitation in awake sleep-disordered breathing subjects. *Eur Respir J* 1999;14:185–190.
- ATS/ERS Workshop Summary. The raised volume rapid thoracoabdominal compression technique. *Am J Respir Crit Care Med* 2000;161:1760–1762.
- van Lunteren E, Van de Graaff WB, Parker DM, Mitra J, Haxhiu MA, Strohl KP, Cherniack NS. Nasal and laryngeal reflex responses to negative upper airway pressure. *J Appl Physiol* 1984;56:746–752.
- Anch AM, Remmers JE, Bunce HI. Supraglottic airway resistance in normal subjects and patients with occlusive sleep apnea. *J Appl Physiol* 1982;53:1158–1163.
- Smith TC, Marini JJ. Impact of PEEP on lung mechanics and work of breathing in severe airflow obstruction. *J Appl Physiol* 1988;65:1488–1499.
- Marini JJ. Should PEEP be used in airflow obstruction? *Am Rev Respir Dis* 1989;140:1–3.
- Petrof BJ, Legaré M, Goldberg P, Milic-Emili J, Gottfried SB. Continuous positive airway pressure reduces work of breathing and dyspnea during weaning from mechanical ventilation in severe chronic obstructive pulmonary disease. *Am Rev Respir Dis* 1990;141:281–289.
- Ninane V. "Intrinsic" PEEP (PEEPi): role of expiratory muscles. *Eur Respir J* 1997;10:516–518.
- Younes M. Dynamic intrinsic PEEP (PEEP_{i,dyn}): is it worth saving? *Am Med J Respir Crit Care* 2000;162:1608–1609.
- Tuxen DV. Detrimental effects of positive end-expiratory pressure during controlled mechanical ventilation of patients with severe airflow obstruction. *Am Rev Respir Dis* 1989;140:5–9.