ORIGINAL ARTICLE

Respiratory mechanics at different PEEP levels during general anesthesia in the elderly: a pilot study

E. MARANGONI [1], V. ALVISI [1], R. RAGAZZI [1], F. MOJOLI [2], R. ALVISI [1]
G. CARAMORI [3], L. ASTOLFI [1], C. A. VOLTA [1]

[1]Section of Anesthesia and Intensive Care, Department of Surgical, Anesthesiological and Radiological Science, University of Ferrara, Ferrara, Italy; [2]Policlinico S. Matteo, University of Pavia, Pavia, Italy; [3]Section of Respiratory Disease, Department of Clinical Medicine, University of Ferrara, Ferrara, Italy

ABSTRACT

Background. General anesthesia could imply that the closing capacity exceed the functional residual capacity. This phenomenon, associated with a reduction of maximal expiratory flow, could lead to expiratory flow limitation (EFL). The aim of our study was to verify 1) a new method of determining EFL during anesthesia (PEEP test); 2) if anesthesia could be associated with the development of EFL; 3) if the use a small amount of PEEP is able to reverse the possible negative effects of low lung volume ventilation.
Methods. Fifty two patients scheduled for abdominal surgery were prospectively randomized in: 1) group ZEEP, ventilated at PEEP 0 H_2O and 2) group PEEP ventilated at PEEP 5 cm H_2O. The presence of EFL was determined by the negative expiratory pressure (NEP) test the day before surgery and by the PEEP test during surgery. Data of respiratory mechanics were calculated at the beginning and at the end of anesthesia.
Results. 1) The PEEP test allows the detection of EFL; 2) anesthesia was associated with EFL: 8 patients developed EFL after induction. At the end of surgery, 7 more patients became flow limited in the group ZEEP, while only 1 in the group PEEP. The group ZEEP exhibited a marked decrease of expiratory flow and a worsening of respiratory mechanics at the end of surgery.
Conclusion. The PEEP test allowed to verify that EFL during anesthesia is a valuable phenomenon. The use of 5 cmH_2O of PEEP was helpful to prevent the deterioration of lung mechanics that occurs during surgery. *(Minerva Anestesiol 2012;78:1205-14)*

Key words: Anesthesia, general - Positive-pressure respiration - Respiratory mechanics.

General anesthesia is associated to a decreased functional residual capacity (FRC),[1] which is related to various mechanisms such as anesthesia induction by itself,[2] atelectasis development with high fraction of inspired oxygen,[3] muscle paralysis, supine position,[2, 4] increased extravascular lung water due to peri-operative fluids therapy and pro-inflammatory mediators produced during surgery.[5, 6] Moreover, this reduction of FRC can be enhanced by the presence of several co-morbidities, such as obesity or heart failure.[7, 8]

The reduction of FRC could imply that the closing capacity (CC) exceeds the FRC.[9] Leblanc *et al.* found a marked age-dependence of closing capacity.[9] The age-related increase of CC reflects both loss of lung recoil and decreased resistance to collapse of the peripheral airways.[10, 11] In supine position CC exceeds FRC at the mean age of about 44 years, because of the gravity-dependent decrease in FRC.[9] This phenomenon happens much earlier during anesthesia (about 30 years).[12] Hence

Comment in p. 1193.

the decreased FRC related to general anesthesia, associated with an unaltered CC,[13] renders older individuals more susceptible to "tidal airway closure", particularly in supine position.[12]

With advancing age there is a preferential reduction of maximal expiratory flow (V'max) at low lung volume.[14] Although the nature of this phenomenon is multifactorial, the increase in closing volume with advancing age probably plays a pivotal role. Indeed, since the peripheral airways close at higher lung volume in the elderly, their V'max decreases because the lung units served by the closed airways cease to contribute to expiratory flow. As a result of the preferential reduction of V'max in the tidal volume range, elderly patients are susceptible to tidal expiratory flow limitation (EFL), particularly in supine position.[15] The presence of tidal EFL implies increased inhomogeneity of ventilation distribution [16] with risk of peripheral airway injury, which is characterized histologically by rupture of the alveolar attachments to the respiratory bronchioles, damage of the brochiolarepithelium and increased number of polymorphonuclear leucocytes in the alveolar walls, and functionally by increased airway resistance.[17, 18] Hence it could be of clinical interest to verify whether a patient could develop EFL during surgery. In spontaneously breathing patients, the use of the negative expiratory pressure (NEP) test is considered the gold standard for detecting the presence of EFL. However, this test is cumbersome and difficult to apply in ventilated patients during anesthesia because of the use of a closed circuit and other technical difficulties (connection between the NEP system and the expiratory port of the ventilator). An alternative method has been previously proposed;[19] it is based on the variation of the tidal expiratory flow in presence or absence of low level of PEEPe. However, its application in the clinical setting is not established yet. The first aim of our study was to verify the ability of this method to detect the presence of EFL and, conversely, if anesthesia is associated with EFL in elderly patients undergoing major abdominal surgery.

Moreover, although postoperative impairment could be transient and respiratory function can recover shortly after surgery, some patients may develop respiratory complications both in the intraoperative or postoperative period. Postoperative pulmonary complications occur in 3 -10% of patients undergoing elective abdominal surgery.[20] We hypothesized that the consequence of low lung volume ventilation can be avoided by application of small levels of positive end expiratory pressure (PEEP). Hence the second aim of our study was to verify if the use of PEEP is able to reverse the negative effects of low lung volume ventilation eventually associated with EFL.

Materials and methods

Study population

Candidates for this prospective randomized study were patients with age >65 years undergoing major abdominal surgery from January to May 2010 at the S. Anna University Hospital of Ferrara. This study was approved by the ethics committee of our institution and informed consent was obtained from each subject. The EudraCT number is 2011-00513339.

Detection of expiratory flow limitation

The day before surgery, the presence of EFL was evaluated by using the NEP test. Patients were evaluated both in supine and seated position while breathing through a flanged mouthpiece and wearing a nose-clip. The NEP method used to detect tidal expiratory flow limitation has been previously described in detail.[21] Flow (V') was measured with heated pneumotachograph linear over the experimental range of V'. Volume was obtained by numerical integration of the V' signal. Pressure at the airway opening was measured through a side port of the pneumotachograph. After reaching steady state breathing, a series of three to five test breaths were performed in which NEP of -3 cmH_2O was applied at the beginning of expiration and maintained throughout the ensuing expiration. The expiratory flow-volume loops generated with NEP are compared by superimposition with those obtained during the immediately preceding breaths. Patients in whom V' is greater with NEP over the entire range of the tidal expiration are considered as not flow limited (Figure

1). By contrast, subjects in whom the application of NEP does not elicit an increase in V' are considered flow limited.[21]

The day of surgery, patients were randomized by computerized method in two groups, the first in which the level of PEEPe was set to zero (group ZEEP) for the entire duration of surgery; and the second in which that level was set to 5 cmH_2O (group PEEP) for the entire duration of surgery. Anesthesia was induced with propofol (1.5 mg/kg), fentanyl (3 mcg/Kg), and vecuronium bromide (0.1 mg/kg) and maintained with sevoflurane and air-oxygen mixture 50%-50%.

All patients were intubated via endotracheal low pressure cuffed tube, with an internal diameter ranging between 7.5 and 8.0 mm. They were ventilated in volume controlled mode, with a tidal volume and a respiratory rate aimed to maintain normocapnia. The presence of EFL during general anesthesia was assessed by using the PEEP test. The latter is based on a sudden decrease of expiratory resistance obtained by a subtraction of 3 cmH_2O of PEEPe during expiration.[19] A patient was judged having EFL when the subtraction of PEEPe was not able to increase the expiratory flow when compared to the previous test breath; otherwise, the patient was considered not flow limited (Figures 1, 2).

The PEEP test was performed at the beginning and at the end of surgery, together with calculation

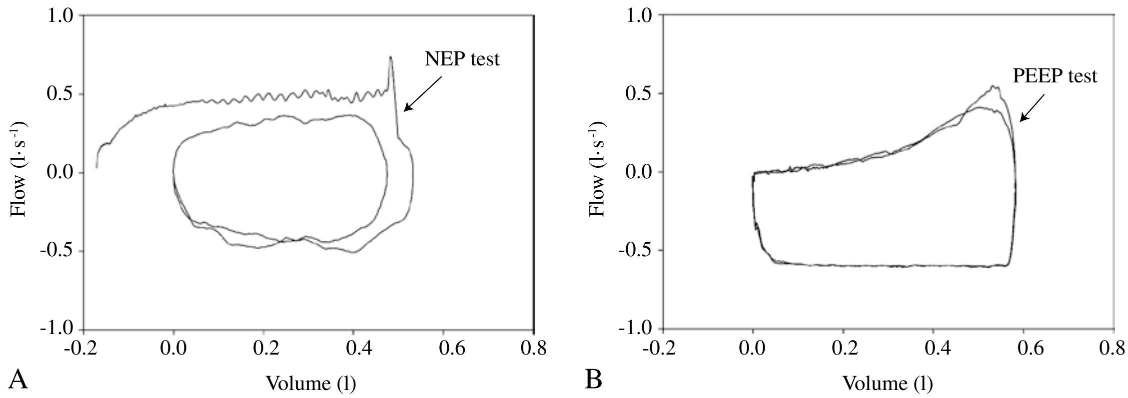

Figure 1.—A) Flow – volume curves of a representative patient in which the NEP test was performed the day before surgery in supine position. The application of 3 cmH_2O of NEP was able to increase the expiratory flow and hence the patient was classified as not flow limited; B) flow – volume curves of the same patient at the end of anesthesia. The subtraction of 3 cmH_2O of PEEP did not increase the expiratory flow. Hence the patient became flow limited at the end of surgery.

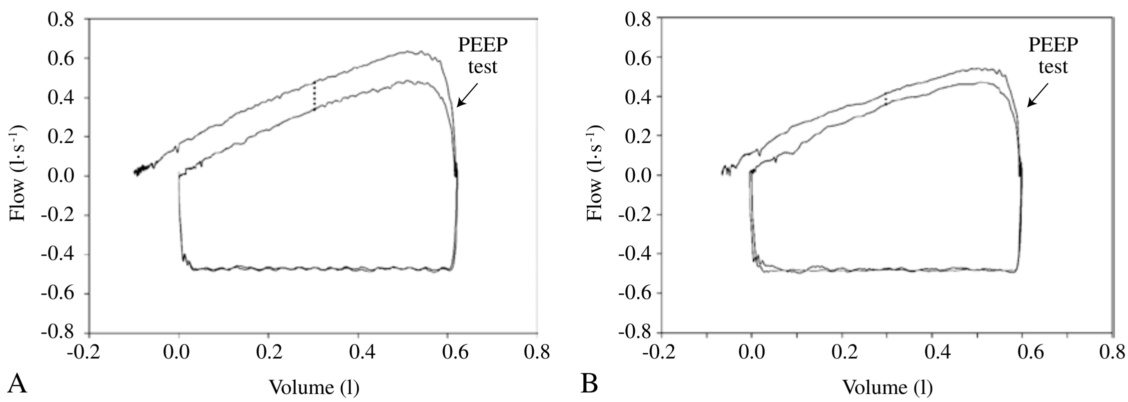

Figure 2.—Flow – volume curves of a representative patient (group ZEEP) undergoing PEEP test immediately (A) and after the end (B) of anesthesia. Note that the expiratory flow increases due to the subtraction of 3 cmH_2O of PEEP was much higher at the beginning compared to the end of anesthesia. Dotted line represents the ΔV' at 50% of the expired volume.

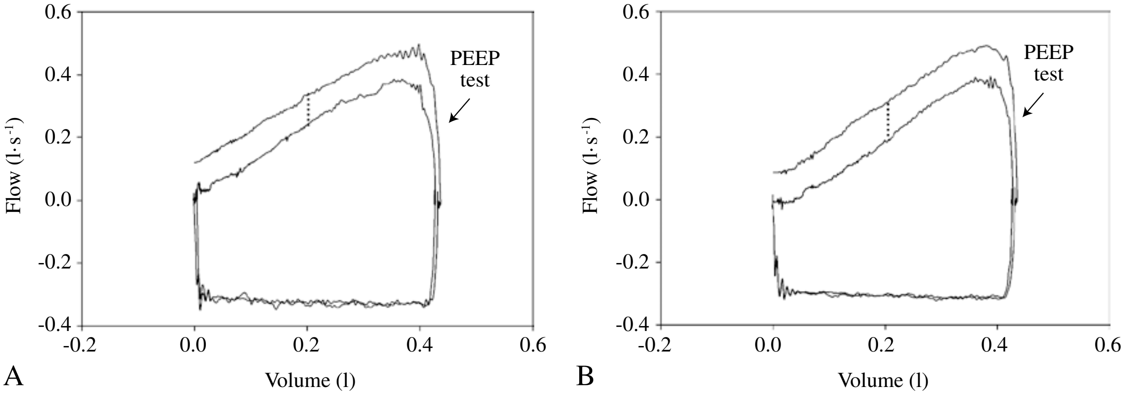

Figure 3.—Flow – volume curves of a representative patient (group PEEP) undergoing PEEP test immediately (A) and at the end (B) of anesthesia. Note that the expiratory flow increase due to the subtraction of 3 cmH_2O of PEEP was equal at the beginning and at the end of anesthesia. Dotted line represents at ΔV' at 50% of the expired volume.

of quasi-static compliance (Cqst,rs) of respiratory system and airway flow resistance (Rmin,rs).

Determination of respiratory mechanics parameters

Respiratory mechanics parameters were calculated by using the end-inspiratory and end expiratory occlusion technique. Cqst,rs was calculated as tidal volume / (end inspiratory plateau pressure – PEEPtot), where PEEPtot is the end-expiratory pressure at period of no-flow.[22] Rmin,rs was determined as (Peak – P_1) / V', where Ppeak is the peak inspiratory pressure, P_1 is the airways pressure at the point of zero flow and V' is the inspiratory flow.[23]

Finally, in patients without EFL detected both before and during surgery, the difference in expiratory flow (ΔV') between the test breath and the ensuing breath during which PEEPe was subtracted, was calculated at 50% of the expired V_T (Figures 1, 3).

The degree of muscle paralysis was monitored by ulnar nerve stimulation. Determination of respiratory mechanics parameters was performed in presence of no reaction at the train of four test.

Additional experiment

Since the presence of EFL was assessed by two different methods (i.e. the NEP and the PEEP test), we performed an additional experiment to assess the validity and the congruity of both methods in detecting the presence of EFL. The determination of the presence of EFL is part of daily monitoring of the respiratory function of our ICU patients. The NEP and the PEEP test were applied in random order in 10 consecutive intensive care patients able to breathe spontaneously (Table I). The set up used for the NEP and the PEEP test was previously described in the Methods section. The NEP test was applied when the patients were spontaneously breathing, while the PEEP test was done when the same patients were mechanically ventilated. As previously pointed out,[19] the results of the NEP and PEEP test were in good agreement since both tests were able to detect the presence / absence of EFL (Figure 1). In this connection it should noted that

Table I.—*Clinical characteristics of the 10 ICU patients enrolled in the study. Value are mean ± SD.*

Age (years)	71±3
BMI (kg/m²)	25±2
Sex (M/F)	6/4
Smokers (number)	6
Tidal volume (mL)	420±30
EFL (number)	5
Cause of ARF	
COPD	3
Recent surgery	6
Pneumonia	1

ARF: acute respiratory failure; COPD: chronic obstructive pulmonary disease; EFL: expiratory flow limitation; BMI: body mass index.

the 7 patients who were flow limited the day before surgery continued to be flow limited after anesthesia induction and at the end of surgery.

Data analysis

The recorded pressure and flow signals were stored on a portable computer and amplified, filtered and digitized by an analogue-to-digital-converter (Direc Physiologic Recording System, Canada). Data analysis was performed with two software: ANADAT (ANADAT 5.1, RHT-InfoDat, Montreal, Quebec, Canada) and ANALYSER 2.2 (ICU-Lab KleisTEK 2.2).

Statistical analysis

Statistical analysis was carried out using a software package SigmaStat for Windows v. 3.5. To detect a difference in compliance of 5 with an SD of 4, with a type I error of 0.05 and a power of 0.80, 24 patients had to be recruited, 12 in each group. We decided to enrol 15 patients each group because of a possible drop out of selected patients.

The normal distribution of data was calculated for each parameter by using the Kolmogorov-Smirnov test. In presence of normally distributed data, as it was the case of our study, differences between baseline and end of surgery or between the two groups were calculated with the Student t test.

All data are expressed as mean (SD). The difference between the two groups were considered statistically significant for probability (P) values <0.05.

Results

Fifty two (52) patients were enrolled, 26 each group. Respiratory mechanics parameters were calculated in 30 patients, 15 each group.

The two groups were not statistically different in terms of age, sex, BMI, duration of surgery, amount of fluids administered and number of co-morbidities (Table II).

None of the patients was flow limited before surgery in seated position, while 7 patients were flow limited in supine position (Table III). The presence of EFL in these patients was associated to a smoke history (1 patient), BMI >30, <35 (2 patients), asthma (1 patient), advanced age (1 patient, 90 year old), chronic heart failure (1 patient), hypertension (1 patient).

The PEEP test was able to correctly detect the presence of EFL during surgery (Figure 4). Immediately after anesthesia induction, 8 patients (15%) developed EFL, 4 in both groups

Table II.—*Clinical characteristics of the 52 patients enrolled in the study. Data are expressed as mean±SD. Comorbidities are expressed as a total number; in brackets the number of patients who exhibits expiratory flow limitation during the perioperative period.*

	Group ZEEP	Group PEEP
Age (years)	74±8	74±6
BMI (kg/m²)	27±4	25±5
Sex (M/F)	13/13	10/16
ASA physical status I/II/III	1/6/8	1/5/9
Tidal volume (ml)	578±88	544±83
Duration of surgery (min)	181±65	179±60
Intraoperative fluids (ml/kg·h^{-1})	13.1±5	13.6±6
Co - morbidities		
Smokers	9 [4]	9 [2]
Hypertension	11 [3]	10 [0]
COPD	2 [0]	3 [1]
Chronic heart failure	3 [2]	3 [2]
Asthma	1 [0]	2 [2]
Obesity (BMI>30<35)	6 [5]	7 [0]
Diabetes mellitus	2 [0]	3[0]
Age > 80 year	7 [2]	5 [0]

COPD: chronic obstructive pulmonary disease; BMI: body mass index; ASA: American Society of Anesthesiologists physical status.

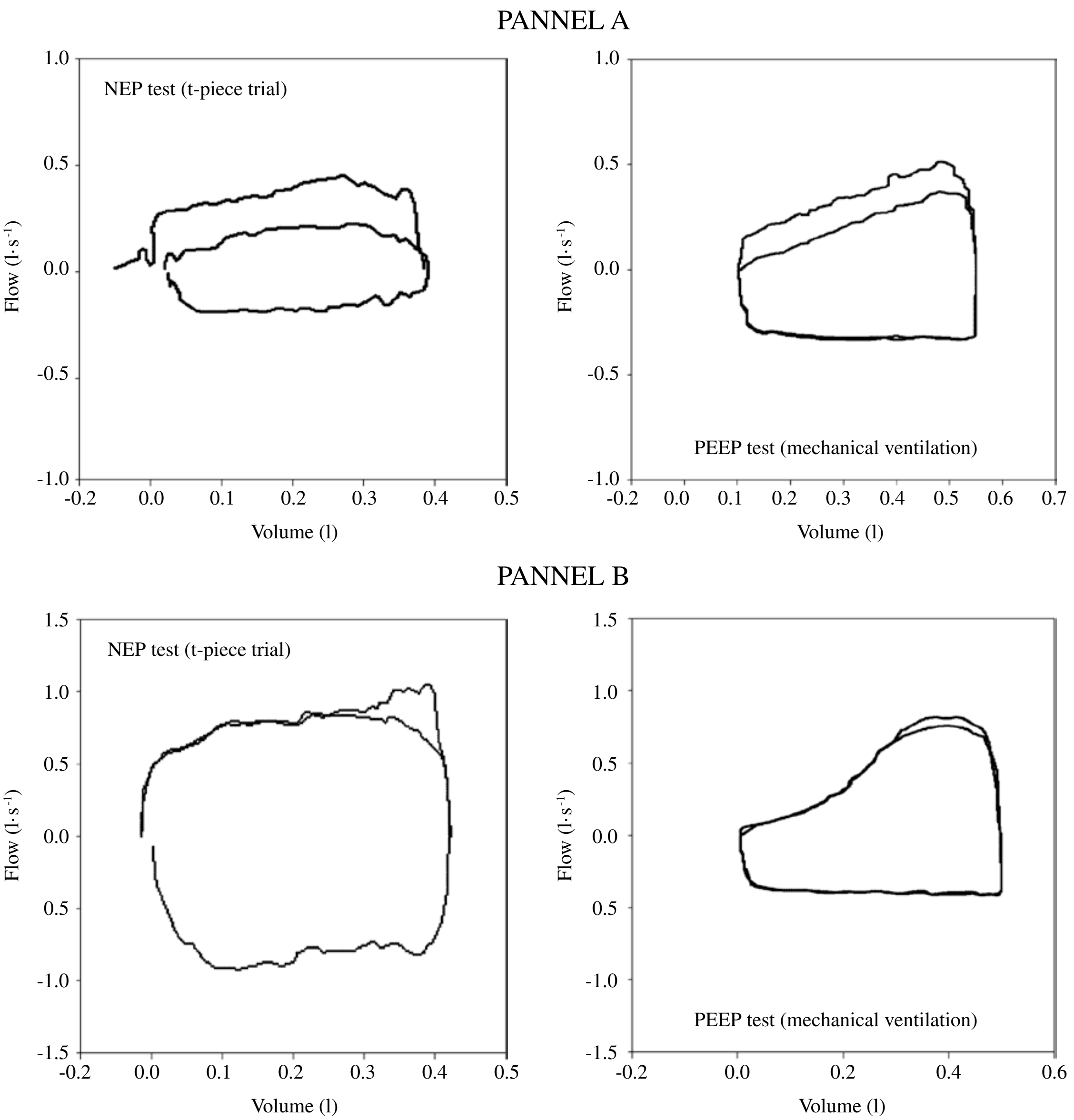

Figure 4.—Expiratory flow-volume curves of representative ICU patients in which both NEP and PEEP test were applied. A) Both NEP and PEEP test detected the absence of EFL; B) both NEP and PEEP test detected the presence of EFL. Note that the NEP test was applied in spontaneously breathing patient, while the PEEP test was used in the same patient during mechanical ventilation.

Table III.—*Number of patients with expiratory flow limitation (EFL) before surgery and of those who developed EFL during surgery.*

	Group ZEEP	Group PEEP
Day before surgery	4	3
After anaesthesia induction	4	4
End of anesthesia	7	1
Total	15	8

Table IV.—*Respiratory mechanics parameters at the beginning and the end of surgery. Values are mean±SD.*

	Group ZEEP		Group PEEP	
	Beginning	End	Beginning	End
Cqst,rs (ml/cmH_2O)	44±2.5	37±1.6 *^	46±3.3	46±3.7 ^
Rmin,rs (cmH_2O*l/s)	5.7±2.3	6.4±2.5 *	5.9±3.5	5.9±3.9
ΔV' (l/s)	0.1±0.01	0.06±0.01 *^	0.09±0.04	0.09±0.02 ^

*P<0.05: comparison with baseline values
^P<0.05: comparison between the two groups
Cqst,rs: quasi static compliance of the respiratory system
Rmin,rs: airflow resistance of the respiratory system
ΔV': difference in flow at 50% of the expired volume

(Table III). At the end of surgery, 7 more patients became flow limited in the group ZEEP, while only 1 in the group PEEP. Hence 42% of the patients ventilated at ZEEP exhibited EFL during surgery (Table III). Furthermore the two groups behave differently in terms of respiratory mechanics parameters calculated during surgery (Table IV). Although the values of quasi-static compliance and flow resistance were similar among the two groups at the beginning of surgery, only the group ZEEP exhibited a worsening of respiratory mechanics at the end of surgery (Table IV). Finally, the expiratory Δflow was markedly reduced in the group ZEEP compared to the group PEEP (Table IV; Figures 2, 3).

Discussion

The most relevant results of the present study are that: 1) The PEEP test allows to verify the presence of EFL; 2) anesthesia induction can promote the development of EFL; 3) during surgery, the respiratory system compliance and airways resistance can worsen and the expiratory flow can decrease up to the development of EFL (Tables III, IV, Figure 3); 4) the worsening of respiratory mechanics during surgery can be limited by the use of low level of PEEP (Table IV, Figure 3).

The presence of EFL during anesthesia should be considered carefully. Anesthesia induction is associated to a decreased FRC. This reduction could imply that the closing capacity might exceed FRC.[9] Moreover, with advancing age there is a preferential reduction of maximal expiratory flow at low lung volume and hence elderly patients are susceptible to tidal EFL. The presence of EFL can produce lung injury, which is generally attributed to cyclic opening/closure of the relatively small airways with concomitant generation of abnormal shear stresses, responsible for the mechanical and histological damage in bronchioles with a concomitant increase of airway resistance.[17, 18] In this connection it should be pointed out that the increase in airways resistance (Table IV) is associated with an inflammatory response and marked alteration of alveolar-bronchiolar coupling.[17, 18] Till now, determination of EFL during surgery was difficult. The use of NEP test, which is the gold standard for detecting the presence of EFL, is cumbersome and complicated during anesthesia, the main reasons for this inconvenience being the use of a closed circuit and the connection between the NEP system and the expiratory limb of the ventilator. Hence a simpler method was required for detecting the presence of EFL during anesthesia. Rossi *et al.*[19] proposed a new method for detecting EFL in ventilated patients, which is based on the effect on the tidal expiratory flow of application/removal of low level of PEEPe. However, the validity of this method was not corroborated in subsequent studies, nor in ICU patients neither in patients undergoing general anesthesia, remaining only a speculative test. Our data clearly show that the results obtained with the application of the PEEP test are superimposed to those obtained with the NEP test (Figure 4). Hence the PEEP test is able to easily detect the presence of EFL during anesthesia.

Expiratory flow limitation was detected in supine position in the 10% of the patients at the pre-surgery evaluation. However, this percentage increased to 52% at the end of surgery. In other words, 42% of the patients of the group ZEEP became flow limited during surgery. These results underline that EFL could be an important phenomenon during surgery not only because elderly patients can be flow limited before surgery, but, more interestingly, because they can develop EFL during surgery. There are numerous clinical situations associated with the presence of EFL, such as heart failure,[8, 24] chronic obstructive pulmonary disease,[21] obesity,[25] sleep apnea,[26] bronchiectasis.[27] Surprisingly, anesthesia is not considered as a risk factor for developing EFL, although the induction of a general anesthesia is characterized by a reduction of FRC. In presence of a reduced expiratory flow, as it is in elderly patients, the decrease of FRC can cause the maximal expiratory flow to be equal to the expiratory flow obtained during tidal ventilation. The direct consequence is the development of EFL. This is clearly shown in Figure 1, in which the flow-volume curves of a representative patient are presented. Although no flow limitation was detected before surgery (A), the patient became flow limited during anesthesia. However, patients can develop EFL not only because of lung aging, but also because of the presence of comorbidities that can further influence the lung volume and the expiratory flow, such as obesity, chronic heart failure, COPD, and asthma (Table II).

About 27% of patients not flow limited after anesthesia induction developed EFL toward the end of surgery, making evident that the worsening of the respiratory parameters is a phenomenon that continues till the end of surgery and it is not related only to anesthesia induction. In this connection it should be noted that surgery is associated with progressive decline of the expiratory flow, the reduction of which is around 50% of the value obtained immediately after anesthesia induction (Table IV, Figure 2). This reduction could be due to 1) a further reduction of FRC; 2) a progressive increase of expiratory resistance in presence of decreased compliance, as it was the case of the group ZEEP; 3) both mechanisms. In any case, this phenomenon could indicate a deterioration of respiratory mechanics which is easily and frequently evaluated bedside by the PEEP test. From the physiological point of view, FRC can be increased by using PEEPe. The latter should partially counterbalance the negative effect of low lung volume ventilation. Indeed PEEPe seems helping patients to avoid the reduction of the expiratory flow (Table IV, Figure 1), in this way decreasing the possibility of developing EFL at the end of surgery. Indeed the leading mechanism responsible of the development of EFL is the decrease of expiratory flow during tidal ventilation.

As for the Δ expiratory flow (Table IV), the respiratory mechanics parameters had a different behaviour whether patients were ventilated at ZEEP or PEEP 5 cmH_2O. Our results show that respiratory mechanics parameters, such as respiratory system compliance and airways resistances worsen during anesthesia only in the ZEEP group (Table IV). These variations can be partially prevented by application of 5 cmH_2O of PEEP (Table IV, Figure 3). The explanation why the respiratory mechanics parameters worsen and the expiratory flow decreases during surgery is not completely understood yet. However, we can hypothesize that several factors may be involved. As previously pointed out, anesthesia implies a reduced FRC. Since flow resistance increases as lung volume decreases, it is axiomatic that the reduction of FRC implies greater inspiratory flow resistance. However resistance, compliance and expiratory flow continued to worsen toward the end of surgery only in the ZEEP group. Hence other factors promoting a further FRC reduction should be involved, such as low lung volume ventilation, monotone ventilation without deep breath, fluids therapy and pro-inflammatory cytokines. It has been previously demonstrated that surgery is associated with an over-production of pro-inflammatory mediators.[5] These mediators can alter microvascular permeability and thus they increase lung oedema. Furthermore, FRC might be reduced in case of obesity and heart failure.[24, 25] Finally, atelectasis could be considered as a possible explanation for the worsening of respiratory mechanics. However, the development of more atelectasis than those obtained immediately after anesthesia induction is questionable the since abdominal surgery adds little to atelectasis.[28] In any case, whatsoever is the cause(s) of the reduction of the expiratory flow and worsening of respiratory parameters, our results show that the use of 5 cmH_2O of PEEP can prevent this fall of the expiratory flow, as well as the decrease of Cqst,rs and the increase of flow resistance (Table IV).

Our results are partially in contrast with those of Pelosi and co-workers, who found no differences in terms of respiratory mechanics and gas exchange by using 10 cmH_2O of PEEP in normal patients undergoing general anesthesia.[7] The opposite was true for obese patients in whom the same level of PEEP ameliorates resistance, compliance and oxygenation. Hence the authors concluded that the use of PEEP during anesthesia is recommended only in obese patients. However, there are significant differences between the two studies. First, our patients were much older (43 vs. 73 years) and hence with the possible occurrence of a closing capacity higher than FRC in supine position. In this position, after induction of anesthesia, this phenomenon could happen even in normal subject at the age of about 30 years. Furthermore we calculate the respiratory mechanics parameters not only at the beginning but also at end of surgery, measuring the changes following anesthesia induction that can further reduce the respiratory function during surgery. Finally, we applied a lower value of PEEP (5 cmH_2O vs. 10 cmH_2O).

Conclusions

The presence of EFL can be easily detected during general anesthesia by using the PEEP test. The latter could also help to evaluate the progressive reduction of the expiratory flow that might occur during surgery (Figure 2, 3) since this phenomenon implies a worsening of respiratory mechanics. The use of low level of PEEP seems able to prevent the deterioration of respiratory mechanics that occurs during surgery.

Key messages

— The PEEP test can detect the presence of expiratory flow limitation during anesthesia; anesthesia can be associated to the development of expiratory flow limitation.

— The expiratory flow continues to decrease toward the end of surgery; the use of 5 cmH_2O of PEEP partially prevents the effects of low lung volume ventilation.

References

1. Lumb AB, Pearl RG. Anesthesia. In: Nunn's applied respiratory physiology, 6th edition. Philadelphia: Elsevier; 2005. p. 297-326.
2. Wahba RWM. Perioperative functional residual capacity. Can J Anesth 1991;83:384-400.
3. Gunnarsson L, Tokics L, Gustavsson H, Hedenstierna G. Influence of age on atelectasis formation and gas exchange impairment during general anesthesia. Br J Anesth 1991;66:423-32.
4. Westbrook PR, Stubbs SE, Sessler AD, Rehder K, Hyatt RE. Effects of anesthesia and muscle paralysis on respiratory mechanics in normal man. J Appl Physiol 1973;34:81-6.
5. Baigrie RJ, Lamont PM, Kwiatkowski D, Dallman MJ, Morris PJ. Systemic cytokine response after major surgery. Br J Surg 1992;79:757-60.
6. Volta CA, Alvisi VM, Marangoni E, Alvisi R, Castellazzi M, Fainardi E *et al.* Influence of different strategies of volume replacement on the activity of matrix metalloproteinases: an in vitro and in vivo study. Anesthesiology 2007;106:85-91.
7. Pelosi P, Ravagnan I, Giurati G, Panigada M, Bottino N, Tredici S *et al.* Positive end-expiratory pressure improves respiratory function in obese but not in normal subjects during anesthesia and paralysis. Anesthesiology 1999;91:1221-31.
8. Torchio R, Gulotta C, Greco-Lucchina P, Perboni A, Montagna L, Guglielmo M *et al.* Closing capacity and gas exchange in chronic heart failure. Chest 2006;129:1330-6.
9. Leblanc P, Ruff F, Milic-Emili J. Effects of age and body position on "airway closure" in man. J Appl Physiol 1970;28:448-51.
10. Holland J, Milic-Emili J, Macklem PT, Bates DV. Regional distribution of pulmonary ventilation and perfusion in elderly subjects. J Clin Invest 1968;47:81-92.
11. Turner JM, Mead J, Wohl ME. Elasticity of human lung in relation to age. J Appl Physiol 1968;25:664-71.
12. Hedenstierna G, Edmark L. The effects of anesthesia and muscle paralysis on the respiratory system. Intensive Care Med 2005;31:1327-35.
13. Hedenstierna G, Santesson J. Airway closure during anesthesia: a comparison between resident-gas and argon bolus techniques. J Appl Physiol 1979;47:874-81.
14. Knudson RJ, Clark DF, Kennedy TC, Knudson DE. Effect of aging alone on mechanical properties of the normal adult human lung. J Appl Physiol 1977;43:1054-62.
15. Milic-Emili J. Ventilation distribution. In: Hamid Q, Shannon J, Martin J, editors. Physiologic basis of respiratory disease. Hamilton, Ontario: BC Decker; 2005. p. 133-41.
16. Nucci G, Suki B, Lutchen K. Modeling airflow related shear stress during heterogeneous constriction and mechanical ventilation. J Appl Physiol 2003;95:348-56.

17. D'Angelo E, Pecchiari M, Baraggia M, Setta M, Balestro E, Milic-Emili J. Low-volume ventilation causes peripheral airway injury and increased airway resistance in normal rabbits. J Appl Physiol 2002;92:949-56.
18. D'Angelo E, Pecchiari M, Setta M, Balestro E, Milic-Emili J. Dependence of lung injury on inflation rate during low-volume ventilation in normal open-chest rabbits. J Appl Physiol 2004;97:260-68.
19. Rossi A, Polese G, Milic-Emili J. Monitoring respiratory mechanics in ventilator-dependent patients. In: Tobin MJ, editor. Principles and practice of intensive care monitoring. New York: McGraw-Hill; 1998.
20. McAlister FA, Bertsch K, Man J, Bradley J, Jacka M. Incidence of and risk factors for pulmonary complications after non thoracic surgery. Am J Respir Crit Care Med 2005;171:514-7.
21. Eltayara L, Becklake M.G, Volta C.A, Milic-Emili J. Relationship between chronic dyspnea and expiratory flow limitation in patients with chronic obstructive pulmonary disease. Am J Respir Crit Care Med 1996;154:1726-34.
22. Futier E, Constantin JM, Pelosi P, Chanques G, Kwiatkoskwi F, Jaber S *et al.* Intraoperative recruitment maneuver reverses detrimental pneumoperitoneum-induced respiratory effects in healthy weight and obese patients undergoing laparoscopy. Anesthesiology 2010;113:1310-9.
23. Volta CA, Ferri E, Marangoni E, Ragazzi R, Verri M, Alvisi V *et al.* Respiratory function after aortic aneurysm repair: a comparison between retroperitoneal and transperitoneal approaches. Intensive Care Med 2003;29:1258-64.
24. Duguet A, Tantucci C, Losinguez O, Isnard R, Thomas D, Zelter M *et al.* Expiratory flow limitation as a determinant of orthopnea in acute left heart failure. J Am Coll Cardiol 2000;35:690-700.
25. Ferretti A, Giampiccolo P, Cavalli A, Milic-Emili J, Tantucci C. Expiratory flow limitation and orthopnea in massively obese subjects. Chest 2001;119:1401-8.
26. Liistro G, Veriter C, Dury M, Aubert G, Stanescu D. Expiratory flow limitation in awake sleep-disordered breathing subjects. Eur Respir J 1999;14:185-90.
27. Koulouris NG, Retsou S, Kosmas E, Dimakou K, Malagari K, Mantzikopoulos G *et al.* Tidal expiratory flow limitation, dyspnoea and exercise capacity in patients with bilateral bronchiectasis. Eur Respir J 2003;21:743-8.
28. Lindberg P, Gunnarsson L, Tokics L, Secher E, Lundquist H, Brismar B *et al.* Atelectasis, gas exchange and lung function in the postoperative period. Acta Anesthesiol Scand 1992;36:546-53.

Funding.—The study was supported by a grant from the Italian Ministry of University

Received on January 25, 2012. - Accepted for publication on June 29, 2012.

Corresponding author: C. A. Volta, Section of Anesthesia and Intensive Care, Department of Surgical, Anesthesiological and Radiological Science, S. Anna Hospital, University of Ferrara, Via Aldo Moro 8, 44121 Ferrara, Italy. E-mail: vlc@unife.it

This article is freely available at www.minervamedica.it