

Lung hyperinflation and flow limitation in chronic airway obstruction

R. Pellegrino*, V. Brusasco**

Lung hyperinflation and flow limitation in chronic airway obstruction. R. Pellegrino, V. Brusasco. ©ERS Journals Ltd 1997.

ABSTRACT: We reasoned that if flow limitation plays an important role in lung hyperinflation, then bronchodilatation should be associated with a decrease of functional residual capacity (FRC) only in subjects breathing under conditions of flow limitation.

This hypothesis was tested in 33 subjects with chronic airway narrowing due to asthma or chronic obstructive pulmonary disease (COPD). Flow limitation during tidal breathing was inferred from the impingement of the tidal flow-volume loop on the flow recorded during submaximally forced expiratory manoeuvres initiated from end-tidal inspiration.

At baseline, flow limitation during tidal breathing was present in seven asthmatic (Group 1) and eight COPD subjects (Group 2), but absent in 11 asthmatic (Group 3) and seven COPD subjects (Group 4). FRC (mean \pm SEM) was similar in the four groups (range 117 \pm 7 to 134 \pm 6% of predicted). Inhalation of salbutamol (200 μ g) caused significant increments of the forced expiratory volume in one second (FEV₁) (range 6 \pm 1 to 21 \pm 8% of baseline) and forced expiratory flows at 30% of baseline forced vital capacity (V'30) (range 58 \pm 13 to 235 \pm 93% of baseline) in all groups. In groups with flow limitation during tidal breathing at baseline the FRC measured by plethysmography decreased significantly (12 \pm 2% in Group 1, and 9 \pm 2% in Group 2), and the inspiratory capacity (IC) measured by spirometry increased significantly (17 \pm 3% in Group 1 and 7 \pm 3% in Group 2). This was associated with flow limitation disappearing at the volume of baseline end-tidal expiration. In Groups 3 and 4 neither FRC nor IC changed significantly. The breathing pattern was not modified in any group after salbutamol.

These findings suggest that flow limitation may contribute to generation of lung hyperinflation both in asthma and chronic obstructive pulmonary disease. We speculate that the increment of functional residual capacity could be triggered by dynamic airway compression downstream from the flow-limiting segment.

Eur Respir J 1997; 10: 543–549.

Functional residual capacity (FRC) is generally increased in patients with airway narrowing due to chronic obstructive pulmonary disease (COPD) or asthma [1]. Part of this increment may be caused by the low elastic recoil of the lung, which passively sets FRC at a volume higher than predicted. Nevertheless, bronchodilators may increase expiratory flow and decrease FRC in these individuals [1], suggesting that lung volume during tidal breathing is also dynamically regulated.

Recent observations have raised the suspicion that there is an interesting relationship between FRC and expiratory flows. For example, unlike normal individuals, patients with mild-to-moderate COPD increase FRC during exercise as soon as the tidal expiratory flow encroaches on the maximal flow-volume loop [2]. If a threshold load, which reduces tidal flow, is suddenly applied during expiration under these circumstances, then FRC consistently and paradoxically decreases, in contrast to the situation when ventilation is not flow-limited [3]. Further evidence that FRC is coupled to expiratory flow comes from the observation that when bronchoconstriction is induced in asthmatics, FRC does

not increase until the decrement of forced expiratory flow is such as to impinge on tidal expiratory flow [4].

On this basis, we hypothesized that in subjects with mild-to-moderate chronic bronchoconstriction who utilize maximal expiratory flow during tidal expiration, *i.e.* breathing in flow limitation, bronchodilatation would be associated with a decrease of FRC, whereas in patients who do not utilize maximal flow at any volume during tidal breathing, even if obstructed, bronchodilatation would not affect FRC. In addition, we investigated whether the modulation of FRC by flow limitation is different in COPD and bronchial asthma.

Methods

Subjects

The study included 33 subjects with chronic bronchoconstriction due to bronchial asthma or COPD [5]. To enter the study, all individuals were required to have a

*Servizio di Fisiopatologia Respiratoria, Azienda Ospedaliera S. Croce e Carle, Cuneo, Italy. **Cattedra di Fisiopatologia Respiratoria, Dipartimento di Scienze Motorie e Riabilitative, Università di Genova, Genova, Italy.

Correspondence: V. Brusasco
Facoltà di Medicina e Chirurgia
Università di Genova
Largo R. Benzi 10
16132 Genova
Italy

Keywords: Breathing pattern
bronchodilatation
flow-volume curve
functional residual capacity

Received: May 23 1996
Accepted after revision December 2 1996

forced expiratory volume in one second (FEV₁) >40% of predicted and a FEV₁/forced vital capacity (FVC) ratio below the normal range. The predicted values used were from QUANJER *et al.* [6]. None of the subjects was affected by other pulmonary or systemic disease. Before the study, oral corticosteroids and theophylline were avoided for 24 h, inhaled corticosteroids for 12 h, and short-acting inhaled bronchodilators for 12 h. None of the subjects was receiving long-acting bronchodilators. Informed consent was obtained before the study.

Lung function measurements

Flow was measured at the mouth by a screen-type pneumotachograph, linear up to 16 L·s⁻¹, coupled to a differential pressure transducer (Jaeger, Würzburg, Germany). Volume was obtained by integration of the flow signal after careful correction for drift by manual adjustment of a potentiometer.

All lung function measurements were obtained, whilst the subjects were in a sitting position, at least in triplicate before and 20 min after salbutamol (200 µg, metered dose) was inhaled through a spacer.

Lung volumes. Thoracic gas volume (TGV) at end-tidal expiration (FRC) was measured in a constant-volume body plethysmograph (Jaeger, Würzburg, Germany) by slowly panting against a closed shutter at the end of expiration [7]. Total lung capacity (TLC) was calculated by adding to TGV the volume that could be maximally inhaled immediately after the opening of the shutter. Inspiratory capacity (IC) was measured on the spirogram as the difference between the straight line that best connected, by eye, the end-expiratory lung volumes of the last 6–7 regular breaths and TLC.

Breathing pattern. After about 60 s of quiet and regular breathing through the mouthpiece, 6–7 tidal regular breaths were plotted as a spiographic tracing on an XY recorder (LY 1400 Linseis, Selb, Germany), at a speed of 2 cm·s⁻¹. Inspiratory (V_{TI}) and expiratory (V_{TE}) tidal volumes, respiratory frequency (*f*_R), and inspiratory (*t*_I) and expiratory (*t*_E) times were measured. Mean inspiratory (V_{TI}/*t*_I) and expiratory (V_{TE}/*t*_E) flows, ratio of inspiratory time to total respiratory cycle time (*t*_I/*t*_{tot}), and minute ventilation (V_E) were then computed.

Flow-volume curves. After regular breathing with no volume drift, the subjects performed a forced expiration from end-tidal inspiration without breathholding (partial expiratory manoeuvre). Special care was taken to coach the subjects not to slow down the inspiration preceding the partial forced manoeuvre, thus minimizing the dependence of forced flows on the time of the preceding inspiration [8]. The subjects then took a fast deep breath to TLC and, without breathholding, forcefully expired to residual volume (RV) (full expiratory manoeuvre), which was followed by another deep breath to TLC to check for volume drift. The signals were first displayed on a screen (Body Test Screen; Jaeger, Würzburg, Germany) and then slowly plotted on the XY recorder as spiograms and flow-volume loops. FVC was calculated on the spiograms as the distance between the RV

attained after the maximal expiratory manoeuvre and the straight line joining the two TLCs (preceding and following the full expiratory manoeuvre). FEV₁ was calculated by back-extrapolating the volume to TLC [6]. Flow from the partial expiratory manoeuvre was measured at 30% of control FVC (V₃₀). Changes in V₃₀ give a reliable estimate of the reversibility of airway obstruction, as they are independent of the effects of deep inhalation [9] and the time course of the preceding expiration. Flow-volume curves without sharp peak flow were discarded and repeated.

Flow limitation. Flow limitation was detected by comparing the flow-volume loops recorded during tidal breathing and after a gentle forced expiration (with smooth peak flow) initiated from end-tidal inspiration without breathholding. A deep inspiration to TLC recorded soon after the gentle forced manoeuvre allowed the loops to be superimposed and compared at absolute lung volume. Particular care was taken that the inspiratory flow before the gentle forced expiration was similar to that of the previous tidal breaths. Flow limitation was defined as the condition of tidal expiratory flow impinging on the maximal flow generated during the gentle forced expiratory manoeuvre (fig. 1).

Statistical analysis

Between- and within-groups analysis of variance (ANOVA) with Newman Keuls *post-hoc* test was used to assess the significance of differences between groups and the changes after bronchodilatation. All data are presented as mean ± SEM. A p-value less than 0.05 was considered statistically significant.

Results

Control condition

According to the presence or absence of flow limitation and the clinical diagnosis, the subjects were divided at the end of the study in four groups. Subjects with flow limitation during tidal breathing at baseline

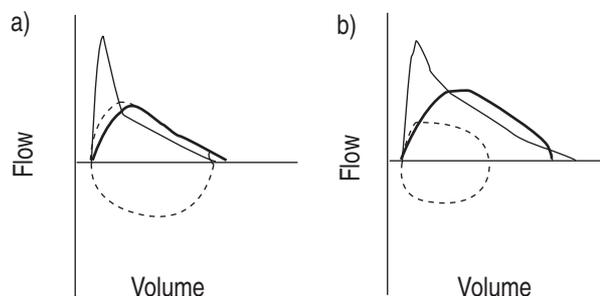


Fig. 1. — Method used to detect flow limitation by comparing tidal to forced expiratory flow-volume loops started from end-tidal inspiration. a) Tidal breathing is flow-limited, as tidal expiratory flow (interrupted line) impinges on submaximally forced expiratory flow (thick continuous line). Note that if expiratory effort is maximal (thin continuous line), then expiratory flow decreases due to thoracic gas compression. b) Tidal breathing is not flow-limited, as tidal expiratory flow (interrupted line) is much less than submaximally forced expiratory flow (thick continuous line).

Table 1. – Anthropometric and pulmonary function data at baseline

	Group 1	Group 2	Group 3	Group 4	Significant differences
Sex M/F	4/3	8/0	9/2	7/0	
Age yrs	44±8	51±6	38±4	53±4	
Height cm	170±3	171±3	168±2	171±3	
BMI kg·m ⁻²	22±1	26±2	25±1	24±1	
FEV ₁ L	2.07±0.22	2.13±0.16	2.93±0.19	3.07±0.40	1 vs 3, 1 vs 4, 2 vs 3, 2 vs 4
% pred	67±5	70±6	83±3	91±8	1 vs 4, 2 vs 4
FVC L	3.48±0.32	3.58±0.19	4.36±0.26	4.54±0.57	1 vs 3, 1 vs 4, 2 vs 3, 2 vs 4
% pred	91±6	89±5	99±3	105±9	
V'30 L·s ⁻¹	0.33±0.04	0.52±0.06	0.84±0.07	0.89±0.19	1 vs 3, 1 vs 4, 2 vs 3, 2 vs 4
FRC L	4.00±0.22	4.47±0.32	3.69±0.28	4.22±0.34	1 vs 3, 1 vs 4, 2 vs 3, 3 vs 4
% pred	134±6	131±10	117±7	124±8	
IC L	2.53±0.22	2.76±0.17	2.89±0.16	2.91±0.32	1 vs 2, 1 vs 3, 1 vs 4
TLC L	6.48±0.34	7.19±0.25	6.75±0.32	7.38±0.36	
% pred	113±3	114±7	109±3	110±2	

Values are presented as mean±SEM. M/F: male/female; BMI: body mass index; FEV₁: forced expiratory volume in one second; FVC: forced vital capacity; V'30: expiratory flow at 30% of control FVC during a forced expiratory manoeuvre started from end-tidal inspiration; FRC: functional residual capacity; IC: inspiratory capacity; TLC: total lung capacity; % pred: percentage of predicted value. Significant differences (analysis of variance (ANOVA) Newman Keuls test) between groups are reported in the last column.

Table 2. – Breathing pattern data at baseline

	Group 1	Group 2	Group 3	Group 4	Significant differences
VTE L	1.12±0.10	1.07±0.12	0.90±0.07	1.07±0.15	
fR breaths·min ⁻¹	13±1	18±1	15±1	15±1	
V'E L·min ⁻¹	14.2±1.0	18.6±2.0	13.3±0.9	16.0±1.6	1 vs 2, 2 vs 3, 2 vs 4, 3 vs 4
tI s	1.83±0.20	1.46±0.10	1.61±0.13	1.67±0.14	
tE s	3.07±0.49	1.99±0.17	2.52±0.17	2.29±0.16	
VTI/tI	0.61±0.04	0.71±0.04	0.59±0.05	0.63±0.06	
VTE/tE	0.40±0.04	0.55±0.06	0.36±0.02	0.47±0.06	1 vs 2, 1 vs 4, 2 vs 3, 2 vs 4, 3 vs 4
tI/t _{tot}	0.38±0.03	0.42±0.02	0.39±0.01	0.42±0.02	

Values are presented as mean±SEM. VTE: expiratory tidal volume; fR: respiratory frequency; V'E: minute ventilation; tI and tE: inspiratory and expiratory times; VTI/tI and VTE/tE: mean inspiratory and expiratory flows; tI/t_{tot}: ratio of inspiratory to total respiratory time. Significant differences (analysis of variance (ANOVA), Newman Keuls test) between groups are reported in the last column.

were assigned to Group 1 (seven asthmatics) and Group 2 (eight with COPD). Subjects without flow limitation were assigned to Group 3 (eleven asthmatics) and Group 4 (seven with COPD). One individual from Group 1 and two from Group 3 were current smokers, whereas all individuals from Groups 2 and 4 were smokers. The anthropometric and pulmonary function data of the four groups are presented in table 1. Two subjects from Group 1, four from Group 2, and four from Group 3 were overweight (body mass index (BMI) 25–30 kg·m⁻²), and only one patient from Group 2 was obese (BMI >40 kg·m⁻²). Mean BMI was not significantly different between groups.

All individuals from the four groups were moderately obstructed (table 1), though FEV₁ and FVC (% pred) were slightly less (p<0.05) in the individuals with flow limitation (Groups 1 and 2) compared to those without flow limitation (Groups 3 and 4). Also, V'30 was significantly less (p<0.01) in Groups 1 and 2 than in Groups 3 and 4. Flow limitation was present in all subjects from Groups 1 and 2 over a substantial part of tidal expiration.

FRC (% pred) was not significantly different between groups, although there was a trend for individuals breathing in flow limitation (Groups 1 and 2) to have higher values than those without flow limitation (Groups 3 and 4).

The analysis of breathing pattern (table 2) revealed slightly greater V'E and higher VTE/tE in COPD (Groups 2 and 4) than in asthmatics (Group 1 and 3) subjects.

After salbutamol

FEV₁ and V'30 increased significantly in all groups after inhaling salbutamol (table 3), and flow limitation disappeared at the volume corresponding to control FRC in all individuals from Groups 1 and 2.

FRC decreased significantly (p<0.001) and IC increased significantly (p<0.001) in Groups 1 and 2, but remained unchanged in Groups 3 and 4 (table 3 and fig. 2).

Table 3. – Percentage changes of pulmonary function data after bronchodilatation

	Group 1	Group 2	Group 3	Group 4
FEV ₁ %	21±8***	10±2*	14±1***	6±1*
FVC %	15±5***	7±2**	3±1	1±2
V'30 %	235±93***	96±34*	71±14***	58±13**
IC %	17±3***	7±3*	0±1	0±2
FRC %	-12±2***	-9±2*	-1±1	-1±3
TLC %	0±1	-4±1	-1±1	0±2
VTE %	1±3	-3±6	-6±4	-6±3
fR %	4±3	6±3	8±5	0±4
V'E %	5±5	8±5	0±3	-7±4
tI %	2±5	-2±3	-3±2	-2±3
tE %	-5±5	-6±4	-6±5	3±5
VTI/tI %	1±7	6±6	-6±4	-5±3
VTE/tE %	8±6	10±5	2±4	-8±5
tE/t _{tot} %	6±6	3±4	3±4	-3±3

Values are presented as mean±SEM. For abbreviations see tables 1 and 2. *: p<0.05; **: p<0.01; ***: p<0.001, versus baseline.

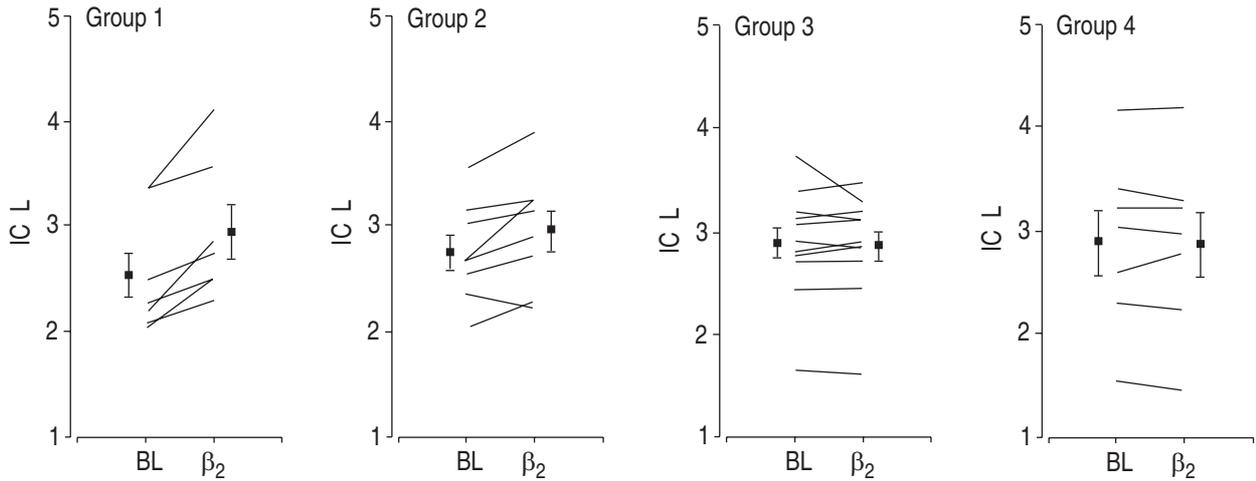


Fig. 2. — Inspiratory capacity (IC) at baseline (BL) and after inhaling salbutamol (β_2) in all individuals from the four groups. Squares represent mean values and bars standard errors.

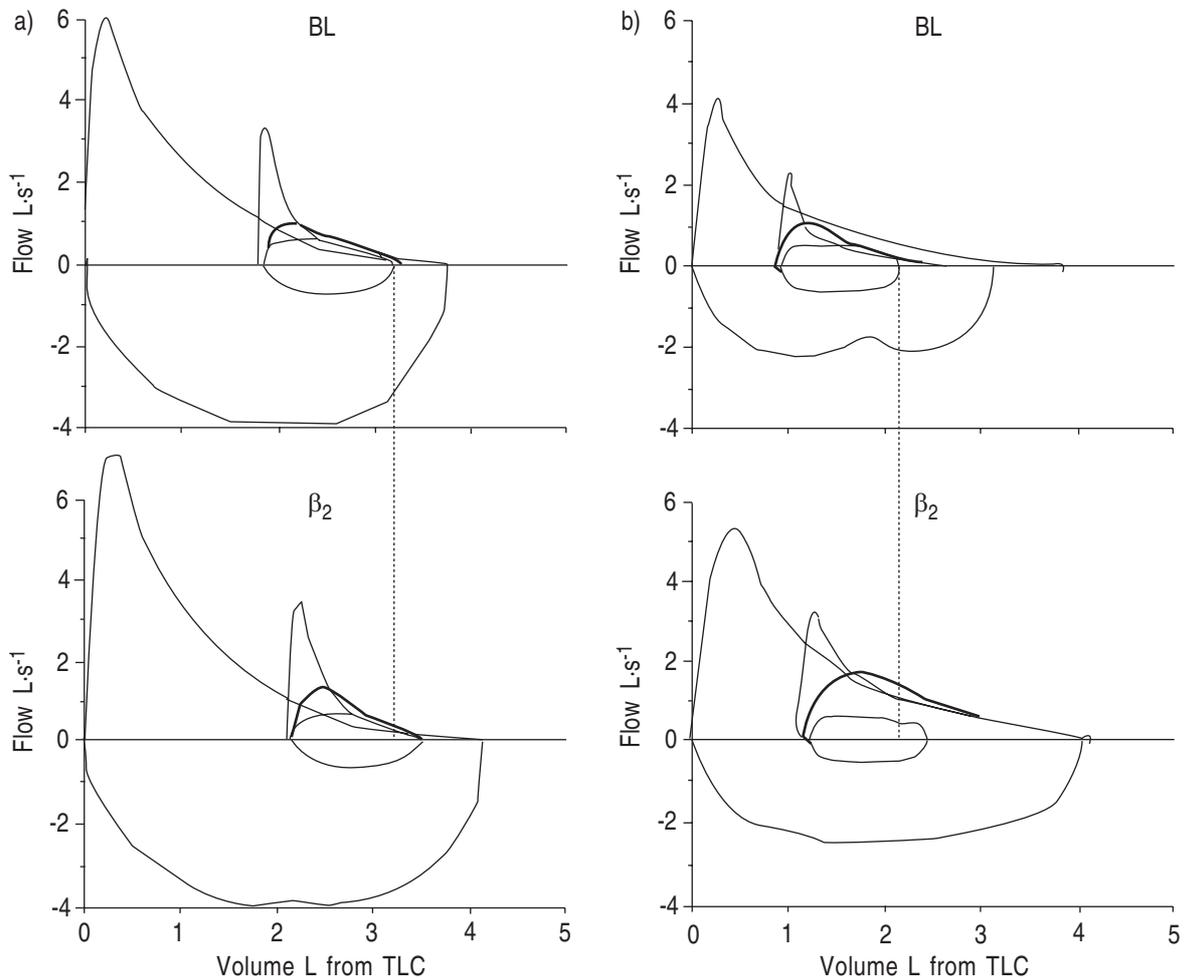


Fig. 3. — Typical patterns of tidal, partial, and full flow-volume curves at baseline (BL) (upper panels) and after inhaling salbutamol (β_2) (lower panels) in: a) an asthmatic subject from Group 1; and b) a subject with COPD from Group 2. Thick lines represent the submaximally forced expiratory flows. The dotted vertical lines indicate baseline FRC. a) Tidal breathing is flow-limited at baseline, as shown by the impingement of tidal flow on submaximally forced flow near end-expiration. After β_2 , maximal expiratory flow increases and FRC decreases by about 0.25 L, to a new volume at which tidal expiration impinges again on submaximally forced expiratory flow, suggesting flow limitation at a lower lung volume. b) Tidal breathing is flow-limited at baseline. After β_2 , maximal expiratory flow increases and FRC decreases by about 0.3 L, but well above the volume at which tidal flow would be limited. COPD: chronic obstructive pulmonary disease; FRC: functional residual capacity; TLC: total lung capacity.

Four individuals from Group 1 and five from Group 2 decreased FRC to a new volume at which tidal expiratory flow impinged on submaximally forced flows, as in the example shown in figure 3a. Three individuals from Group 1 and two from Group 2, however, decreased FRC by a volume less than necessary for flow limitation to reappear, as in the example shown in fig. 3b. Only one subject from Group 2 did not decrease FRC at all, despite the increase of maximal expiratory flows. In Groups 3 and 4, the increment of maximal expiratory flow was not associated with a decrement of FRC, as shown for the typical example in figure 4. The absolute changes of IC were not correlated with the changes of FEV₁.

The breathing pattern was not significantly modified after salbutamol, without consistent differences between groups (table 3).

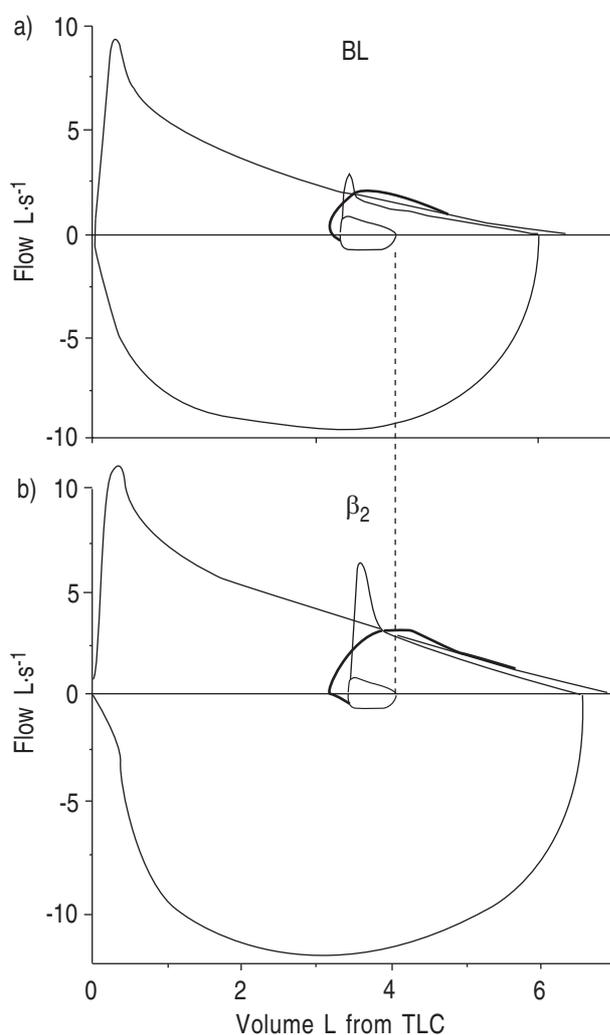


Fig. 4. — Representative example of tidal, partial and full flow-volume curves: a) at baseline (BL); and b) after inhaling salbutamol (β_2) in an individual from Group 3. Thick lines are submaximal expiratory flows. Note that tidal breathing at control is not flow-limited, as indicated by the presence of an expiratory flow reserve, *i.e.* a difference between submaximally forced flows and tidal expiratory flow near end-tidal expiration. After β_2 , maximal expiratory flows increase, but functional residual capacity (FRC) does not change. The dotted vertical line indicates baseline FRC. TLC: total lung capacity.

Discussion

The results of this study indicate that FRC may decrease after bronchodilatation only in those subjects who are apparently flow-limited during tidal breathing. In the subjects who are bronchoconstricted but apparently not flow-limited at rest, bronchodilatation does not appear to be consistently associated with changes of FRC. These findings are in keeping with the hypothesis that flow limitation may regulate FRC in subjects with bronchoconstriction.

Detection of flow limitation is a crucial issue in this study. A definite method of recognizing the occurrence of flow limitation during tidal breathing is to compare the transpulmonary pressure (P_L) recorded during tidal expiration to the critical pressure (P_{crit}) necessary for the pulmonary system to generate maximal expiratory flows [2, 10], which mainly depends on the elastic properties of the airways and the bronchial calibre [11]. Flow limitation is defined as P_L exceeding P_{crit} at some lung volume during tidal expiration. P_{crit} is determined by recording the isovolume pressure-flow curves, which requires a high level of training to perform respiratory manoeuvres, the positioning of an oesophageal balloon, and the knowledge of absolute lung volumes.

Recently, a simple method was proposed [12] for detecting the presence of flow limitation, *i.e.* comparing the tidal expiratory flow with that produced by applying a small negative pressure at the mouth during tidal expiration (NEP). The lack of increment of expiratory flow by NEP would indicate flow limitation. This method is very easy to apply even in non co-operative patients, and has the advantage of avoiding the effects of time and volume history on airway calibre, as well as the artefacts due to thoracic gas compression.

Based on the same principle, we compared the tidal expiratory flow with that generated by a gentle forced expiratory manoeuvre started from end-tidal inspiration immediately after a normal inspiration and without breath-holding. Such a gentle forced expiratory manoeuvre was never associated with the typical sharp peak expiratory flow generated by the forced expiratory manoeuvres, as shown in figures 1, 3 and 4. Thereafter, the expiratory flow always exceeded the flow of the forced manoeuvre, which indicates that thoracic gas compression was minimal or absent during the manoeuvre. We assumed the impingement of tidal expiratory flow on the flow recorded after a gentle forced expiratory manoeuvre to be strongly suggestive of flow limitation during tidal breathing. On the other hand, we assumed that tidal expiration was not flow-limited when the flow generated during the gentle forced expiratory manoeuvre was always greater than the tidal flow. As expiratory flow recorded during submaximal efforts is scarcely affected by inhomogeneities of lung emptying, we think that our method reliably detected the presence of flow limitation during tidal breathing.

In normal individuals, tidal expiration is not totally passive because narrowing of the larynx and postinspiratory tonic activity of inspiratory muscles [13] decrease the lung emptying rate, and yet FRC reaches the relaxation volume of the respiratory system. In asthmatic and COPD subjects, FRC may increase because the time constant of the respiratory system (the ratio of

resistance to elastance) is increased [14, 15]. Any decrease of resistance and/or increase of elastance should allow more volume to be expired for a given t_E , and FRC to be attained at a lower lung volume, unless the mechanisms that brake expiration become more active. The electric postinspiratory activity of the inspiratory muscles has been shown to decay faster in patients with COPD than in normal subjects [16], indirectly suggesting that it may decay less after bronchodilatation, thus counterbalancing any potential decrease of FRC due to the decrement of the time constant. However, as there is no reason for inspiratory muscles to be differently activated during early expiration in subjects with or without flow limitation, the change in time constant does not appear to be a plausible mechanism regulating FRC in the individuals with chronic airway narrowing.

Furthermore modifying V_T and/or t_E [14] could change FRC, as suggested by PARDY *et al.* [17] in patients with COPD. If so, one would expect that bronchodilatation reduces FRC by reducing f_R . The present data, however, show that bronchodilatation occurred in all groups with no substantial or significant changes of breathing pattern, but FRC consistently decreased in subjects breathing under conditions of flow limitation only, which would mean that dilating the airways in itself was not the main cause for the FRC to decrease.

We have previously reported observations consistent with flow limitation being a trigger of acute hyperinflation in humans [3, 4], and we suggested that premature termination of expiration may occur during bronchoconstriction in coincidence with achieving maximal expiratory flows during tidal breathing. Consistent with this hypothesis, the individuals from Groups 3 and 4 would not have decreased FRC even if maximal expiratory flow increased, because no one was breathing under conditions of flow limitation. The FRC of these subjects remained higher than predicted even after bronchodilatation, which would suggest that other mechanisms (low elastic recoil pressure of the lung ($P_{el,L}$)?) contributed to lung hyperinflation. On the contrary, the individuals from Groups 1 and 2, who were probably all flow-limited at baseline, decreased their FRC after increasing maximal expiratory flow. However, were flow limitation the only cause of hyperinflation in these individuals, then the decrement of FRC should have been such as to reach the hypothetical predicted value or a new volume where flow limitation occurred again. In three asthmatics and two subjects with COPD, the FRC decreased to a volume at which flow limitation did not reappear, in spite of evident bronchodilatation. It is possible that even in the early stages of chronic bronchoconstriction other mechanisms, such as a reduced $P_{el,L}$, may contribute to increase FRC. Alternatively, a reduction of $P_{el,L}$ by the bronchodilator [18] could have increased the relaxation volume of the respiratory system, thus preventing FRC from decreasing further.

We can speculate on the mechanism by which flow limitation might modulate FRC. During tidal breathing under conditions of flow limitation, the pleural pressure necessary to empty the lungs exceeds P_{crit} and the airways tend to collapse [10, 11]. Consequently, the mechanoreceptors located in the airway wall downstream from the flow-limiting segment might be stimulated, which could cause an unpleasant sensation of breathing [19,

20]. The neural reflexes from the collapsed airways might reach the respiratory centres, which in turn could prematurely stimulate the inspiratory muscles [21] to keep FRC high enough to avoid flow limitation. When the subjects from Groups 1 and 2 were given salbutamol, the opposite situation possibly occurred. Flow limitation at control FRC disappeared, inspiratory muscles were deactivated, and FRC could decrease.

The fact that no changes of breathing pattern were observed in Groups 1 and 2 after inhaling salbutamol does not necessarily imply that they did not occur. Assume, for instance, that an individual from these groups has a \dot{V}'_E of about $10 \text{ L}\cdot\text{min}^{-1}$ and a V_T of 0.75 L at a given lung volume (fig. 5). Inhaling salbutamol increases the airway calibre and abolishes airway compression at end-expiration. The next V_{TE} and t_E will increase, as there are no more obstacles causing expiration to terminate prematurely. In a few breaths, a new lung volume is attained, which could either be the relaxation volume of the respiratory system or the new volume at which flow limitation occurs again. The subject may then maintain the same breathing pattern as before. These transient changes of V_{TE} and t_E , which may be responsible for the decrement of FRC, could not be detected by our method.

From a qualitative point of view, the pattern of response of FRC to bronchodilators was similar in asthmatics and COPD, suggesting that dynamic regulation of lung volume during tidal breathing is relatively independent of the underlying disease. However, the decrement of volume in COPD was less than in asthmatics, probably

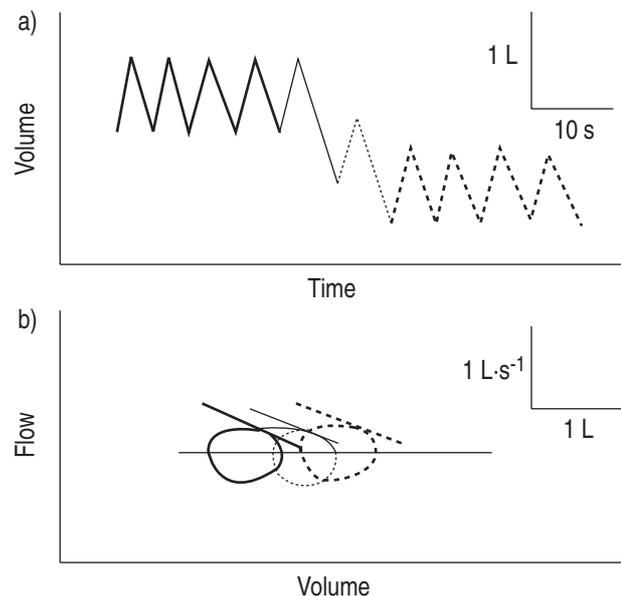


Fig. 5. – Hypothetical changes of breathing pattern when functional residual capacity (FRC) decreases after bronchodilatation. The same tidal breaths are represented as: a) a spirogram; and b) flow-volume loops. At baseline (thick lines), tidal expiration prematurely terminates when the tidal expiratory flow impinges on maximal flow (thick continuous oblique line in the lower panel). After bronchodilatation, the maximal expiratory flow increases (dashed oblique line in the lower panel), thus averting flow limitation. If we assume that flow limitation is the cause of hyperinflation, then the next two not flow-limited expirations (thin continuous and dotted lines) are no longer impeded and can reach a lower volume, until flow limitation occurs again. Ultimately, tidal volume and breathing pattern (dashed lines) may be the same as at baseline, but FRC is decreased.

because of less bronchodilatation or reduced $P_{el,L}$. This is in keeping with our interpretation that the starting signal for increasing FRC possibly arises when airways collapse, whatever the structural rearrangement of the airway wall.

In conclusion, the findings of the present study further support (even if they cannot prove) the hypothesis that dynamic compression of the airways downstream from the flow-limiting segment might act as a trigger for regulating functional residual capacity. The increase in functional residual capacity during chronic airway obstruction may represent a strategy aimed at breathing at a volume at which airway calibre is larger, thus avoiding dynamic compression. The clinical implications of this study are that the subjects who take greater advantage from bronchodilator treatment are possibly those who can decrease functional residual capacity, thus further reducing the elastic work of breathing.

Acknowledgement: The authors are very grateful to J.R. Rodarte for his criticism and suggestions.

References

- Pride NB, Macklem PT. Lung mechanics in disease. In: Handbook of Physiology. Section 3, Vol. III, Part 2. The Respiratory System. Mechanics of Breathing. Bethesda, MD, American Physiological Society, 1986; pp. 659–692.
- Babb TG, Viggiano R, Hurley B, Staats B, Rodarte JR. Effect of mild-to-moderate airflow limitation on exercise capacity. *J Appl Physiol* 1991; 70: 223–230.
- Pellegrino R, Brusasco V, Rodarte JR, Babb TG. Expiratory flow limitation and regulation of end-expiratory lung volume during exercise. *J Appl Physiol* 1993; 74: 2552–2558.
- Pellegrino R, Violante B, Nava S, Rampulla C, Brusasco V, Rodarte JR. Expiratory airflow limitation and hyperinflation during methacholine-induced bronchoconstriction. *J Appl Physiol* 1993; 75: 1720–1727.
- American Thoracic Society. Chronic bronchitis, asthma and pulmonary emphysema. *Am Rev Respir Dis* 1962; 84: 762–768.
- Quanjer PhH, Tammelin GJ, Cotes JE, Pedersen OF, Peslin R, Yernault J-C. Lung volumes and forced ventilatory flows. Report Working Party "Standardization of Lung Function Tests". European Coal and Steel Community. *Eur Respir J* 1993; 6 (Suppl. 16): 5–40.
- Shore SA, Huk O, Mannix S, Martin JG. Effect of panting frequency on the plethysmographic determination of thoracic gas volume in chronic obstructive pulmonary disease. *Am Rev Respir Dis* 1983; 128: 54–59.
- D'Angelo E, Prandi E, Marazzini L, Milic-Emili J. Dependence of maximal flow-volume curves on time course of preceding inspiration in patients with chronic obstructive lung disease. *Am J Respir Crit Care Med* 1994; 150: 1581–1586.
- Barnes PJ, Gribbin HR, Osmanliev D, Pride NB. Partial flow-volume curves to measure bronchodilator dose-response curves in normal humans. *J Appl Physiol: Respirat Environ Exercise Physiol* 1981; 50: 1193–1197.
- Olafsson S, Hyatt RE. Ventilatory mechanics and expiratory flow limitation during exercise in normal subjects. *J Clin Invest* 1969; 48: 564–573.
- Hyatt RE. Forced expiration. In: Handbook of Physiology. Section 3, Vol. III, Part 1. The Respiratory System. Mechanics of Breathing. Bethesda, MD, American Physiological Society, 1986; pp. 295–314.
- Koulouris NG, Valta P, Lavoie A, et al. A simple method to detect expiratory flow limitation during spontaneous breathing. *Eur Respir J* 1995; 8: 306–313.
- Remmers JE, Bartlett D, Jr. Reflex control of expiratory airflow and duration. *J Appl Physiol* 1977; 42: 80–87.
- Vinegar A, Sinnott EE, Leith ED. Dynamic mechanisms determine functional residual capacity in mice, *Mus musculus*. *J Appl Physiol: Respirat Environ Exercise Physiol* 1979; 46: 867–871.
- Kimball WR, Leith ED, Robins AG. Dynamic hyperinflation and ventilator dependence in chronic obstructive pulmonary disease. *Am Rev Respir Dis* 1982; 126: 991–995.
- Citterio G, Agostoni E, Del Santo A, Marazzini L. Decay of inspiratory muscle activity in chronic airway obstruction. *J Appl Physiol: Respirat Environ Exercise Physiol* 1981; 51: 1388–1397.
- Pardy RL, Rivington RN, Milic-Emili J, Mortola JP. Control of breathing in chronic obstructive pulmonary disease. *Am Rev Respir Dis* 1982; 125: 6–11.
- McFadden ER, Newton-Howes J, Pride NB. Acute effect of inhaled isoproterenol on the mechanical characteristics of the lung in normal man. *J Clin Invest* 1970; 49: 779–790.
- O'Donnell DE, Sani R, Anthonisen NR, Younes M. Effects of dynamic airway compression on breathing pattern and respiratory sensation in severe chronic obstructive pulmonary disease. *Am Rev Respir Dis* 1987; 135: 912–919.
- O'Donnell DE, Sani R, Giesbrecht G, Younes M. Effects of continuous positive airway pressure in patients with chronic obstructive pulmonary disease during submaximal exercise. *Am Rev Respir Dis* 1988; 138: 1185–1191.
- Meessen NEL, Van Der Grinten CPM, Folgering HThM, Luijendijk SCM. Role of lung receptors in generation of histamine-induced tonic inspiratory activity. *Eur Respir J* 1990; 3 (Suppl. 10): 140S.