Partial flow/volume curves and airway resistances in obese subjects: new tools for investigating flow limitation?

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Background, aims and methods

The number of obese patients referred to our laboratory for pulmonary function tests is increasing: sleep breathing disorders, unexplained effort dyspnea, evaluations before surgical procedures are the main problems we are expected to cope with. In some patients with normal FEV_1 and FEV_1/VC values, we have observed an overlap between the tidal volume expiratory flow and the maximal forced expiratory flow, a pattern that suggests expiratory flow limitation (EFL) [1]. EFL has been reported in obese patients without bronchial obstruction [2] and it is not surprising that some of our obese patients may be flow limited at rest.

Partial sub-maximal flow/volume curves (PSCs) have been reported as a tool for detecting expiratory flow limitation in patient with airway obstruction [3]. In COPD we described that when PSCs suggest the occurrence of EFL, a loop in the expiratory phase of quiet breathing airway resistance (Raw-qb) is frequently seen. We hypothised that a loop in the expiratory portion of Raw-qb could be a marker of EFL [4].

With the aim of seeing if the same issue was true for obese patients, we studied 45 consecutive obese subjects with no history of asthma, no bronchial hyperreactivity to methacoline challenge, and no acute or chronic obstructive lung disease. Thirteen patients had no graphic overlap between maximal flow-volume curves and tidal volume; the others had tidal volume expiratory flows impinging maximal forced expiratory flows in all manoeuvers, suggesting the likelihood of EFL.

The Raw-qb were obtained twice, when a patient was breathing at tidal volume, trying to minimise factors that could artificially create a loop (phase delay in flow measurement, artefacts due to gas temperature changes, air losses from the mouthpiece and cheek movements, plethysmographic losses). After at least eight stable tidal breaths, patients were invited to sligthly increase their respiratory rate to 18-24 breath/minute paced by technician: during this phase Raw - qb were collected.

PSCs, obtained according to the description by Pellegrino et alii, are extensively described elsewhere [3, 4]. The manoeuvres, were repeated 2-4 times.

All measurements were obtained at the same session with patients seated, using the Vmax 20 Sensor Medics.

The data was analysed using Systat statistical software, rel. 11.05 for Windows (SPSS Inc. Chicago). The results were expressed as means ± standard deviation and as frequency percentages.

The differences in variables between groups were evaluated by Student's unpaired two tailed *t*-test and ANOVA. The level of statistical significance for each test was set at <0.05. The association between variables was examined using bivariate correlations and Spearman's coefficient calculation.

Results

On the basis of spirometry and PSCs, patients were divided into four groups (figure 1):

Group 0: the 13 patients without suspected EFL at spirometry, with a wide flow reserve between tidal volume and maximal flows. These patients were "not flow-limited" (figure 1A).

Group 1: 10 patients with suspected EFL at spirometry but without any graphic overlap between PSCs and tidal volume. These patients were also defined as "not flow-limited" (figure 1B).

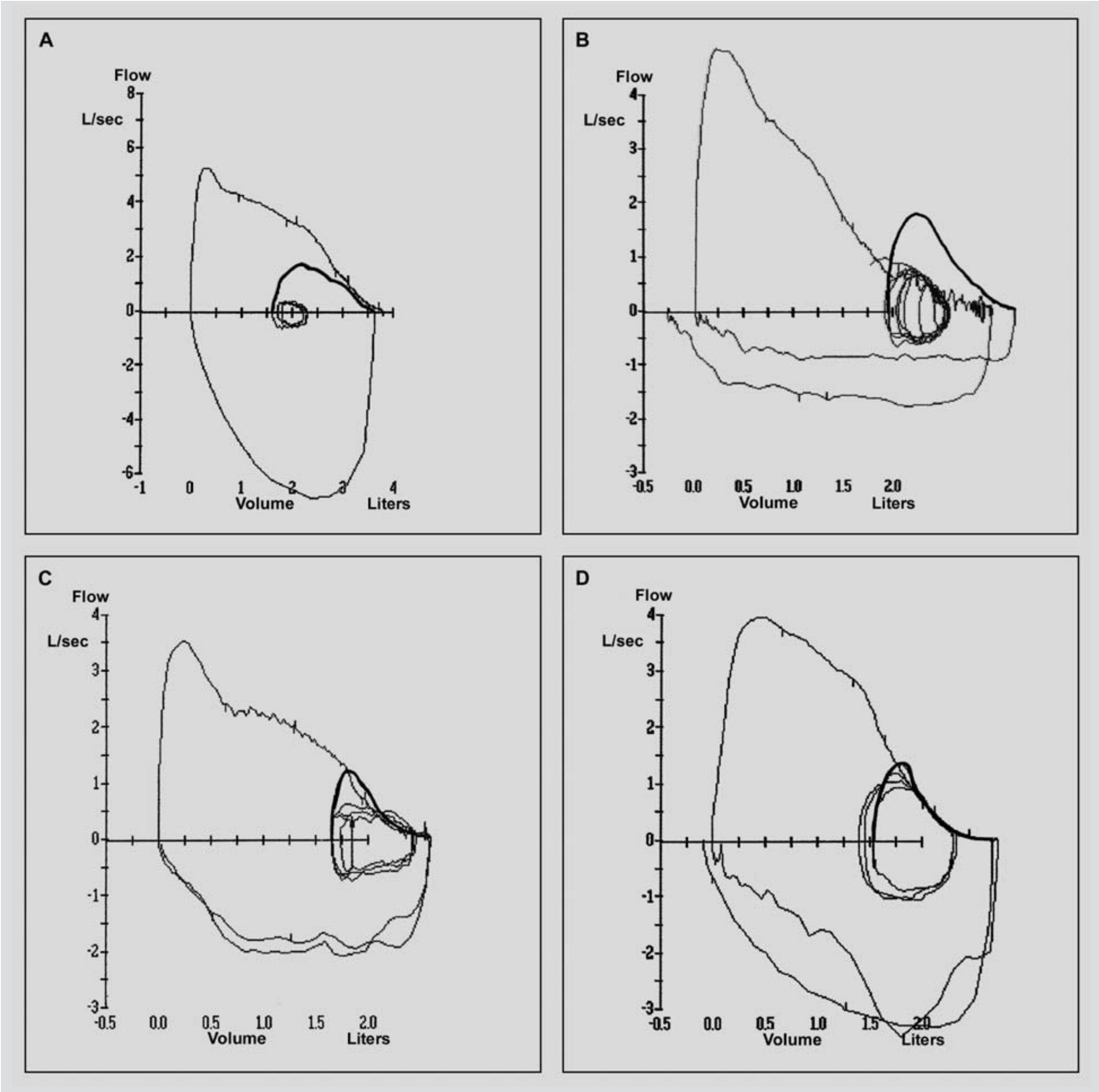

Fig. 1. - The diagrams show four examples of maximal flow/volume loops with the tidal volumes and PSC, for each study group. PSC are in boldface.
Fig. 1A, subjects without suspected EFL on standard spirometry (group 0).
Fig. 1B, subjects with suspected EFL on standard spirometry, not confirmed by PSC (group 1).
Fig. 1C, subjects with suspected EFL on standard spirometry confirmed by PSC, with a graphic overlap between PSL and tidal volume < 50% (group 2).
Fig. 1D, subjects with suspected EFL on standard spirometry confirmed by PSC, with a graphic overlap between PSL and tidal volume > 50% (group 3).

Group 2: 8 patients with suspected EFL at spirometry and a graphic overlap < 50% between PSCs and tidal volume: these patients were defined as very likely to have EFL < 50% of tidal volume (figure 1C).

Group 3: 14 patients with suspected EFL at spirometry and a graphic overlap > 50% between PSCs and tidal volume: these patients were defined as very likely to have EFL > 50% of tidal volume (figure 1D).

Table 1 shows the anthropometric parameters and baseline functional values for the subjects divided into two groups, i.e. not flow-limited (non-EFL, groups 0 and 1) and flow-limited (EFL, groups 2 and 3).

Baseline functional values, age and BMI among non-EFL subjects (groups 0 and 1) and EFL subjects (groups 2 and 3) did not differ significantly, apart from the vital capacity which was considered as an absolute value (abs.VC), and expiratory reserve volume as an absolute value (abs.ERV).

Patients were then split into two groups: type A (30 patients with no loop in the Raw-qb diagram) and type B (15 patients with the loop) (figures 2A and 2B).

The baseline functional values of type A patients differed significantly from type B for abs.VC and abs.ERV (table 2).

Type B patients (with the loop) belonged to groups 2 and 3. The percentage of type B subjects

Table 1. - Morphological characteristics and functional baseline values of subjects divided into non-EFL (group 0 and 1) and EFL(group 2 and 3), according to the outcome of PSC

	GROUP 0-1 (N 23; M/F=18/5)	*GROUP 2-3 (N 22; M/F=9/13)*
	Mean ± SD	Mean ± SD
AGE (years)	61.6 ± 12.1	66.1 ± 9.1
VC abs. (ml)	3917.3 ± 956.0	2922.3 ± 664.2*
VC % pred.	87.7 ± 14.2	84.8 ± 14.6
FEV_1 % pred.	91.5 ± 16.2	86.1 ± 15.1
TIFF abs.	74.5 ± 5.9	72.5 ± 5.1
TIFF % pred.	104 ± 7.1	103.8 ± 6.5
IC % pred.	104.8 ± 20.1	107.2 ± 19.5
FEF_{25-75}/VC	0.64 ± 0.18	0.57 ± 0.18
ERV (ml)	785.2 ± 339.2	393.2 ± 181.3*
Raw-qb	5.0 ± 2.0	5.5 ± 1.9
Sgaw-qb	0.08 ± 0.03	0.07 ± 0.02
BMI (Kg/m^2)	35.6 ± 4.1	36.2 ± 3.7

N: number of subjects; M/F: male/female ratio; SD: standard deviation; abs: absolute value; % pred: percentage of the predicted value; VC: vital capacity; FEV: forced expiratory volume; TIFF: Tiffenau index; IC: inspiratory capacity; FEF_{25-75}/VC: forced mid-expiratory flow; ERV: expiratory reserve volume; Raw-qb: quiet breathing airway resistance; Sgaw-qb: quiet breathing specific airway guidance; BMI: body mass index; *: p<0.001 in the differences between the means for the two groups.

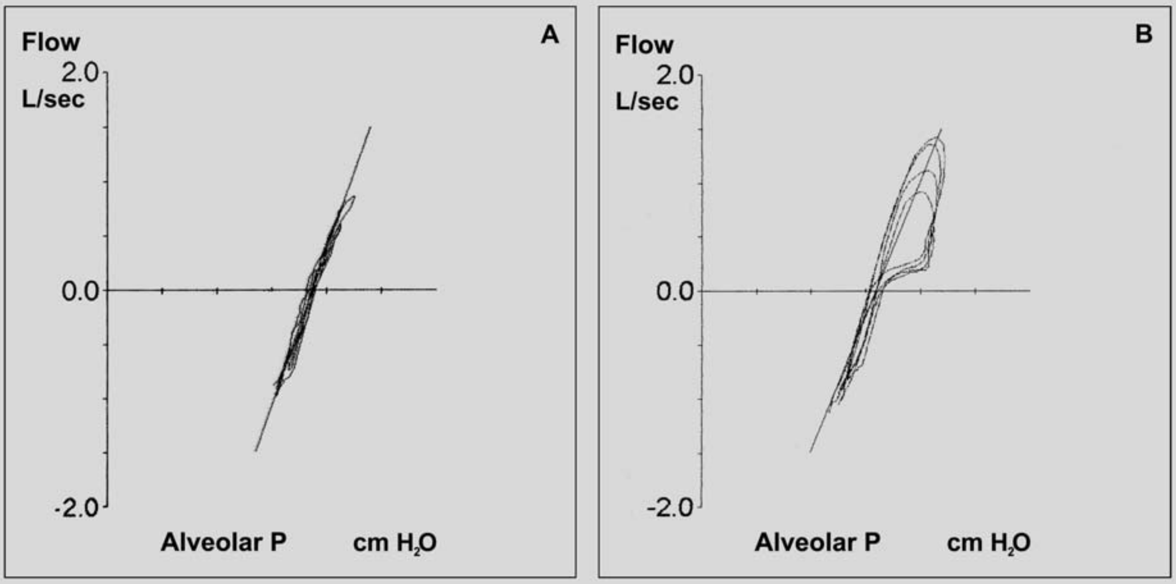

Fig. 2. - Examples of flow/pressure diagrams of Raw-qb with no loop (fig 2A, type A subjects) and with a loop (fig. 2B, type B subjects).

was significantly higher in group 3 than in group 2 (tables 3 and 4).

The Spearman test showed a significant correlation between EFL and abs.ERV (r: -0.67, p < 0.001), and between EFL and abs.VC (r: - 0.56, p < 0.001).

Brief comment

Our results suggest a relationship between the presence of a loop in the expiratory portion of the Raw-qb and the presence of EFL as suggested by PSCs.

The gold standard of EFL requires the demonstration of an increase in transpulmonary pressure with no increase in expiratory flow [5], but the method is time-consuming and invasive, and doesn't fit in to the clinical practice. Impinging of maximal flow/volume loop with tidal expiratory flow at standard spirometry may only rouse the suspicion of EFL, but it is not reliable for the diagnosis of EFL [6]. The NEP (negative expiratory pressure) technique is widely used to diagnose EFL. It does however require a specific device, and in obese patients has some drawbacks [2, 7, 8]. PSCs do not require specific devices, but the patient must be very cooperative [4].

Table 2. - Demographic characteristics and baseline functional values of subjects divided into groups according to the shape of the Raw-qb

	Type A (N 30; M/F=20/10)	Type b (N 15; M/F=7/8)
	Mean ± SD	Mean ± SD
AGE (years)	61.1 ± 11.4	69.2 ± 7.5°
VC abs. (ml)	3727.3 ± 958.0	2838.0 ± 653.6*
VC % pred.	87.7 ± 13.3	83.5 ± 16.2
FEV_1 % pred.	90.4 ± 16.1	85.8 ± 15.1
TIFF abs.	74.4 ± 5.8	71.8 ± 4.7
TIFF % pred.	103.9 ± 7.1	103.9 ± 6.1
IC % pred.	106.4 ± 21.2	105.0 ± 16.4
FEF_{25-75}/CV	0.63 ± 0.19	0.56 ± 0.16
ERV (ml)	702.3 ± 346.9	376.0 ± 168.0*
Raw-qb	4.9 ± 1.9	5.8 ± 2.1
Sgaw-qb	0.08 ± 0.02	0.07 ± 0.2
BMI (Kg/m^2)	35.6 ± 4.0	36.4 ± 3.7

N: number of subjects; M/F: male/female ratio; SD: standard deviation; abs: absolute value; % pred: percentage of the predicted value; VC: vital capacity; FEV: forced expiratory volume; TIFF: Tiffenau index; IC: inspiratory capacity; FEF_{25-75}/VC: mean expiratory forced flow in the 25-75 % part of forced vital capacity on vital capacity ratio; ERV: expiratory reserve volume; Raw-qb: quiet breathing airway resistance; Sgaw-qb: quiet breathing specific airway guidance; BMI: body mass index; °: $p<0.05$ in the differences between the means for types A and B; *: $p<0.001$ in the differences between the means for types A and B.

Table 3. - Frequency of expiratory loop in subjects divided into groups according to outcome of PSC

	GROUP 0 (N 13)		*GROUP 1 (N 10)*		*GROUP 2 (N 8)*		*GROUP 3 (N 14)*	
Type a	13	100%	9	90%	4	50%	4	28.6%
Type b	0	0%	1	10%	4	50%°	10	71.4%*

N: number of patients; Type a: number of patients with no expiratory loop in the Raw-qb diagram, expressed in absolute value and as a percentage, in groups 0-1-2-3; Type b: number of patients with an expiratory loop in the Raw-qb diagram, expressed in absolute value and as a percentage, in groups 0-1-2-3; °,*: $p<0.01$ in the differences of percentages between groups 2-1 and 3-2, respectively.

Table 4. - Frequency of expiratory loop in subjects divided in two groups (No FL: group 0 + group 1; FL: group 2 + group 3) according to outcome of PSC

	No FL (PSCs) (N 23)		*FL (PSCs) (N 22)*	
Type a (N 30)	22	73%	8	27% *
Type b (N 15)	1	7%	14	93% ***

N: number of patients; Type a: number of patients with no expiratory loop in the Raw-qb diagram, expressed in absolute value and as a percentage, in groups 0+1 (No FL) and 2+3 (FL); Type b: number of patients with an expiratory loop in the Raw-qb diagram, expressed in absolute value and as a percentage, in groups0+1 (No FL) and 2+3 (FL); *: $p<0.05$; ***: $p<0.001$ in the differences of percentages between FL and not FL subjects.

If a loop in the expiratory phase of Raw-qb were a marker of EFL, we should have a tool for the diagnosis of EFL easy to obtain from any laboratory testing Raw. We first advanced this hypothesis in COPD patients [4]. Now we have seen that while the PSCs strongly suggest EFL, Raw-qb diagram have an expiratory loop in obese patients too. Very recently other Authors [9] have proposed the loop in the pressure/flow diagram as a marker of EFL. Dellaca' *et al.* [9] used the Mead and Whittemberger method for measuring pulmonary resistance to detect EFL. They plotted flow resistive pressure (pfr) versus flow: when the graphs showed a loop where the flow decreased during expiration while Pfr increased, the breath was classified as “flow-limited”. We suggest that a loop in the Raw-qb may have the same functional meaning as the loop observed by Dellacà *et al.* [9]. Obviously more studies are needed, but we think that the topic deserves attention.

Our data also suggests also that in obesity EFL doesn’t seem to be only a BMI-related problem, but a ERV related problem too: the lower is the absolute ERV value, the greater is the likelihood of observing EFL. This means that obese patients with high BMI but preserved ERV may be not flow limited, and that obese patients with BMI close to 30 but breathing near to FRC (low ERV) may be flow-limited.

It is known that EFL contributes to the mechanism of dyspnea [10]. We suggest that a low ERV and the EFL could play a role in the effort dyspnea of obese patients. As a matter of fact, it is unclear why some obese subjects who have the same BMI are affected by dyspnea more than others [11]. Our hypothesis constitutes a possible explanation: weight is not the solely important factor, how much fat has "worn off" your ERV is also important. This easily happens if 1) ERV is low before weight gain 2) weight distribution is the visceral one (adipose tissue is distributed mostly at visceral level). For example, short elderly women with BMI ranging 25 to 35, and visceral fat distribution are often referred to our laboratory for effort dyspnoea. Short elderly women have the smallest ERV as an absolute value. In these patients even have a moderate fat increase in the abdomen (visceral fat distribution) which could easily lead to the virtual absence of ERV, EFL, dynamic hyperinflation [12] and effort dyspnea.

References

1. Hyatt RE. The interrelationship of pressure, flow and volume during various respiratory manoeuvres in normal and emphysematous patients. *Am Rev Respir Crit Care Med* 1961; 83: 676-683.
2. Ferretti A, Giampiccolo P, Cavalli A, Milich-Emili J,Tantucci C. Expiratory flow limitation and orthopnea in massively obese subjects. *Chest* 2001; 119: 1401-1408.
3. Pellegrino R, Brusasco V. Lung hyperinflation and flow limitation in chronic airway obstruction. *Eur Respir J* 1997; 10: 543-549.
4. Drigo R, Enzo E, Fontana M, Ferraresso A, Zambotto F. Curve flusso volume sottomassimali e resistenze delle vie aeree "quiet breathing" nella valutazione della limitazione di flusso in pazienti con BPCO. *Rassegna di Patologia dell'Apparato Respiratorio* 2002; 17; 367-376.
5. Mead J, Whittenberger JL. Physical properties of human lungs measured during spontaneous respiration. *J Appl Physiol* 1953; 5: 779-796.
6. Babb TG. Mechanical ventilatory constraints in aging, lung disease, and obesity: perspectives and brief review. *Med Sci Sports Exerc* 1999; 31: 12-22 (suppl).
7. Liistro G, Veritier C, Dury M, Aubert G, Stanescu D. Expiratory flow limitation in awake sleep disordered breathing subjects. *Eur Respir J* 1999; 14: 185-190.
8. Ninane V, Leduc D, Kafi SA, Nasser M, Houa M, Sergysels R. detection of expiratory flow limitation by manual compression of the abdominal wall. *Am J Respir Crit Care Med* 2001; 163: 1326-1339.
9. Dellacà RL, Santus P, Aliverti A, Stevenson N, Centanni S, Macklem PT, Pedotti A, Calverley PMA. Detection of expiratory flow limitation in COPD using the forced oscillation technique. *Eur Respir J* 2004; 23: 232-240.
10. Tantucci C. Limitazione dei flussi. In: Il volto della BPCO che cambia. Utet 2001, pp. 21-27.
11. El Gamal H, Khajat A, Shikora S, Unterborn JN. Relationship of dyspnea to respiratory drive and pulmonary function tests before and after weight loss. *Chest* 2005; 128: 3870-3874.
12. Babb TG, Buskirk ER, Hodgsar JL. Exercise and expiratory lung volumes in lean and moderately obese women. *Int J Obes* 1989; 13: 11-19.