WORK OF BREATHING–TIDAL VOLUME RELATIONSHIP: ANALYSIS ON AN *IN VITRO* MODEL AND CLINICAL IMPLICATIONS

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ABSTRACT. Objective. Work of breathing (WoB) is currently employed to assess the afterload on the respiratory muscles and to estimate the energy expenditure for breathing. Since WoB depends on the ventilated tidal volume (TV), $WoB*L^{-1}$, the indicized form of WoB has been employed as a measure of WoB which is independent of TV. Actually, the independence of $WoB*L^{-1}$ from the ventilated TV has never been demonstrated. The aim of this study was to verify the predicted TV-independence of $WoB*L^{-1}$ on an *in vitro* model. **Methods.** Our experimental model was constituted as follows: two endotracheal tubes, with internal diameter measuring respectively 6.5 and 8.5 mm, were alternatively connected with two rubber balloons whose compliance was respectively 0.02 and 0.06 L/hPa; the system was mechanically ventilated at ten different tidal volumes, ranging from 0.3–1 l. Flow rate was kept constant (35 l/m) during the whole experiment. **Results.** Both elastic components of the model showed a static volume–pressure relationship which was linear in the experimental range of TV. In all combinations of resistance and compliance WoB increased quadratically whereas $WoB*L^{-1}$ increased linearly with the growing TV ($p < 0.001$). **Conclusions.** These results demonstrate the TV-dependence of $WoB*L^{-1}$ and suggest that $WoB*L^{-1}$, if TV changes, cannot be considered as an index of respiratoy muscle afterload and should not be used as a guide for weaning patients from the mechanical ventilation. Finally, we introduced a new parameter (WoB_{1L}) which seems to be a more TV-independent measure of respiratory work.

KEY WORDS. Weaning, work of breathing, respiratory mechanics.

INTRODUCTION

Work of breathing (WoB) is defined as the work done by the ventilatory pump to accomplish a certain level of ventilation [1]. This parameter is currently employed both in clinics and in research to estimate the afterload on the respiratory muscles, to diagnose specific pathological conditions of the breathing system and to optimize mechanical ventilator setting as well as patient–ventilator interaction [2]. Moreover, WoB has been proposed as a predictive index for mechanical ventilation weaning [3]. Frequently in the literature WoB is normalized to the ventilated tidal volume (TV) as follows: $WoB*L^{-1}(J*L^{-1}) = WoB/TV$, evidently with the intention of comparing work performed at different TV [4, 5]. Furthermore, clinicians are now using $WoB*L^{-1}$, due to the availability of monitors for bedside evaluation of respiratory system mechanics whose software provide $WoB*L^{-1}$ value [6, 7].

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WoB contains an elastic (WoBel) and a resistive (WoBres) component due respectively to the elastic recoil of the lungs and chest wall and the non-elastic, mainly frictional, resistance to gas flow [8].

It has been known for many years that, if the compliance (C) of the system is constant in the considered range of TV, WoBel is proportional to TV^2 [9]. WoBel is the quantitatively major component of WoB in many published clinical data [10–14]; thus, the indicization WoB^*L^{-1} could not be adequate to compare work performed at different TV if such an important component of work is proportional to TV^2.

The aim of the present study was: (1) to evaluate on an *in vitro* model the the dependence of the whole WoB value (WoBel + WoBres) on TV variations; (2) to verify the adequacy of the widely diffuse use of WoB^*L^{-1} as a way to compare work performed at different volumes of ventilation.

MATERIALS AND METHODS

Model

The experiments were carried out on an *in vitro* model consisting of a resistive and an elastic component. Resistance (R_{aw}) was alternatively given by two endotracheal tubes (ETT) (Mallinkrodt, Glens Falls, NY) which different internal diameters: 6.5 mm ("R") and 8.5 mm ("r"). The elastic component was alternatively represented by two rubber balloons with different compliances: 0.02 L/hPa ("c") and 0.06 L/hPa ("C"). All four possible combinations between different resistance and compliance were studied: (a) "rc"; (b) "Rc"; (c) "rC"; (d) "RC".

Experimental protocol

In each condition the model was mechanically ventilated by a Puritan Bennet 7200a ventilator (Puritan Bennet, Carlsbad, CA) with ten different tidal volumes (TV), ranging from 0.3–1 l. Inspiratory flow rate (V'_{insp}) was constant (35 l/m) during the whole experiment and a square inspiratory flow waveform was selected. A two second end-inspiratory pause and a six breath per minute respiratory rate (RR) were used. The resulting expiratory time allowed the model to perform a complete expiration before the next cycle. The inspiratory oxygen fraction (FiO_2) was set at 0.21.

Measurements

A flow (V', l/m) and pressure (P, hPa) transducer (Varflex, Bicore, Irvine, CA) was placed between ET and Y piece of the ventilator's breathing circuit. Five respiratory cycles were studied in each condition of applied TV. V'_{insp} and P data were collected by the Bicore CP100 (Bicore) pulmonary monitor (sampling rate: 50 Hz), and processed by a personal computer using CP100UTL (Bicore) and Excel 5.0 (Microsoft) softwares.

After one of the components of the model and/or the entered TV was changed ten respiratory cycles were wasted before collecting data.

In all experimental conditions P values at the end of the inspiratory pause (Pel) were measured.

Calculated parameters

Data were calculated as the mean of five measurements. **TV** (l) values were obtained by integration of V'_{insp} trace by time. **WoB** (J) was calculated by integration of TV data by the corresponding P values. **WoBel** (J) values were calculated, assuming a linear static volume–pressure relationship, as the area of the right angled triangle whose cathetes are Pel (expressed in kPa) and TV [8]:

$$\mathrm{WoBel} = (\mathrm{Pel}^*\mathrm{TV})/2$$

WoBel values were than subtracted to WoB to obtain **WoBress** (J). $\mathbf{WoB^*L^{-1}}$ (J/L) values were computed dividing WoB by the ventilated TV.

Statistics

Regression analysis and correlation were used to describe the TV dependence of WoB and WoB^*L^{-1}.

RESULTS

Both elastic components of our model showed a static volume-pressure relationship which was linear over the whole experimental range of TV (Figure 1). In all combinations of resistance and compliance WoB increased quadratically with the increasing TV (Figure 2). WoBres, instead, increased linearly with TV (Figure 3). Despite the supposed indicization, WoB^*L^{-1} also increased linearly with the increasing TV (Figure 4).

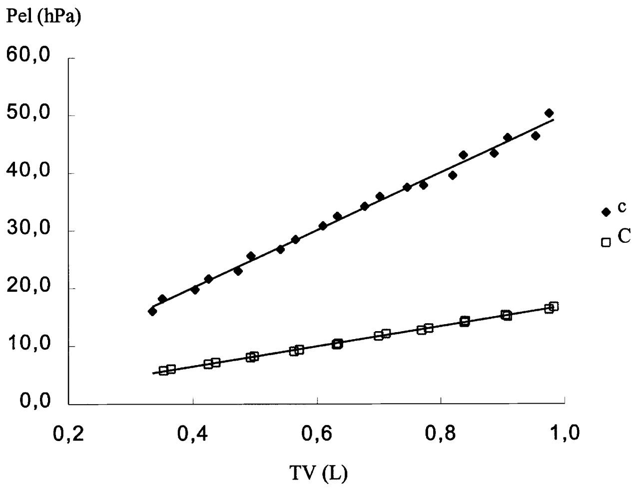

*Fig. 1. Static pressure–volume relationships of the two elastic components of the model. "C" setting (empty squares): Pel = −0.5 + 17.4 * TV, r = 0.999, p = 0.001; "c" setting (filled squares): Pel = 0.49 + 49.9 * TV, r = 0.997, p < 0.001.*

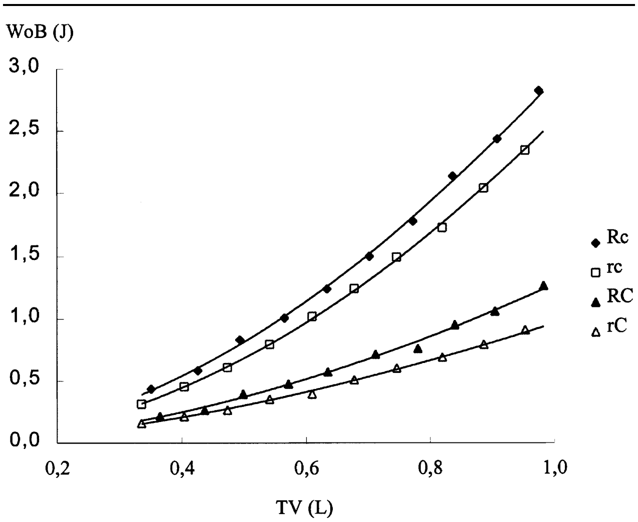

*Fig. 2. Volume-dependence of WoB. "Rc" setting: WoB = −0.01 + 0.36 * TV + 2.58 * TV^2, r = 0.999, p < 0.001; "rc" setting: WoB = −0.05 + 0.37 * TV + 2.22 * TV^2, r = 0.999, p < 0.001; "RC" setting: WoB = −0.03 + 0.29 * TV + 1.02 * TV^2, r = 0.995, p < 0.001; "rC" setting: WoB = 0.02 + 0.13 * TV + 0.8 * TV^2, r = 0.998, p < 0.001.*

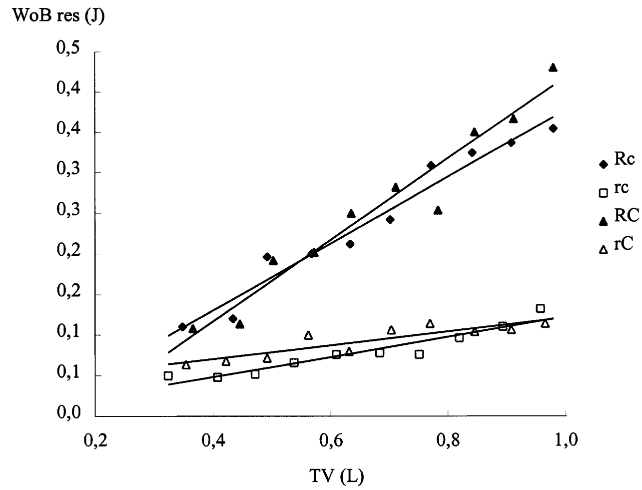

*Fig. 3. Volume-dependence of WoBres. "Rc" setting: WoBres = −0.03 + 0.41 * TV, r = 0.977, p < 0.001; "rc" setting: WoBres = 0.001 + 0.12 * TV, r = 0.96, p < 0.001; "RC" setting: WoBres = −0.09 + 0.51 * TV, r = 0.972, p < 0.001; "rC" setting: WoBres = 0.04 + 0.08 * TV, r = 0.867, p < 0.001.*

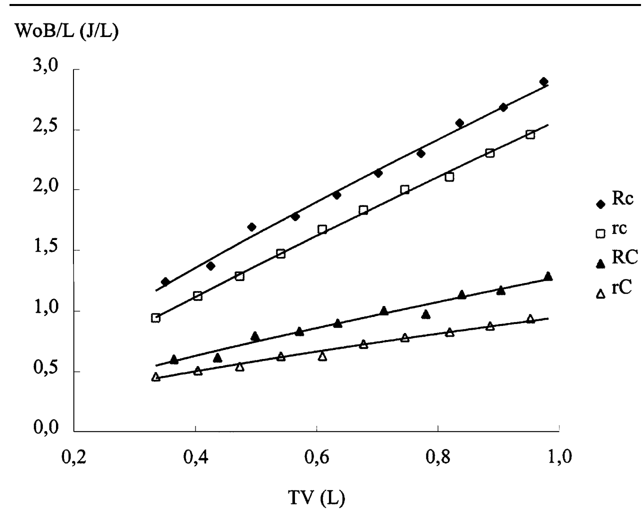

*Fig. 4. Volume-dependence of WoB*L^{-1}. "Rc" setting: WoB*L^{-1} = 0.3 + 2.63 * TV, r = 0.097, p < 0.001; "rc" setting: WoB*L^{-1} = 0.17 + 2.38 * TV, r = 0.099, p < 0.001; "RC" setting: WoB*L^{-1} = 0.19 + 1.1 * TV, r = 0.983, p < 0.001; "rC" setting: WoB*L^{-1} = 0.19 + 0.77 * TV, r = 0.096, p < 0.001.*

DISCUSSION

Our results show that: (1) WoB is exponentially related to TV; (2) WoB*L^{-1} varies linearly with changing TV.

In a previous study, the dependence of WoBel on TV^2 was demonstrated [9]. In accord with the clinical data published in the literature, in our model WoBel was also the main component of WoB (Table 1). The exponential increase of WoB we observed with increasing TV must almost entirely be attributed to the behaviour of the WoBel component previously described. In our model we kept constant in the inspiratory flow and varied TV just by prolonging the inspiratory time (T_i.

Table 1. Elastic and resistive components of WoB at the smallest and greatest values of TV, in the four experimental settings

TV	Rc		rc		RC		rC	
	WoBres	WoBel	WoBres	WoBel	WoBres	WoBel	WoBres	WoBel
0.35 ±0.01	0.11 ±0.01	0.32 ±0.00	0.05 ±0.00	0.26 ±0.00	0.11 ±0.00	0.11 ±0.00	0.06 ±0.00	0.10 ±0.00
0.98 ±0.01	0.35 ±0.00	0.46 ±0.03	0.13 ±0.00	0.22 ±0.03	0.43 ±0.00	0.82 ±0.00	0.11 ±0.00	0.79 ±0.02

In this way we did not vary the regimen of V'_{insp} values toward the turbulent flow.

Increases of V'_{insp} concomitant to TV increases are possible and probably frequent in the clinical setting and they are expected to increase, perhaps significantly, the exponentiality of the relationship between WoB and TV.

However, as our results suggest, this relationship remains exponential even if variations in V'_{insp} do not occur, due to the perceptually heavy influence of WoBel in determining the total WoB value.

The residual dependence of WoB*L^{-1} on TV is confirmed by our study. It follows that such indicization of work is not useful with inconstant TV. The WoB*L^{-1} value could be affected by the influence of ventilation as well as by true differences in the impedance offered by the breathing system to the ventilatory pump.

This could lead to misinterpretation of bedside collected data, both with regard to diagnostic conclusions and in evaluating the effects of ventilatory or pharmacological therapies.

We are identified some possibilities of errors arising when WoB*L^{-1} is employed to compare situations characterised by inconstant TV:

(1) Both TV and WoB*L^{-1} vary in the same direction (decrease or increase): the variation of WoB*L^{-1} could be totally or partially due to the changed TV, suggesting a false or erroneously quantified variation in the impedance of the respiratory system [11, 16, 17].
(2) TV and WoB*L^{-1} vary in opposite directions: a change of the impedance of the respiratory system is missed or erroneously quantified [4, 13, 18–20].

Among the examined literature, we cited just a few recent studies whose conclusions could be affected by interpretative errors due to an inappropriate use of WoB*L^{-1}.

Furthermore, it is not infrequent to read articles in which WoB, or WoB*L^{-1} values are presented without showing the measured TV data; in these cases the reader is not allowed even to exclude or suspect the "direction" of a possible error in the estimation of respiratory work [21, 22].

Because of these considerations, since WoB*L^{-1} cannot be used in conditions of inconstant TV, one could question the usefulness of this parameter, because in the authors' opinion it does not add any new information to the concept of WoB and moreover it can lead to incorrect conclusions: consequently, it should perhaps be abandoned.

Theoretically, a possible way to indicize WoB per volume of ventilation would be the calculation of a parameter which we call $\text{WoB}_{1\text{L}}$ (J*1L^{-1}), namely the theoretic work performed on the same breathing system ventilating a litre TV. This approach requires two assumptions: first, the compliance of the respiratory system has to remain constant until one litre TV in a given patient. Second, the ratio WoB/WoBel has to remain unchanged at various levels of TV. That is, WoBel and WoBres have to contribute in a perceptually constant amount to the total WoB value. Since WoBel changes quadratically with TV, this could occur when a TV change is exclusively due to a flow rate variation in regimen of turbulence: in this case the resistive pressure varies quadratically with flow [15] and a quadratic variation of Wres could be expected.

If we accept these conditions we may calculate $\text{WoB}_{1\text{L}}$ as follows: first we estimate $\text{WoBel}_{1\text{L}}$, namely the theoretic WoBel accomplished at one liter TV:

$$\text{WoBel}_{1\text{L}} = (1/C)/2$$

then, assuming constant the ratio WoB/WoBel at any level of TV,

$$\text{WoB}_{1\text{L}} = \text{WoB}^{*}\text{WoBel}_{1\text{L}}/\text{WoBel}$$

Despite these assumptions, $\text{WoB}_{1\text{L}}$ could reveal itself a useful TV-independent measure of WoB at bedside. In fact, it should eliminate the influence of the variable TV from the measure of WoB reporting the WoB value to an established level of TV. Further investigations are eventually needed to confirm the feasibility of its application and provide *in vivo* validation.

We conclude that every time TV is inconstant both WoB and WoB*L^{-1} cannot be considered as indexes of respiratory muscle afterload nor of energy expenditure for breathing. Therefore they should not be used as a guide for muscle fatigue judgement and for weaning patients from mechanical ventilation.

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