

A new approach to the determination of airway resistance: interrupter technique vs. plethysmography*

Uma nova abordagem na determinação da resistência das vias aéreas: técnica do interruptor vs. pletismografia

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Abstract

Objective: To determine the agreement between interrupter resistance (Rint) and airway resistance (Raw) by plethysmography in order to verify the clinical applicability of the interrupter technique. **Methods:** The Rint technique was performed with the patients in a sitting position, during exhalation, with a nose clip and cheek support. Plethysmography was carried out in accordance with standard protocols. All measurements were taken prior to and after the administration of an inhaled bronchodilator via a metered dose inhaler with a spacer. **Results:** The study comprised 99 consecutive patients referred to the Porto Alegre *Hospital de Clínicas*, located in the city of Porto Alegre, Brazil, for pulmonary function testing. Patient ages ranged from 18 to 82 years, and 52 of the patients were women. In the patients with $FEV_1 \geq 60\%$ of predicted, there was good agreement between the methods ($r = 0.8$; intraclass correlation coefficient = 0.8). The Rint values were lower than were those of Raw by plethysmography in the patients with more severe disease. However, there was good agreement between $Rint \geq 4 \text{ cmH}_2\text{O} \cdot \text{L}^{-1} \cdot \text{s}^{-1}$ and Raw by plethysmography $> 2.5 \text{ cmH}_2\text{O} \cdot \text{L}^{-1} \cdot \text{s}^{-1}$ (likelihood ratio > 8 ; kappa coefficient = 0.73). **Conclusions:** In the patients with less severe disease, there was good agreement between Rint and Raw by plethysmography. The agreement between the two methods was also strong regarding the detection of an increase in Raw. The Rint technique is a potentially useful method for the evaluation of adult patients.

Keywords: Plethysmography; Airway resistance; Diagnostic techniques, respiratory system; Respiratory function tests; Airway obstruction/diagnosis.

Resumo

Objetivo: Determinar a concordância da medida da resistência das vias aéreas (RVA) pela técnica *interrupter resistance* (Rint, resistência do interruptor) com a do método pletismográfico para fins de aplicabilidade clínica. **Métodos:** A técnica Rint foi realizada com os pacientes em posição sentada, em expiração, utilizando clipe nasal e com suporte das bochechas. O exame pletismográfico foi realizado de acordo com protocolos padronizados. As medidas foram realizadas antes e após a administração inalatória de um broncodilatador via spray dosimetrado com espaçador. **Resultados:** Avaliamos 99 pacientes consecutivos encaminhados para o Hospital de Clínicas de Porto Alegre, Porto Alegre (RS), para a realização de testes de função pulmonar, com idades entre 18 e 82 anos. Desses, 52 eram mulheres. Houve boa concordância entre os métodos ($r = 0,8$; coeficiente de correlação intraclass = 0,8) nos pacientes com $VEF_1 \geq 60\%$ do previsto. Os valores de Rint foram menores que os da RVA por pletismografia em indivíduos mais graves. Entretanto, houve boa concordância entre $Rint \geq 4 \text{ cmH}_2\text{O} \cdot \text{L}^{-1} \cdot \text{s}^{-1}$ e RVA por pletismografia $> 2,5 \text{ cmH}_2\text{O} \cdot \text{L}^{-1} \cdot \text{s}^{-1}$ (razão de verossimilhança > 8 e coeficiente kappa = 0,73). **Conclusões:** A concordância entre o Rint e a RVA por pletismografia foi boa nos indivíduos menos graves. A concordância para um diagnóstico de aumento da RVA entre os dois métodos também foi forte. A técnica Rint é um método potencialmente útil na prática assistencial em adultos. **Descritores:** Pletismografia; Resistência das vias respiratórias; Técnicas de diagnóstico do sistema respiratório; Testes de função respiratória; Obstrução das vias respiratórias/diagnóstico.

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Introduction

Airway resistance (R_{aw}) is understood as the degree of difficulty that the air has in moving through the airways, being an important parameter in pulmonary function testing.⁽¹⁻³⁾ It is calculated as the difference in pressure between the alveolus and the mouth, divided by the airflow rate.

Although it is possible to determine R_{aw} with the aid of plethysmography, a sensitive and reproducible method, plethysmography is complex, costly, and available at few facilities.⁽⁴⁾

The interrupter resistance (Rint) technique estimates alveolar pressure and measures total airway resistance by interrupting airflow briefly and transiently. By means of this technique, R_{aw} is determined, as is the elastic resistance of the chest wall and lung tissue, not being corrected for the lung volume at which it was determined. The technique is performed with the patients breathing at tidal volume, near functional residual capacity (FRC).^(1,5)

In measurements taken near FRC, the relative importance of R_{aw} (in determining airflow) increases, whereas that of elastic recoil, compliance, and patient effort is reduced. ⁽¹⁾ In addition, tissue resistance accounts for approximately 20% of the total resistance in normal subjects.⁽²⁾

The Rint technique is simple, is easy to perform, requires little cooperation, is portable, is noninvasive, and is inexpensive compared with plethysmography.^(3,6-8) In children, there are reference values and the correlation with R_{aw} by plethysmography is well documented,^(3,6,8-12) However, there are few data regarding this correlation in adults.

Patients with lung disease have been evaluated mainly by spirometry and whole-body plethysmography. Spirometry measures ventilatory capacity and is based on the presence of airflow limitation, defined by the FEV_1/FVC ratio. However, in situations in which FVC is reduced, such as in cases of obesity, this ratio can be normal. In such cases, an increase in R_{aw} or a reduction in specific airway conductance indicates airflow limitation.⁽¹⁾

Plethysmography allows the determination of lung volumes and R_{aw} .

The objective of the present study was to compare interrupter resistance (Rint) and R_{aw} by plethysmography in adults in order to determine

the clinical applicability of the interrupter technique.

Methods

The study comprised 99 consecutive patients referred to the Pulmonary Function Laboratory of the Porto Alegre *Hospital de Clínicas*, located in the city of Porto Alegre, Brazil, for pulmonary function testing between June of 2006 and January of 2007. Patient ages ranged from 18 to 82 years.

The Rint measurements were taken during routine practice at the facility, and the required variables, such as weight, height, gender, and age, were obtained for all patients.

A MicroRint device (Micro Medical Ltd., Kent, United Kingdom), which has been used in previous studies,^(3,10) was used for measuring Rint. The measurements were taken with the patients in a sitting position, with a mild cervical hyperextension, while using a nose clip and cheek support.^(10,13) Mouth pressure was estimated by two-point linear back-extrapolation (70 and 30 ms) from occlusion up to 15 ms after the valve was closed. Automatic random release of the occlusion valve occurred at PEF.

Six occlusions were performed prior to and after the use of inhaled albuterol (400 µg) via a metered dose inhaler with a small volume spacer.

The following equation was used for calculating R_{aw} ^(1,12):

$$R_{aw} = \text{Pressure} / \text{Flow}$$

We evaluated only patients with at least three technically satisfactory Rint measurements, in accordance with previously published criteria.^(3,10)

Prior to initiation of the measurements, the device was calibrated by the company responsible for providing technical assistance to that brand.

Spirometric measurements, as well as lung volume measurements and R_{aw} measurement by plethysmography, were performed with a MasterScreen Body device (Jaeger, Würzburg, Germany), by the Dubois method.⁽¹⁴⁾ The type of lung disease was defined by spirometry. The predicted values, the technique of performing the tests, and the test interpretation algorithm followed the Brazilian Thoracic Association Guidelines for Pulmonary Function Testing.⁽¹⁾ The Rint values and those of total

Raw by plethysmography are expressed in $\text{cmH}_2\text{O} \cdot \text{L}^{-1} \cdot \text{s}^{-1}$.

The patients underwent Rint measurements and, subsequently, Raw measurements by plethysmography. All measurements were repeated 15 min after inhaled bronchodilator use.

The analysis included determining correlation and agreement—with the use of Pearson's correlation coefficient and intraclass correlation coefficient (ICC)—between the Rint technique and plethysmography. The likelihood ratio (LR), kappa coefficient, the Youden index, the ROC curve, and the t-test were also used in the data analysis.⁽¹⁵⁻²⁰⁾ We also analyzed the correlations between the methods also after stratification by FEV_1 ($\geq 60\%$ or $< 60\%$ of predicted). We employed the Statistical Package for the Social Sciences, version 17.0 (SPSS Inc., Chicago, IL, USA). The study was approved by the Research Ethics Committee of the Porto Alegre *Hospital de Clínicas*.

Results

Initially, 99 consecutive patients were admitted. In 22 of those patients (12 in the pre-bronchodilator phase and 10 in the post-bronchodilator phase), it was not possible to measure Raw by plethysmography or to obtain at least three satisfactory Rint measurements. Therefore, we analyzed the data regarding 87 and 90 patients, respectively, prior to and after bronchodilator use.

Of the 99 patients, 52 (52.5%) were women. The mean age, height, and weight were 57.3 ± 14.6 years, 161.9 ± 8.6 cm, and 71.33 ± 15.1 kg, respectively. The mean FVC values in the pre- and post-bronchodilator phases were 74.42% and 78.48%, respectively, whereas those for FEV_1 were 63.61% (range: 22.2-118.3) and 67.47% (range: 26.0-123.4), respectively.

Regarding the type of lung disease (as defined by spirometry), 24 patients (24.2%) had normal results, 9 (9.1%) had restrictive lung disease, 6 (6.1%) had mixed lung disease, and 60 (60.6%) had obstructive lung disease.

In approximately half of the subjects (53%), FEV_1 was $\geq 60\%$ of predicted in the pre-bronchodilator phase.

The evaluation of the reproducibility of the Rint measurements showed a coefficient of variation (CV) of $14.5 \pm 8.31\%$ and $14.8 \pm 10.03\%$ in the pre- and post-bronchodilator phases, respectively, whereas the ICC values in the same phases were 0.87 and 0.88, respectively.

The correlation between the methods is shown in Table 1 and graphically represented in Figure 1.

As seen in the analysis of agreement between the two methods (Table 1), the CV was found to be 25.6% and 23.9% in the pre- and post-bronchodilator phases, respectively, whereas ICC was found to be 0.55 and 0.53 in the respective phases.

This overall agreement can be seen in the graph of the difference in means (Figure 2).

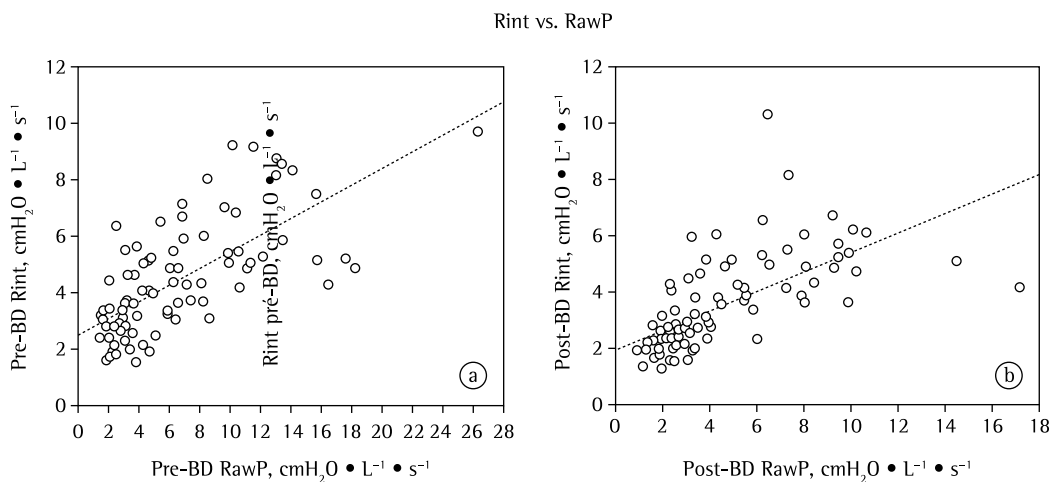


Figure 1 – In a), correlation between interrupter resistance (Rint) and airway resistance by plethysmography (RawP) in the pre-bronchodilator phase (pre-BD; $r = 0.74$). In b), correlation between Rint and RawP in the post-bronchodilator phase (post-BD; $r = 0.64$).

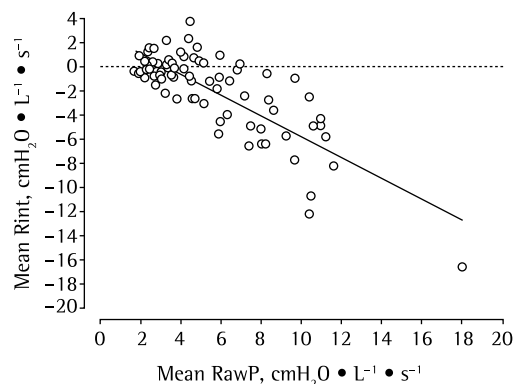
Table 1 – Analysis of the correlation between the interrupter technique and plethysmography.

Variable	Overall	FEV ₁ ≥ 60% of predicted	FEV ₁ < 60% of predicted
Pre-BD	0.74	0.80	0.67
r	(p < 0.01)		
Post-BD	0.64	0.72	0.49
r	(p < 0.01)		
Pre-BD	25.6	17.2	37.6
CV, %			
Post-BD	23.9	18.9	30.1
CV, %			
Pre-BD	0.55	0.80	0.28
ICC			
Post-BD	0.53	0.68	0.23
ICC			

r: Pearson's linear correlation coefficient; BD: bronchodilator; CV: coefficient of variation; and ICC: intraclass correlation coefficient.

In Figure 3, we illustrate the difference in the means, stratifying the patients by FEV₁ in % of predicted in the pre-bronchodilator phase. These graphs show that, in patients with an FEV₁ ≥ 60% of predicted, the Rint values oscillate near the mean, whereas, in patients with an FEV₁ < 60% of predicted, the Rint underestimates Raw in comparison with plethysmography.

The Pearson's correlation coefficient, ICC, and CV values reveal that the correlation between the two methods is weaker in the post-bronchodilator phase (Table 1). Graphically, the behavior of the values obtained in this phase is similar to that of those obtained in the pre-bronchodilator phase.

**Figure 2** – Bland & Altman plot of the difference between mean interrupter resistance (Rint) and mean airway resistance by plethysmography (RawP). The intraclass correlation coefficient is 0.55.

For the two methods, Raw decreased in parallel with increases in FEV₁.

In addition, we evaluated the agreement between the methods by analyzing sensitivity, specificity, and LR, as well as by using kappa statistics, as follows: we dichotomized our sample into normal patients (Raw ≤ 2.5 cmH₂O • L⁻¹ • s⁻¹) and impaired patients (Raw > 2.5 cmH₂O • L⁻¹ • s⁻¹), based on plethysmography (gold standard), and constructed a ROC curve, the area under the curve (AUC) being 0.87. For these data, the Youden index was 0.62, showing that Rint had a sensitivity of 69.1% and a specificity of 92.8% for a plethysmographic diagnosis of altered Raw.

The prevalence-adjusted kappa was 0.73 (95% CI: 0.34-0.78), indicating a diagnostic agreement of 87%.

For the LR, in addition to the cut-off point of 2.5 cmH₂O • L⁻¹ • s⁻¹ for normal Raw by plethysmography, we defined different cut-off points for Rint (1, 2, 3, and 4 cmH₂O • L⁻¹ • s⁻¹). These data are shown in Table 2.

Therefore, we obtained an LR of 8.24 and 0.13 when the Rint values were ≥ 4 cmH₂O • L⁻¹ • s⁻¹ or < 2 cmH₂O • L⁻¹ • s⁻¹, respectively.

In the 15 patients with bronchodilator response as measured by spirometry, the Rint values decreased by 34.2% and those of Raw by plethysmography decreased by 39.5% compared with the values obtained in the pre-bronchodilator phase, and this difference was not statistically significant (p = 0.27). In 1 of those patients, Rint increased after bronchodilator use.

Of the patients in whom there was a reduction in resistance in the post-bronchodilator phase, the variation between the pre- and post-bronchodilator phases was ≥ 30% in 44% (34/77) and 48.6% (35/72) for Rint and for Raw by plethysmography, respectively.

In the post-bronchodilator phase, Rint and Raw by plethysmography increased in 18 and 19 patients, respectively.

Discussion

We compared Rint and Raw by plethysmography in order to find a potentially useful correlation confirming the applicability of the Rint technique in clinical practice.

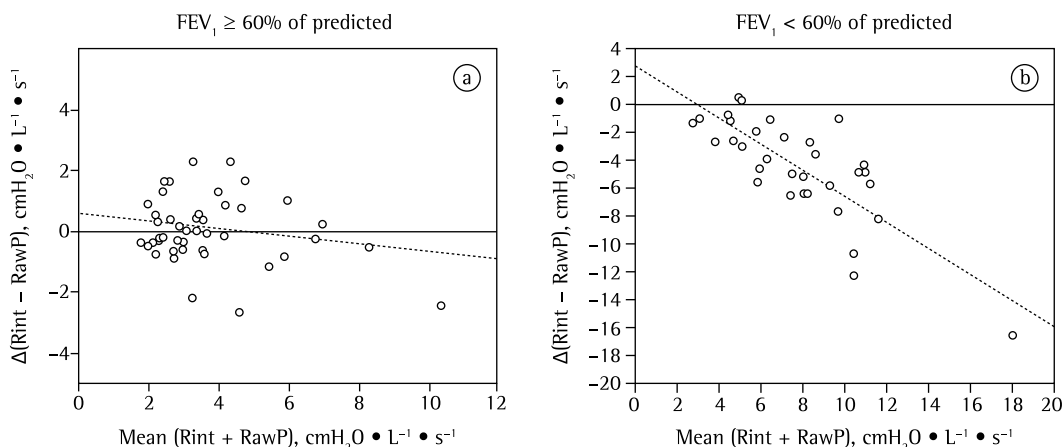


Figure 3 – Correlation of the difference between interrupter resistance (Rint) and mean airway resistance by plethysmography (RawP) with mean Rint+RawP in the pre-bronchodilator phase using the cut-off point of 60% of FEV₁ in % of predicted. In A, FEV₁ ≥ 60% of predicted (r = 0.80 and intraclass correlation coefficient [ICC] = 0.80). In B, FEV₁ < 60% of predicted (r = 0.67 and ICC = 0.28).

The characteristics of each method are well known and are available in the literature reviewed.

In the present study, FEV₁ in % of predicted ranged from 22.2% to 118.3%, indicating the presence of subjects whose status ranged from severely impaired to normal, from the standpoint of spirometry.

The data regarding Rint variability reported in our study are similar to those found in the literature. In the pre-bronchodilator phase, we found a mean CV of 14.5%, which is comparable to the values found by two other groups of authors, who reported mean CVs of 16.3% and 14.4%, respectively.^(3,4)

Another group of authors found a mean CV of 16% when using linear back-extrapolation in order to determine occlusion pressure.⁽²¹⁾

In children between 30 months and 5 years of age, one group of authors found the CV for expiratory Rint to be 15.5% and 18.1% in the pre-

and post-bronchodilator phases, respectively.⁽²²⁾ In our study, Rint was 14.8% in the post-bronchodilator phase. In contrast, another group of authors found mean CV values lower than 10% in adults.⁽²³⁾ In our study, we used the final result of Raw by plethysmography, because we do not have the mean CV for this method. However, data in the literature indicate that the mean CV for plethysmography (13.2%) is slightly lower than is that for the Rint technique.⁽³⁾

In our study, the reproducibility of the Rint measurements was considered good (ICC = 0.87). According to another study, ICC values below 0.6 are not useful.⁽¹⁵⁾

Regarding mean Raw values obtained by the two methods, previous studies^(3,11) have shown that Rint measurements are usually higher than are those of Raw by plethysmography. Higher Rint values might be explained by the fact that the Rint technique measures not only Raw but

Table 2 – Likelihood ratio between the interrupter technique and plethysmography, calculated by stratifying four interrupter resistance measurements by the number of patients above and below the cut-off point of 2.5 cmH₂O • L⁻¹ • s⁻¹ for Raw by plethysmography.

Rint, cmH ₂ O • L ⁻¹ • s ⁻¹	Patients, n		LR
	RawP > 2.5 cmH ₂ O • L ⁻¹ • s ⁻¹	RawP ≤ 2.5 cmH ₂ O • L ⁻¹ • s ⁻¹	
1	1	3	0.07 0.13
2	5	6	0.17
3	22	4	1.13
4	40	1	8.24

Rint: interrupter resistance; RawP: airway resistance by plethysmography; LR: likelihood ratio.

also a component of the chest wall and lung parenchyma.⁽⁵⁾

The algorithm used for estimating alveolar pressure can also have an influence, because measures based on the determination of pressure at the end of occlusion have resulted in higher Rint values compared with other algorithms, such as that of linear back-extrapolation.^(21,23)

Other factors that might explain differences in measurements between the two methods are the heterogeneity of airway impairment and to the fact that the time interval (100 ms) might not be sufficient for balancing alveolar pressure measured by the Rint technique.⁽¹¹⁾ These two last factors, however, would result in lower Rint values.^(11,23) In our study, using the analysis of the differences around the mean⁽¹⁶⁾ and not stratifying by the severity of airway obstruction, we found that the Rint typically underestimated Raw when compared with plethysmography.

However, when we stratified patients by disease severity based on FEV₁ in % of predicted, we found that the Rint values oscillated around the mean in the patients with FEV₁ ≥ 60% of predicted and that, in the patients with disease that was more severe (FEV₁ < 60% of predicted), Rint unequivocally underestimated Raw in comparison with plethysmography.

This dichotomous behavior of the Rint technique in relation to plethysmography can be easily seen in the graphic analysis (Bland & Altman)⁽¹⁶⁾ in Figures 2 and 3. These figures show that the difference between the Rint and plethysmography values for Raw is greater when the plethysmography values are more elevated.

One group of authors⁽¹¹⁾ found that the Rint values were higher than were those of Raw by plethysmography, except in patients with disease that was more severe, in whom, as in our study, the Rint values were lower than were those of Raw by plethysmography. However, those authors might have underestimated the Raw by plethysmography values, because the measurements were taken with the patients breathing at tidal volume and without panting.

Our finding that values obtained by the Rint technique were lower in the patients with disease that was more severe might be explained by the presence of lung hyperinflation and by the fact that resistance depends on the lung volume at which it was measured. In addition, on the Rint curve, the initial oscillation is dampened, and

there is a trend toward rounding of the pressure line (pressure-time curve) in patients with a greater degree of obstruction, which can cause difficulties in the back-extrapolation.⁽¹¹⁾

Naturally, two different methods are not expected to correlate perfectly.⁽¹⁶⁾ In the present study, we found the overall agreement, as measured by the ICC and without stratification by FEV₁ in % of predicted, to be low.

In general, the Rint underestimated Raw compared with plethysmography, especially in patients with disease that was more severe. Nevertheless, in subjects with disease that was less severe (FEV₁ ≥ 60% of predicted), we found that, as reported in other studies,^(3,15) the two methods correlated strongly with each other (r = 0.80) and had good agreement (ICC = 0.80).

In our ROC curve, we dichotomized the results into those for normal patients and those for impaired patients, based on plethysmography, and we obtained an AUC of 0.87. According to Bland & Altman,⁽¹⁷⁾ the AUC represents the probability of a person with the disease obtaining a higher value in the test under study in comparison with a person without the disease. Considering that a test is useless if the AUC = 0.5 and that a test is perfect if the AUC = 1.0 (maximum value),⁽¹⁸⁾ the value found in our study is considered good. Similarly, we obtained a Youden index of 0.62, indicating that Rint had a sensitivity of 69.1% and a specificity of 92.8% for the detection of an increase in Raw (Rint ≥ 4 cmH₂O • L⁻¹ • s⁻¹, corresponding to Raw by plethysmography > 2.5 cmH₂O • L⁻¹ • s⁻¹).⁽¹⁹⁾

For the upper cut-off points (Rint ≥ 4 cmH₂O • L⁻¹ • s⁻¹ and Raw by plethysmography > 2.5 cmH₂O • L⁻¹ • s⁻¹), we obtained an LR > 8 and a kappa index of 0.73, both of which are considered good.^(20,24)

According to Grimes & Schulz,⁽²⁰⁾ an LR near 1 has little effect on decision-making, whereas high or low values can significantly change the probability of disease. According to the same authors, an LR between 5 and 8 is considered moderate, whereas an LR above 10 is considered excellent. Therefore, given that the Rint technique is easy to perform and has practical and economic advantages over plethysmography, we believe that the results above are satisfactory.

Regarding the LR for Rint values ≤ 2 cmH₂O • L⁻¹ • s⁻¹, the value obtained (LR = 0.13) indicates a lower probability of Raw

being altered in these patients. However, the small number of patients ($n = 15$) with $R_{int} \leq 2 \text{ cmH}_2\text{O} \cdot \text{L}^{-1} \cdot \text{s}^{-1}$ imposes limits on this assertion.

Both methods revealed an inverse relationship between R_{aw} and FEV_1 in % of predicted.

The evaluation of bronchodilator response revealed that, in those patients with bronchodilator response as measured by spirometry, the drop in R_{aw} was similar in the two methods, a finding that is in agreement with those of other studies.⁽³⁾

In several of the patients in whom R_{aw} increased after bronchodilator use, we observed a reduction (of variable amplitude) in residual volume. However, conclusions regarding this issue require specific studies.

It should be borne in mind that plethysmography is available only in a few urban areas and research centers. In addition, there is little information available regarding the use of the R_{int} technique in adults. Few studies have attempted to obtain reference values⁽⁴⁾ or have compared the use of the R_{int} technique with that of impulse oscillometry in the diagnosis of COPD in elderly subjects⁽²⁵⁾ or have compared the use of the R_{int} technique with that of spirometry in bronchial challenge testing.⁽²⁶⁾

In 2009, one group of authors presented algorithms for estimating alveolar pressure by the R_{int} technique in adults, although no correlation was made with plethysmography.⁽²³⁾

In our analysis, the diagnostic agreement between the methods was strong in the subjects with disease that was less severe, as demonstrated by the fact that Pearson's correlation coefficient and the ICC were both 0.80. In these subjects, the R_{int} values differed from those of R_{aw} by plethysmography by being either higher or lower. In contrast, in the subjects with disease that was more severe, R_{int} clearly underestimated R_{aw} compared with plethysmography.

Our study sought to expand the comparative analysis of the R_{int} technique, attempting a more practical approach and employing more objective elements of correlation with plethysmography. Therefore, we believe we can provide some support for the cautious use of this technique in clinical practice in adults.

We conclude that the R_{int} technique is a useful tool and that it can be an alternative to plethysmography in certain cases, especially

if R_{int} is $\geq 4 \text{ cmH}_2\text{O} \cdot \text{L}^{-1} \cdot \text{s}^{-1}$, providing an acceptable degree of diagnostic certainty.

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