Arch Bronconeumol. 2009;**45(7)**:320-324

ARCHIVOS DE BRONCONEUMOLOGIA

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Original Article

Measuring Breathing Pattern in Patients With Chronic Obstructive Pulmonary Disease by Electrical Impedance Tomography

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ARTICLE INFO

Article history:
Received September 3, 2008
Accepted January 28, 2009
Available online June 3, 2009

Keywords:
Electrical impedance tomography (EIT)
Breathing pattern
Pneumotachometer
Calibration

ABSTRACT

Background and Objective: The measurement of breathing pattern in patients with chronic obstructive pulmonary disease (COPD) by electrical impedance tomography (EIT) requires the use of a mathematical calibration model incorporating not only anthropometric characteristics (previously evaluated in healthy individuals) but probably functional alterations associated with COPD as well. The aim of this study was to analyze the association between EIT measurements and spirometry parameters, static lung volumes, and carbon monoxide diffusing capacity (DLCO) in a group of male patients to develop a calibration equation for converting EIT signals into volume signals.
Materials and Methods: We measured forced vital capacity (FVC), forced expiratory volume in 1 second (FEV_1), FEV_1/FVC, residual volume, total lung capacity, DLCO, carbon monoxide transfer coefficient (KCO) and standard anthropometric parameters in 28 patients with a FEV_1/FVC ratio of <70%. We then compared tidal volume measurements from a previously validated EIT unit and a standard pneumotachometer.
Results: The mean (SD) lung function results were FVC, 72 (16%); FEV_1, 43% (14%); FEV_1/FVC, 42% (9%); residual volume, 161% (44%); total lung capacity, 112% (17%); DLCO, 58% (17%); and KCO, 75% (25%). Mean (SD) tidal volumes measured by the pneumotachometer and the EIT unit were 0.697 (0.181) L and 0.515 (0.223) L, respectively (P<.001). Significant associations were found between EIT measurements and CO transfer parameters. The mathematical model developed to adjust for the differences between the 2 measurements (R^2=0.568; P<.001) was compensation factor=1.81 – 0.82 × height (m) – 0.004×KCO (%).
Conclusions: The measurement of breathing pattern by EIT in patients with COPD requires the use of a previously calculated calibration equation that incorporates not only individual anthropometric characteristics but gas exchange parameters as well.
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Medición del patrón ventilatorio mediante tomografía por impedancia eléctrica en pacientes con EPOC

Palabras clave:
Tomografía por impedancia eléctrica (TIE)
Patrón ventilatorio
Neumotacómetro
Calibración

RESUMEN

Introducción: La medición del patrón ventilatorio (PV) en pacientes con enfermedad pulmonar obstructiva crónica (EPOC) mediante tomografía por impedancia eléctrica (TIE) requiere disponer de un modelo matemático de calibración que tenga en cuenta no sólo las características antropométricas (ya evaluadas en la persona sana), sino probablemente también las alteraciones funcionales propias de la enfermedad. El objetivo del presente estudio ha sido relacionar, en un grupo de pacientes (varones) con EPOC, las variables de la función pulmonar —espirometría, volúmenes estáticos, transferencia de monóxido de carbono (CO)— con las determinaciones de TIE y obtener una ecuación de calibración que permita convertir la señal eléctrica de la TIE en una señal de volumen.

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Material y métodos: Se estudió a 28 pacientes —volumen espiratorio forzado en el primer segundo (FEV_1)/capacidad vital forzada (FVC) < 70%— con un equipo TIE-4 previamente validado y se compararon los resultados con los de un neumotacómetro estándar. Previamente se determinaron los siguientes parámetros: FVC, FEV_1, FEV_1/FVC, volumen residual, capacidad pulmonar total, capacidad de difusión de CO y coeficiente de transferencia de CO (KCO), además de las variables antropométricas habituales.
Resultados: Los valores medios (± desviación estándar) de las diferentes pruebas funcionales fueron: FVC del 72 ± 16%; FEV_1 del 43 ± 14%; FEV_1/FVC del 42 ± 9%; volumen residual del 161 ± 44%, capacidad pulmonar total del 112 ± 17%; capacidad de difusión de CO del 58 ± 17%, y KCO del 76 ± 25%. Los valores medios de volumen circulante de las determinaciones obtenidas con el neumotacómetro y la TIE fueron de 0,697 ± 0,181 y 0,515 ± 0,223 l, respectivamente ($p < 0{,}001$). Se encontraron relaciones significativas entre las medidas de la TIE y la transferencia de CO. El modelo matemático para ajustar las diferencias entre ambas determinaciones ($R^2 = 0{,}568$; $p < 0{,}001$) fue: factor de compensación = 1,81 − 0,82 × talla (m) − 0,004 × KCO (%).
Conclusiones: La medición del PV mediante un equipo de TIE en pacientes con EPOC requiere una calibración previa que tenga en cuenta no sólo las características físicas de cada individuo, sino además la situación funcional del área de intercambio gaseoso.
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Introduction

The measurement, and, in particular, the monitoring of breathing pattern for long periods of time are processes that respiratory medicine has not yet fully resolved. Pneumotachography, which is the current method of choice, alters breathing dynamics as it requires the use of a mouthpiece or a mask. Alternative methods, in particular respiratory-inductive plethysmography, have been all but abandoned because of calibration problems, which in many cases, are unsurmountable.[1] Another more recently proposed alternative is the use of vibration response imaging, although further analysis of this system for measuring breathing pattern over long periods of time is required.[2] Studies of the use of electrical impedance tomography (EIT) to measure single lung function[3-5] and, more recently, breathing pattern in healthy individuals have shown that system calibration is a major problem in EIT as well.

EIT converts an output impedance signal into a series of chest images, which must subsequently be converted into a volume signal.[6] This conversion requires the use of mathematical models that incorporate key anthropometric variables for the individual being studied. Our studies of healthy individuals have shown that these variables are sex (calibration is more difficult in female patients), skinfold thickness (front, side, back, and subscapula), and chest circumference (different fat distribution and presence of mammary glands).[7]

Our initial observations in patients with respiratory disease indicated that the calibration of EIT units would be further complicated by internal chest alterations, which, like external factors, vary from patient to patient. The presence and extent of air trapping in addition to varying gas exchange surface areas, for example, could alter electrical transmission. We thus realized that if we were to use EIT to measure breathing pattern (tidal volume) in patients with chronic obstructive pulmonary disease (COPD), we would need to take account of both internal and external chest characteristics.

The aim of the present study was to analyze the association between a range of lung function parameters and electrical impedance measurements to establish a mathematical calibration model which, when used in addition to the existing model for external chest factors, would allow EIT to be used in the measurement and monitoring of breathing pattern in male patients with COPD.

Materials and Methods

EIT-4

The EIT-4 is a fourth-generation EIT prototype unit designed by the electronic engineering department at Universitat Politècnica de Catalunya, Spain. It permits the recording of volume-time signals from a sequence of images obtained using 16 electrodes (Red Dot 2560; 3 M, London, Ontario, Canada) arranged on the chest of the individual being studied.

The images are obtained following the injection of a 1-mA current at a frequency of 48 kHz through the 16 electrodes. The current is routed to a pair of multiplexers, which subsequently inject the current into the individual's body through a pair of electrodes. Using a special detector system, the other electrodes sequentially measure the voltages generated on the chest surface. Once the measurements have been recorded for this pair of electrodes, the injection and detection points are moved to an adjacent pair of electrodes and a new cycle begins.[8] This procedure is repeated until all the electrodes have been used as injectors and detectors. The EIT-4 has been tested in previous studies[3-9] and is used for other measurements at the lung function laboratory at our center.

The procedure described produces a matrix of surface transconductances, which are converted into regional changes in conductivity inside the body using an appropriate reconstruction algorithm. Finally, the scale of impedance values must be individualized as these values, as has already been mentioned, vary according to the physical characteristics of each person. The tidal volume for healthy males is thus estimated using the following formula:

$$\Delta V_{male} = (\Delta IC)/(2908 - 13.2 \times W(kg) - 3.7 \times SS\_Sk\,(mm))$$

Where ΔIC is the sum of the conductivity changes in the region studied, W is the weight, and SS_Sk is the subscapular skinfold.

Volunteers

We studied 28 men with an existing diagnosis of COPD (forced expiratory volume in 1 second [FEV_1]/forced vital capacity [FVC] <70%) who were consecutively enrolled as they visited our laboratory for lung function tests. All the tests were performed between 9 AM and noon in a quiet room at sea level with an ambient temperature of 25°C and a relative humidity of 60%. The patients all voluntarily consented to participate in the study, which had been previously approved by the ethics committee at our center.

Procedure

The pneumotachometer and the EIT-4 were mounted in parallel and operated independently of each other, with no mutual influence. Prior to use, they were calibrated as follows:

- The pneumotachometer was calibrated using a 3-L gas syringe in accordance with standard laboratory protocols (acceptable deviation, <1%).
- The EIT-4 was calibrated using a previously validated equation for healthy individuals.[6,7] Finally, image capture speed (16-18 images per second) was tested at the moment of measurement.

Before each measurement, we recorded anthropometric data (age, weight, height, and body mass index) and measured skinfolds (front, side, back, and subscapula) using electronic skinfold calipers. We then performed the corresponding lung function tests (spirometry, static lung volumes, and carbon monoxide transfer), and finally, following a 15-minute rest period, proceeded to measure breathing pattern. For each patient, once the 16 electrodes had been positioned and the units calibrated and connected, 3 different readings were recorded and stored in txt- and asc-extension files for subsequent processing. Tidal volume measurements over periods of 30 seconds (between 5 and 8 respiratory cycles) were recorded both graphically and numerically, with a 3-minute interval between measurements. A total of 20 to 25 cycles were recorded for each patient.

Statistical Analysis

Data were expressed as means (SD), and pneumotachometer and EIT-4 measurements were compared using the *t* test for nonparametric variables. Relationships between variables were analyzed using the Spearman correlation coefficient and differences in tidal volume measurements were evaluated using Bland-Altman analysis. Statistical significance was set at a value of *P* less than .05 in all cases. Finally, all the variables were studied using multivariate regression analysis to obtain an equation model that could be used to calibrate the EIT-4 for patients with COPD.

Results

The mean (SD) anthropometric parameters for the series (which included men only) were an age of 69 (9) years, a height of 1.65 (0.07) m, a weight of 76 (12) kg, and a body mass index of 28 (4.2) kg/m^2. The skinfold measurements were 23 (6) mm (front), 25 (8) mm (side), 24 (8) mm (back), and 26 (9) mm (subscapula).

FVC and FEV_1 values were 72% (16%) and 43% (14%) of predicted, respectively, and the FEV_1/FVC ratio was 42% (9%). For the 22 patients in whom we were able to measure static lung volumes, we found a mean residual volume of 161% (44%) of predicted and a total lung capacity of 112% (17%) of predicted. Based on CO transfer measurements performed in 19 patients, we found a mean carbon monoxide diffusing capacity (DLCO) of 58% (17%) of predicted and a CO transfer coefficient (KCO) of 76% (25%) of predicted (Table 1).

Mean tidal volume measured by the pneumotachometer and the EIT-4, respectively, was 0.697 (0.181) L and 0.515 (0.223) L (P<.001). The mean of the differences between the measurements obtained using both units was 0.182 (0.125) L, with a Spearman correlation coefficient of r=0.825 (P<.01).

The correlation between the lung function parameters studied and the impedance index, together with the differences in tidal volume measurements from both units, are shown in Table 2. Statistically significant correlations were found between the impedance index and FEV_1/FVC, DLCO, and KCO on the one hand and between the difference in tidal volume measurements from the 2 systems and DLCO and KCO, on the other.

The Figure shows the differences in tidal volume measurements from both units with respect to values obtained using the pneumotachometer. The mean of the differences was 0.432 L, with limits of agreement ranging from +0.422 to −0.068 L. All the measurements fell within this interval. Nonetheless, this mean difference can be corrected using the following expression: (R^2=0.568, P<.01).

$$\text{Differences} = 1.81 - 0.82 \times \text{height (cm)} - 0.004 \times \text{KCO (\%)}$$

The estimation for COPD patients would therefore be as follows:

$$\Delta VCOPD = \Delta V_{males} + \text{Differences}$$

Discussion

The findings of the present study indicate not only that tidal volume measured by EIT in patients with COPD should be adjusted for external factors (basically height) but also that lung alterations,

Table 1
Lung Function Variables in the Study Population [a]

Patient	Spirometric Values, %			Static Volumes, %		CO Transfer Values, %	
	FVC	FEV_1	FEV_1/FVC	RV	TLC	DLCO	KCO
1	55	33	41		–	–	–
2	74	36	35	213	129	41	67
3	58	37	42	109	86	72	111
4	60	30	34	–	–	–	–
5	71	46	44	–	–	–	–
6	52	37	53	168	93	77	112
7	76	52	48	136	106	–	–
8	76	50	49	159	110	66	81
9	88	64	54	118	106	78	83
10	75	65	59	–	–	–	–
11	47	30	47	–	–	–	–
12	56	38	49	146	94	80	139
13	64	48	54	–	–	–	–
14	71	39	39	159	113	59	80
15	94	57	45	148	120	–	–
16	70	25	25	173	116	50	60
17	114	68	42	113	125	49	52
18	90	47	37	–	–	41	55
19	44	22	36	–	–	–	–
20	87	48	41	195	130	67	61
21	96	75	54	133	113	70	82
22	64	42	46	68	70	66	86
23	84	39	32	191	127	80	79
24	63	35	39	219	128	53	80
25	70	30	30	136	102	37	74
26	65	25	28	215	123	23	34
27	76	49	44	161	117	47	59
28	78	43	41	251	141	47	48
Mean	72	43	42	161	112	58	76
SD	16	14	9	4	17	17	25

Abbreviations: CO, carbon monoxide; DLCO, CO diffusing capacity; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; KCO, CO transfer coefficient; RV, residual volume; TLC, total lung capacity.
[a] All the values are presented as percentages of predicted.

Table 2
Correlation Matrix for Lung Function Variables Analyzed With Impedance Index and Difference Between Tidal Volume Measurements From Pneumotachometer and Electrical Impedance Tomography Unit

Parameters	Impedance Index		Tidal Volume Difference	
	r	P	r	P
FVC, % predicted	0.159	.419	0.090	.962
FEV_1, % predicted	−0.024	.253	−0.116	.557
FEV_1/FVC, % predicted	−0.559	.020	−0.263	.176
RV, % predicted	0.054	.822	0.099	.677
TLC, % predicted	0.108	.650	0.121	.611
DLCO, % predicted	−0.599	.007	−0.576	.010
KCO, % predicted	−0.630	.004	−0.642	.003

Abbreviations: DLCO, carbon monoxide (CO) diffusing capacity; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; KCO, CO transfer coefficient; RV, residual volume; TLC, total lung capacity.

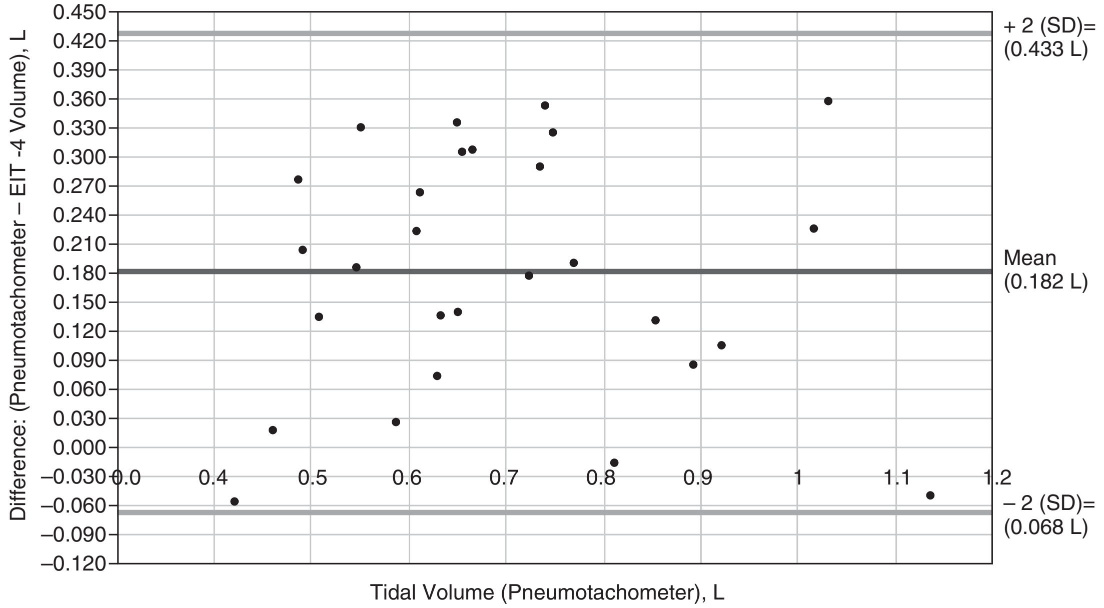

Figure. Band-Altman Plot. Distribution of tidal volume measurements with respect to pneumotachometer values. EIT, electrical impedance tomography; SD, standard deviation.

expressed in terms of reduced gas exchange area, change the value of the EIT signal recorded.

These conclusions are essentially based on the association observed between the overall impedance value and variables that reflect the size of the gas exchange area. Although we also observed a significant relationship between impedance and airflow obstruction, this parameter was not included in the final equation. No significant correlation was found between impedance and residual volume, indicating that air trapping, regardless of its extent, does not have a significant effect on the transmission of the electrical signal.

While tidal volume measurements obtained using both the pneumotachometer and the EIT-4 were, logically, significantly associated, the distribution of these measurements on a Bland-Altman plot (Figure) shows that almost all of the EIT measurements were lower than those obtained using the pneumotachometer. Furthermore, the difference between the measurements was statistically significant. Nonetheless, as shown in the multivariate equation, this difference can be compensated for with a mathematical process that corrects this practically systematic error.

The main problem associated with using EIT to measure tidal volume during breathing at rest lies in the difficulty of calibrating the electrical signal and obtaining a comparable and lasting volume signal. Anthropometric parameters, and particularly those that refer to the chest (skinfolds and weight) must be taken into account when adjusting EIT measurements in healthy individuals.[7] In patients with COPD, however, lung parameters, such as airflow obstruction, air trapping, and reduced gas exchange area, must also be taken into account. Of these variables, the only one that had a significant effect on measurements in our case, and consequently should be incorporated into the adjustment equation for COPD, was KCO. Because we only studied men, skinfold thickess did not have a significant effect on our measurements. Indeed, as occurs in spirometry, height was the factor that had the greatest influence. The above observations are particularly relevant for studies involving female patients with COPD.

Numerous international research groups are involved in the study of how to calibrate EIT volume-time measurements using different mathematical equations that model individual characteristics. The main problem lies in finding a method capable of converting the electrical signal into a volume signal. The research group at the clinical engineering department of the University of Kiatasato in Sagamihara, Japan proposed a calibration method based on adjusting measurements to a mathematical model incorporating lung tissue density and conductivity variables obtained in experimental models.[10] They actually proposed using this model to measure spirometric and static lung volume parameters in addition to tidal volume. Their findings have only been validated, however, in a small, homogeneous group of young, healthy, and very thin individuals.

An alternative approach proposed by the research group at the University of Biomedical Engineering of Tel-Aviv in Israel is based on a calibration method involving the characterization of the right and left lung using a theoretical reconstruction algorithm that measures the resistivity of each lung.[11] They validated their model in 33 healthy individuals and obtained volume-time results that were not significantly associated with anthropometric parameters.

Frerichs,[12] in a magnificent review of the literature, evaluated the efforts made by different groups to resolve this calibration problem. Her analysis of 37 articles published between 1985 and 1999 highlighted the vast diversity of applications proposed, the small size of the groups (healthy individuals and patients) studied, the complexity of the methods described, and finally, the need to find a simple solution to adjust EIT measurements to changes in lung volume. The only efforts made in this respect in recent years have been by Nebuya et al[10] and Zlochiver et al.[11] Our findings are both novel and practical as our method involves the use of simple variables (anthropometric data) and basic lung function parameters, readily available for patients with COPD. They do, however, need to be validated in a second group of patients with COPD and similar physical characteristics.

The behavior of an electric current flowing through body tissue is influenced by the characteristics of the current. A wide range of factors such as the distribution of body fat around the chest, lung volume, skin rigidity, height, and weight all influence current transmission, and consequently, changes in tissue impedance. Other factors that occur within the chest in different diseases, such as rigidity, obstruction, and air trapping, can also alter current flow. This complicates the matter of calibration even further as different diseases alter lung tissues in a different manner, meaning that separate calibration systems would be required for different types of disease.

One solution would be to use EIT to monitor breathing pattern only and not to measure volume. Given the lack of a simple, quick procedure that could be used to evaluate from the outset the main variables that might modify current flow through the chest, EIT should be used only to assess changes over time, regardless of true tidal volume. An alternative would be to perform measurements simultaneously with an EIT unit and a pneumotachometer, but this would not eliminate the need for consecutive measurements over a long period of time.

Funding

This study was funded by grants from the Breathe Network (Red Respira) of the Instituto de Salud Carlos III, the Spanish Society of Pulmonology and Thoracic Surgery (SEPAR), and La Marató de TV3.

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