Evaluation of transthoracic bioelectrical impedance analysis in monitoring lung water during diuresis

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ABSTRACT

Objective: To evaluate if noninvasive monitoring of lung water by transthoracic bioimpedance analysis adds useful information to standard clinical parameters while diuresing patients with edematous lungs. *Design:* Prospective, observational study . *Setting:* University tertiary care teaching hospital. *Patients and interventions:* Fifty-one healthy controls had right chest transthoracic BIA measured to determine normal right chest resistance and right lung resistivity. Fourteen hospitalized fluid-overloaded patients with edematous lungs were subsequently evaluated by serial right transthoracic BIA measurements before and after four days of diuresis. *Measurements and main results:* Although right transthoracic resistances were significantly higher in healthy women than men, there were no significant between-sex differences in calculated right lung resistivities. Combined male and female right lung resistivities were normally distributed. Natural log conversion of chest resistivity (named t-BIA) yielded a mean of 6.54 ± 0.23, with a coefficient of variation of 3.5%. Hospitalized patients had right lung t-BIAs significantly lower than normals before diuresis (6.22 ± 0.48; $p < 0.01$). After diuresis, these rose into the normal range (6.40 ± 0.51). Eight patients (57%) had an increase in chest resistivity, i.e., drier lungs and weight loss. Four patients (29%) who lost weight had wetter lungs and two patients (14%) who gained weight had drier lungs. Chest resistivity changes did not correlate with changes in body weight, chest exam or fluid balance. Conclusion: During diuresis, t-BIA measured changes in lung water add useful additional information to standard clinical parameters by both monitoring the dynamic changes that occur during treatment and by helping to establish meaningful therapeutic endpoints.

INTRODUCTION

Fluid overloaded patients with edematous lungs requiring diuresis comprise a significant hospitalized population. During diuresis, standard monitoring includes the evaluation of clinical signs and symptoms, chest radiographs and/or weight change. However, quantifying the extent of pulmonary edema and monitoring lung water changes in these patients is difficult. A number of studies have shown that clinical and radiographic findings of pulmonary congestion from congestive heart failure show poor correlation with invasive measurements of pulmonary capillary wedge pressures [1-3]. Other methods that directly measure lung water (e.g., double dilution techniques) are invasive, expensive, complicated and time-consuming or no longer clinically available [4, 5]. A simple, fast, easily implemented, non-invasive tool to objectively measure lung water might be clinically useful when diuresing patients. One technology that has the potential to do this is transthoracic bioetectrical impedance analysis [612]. In BIA, an alternating electrical current is passed through biologic tissue and the resistance to that current measured [13-15]. This resistance is inversely proportional to the amount of water contained by the tissues within the electric field. We have developed a new transthoracic bioimpedance analysis system with which we measure the electrical resistance of the right lung. From this, we then calculate a standardized index of right lung water termed resistivity [12]. In a porcine model of endotoxin induced increased permeability pulmonary edema, we have shown that right lung resistivity correlates with both total lung water and extravascular lung water obtained by direct postmortem gravimetry [12]. In this study, we evaluate whether our bioimpedance system adds useful information to standard clinical parameters in monitoring patients with hydrostatic pulmonary edema as they are being diuresed.
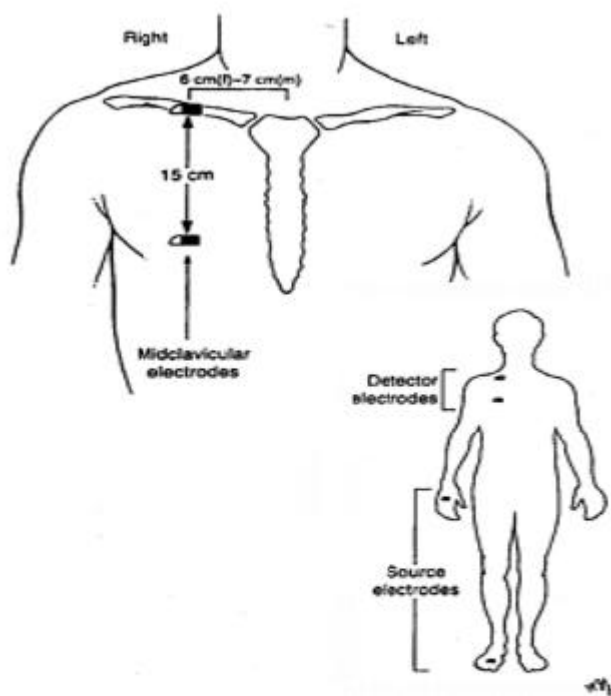
Figure 1. Placement of leads for right transthoracic BIA measurements. Source electrodes remain on the right hand and right foot. Detector electrodes are placed in the right midclavicular line. The midclavicular point is standardized to 7 cm from the middle of the sternum for males (m), and 6 cm from the middle of the sternum for females (f). The distance between the pair of detector electrodes is 15 cm.

MATERIAL AND METHODS

This project was approved by the Mt. Sinai Medical Center's Institutional Review Board and all subjects gave nformed written consent.

Subjects

Normals
Healthy subjects less than fifty years old without known heart or lung disease were recruited from the medical and nursing staff to determine normal values for right transthoracic resistance and right lung resistivity. Heights and weights were measured standing in stocking feet. After voiding, whole body and right chest bioimpedance measurements were performed as described below.

Patients
Hospitalized patients with total body fluid overload and congested lungs who where being diuresed by their primary physicians were studied. All tests and therapy were determined by the patient's treating physicians who were blinded to the BIA results. Patients had heel-crown heights measured supine in bed by tape measure, and were weighed using either a bed scale, a sitting scale or a standing scale, with the same scale used for each patient on both days. Thoracic circumferences at end-expiration (functional residual capacity) were measured high in the axilla and at the xiphoid process, and the mean of these two was used as the circumference for the lung resistivity calculation. After enrollment and anthropometric measurements, baseline whole body and right transthoracic BIA measurements were made. Both BIA measurements were repeated at approximately the same time four days later. To reduce measurement error, care was taken' to place the electrodes on exactly the same spots as they had been for the previous measurements with the patient in the same position. Data abstracted from patients charts included the etiology of the fluid overload, the medications used, fluid balance and weight changes. Documentation of findings consistent with fluid overload on lung, sacrum and leg exam were sought for days one and four.

Whole body measurements
BIA measurements were performed using a tetrapolar electrode array and a specially modified QuantUMd,, System Analyzer interfaced to a Zenith DataSystems laptop computer containing BIA interpretation software (RJL Systems, Inc., Clinton Twp., MI). This system delivers an imperceptible constant 800 pA alternating current at 50 KHz frequency. The analyzer was modified by RJL Systems to include a low and a high gain setting. On the standard high gain setting for whole body measurements, resistances and reactances are displayed as whole numbers, from 0 to 2,500 ohms (Q). On the more sensitive low gain setting for chest measurements, these values are displayed to one decimal place from 0.0 to 250.0 Q. BIA measurements were made with each subject reclining at 30 degrees, not flat as in standard BIA technique [14]. This was done in anticipation of studying dyspneic patients with edematous lungs who might be unable to .remain supine during the measurement interval. The skin surface for each electrode was cleaned with alcohol. We used Ag/AgCl spot ECG electrodes (Marquette Electronics; Jupiter, FL) cut in half lengthwise for all measurements. Studies were conducted throughout the day at ambient temperature with no attempt made to, standardize measurement times to food or fluid intake. Whole body measurements were done using standard right- sided, tetrapolar electrode placement. Two distal signal introducing source electrodes were placed on the dorsal surfaces of the right hand and foot just proximal to the metacarpal-phalangeal and metatarsalphalangeal joints, respectively [14]. Voltage sensing detector electrodes were placed between the medial and lateral malleoli at the ankle and at the pisiform prominence on the wrist. Whole body data was collected through the QuantUmd., analyzer software package that uses measured resistance and reactance values to calculate total body, intracellular and extracellular water based on proprietary equations.

Right transthoracic measurements
Right chest resistance measurements were made at FRC (end-expiration) with the BIA analyzer on its low gain setting. The most stable resistance values were recorded, usually obtained within ten to fifteen seconds. To make the chest measurements, source electrodes remained on the right wrist and ankle, and only the detector electrodes were moved to the right chest. The detector electrode pair was placed 15 cm apart in the right mid- clavicular line, with the upper electrode 6 cm (in females) or 7 cm (in males) lateral to the sternal notch along the lower clavicular border (Figure 1).

This positioning contrasts with other segmental BIA studies in which both source and detector electrodes are moved proximally together [16]. Spacing the current-injecting electrodes widely with respect to the potential-measuring electrodes gives the best chance of achieving a uniform current distribution within the potential-measuring electrodes and increases measurement reproducibility [17]. Clear respiratory variations can be seen with the detector electrodes in this position.

Right lung resistivity calculation

The ability of any biological tissue to resist a constant electric current depends on the relative proportions of water and electrolytes it contains, and is called resistivity (in Ohms/cm ^{3}). Resistivity is inversely proportional to the number of free electrolytic ions per unit volume in the tissue [17]. To calculate in vivo right lung resistivity, we assumed the thorax to approximate a cylindrical electrical conductor and used the following equation:

$$p = (\text{resistance}) * (\text{circumference}^2) / (4 * PI * \text{distance})$$

Where rho (p) = resistivity (Ohms/cm^3),

circumference mean chest circumference (cm),

resistance = midclavicular parallel resistance

length = distance between detector electrode

(pair = 15 cm.)

Statistical analysis

All results are expressed as mean ± S.D., with a p value of < 0.05 considered statistically significant. Baseline between-sex or between group differences were compared by independent samples t test using Statistica for Windows, Release 5.0 (Tulsa, OK). The ShapiroWilk's W test was used to test for the normal distribution. Changes in measurements between day one and day four of diuresis within each group were analyzed by paired t tests for quantitative data and by Chi-square for qualitative data.
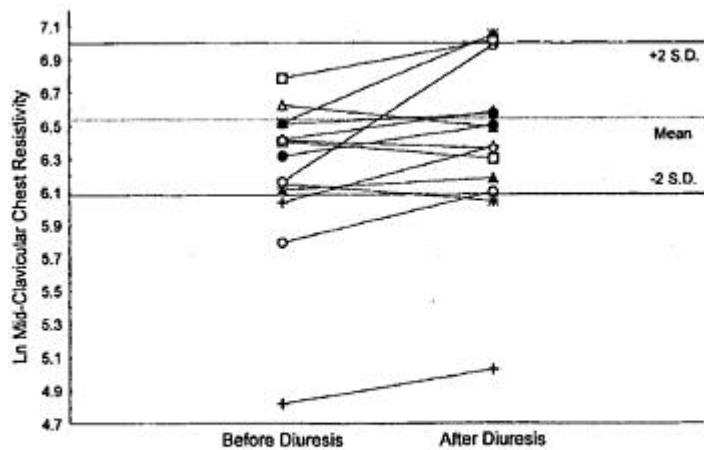
RESULTS

Figure 2. Ln right mid-clavicular resistivities (t-BIA) of patients on day one and day four (N = 14). Mean ± 2 S.D. is the normal range generated from healthy controls.

Normals

Fifty-one healthy normal volunteers, 32 men and 19 womn, with a mean age of 30 ±361 5 years were studied. Mean heights and weights were 173 ±361 7 cm and 77 ± 361 10 kgs for men and 162 ± 361 6 cm and 59 ± 361 8 kgs for women. Whole body measurements for both men and women were consistent with results in normal adults published elsewhere (18]. Women had smaller chest circumferences than men (81 ±361 5.7 cm vs. 96.8 :E 6.3 cm; p < 0.05) and higher right transthoracic resistances (19.0 ±361 2.9 0 vs. 14.6 ±361 3.7 Q; p < 0.05). However, right lung resistivities calculated from these resistances showed no significant between-sex difference (727± 169 Q-cm [female] vs. 674± 361 125 Q-cm [male]). Resistivities for all normals were combined and a distribution histogram was plotted. Combined resistivities were normally distributed (Shapiro-Wilk's W = 0.97, p < 0.3 1) with a mean of 707 ±361 155 Q-cm and a coefficient of variation of 22%. Further attempts to normalize chest resistivity by other geometric parameters such as height, weight, body surface area and body mass index did not reduce this variability. However, a natural logarithmic transformation of mid-clavicular resistivities yielded a mean of 6.54 ±361 0.23, with a coefficient of variation of only 3.5%. We termed this conversion t-BIA: and used it as our final value.

Patients

Fourteen patients were recruited (9 men and 5 women), with a mean age of 56 ±361 17 years. Mean heights and weights were 168 ±361 5 cm and 76 ±361 17 kgs for men and 157 + 6 cm and 68 ±361 16 kgs for women. Female patients were significantly heavier than normals (p = 0.02). The reasons for fluid overload and pulmonary congestion included severe congestive heart failure (N = 12) and fluid overload following large volume resuscitation for pancreatitis (N = 1) and gastrointestinal bleeding (N = 1). All patients were receiving intravenous furosernide, 40 to 200 mg/day, with some receiving additional bumetanide or zaroxolyn. In addition, many of the patients were receiving cardiotonic medications, such as dopainine (57%), dobutamine (57%), digoxin (57%) or an angiotension converting enzyme inhibitor (36%). One patient in renal failure was hemodialyzed for fluid overload. On initial exam, 13 of the 14 patients had documentation of abnormal lung findings, including rales (79%), wheezing (7%) and decreased breath sounds (7%). By the fourth day, chest exam had improved in seven patients, and was the same or worse in seven. Ten patients had leg edema on initial exam, with improvement in three and worsening or no change in the remainder. No patient had documentation of examination for sacral edema, although all these patients were confined to bed. Twelve of the patients had chest radiographs done on day one. Seven of these (58%) showed cardiomegaly, nine (57%) showed pulmonary vascular congestion and two (17%) showed frank pulmo nary edema. No patient had serial chest radiographs done on both days one and day four. Chest radiographs did not seem to be used by these clinicians to guide diuretic therapy. Over the four days of diuresis patients avetaged a loss of 4.6 ±361 4.4 kgs in weight (range 1.7-13.5 kgs) which was 6.0 ± 361 5.7% of their baseline weights. Two (14%) patients gained weight. There was no correlation between weight lost and the baseline weight (r - 0.37, p = 0.19). Out of the ten of thepatients who had complete fluid balances documented, all were in negative balance, losing an average of - 4,176 ±361 2,938 ml (range - 242 to - 9,549). There was poor correlation between changes in weight and fluid balance (r = 0.56, p = 0.09). As a group, patient t-BIAs at baseline were significantly lower than normals with a mean of 6.22 ±361 0.48 (p < 0.01). Only 3 patients had values that were more than 2 standard deviations below the normal mean, with all of the rest in the normal to low normal range (Figure 2). Following four days of diuresis, patient t-BlAs rose to 6.40 \361 0.51 (p = 0.14 compared to normals). Three patients who initially had t-BlAs in the normal range were diuresed to chest resistivities above the normal range. These patients lost an average of 7.63 kgs, compared to 3.43 kgs for the other patients. Four (29%) patients had decreases in t-BlAs, including one that went from normal to below normal despite losing 4.4 kgs. Changes in t-BIA, i.e., lung water, did not correlate with changes in body weight (r = - 0.25, p = 0.39) (Figure 3). Likewise, although there appeared to be a trend, there was no statistical difference between tBIA changes in patients whose chest exam improved (0,27 ±361 0.32) and
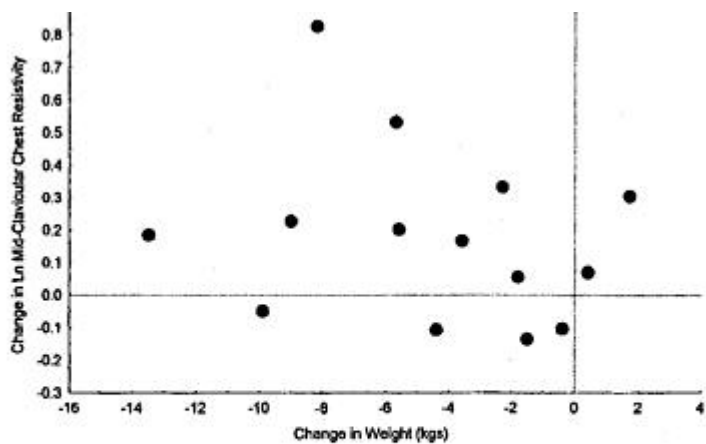
Figure 3. Lack of correlation between changes in ln mid-clavicular chest resistivity (t-BIA) and changes in weight following four days of diuresis (r = − 0.25, p = 0.39).

in those who did not (0.09 ±361 0.17) (P = 0.19). Eight (57%) patients had the desired response to diuretic therapy, i.e., both an increase in t-BIA, (drier lungs) and weight loss. In contrast, four (29%) patients had worsened lung water although they lost weight and two (14%) patients had drier lungs although they gained weight. In the six patients who lost more than 5 kgs in the four days of diuresis, the four who had improved chest exams also had increased t-BIAs. In ptients who diuresed less than five kilograms, there was no consistent relationship between weight loss, changes in chest exam and changes in tBIA. In fact, the two patients who gained weight had an improved chest exam documented, and both had slightly improved resistivity.

DISCUSSION

The end points currently used by clinicians to decide when adequate pulmonary diuresis has been achieved include improvements in clinical signs and symptoms and chest radiographs. These end points are inexact and qualitative, which can lead to therapeutic uncertainty [19]. While a general mobilization of fluid from an overloaded patient with pulmonary congestion may be suggested by a decrease in total body water and body weight, a method with which to directly measure lung water would specifically establish the presence or absence of effective diuresis of parenchymal lung tissue. BIA is a safe, noninvasive and affordable technique for repeated measurements of body fluid compartments [13, 14]. Previous attempts in the 1970s to use transthoracic BIA to estimate lung water were disappointing due to technical and methodological difficulties [6-9]. Recently, improved technology and a more sophisticated understanding of BIA have yielded more consistent results [10-12]. Transthoracic bioimpedance measurements of lung water are simple to perform, can be monitored continuously, and yield objective data [12]. Although less precise than invasive measurements of lung water, the growing awareness of the morbidity and possible mortality that may result from invasive monitoring suggests that using a less precise but safer noninvasive technique may be preferable [20]. Transthoracic BIA measured changes in lung water appeared to provide worthwhile additional information to body weights, chest exam and fluid balance by both monitoring the dynamic changes that occurred during treatment and by helping to establish meaningful therapeutic endpoints. Six of the patients that we studied were very aggressively diuresed, losing more than five kgs in four days for an average of 11% loss of body weight. This very rapid diuresis can lead to electrolyte depletion and hemodynamic instability, and is therefore usually done in a monitored setting. In this extreme weight loss group, chest exam and t-BIA were consistent with each other, with four patients having both improved chest exams and t-BIAs and two with unchanged exams and resistivities. However, within this group, the two patients with the greatest diuresis had smaller improvements in resistivity than the other two patients. This suggests that, although better, these two patients still had increased lung water and could have been diuresed more. In our study, 43% of patients undergoing diuresis had changes in body weight that diverged from changes in lung water as measured by transthoracic BIA. If the treating physicians had known the results of the t-BIA measurements, they might have modified their therapy for these patients. Moreover, there is no a priori reason why whole body diuresis should predictably result in drier lungs. Most of our patients had advanced congestive heart failure and many were receiving cardiotonic medications. Changes in cardiac function may also result in changes in lung water that may be entirely separate from total body fluid status. In addition, changes in body weight may not agree with measured fluid balance [21] and can be misleading due to both technique and equipment measurement error ,[22]. Many hospital scales are inaccurate, with up to 21% not meeting a tolerance of ± 361 I pound at loads below 200 pounds or \361 2 pounds for loads above 200 pounds[22]. The main limitation of this study is the relatively small number of patients which may contribute to type11 statistical error. Although this may limit a broader generalization from the data, it does not invalidate the conclusion, namely, that t-BIA adds information to the clinical picture of pulmonary edema which may assist decisions related to diuresis. Given the frequency with which fluid-overloaded states are encountered, optimizing diuretic therapys important implications for patient outcome and resource allocation. As an example, in acute lung injury, fluid management directed toward minimizing extravascular lung water (EVLW) measured invasively has been shown to result in decreased use of mechanical ventilation and fewer ICU days [23, 24]. Other potential applications of t-BIA include monitoring lung water with volume resuscitation, in post CABG patients during and after extubation [25] and in chronic heart failure patients [19, 261.

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