Monitoring Pleural Effusion in Elderly Patients Using Internal Thoracic Impedance

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ABSTRACT: **Background:** Internal thoracic impedance (ITI) measurement is a sensitive method for detecting preclinical pulmonary edema and pleural effusion.

Objectives: To investigate the efficacy of this non-invasive method for detecting early pleural effusion among geriatric patients and to monitor increased ITI during its resolution.

Methods: This prospective, controlled study was conducted between July 2012 and August 2015. The study comprised 70 patients aged 65 to 94 years; and 39 of the patients had pleural effusion. ITI was measured continuously with a RS-207 monitor. The predictive value of ITI monitoring was determined based on a total of eight measurements taken at 12-hour intervals over 84 hours.

Results: As a result of medical treatment, the median ITI of the study group increased from 31 (interquartile range [IQR] 28–33 ohms) to 41 ohms (IQR 38–41 ohms; $P < 0.001$) compared to non-significant changes in the control group. Average respiratory rate (per minute) in the study group decreased from 29 (IQR 28–34) to 19 (IQR 18–20).

Conclusions: ITI monitoring is efficient for diagnosis and for ongoing clinical evaluation of the treatment of elderly patients with pleural effusion. Timely treatment may prevent serious complications of effusions avoiding extended hospitalization.

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KEY WORDS: elderly, impedance, internal thoracic impedance (ITI), plethysmography, pleural effusion

Patients above the age of 65 years comprise a growing segment of the heart failure (HF) population. While HF is the most frequent cause of pleural effusion, it is often difficult to diagnose in geriatric patients because of co-morbidities such as chronic kidney disease, cognitive disorders, cerebrovascular disease, anemia, and malignancy [1,2]. This difficulty results in delayed diagnosis of pleural effusion, which frequently leads to hospitalization, functional decline, and subsequent fatal outcome.

Early detection of exacerbation of large amounts of pleural fluid prior to the appearance of symptoms, such as severe dyspnea, and proper preventive treatment may interrupt this pathological sequela. However, the detection requires continuous or frequent periodic monitoring of at-risk patients who experienced recurrent pleural effusion [3,4]. Frequent chest X-rays (the gold standard for diagnosing pulmonary fluid) may be harmful due to radiation, and the possibility of repeated imaging may pose a major challenge due to mobility issues, especially when the patient is not hospitalized.

Accumulation of pleural fluid can be easily detected by thoracic impedance monitoring, which is based on measuring electrical resistance in impedance plethysmography [5-11]. We previously described the use of the Edema Guard Monitor (EGM) model RS-207 (R. S. Medical Monitoring, Ltd., Jerusalem, Israel) [9,11,12] for early detection and treatment of pleural effusion. This modality is unique in that it measures the internal thoracic impedance (ITI) of only the lungs and not total thoracic impedance (TTI). ITI is much more sensitive than other available plethysmography techniques. When TTI is measured, skin resistance is a major component of the measurement and lung electrical impedance is negligible, representing only 1–5% of TTI [9-16].

The use of EGM is straightforward and simple. It requires placing three electrodes on the anterior chest wall and three on the upper back. ITI readings are high quality, with inter-reading variations of less than 5%. The measurements are reproducible and they were shown to have high specificity and sensitivity [8-13]. Determining pleural effusion with EGM is easy to perform at the bedside. The device is intended to replace other modalities for assessing pleural effusion, including chest X-ray, ultrasound, and computed tomography (CT). Therefore, it is suitable for follow-up of severely ill patients who often cannot be transported to imaging facilities. Moreover, CT scanning is usually not performed daily due to high costs and possible excessive radiation. Chest X-ray is not optimal for many patients, as they cannot assume an upright position. Ultrasound availability may also be limited. Thus, ITI measurement is a useful alternative and provides an effective solution for monitoring the dynamics of pleural effusion. The monitor is low cost and user friendly, which allows for its use in hospitals and outpatient venues for the early diagnosis of pleural fluid accumulation.

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This modality has been proven effective for preclinical diagnosis of pulmonary edema [9-13,15]. It successfully detected early pleural effusion in the general, mixed age population [16]. In an earlier study, we evaluated 100 consecutive patients, ages 25 to 96 years [9]. However, to the best of our knowledge, there are no published reports of its use in elderly patients, who constitute the majority of HF patients.

The current study focused on a geriatric population because HF is the most common cause of pleural effusion and it is very prevalent among the elderly. Moreover, because elderly patients tend to be frail, optimal monitoring of pleural effusion for the purpose of diagnosis and treatment is often critical to their medical management. In addition, we hypothesized that ITI values in the elderly might be within different ranges than do those of young adults.

The aim of the current study was to evaluate the suitability of the RS-207 EGM for detecting and monitoring pleural effusion in the preclinical and clinical stages among patients older than 64 years.

PATIENTS AND METHODS

This prospective study comprised a cohort of consecutive patients, older than 65 years of age who had been admitted to the department of internal medicine at the Tel Aviv Medical Center from July 2012 through August 2015. The inclusion criteria for the study group (Group 1) were HF due to ischemic or valvular heart disease, kidney disease, infectious disease complicated by pleural effusion, or malignant diseases complicated by pleural effusion. The inclusion criteria for the controls (Group 2) were the same as Group 1, but without pleural effusion. Exclusion criteria were an attached pacemaker, coma or respiratory failure due to pulmonary edema or embolism, a thoracic deformation, or inability to provide informed consent.

The protocol followed the principles outlined in the Declaration of Helsinki, and was approved by the local ethics committee of the Tel Aviv Medical Center and the Israeli Ministry of Health (#0504-11-TLV). All participants provided written informed consent prior to study enrollment.

To monitor pleural effusion, three electrodes were placed on the front and back of the right thorax [9,12,15], providing a value of internal thoracic electrical resistance (impedance). ITI is estimated by a precise method described in detail elsewhere [9,15]. ITI was monitored continuously but recorded every 12 hours. ITI was expected to decrease before symptoms and signs of pleural effusion appeared. Since the primary objective of this study was to verify the decrease in ITI in elderly patients, ITI was measured repeatedly (eight readings over 4 days). By measuring ITI, we would be able to identify pleural effusion before it became clinically evident and use it as a predictive measurement.

Pleural effusion was diagnosed based on chest X-ray findings and arterial hypoxemia (< 92%) in addition to the following signs and symptoms: progressive dyspnea at rest (> 20 respirations), tachycardia (> 90 beats/min), diaphoresis, cyanosis, dullness on percussion, and crepitation rales [15].

Diuretics (furosemide and spironolactone) or pleural paracentesis were used to treat elderly patients with pleural effusion. Conservative treatment or pleural puncture was successfully achieved after a 12-hour repeat of the clinical examination and measurements of oxygen saturation (O_2%), respiratory rate, pulse, systolic (sBP) and diastolic blood pressure (dBP), and ITI. At the end of the 84-hour monitoring period, a follow-up chest X-ray was performed. Data necessary to analyze and characterize the efficiency of RS207 monitor in the study setting was obtained by repeated measurements of ITI.

STATISTICAL ANALYSIS

Categorical variables were described using frequency and percentage. A histogram was used to test normal distribution of continuous variables. Means and standard deviations (SD) are presented for normally distributed continuous variables, and medians and interquartile ranges (IQR) for abnormally distributed continuous variables. Chi-square test or Fisher's exact test were used to compare categorical variables and the independent samples *t*-test. The Mann-Whitney test to compare continuous variables. Spearman's correlation coefficient was used to evaluate the correlations between continuous variables. The Wilcoxon test was used to compare ITI, sBP, dBP, respiratory rate, O_2 saturation, and pulse from time 0 to 84 hours. Univariate and multivariate linear mixed model analyses were employed to evaluate changes in ITI, sBP, dBP, respiratory rate, O_2 saturation, and pulse over time and to compare patients with or without pleural effusion. To evaluate the association of sBP, dBP, respiratory rate, O_2 saturation, pulse, and ITI, a linear mixed model analysis was used. A P value < 0.05 was considered statistically significant. Statistical analyses were performed using IBM Statistical Package for the Social Sciences statistics software, version 21 (SPSS, IBM Corp, Armonk, NY, USA).

RESULTS

The study cohort included 70 patients above 65 years of age who had been admitted to an internal medicine ward for dyspnea due to heart failure. The study group included 39 patients with pleural effusion (22 females and 17 males, median age 79 years, IQR 77–83 years). The control group included 31 patients who did not have pleural effusion (25 females and 6 males, median age 80, IQR 75–86 years). Table 1 describes the baseline clinical characteristics of the groups. Initial ITI was 31 ohms in Group 1 and 63 ohms in Group 2. The median body mass index (BMI) of Group 1 was 24 (IQR 23–27) and was significantly lower compared to Group 2 with a BMI of 26 (IQR 24–29, P < 0.001). This difference persisted throughout the monitoring and treatment periods.

Table 1. General clinical patient data

Variable*	Pleural effusion (Group 1) n=39 (IQR)		Controls (Group 2) n=31 (IQR)		*P* value
Age, years	79	(77–83)	80	(75–86)	‹ 0.001
Gender (male)	17	(44%)	6	(19%)	0.032
Body mass index	24	(23–27)	26	(24–29)	‹ 0.001
Initial internal thoracic impedance	31	(28–33)	63	(60–66)	‹ 0.001
Oxygen (%)	86	(78–88)	94	(93–95)	‹ 0.001
Respiratory rate (per minute)	29	(28-34)	14	(13–16)	‹ 0.001
Pulse (per minute)	100	(94–102)	70	(58–82)	‹ 0.001
Systolic blood pressure (mmHg)	160	(149–170)	140	(136–150)	‹ 0.001
Diastolic blood pressure (mmHg)	88	(77–100)	70	(65–80)	‹ 0.001

*Continuous variables are presented as median (IQR) and categorical variables as number (%)

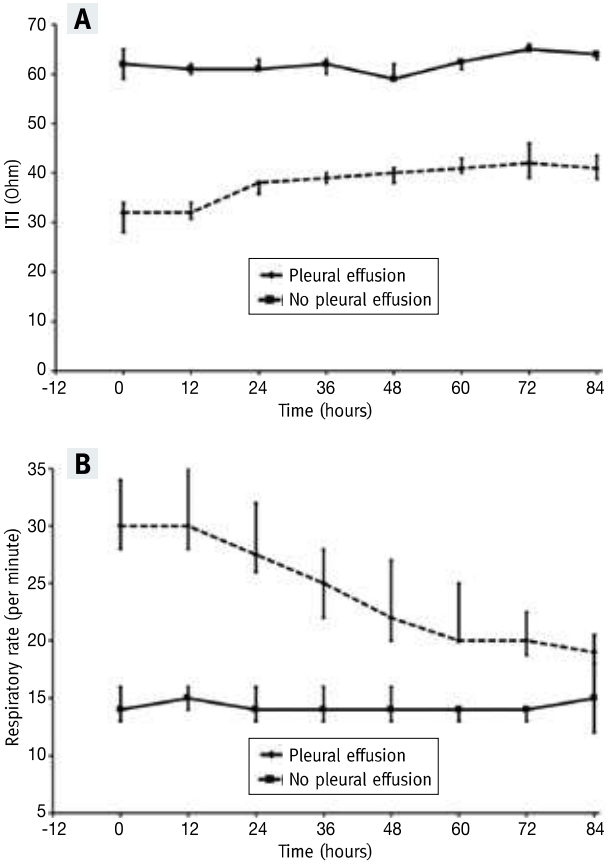
IQR = interquartile range

The etiologies of the pleural effusion were ischemic or valvular heart failure (44%), malignant disease (36%), parapneumonic fluid or empyema (11%), uremic pleural effusion (6%), or pericarditis (3%). Non-insulin-dependent type 2 diabetes was confirmed in 38% of the patients, 59% had hypertension, and 21% were current or past smokers. The mean left ventricular ejection fraction in patients with heart failure was 38%, and the mean New York Heart Association (NYHA) class was 2.7. Pleural puncture was performed on 26 patients (67%) with pleural effusion. A mean of 780 cc pleural effusion was extracted. Among the control patients (N=31), 9 patients (28%) were diagnosed with ischemic heart disease, 12 patients (38%) with infectious diseases (urinary tract infections, pneumonia/bronchitis, or cellulitis), 7 patients (25%) had malignant disease, and 3 patients (9%) anemia.

ITI was recorded once every 12 hours over 84 hours (4 days) to explore the relationship between decreased ITI and the appearance of clinical signs compatible with pleural effusion. Some patients who were hospitalized with pleural effusion developed severe dyspnea (aggravation of pleural effusion). The significant differences between the control and study groups in ITI from beginning of treatment and during monitoring are displayed in Figure 1A. The median ITI in Group 1 at the onset of monitoring was 31 ohms (IQR 28–33 ohms) compared to 63 ohms (IQR 60–66 ohm) for Group 2 ($P < 0.001$).

The mean ITI increased by 32.2% ohm over the treatment period ($P < 0.001$) in Group 1, while no changes were observed in Group 2 during the same monitoring period. Group 1 underwent significant changes in O_2 saturation levels. The baseline median O_2% saturation was 86% (IQR 78–88) in Group 1 and rose to 92% at the end of the monitoring period, as compared to a consistent level of 94% in Group 2. The most significant changes between the two groups in clinical signs were seen in respiratory rate (Figure 1B). The median respiratory rate in

Figure 1. [A] Internal thoracic impedance changes during monitoring and treatment (median values and interquartile range). **[B]** Respiratory rate and internal thoracic impedance changes during monitoring and treatment (median values and interquartile range)



ITI = internal thoracic impedance

Group 1 decreased from 29 (IQR 28–34) per minute to 19 (IQR 18–20) per minute ($P < 0.001$), representing a 31% decrease in the patients with pleural effusion, while it did not change (14 per minute) in the control group (P = NS).

The median baseline pulse rate of 100 per minute in Group 1 (IQR 95–102) decreased to 72 (IQR 71–77) per minute after treatment, representing a decline of 28% ($P < 0.001$), in comparison to Group 2 in which there were no changes (P = NS). The same trend was seen in sBP. Median sBP at baseline was 160 mmHg (IQR 149–170) and 132 mmHg (IQR 131–138) at the eighth measurement, representing a decrease of 17.5% ($P < 0.001$) for Group 1 in comparison to no changes in Group 2 (P = NS). Significant changes were seen in dBP in both groups. They were more apparent in Group 1, in which dBP decreased by 13.6%. Interestingly, the ITI and the clinical parameters of oxygen saturation, respiratory rate pulse, sBP, and dBP did not change significantly between measurements six and eight. This finding could be because most of the fluid had already

been evacuated and the changes in the residual amounts were not significant. Table 2 summarizes the changes in the clinical parameters from baseline (time 0) to the end of the monitoring period (84 hours) among patients with pleural effusion.

Among the patients with pleural effusion, 26 underwent right-sided pleural paracentesis. The mean fluid volume was 780 ml. These patients were kept under close surveillance. Their ITI increased rapidly an hour after the procedure (median of 6.3 ohms), compared to a mean of 2.7 ohms for all Group 1 patients. By the end of the 84 hour observation period, the mean overall ITI of the 26 patients who underwent paracentesis had increased by 12.6 ohms (33.7%, $P < 0.01$) as compared to an increase of 10 ohms in the entire Group (31.5%, $P < 0.01$). O_2%, respiration rate, pulse rate, sBP and dBP improved more rapidly among Group 1 compared to Group 2, as expected.

Spearman correlations of the ITI and clinical parameters at baseline and at each stage of monitoring were O_2% = 0.85 ($P < 0.001$); respiratory rate = 0.70 ($P < 0.001$); pulse = 0.75 (P = NS); sBP = 0.57 ($P < 0.001$), and dBP = 0.35 ($P < 0.001$). There were no correlations among ITI levels and clinical parameters with age or BMI.

A linear mixed model analysis of Group 1 showed that an ITI elevation of 10 ohms led to an increase of 6.4% in oxygen saturation (IQR 5.6–7.1), a decrease in the respiratory rate of 3.7% (IQR 2.9–4.7), and a decrease in pulse rate of 8.8% (IQR 1.05–0.71). An elevation of 10 ohm (Group 1) led to a decrease in sBP of 10.8 mmHg (IQR 1.34–0.81) and a decrease in dBP of 7.8 mmHg (IQR 0.56–0.99; $P < 0.001$).

At a threshold ITI value of 40 ohms, the sensitivity of the RS 207 in ITI monitoring was 100% and the specificity was 96.5%, indicating a high level of reliability to detect pleural effusion. There were no differences in the initial main vital clinical parameters of patients who had exudative pleural effusion and those who had transudate fluid [Table 3], except that the dBP was higher in the exudate group 96 mmHg (IQR 62–72) vs. 88 mmHg (IQR 77–100) in the transudate group ($P = 0.006$).

Table 2. Median differences and interquartile range from baseline and after 84 hours of treatment among patients with pleural effusion (n=39)

Variable*	Baseline Median (IQR)		Post-84 hours Median (IQR)		*P* value
Internal thoracic impedance (ohms)	31	(28–33)	41	(38–43)	‹ 0.001
Oxygen (%)	86	(78–88)	92	(92–93)	‹ 0.001
Respiratory rate (per minute)	29	(28–34)	19	(18–20)	‹ 0.001
Pulse (per minute)	100	(94–102)	72	(71–77)	‹ 0.001
Systolic blood pressure (mmHg)	160	(149–170)	132	(131–138)	‹ 0.001
Diastolic blood pressure (mmHg)	88	(77–100)	70	(62–74)	‹ 0.001

*Continuous variables are presented as median (interquartile range)
IQR = interquartile range

DISCUSSION

Over 75% of HF patients in the United States are older than 65 years of age. HF is the main reason for hospitalization among older individuals and a major cause of chronic disability [1,2]. Yearly costs related to HF are over $10 billion. Aging adults are predisposed to develop HF due to age-related changes in the cardiovascular system [1,2,14-21], the most frequent of which has been termed the cardio-geriatric syndrome.

Our results demonstrate that continuous ITI monitoring is a useful and accurate method for diagnosing pulmonary effusion early and for predicting the onset of respiratory distress. It can also assist in managing preventive treatment. ITI monitoring provides objective, independent data sufficient to reflect the pleural effusion status. Eliminating the need to perform repeated chest X-ray films to accurately assess pleural effusion offers a significant advantage. Moreover, the RS207 monitor can be used at home. A 10 ohm decrease in ITI reflects significant accumulation of fluid, alerting the patient or family members to seek medical advice, increase diuretics, or go to the emergency room.

Dynamic changes in ITI values during treatment in patients with pleural effusion were monitored together with other major clinical parameters, including pulse, respiration rate, O_2% saturation, sBP, and dBP. Improvement in these values was linked to an increase in ITI, which occurred in parallel to the elimination of fluid from the pleural space. In the current study, the ITI levels were 51% lower (by a significant 32 ohm) in patients with pulmonary effusion, compared to the ITI levels in patients without pulmonary effusion. These levels were also significantly higher than those found in a general, mixed-age adult population [16]. In the latter group, the initial ITI differed by 40% when related to patients with and without pulmonary effusion [16]. The ITI of symptomatic patients was very low, the same as in the general mixed-aged population [16] (31 ohms vs. 32 ohms, respectively), and similar to the ITI level (33 ohms) in patients with overt pulmonary edema [15]. We measured a 32

Table 3. Differences between initial main vital clinical parameters in exudate and transudate subgroups of patients (n=39)

Variable*	Baseline parameters transudate n=13 median IQR		Baseline parameters exudate n=26 median IQR		*P* value
Internal thoracic impedance	31	28–33	31	38–43	0.965
Oxygen (%)	86	78–88	83	92–93	0.586
Respiratory rate (per min)	29	28–34	31	18–20	0.965
Pulse (per min)	100	94–102	99	71–77	0.941
Systolic blood pressure (mmHg)	165	149–170	157	131–138	0.452
Diastolic blood pressure (mmHg)	88	77–100	96	62–74	0.006

*Variables are presented as median (interquartile range)
IQR = interquartile range

ohm decrease in the ITI in cases of pleural effusion, compared to the control group (63 ohms) and a 10 ohm elevation of ITI in the pleural effusion group after a total treatment period of 84 hours. These results indicate that this diagnostic method can be widely used for hospitalized patients and outpatients. It is important to stress, as previous studies on pulmonary edema and pleural effusion have also shown [15,16], that ITI was still significantly low after the resolution of dyspnea, indicating the presence of residual fluid and a wet lung [13,15,16]. This finding is not surprising because it is impossible to evacuate all the fluid during a short treatment period [16].

The study groups differed in BMI. ITI plethysmography has a unique advantage over the TTI method in that chest wall impedance (especially from subcutaneous adipose tissue, which has a much higher electrical resistance than the lungs do) [8] is removed from the equation of lung impedance. The device has a special algorithm that subtracts skin and other tissue impedance. Therefore, patients with higher BMIs have the same ITI variations as those with normal BMI. We found no correlation between BMI and the ITI values during the current study. Group 1 patients were treated mainly with furosemide, often together with spironolactone or pleurocentesis, according to clinical signs and symptoms and findings on chest X-ray. The ITI measurements showed a 32.3% elevation following treatment, compared to 31.3% in a general, mixed-age population [16].

Along with symptomatic improvement, the following objective improvements in clinical parameters were noted among the Group 1 patients: 7% increase in oxygen saturation, 34.8% decline in respiratory rate, 28% decrease in pulse rate, and decreases of 17.5% and 20.4% in sBP and dBP, respectively. All changes, with the exception of pulse rate, were less prominent in the geriatric, as compared to the general population [16].

The improvement in all five clinical parameters, as well as the ITI levels were observed in the first four to five measurements (48 hours) and were less significant than in the general patient population [16,22]. The ITI values after treatment remained lower in Group 1 as compared to the controls (explained by the presence of residual fluid). However, all five clinical parameters in Group 1 were similar to those in Group 2 and did not change significantly during further follow-up to the endpoint of 84 hours. For example, when the respiratory rate decreased to 16 per minute after the 48-hour period, it did not change significantly until the eighth measurement. A similar pattern was observed in the oxygen saturation and pulse rates, which underwent a significant decline during the first five measurements (48 hours). Patients in Group 2 displayed mild and non-significant ITI variations, most likely explained by stress-inducing factors of the active disease (i.e., fever or dyspnea).

All Group 1 patients had lower ITI levels (28–33 ohms) compared to Group 2 (60–66 ohms). There were no overlapping values between the two groups. The sensitivity and specificity of the method were 100% and 96.7%, respectively, at a threshold ITI value of 40 ohms. This finding was significantly different in patients with and without pulmonary fluid, indicating that the RS207 monitor is a reliable modality for detecting pleural effusion. The method cannot, however, differentiate pleural effusion from pulmonary edema because it measures the ITI of pulmonary fluid without regard to its compartmentalization.

The median baseline difference in ITI between the two groups was approximately 32 ohms, which decreased to approximately 22 ohms after treatment. This result is comparable to the mean value of 25 ohms among individuals with pleural effusion in a general population and to the mean difference of 21 ohms between the peak value of pulmonary edema in the Group 1 patients and the ITI value in the Group 2 patients [16]. Significant correlations were found between the ITI levels and the clinical parameters (O_2%, respiratory rate, pulse rate, sBP, and dBP) measured at baseline and during treatment monitoring. These correlations remained significant for at least 48 hours of monitoring.

An advantage of ITI monitoring is that it allows continuous measurement and is not operator dependent. Ultrasound is reliable for detecting pleural effusion; however, changes in values of ITI during continuous monitoring can indicate imminent, symptomatic pleural effusion. The modality does not replace ultrasound. ITI allows early identification of pleural fluid in the elderly, compared to relying on clinical signs (O_2%, respiratory rate, pulse rate, sBP, and dBP) alone [15]. ITI in an asymptomatic patient decreases before the appearance of clinical symptoms and signs because of an increase in the amount of fluid. The clinical signs are evident only after a substantial amount of fluid has accumulated. During treatment, the ITI rises slowly compared to the speed of improvement of the clinical parameters because of residual pleural effusion.

The monitoring method described here is important for early diagnosis of non-malignant pleural effusion and subsequent initiation and titration of diuretic therapy. This finding is especially relevant for patients with HF who, in contrast to patients with inflammatory or malignant pleural effusion, respond well to treatment with diuretics.

The evacuated volume by paracentesis was 780 cc in the elderly compared to 960 cc in a general unselected group of patients [16], which explains the slightly higher ITI levels in elderly patients. ITI can be measured once daily by monitor, in the same way that pulse, oxygen saturation, and BP are measured. Appropriate treatment may be given to ambulatory patients with recurrent pleural effusion when there is a decrease in impedance, as it reaches values below 33 ohms. ITI values less than 33 ohms were found to be diagnostic for the presence of pleural fluid, necessitating special attention and appropriate treatment. Diagnosis of significant pleural effusion is often crucial for asymptomatic patients in order to prevent respiratory distress, especially for those at imminent risk for mechanical ventilation.

CONCLUSIONS

Monitoring ITI in geriatric HF patients is an effective method for diagnosing aggravating pleural effusion even before appearance of clinical symptoms. This technology is applied through the use of a small, portable machine. It may be especially effective for ambulatory elderly patients with mobility difficulties due to chronic or recurrent pleural effusion and who require frequent medical assessment and changes in treatment.

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Capsule

Clonally expanded CD8 T cells patrol the cerebrospinal fluid in Alzheimer's disease

Alzheimer's disease is an incurable neurodegenerative disorder in which neuroinflammation has a critical function. However, little is known about the contribution of the adaptive immune response in Alzheimer's disease. Using integrated analyses of multiple cohorts, **Gate** et al. identified peripheral and central adaptive immune changes in Alzheimer's disease. First, they performed mass cytometry of peripheral blood mononuclear cells and discovered an immune signature of Alzheimer's disease that consists of increased numbers of CD8+ T effector memory CD45RA+ (T_{EMRA}) cells. In a second cohort, they found that CD8+ T_{EMRA} cells were negatively associated with cognition. Furthermore, single-cell RNA sequencing revealed that T cell receptor (TCR) signaling was enhanced in these cells. Notably, by using several strategies of single-cell TCR sequencing in a third cohort, the authors discovered clonally expanded CD8+ T_{EMRA} cells in the cerebrospinal fluid of patients with Alzheimer's disease. Finally, they used machine learning, cloning and peptide screens to demonstrate the specificity of clonally expanded TCRs in the cerebrospinal fluid of patients with Alzheimer's disease to two separate Epstein–Barr virus antigens. These results reveal an adaptive immune response in the blood and cerebrospinal fluid in Alzheimer's disease and provide evidence of clonal, antigen-experienced T cells patrolling the intrathecal space of brains affected by age-related neurodegeneration.

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