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Is it possible to predict whether BAL salvage is going to be diagnostic?

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Abstract

Introduction: Bronchoalveolar lavage (BAL) is used in the diagnosis of interstitial lung diseases. BAL is diagnostic when ≥ 60% of the instilled volume is recovered. There are no reliable markers useful to predict whether BAL volume is going to be diagnostic. Our goal was to search for pulmonary function markers which could anticipate whether the recovered volume of instilled fluid would be ≥ 60% of administered volume.

Material and methods: BAL volumes and quality were analyzed in the context of disease, medical condition and lung function test results of the subjects hospitalized at the Pulmonology Ward from January 2015 to October 2016. The patients' average age was 61 (29–89).

Results: Among 80 procedures, diagnostic BAL (≥ 60%) has been obtained in 58 cases. The analysis of the group of patients with an interstitial lung disease confirmed that there is a correlation between decreasing BAL recovered volume and an increase of RV[%pred] (r = –0.34) and RV/TLC[%pred] (r = –0.41); $p < 0.05$. There was no significant correlation with DLCO. RV/TLC[%pred] was the parameter with the highest predictive value for an anticipated correct BAL recovery. The curve analysis of the receiver operating characteristic (ROC) showed a diagnostic accuracy (AUC 0.73, 95% CI 0.61–0.86).

Conclusions: Pulmonary hyperinflation may have a predictive role in anticipating a proper recovery of the BAL fluid volume.

Key words: interstitial lung diseases, bronchoalveolar lavage, spirometry, body pletysmography, DLCO

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Introduction

Interstitial lung diseases (ILDs) constitute a very heterogeneous group of non-infectious and non-cancerous illnesses, which includes more than 200 disease entities of a similar clinical, radiological and pathophysiological picture [1, 2]. Individual disease entities do not occur very often, but all ILDs account for about 16% of the respiratory system diseases [2]. It means that their correct diagnosis, differentiation and, consequently, effective treatment are an essential task for physicians.

The main changes in ILDs are hypoxia during rest and/or during exercise, bilateral pulmonary disseminated lesions on thoracic imaging and a restrictive pulmonary disorder with an abnormal gas transfer [3].

The diagnostic approach includes: clinical history and examination, pulmonary function tests, selective blood tests, imaging examinations: chest radiography and high resolution computed tomography, bronchoscopy with bronchoalveolar lavage (BAL) and/or endobronchial/transbronchial biopsies and/or a surgical biopsy [4].

The essence of the disease process in the course of ILDs are lesions in the peripheral structures of the respiratory system. A medical procedure that allows to obtain material from the bronchoalveolar space is BAL performed during

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bronchoscopy. It is characterized by low invasiveness and high safety [5].

The fluid obtained during this procedure can be used in the research and the diagnostic processes only if the procedure has been carried out in compliance with the guidelines. One of the primary condition is the recovery of 50–70% of the volume of fluid introduced during the procedure [6]. It is believed that in addition to its usage in the diagnostic process, BAL can replace other, more invasive examinations useful for the long-term monitoring of the disease activity [1]. Since the 1990s there has been an ongoing process directed to standardize each stage of bronchoalveolar lavage [3, 6–10].

A variety of clinical situations that may reduce the volume of the recovered fluid have been identified. These include old age, cough, smoking and emphysema [11–13]. However, there are no parameters or tests that would allow us to predict before performing bronchoscopy whether the obtained material will have the researching and diagnostic value. The identification of such predictors might help extract methods allowing for increased BAL fluid recovery, and then their use in patients without the risk of obtaining a non-diagnostic result of BAL.

The aim of the research was to find spirometric, plethysmographic and lung diffusion parameters, which could become predictors for achieving the ≥ 60% volume of the fluid administered during bronchoalveolar lavage.

Material and methods

Study group

The retrospective analysis included the patients with interstitial lung disease from the Department of Pneumonology who have undergone BAL procedure in the period between January 2015 and October 2016.

The study group consisted of 80 people (44 women and 36 men) aged between 29–89 (average age 61.4 ± 12.15). The patients were divided into two groups: those who did not demonstrate correct recovery (Group 1) and those with correct recovery (Group 2).

Bronchoscopy with BAL

The bronchofiberoscopy with BAL took place after obtaining written consent of patients. All procedures were performed under local airway anaesthesia (1% lignocaine solution) after premedication (midazolam with or without the addition of tramadol). Lavage was carried out in segments 4 or 5 of either right or left lung or in the area with the most severe interstitial lesions confirmed by medical imaging. If the lesions were evenly spread, the lavage was performed in the bronchi of the middle lobe or uvula based on the voluntary decision of a physician.

BAL was performed in accordance with the recommendation of the Polish Respiratory Society for bronchoalveolar lavage (BAL) sampling, processing and analysis methods [6].

During the procedure, 200 mL of 37ºC; 0.9% sodium chloride solution was applied in 25 ml fractions.

Lung function tests

All procedures have been carried out in the Laboratory of Functional Testing of the Respiratory System at the Department of Pneumonology by qualified medical personnel before bronchoscopy performance. The spirometry test, plethysmographic measurement of lung volumes and measurement of lung diffusion capacity for carbon monoxide were performed using (MasterLab, Jaeger, Germany).

All procedures were carried out in accordance with the Guidelines of the Polish Respiratory Society concerning the performance of spirometry tests [14].

Statistical analysis

The obtained data was subjected to statistical analysis using Statistica 13.1 tool. The Mann-Whitney U Test and chi-squared test were applied to calculate the differences between the groups. The analysis of the correlation between age and the results of lung function tests and BAL fluid recovery was determined using the Pearson correlation coefficient and Spearman's rank correlation coefficient depending on the distribution type of compared variables. For parameters that demonstrate statistically significant correlations, their predictive ability to obtain the correct volume of fluid recovery during bronchoalveolar lavage was tested. For this purpose, the area under receiver operating characteristic (ROC) curves were determined. The level of significance $p < 0.05$ was adopted as statistically significant.

Results

The average values of all parameters measured during lung function tests were reduced. The nearest value to the normal one was shown by the pulmonary distension indicator RV/TLC[%pred].

According to the specificity of interstitial lung diseases, the largest reduction to the parameters based on lung diffusion capacity was also noted in this study.

The average fluid recovery from broncho-alveolar lavage was 64% (128 ml).

In 58 cases (72.5%), this recovery amounted to ≥ 60%.

Table 1 shows differences between the lung function parameters in Group 1 (without correct recovery) and Group 2 (with correct recovery).

All spirometry parameters and those based on lung diffusion capacity were reduced in Group 1, but only in some of them, the difference turned out to be statistically significant. On the other hand, parameters measured during plethysmography were lower in the group with the correct recovery.

For each of the studied parameters in lung function tests, the correlation between their value and percentage recovery of BAL fluid was calculated. Correlations for RV[%pred] (r = –0.34; p = 0.003) and RV/TLC[%pred] (r = –0.41; p < 0.001) were statistically significant.

Correlations between the recovery and the patients' age were not demonstrated.

In order to evaluate the usefulness of these parameters as predictors of correct BAL fluid recovery, ROC curves were determined for them. Bronchoalveolar lavage retrieval was classified as a dichotomous variable, while as a cut-off point for correct recovery, the value of ≥ 60% of the given fluid volume was adopted.

Continuous predictors in compliance with the direction of previously calculated correlations were classified as destimulants (RV[%pred] and RV/TLC[%pred]) to achieve the diagnostic results of BAL. A parameter featuring the greatest accuracy of the model matching is RV/TLC[%pred], for which AUC = 0.73 (95% CI [0.60–0.85]) p = 0.002. ROC curves for RV/TLC[%pred] are shown in Figure 1.

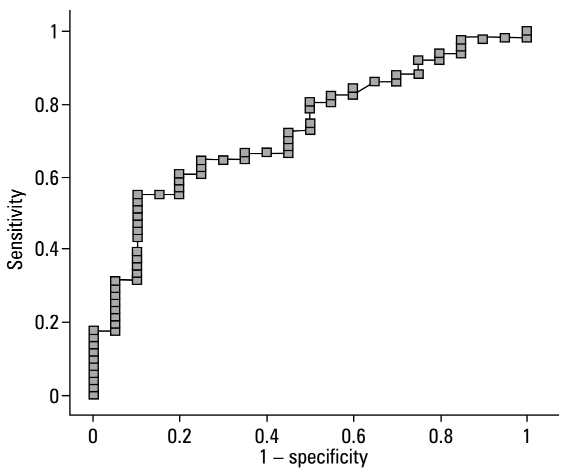

Figure 1. ROC curves for RV/TLC[%pred] RV/TLC [%pred]; AUC 0.73, –95% CI 0.60; +95% CI 0.85; Value p = 0.002. RV: residual volume; TLC: total lungs capacity; % pred: percentage of predicted values; AUC: area under curve; CI: confidence interval; p: probability in the test of significance

Table 1. Comparison of the patients with and without correct BAL recovery

Parameter	Total		Group 1 (without correct recovery)		Group 2 (with corect recovery)		p-value
	n	Mean ± SD	n	Mean ± SD	n	Mean ± SD	
Age	80	61.4 ± 12.2	22	61.1 ± 11.7	58	61.5 ± 12.4	0.78
Sex (Male/Female)	36/44		10/12		26/32		0.96
FEV_1/FVC	78	80.2 ± 9.8	20	78.8 ± 9.8	58	81.9 ± 7.4	0.10
FEV_1[%pred]	78	85.5 ± 23.8	20	80.1 ± 21.7	58	89.2 ± 22.5	0.11
FVC[%pred]	78	86.7± 23.6	20	84.0 ± 25.5	58	88.6 ± 22.7	0.53
TLC[%pred]	71	83.0 ± 19.4	20	85.7 ± 22.1	51	81.9 ± 18.4	0.60
ITGV[%pred]	71	88.2 ± 22.9	20	95.8 ± 21.4	51	85.3 ± 22.9	0.08
RV[%pred]	71	83.5 ± 26.9	20	96.2 ± 30.3	51	78.6 ± 24.1	0.02
RV/TLC[%pred]	71	97.0 ± 20.8	20	108.7 ± 18.9	51	92.5 ± 19.9	0.002
DLCO[%pred]	76	63.9 ± 23.6	21	57.7 ± 24.2	55	66.2 ± 23.1	0.13
DLCO/VA[%pred]	76	79.3 ± 19.6	21	72.3 ± 18.7	55	82.0 ± 19.5	0.09

*Mann-Whitney U test or chi-squared test: FEV_1: forced expiratory volume in 1 second; FVC: forced vital capacity; TLC: total lungs capacity; ITGV: intrathoracic residual volume; RV: residual volume; DLCO: diffusing capacity of the lungs for carbon monoxide; VA: alveolar volume; % pred: percentage of predicted values; p: probability in the test of significance

Discussion

To the best of our knowledge, we have shown for the first time that RV/TLC may be predictive in terms of whether BAL volume could be diagnostic. Bronchoalveolar lavage plays an important role in the differential diagnosis of interstitial lung diseases [3, 6]. Moreover, it can be used in the diagnosis of inflammatory diseases and infections, which is especially important in immunocompromised patients [15]. BAL may help in obtaining diagnosis and may be used for changing the management of immunocompromised patients. Furthermore, it may result in respiratory failure exacerbation, which may cause hypoxemia leading even to intubation [16]. We have shown that in the future it may be possible to predict on the basis of the pulmonary function test whether BAL will be diagnostic in terms of salvage volume.

In clinical practice, there are cases in which it is impossible to recover the right volume of BAL fluid. There are some scientific reports that show attempts to find reasons for reduced BAL regaining [11–13]. A correlation between age and reduced recovery has been demonstrated so far [12]. However, the results of our study do not confirm this correlation. This may be because the previous study has been based on carrying out BAL procedure on healthy individuals [12]. As people get older, the lung tissue elasticity decreases. Low lung elasticity affects the recovery volume. Meanwhile, our study involves patients with interstitial lung diseases in which lesions present in the lung tissue are less dependent on age and more on the severity of the disease process.

In a study of patients with chronic obstructive pulmonary disease (COPD) carried out by Löfdahl *et al*. [13], a relationship between reduced recovery and the severity of emphysema was shown, which was measured as an index of distension in HRCT. Our research confirms the dependence of recovery on the severity of emphysema, but it is worth bearing in mind that the degree of pulmonary distension was measured using plethysmographic parameters. An increase in RV[%pred] as well as RV/TLC[%pred] ratio negatively correlated with the volume of recovered BAL fluid. However, this relationship has proved to be of less importance than that associated with pulmonary distension DLCO. The same publication demonstrated a moderately positive correlation between recovery from BAL and lung diffusion capacity for carbon monoxide [13]. This relationship was not detected in our study. The reason for this difference can be probably explained by different histological pattern of pulmonary parenchyma in interstitial lung diseases and COPD. While in the case of ILDs, the degree of DLCO impairment does not correlate with the severity of pathological lesions. Extensive areas of fibrosis in the course of ILDs are not always reflected in impaired lung diffusion capacity, while a significant reduction in lung volume and severe hypoxemia have no correlation with a considerable reduction of DLCO [17].

One of the factors which influence BAL salvage is the area where it was performed. The volume of the recovered fluid is the highest when lavage is performed in the bronchi of the middle lobe or lingula [18]. Therefore, the procedure is usually performed in the middle and lingual lobe unless local abnormalities justify BAL performance in different segments. However, this has not played any role in our results because included patients have had BAL collected from the segment 4 and 5 bilateral. On the other hand, there is an increasing number of indications to perform various forms of BAL in other segments than only 4–5. This may be especially important in therapeutic lavage such as the one performed in pulmonary proteinosis [19], however, therapeutic BAL was not a subject of analysis in the present study.

Conclusions

RV/TLC [%pred] seems to have the highest predictive value for the anticipated correct BAL recovery. However, on the basis of retrospective data, it is impossible to indicate a good cutoff point for sensitive and specific prediction whether BAL salvage will be diagnostic. Therefore, it is necessary to perform a multicenter randomized controlled trial, in order to verify our observation and find an accurate cutoff point, which would discriminate between BAL salvage ≥ and < 60%.

Conflict of interest

The authors declare no conflict of interest.

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