



BENEFICIAL EFFECT OF WEIGHT LOSS ON RESPIRATORY FUNCTION IN PATIENTS WITH INTERSTITIAL LUNG DISEASES AND OBESITY

Zakiryayeva Parvina Odilovna

Axatova Vazira Pardakulovna

Assistant

Samarkand State Medical University, Uzbekistan

Annotation: study aimed to clarify the effect of weight loss on pulmonary function test (PFT) in ILD patients with obesity.

Keywords: interstitial lung disease, overweight, lung function test, body mass index, carbon monoxide

Methods: In a case-control study, 76 patients with bladder cancer with IL-1B-511 biallelic polymorphism were included, the number of tandem repeats was genotyped.

Results: Among all consecutive ILD patients with a body mass index (BMI) 27 kg/m^2 who received nutrition education for improving obesity between June 2018 and December 18, we retrospectively included patients who successfully decreased their body weight by over 2 kg and underwent follow-up PFT within 6 months. The results of PFT at baseline and follow-up and the level of Krebs von den Lungen-6 (KL-6) were compared. A significant association was found between IL-1 polymorphism and an increased risk of recurrence in patients with urothelial bladder cancer. There was no significant relationship in patients with G1. Carriers homozygous for IL-1B-511T / C had an increased risk of recurrent bladder cancer with odds ratios 2.7 (95% confidence interval [CI], 1.5-4.9) and 3.1 (95% CI, 1.5-6.5) respectively. Statistical analysis showed an interaction between the two loci with risk associated with IL-1B. The -511T allele increased significantly (odds ratio, 9.0; 95% CI, 3.5-23.0).

Conclusions. In ILD patients with obesity, weight loss is important and potentially improves their disease course.

Аннотация выяснение влияния потери веса на тест функции легких (ТФЛ) у пациентов с ИЗЛ с ожирением

Ключевые слова: интерстициальным заболеванием легких, избыточным весом, тест функции легких, индексом массы тела, монооксиду углерода

Методы: Среди всех последовательных больных ИЗЛ с индексом массы тела (ИМТ) - 27 кг/м² которые прошли обучение по питанию для уменьшения ожирения в период с июня 2018 г. по декабрь 2021 г., мы ретроспективно включили пациентов, которые успешно снизили массу тела более чем на 2 кг и прошли контрольную ТФЛ в течение 6 месяцев. Сравнивали исходные и последующие результаты ТФЛ и уровень Кребс фон ден Лунген-6 (КЛ-6).

Полученные результаты: Одиннадцать пациентов (5 мужчин и 6 женщин; средний ИМТ 34,1 кг/м²), были зачислены. Для ТФЛ на исходном уровне проценты форсированной жизненной емкости легких (%ФЖЕЛ), функциональной остаточной емкости (%ФОЕ) и диффузионной способности легких по монооксиду углерода (%ДЛМУ) составляли 69,3%, 59,9% и 54% соответственно. Медиана кл-6 составила 1035 ЕД/мл. Медиана интервала от исходного уровня до последующих PFT составила 41 день. По сравнению с исходными результатами ТФЛ, % ФЖЕЛ, % ФОЕ и % ДЛМУ значительно увеличились (p=0,018, 0,0006 и 0,024 соответственно), а изменения массы тела и ФЖЕЛ сильно коррелировали (p=0,0004). Кроме того, средний уровень КЛ-6 в сыворотке крови при последующем наблюдении имел тенденцию к снижению на 206,5 ЕД/мл. (p=0,083).

Выводы. У пациентов с ИЗЛ с ожирением потеря массы тела важна и потенциально улучшает течение болезни.

Introduction. Interstitial lung disease (ILD) is characterized by varying degrees of fibrosis and inflammation of the pulmonary parenchyma[1]. Idiopathic pulmonary fibrosis (IPF) is the most common type of pulmonary fibrosis and is

characterized by an unfavorable prognosis. In patients with IPF, forced vital lung capacity (VVC) decreases annually by 150-200 ml [2], and a decrease in VVC correlates with disease activity and mortality [3]. More recently, progressive fibrotic ISL, other than ILF, has been reported as a phenotype associated with decreased lung function, worsening symptoms, and early mortality.4]. Therefore, changes in VVC were used as the primary endpoint in some clinical studies of ILF[5] and fibrosing treatment without ILF [6,7]. Patients with ILD are usually obese or overweight due to impaired daily activity (PD) and prednisone side effects. As a rule, obesity can negatively affect the physiology of respiration and cause a decrease in VVC. However, whether it makes sense to improve the condition associated with obesity in patients with IPF[1]. However, the effect of weight loss on lung function (TFL) test results has been reported in severely obese patients with LVD who underwent bariatric surgery. In this study, the average body mass index (BMI) decreased from 39 kg/m² to 30 kg/m² in one year, and the %FVC significantly improved from 62% to 74%.[8] These results strongly suggest that weight loss is important for patients with severe obesity. However, in clinical practice, bariatric surgery is not easy for patients with ILD, and the effect of weight loss through nutrition education and physical therapy on TFL remains unclear. To investigate this research question, we conducted a retrospective study.

Objective: to compare the prognosis in patients with NSID, stratified depending on the underlying cause (idiopathic, NDST, DST, and CRF), in terms of survival, response to therapy, and long-term functional outcomes. MATERIALS AND METHODS. All patients who received dietary recommendations and were informed about dietary restrictions to reduce obesity were examined by registered nutritionists. World Health Organization defines obesity as a BMI of >30 kg/m² and overweight as a BMI of 25-30 kg/m². However, in Asians, obesity is defined as BMI > 25 kg/m² due to differences in physique between Asians and Europeans. Because some studies define obesity as BMI > 27 kg/m²[9], we examined all ILE patients with a BMI of > 27 kg/m² and received nutrition training from June 2014

to December 2018. Patients with weight loss of less than 2 kg or no TFL at baseline or with follow-up for 6 months were excluded. Patients who received additional treatment for ILD or surgical lung biopsy between baseline and subsequent TFL were also excluded. Serum IL-6 levels and TFL results, including FEV%, %FVC of lung carbon monoxide diffusion capacity (DLMU) and % functional residual capacity (FOE), were compared between baseline and follow-up. In addition, the correlation between changes in VVC and body weight was investigated. Statistical analysis: The parameters %VVC and %FEV were compared between baseline and follow-up using the paired Wilcoxon Landmark rank criterion. The correlation between changes in VVC and weight loss was analyzed using the Pearson and Spearman rank correlation coefficients. N-values of less than 0.05 were considered statistically significant. All analyses were performed using the JMP 10 software.

Results and discussion: Characteristics of patients at the initial level Among the 110 patients who received nutrition training, 43 had an ED. Among 33 patients with a BMI of $< 27 \text{ kg/m}^2$, 22 patients were excluded due to lack of follow-up TFL, lack of weight loss of $< 2 \text{ kg}$ or additional treatment. Finally, 11 patients were included, including five men and six women, with an average age of 67 years. Seven patients had a history of smoking, and the average weight and BMI were 87.6 kg and 34.1 kg/m^2 , respectively. Regarding the clinical diagnosis of ISL, 10 patients had idiopathic interstitial pneumonia with ILF (6 patients), NIP(2 patients) and unclassified (2 patients). Initially, seven patients did not receive any treatment for ISL, while the remaining four patients received prednisone, tacrolimus, pirfenidone and/or cyclosporine. The serum KL-6 level was assessed in all patients, and it turned out to be elevated with an average value of 1035 U/ml (normal value $< 500 \text{ U/ml}$). As for , the median VVC and %VVC were below 2310 ml and 69.3%, respectively, although the median FEV0% was within the normal range. % DLMU and FEV% were noticeably low with median values of 54% and 59.9%, respectively, while the predicted ratio of DLMU adjusted for alveolar ventilation (%DLMU/AV) was within the normal range. Changes from the baseline The interval from the initial TFL

to the subsequent TFL ranged from 14 to 182 days, with an average of 41 days. During the follow-up period, nine patients were admitted to our hospital for dietary restriction and received physical therapy to prevent immobilization syndrome due to decreased activity during their hospitalization. One patient was admitted to another hospital for bacterial pneumonia complicated by heart failure. The weight loss was 2.2 to 16.5 kg, with a median of 5.9 kg. It should be noted that KL-6 decreased in almost all examined patients (8/10, 80%), although the difference was not significant. TFL showed that the median D%FVC and %FEV1 was 80 ml, 3.8% and 4.9%, respectively. FVC, %FVC, and %OFV have improved significantly. In addition, % DLMU and % FEV improved with a median DLMU of 5.2% and D%FVC of 7.9%, meanwhile, there was no significant improvement in % DLMU/AB($p < 0.79$). The correlation between the amount of weight loss and the increase in VVC was significant.

Discussion. This study showed the following two conclusions. First, %VVC, % DLMU, and %FEV improved significantly after short-term treatment for obesity, and there was a significant positive correlation between the amount of weight loss and an increase in VVC. Secondly, KL-6 levels tend to decrease after weight loss. As a rule, it is not surprising that VVC and FEV improve in obese people after weight loss. However, it remains unclear whether obese patients show the same results after weight loss[1]. The effect of obesity on respiratory function is complex. An increase in adipose tissue around the chest and abdomen leads to a decrease in the pliability of the chest and an increase in resistance, which increases the massive load on the respiratory muscles and leads to a decrease in VVC and FEF.[8,9]. In addition, a recent report has shown that adipose tissue is present under the bronchial mucosa in patients with asthma and obesity, which contributes to direct airway obstruction. An important conclusion of the present study is that % of DMU also improved significantly after short-term treatment for obesity. As a rule, % of DMU is normal even in people with pathological obesity and does not show any changes after the improvement of the condition in obesity.[9]. However, a previous study of bariatric

surgery in patients with ISL showed that % of DLMU improved from 53% to 60% one year after bariatric surgery. Considering this report, together with the results of this study, weight loss in obese ILD patients will improve % of DLMU, we believe that ILD itself improved due to weight loss due to a decrease in KL-6 and an increase in % of DLMU. In patients with ISL, an increase in KL-6 is considered to be the result of increased production of KL-6 by regenerated type 2 alveolar pneumocytes and/or increased permeability after the destruction of the air-hematological barrier in the affected lungs. Given the short follow-up period in this study, we believe that the decrease in KL-6 in our patients occurred as a result of an improvement in the impaired permeability of the air-hematological barrier. As a rule, the FEV in obese people decreases and eventually approaches the closing capacity of the small airways, which causes collapse and atelectasis. This repeated opening and closing of the small airways can lead to lung damage[9]. Since patients with ISL have a low % VVC, reducing obesity in patients with ISL is likely to lead to an increase in VVC and, finally, reduce lung damage during calm breathing. This hypothesis It is confirmed by the improvement of TFL after short-term treatment of obesity. In clinical practice, patients with ILD are usually obese due to a decrease in ADL and the side effects of prednisone. Many clinical trials and studies have shown that patients with ILD were overweight (median BMI, 25e30 kg/m²), indicating a significant number of obese patients. In patients with ILF, a decrease in VVC and DLMU correlates with a decrease in survival, and DLMU at baseline is a reliable predictor of survival. Taking into account the results of this study, reducing body weight can improve the course of the disease in obese patients. In addition, two antifibrotic agents, pirfenidone and nintedanib, can reduce the annual decrease in VVC, but often cause anorexia and/or diarrhea, which leads to weight loss.[2,7]. Thus, pulmonologists should be aware of the effect of weight loss on TFL in patients with obese heart disease when evaluating the effect of antifibrotic drugs. Despite the important results of this study, there are several limitations. First, this is a retrospective, single-center study that included only 11 patients without a control

group. It would be more useful to compare the results between obese patients with and without weight loss in a larger scale study. Secondly, this study evaluated short-term outcomes over a period of 6 months for the included patients, and therefore it is necessary to clarify the long-term effects of weight loss on lung function.

Conclusion: In obese patients with ISL, short-term weight loss improved TFL results, including % VVC, % FEV, and % DOM, and led to a decrease in KL-6 levels. Weight loss can improve the course of the disease in obese patients.

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