Review

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What is worth measuring in patients with COPD?

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ABSTRACT

A personalized approach to management of a COPD patient is currently required due to heterogeneity of this disorder. A functional evaluation of each COPD patient is a fundamental part of the process to achieve this objective and should require a rational step-by-step procedure starting from the etiology of COPD, determination of the predominant underlying disease, assessment of risk severity, therapeutic role of ICS and finally monitoring of disease activity and its impact on the patient's life under the chosen treatment. Aim of this review is to indicate a series of easy sequential measurements that are worth to have for obtaining all this information crucial to taking care of a patient with a new diagnosis of COPD.

Key words: COPD, chronic bronchiolitis, emphysema, multidimensional risk assessment, patient's management

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Introduction

Although today measurements based on imaging of the lung or biomarkers from various biological sources (blood or sputum etc.) are able to profile peculiar phenotypes in individual patients suffering from chronic obstructive pulmonary disorder (COPD), this short review will be substantially limited to simple measurements of respiratory function that are useful in a patient who received for the first time the diagnosis of COPD.

First step

Although this is not a functional measurement, the first measure should be the plasma levels of alpha-$_1$-antytrypsin (A_1AT) in a stable condition (with CRP within normal limits) to exclude or confirm a A_1AT deficiency. In fact, about 2% of COPD patients is believed to suffer from severe A_1AT deficiency [1] and we have a specific treatment that is effective to reduce the progression of the disease sustaining COPD in these individuals which is mostly a panlobular emphysema [1].

Second step

Since the response to available pharmacological treatment for a patient with COPD is remarkably different according to the predominant disease responsible of the chronic airflow obstruction in terms of respiratory function [2], functional decline [3] and all-cause and respiratory mortality [4] is very important distinguishing between chronic bronchiolitis (without or with mild centrilobular emphysema) and pulmonary emphysema (confluent/advanced centrilobular or panlobular).

Some functional parameters can be of great help in separating these two different pathological conditions [5].

Overinflation due to abnormally high lung compliance and loss of pulmonary capillaries caused by progressive alveolar septa destruction are pathophysiological hallmarks of emphysema. Therefore, plethysmographic total lung capacity (TLC) is markedly increased (above upper limit of normality or 120% of predicted) only in the presence of significant emphysema as well as a reduced lung diffusing capacity (DL_{CO}) due to a low transfer factor (KCO). These parameters are all in the normal range in case of chronic bronchiolitis with the possible exception of DL_{CO} that sometimes can be reduced if the alveolar volume (VA) is diminished (relatively to plethysmographic TLC) because of inhomogeneity of ventilation.

Also the MEF/MIF ratio at 50% of forced vital capacity obtained during the maximal expiratory and inspiratory vital capacity maneuver is highly indicative of the predominant emphysema, when less than 20%, highlighting a marked expiratory collapse of non cartilaginous small airways, due to paucity or lack of alveolar attachments, coupled with a decreased elastic recoil pressure of the lung.

Recently, a novel index so called emphysema severity index (ESI) has been proposed looking at the maximal expiratory flow/volume curve and validated by means of various platforms of quantitative densitometric analysis of lung CT scan [6,7]. The ESI calculation is based on biomechanical model that approximates the morphology of the expiratory limb during forced vital capacity (FVC) maneuver by using an algorithm, elaborate by a dedicated software, fitting its profile. By providing the values of peak expiratory flow, maximal expiratory flow rates at 75%, 50% and 25% of FVC and FVC, the algorithm gives a categorical score from 0 to 10 for any maximal expiratory flow/volume curve suggesting the absence (below 2) or the presence (above 4) of a significant emphysema.

Third step

In order to decide the adequate initial pharmacological treatment to offer is mandatory knowing if a COPD patient is at low risk or at high risk in terms of prognosis related to all-cause mortality. This relies on a multiparametric assessment that requires measurement of body mass index (above/equal or below 21), airflow obstruction by FEV_1 (above/equal or below 50% predicted), chronic dyspnea by mMRC scale (below or equal/above 2), exercise capacity by six minute walking test (above/equal or below 350 mt), Inspiratory Capacity at rest (above/equal or below the lower limit of normality or 80% of predicted) and gas exchange by pulse oximetry (SpO_2 above/equal or below 90%). The history of one or more moderate-to-severe acute COPD exacerbation (AECOPD) by default puts a COPD patient at high risk [8].

In addition, the presence of some comorbidities increases significantly the risk of all-cause mortality in every COPD patient [9] and each one needs to be treated accordingly.

A COPD patient at low risk should be treated with one long-acting (or ultra-long-acting) bronchodilator, whereas a COPD patient at high risk or who has become at high risk must have two long-acting (or ultra-long-acting) bronchodilators (better if taken together).

Fourth step

In both cases the question is whether or not to add inhaled corticosteroids (ICS) on top of one long-acting (or ultra-long-acting) bronchodilator, i.e.: combination therapy in a low risk patient or two long-acting (or ultra-long-acting) bronchodilators, i.e.: triple therapy in a high risk patient, as maintenance treatment even in the absence of AECOPD [10].

BERN acronym may help to decide which COPD patient may benefit of ICS [8]. BERN stands for chronic Bronchiolitis (and not emphysema, as predominant disease), blood Eosinophilia (more than 300 el/mcl assessed twice in stable conditions), consistent significant Responsiveness to acute bronchodilator (especially with an increase of the FEV_1/FVC ratio) and Non-smoker (never smoker or ex-smoker).

A COPD patient BERN positive (with the above mentioned characteristics) should receive ICS; in

contrast, a COPD patient BERN negative (without the above mentioned characteristics) should not be treated with ICS [8].

A COPD patient with history of AECOPD who is by definition at high risk, always requires two long-acting (or ultra-long-acting) bronchodilators and ICS (i.e.: triple therapy) only if AECOPD are predominantly eosinophilic in the sputum, which more often occur in COPD patients with high number (>300 el/mcl) of blood eosinophils. The other different AECOPD should be prevented according to their prevalent nature with specific and adequate treatment [8].

Fifth step

A COPD patient under therapy has to be monitored at least every twelve months.

Besides the smoking cessation (in smokers), measurements of BMI (to control weight), FEV_1 (to control functional decline in ml/yr), mMRC (to control chronic dyspnea) and occurrence of AECOPD are necessary to establish the effectiveness of the treatment to control the activity of disease [11].

Sixth step

At the same time it would be worth evaluating the feeling of the patient about his/her condition under treatment, by administering validated questionnaires about quality of life in COPD like St. George's Respiratory Questionnaire and/or the less demanding CAT questionnaire, looking at perceived impact of disease on the patient's life.

Finally, if possible, the average daily physical activity of a COPD patient should be assessed by a personal actigraph or using a simpler step marker [11].

The two last steps have been implemented to define the new concept of clinically important deterioration (CID) [12]. A reduction of through FEV_1 greater than 100 ml, an increment of the SGRQ score higher than 4 and the presence of AECOPD in a given period of time (i.e.: one year), these as a whole constitute a loss of efficacy of the treatment offered to a COPD patient and may require a re-evaluation of the his/her clinical management.

Table 1. Measurement that it is worth to do in a patient with new diagnosis of COPD.

First step	Etiology of COPD	Alfa-1-antitrypsin plasma level
Second step	Prevalent Disease	TLC – DL_{CO}, KCO – MEF/MIF50% - ESI
Third step	Severity of risk	BMI - FEV_1 - mMRC - 6MWT- SpO_2 - IC, AECOPD
Forth step	ICS administration	BERN
Fifth step	Control of activity	Smoking, BMI - FEV_1- mMRC, AECOPD
Sixth step	Impact on patient	SGRQ – CAT – Daily physical activity

Conclusion

Finally, a Table (Table 1) to summarize what is useful to measure in a patient with new diagnosis of COPD is provided at the end to complete this review.

References

1. Miravittles M, Dirksen A, Ferrarotti I, Koblizek V, Lange P, Mahadeva R, et al. European Respiratory Society statement: diagnosis and treatment of pulmonary disease in alfa-1-antitrypsin deficiency. Eur Respir J 2017;50(5).
2. Lee JH, Lee YK, Kim EK, Kim TH. Responses to inhaled long-acting beta-agonist and corticosteroids to COPD subtype. Respir Med 2010;104:542-9.
3. Nishimura M, Makita H, Nagai K, Konno S, Nasuhara Y, Hasegawa M, et al. AJRCCM 2012;185:44-52.
4. Johannessen A. Skorge TD, Bottai M, Grydeland TB, Nilsen RM, Coxson H, et al. Mortality by level of emphysema and airway wall thickness. AJRCCM 2013;187:602-8.
5. Tantucci C, Pini L. COPD: it is time to change! Int J of COPD 2015;10:2451-7.
6. Occhipinti M, Paoletti M, Bartholmai BJ, Rajagopalan S, Karwoski RA, Nardi C, et al. Spirometric assessment of emphysema presence and severity as measured by quantitative CT and CT-based radiomics in COPD. Respir Res 2019;20:101.

7. Occhipinti M, Paoletti M, Crapo JD, Make BJ, Lynch DA, Brusasco V, et al. Validation of a method to assess emphysema severity by spirometry in the COPD gene study. Respir Res 2020;21:103.
8. Tantucci C, Pini L. COPD: Inhaled corticosteroids in COPD: trying to make a long story short. Int J of COPD 2020;15:821-9.
9. Divo M, Cote C, deTorres JP, Casanova C, Marin JM, Pinto-Plata V, et al. Comorbidities and risk of mortality in patients with chronic obstructive pulmonary disease. AJRCCM 2012;186:155-61.
10. Ernst P, Saad N, Suissa S. Inhaled corticosteroids in COPD: the clinical evidence. Eur Respir J 2015;45:525-37.
11. Agusti A, MacNee W. The COPD control panel: towards personalised medicine in COPD. Thorax 2013;68:687-90.
12. Sing D, Criner GJ, Naya I, Jones PW, Tombs L, Lipson A, et al. Measuring disease activity in COPD: is clinically important deterioration the answer? Respir Res 2020;21:134-47.

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