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COPD – moving beyond bronchodilation

Jean-Marie Tschopp

Summary

The burden of chronic obstructive pulmonary disease (COPD) remains very high. Till recently clinical approach of COPD patients was focused on measuring airflow limitation during exercise and treating airway obstruction with inhaled bronchodilators and corticosteroids.

This approach stems from an old definition of COPD, mainly consisting of airflow limitation with poor reversibility after bronchodilation.

The concept of COPD has changed strikingly in the last years. Many recent studies have shown that COPD is a systemic disease affecting not only the lungs but many other organs of the patient. Laboratory cardiopulmonary exercise testing assesses physiological and biological reserves. However, it is not the most suitable test to assess the functional state of a systemic disease such as COPD. We need simpler exercise tests that can be used on larger scales. The 6-minute walk test has been shown to be highly reproducible and reflects real life limitations of these patients better. It allows precise measurements of medical intervention and is a good predictor of mortality, provided clinicians respect the defined standards of this test. It should be associated with a more systemic index such as the BODE index to better find disease-modifying interventions and improve the outcome of COPD patients.

On the other hand routine measurement of spirometry in the general population by primary care physicians should be promoted as it decreases smoking habits and helps better detecting and management of COPD patients.

Specialists should support primary care physicians to spread these new concepts of COPD throughout the medical community.

Key words: COPD; systemic disease; spirometry

Introduction

Chronic obstructive pulmonary disease (COPD) is a very common and costly disease spreading all over the planet [1]. The prevalence of clinically relevant cases is about 4–6% in the European adult population with estimated numbers of COPD patients of 3.0 million in the UK, 2.7 million in Germany and 2.6 million in France. It is the fourth leading cause of death in the United States and in Europe. Moreover, COPD mortality has more than doubled in females over the last 20 years [2]. It is mainly related to smoking habits making this very frequent disease the most preventable disease of the world [3].

COPD was defined by airflow limitation with poor reversibility after bronchodilation. Till recently a prerequisite for diagnosis was the measurement of FEV_1 by spirometry. An epidemiological study in London postmen by Fletcher and colleagues [4] clearly demonstrated the role of FEV_1 as a predictor of mortality and individual outcome of these patients. However as Wullf [5] stated, the description of diseases changes over time and "textbooks of medicine must be rewritten from time to time not only because of the development of new technology and new treatments, but because diseases change." The most striking change in the concept of COPD in the last years is that this disease is a systemic disease affecting not only the lungs but many other organs of the patient [6]. Exercise testing assesses physiological and biological reserves and it should ideally be considered as the most suitable test to assess the functional limitations of patients with a systemic disease such as COPD [7]. Laboratory exercise testing has been developed more than 20 years ago [8, 9] and is commonly known as spiroergometry when simultaneously recording respiratory and cardiac parameters. What is the place of this test in the assessment of COPD and in the development of new therapeutic tools? Should we do more spirometry in daily medical practice to better diagnose COPD and decrease the burden of this disease?

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Exercise testing as a component of disease assessment

In 1982, Jones wrote a manual of exercise testing summarizing knowledge of that time [7, 10] and clearly showed that exercise testing should be considered an extension of the clinical examination because, testing under load is mandatory in the assessment of any machine and especially of the human machine. Since then, exercise testing has spread in the medical community. Laboratory exercise testing is very reproducible with simultaneous measurement of many physiological parameters allowing precise definition of limitations of any individual patient. It can be considered as a gold standard in the evaluation of any patient suffering from cardiac, respiratory, neurologic or muscular diseases [11].

There are many indications for exercise testing in respiratory diseases (table 1). The treating physicians possess well defined graph plots with the response predicted for a normal individual having the anthropometric characteristics of the patient [12]. It is easy to rapidly recognise patterns of abnormalities and the associated clinical disorders. However, even if laboratory exercise testing provides important and pertinent information about metabolic, cardiac, ventilatory or muscular limitations in diseases such as COPD, it remains an expensive and "high tech" clinical test requiring specialised staff (figure 1). It cannot be used on a large scale to assess large groups of patients or new treatments of respiratory or cardiac diseases. There was a need to develop simpler tests that can be used in routine practise [13].

Exercise testing as a tool to better assess severity of COPD and to find disease-modifying interventions

In the 1960s, Cooper developed a simple test to evaluate the walking distance during a defined period of time, eg the 12-minute walk test [14], because this test would better represent functional activity in daily life. Later on a 6-minute walk test (6MWT) was found to perform as well as the 12-minute walk test [15]. It was easier to administer and reflected daily activities better than other tests [16]. It is now largely used because it is very simple and does not require special equipment (fig. 2 and table 2) and trained technicians [17]. The 6MWT has now many recognised indications such as measuring results of medical interventions in patients with heart or lung diseases, assessing the

Figure 1

Cardiopulmonary exercice testing requires sophisticated technologies and specialised staff.

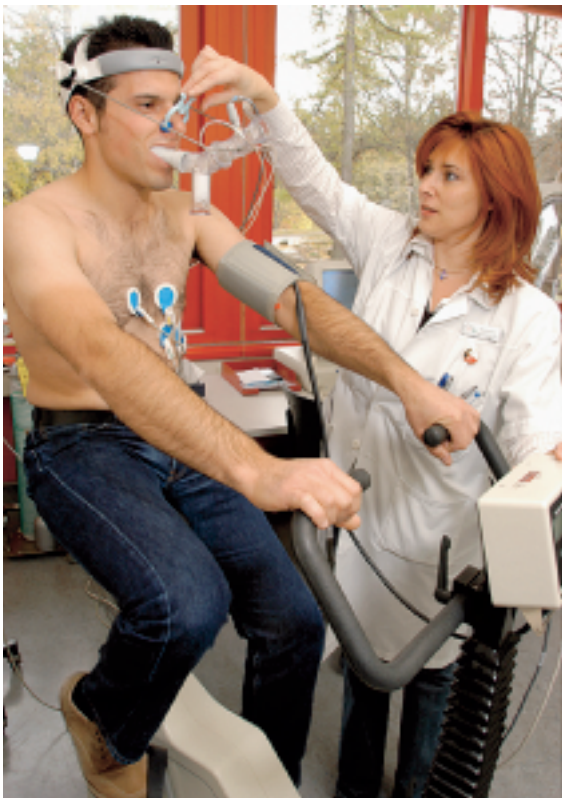

Table 1

Indications for exercise testing in respiratory diseases.

Assessment of physical function
patient evaluation
exercise prescription
disability evaluation
Differential diagnosis of dyspnoea
cardiovascular
respiratory
metabolic
neuromuscular
muscular
psychological
Evaluation of therapeutic interventions
pharmacological
surgical
oxygen
rehabilitation
transplantation

Figure 2

The 6-minute walk test requires good explanation to the patient and well standardised encouragements.

Table 2

Minimal requirements for a 6MWT (adapted from reference [17]).

Free Corridor of 30 m and 2 cones
Standardised instructions
At least two practice walks
Graded scale in meters
Standard encouragement
Supervision from behind
End exercise Borg scale

Table 3

Indications for a 6-minute walk test (adapted from reference [17]).

Pre- and post-treatment comparisons	
	lung transplantation
	rehabilitation
	lung resection, LVRS
	COPD
	heart failure
Functional status	
	COPD
	cystic fibrosis
	older patients
	heart failure
	peripheral vascular disease
Predictor of morbidity and mortality	
	COPD
	primary pulmonary hypertension
	heart failure

functional status of an individual or as a predictor of mortality (table 3). However, technical aspects must be respected if we want to get reliable and reproducible results as recently noticed by cardiologists and even veterinarians [18, 19]. In this last paper, Refsgaard commented on randomised controlled trials that measured 6MWTs assessing the efficacy of pharmacological interventions in heart failure. He insisted in a rather provocative editorial, on the necessity of a rigorous protocol when doing a 6MWT. Such a test cannot be done in general practice as it requires a free corridor of at least 30 m. Clinicians are therefore responsible for instructing technicians performing the test to assure continuous quality in acute and rehabilitation hospitals. It is the only way to get reliable data about a patient's improvement related to medication or any other therapeutic intervention.

The test should be very well standardised [17] and it is mandatory that clinicians consult these guidelines which provide a step-by-step protocol and safety measures, define the preparation of the patient and procedures, and offer recommendations for the interpretation of results. They should supervise the testing in their clinical setting which does not require high powered technology.

For example: the corridor must be free of any walk obstacle and distances must be well marked every 3 meters, a treadmill is not recommended because patients are not able to walk at their own pace, patients should sit in a chair before doing the test, a technician should not accompany the patient and encouragements need to be well standardised etc. Although not formally recommended in the above cited guidelines, we have now very small portable and more precise oxymeters allowing continuous measurements during a test and providing useful clinical data on pulse rate and peripheral oxygenation.

When all these conditions are fulfilled, the 6MWT provides very reliable and reproducible results. For example, recently Pinto et al. [20] predicted mortality of COPD patients by such a simple test despite no significant change in FEV_1 over 4 years. If we use the 6MWT for interpretation of the results of an individual patient before and after any medical intervention, we want to know whether the measured improvement is clinically significant. It is mandatory to do one or two practice walks before the first measurement. It is generally admitted to express results in absolute distances and an improvement of >50 m is considered as clinically significant as shown by Redelmeyer et al. [21] in COPD patients.

In conclusion, if we follow the recommended guidelines, this test is a very useful tool to assess the functional status of COPD patients and measure impairment in their daily life activity.

Towards a systemic approach of COPD

From a biological and epidemiological point of view, there are many evidences suggesting that chronic low-grade systemic inflammation exists in stable COPD as in other chronic diseases such as cardiovascular diseases [22]. That is not entirely surprising since cigarette smoking is a main risk factor not only for COPD but also for myocardial infarctions, peripheral or cerebral vascular diseases.

Table 4

Modified MRC dyspnoea scale.

Grade 1	breathlessness with strenuous exercise
Grade 2	short of breath when hurrying on the level or walking up a slight hill
Grade 3	walks slower than people of the same age on the level or stops for breath when walking at own pace on the level
Grade 4	stops for breath after walking 100 meters
Grade 5	too breathless to leave the house when dressing

Table 5

Variables and point values used for assessing the BODE index (adapted from reference [22]).

Variable	Points on BODE index			
	0	**1**	**2**	**3**
FEV_1 (% of predicted)	≥65	50–64	36–49	≤35
Distance walked in 6 min (m)	≥350	250–349	150–249	≤149
MMRC dyspnoea scale	0–2	3	4	5
body-mass index ($kg.m^{-2}$)	>21	≤21		

Celli et al. [23] hypothesised that a multi-systemic grading assessing respiratory and systemic expressions of COPD would better predict outcome in these patients. They developed the BODE index including four parameters, ie the body mass index (B), the degree of airflow obstruction (O) as defined by FEV_1, the level of dyspnoea (D) according to the modified Medical Research Council questionnaire (MMRC; table 4) and the exercise (E) capacity expressed as the distance walked in 6 minutes. One can therefore – for each patient – assess his/her own BODE index (table 5).

This index was retrospectively and prospectively validated and has proven to be a much better predictor of survival than all the commonly used parameters. Since then, the definition of disease intervention in COPD has changed. Imfeld et al. [24] used the BODE index 3 months after lung volume reduction in COPD and showed it to be a better predictor of mortality than FEV_1, of the dyspnoea score and of the 6-minute walk distance. The same was true for pulmonary rehabilitation where the improvement in BODE index after intervention correlated with survival in COPD [25]. In the last years, the disease concept of COPD changed, emphasising that disease-modifying interventions should not only address bronchial obstruction as recommended 30 years ago [4], but also poor nutrition, worsened dyspnoea, limitation in exercise capacity, and muscle weakness [26].

COPD case finding by primary care physicians

At first sight, it might be useful to promote the use of routine measurement of FEV_1 by simple spirometry to diagnose more cases of COPD in the general population. A recent study involving more than 500 primary care physicians who received a special training by 57 chest physicians, did not find any benefit of such a screening programme [27]. Enright in an accompanying editorial [28] casts doubts upon the real advantage of such a screening, based on a report of the US Agency for Healthcare Research and Quality. He argued mainly that many detected COPD patients with an FEV_1 >50% would receive inhaled bronchodilators without proven benefit, apart from increasing the market of these drugs. However, two recent studies clearly showed a benefit of primary-care spirometry. Walker et al. [29] provided an open-access spirometry to a local primary-care area, to which 1508 subjects were referred. They found 130 new cases of COPD, who were not only better detected but better managed in terms of using current medication. Bednarek et al. [30] investigated more than 4000 smokers with spirometry and gave them at the time of screening advice about smoking cessation. They showed a controlled smoking cessation rate of 16.3% at one year, which was higher than the expected 4–6%. These results are remarkable and strongly suggest that spirometry screening works not only for helping patients to stop smoking, but also to offer COPD patients a better clinical management. Such a health policy ought to be largely promoted in the adult population, especially in smokers.

Conclusion

COPD is a very frequent disease encountered by primary care physicians as well as by chest physicians. The most striking change that occurred in these last years regards the concept of COPD as a systemic disease [6]. To asses the severity of the disease, we cannot focus our clinical work only on spirometry and any measurement of airway obstruction. Similarly, exercise testing should be done not only in laboratories with high powered and expensive technologies but also in routine practise using simpler exercise tests such as the 6-minute walk test associated or not to the BODE index to better find disease-modifying interventions and to improve the outcome of COPD patients [31]. Unfortunately there is still a lot to do to promote these new concepts within the medical community.

Correspondence:
Prof. Jean-Marie Tschopp
Médecin-Directeur
CHCVs – Centre Valaisan de Pneumologie
CH-3963 Crans Montana
E-Mail: jean-marie.tschopp@admin.vs.ch

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