REVIEW

Diagnostic management of chronic obstructive pulmonary disease

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ABSTRACT

Detection of early chronic obstructive pulmonary disease (COPD) in patients presenting with respiratory symptoms is recommended; however, diagnosing COPD is difficult because a single gold standard is not available. The aim of this article is to review and interpret the existing evidence, theories and consensus on the individual parts of the diagnostic work-up for COPD.

Relevant articles are discussed under the subheadings: history taking, physical examination, spirometry and additional lung function assessment.

Wheezing, cough, phlegm and breathlessness on exertion are suggestive signs for COPD. The diagnostic value of the physical examination is limited, except for auscultated pulmonary wheezing or reduced breath sounds, increasing the probability of COPD. Spirometric airflow obstruction after bronchodilation, defined as a lowered ratio of the forced volume in one second to the forced vital capacity (FEV1/FVC ratio), is a prerequisite, but can only confirm COPD in combination with suggestive symptoms. Different thresholds are being recommended to define low FEV1/FVC, including a fixed threshold, and one varying with gender and age; however, the way physicians interpret these thresholds in their assessment is not well known. Body plethysmography allows a more complete assessment of pulmonary function, providing results on the total lung capacity and the residual volume and is indicated when conventional spirometry results are inconclusive. Chest radiography has no diagnostic value for COPD but is useful to exclude alternative diagnoses such as heart failure or lung cancer.

Extensive history taking is of key importance in diagnosing COPD.

KEYWORDS

COPD, diagnosis, history taking, physical examination, spirometry

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a cluster of heterogenic disorders, characterised by expiratory flow limitation that is not completely reversible and in most cases progressive.[1] Patients with COPD show an abnormal inflammatory reaction to tobacco smoke or other air pollution exposures, resulting in airway obstruction, destruction of lung tissue and hyperinflation. COPD is among the leading chronic disorders worldwide regarding frequency, impact on quality of life and mortality.[1]

Often COPD stays undiagnosed until it has developed to a more severe stage. This underdiagnosis of early COPD[2,3] is illustrated by the relatively low number of mild COPD cases in the Netherlands: of all patients with established COPD in the year 2000, 27% had mild, 55% moderate, 15% severe and 3% very severe disease.[4]

Early detection of COPD is relevant because adequate treatment, especially stop smoking interventions, but also inhaled medication, lifestyle counselling and influenza vaccination reduce exacerbations and improve quality of life.[1] Nonetheless, diagnosing COPD is difficult, because a single gold standard is not available. A diagnosis requires the assessment of symptoms, signs and spirometry results combined, while spirometry abnormalities can be subtle in the early phase.[1,5] Possibly, these diagnostic difficulties contribute to the present underreporting of COPD.

This manuscript discusses the diagnostic management of COPD, with an emphasis on early COPD. The viewpoint will be from a primary care perspective, where the majority of the patients are diagnosed and treated.

WHICH PATIENTS ARE AT RISK?

International guidelines discourage screening non-symptomatic subjects for COPD because there is no evidence of the long-term effects,[1,5-7] but strongly recommend to evaluate COPD in (former) smokers older

than 40 - COPD is rare below this age – who seek healthcare for respiratory symptoms,[1,5] such as cough, wheeze or dyspnoea. These symptoms are probably not always perceived as signs of possible COPD, but frequently labelled as respiratory infections. A first step in the diagnostic process is therefore increased awareness that such respiratory symptoms, which are among the most frequently seen in primary care, can suggest COPD. Hereafter, the results of history taking, physical examination, spirometry and additional lung function assessment can be helpful in the diagnostic work-up for COPD. This manuscript will discuss these diagnostic tests, in the order they are used in daily practice.

HISTORY TAKING

History taking for COPD includes the assessment of possible aetiological risk factors on the one hand and suggestive symptoms on the other hand. The biggest risk factor, tobacco smoking, is often quantified in 'pack-years', with one unit representing one year of smoking 20 cigarettes a day. There is a dose-response relation between smoking duration and lung function decline,[8] but the genetic susceptibility for COPD varies largely between individuals,[9] and COPD sometimes even develops in never smokers.[10] Accordingly, no threshold for smoking duration can be recommended; however, several studies found that more than 20 pack-years substantially increased the risk of COPD.[11,12] Other airway exposures such as dust, chemicals or fumes, which are often occupation related, (for example farmers, bakers or drivers), should also be evaluated. In general, the risk of COPD increases with the air pollution level, including indoor air pollution from biomass fuel which is only relevant in developing countries.[10]

Other risk factors for COPD that can easily be evaluated by history taking or reviewing the medical file are: low birth weight, asthma, respiratory tract infections including tuberculosis and a family history of COPD.[1,13] The exact causal mechanisms for COPD are less straightforward here than for the respiratory exposures, but the aetiology of COPD is beyond the scope of this article.

Regarding symptoms, cough, wheeze, and phlegm have diagnostic value for COPD, especially if chronic (longer than three months) or recurrent.[1,14-17] Screening the medical file for diagnostic codes of 'acute bronchitis' or 'cough' may help to identify earlier episodes of respiratory symptoms, which might have been exacerbations of hidden COPD. Another symptom is shortness of breath on exertion. This is common in early COPD, despite limited spirometric obstruction, merely caused by an increasing functional residual volume (air trapping) during higher breathing frequency, also called 'dynamic hyperinflation'.[18] Shortness of breath at rest is often present in severe COPD, but unusual as presenting symptom[1] and requires evaluation of alternative more acute disorders, including for example pulmonary embolism, pneumonia and acute heart failure.

PHYSICAL EXAMINATION

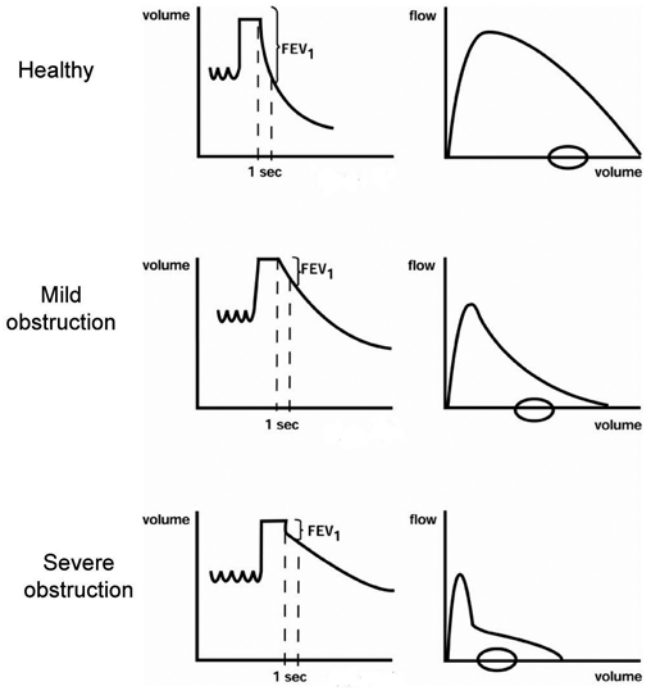
In most cases the diagnostic value of physical examination for COPD is limited. The most useful diagnostic items are 'diminished breath sounds' and 'wheezing' on lung auscultation, which have higher positive than negative predictive values and can therefore not exclude COPD.[11,12,19-23] There are various other well-known and evidence-based physical manifestations of COPD, including barrel chest, accessory muscle use,[14] weight loss[24] and peripheral oedema,[25] but these are merely confined to severe and usually established COPD. Nonetheless, these typical pulmonary signs can aid to assess and monitor exacerbations of established COPD. Other evidence-based signs, for example forced expiratory time,[22,23,26] laryngeal height,[11] and subxyphoid apical impulse,[14] are not part of the routine physical examination and therefore less helpful for practice. Resuming, wheezing and reduced breath sounds suggest COPD, but normal physical examination results do not exclude COPD.

SPIROMETRY

Spirometry is a non-invasive test quantifying flow and volume of the vital capacity, which is the amount of air that can be inhaled and exhaled. Results should be measured before and after an inhaled bronchodilator. The measurement validity depends on the technician's instruction skills regarding the patient's required forced breathing manoeuvres. Spirometry has been implemented in many primary care settings during the last decade, where rigorous training of practice staff has shown to allow for adequate measurement quality.[27] Results are visualised in a time-volume and flow-volume curve (a simplified representation is given in *figure 1*) and the most relevant results for COPD are the forced expiratory volume in one second (FEV1) and the forced vital capacity (FVC).

For a COPD diagnosis, spirometric airflow obstruction is a prerequisite, defined as a lowered ratio of the FEV1 to the FVC (FEV1/FVC ratio), persisting after bronchodilation. Several thresholds are recommended to define low FEV1/FVC. An often recommended threshold is a fixed value of <0.7. However, this fixed value causes potential overdiagnosis of COPD in the elderly, and underdiagnosis in the young because FEV1 decreases with ageing resulting in a FEV/FVC ratio <0.7 in more than 20% of healthy elderly people (>60 years).[28,29] Therefore, others define low FEV1/FVC by the 'lower limit of normal' according

Figure 1. *Simplified volume-time and flow-volume spirometry curves*



	result	pred	%pred
FEV1 (l)	2.98	2.91	102
FVC (l)	3.95	3.39	117
FEV1/FVC	0.75	0.86	87

	result	pred	%pred
FEV1 (l)	2.55	2.92	87
FVC (l)	3.86	3.39	114
FEV1/FVC	66	86	77

	result	pred	%pred
FEV1 (l)	1.2	2.79	43
FVC (l)	2.26	3.59	63
FEV1/FVC	53	75	71

Results of forced breathing spirometry manoeuvres are shown. FEV1 = forced expiratory volume in one second; FVC = forced expiratory volume; pred = predicted value according to age, gender and height; % pred = percentage of the predicted value. Post-bronchodilator results are shown of three individuals.

to age and gender, instead of a fixed value, identifying the lowest 5% of a population.[30,31] To define the normal range, several regression equations were derived from different populations, with the National Health and Nutrition Examination Survey (NHANES III) as most used standard.[32] Most modern spirometry software allows calculation of thresholds by several methods. How physicians interpret spirometry results and thresholds in their assessment of COPD is unknown; however, the controversy on spirometric definitions illustrates that COPD is a clinical diagnosis which can not be based on spirometry results only.[1,5]

Besides the size of the volumes, one should judge the shape of the spirometric flow volume curve, to verify the quality and reproducibility of the measurements. Moreover, in many patients with severe COPD the descending limb of the expiratory loop is typically concave (*figure 1*);[1,33] however, standardised measures for this assessment are lacking.

ADDITIONAL LUNG FUNCTION ASSESSMENT

When there is diagnostic uncertainty, for example when symptoms are suggestive but spirometry is normal, or when a patient cannot sufficiently perform the forced breathing manoeuvres of conventional spirometry, additional lung function tests in a laboratory are helpful. Only those tests that are most efficient and commonly used in the diagnostic workup for COPD will be briefly discussed: body plethysmography and diffusion capacity of the lungs.

Besides the vital volumes, body plethysmography results include the total lung capacity (TLC) and the residual volume (RV) which is the TLC minus the vital capacity. Moreover, it allows quantification of the pulmonary gas diffusion capacity, most commonly using carbon monoxide (CO) as tracer gas.[34] Body plethysmography measurements are non-invasive tests performed on a patient sitting in a small enclosed space (body box). Results are expressed as absolute numbers and percentage predicted according to age, height and gender reference values[31] and the normal variability range is commonly defined as 80% to 120% predicted.[31,35] Body plethysmography allows a more complete assessment of gas exchange and chest mechanics than conventional spirometry. Although not specific, abnormal results can strongly suggest COPD. An enlarged RV and TLC are indicative of COPD, representing hyperinflation and enlarged air spaces (emphysema). A low DLCO suggests COPD[36] as well but can also be found in other disorders, for example interstitial lung diseases, pulmonary embolism, and pulmonary hypertension.[37] Finally, a low FVC limits interpretation of spirometry

results and requires referral for body plethysmography, to discriminate restrictive (low TLC) from obstructive lung disorders (normal/high TLC and high RV).[5,35]

REVERSIBILITY TESTING

For a long time airflow obstruction in COPD was considered to be completely irreversible and accordingly, a large improvement of the spirometric FEV1 - often called reversibility – was assumed to suggest reversible airway disorders such as asthma, and a lack of improvement typical for COPD. However, nowadays it is increasingly acknowledged that although obstruction in COPD by definition cannot normalise, it varies largely within individuals.[38] Contrary to earlier assumptions, a 12% FEV1 increase after inhaled bronchodilators or oral steroids is common in COPD, and more frequent than in healthy subjects.[39-41] Therefore, reversibility after treatment or time does not exclude COPD, except when lung function results normalise completely.

When spirometry results show both reversibility and persistent obstruction, differentiation between asthma, COPD, or a combination of both can be challenging but is nonetheless relevant because therapeutic management differs, with an emphasis on inhaled corticosteroids and other anti-inflammatory drugs in asthma, and inhaled bronchodilators in COPD.[1,42] In the elderly, asthma and COPD characteristics overlap; especially patients with asthma exposed to cigarette smoke or other inhaled exposures can develop incompletely COPD-like reversible obstruction.[43] Careful history taking is the most efficient tool to differentiate between COPD and asthma,[44] with allergy, eczema, symptoms in childhood, fluctuating symptoms with symptom-free periods, bronchial hyper-reactivity, and eczema being more suggestive of asthma.

INFLAMMATION MARKERS

Several acute-phase proteins including C-reactive protein and ferritin are increased in subjects with COPD, attributed to assumed systemic ongoing inflammation.[45,46] Whether these markers have added diagnostic value over symptoms, signs and spirometry is unknown and therefore measurement is not recommended in the diagnostic work-up for COPD.

SEVERITY STAGING

The GOLD criteria define COPD severity according to the post-bronchodilator FEV1 as percentage predicted (% pred): mild (FEV1 >80% pred), moderate (FEV1 50-80% pred), severe (FEV1 30-50% pred) and very severe (FEV1 < 30% pred). Most newly diagnosed subjects show mild or moderate disease.[16,47,48]

The association between spirometric obstruction and symptoms is, however, limited and additional assessment of severity should address symptoms, frequency and severity of exacerbations, and complications as respiratory failure, right heart failure and weight loss.[1] Validated questionnaires to judge and monitor health state are the British Medical Research Council (MRC) dyspnoea scale[49] and the Clinical COPD Questionnaire (CCQ)[50] on COPD-related symptoms, daily functioning and mental health.

DIFFERENTIAL DIAGNOSIS

In patients presenting with persistent or recurrent cough, wheeze and/or breathlessness, the differential diagnosis besides COPD is extensive, and includes asthma as previously addressed, heart disorders, pulmonary hypertension, lung infections, malignancy, interstitial lung disease and gastro-oesophageal reflux.[1] Of these, congestive heart failure, lung cancer and chronic bronchiectasis will be briefly discussed.

In the elderly, especially those older than 70, unrecognised heart failure is frequent, but also the combination of COPD and heart failure, because of overlapping aetiology (smoking history) and susceptibility.[51] Brain natriuretic peptide (BNP) measurement in blood, chest radiography and electrocardiography help to make heart failure more or less likely. If results suggest possible heart failure, echocardiography is indicated to diagnose heart failure with certainty. Lung cancer should be considered in all smokers presenting with a persistent cough, with chest radiography as a useful first diagnostic step. Because chest radiography is not 100% sensitive to exclude pneumonia, clinical suspicion of lung cancer warrants more advanced imaging (computerised tomography (CT) scanning). Bronchiectasis is characterised by complaints of large volumes of purulent phlegm, sometimes low-grade fever and is usually associated with bacterial infections. Bronchial wall thickening and bronchial dilatation are suggestive signs on chest radiography or CT scanning.[1]

Overall, a chest radiography is helpful to evaluate alternative diagnoses, but has limited diagnostic value for COPD, except in case of apparent bullae which are rare in early COPD.[1]

IMPLICATIONS FOR PRACTICE AND RESEARCH

In most patients presenting with persistent respiratory symptoms, COPD can be diagnosed or excluded by

history taking, physical examination and spirometry. History taking is most relevant, not only to evaluate COPD presence but also to alternative diagnoses. Physical examination can be completely normal in early COPD. In case of doubt, repeated spirometry and/or more extensive lung measurements are helpful. Chest radiography and electrocardiography are useful to exclude or suggest alternative diagnoses.

Finally, there is debate on the benefit of detection of early COPD. Arguments for detection include evidence that smokers diagnosed with COPD are more successful in quitting,[52,53] and improved quality of life and reduced exacerbations after treatment.[1] Moreover, a diagnosis could help to reduce unnecessary treatments (antibiotics and antitussives) and diagnostic procedures, but whether this is true is unknown. Arguments against detection are the associated costs for detection and treatment, the unpredictable individual course of mild COPD, lacking evidence on treatment of mild COPD and possible fear and distress of the patients by being labelled with COPD. Studies on the effects of standard treatment of mild COPD including quality of life and patient perception are needed to estimate the cost effectiveness of early COPD detection.

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