Review

Lung Function Tests in Clinical Decision-Making

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Abstract

In this article, we review the utility of the most common lung function tests (spirometry, reversibility test, peak expiratory flow, lung volumes, maximal respiratory pressure, carbon monoxide transference, arterial blood gas, 6-min walk test and desaturation with exercise and ergospirometry) related to the most frequent pathologies (dyspnea of undetermined origin, chronic cough, asthma, COPD, neuromuscular diseases, interstitial diseases, pulmonary vascular diseases, pre-operative evaluation and disability evaluation). Our analysis has been developed from the perspective of decision-making, clinical interpretation or aspects that the physician should take into account with their use. Consequently, the paper does not deal with aspects of quality, technique or equipment, with the exception of when regarding costs as we believe that this is an important element in the decision-making process. The document is extensively supported by references from the literature.

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Introduction

Lung function studies are a key part of the diagnostic evaluation and follow-up of patients with respiratory diseases. In addition, they have other very important clinical applications, such as evaluating surgical risk, disability, and prognosis. The information they provide is objective, precise, reproducible, and reliable.

There are several different lung function tests (LFT), and each has its indications. Those that are referred to as basic LFT are baseline spirometry and flow–volume curve, bronchodilator test, and arterial blood gases. Other important tests in clinical practice are the carbon monoxide transference test (DLCO), lung volume determination, bronchial provocation tests, exercise tests and the determination of maximal pressures. In this review, we will present their most relevant aspects.

In order to carry out all these tests, different equipment is needed, which must meet the technical requirements established by current guidelines. Likewise, it is essential to check the calibration of the devices prior to their use, as well as to follow the established regulations for hygiene and control of infection. The personnel who administer the tests should be familiarized with the equipment and have sufficient experience in their duties to obtain quality results. Patients should follow the previous preparation instructions, and they should be explained how to correctly perform the tests.
Spirometry and Flow–Volume Curve

Spirometry measures the forced expiratory volume in 1 s (FEV\(_1\)) and the forced vital capacity (FVC), and it is the most accessible and useful lung function test. It takes 10–15 min to perform and the equipment costs from 2000 to 6000€. The test entails practically no risk, and each test costs approximately 40€. If the spirometer is able to collect data for more than 30 s, slow vital capacity (SVC) can also be measured. SVC increases the sensitivity of spirometry for detecting obstruction,\(^1\) but it does require the test to be longer. Other parameters are mesoexpiratory flow (MEF 25%–75%) and instantaneous maximum flow at 75%, 50%, or 25% of FVC (MEF 75%, 50%, 25%). These parameters are considered indicators of the state of the small airway and a statistical correlation has been observed in subject groups. They are not, however, very sensitive due to their variability, and the cut-points (5% percentile) are nearly 50%\(^5\) in subjects >50 years of age.

The morphology of the flow–volume curve is very useful for detecting the characteristic concavity of the slowing of expiration at low volumes in obstructive patterns\(^6\) and the convexity in restrictive patterns\(^6\) (Fig. 1); moreover, it has a distinctive shape in upper airway obstruction, as shown in Fig. 2. It must be noted, however, that the sensitivity is low in tracheal stenoses measuring more than 1 cm in diameter.\(^7\)

Correctly interpreting spirometry requires it being analyzed within the context of the patient’s clinical data, but we can refer to general respiratory function patterns: obstructive, restrictive, and mixed (Fig. 3). The most important parameter for identifying an obstruction is an FEV\(_1\)/VC ratio <70%.\(^2,6\) This cut-point can lead to a significant number of false positives in males over the age of 40 and in women over the age of 50, as well as to the overdiagnosis of obstruction in seniors, asymptomatic subjects and non-smokers.\(^6,8\)

It has therefore been recommended to use the lower limit of the confidence interval (LLN)=mean predicted value−(standard error of the residuals×1.645),\(^2,6\) but tradition and the fact that this percentile is not available in the majority of the devices mean that it is not often used.

Spirometry also is able to evaluate the severity of ventilatory alterations.\(^2,6\) To do so, categories have been defined as a simple conceptual framework depending on post-bronchodilator FEV\(_1\) for obstructive defects and according to vital capacity (VC) or total lung capacity (TLC) for restrictive defects.\(^2,6\) The cut-points of the different guidelines are shown in Table 1. These cut-points are related with the ability to perform daily activities, morbidity and mortality in COPD.\(^9–13\) but these are less relevant in asthma, where hyperactivity, variability in function (and symptoms), and the response to treatment are more relevant factors than momentary FEV\(_1\).\(^14\)

The cut-points are also not relevant in the obstruction of the upper airway.\(^5\)

Although in most restrictive disorders worsened symptoms are accompanied by a drop in VC, VC may only be moderately reduced in diffuse interstitial lung diseases (DILD) with a marked loss in diffusion capacity and severe blood gas alterations.\(^6,15–17\) Severe respiratory failure may occur in patients with rapidly progressive neuromuscular diseases who had had normal or slightly reduced VC shortly before.\(^5\)

Another aspect of FEV\(_1\) and VC is that they are general indicators of health related with life expectancy, even in non-smoker patients.\(^18\) (Fig. 4).

Spirometry is very useful for following evolution and monitoring functional changes over time. Table 2 describes the cut-points in
Table 1
Gradation of The Severity According to Different Guidelines.

<table>
<thead>
<tr>
<th>Obstructive Alteration</th>
<th>Restrictive Alteration</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ATS/ERS</strong></td>
<td><strong>VC</strong></td>
</tr>
<tr>
<td>Mild</td>
<td>&gt;70%</td>
</tr>
<tr>
<td>Moderate</td>
<td>60%–69%</td>
</tr>
<tr>
<td>Moderate–severe</td>
<td>50%–59%</td>
</tr>
<tr>
<td>Severe</td>
<td>35%–49%</td>
</tr>
<tr>
<td>Very severe</td>
<td>&lt;35%</td>
</tr>
<tr>
<td><strong>SEPAR</strong></td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>&gt;65%</td>
</tr>
<tr>
<td>Moderate</td>
<td>50%–64%</td>
</tr>
<tr>
<td>Severe</td>
<td>35%–49%</td>
</tr>
<tr>
<td>Very severe</td>
<td>&lt;35%</td>
</tr>
</tbody>
</table>

**Classification (GOLD) of COPD severity**

- Stage I, mild: ≥80%
- Stage II, moderate: 50%–80%
- Stage III, severe: 30%–50%
- Stage IV, very severe: <30%


Fig. 3. Algorithm for interpreting the respiratory function tests. FEV₁: forced expiratory volume in 1 s; FVC: forced vital capacity; LLN: lower limit of normal; TLC: total lung capacity.

The reversibility test costs 40€ more than spirometry (app. 80€ in total). It is indicated in all asthmatics at the time of diagnosis and, if there is still obstruction, at follow-up. As in many laboratories the medicine is routinely withdrawn, we should warn the patient and the laboratory not to withdraw it if our objective is to verify the response to treatment (individual therapeutic assay).

The definition of COPD itself indicates that this disease is characterized by "airflow limitation that is not reversible" and "there are no marked changes in the function over the course of several months". This means that the condition should be met that, if there is reversibility, it is not total, and therefore the measured FEV₁/VC ratio should be <70% after bronchodilators. In fact, epidemiological studies have shown that the prevalence of COPD reduces between 10% and 40% using post-bronchodilator FEV₁/VC, although the socioeconomic impact of said difference is not known.

A positive result to bronchodilators cannot distinguish between COPD and asthma, although improvements of more than 400 ml after bronchodilators or glucocorticoids suggest the second possibility or at least a mixed phenotype.

Fig. 4. Alveolar diffusion–volume ratio. DLCO: diffusing capacity for carbon monoxide in one single breath; Vₐ: alveolar volume. From Frans et al.

Table 2
Significant Changes in the Spirometric and Carbon Monoxide Diffusing Capacity Variables.

<table>
<thead>
<tr>
<th></th>
<th>FVC</th>
<th>FEV₁</th>
<th>MEF 25%–75%</th>
<th>DLCO</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Daily</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>≥5%</td>
<td>≥5%</td>
<td>≥13%</td>
<td>≥7%</td>
</tr>
<tr>
<td>COPD patients</td>
<td>≥11%</td>
<td>≥13%</td>
<td>≥23%</td>
<td></td>
</tr>
<tr>
<td><strong>Weekly</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>≥11%</td>
<td>≥12%</td>
<td>≥21%</td>
<td>≥2ᵃ</td>
</tr>
<tr>
<td>COPD patients</td>
<td>≥20%</td>
<td>≥20%</td>
<td>≥30%</td>
<td>≥1.3</td>
</tr>
<tr>
<td><strong>Annually</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>≥15%</td>
<td>≥15%</td>
<td>≥10%</td>
<td></td>
</tr>
</tbody>
</table>

FVC: forced vital capacity; FEV₁: forced expiratory volume in 1 s; MEF 25%–75%: mesoexpiratory flow at 25%–75%; DLCO: single-breath transference of carbon monoxide.

ᵃ In mmol min⁻¹ kPa⁻¹; in order to transform into the units most frequently used in the United States (mL min⁻¹ mmHg⁻¹), multiply by ~3 (3.013). Taken from Pelligrino et al.
One concept that has changes in recent years, based on large clinical assays, is that the presence or absence of bronchodila-
tion, except when very pronounced (>400 ml), does not seem to
to precisely predict symptom alleviation, changes in exercise capacity,
long-term response or response to either corticosteroids or bronchodilators. Therefore, the bronchodilator test is not a valid
guideline for treatment.

As for the diagnosis, there is abundant evidence that iden-
tifies FEV$_1$ as a risk factor in COPD and, in this case as well as in the diagnosis, the optimal parameter is post-
bronchodilator FEV$_1$. Reversibility has been found to be associated
with an accelerated decrease in FEV$_1$, but not all studies find this
association.

The percentage of COPD patients who respond to bronch-
dilators is variable. In the UPLIFT study, which administered ipratropium bromide and salbutamol with spirometries repeated
30 min afterwards, 52% of the patients responded to bronchodila-
tors. Nevertheless, these levels were 64%, 48%, and 18% when the
patients were classified into GOLD stages II, III, or IV. It has been seen that up to 35% of patients with an initial nega-
tive bronchodilator test, the result may be positive in later tests.
However, two tests can detect the majority of patients (88%) who occasionally may respond to bronchodilators, and therefore
its routine use would not be justified in patients with COPD
who already have one or at most two previous bronchodilator
tests.

Any drug may be used, but due to questions of effectiveness, an
inhaled, fast-acting $\beta_2$-agonist is almost always used (salbutamol is
most often used at a dose of 400 µg or 4 puffs taken 30 s apart
and with a proper inhalation technique). The effect begins 5 min
after the inhalation and reaches its maximum after 20 min. If iprat-
ropium is used, the recommended dose is 160 µg (8 puffs) and the
“post” spirometry is done 45 min later. Another way to evaluate
reversibility is to administer a test treatment (individual therapeu-
tic assay) and to evaluate the patient 30 days later, making the
laboratory and the patient aware that the medication prescribed
should not be withdrawn before doing the effectiveness evaluation
test.

Peak Expiratory Flow

Peak expiratory flow (PEF) is the maximal flow that a person
can exhale during a short maximal expiratory effort after complete
inspiration. In patients with asthma, PEF correlates with FEV$_1$, but
it should not be used as its substitute. Peak expiratory flow is a
measurement that is easy to do with a device that costs 30€, but it
is not very popular. It has the following uses:

Diagnosis

Variations of more than 20% are diagnostic for asthma in the
proper context. PEF can also allow us to observe the variability
in certain situations, such as an improvement during vacation
or worsening when exposed to certain environments, which,
if there are economic or legal implications, should be checked
seriously.

Monitoring Disease

In order to do so, we should establish the initial value by taking
measurements for 15 days in conditions of clinical stability and
maximum treatment and use this reference in order to establish
plans of action; however, it is not easy to maintain long-term
adherence, which limits its use.

Non-Specific Provocation Tests

There are different non-specific provocation tests (ATP, mani-
notol, isocapnic hyperventilation, exercise, food coloring) that are
useful in specific contexts. These tests take time and cost 200€.

The test may be indicated when the asthma diagnosis is in ques-
tion (atypical symptoms, normal spirometry), when a patient is
suspicous of having occupational asthma or asthma induced by
irritants, and when a test is required to rule out asthma in divers,
athletes, military personnel or other individuals in whom bron-
chospasm would be an unacceptable risk for themselves or for other
people, or it is required by regulations in order to use anti-asthma
medication, and it is not contraindicated. In the cases in which
asthma is triggered by exercise, exertional asthma has professional
implications; given the persistence of symptoms with exercise in a
correctly treated asthmatic, exercise provocation tests or isocapnic
hyperventilation tests may be indicated.

Although non-specific bronchial provocation tests can evaluate
asthma severity and monitor its treatment, they are not used for
this objective in clinical practice.

Interpretation of a Negative Test

In general, a negative test rules out asthma, except in certain
cases of allergic asthma or asthma induced by irritants in which
the test was done a time after the exposure and the symptoms.

Interpretation of a Positive Test

Approximately 1%–7% of the general asymptomatic popula-
tion has bronchial hyperreactivity (up to 26% if smokers or atopic
patients are included), although there are those who believe
that these patients are mild asthmatics who do not perceive their
symptoms. Therefore, the diagnosis should not be based on a
positive hyperreactivity test, and it should be confirmed that the
symptoms of the patient disappear with the treatment.

Determination of Static Volumes and Lung Resistances

The determination of pulmonary volumes and capacities can-
not be measured with spirometry, including: residual volume (RV),
functional residual capacity (FRC), and total lung capacity (TLC). It costs about 150€. The most widely used methods
are the helium dilution technique and nitrogen washout (FRC),
which can usually be measured with the same device as carbon
monoxide diffusion and body plethysmography (FRC$_{\text{pleth}}$), which
requires a booth that costs approximately 36 000€. Plethysmog-
raphy gives results that are somewhat higher than the other
two methods, but it is the fastest, most precise and reproducible
method.

The TLC measured during the determination of DL$_{\text{CO}}$
should never be used as a measurement of actual TLC because it
is underestimated, and the greater the obstruction the greater the
underestimation.

When studying lung volumes, we can find two pathological pat-
terns: restriction, defined by a TLC less than 80% of the reference
value, and hyperinflation, defined by either an FRC% or an RV/TLC
ratio above 120%. There are no data to document the use of FRC or
RV categories in airflow obstruction or TLC in pulmonary restriction
in order to classify severity, as done in spirometry.

Cases of low TLC and normal VC are exceptional; therefore
these measurements are generally not very useful in subjects
with normal VC. Its use has not been demonstrated in the dif-
fential diagnosis between emphysema and chronic bronchitis,
or between COPD and asthma. There is a general correlation
between the reduction in FEV$_1$ and the increase in RV, although
the agreement is not good in up to 15%, thus it could help to
interpret some cases of unjustified dyspnea in obstructive patients
when unexpected hyperinflation is detected. In patients with COPD
with or without normal VC, these measurements are useful for selecting patients for volume reduction, requiring more than 100% TLC and 135% FRC.39

The measurements of volumes can be useful in the study of subjects with low VC. In cases of mixed pattern, only approximately 10% have low TLC (the majority of them have an FEV1/VC ≥60% and an FEV1 >40%).3,36 so this would be the target population for measuring lung volumes.

In restrictive diseases, TLC has prognostic value,16 but VC is almost always used as it is easier to measure. In cases with typical restrictive spirometries (meaning when VC is lower, the FEV1/VC is higher [85%–90%] and the flow–volume curve has the characteristic convex pattern [Fig. 1]6, and if the symptoms are compatible, it is probably not necessary to confirm the restriction by measuring TLC. If the lower VC on spirometry is not accompanied by a normal or slightly increased FEV1/VC, this is frequently due to the fact that the inspiration or expiration has not been maximal and in up to 50% of these patients the repetition of the spirometry demonstrates that the subject is normal.3,6,40 In these cases, it would also be indicated to measure volumes if the VC continues to be low after repeating spirometry.

Airflow resistance can be measured by plethysmography, but this is rarely used in clinical practice due to its variability and because even the most sensitive parameter, specific resistance, generally reflects more of the obstruction of the large airways than of the more peripheral areas.6,3,4,41 It may be useful in patients who are incapable of correctly doing spirometry, as it requires less patient collaboration.

Maximal Respiratory Pressures

Maximal inspiratory pressure (PI\textsubscript{MAX}) is the maximal pressure that the patient can produce when trying to inhale through a blocked mouthpiece after maximum expiration (from RV). PI\textsubscript{MAX} pressure can be measured in the nose by inserting a nasal plug and sniffing with the other open nostril. This procedure is called sniff nasal-inspiratory pressure (SNIP), and it has the same indications as PI\textsubscript{MAX}. Its advantage is that it can measure pressure in patients with neuromuscular diseases who are unable to close their mouths properly because sniffing is a natural maneuver that is more easily understood by patients and which they are sometimes able to perform better. Usually, both are measured (PI\textsubscript{MAX} and SNIP), and the better of the two is considered more representative, which is later used in the follow-up. Maximal expiratory pressure PE\textsubscript{MAX} is the maximal pressure exerted into a blocked mouthpiece, measured during forced expiration after complete inhalation (from TLC), with inflated cheeks. It is easy to measure with a simple pressure manometer connected to a mouthpiece that costs between 1500 and 2000€. The cost of the test is 60€ plus an additional 80€ if combined with sitting and standing spirometry. PI\textsubscript{MAX} and PE\textsubscript{MAX} are measurements of the capacity for generating effort of the inspiratory and expiratory muscles, and therefore they can be affected by the configuration of the thorax, particularly the diaphragm, without any alterations that are muscular, as occurs in hyperinflated COPD. PI\textsubscript{MAX} (SNIP) and average PE\textsubscript{MAX} for adult men are −100 cmH\textsubscript{2}O (−98 hPa) and 170 cmH\textsubscript{2}O (167 hPa), respectively, meanwhile the corresponding values for adult women are approximately −70 cmH\textsubscript{2}O (−69 hPa) and 110 cmH\textsubscript{2}O (108 hPa), respectively.42,43 The lower limit of the normal range is about two-thirds of these values.6

Whenever there is an inexplicable reduction in vital capacity or there is clinical suspicion of respiratory muscle weakness, Monitoring PI\textsubscript{MAX} (SNIP) and PE\textsubscript{MAX} is useful, together with VC, for following the evolution of patients with neuromuscular disorders (Table 3). However, they are only able to verify the situation at the time of the measurement and their prognostic value is limited, as some of them evolve with flare-ups and the muscular function may unpredictably worsen at any time.

Single-Breath Carbon Monoxide Transference

The diffusing capacity of the lung for carbon monoxide in a single breath (DL\textsubscript{CO}), also known as carbon monoxide transference factor (Tl\textsubscript{CO}), is useful in the evaluation of both restrictive and obstructive disease.44 It requires a device that costs between 18,000 and 24,000€. The cost of a test is about 100€. DL\textsubscript{CO} should always be given as corrected for hemoglobin, which in the majority of devices appears as Dl\textsubscript{CO}, and, if possible, for carboxyhemoglobin.

A reduction in DL\textsubscript{CO}, with normal pulmonary vascular disorders,5 but it can also be seen in incipient DILD or emphysema.5A reduced DL\textsubscript{CO} in the presence of restriction suggests DILD,15,16 although sometimes restriction is seen in pulmonary vascular diseases.45

A reduced DL\textsubscript{CO} in the presence of obstruction suggests emphysema46 and also with other much rarer diseases such as histiocytosis X, lymphangioleiomyomatosis, and tuberous sclerosis with lung affection.47,48

In heart failure due to left ventricular failure, a low DL\textsubscript{CO} can be observed that is directly related with severity and is a powerful prognostic factor of the disease.15

A high DL\textsubscript{CO} can be seen in asthma,49 obesity,50 and in intrapulmonary hemorrhage.51

DL\textsubscript{CO} can also be used to categorize disease severity.6

The DL\textsubscript{CO}/VA, also known as K\textsubscript{co} diffusion constant, is theoretically able to differentiate between the processes that reduce alveolar volume (VA) that limit the normal expansion of the chest (that behave as a loss in V\textsubscript{L}A) or that, as in COPD, the effective VA is reduced in such a way that the gases used to measure DL\textsubscript{CO} are not completely diluted by the entire alveolar space (reduced in proportion with the VA) from other diseases that reduce the DL\textsubscript{CO} because they affect diffusely the exchange surface either due to thickening of the alveoli or due to the loss in capillarization. However, the comparison with the predicted value obtained in subjects with normal VA can lead to errors when the VA is low52 as the Tl\textsubscript{CO}/VA does not vary linearly with VA (Fig. 1).53 Therefore, there is a great debate about their clinical use.6,45,55 Our experience is that, knowing the clinical symptoms of the patient, DL\textsubscript{CO}/VA usually provides little information (Table 4).

Arterial Blood Gas Analysis

In stable ambulatory patients, baseline arterial blood gas analysis (without oxygen supplementation), or ABG, can be a useful complement for lung function tests in specific patients. It costs about 30€. It is used to confirm hypoventilation when it is
suspected based on the clinical history (e.g. neuromuscular disease or advanced COPD). ABG is also used to confirm chronic hypoxemia and to provide a more detailed evaluation of the severity. It is a painful test, so its use should not be routine and it is only indicated in patients who have low SatO₂ on pulse-oximetry.

Measurement of Exhaled Nitric Oxide

In recent years, there has been growing interest in the determination of the nitric oxide fraction in exhaled air (FE\textsubscript{NO}), which has become a routine test after standardized guidelines were published.\textsuperscript{56} The cost of the test is about 50€. It is a quantitative, simple, non-invasive, safe method for measuring the inflammation of the airways, and it is a tool that complements other LT. for the evaluation of bronchial diseases like asthma.

Even though its role is still not free from controversy due to the fact that the evidence on which the recommendations are based are not from clinical assays, measuring FE\textsubscript{NO} can be used for\textsuperscript{57}:

- Detecting eosinophilic inflammation of the respiratory tract (FE\textsubscript{NO} >35–50 ppb),\textsuperscript{19,57} which in the presence of compatible symptoms or airflow obstruction (FE\textsubscript{V1}/VC <70%) can establish a diagnosis of presumed asthma (or at least presumed response to treatment with inhaled corticosteroids similar to asthma) that obligatorily should be confirmed with the demonstration of acute reversibility or an “individual therapeutic assay” with inhaled or oral corticosteroids (see reversibility test) that improves the function or at least symptoms.\textsuperscript{19}
- Determining the probability of response to corticosteroids in patients with chronic respiratory symptoms. The recommendation is:
  - To use a cut-point of ≤25 ppb to consider a subject as unlikely to respond.
  - To use a cut-point of more than 50 ppb to consider a subject as likely to respond.
  - In the intermediate levels (>25 and ≤50 ppb), evaluate depending on the symptoms.
- Monitoring the inflammation of the respiratory tract in order to determine the dose of corticosteroids. It is recommended to first establish whether the patient is still exposed to the allergens suspicious of being the cause of the airway inflammation. Based on the opinion of experts, the recommendation is to consider significantly those increases (lack of response) or decreases (response) in FE\textsubscript{NO} that are greater than 20% for values of more than 50 ppb or greater than 10 ppb for values lower than 50 ppb from one visit to the next.
- Detecting the lack of compliance with corticosteroid treatment.

The 6-min Walk Test and Oxygen Desaturation During Exercise

The 6-min walk test (6MWT) is a good index for physical function,\textsuperscript{58–61} and it also has prognostic value in many chronic respiratory diseases.\textsuperscript{58,62–64} It costs about 50€. In general, healthy people can walk 400–700 m, depending on age, height, stature, and sex.\textsuperscript{59,61}

Desaturation during exercise, generally measured with a walk test, is an index with prognostic value in pulmonary vascular diseases, interstitial diseases, and COPD.\textsuperscript{65} A fall in SpO₂ greater than 4% (with a total under 93%) suggests important desaturation and it is used to evaluate the need for oxygen and its titration in patients with chronic pulmonary diseases.\textsuperscript{65–67}

Ergospirometry

There are multiple applications for cardiopulmonary exercise tests in pulmonology (Table 5). The equipment costs about 24 000€, plus 9000€ for the cycle-ergometer. The cost per test is 150€. It is beyond the purpose of this article to review in detail such tests, and interested readers are recommended to read more advanced papers.\textsuperscript{56–75} Maximal oxygen uptake has prognostic value in respiratory diseases.\textsuperscript{65,68,70–75}

### Indications

LFT are useful for evaluating all types of pulmonary disease and as a screening for the presence of disease in persons with risk factors, such as smoking. Other indications for lung function tests are:

- Evaluating symptoms such as persistent chronic cough, wheezing, dyspnea, and cough at resting conditions or with exercise.
- Objectively evaluating bronchodilator treatment.
- Evaluating the effects of exposure to agents that are noxious for the lungs (dust or chemical products).
- Assessing patient risk before thoracic surgery and the prevention of any type of surgery in patients in whom unknown treatable lung disease is suspected.
- Objectively evaluating dysfunction or disability.

### Chronic Dyspnea

Many lung diseases start slowly and insidiously and they finally become evident with non-specific symptoms, such as exertional dyspnea. LFT are an essential part of the diagnostic routine in these patients. Spirometry should be the first test and other tests should be ordered depending on its results. If the cause of exertional dyspnea remains unclarified after bronchodilation tests, Dl\textsubscript{CO}, and lung volumes, ergospirometry may be useful (Fig. 5).

### Chronic Cough

This is a very frequent symptom and can be the cause of up to 40% of outpatient consultations in pulmonology.\textsuperscript{76} When asthma or COPD is suspected due to the clinical history and chest radiograph, spirometry, and bronchodilator tests are necessary. Before ordering a hyperreactivity test, it must be verified that the patient has persistent cough (>8 weeks), that he/she is not taking

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**Table 4**

<table>
<thead>
<tr>
<th>Severity of the Alterations in Carbon Monoxide Diffusing Capacity</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>&gt;60% and &lt;LLN</td>
</tr>
<tr>
<td>Moderate</td>
<td>40%–60%</td>
</tr>
<tr>
<td>Severe</td>
<td>&lt;40%</td>
</tr>
</tbody>
</table>

\%: % predicted; LLN: lower limit of normal.

**Table 5**

| Indications for the Exertion Test in Pulmonology |
|---|---|
| Evaluation of the tolerance to exercise and its limiting factors |
| Observation of the limitation of capacity for exertion |
| Analysis of the factors that limit exercise capacity |
| Distinction between dyspnea of respiratory or cardiac origin |
| Study of unexplained dyspnea with tests at rest |
| Functional assessment and prognosis and detection of alterations that are caused by or noticeably worsen with exercise in chronic pulmonary diseases |
| Evaluation of disability in respiratory diseases |
| Exercise prescription in rehabilitation |
| Diagnosis of exercise-induced bronchospasm |
| Evaluation of the effects of therapeutic interventions |
| Pre-surgery evaluation in lung resection surgery |
Spirometry is essential in the follow-up of COPD patients in order to monitor the effectiveness of treatment (Table 2) and the progression of the disease.\textsuperscript{78,80} It does not seem to make sense to do more than one per year without any other reason than just for follow-up.\textsuperscript{78,80} We should expect reductions in FEV\textsubscript{1} between 30 and 40 ml/year. Higher reductions may be related with the emphysema phenotype, the persistence of smoking, poor control of exacerbations or insufficient treatment.\textsuperscript{23,81,82} These changes are below the test variability, so in order to interpret them quality spirometry should be available and done under the same conditions (same laboratory, same pharmacological setting, stable patient) and at several points (2 or 3 years), unless the decrease (or improvement) surpasses the test variability (Table 2). In patients with FEV\textsubscript{1} <1l, spirometry may not be particularly sensitive to change due to the variability of the test (12% or 190 ml). In these patients, other determinations such as measuring symptoms, quality of life, desaturation with exercise or tolerance of exertion can be more sensitive to the interventions and to the progressions of the disease than FEV\textsubscript{1} itself.\textsuperscript{65,83}

Neuromuscular Diseases

Since the advent of non-invasive mechanical ventilation, more and more patients with severe respiratory failure are maintained with this therapy, and the demand for tests to measure muscle strength has increased. From a clinical practice standpoint, VC is a useful screening test and its reduction of more than 25% in decubitus (normal, <5%) when comparing with the patient in an erect position is indicative of neuromuscular disease. The ability to cough effectively is usually lost when the VC is less than 30 ml/kg, and a VC <30% is considered to predict imminent respiratory failure in chronic neuromuscular diseases, but it should be accompanied by other measurements, like PaCO\textsubscript{2} and, sometimes, nocturnal capnography. Respiratory pressures are more sensitive than VC and they would be indicated in the diagnosis and follow-up as a complement, especially in those cases in which the reduction of the vital capacity in decubitus is not clear.

Diffuse Interstitial Lung Disease

Lung function tests should be considered within the context of the radiology results. Spirometry is useful to detect restriction (VC), but it seldom helps to establish the cause.\textsuperscript{84} DL\textsubscript{CO} is useful to screen for interstitial lung affection when interventions are scheduled (bone marrow transplant, chemotherapy) and in order to differentiate between intrinsic lung diseases and other causes of restriction, and it also has prognostic value.\textsuperscript{15,16,84} Desaturation during exercise also has prognostic value in these patients,\textsuperscript{65,84} and the 6MWT can be used to titrate ambulatory oxygen when needed.\textsuperscript{65,66} All these tests play a role in patient follow-up every 6–12 months, or when a change is presumed in the evolution of the disease.
Pulmonary Vascular Disease

Spirometry is indicated in the initial evaluation of pulmonary vascular diseases for their differential diagnosis with other processes. Sometime, there is an observed reduction in VC. DCO can play a screening role in the detection of pulmonary hypertension, for example in rheumatic diseases, and in evaluating its pronosis, although other devices including echocardiography and exertion tests are more often used. Even though the 6MWT is more popular, ergospirometry can have advantages as it gives more physiological information and it is done in a safer setting, which is the lab. The exertion tests are useful in following up these patients and for monitoring treatment effectiveness.

Pre-Surgery Evaluation

Lung function tests are only indicated when there is a suspicion of unknown or exacerbated respiratory disease that may be susceptible to improving with treatment and therefore reducing risk, because necessary surgery should never be contraindicated based on lung function. Exceptions to this rule are surgery of the abdominal aorta and lung resection surgery. In the latter, the combination of spirometry, DCO, and ergospirometry can better stratify the risk.

Evaluation of Disability

Spanish legislation (Real Decreto 1971/1999, of 23 December, regarding the procedure for recognizing, declaring, and determining the degree of disability) establishes that the evaluation of disability should be done based on spirometric criteria, DCO or maximal oxygen consumption.

Conflict of Interests

The authors declare having no conflict of interests.

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