GOLD UPDATE on COPD and the Importance of Accurate Dyspnea Evaluation

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COPD is...

- Preventable and treatable

- Associated with significant concomitant chronic diseases which increase its morbidity and mortality

- Characterized by persistent respiratory symptoms and airflow limitation that is:
  - due to airway and/or alveolar abnormalities
  - usually caused by significant exposure to noxious particles or gases
COPD Is a Nationwide Problem

In the United States, adults ≥18 years of age with COPD...
COPD Is a Nationwide Problem

In the United States, adults ≥18 years of age with COPD...

- are more likely to report being unable to work (24%) than adults who do not have COPD (5%)
- require the use of special equipment (22%) for health problems compared with 7% of adults without COPD
- face activity limitations as a result of health problems (50%) compared with 17% of persons who do not have COPD


COPD Arises From Damage and Inflammation in the Respiratory Tract

Respiratory Anatomy

- Trachea
- Bronchi
- Bronchioles
- Alveoli

Chronic Bronchitis and Airway Inflammation

- In healthy lungs, the airways are elastic and flexible
- With chronic bronchitis, airways can become swollen or thicker than normal
- Chronic bronchitis may cause increased mucus production
- Airways may become partially obstructed, making it harder to get air out of the lung. The resulting hyperinflation also makes inspiration difficult
Emphysema is caused by damage to the alveoli walls.

- Healthy alveoli are elastic and capable of springing back to their original size after active inspiration.
- Emphysema involves damage to the walls of the alveoli.
- In emphysema, alveoli lose their elasticity, which impairs natural passive exhalation, resulting in trapping of air and hyperinflation.

FEV₁ Progression over Time

FEV₁ in percent of predicted maximally attained value

- **TR1**: Normal
- **TR2**: Small lungs but no COPD
- **TR3**: Normal initial FEV₁ with rapid decline leading to COPD
- **TR4**: Small lungs leading to COPD

- **TR1**: 71.5%
- **TR2**: 16.9%
- **TR3**: 5.5%
- **TR4**: 6.1%

No COPD

COPD

Age range under observation

FEV₁=forced expiratory volume in 1 second.

Global Strategy for the Diagnosis, Management, and Prevention of COPD

Key Indicators for a Diagnosis of COPD

**Symptoms and Past Medical History**

- **Dyspnea** – progressive, worse with exercise, persistent
- **Chronic cough** – may be intermittent and unproductive, recurrent wheeze
- **Chronic sputum production** – any pattern of chronic sputum production may indicate COPD
- Recurrent lower respiratory tract infections

**History of Risk Factors**

- Host factors (genetic, congenital/developmental)
- Tobacco smoke
- Smoke from home cooking/heating fuels
- Occupational dusts, vapors, fumes gases or chemicals

**Family History of COPD and/or Childhood Factors**

AND

**Airflow Limitation**

Post-bronchodilator FEV₁/FVC <0.70*

GOLD recommends active casefinding:

i.e. Performing spirometry in patients with symptoms and/or risk factors, but not screening spirometry

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*Required for the diagnosis of COPD.

FEV₁=forced expiratory volume in 1 second; FVC=forced vital capacity.

Use Spirometry to Confirm COPD Diagnosis\(^1\)

Post-bronchodilator FEV\(_1\)/FVC <0.70 indicates COPD diagnosis

**Spirometry – Normal Trace**
- FEV\(_1\) = 4 L
- FVC = 5 L
- FEV\(_1\)/FVC = 0.8

**Spirometry – Obstructive Disease**
- FEV\(_1\) = 1.8 L
- FVC = 3.2 L
- FEV\(_1\)/FVC = 0.56

**FEV\(_1\):** Amount of air exhaled in the first second during the FVC maneuver\(^2\)

**FVC:** Total amount of air a person can forcibly exhale after maximum inhalation\(^2\)

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COPD Exacerbations: Risk Factors and Impact

Risk factors:
- Frequent past exacerbations
- Severity of FEV₁ impairment
- Chronic bronchial mucus hypersecretion
- Daily cough and wheeze
- Increased age
- Persistent symptoms of chronic bronchitis
- Comorbid conditions, mainly cardiovascular disease

Impact:
- More rapid decline of FEV₁
- Increased dyspnea
- Greater decline in health status
- Increased mortality

The Refined ABCD Assessment tool (steps 1 and 2)

### Spirometrically Confirmed Diagnosis
- Post-bronchodilator $FEV_1/FVC < 0.7$

### Assessment of Airflow Limitation

<table>
<thead>
<tr>
<th>GOLD</th>
<th>FEV₁ % predicted</th>
</tr>
</thead>
<tbody>
<tr>
<td>GOLD 1</td>
<td>≥ 80%</td>
</tr>
<tr>
<td>GOLD 2</td>
<td>50% - 79%</td>
</tr>
<tr>
<td>GOLD 3</td>
<td>30% - 49%</td>
</tr>
<tr>
<td>GOLD 4</td>
<td>&lt; 30%</td>
</tr>
</tbody>
</table>

Global Strategy for the Diagnosis, Management, and Prevention of COPD

The Refined ABCD Assessment tool (step 3)

Exacerbation history | Assessment of symptoms/risk of exacerbations

≥ 2 or ≥ 1 leading to hospital admission

0 or 1 (not leading to hospital admission)

C | D

mMRC 0-1
CAT < 10

Symptoms

mMRC ≥ 2
CAT ≥ 10

Goals of COPD Management

Reduce Symptoms
- Relieve symptoms
- Improve exercise tolerance
- Improve health status

Reduce Risk
- Prevent disease progression
- Prevent and treat exacerbations
- Reduce mortality

AND
Nonpharmacologic Management of COPD

<table>
<thead>
<tr>
<th>Patient Group</th>
<th>Essential</th>
<th>Recommended</th>
<th>Depending on Local Guidelines</th>
</tr>
</thead>
<tbody>
<tr>
<td>A (B-D)</td>
<td>Smoking cessation (can include pharmacologic treatment)</td>
<td>Physical activity</td>
<td>Flu vaccination</td>
</tr>
<tr>
<td></td>
<td>Smoking cessation (can include pharmacologic treatment)</td>
<td>Physical activity</td>
<td>Pneumococcal vaccination</td>
</tr>
<tr>
<td></td>
<td>Pulmonary rehabilitation</td>
<td></td>
<td>Flu vaccination</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Pneumococcal vaccination</td>
</tr>
</tbody>
</table>

Fletcher-Peto Curve: Impact of Smoking on Airflow

Figure adapted from Fletcher, C, Peto, R. *Br Med J.* 1977;1(6077):1645-1648.
Pharmacologic Treatment Algorithms

Group C

Group D

Consider PDE-4 inhibitor if FEV₁ < 50% pred. and patient has chronic bronchitis

Consider macrolide (if former smokers)

Further exacerbation(s)

Further exacerbation(s)

Persistent symptoms / Further exacerbation(s)

LAMA + LABA

LAMA + LABA + ICS

LAMA + LABA + ICS

Preferred treatment

Group A

Group B

Continue, stop or try alternative class of bronchodilator

Evaluate effect

A bronchodilator

LAMA + LABA

Persistent symptoms

long-acting bronchodilator (LABA or LAMA)

SABA = short-acting β₂-agonist; SAMA = short-acting muscarinic antagonist; LABA = long-acting β₂-agonist; LAMA = long-acting muscarinic antagonist; ICS = inhaled corticosteroid; PDE-4 = phosphodiesterase-4.

Learning Objectives

Upon completion of this training, learners should be able to:

- Identify physical inactivity as an important problem in COPD and recognize its association with worsened disease
- Explain dyspnea as the driver of COPD inactivity
- Understand the importance of a full evaluation of COPD which includes a complete evaluation of dyspnea and its impact on activity levels
“My goals are probably similar to the goals of many patients as they age, but having COPD and its associated limitations, increases the importance of these goals. First, I want to remain independent. I have three grown daughters, one living close by, but I really prefer to manage my life without troubling my children. They have their own lives and their own needs.”

“Second, I’d like to remain mobile for as long as possible. Mobility, to me as a COPD patient, means being able to get around my home and do household chores, such as bed-making and laundry. Outside the home, I want to continue to drive myself around, shop for groceries, make doctor visits, and do errands unassisted. Finally, I want to stay well and out of hospitals, except as a volunteer!”
Are the Needs of COPD Patients Being Fully Met?

Studies report 30-70% of patients with COPD receive no treatment.¹

Treatments when given are often sub-optimal.¹

The **GOLD guidelines** recommend full symptom evaluation to select treatment in addition to evaluating comorbidities. However, this can be difficult for several reasons:²

- Patients can experience worsening dyspnea even in the setting of stable lung function.³

- Conventional tests used to identify activity limitation may not be able to assess impact of environmental and psychological changes on activity.⁴

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Correlation Between Exercise Tolerance and COPD Outcomes

Mortality progressively decreases as the 6-min walking distance (6MWD) increases.

For distances <100 m, n=19; for 101-200 m, n=61; for 201-300 m, n=57; for 301-400 m, n=46; and for >400 m, n=15.

Daily Activity and Outcomes

In patients with moderate to very severe COPD, daily physical activity was measured providing a mean of 1-min movement epochs as vector magnitude units (VMUs).

- After adjusting for relevant confounders, increases in physical activity showed decreases in mortality risk.
- In a multi-variate model, 3 independent predictors of mortality were comorbidity, endurance time, and daily physical activity.
- The time until first hospital admission due to COPD exacerbation was shorter for the patients with lower levels of physical activity.
Physical Activity is Critically Important to Assess

According to the Copenhagen City Heart Study, regular physical activity in COPD patients was associated with reduced chance of hospital admissions and all-cause death.

As an important determinant of COPD outcomes, limitations to physical activity should be evaluated and managed.
Dyspnea is a Key Reason for Physical Activity Reduction in COPD

Mean daily time spent walking by GOLD stage in COPD compared with healthy subjects

- Activity limitation is a key manifestation of COPD and is in large part caused by dyspnea.
- COPD patients with moderate to mild lung function impairment can also experience a reduction in daily physical activity.
- Fatigue and leg discomfort can be factors in activity limitation.
- The ultimate goal of targeting dyspnea is to improve health status and survival by increasing physical activity.

GOLD=Global Initiative for Chronic Obstructive Lung Disease

What is “Control” in COPD?

After establishing the severity of COPD, the following points should be assessed during patient follow-up:

- Regular visits of COPD patients to the healthcare provider
- Smoking cessation
- Dietary recommendations aimed at achieving and maintaining an optimal bodyweight
- Regular physical activity
- Assessment of symptoms, including their degree of severity
- History of exacerbations
- Assessment of comorbidities that can interfere with COPD control
- Appropriate vaccination
- Periodical review of therapeutic regimens, patient compliance, and evaluation of side effects
- Measurement of patient’s QoL

Anticipatory Dyspnea

Patients may self-manage their disease by limiting their activities because of dyspnea or even to prevent becoming short of breath.¹

Activity limitation may occur even in mild disease.²

The limitation in activity induced by dyspnea can be distressing and may lead to anxiety and depression, which are frequently observed in COPD.³

Investigators studied fMRI imaging to identify brain activity in 41 patients with COPD vs 40 control subjects after exposure to dyspnea-related word cues.

- Participants viewed each word and rated it according to how breathless and how anxious it would make them feel on a visual analog scale (VAS) of 0 (not at all) to 10 (very much).

- In comparison to control subjects, patients with COPD showed stronger activation in the left-side mPFC and the ACC.

- Activity in these areas has previously been linked to pain and dyspnea.

- Depression, fatigue and vigilance may also be associated with activity observed in these areas.

Standardized Assessments Used to Assess Symptoms

Care can be improved with the use of scoring tools that are reliable, standardized, and sensitive to clinical changes. These tools should provide meaningful information and be acceptable for both patient and HCP use.¹

<table>
<thead>
<tr>
<th>Tool</th>
<th>Description</th>
<th>Pro</th>
<th>Con</th>
</tr>
</thead>
<tbody>
<tr>
<td>SGRQ</td>
<td>50 item questionnaire assess QoL over multiple domains²</td>
<td>FDA acceptable endpoint, responsive to therapy²</td>
<td>Time-consuming²</td>
</tr>
<tr>
<td>CAT</td>
<td>8 item questionnaire with comprehensive symptom assessment³</td>
<td>Validated, relatively brief¹</td>
<td>No definite MCID¹</td>
</tr>
<tr>
<td>MMRC</td>
<td>5-item scale to assess the severity of breathlessness³</td>
<td>Relates well to other measures of health status, predicts future mortality risk³</td>
<td>Not sensitive to change with treatment and only measures dyspnea¹</td>
</tr>
<tr>
<td>CCQ</td>
<td>Questionnaire with 10 items within 3 domains (symptoms, functional state, mental state)¹</td>
<td>Validated, correlates with SGRQ and SF-36, has MCID (&gt;0.4) and relatively short¹,²</td>
<td>Has not been widely used in pharmaceutical trials²</td>
</tr>
</tbody>
</table>

Clinical COPD Questionnaire

Patients are asked to answer the following questions. The time frame can be over 7 days.

How often did you feel…?
- SOB at rest
- SOB while doing physical activities
- Concerned about getting a cold or your breathing getting worse
- Depressed because of your breathing problems
- Did you cough
- Did you produce phlegm

Patients are asked to rate how limited they were during the following activities due to breathing problems.
- Strenuous activities (hurrying, climbing stairs, sports)
- Moderate activities (walking, housework, carrying things)
- Daily activities (dressing, washing themselves)
- Social activities (talking, being with children, visiting friends and family)
Potential Ways to Assess Activity

- Questionnaires

- Diaries

- Portable devices that monitor motion

- Patient/physician discussion
  - Questions such as “Have you given up any activities as a result of shortness of breath or fatigue?” can be useful.

Interventions that can affect dyspnea, and/or exercise capacity include:¹
- Pharmacotherapy
- Pulmonary rehab
- Informal counseling
- Oxygen
- Surgical therapy for COPD
- Other interventions used in various combinations tailored to the patient

Summary

Decreased activity is associated with poor COPD outcomes. Regular physical activity reduces hospital admissions and all-cause death.

The GOLD guidelines recommend full symptom evaluation to select treatment in addition to evaluating comorbidities. It is important to quantify the impact on the severity of breathlessness using a validated assessment.

Activity limitation is a key manifestation of COPD and is mainly caused by dyspnea. The ultimate goal of targeting dyspnea is to improve health status and survival by increasing physical activity.
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The Modified Medical Research Council (MMRC) Dyspnoea Scale

<table>
<thead>
<tr>
<th>Grade of dyspnoea</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Not troubled by breathlessness except on strenuous exercise</td>
</tr>
<tr>
<td>1</td>
<td>Shortness of breath when hurrying on the level or walking up a slight hill</td>
</tr>
<tr>
<td>2</td>
<td>Walks slower than people of the same age on the level because of breathlessness or has to stop for breath when walking at own pace on the level</td>
</tr>
<tr>
<td>3</td>
<td>Stops for breath after walking about 100 m or after a few minutes on the level</td>
</tr>
<tr>
<td>4</td>
<td>Too breathless to leave the house or breathless when dressing or undressing</td>
</tr>
</tbody>
</table>
CAT

COPD Assessment Test

Example: I am very happy 0 2 3 4 5 I am sad

I never cough 0 1 2 3 4 5 I cough all the time
I have no phlegm (mucus) in my chest at all 0 1 2 3 4 5 My chest is full of phlegm (mucus)
My chest does not feel tight at all 0 1 2 3 4 5 My chest feels very tight
When I walk up a hill or one flight of stairs I am not breathless 0 1 2 3 4 5 When I walk up a hill or one flight of stairs I am very breathless
I am not limited doing any activities at home 0 1 2 3 4 5 I am very limited doing activities at home
I am confident leaving my home despite my lung condition 0 1 2 3 4 5 I am not at all confident leaving my home because of my lung condition
I sleep soundly 0 1 2 3 4 5 I don't sleep soundly because of my lung condition
I have lots of energy 0 1 2 3 4 5 I have no energy at all

CLICK TO GET YOUR TOTAL SCORE!

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### CLINICAL COPD QUESTIONNAIRE

Please circle the number of the response that best describes how you have been feeling during the past week.
(Only one response for each question.)

<table>
<thead>
<tr>
<th>Question</th>
<th>never</th>
<th>hardly ever</th>
<th>a few times</th>
<th>several times</th>
<th>many times</th>
<th>a great many times</th>
<th>almost all the time</th>
</tr>
</thead>
<tbody>
<tr>
<td>On average, during the past week, how often did you feel:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Short of breath at rest?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>2. Short of breath doing physical activities?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>3. Concerned about getting a cold or your breathing getting worse?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>4. Depressed (down) because of your breathing problems?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>In general, during the past week, how much of the time:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. Did you cough?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>6. Did you produce phlegm?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>On average, during the past week, how limited were you in these activities because of your breathing problems:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7. Strenuous physical activities (such as climbing stairs, hurrying, doing sports)?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>8. Moderate physical activities (such as walking, housework, carrying things)?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>9. Daily activities at home (such as dressing, washing yourself)?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>10. Social activities (such as talking, being with children, visiting friends/relatives)?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
</tbody>
</table>
Back up

- MMRC
  https://www.verywell.com/guidelines-for-the-mmrc-dyspnea-scale-914740

- CAT
  http://www.catestonline.org/english/indexEN.htm

- Clinical COPD Questionnaire
  https://www.biomedcentral.com/content supp/1465-9921-7-62-S1.PDF