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May 06 2012

Chronic obstructive pulmonary disease 2012 update (COPD Review, Lancet)

Clinic and Consults, COPD, Review Articles Add comments

Chronic Obstructive Pulmonary Disease (COPD) 2012 Update

From the excellent **Seminar** in *Lancet* April 2012, the **2004 ATS statement**, and our reviews of **recent articles on COPD**.

Epidemiology of COPD

- Globally, ~10% of people older than 40 have airflow limitation of GOLD stage 2 or worse (FEV1 < 80% predicted); up to 25% may have GOLD stage 1 (FEV1 ≥ 80% predicted but FEV1/FVC < 0.7).
- Up to 60-85% of people with COPD (mostly mild/moderate severity) are undiagnosed.
- Besides tobacco smoking, biomass exposure (wood burning stoves), secondhand smoke, air pollution and work exposures to fumes and dusts cause COPD in susceptible people.
- COPD is the 4th leading cause of death worldwide; its mortality is rising, while cardiovascular disease's is falling; COPD is expected to be the 3rd leading cause of death in the next 20 years.

Pathophysiology of COPD

COPD is characterized both by destruction of lung parenchyma with loss of elastic recoil (causing emphysema) and infiltration of the walls of the small airways by inflammatory cells (causing chronic bronchiolitis / bronchitis). Although students are still taught these two broad phenotypes are distinct entities, in truth they coexist and overlap in varying degrees in virtually everyone with COPD. The reasons for these variable phenotypes and their clinical importance are poorly understood.

Alpha-1 antitrypsin deficiency is present in 1-2% of people with COPD, and is likely underrecognized. Genome-wide association studies have identified various gene polymorphisms associated with increased (and a few with decreased risk) for developing COPD.

COPD continues to be frequently described as chronic and progressive, and this is so in many patients. However, COPD is a highly heterogeneous disease, and this applies to its progression between individuals. Among people with COPD who stop smoking, some will continue to experience accelerated decline in lung function compared to healthy non-smokers; however, **recent evidence suggests** the majority will experience FEV1 declines no more rapid (and in some cases, less rapid) than the average nonsmoker. [1, 2, 3]

COPD Exacerbations

Many (not all) patients with COPD experience days-long episodes of increased dyspnea, cough, and sputum production, called COPD exacerbations. Most COPD exacerbations occur at home, resulting in increased use of bronchodilators, impaired function and enjoyment of life; more severe COPD exacerbations require systemic steroids, antibiotics, and sometimes hospitalization.

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- Early goal directed therapy does not improve outcomes in septic shock (ProCESS)
- Community Acquired Pneumonia (Review)
- Bleeding and Coagulation Disorders in the ICU (Review)
- No benefit from higher mean arterial pressure in most with septic shock
- ACCP Guidelines for Diagnosis and Management of DVT/PE/VTE, 9th edition (Review)
- Catheter directed thrombolysis for submassive PE: better than heparin? (RCT)
- Weaning from Mechanical Ventilation Update (Review)
- Beta blockers safe for most patients with asthma or COPD?
- Mechanical Ventilation in ARDS: 2014 Update
- Enoxaparin prophylaxis: no effect on mortality or fatal pulmonary embolism (RCT)

ACCP 9th Edition Guidelines for DVT, PE, Anticoagulation (February 2012)

Surviving Sepsis Guidelines 2013 Update

Most Viewed All Time

People with moderate COPD have one exacerbation per year on average; those with severe COPD have 2 on average. However, these averages mask wide heterogeneity: many patients with COPD have exacerbations never or very infrequently; a few experience them almost every month.

Recent research using invasive sampling of sputum from patients with COPD exacerbations strongly suggests that infections cause the majority (~80%) of COPD exacerbations, especially severe exacerbations. Common-cold bacteria and viruses including *H. influenzae*, *S. pneumoniae*, *M. catarrhalis*, rhinovirus, coronavirus, and parainfluenza cause the majority of infectious exacerbations (or about 50-60% of all COPD exacerbations), with less common organisms like Pseudomonas aeruginosa, S. aureus, and atypical bacteria (*Mycoplasma*, *Chlamydia pneumonia*) causing a minority of COPD exacerbations.

Congestive heart failure, systemic infections, pulmonary embolism, pneumonia, air pollution, cold air, allergies, and smoking are thought to cause 20-40% of COPD exacerbations.

Treatments for COPD

The **GOLD guideline treatment table** is the most well-known and accepted guideline for the treatment of COPD. It can be summarized as follows:

Stage:*	1 (mild)	2 (moderate)	3 (severe)	4 (very severe)
FEV1/FVC	<0.70	<0.70	<0.70	<0.70
FEV1	>= 80% pred.	50-80% pred.	30-50% pred.	<30% pred., or <50% pred. w/chronic respiratory failure
Treatment	Short-acting bronchodilator as needed for all patients with COPD.			
		Consider pulmonary rehabilitation.	Consider pulmonary rehabilitation.	Consider pulmonary rehabilitation.
		One or more long-acting bronchodilators.	One or more long-acting bronchodilators.	One or more long-acting bronchodilators.
			Inhaled corticosteroid, if repeated exacerbations.	Inhaled corticosteroid, if repeated exacerbations.
				Long-term oxygen if needed; consider lung volume reduction surgery

** All patients should receive smoking cessation counseling and influenza vaccination.*

Long-acting Bronchodilators, Inhaled Corticosteroids, and Tiotropium

Long-acting bronchodilators (formoterol, salmeterol) and long-acting anticholinergics (tiotropium) have similar efficacy:

- Improvements in post-bronchodilator FEV1 (~50-100 mL)
- Improvements in dyspnea (~3 points on the St. George's questionnaire)
- Reduction in daily short-acting beta-agonist use by ~1 inhalation.
- Tiotropium prevented COPD exacerbations better than salmeterol in **one randomized trial**, but the effect was quite small.

Long-acting beta agonists have cardiac effects, but have not been found to cause cardiovascular events, and don't have the very slightly increased risk of death associated with LABA monotherapy for asthma.

Tiotropium has been suspected of causing cardiovascular events based on observational trials, but the current consensus (based mainly on UPLIFT randomized trial data and a

ACCP Guidelines for Diagnosis and Management of DVT/PE/VTE, 9th edition (Review)
Surviving Sepsis Guidelines Updated: Preview from SCCM Meeting
How to manage anticoagulation perioperatively (Guideline)
Mechanical Ventilation in ARDS: 2014 Update
How to start & manage warfarin/coumadin for acute DVT/PE (Guideline)
Initial Treatment of Acute Deep Venous Thrombosis (DVT) of the Leg (Guidelines)
Meet the New ARDS: Expert panel announces new definition, severity classes
Treating acute pulmonary embolism with anticoagulant therapy (Guideline)
Surviving Sepsis Guidelines 2013 – Review & Update
Chronic obstructive pulmonary disease 2012 update (COPD Review, Lancet)

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meta-analysis) is that Spiriva does not cause cardiovascular events.

Inhaled corticosteroid/LABA combination products cause pneumonia in a tiny proportion of patients; however, combination products may also reduce mortality slightly (based on the just-barely-negative TORCH trial). ICS/LABA combination products do not seem to cause an increased risk of death from pneumonia. Inhaled corticosteroids probably cause osteoporosis in a small number of susceptible patients.

The evidence is inconclusive as to whether any drug treatments for COPD modify (slow) the disease course or reduce mortality, but data from several clinical trials suggests that both inhaled corticosteroid/LABA combination products and tiotropium may reduce decline in FEV1 and slightly reduce mortality risk.

An **observational study** also suggested a benefit of "triple therapy" with inhaled corticosteroid, long-acting beta-agonist, and tiotropium.

Roflumilast and Cilomilast

The role of these new phosphodiesterase inhibitors is unclear. They have not been included in GOLD or other society treatment guidelines. Roflumilast only improved postbronchodilator FEV1 by ~50 mL and reduced exacerbation frequency by a relative 17%, among selected patients with GOLD stage 3-4 COPD who had cough with sputum changes and a history of exacerbations. The Cochrane Collaboration published an **analysis** on these new agents in 2011. Postmarketing data will be essential to determine the new agents' real-world efficacy and risk of adverse events.

Azithromycin

A **randomized trial** of 1,577 patients treated with azithromycin or placebo for a year showed a 27% reduction in exacerbations in the azithromycin group, but may also have caused hearing loss. Erythromycin had a similar effect in another trial, but has poor gastrointestinal tolerability.

Lung Volume Reduction Surgery

Consideration for lung volume reduction surgery is recommended for all patients with very severe COPD. The surgery provides a **mortality reduction** and improvement in quality of life, especially in patients with upper-lobe predominant disease and poor exercise capacity. For unclear reasons, however, lung volume reduction surgery has never caught on: only 105 Medicare beneficiaries underwent LVRS in 2006.

Non-Surgical, Bronchoscopic Lung Volume Reduction

Because of the morbidity and risk associated with lung volume reduction surgery, and its subsequent unpopularity, numerous companies and investigators have sought to produce a medical device that could be placed bronchoscopically and that would reduce dead space ventilation — lung volume reduction surgery without the surgery, if you will. To date, none of these devices have worked effectively enough to recommend their use outside clinical trials. The most recent example was the **EASE trial**, published in *Lancet* 2011, showing that bronchoscopically-placed airway stents with one-way valves (the **Exhale device**) did not improve airway mechanics or dyspnea.

Why haven't these bronchoscopically placed devices worked? The most likely answer is collateral ventilation, or interalveolar air drift through the pores of Kohn. These are miniscule anatomic intercommunications that allow air to fill back into emphysematous areas after air is removed through the implanted device.

Treatment of COPD Exacerbations

Guidelines are available for treatment of COPD exacerbations; they mainly recommend:

- Increasing the dose of short acting bronchodilators (albuterol and/or ipratropium).
- Adding oral corticosteroids if bronchodilators are not successful.
- Oxygen and ventilatory support for respiratory failure. A **recent review** showed that non-invasive positive pressure ventilation is likely improving outcomes from COPD exacerbations.
- Consider theophylline for severe exacerbations.

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Palliative Care (6)

Archives

Select Month

Chronic obstructive pulmonary disease. Seminar. Decramer M et al. Lancet 2012;379:1341-1351.

Qaseem A et al. Diagnosis and Management of Stable Chronic Obstructive Pulmonary Disease: A Clinical Practice Guideline Update from the American College of Physicians, American College of Chest Physicians, American Thoracic Society, and European Respiratory Society. Ann Intern Med 2011;155:179-191. [*PulmCCM.org summary*]

Celli BR et al. Standards for the diagnosis and treatment of patients with COPD: a summary of the ATS/ERS position paper. Eur Respir J 2004;23:932-946.

Stoller JK. Acute Exacerbations of Chronic Obstructive Pulmonary Disease. N Engl J Med 2002;346:988-984.

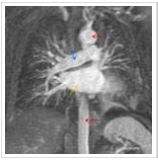
You may also like -

Vitamin D supplements don't prevent COPD exacerbations in RCT (Ann Intern Med)

Antibiotics (azithromycin) to prevent COPD exacerbations (Review, NEJM)

How to prevent COPD exacerbations (Chest)

Indacaterol vs Tiotropium: Tie on FEV1; Spiriva wins on exacerbations



In COPD, larger pulmonary artery assoc. with severe exacerbations (NEJM)

Posted by Pulmonary Central

13 Responses to "Chronic obstructive pulmonary disease 2012 update (COPD Review, Lancet)"

1. **Pr** says:
May 7, 2012 at 6:25 am

I think u made a mistake on the lung volume reduction candidates. It is patients with heterogenous disease and good exercise tolerance

Reply

Pulmonary Central says:
May 7, 2012 at 8:22 am

Hey Pr, thanks for writing.

I think we're both right. Heterogeneous disease means upper-lobe or lower-lobe predominant disease. Those with upper-lobe predominant disease and low exercise capacity (pre-op) were most likely to benefit from LVRS in subgroup analyses of the NETT trial. Those with upper lobe predominant disease and a high exercise tolerance also benefited, but not as much.

http://pulmccm.org/main/review-articles/what-we-know-about-lung-volume-reduction-surgery-thanks-to-nett-review-ajrccm/

Matt

Reply

2. **Ibrahim al Sanouri** says:
May 7, 2012 at 3:42 pm

In the regard of Mortality there is another study called UPLIFT that also cofirmed TOURCH results with triple therapy causing sustained improvement in FEV1

Reply

Pulmonary Central says:
May 7, 2012 at 4:23 pm

Ibrahim –

UPLIFT was a test of tiotropium vs placebo and wasn't designed to test "triple therapy" (tiotropium, inhaled corticosteroid, and long-acting beta agonist). However, you're right that in effect, it did test triple therapy, since patients in either arm were also treated with 'standard therapy' according to their physicians, and these treatments often included LABAs and inhaled steroids.

I haven't looked at the granular data to see if UPLIFT showed a benefit of triple therapy or not, but I wouldn't be surprised if it did. I don't think TORCH could be construed as testing triple therapy though.

-Matt

http://www.nejm.org/doi/full/10.1056/NEJMoa0805800
http://www.nejm.org/doi/full/10.1056/NEJMoa063070

Reply

3. **Mabruk BASHIR** says:
May 14, 2012 at 3:26 pm

I thought that, the review will highlight on the non-surgical options of lung volume reduction directed to COPD patients.

Kind Regards

Reply

Matt Hoffman says:
May 14, 2012 at 3:46 pm

Mabruk: Thanks for your comment. You are right, this is an important area that was missing from the review. I added a section above on bronchoscopic lung volume reduction. None of these therapies have proven successful outside of pilot studies, to my knowledge (someone please correct me if I am wrong). I appreciate your bringing this up.

Reply

4. **baikuntha panda** says:
May 16, 2012 at 11:26 am

a good review with distilled message

Reply

5. **Carol Blawas** says:
September 12, 2012 at 5:41 pm

Excellent information…Can anyone give me info on DLCO results and their meaning ?

Thank you

Reply

6. **Bettye Virginia Labhart** says:
October 8, 2012 at 7:57 am

Thank you so much for the info that you post. It does helps a great deal in coping with COPD.

Reply

7. **Guediri Samir** says:
October 22, 2012 at 5:23 pm

Please gents,
I have question for another subject
Concerning the diffirents scale to evaluate dyspnea, as we know that there are many scales for exampl (MMRC, MRC, Sadoul, NYHA, Borg ……) and there are many pathologies (PID, COPD, Cancer,…..)

What is the indication of each scale or for each pathology which scale we can used
Thanks

Reply

Pulmonary Central says:
October 29, 2012 at 1:46 pm

Hi Guediri, most or all of these scales seem to have been created for research settings in order to detect difference between two tested interventions (and/or placebo). Dyspnea in outpatients is a tricky thing to measure and I have not seen the scales used in regular clinical practice in the U.S., other than the simple NYHA or WHO scales. Thank you for writing. -Matt

Reply

8. **Raju Pangeni** says:
August 18, 2013 at 2:21 am

Researches have consistently shown the role of inflammatory mediators in COPD, often associated with extrapulmonary effects as well.. So, why are steroids and other anti-inflammatory agents not found to be helpful? or are we missing something?

Reply

9. **mm salim** says:
February 24, 2014 at 9:54 am

great reading

Reply

Leave a Comment

Cost shifting of asthma meds to patients had little effect on adherence, outcomes (JAMA)

How to bill for palliative care in the ICU … legally (Chest)