COPD

Common Myths and Misperceptions

(I had some of these)

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• A 70 yr old man comes to see you for exertional dyspnea. He has a 60 pack yr smoking history.

Which of the following statements is correct?

A) Nearly all patients who smoke develop COPD - based on this history he should be started on inhaled bronchodilators
B) Only ~15% of smokers develop COPD
C) Although COPD is more likely given his smoking history – spirometry should be obtained to confirm the diagnosis
D) A chest x-ray would be a sensitive test to help make the diagnosis of COPD
Development of COPD Over 25 years – Copenhagen City Heart Study

Løkke A et al. Thorax 2006;61:935-939

Genetics Influence the Risk of Developing COPD

Matrix Metalloproteinase 12
- Produced by alveolar macrophages and degrades connective tissue
- Essential for developing emphysema in mice exposed to cigarette smoke
- Increased expression in human smokers
- rs2276109 - single nucleotide polymorphism within the MMP12 gene
  - G (minor) allele - associated with reduced expression of MMP12 compared to the A (major) allele
  - G allele associated with a 35% risk reduction of developing COPD

NEJM 2009;361:2599-608
Chest Radiography in the Diagnosis of COPD

FEV1 3.62L (101%)  FVC 5.18L (102%)  DLCO 26.9 (110%)
“The diagnosis requires spirometry”
ATS/ERS Standards for the diagnosis and treatment of patients with COPD – Eur Respir J 2004;23:932-46

39% of patients classified as having COPD by their primary care physician did not have COPD when assessed with spirometry – European Heart Journal 2005;26:1887-1894

~1/3 of individuals with a new diagnosis of COPD have spirometry performed - Chest 2007;132:403-9 and 2006; 129:1509-15

• You order spirometry pre and post bronchodilator on a 62 yr old woman with dyspnea and a 40 pack/yr history of smoking. The report returns - “moderate airflow obstruction without response to bronchodilator”
• Based on this report you decide there is no benefit to prescribing a bronchodilator to this patient - True or False?
Acute Bronchodilator Testing in the PFT Laboratory

- ATS criteria for “significance” - >12% improvement in FEV1 or FVC and > 200ml
- Criteria designed to separate normal response (no lung disease) from abnormal (lung disease)
- Clinical interpretation is complicated by:
  1) Healthy people have improvement in pulmonary function after bronchodilator administration - >100ml in younger adults
  2) In COPD ~100-140ml increase in FEV1 or a 5-10% increase from baseline is felt likely to be a minimally clinically important difference - meaning perceived by the patient as being important.


FEV1 Response After 12 weeks of Ipratropium or Salmeterol - Stratified by Acute Reversibility

- Magnitude of improvement was greater in “reversible” group but was still ~150 ml in “non-reversible” group
- Improvement in Health-Related QOL scores (CRDQ) were similar in the reversible and non-reversible groups
- Similar findings reported for Tiotropium – Chest 2003;123:1441-9

CHEST 2011;140(4):1055-1063
“The lack of increase of FEV1 and/or FVC after a bronchodilator is not a good reason to avoid 1–8 week clinical trial with a bronchoactive medication”

ATS/ERS
Interpretation Strategies for Lung Function Tests

European Respiratory Journal 2005;26 (5): 948-68

• A 40 y/o man comes to your office because of dyspnea when he is out playing soccer with his kids – ages 8 and 10. He is a 30 pack/yr smoker.

You perform spirometry – the post bronchodilator FEV1 and FVC are in the normal range but the FEV1/FVC ratio is 65 (low) – consistent with GOLD stage I COPD

• You conclude that with nearly lung function tests his COPD is so mild it should not be causing his symptoms – True or False?
Exercise Capacity in Early COPD is Significantly Reduced

- 21 individuals with GOLD stage I COPD – mean post-BD FEV1 91% predicted, FEV1/FVC ratio 60 and DLCO 98% underwent exercise testing with comparison to a matched control group.
- Peak V02 78% vs 101% in the control group
- More dyspnea and higher ventilatory requirements – evidence of dynamic hyperinflation

Am J Respir Crit Care Medicine 2008;177:622-29

Dynamic Hyperinflation During Exercise in COPD

[Diagram showing volume (VT) and EELV during exercise in normal and COPD conditions]

A 72 y/o woman with severe COPD sees you in the office for regular follow-up. Her resting oxygen saturation by pulse oximetry is 95%. With walking her Sp02 decreases to 86%.

Based on these measurements which of the following statements is correct?

A) She should wear oxygen ~24 hrs/day.
B) Oxygen with exertion will improve her QOL
C) Oxygen with exertion will help prolong her life
D) Oxygen may improve her exercise capacity on a treadmill

Oxygen Therapy in COPD

- Two randomized trials evaluating the chronic use of oxygen in persistently hypoxemic patients with COPD have shown a mortality benefit

The Lancet 1981;March 28:681-85
Annals Internal Medicine 1980;93:391-98
Oxygen May Improve Exercise Performance in COPD Without Resting Hypoxemia

- Desaturation defined as >5% fall in SpO2 with exertion to <90%
- Patients did not have to carry their oxygen/air equipment during the 6MWT
- SpO2 remained >90% with O2
- Dyspnea ratings decreased similarly with oxygen in both desaturators and non-desaturators

Chest 2001;120:437-43

Effect of Oxygen on Quality of Life in COPD with Exertional Hypoxemia

- 27 patients with COPD and isolated exertional hypoxemia ≤88%
- Completed “N-of-1” RCTs consisting of 3 pairs of 2-week periods with oxygen provided during one and placebo during the other
- Only 2/27 showed a consistent reduction in dyspnea during all three pairs of treatment periods reaching significance (>0.5) on 2 of the 3

AJRCCM 2007;176:343-49
A 55 yr old man with severe COPD (FEV1 28% predicted). He had a MI 2yrs ago and is now having angina. His coronary disease is not amenable to PCI or CABG.

Which of the following statements is true regarding the use of cardioselective beta-blockers in this patient?

1) His COPD is a relative contra-indication
2) A beta-blocker should be started although it will increase the likelihood of an acute COPD exacerbation
3) Patients with COPD and CAD have better outcomes when treated with a beta-blocker
4) Severe COPD is a “black box” warning for beta-blocker use

COPD and Beta-blockers

- Cardioselective beta-blockers have ~20 fold higher affinity for beta-1 receptors than beta-2 receptors
- Meta-analysis of 10 trials evaluating the effects of cardioselective beta-blockers in COPD (mild-moderate) revealed no significant change in FEV1 and no increase in respiratory symptoms – Ann Intern Med 2002;137:715-25
- Due to smoking as a common risk factor many patients (~50%) have heart disease - CAD, CHF, HTN.
Beta-Blockers Improve Mortality After MI in Patients with COPD

- 40% reduction in risk of death at two yrs in pts with COPD receiving a beta-blocker post MI
- 34% of all pts received a beta-blocker post MI vs 22% of pts with COPD

NEJM 1998;339:489-97

Beta-Blockers May Reduce Mortality and Risk of Exacerbations in COPD

- 2230 pts with diagnosis of COPD followed for a mean of 7.2 yrs – 30% on beta-blockers
- Adjusted HR for use of a beta-blocker for mortality = 0.68 (CI 0.56-0.83)
- Adjusted HR for use of a beta-blocker for AECOPD = 0.71 (CI 0.60-0.83)
- Patients without overt cardiovascular disease had similar benefits

Archives of Internal Medicine 2010;170:880-87
• A 65 y/o man is admitted to the ICU with acute hypercapneic respiratory failure. He has very severe COPD - FEV1 26% predicted – and is still smoking ½ ppd.

Counseling the pt and his family you should tell them:

1) He has “end stage” COPD and based on his FEV1 he will likely die from this in the next 2 yrs.
2) A trial of NIPPV is reasonable but he should not be intubated as he would very likely not get off the ventilator
3) If he requires intubation he will likely get off the ventilator but will probably have a prolonged hospitalization/recovery and poorer prognosis
4) If he survives the hospitalization there is no reason to quit smoking because the damage is already done

**Survival in COPD**

- Patients with severe COPD can live a long time.
- Stage III – FEV1 ≤ 35% - ~40% 4 year survival
- BODE Index
  - B = BMI - </> 21
  - O = Obstruction – (FEV1)
  - D = Dyspnea (MMRC scale)
  - E = Exercise Capacity (6MWT)

NEJM 2004;350:1005-12
ICU Outcomes in COPD

- 170 mechanically ventilated patients – 16% ICU mortality (most got off the ventilator), 32% hospital mortality and mean LOS 30 days – *JAMA* 1995;274:1852-57

- ICU mortality best predicted by variables which reflect the severity of acute illness – *Q J Medicine* 2012;105:115-126

- Chronic underlying respiratory physiology (pfts) and functional status better predict the longer term outcomes

Does Smoking Cessation Make a Difference in Severe COPD?

- Survival of 129 patients with severe COPD
- Mean 52 pack yrs smoking and FEV1 610 ml
- Stratified by smoking status at entry into the study

*ARRD* 1989;140:S100-105
Take Home Points

- Not all smokers get COPD – perform spirometry to make the diagnosis
- A chest x-ray is neither sensitive nor specific for COPD
- The lack of an acute “significant” bronchodilator response does not preclude clinical benefit from inhaled bronchodilators
- Even mild COPD limits functional capacity

Take Home Points

- Oxygen therapy has limited benefit in pts with isolated exertional hypoxemia
- Beta-blockers are safe and improve outcomes in COPD
- Most patients with acute respiratory failure get off the ventilator – but a prolonged recovery and diminished QOL are common
- It is never too late to stop smoking!