COPD Management: Sorting Realities from Myths

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COPD—Leading Cause of Death & Disability

• US prevalence ~10-24 million (~6%)
  – ~10 million diagnosed (Chronic bronchitis >> emphysema)
  – ~14 million undiagnosed

• 4th leading cause of death in US
  – ~120,000 deaths in 2000
  – In 2000, mortality in women surpassed men

• Second leading cause of disability (after heart disease)

• Frequent diagnosis in older population
  – Long latency period (~35 years)
  – Aging of US population
  – …Yet 70% younger than 65

Mannino et al: MMWR 2002
Mannino et al: Arch Int Med 2000
AHRQ pub. 02-M016
68 yo retired ER nurse wants help with dyspnea on exertion. Smoked 1-2 ppd since starting in Army Nursing Corps late 1950s (>50 pk years).
Which of the following statements are true?

- Physical exam provided clues necessary to determine that she has COPD, you recommend inhalers.
- Chest x-ray is the best way to determine if COPD is the cause of her DOE.
- Nearly all patients who smoke develop COPD. She probably has COPD & should be started on inhalers.
How do you make diagnosis of COPD?

What per cent of continuous smokers (> 25 pk yrs) develop COPD?

- 25% = Absolute risk over 25 years of f/u (N=8045)
- Most are mild to moderate severity

Smoking history & Dyspnea does not automatically → COPD Dx

How do you make diagnosis of COPD?

Are there diagnostic physical exam findings?

What about Dahl’s Sign?

There are no diagnostic physical findings which confirm COPD.
How do you make diagnosis of COPD?

Is the CXR sensitive way to detect COPD?

CXR seldom diagnostic, but valuable for excluding alternative dx & presence of comorbidities

Reich SB et al. AJR 1984
Which of the following statements are true?

- Physical exam provided clues necessary to determine that she has COPD, you recommend inhalers
- Chest x-ray is the best way to determine if COPD is the cause of her DOE.
- Nearly all patients who smoke develop COPD. She probably has COPD & should be started on inhalers.

NONE OF THESE!
Spirometry Required to Diagnose COPD

• Only ~33% newly diagnosed COPD have had spirometry...

• 39% diagnosed as COPD by primary care provider, did not, upon checking spirometry...

• ATS/ERS & GOLD Standards for diagnosis of COPD -> **Spirometry**

Eur Heart J 2005
Chest 2006; Chest 2007
Eur Respir J 2004; GOLD 2013
68 yo retired ER nurse wants help with dyspnea on exertion. Smoked 1-2 ppd since starting in Army Nursing Corps late 1950s (>50 pk years).

Spirometry pre- & post-bronchodilator:
• Moderate obstructive physiology
• Significant improvement post-bronchodilator
Based on these data you:
- Explain to her she has COPD (not asthma) &
- Reassure her that she should experience substantial improvement in dyspnea using the bronchodilators you will prescribe…

Correct…?

Incorrect…?
COPD & FEV1 post Bronchodilator (BD)

- **Reversibility** post BD (ATS)
  - 12% increase AND
  - 200 mL
- Reversibility in COPD common (54-73%)
- 150-200 mL ≈ Threshold for perception of benefit
- Data shows:
  - Reversible: max ~300 mL
  - Nonreversible: max ~150 mL
  - Health related QOL score same for reversible & nonreversible
- Other BD studies show similar results (eg, tiotropium)

Hanania NA. *Chest* 2011; Chest 2003
Based on spirometry data you:
- Explain to her she has COPD (not asthma) ✓
- Reassure her that she should experience substantial improvement in dyspnea using the bronchodilators you will prescribe…

COPD & bronchodilator Rx:
- Post BD spirometry response does not correlate with patient response to chronic bronchodilator Rx.
- Magnitude of improvement small enough that substantial fraction of patients won’t recognize benefit
- Neither reason should preclude bronchodilator therapeutic trial (1-3 months)
- Post BD spirometry (reversibility) does not differentiate asthma from COPD

Hanania NA. *Chest* 2011
Bronchodilators in Chronic COPD
Anti-cholinergics & $\beta_2$ Agonists

- Symptom management (prevent &/or reduce)
- Long-acting bronchodilators
  - More convenient & effective compared to short acting
  - May reduce exacerbation frequency
- No risk to using LABA alone (unlike asthma)
- CV risk of tiotropium seems to be low/nil.
- Short acting combination improves efficacy & reduces side effects compared to pushing dose of single Rx (Long acting combo data emerging)

--GOLD 2013
68 yo retired ER nurse wants help with dyspnea on exertion. Smoked 1-2 ppd since starting in Army Nursing Corps late 1950s (>50 pk years; FEV1 55%, DLCO 45%).

Long acting inhaled BD & rescue albuterol MDI \implies Less dyspnea…

…She wants more Rx to improve dyspnea. You recommend inhaled steroid reasoning that the root cause is chronic Inflammation (as w/ asthma)

Correct? Incorrect?
<table>
<thead>
<tr>
<th>INFLAMMATION</th>
<th>ASTHMA</th>
<th>COPD</th>
</tr>
</thead>
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<tr>
<td><strong>Cells</strong></td>
<td>Mast cells</td>
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<td></td>
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<td>CD8⁺ T cells</td>
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<tr>
<td></td>
<td>CD4⁺ T cells</td>
<td>Macrophages +++</td>
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<td><strong>Mediators</strong></td>
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<td>LTB₄</td>
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<td>IL-4, IL-5</td>
<td>IL-8, TNF-α</td>
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<tr>
<td></td>
<td>ROS +</td>
<td>ROS +++</td>
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<tr>
<td><strong>Effects</strong></td>
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<td></td>
<td>Little fibrosis</td>
<td>Lung destruction</td>
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<tr>
<td></td>
<td>Ep shedding</td>
<td>Fibrosis +</td>
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<td></td>
<td></td>
<td>Sq metaplasia</td>
</tr>
<tr>
<td><strong>Response to steroids</strong></td>
<td>+++</td>
<td>-</td>
</tr>
</tbody>
</table>
COPD Pharmacologic Rx
Corticosteriod Data

• Chronic inflammation of COPD not suppressed by inhaled or oral steroids
  (Culpitt SV et al AJRCCM 1999; Keatings et al AJRCCM 1997)

• 10-20% chronic stable COPD pts show objective improvement
  – Probably have asthma also
  – Airway hyperresponsiveness predicts faster decline in FEV1
    (Tashkin DP et al AJRCCM 1996)

• Long-term inhaled steroids do not effect progression of COPD (even started before patients symptomatic)
**Steroids in Chronic COPD**

**Inhaled Steroid Treatment**

- General rule: Chronic COPD resistant to steroid Rx
- Up to 20% responsive (FEV1 improves)
- Predicting inhaled steroid effect (asthma subgroup)
  - Acute PFT bronchodilator response -> No
  - Response during acute exacerbation -> No
  - Carefully monitored therapeutic trial -> Maybe
- Decreases frequency of exacerbations
  **GOLD** C or D, ≥2 exacerbations/year
- Combo Rx, Mod - Severe COPD, RDBPC trials...
  - Fluticasone-Salmeterol (500/50), N~4000 x 3 yrs: Small effect, better than either alone (TORCH, NEJM 2/07)
  - Tiotropium + Fluticasone-Salmeterol (500/50), N~450 x 1 yr: Small effect, ↑FEV1, ↓Hospitalizations (UPLIFT, AIM 4/07)
  - Difficult studies to do/interpret...Attrition rate 40%
COPD Recommendation: Inhaled Steroid

Add to long acting inhaler(s):

- Recurrent Exacerbations (≥ 2 exacerbations prior 12 months)
- Concurrent Asthma
- (Persistent symptoms)

NB: ICS alone not recommended

↑ Risk pneumonia

± Risk osteopenia/fractures

---GOLD 2013
COPD: Combination Inhalers

Budesonide/Formoterol MDI 80,160/4.5  2 puffs bid

Mometasone/Formoterol MDI 200,400/5 MDI 2 puffs bid

Fluticasone/Salmeterol
   – DPI 100,250,500/50 1 puff bid

Fluticasone/Vilanterol DPI 100/25 1 puff daily
68 yo retired ER nurse wants help with dyspnea on exertion. Smoked 1-2 ppd since starting in Army Nursing Corps early 1960s (>50 pk years; FEV1 55%, DLCO 45%).

Long acting inhaled BD & rescue Albuterol MDI⇒ Less dyspnea...
She wants more Rx to improve dyspnea.
You recommend inhaled steroid reasoning that root cause of bronchospasm is chronic inflammation (as w/ asthma)

What could you do now?
COPD: Hyperinflation, Air Trapping Beyond Bronchospasm to Explain Dyspnea

Reduced expiratory flow rate due to compression, mucous, inflammation/edema

• Increased time for exhalation required

• Physiologic (PFT) changes:
  – Reduced FEV1
  – Increased Residual Volume (RV) & Total Lung Capacity (TLC)
Mild COPD $\Rightarrow$ Dynamic Hyperinflation

Exercise Test: N = 21 w/ GOLD Stage I vs Control

- Mean post BD FEV1 = 91% predicted
- All w/ FEV1/FVC <70%
- DLCO 98% predicted

Results…

- COPD: VO2 max 78% (nl 85%)
- Control: VO2 max 101%
- COPD group: Dynamic Hyperinflation
Dynamic Hyperinflation Treatment

• Patient recognition/comprehension
  – Not bronchospasm
  – Same amount of activity, but allow more time

• Bronchodilators
  – Long acting $\beta$-agonists & anti-cholinergics > Short acting

• Pulmonary Rehab
  – Education (Comprehension, Pursed lip breathing)
  – Training → Improved IC, Reduced RR for effort

• Additive: Long acting bronchodilator Rx + Training

68 yo retired ER nurse wants help with dyspnea on exertion. Smoked 1-2 ppd since starting in Army Nursing Corps early 1960s (>50 pk years; FEV1 55%, DLCO 45%).

Long acting inhaled BD & rescue Albuterol MDI plus Exercise ⇒ Less dyspnea, BUT…
…I wonder if O2 will help her dyspnea.

O2 Sat: Resting 95%; 6 min walk (6MWT) 85%

Based on data which recommendation is correct:
1. Continuous O2 24/7: Prevents heart failure & prolongs life OR
2. O2 for exertion: Prevents heart failure & prolongs life OR
3. O2 for exertion: Perhaps improves dyspnea & exercise OR
4. O2 won’t help
Supplemental O2 May Improve Exercise Performance

- Desaturators distance improved by 22% \((P<0.02)\)
- Dyspnea rating ↓ in Desaturators & Non-
- For both, within Group responses variable & unpredictable...

Desaturators (N=10) vs Non-desaturators (N=10)
DBPC 6MWT: O2 vs Compressed Air
Supplemental O2 May Improve Quality of Life

- N=27 COPD, exertional desaturation (<88%)
- "N-of-1 RCT" x3 (2 weeks) O2 vs RA
- Only 2/27 showed consistent reduction in dyspnea

Nonoyama M et al, AJRCCM 2007
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Long acting inhaled BD & rescue Albuterol MDI plus Exercise ⇒ Less dyspnea, BUT…

…She wonders if O2 will help her dyspnea.

Data from 1980s: If resting O2 sat ≤88% (PO2 ≤50), THEN Supplemental O2 >18 hr/day reduces mortality

*Lancet* 1981; *AIM* 1980

3. O2 for exertion: Perhaps improves dyspnea & exercise OR
4. O2 won’t help
Cumulative Benefits of Interventions Targeting Dyspnea

Dyspnea (Borg Scale)

- Severe
- Somewhat severe
- Moderate
- Slight
- Very slight
- Nothing at all

Endurance Exercise Time (minutes)

Bronchodilators
Oxygen Therapy
Exercise Training

Keep it realistic!!

--ATS Consensus Statement 1999
68 yo retired ER nurse wants help with dyspnea on exertion. Smoked 1-2 ppd since starting in Army Nursing Corps early 1960s (>50 pk years; FEV1 55%, DLCO 45%).

She needs Hip surgery which is planned 3 weeks hence. Which of the following regarding short-term pre-op smoking cessation is correct:
1. Stop smoking now because it is a good idea
2. Keep smoking until day of surgery, because complications are increased in those stopping over short term (<8 weeks pre-op)
Pre-Op Smoking Cessation Dilemma

Smokers (456)

- Never stopped (124)
- Stopped < 2 wks (84)
- Stopped 2-4 wks (44)
- Stopped 4-8 wks (28)
- Stopped > 8 wks (176)

Nonsmokers (44)

- Increased risk a/w short term smoking cessation pre-op persists in Textbooks, Consensus documents & subsequent studies since 1990, reflecting the power of “interpretive bias”

- Smoking cessation both good and bad…
  - Short term quitters increases complications (57%) vs smokers (33%)
  - Nonsmokers & Quitters (>8 weeks) ↓ complications (P <0.01)
Pre-op Smoking Cessation Paradox Refuted

• Multiple studies past ~5 years demonstrate that pre-op smoking cessation does not paradoxically increase post-op complications.

• Anticipated surgery should be seen as a compelling teaching opportunity for stressing both short & long-term value of smoking cessation.

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During immediate post-operative period, she suffers NSTEMI. The consult cardiologist recommends adding β-blocker Rx.

Which of the following is correct:

1. COPD is a relative contraindication for beta-blocker Rx
2. Patients w/ COPD & CAD do better on beta-blocker Rx
Avoid β-blockers in COPD pts d/t broncho-constrictive property & competition w/ β-agonist

- Cardiovascular disease (eg, CAD, HTN, CHF) concurrent commonly (~50%) in COPD pts
- Meta-analysis showed that cardio-selective beta-blockers in mild-moderate COPD produced no negative effect on FEV1 & respiratory symptoms
- Do COPD pts benefit w/ cardio-selective β-blocker?

Salpeter et al. Annals Int Med 2002
**β-Blockers Reduce Mortality (post MI) & Risk of Exacerbations**

- **Left Panel** → 40% reduction in 2 year post MI mortality in COPD attributable to β-blocker Rx
- **Right Panel** → N=2230 COPD pt f/u x 7.2 yr, 30% β-blocker Rx
  Beta blocker Rx reduced mortality & # acute exacerbations

COPD Roses Among the Thorns…

Conclusions

• Perform Spirometry to diagnose COPD
  – Only 25% of smokers develop COPD
  – Physical exam (Pink Puffer/Blue Bloater/Dahls) & CXR too insensitive

• Reversibility post bronchodilator does not…
  – Identify true asthmatic from COPD
  – Discern whether an individual with COPD will benefit from bronchodilator Rx…

• Dynamic Hyperinflation causes dyspnea in many COPD patients (even mild). Improves with
  – Education & Exercise (Pulmonary Rehab)
  – Long acting inhalers
COPD Roses Among the Thorns…Cont’d

• Inhaled steroids beneficial when added to long acting inhalers
  – ≥ 2 exacerbations/year
  – Not necessarily d/t effect on airway inflammation

• O2 supplementation benefits COPD w/ resting hypoxemia (SaO2<88%), but limited benefit in those w/ only exertion hypoxemia

• Pre-op: Compelling teaching opportunity for stressing both short & long-term value of smoking cessation

• Cardio-selective β-blockers not only safe but may improve outcomes in COPD