

*COPD  
and  
Interstitial Lung Disease*

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# Chronic Lung Disease

## ◆ COPD – 6 Cases

- *Morbidity and Prognosis*
- *First Bronchodilator ?*
- *Frequent Exacerbations (2) – not just azithro*
- *Dyspnea – not always due to COPD*
- *Acute Exacerbation - management*

## ◆ Interstitial lung disease – 3 Cases

- *Aging Population = more interstitial disease*
- *Dying with vs dying of ILD, or dying of a complication?*

➤ *New treatments – that actually work*



# *Asthma Vs COPD*

## *One Disease?*

- ◆ Shortness of breath
- ◆ Wheezing episodes
- ◆ Rescue treatment with puffers
- ◆ Systemic steroids for flare-ups
- ☑ No – Eos vs PMNs, Reversibility

# *COPD – Death and Disability*

## ◆ **Top 10 causes of death, US 2010**

CJMurray, *NEJM* 2013; 369:448

- *Ischemic heart disease*
- *Stroke*
- *Lung cancer*
- *Alzheimers*
- *COPD*

## ◆ **Disability-Adjusted life years (DALYs)**

- *Ischemic heart disease*
- *COPD*
- *Low back pain*
- *Lung cancer*
- *Depression*

✓ **ACOs**

✓ **CMS: *Hospital Compare***



# COPD – So What's New?

- ◆ **Classic care – early 1990s to the present**
  - *Smoking cessation*
  - *Vaccination – flu and pneumovax, PCV 13*
  - *Oxygen, post hospitalization Pulm Rehab*
  - *Inhalers*
    - ◆ **Bronchodilators**
      - Short acting beta-agonists – albuterol
      - Long-acting beta-agonists (LABA) - *Salmeterol, formoterol*
      - Long-acting musc. antagonists (LAMA) - *Tiotropium, aclidinium*
    - ◆ **Inhaled corticosteroids – if frequent exacerbations**
- 1. **Preventive meds for frequent exacerbations**
  - Guidelines: ACCP/CTS, *Chest* April, 2015; 147:894-942
- 2. **COPD as a marker for severe comorbidities**

# *COPD and Prognosis*

- ◆ 63 yo woman with severe COPD, FEV1 = 0.8L, on 2 liter/min O2
- ◆ Functional status – walking around apt
  - *Desaturates to 70s*
- ◆ Every new VNA – phone call re dyspnea
- ◆ PCP and case mgr – referral to hospice?

# COPD: Stage and Tx per GOLD

I: Mild

II: Moderate

III: Severe

IV: Very Severe

- FEV<sub>1</sub>/FVC < 0.70
- FEV<sub>1</sub> ≥ 80% predicted

- FEV<sub>1</sub>/FVC < 0.70
- 50% ≤ FEV<sub>1</sub> < 80% predicted

- FEV<sub>1</sub>/FVC < 0.70
- 30% ≤ FEV<sub>1</sub> < 50% predicted

- FEV<sub>1</sub>/FVC < 0.70
- FEV<sub>1</sub> < 30% predicted or FEV<sub>1</sub> < 50% predicted plus chronic respiratory failure

Active reduction of risk factor(s); influenza vaccination

Add short-acting bronchodilator (when needed)

Add regular treatment with one or more long-acting bronchodilators (when needed); Add rehabilitation

Add inhaled glucocorticosteroids if repeated exacerbations

Add long term oxygen if chronic respiratory failure.  
Consider surgical treatments

# Prognostic Stage: More than FEV1

- ◆ FEV1 – how fast can you puff?
- ◆ Functional Status – what can you do?
  - $B = BMI \leq 21$
  - $O = Obstruction - FEV1$
  - $D = Dyspnea - MRC\ scale$
  - $E = Exercise\ Capacity$
- ◆ Exacerbations – How often are you sick?



# *COPD: Prognosis*

## ◆ **BODE Index – Looking and Listening**

*63 yo woman, FEV1 = 0.8L, 2 L/min O2*

➤ *Skinny? – BMI* *0 pts*

➤ *Low FEV1? -- Severe Obstruction* *3 pts*

➤ *Breathless? – Dyspnea score* *3 pts*

➤ *Activity limitations? -- Exercise cap. 3 pts*

*SCORE = 9/10 pts*

# *Common Knowledge: Severe COPD*

## *GOLD Class 3-4*

- ◆ Poor QOL
- ◆ High mortality in ICU
- ◆ Difficult to extubate
- ◆ Mech ventilation is burdensome and feared
  
- ◆ Predictable course
- ◆ Die of COPD



# *Humility re: Severe COPD*

## *Severe COPD Myths*

- ◆ Poor QOL
- ◆ High mortality in ICU
- ◆ Difficult to extubate
- ◆ Mech ventilation is burdensome and feared
- ◆ Predictable course
- ◆ Die of COPD

## *Reality*

- ◆ Compared to ?
- ◆ Lowest mort 20-25%
- ◆ Easier than ARDS, etc
- ◆ 96% said Yes, Again
  - *Wildman MJ (UK ICUs). Thorax. 2009;64:128-32*
- ◆ Unpredictable
- ◆ 2-3x more CV deaths

# *COPD Prognostication: Humility*

- ◆ 63 yo woman, FEV1 0.8L, 2 L/min O2
- ◆ Discussion 2003.... 10 years later
- ◆ 2013: FEV1=0.8L, 3-4L/m O2, SOB walking around apt

- *Casanova et al. The Progression of COPD is Heterogeneous: BODE Cohort. Am J Respir Crit Care Med 2011;184: 1015-21*
- *FEV1 ~45% pred, 12 yr of follow-up*
- *75% had no change in FEV1 or BODE score*

◆ **Key – No exacerbations**

➤ **BODEX Score**

# 75 yo man w/COPD – 1<sup>st</sup> Inhaler?

- ◆ Retired lawyer, likes competitive tennis
  - *Dyspnea, decr FEV1 to 1.4L, 46% pred.*
  - *Exacerbations – 0-2 per yr.*
- ◆ Inhaled corticosteroid?
- ◆ Long-acting bronchodilator?
  - *LA anti-muscarinic: Tiotropium, aclidinium*
  - *LA beta-agonist: Salmeterol, formoterol*

# COPD: Stage and Tx per GOLD

**I: Mild**

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**IV: Very Severe**

- $FEV_1/FVC < 0.70$
- $FEV_1 \geq 80\%$  predicted

- $FEV_1/FVC < 0.70$
- $50\% \leq FEV_1 < 80\%$  predicted

- $FEV_1/FVC < 0.70$
- $30\% \leq FEV_1 < 50\%$  predicted

- $FEV_1/FVC < 0.70$
- $FEV_1 < 30\%$  predicted or  $FEV_1 < 50\%$  predicted plus chronic respiratory failure

Active reduction of risk factor(s); influenza vaccination

Add short-acting bronchodilator (when needed)

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Consider surgical treatments

**Tiotropium**

**LABA (beta-agonists)**

**Salmeterol**

**Formoterol**

**COPD, not Asthma**

# 75 yo man w/COPD – 1<sup>st</sup> Inhaler?

## ◆ Retired lawyer, tennis

➤ *Dyspnea, FEV1 46% pred, occ Exac*

## ◆ ~~Inhaled corticosteroid~~

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## ◆ Long-acting bronchodilator –LAMA, LABA

➤ *LA anti-muscarinic: Tiotropium, aclidinium*

◆ Grade 1C recommendation (ACCP, 2015)

➤ *LA beta-agonist: Salmeterol, formoterol*

# 75 yo man w/ COPD – Steroids?

## ◆ Inhaled steroids + LABA in COPD

- *Moderate to severe COPD with recurrent exacerbations*
- *As combination inhaler w/long-acting beta-agonist (LABA)*
- *No benefit on preserving lung fcn over time*
- *Decreased exacerbations, modest survival benefit*
- *Adverse Effects: hoarseness, pneumonia, skin spots*



# *COPD – Recurrent Exacerbations*

- ◆ 65 yo man w/severe COPD, 7 flares in past 2.5 yrs
- ◆ 73 yo woman w/severe COPD, 5<sup>th</sup> hospitalization in 10 mos

# Exacerbations: Preventable?

## ◆ 65 yo M undertaker with COPD

- *FEV1 = 1.2L, 25% predicted, no O2*
- *7 flares/2.5 yrs, despite vaccinations etc*
- *Meds: Salmeterol/flutic.250/50,  
Tiotropium*
  - ◆ Another inhaler?
  - ◆ Maintenance prednisone?
  - ◆ Prophylactic antibiotics? Vit D?
  - ◆ Roflumilast (PDE4 inhibitor) ?
  - ◆ Care management/Self-management?

# *Exacerbations: Preventive antibiotics:*

- ◆ **Olden days – rotating antibiotics**
- ◆ **Azithromycin – Guidelines *Chest* 4/2015 – Grade 2A**
  - *5 RCTs, Largest NEJM- lead article 8/25/11 RCT of azithro 250 mg/d*
    - ◆ *Pts on O2 or prednisone chronically, with at least one exac in past yr*
  - *Less freq exac (1/4-1/3 less), occurring later*
  - *BUT hearing loss, resistant organisms*
  - *CV events? – Baseline EKG*
- ◆ **Considering azithro, other antibx?**
- ◆ **REFER for evaluation of “COPD”**
  - *Bronchiectasis?*
  - *Mycobacterium avium (MAC)?– drug resistance*

# Recurrent Exac. in COPD

- ◆ Maintenance prednisone?---- No!
- ◆ A pt who is “steroid-dependent”?
  - *Not quite Nevah, but almost*
  - *Needs referral for an alternative dx*
    - ◆ Bronchiectasis
    - ◆ Pt confuses steroid-withdrawal w/ flaring disease
- ◆ Vitamin D?
  - *Multiple studies – Maybe ....in severe deficiency*

# *Recurrent Exac. in 65 y.o. man*

## ◆ **Magic prophylactic pill? - PDE4 inhibitor**

➤ *Roflumilast (Daliresp) – approved 2011*

➤ *Pts with severe to v. severe COPD*

➤ *To reduce the risk of exacerbations*

➤ *Adverse effects*

◆ Wt loss (2 kg), GI upset

◆ Suicidal ideation, other psychiatric symptoms

◆ Drug interactions at P450 CYP3A4 and 1A2

➤ ***Not Yet!***



# *COPD – Recurrent Exacerbations*

◆ 65 yo undertaker, FEV1 25% pred, 7 flares in the past 2.5 yrs, triple inhalers

➤ *COPD and bad prognosis?*

➤ *Another lung disease?*

◆ Interstitial lung disease ---- PFTs

➤ *COPD + ?*

◆ Bronchiectasis

➤ *CHF or CAD*

# *COPD + Bronchiectasis*

## ◆ **First Question – truly COPD?**

➤ *Smoking history, chronic bronchitis?*

## ◆ **University hospitals cohort in Spain**

▫ *Am J Respir Crit Care Med April 2013; 187:823*

➤ *Moderate-severe COPD (FEV1 <80% pred)*

◆ *FEV1 = 1.4L, 49% pred*

➤ *Bronchiectasis on CT in 57%*

➤ *Associated with*

◆ *More exacerbations, mortality (2.5x)*

# *COPD :Recurrent Exacerbations*

◆ 65 yo M, 7 flares /2.5 yr

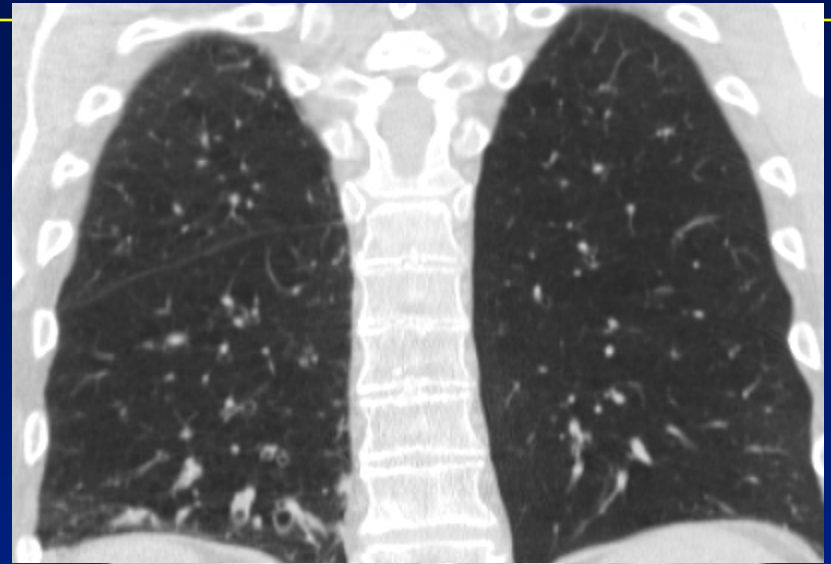
➤ *COPD + ?*

➤ *Bronchiectasis*

◆ Chronic productive cough

◆ Pseudomonas, H.flu, Strep pneumo

◆ IgG v. low, IgG subsets v. low, no response to Pneumovax





# Approach to Bronchiectasis

- ◆ High-resolution CT of chest
- ◆ Sputum culture: bacterial, AFB, fungus
- ◆ Immunological defect?
  - *Quant. Ig, SPEP, subclasses*
  - *Alpha-1-antitrypsin level*
- ◆ Cystic fibrosis?
  - *CFTR testing, Sweat test*
- ◆ Misc: Ciliary dysf, RA, ABPA...MAvium

# *COPD + Bronchiectasis*

- ◆ **Classical bronchiectasis**
  - *Purulent, bacterial flares*
  - *Due to immunodeficiency or idiopathic*
- ◆ **Nodular bronchiectasis**
  - *Mycobacterium avium (MAC)*
  - *Higher mortality with macrolide alone*
- ◆ **Azithro prophylaxis – Wrong!**
- ◆ **65 yo undertaker – no MAC ---- IV IgG**

# 73 yo F w/COPD, 5<sup>th</sup> hosp/yr

- ◆ 73 yo woman admitted for the 5<sup>th</sup> time in 10 mos with sudden dyspnea, hypoxemia
  - Severe COPD (FEV1 0.7L, 34% pred)
  - On home oxygen, 4 lpm
  - Morbid obesity – 64 inches, 265 lbs
  - Sleep apnea

# 73 yo F w/COPD, 5<sup>th</sup> hosp/yr

## ◆ Typical COPD flare?

- *New cough, sputum, preceding URI.....Not always*

## ◆ Dual diagnosis? COPD +

- *Sleep apnea – rather compliant*
- *COPD variant...Bronchiectasis?.....No sputum, CT neg*

## ◆ Atypical CHF?

- *Rarely crackles on exam or leg edema or CXR*
- *Elevated BNP - not always*
- *Key – Pizza boxes*

➔ **No hospitalizations for > 2 yrs**



# COPD Self-Management? RCTs

- ◆ **Bucknall CE et al. Glasgow *BMJ* 2012; 344**
  - Eligible for RCT during COPD hospitalization
    - ◆ *Regimen optimized, smoking cess'n, rehab (if >2 yr), educational sessions, visits q6wk, Action plan*
    - ◆ *~50% readm/died in 12 mos, no diff. QOL – no diff*
- ◆ **Fan V et al RCT in VA. *Ann Intern Med.* 2012;156:673**
  - ◆ *Intervn: Education, individualized action plan (meds and call)*
  - Trial Halted - at 44% of enrollment
    - ◆ *Overall mortality: 28 deaths vs 10 deaths in control arm*
- ◆ **ACCP/CTS Guidelines April 2015 - Exacerbators**
  - Self-management
  - Individual components
  - Specialist Access + Educ'n + Case mgt + Action plan (Grade 1C)

# 82 yo man w/ COPD, dyspnea

- ◆ Smoked 50 PY, mild clinical COPD
- ◆ New dyspnea over 6 mos
  - *Couldn't do chores, yard work*
- ◆ Barrel-chested, no distress, faint end-expiratory wheezes
- ◆ Meds: Tiotropium

# COPD

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- ◆ Your choices are:
  1. *Prescribe another MDI*
  2. *Refer to pulmonary rehabilitation*
  3. *Order spirometry*
  4. *Order a stairlift or scooter*

# *Spirometry in Primary Care?*

## ◆ **Newly diagnosed COPD**

- *Only 1/3 have spirometry done*
- *Overdiagnosed – Smoking*

## ◆ **Underdiagnosed**

- *Pts w/ $FEV_1 < 50\%$  pred (Petty, Arch Int Med 2001)*
- *Less than half were MD-diagnosed*

## ◆ **Guidelines – Perform spirometry to diagnose and stage COPD**



# *Spirometry in Primary Care?*

- ◆ **Overdiagnosis / Misdiagnosis – other Dx**
  - *Life's not fair – only 30-40% of smokers get COPD*
    - ◆ *Chest 2006 Oct;130:1129 - Finland*
- ◆ **Underdiagnosis - Severe COPD (FEV1 <50%)**
  - *Only half diagnosed by MD (NHANES, Arch Int Med 2000; 160:1683)*
- ◆ **Practice Guidelines – Require spirometry to dx and stage COPD in pts >age 40 w/ resp symp.**
  - *NCQA/HEDIS measure 2006, 2010, Medicare*
- ◆ **Reality - New dx COPD, Only 1/3-1/2 have spirom**

# Why not Spirometry in Primary Care?

- ◆ **76% of PCPs diagnose COPD clinically**
  - ◆ Moore PL. Am J Med 2007; 120:S23-27
- ◆ **Focus group of 12 PCPs – Why not spirometry?**
  - ◆ J COPD 2013; 10: 444
- ◆ **Newly suspected COPD**
  - *Confident in history and results of inhaler trial*
  - *Uncertain utility of spirometry, pulm interpretation*
- ◆ **Pre-existing Dx of COPD**
  - *Middle-aged-elderly, smoking history, inhalers....Lots of other problems*
- ◆ **Priority of COPD during visit**
  - *Most other chronic diseases have a simple, point of care measure eg A1c*
  - *Monitoring – pt's subjective report*
- ◆ **Health system barriers**
  - *PFT appt, insurance – most admitted lack of value, not logistics*

# 82 yo man w/ COPD, dyspnea

- ◆ Smoked 50 PY, mild clinical COPD
- ◆ New dyspnea doing yardwork
- ◆ FEV1 1.2L, 40% pred
- ◆ 3 yr ago - FEV1 = 1.2L
- ◆ ETT equivocal....
- ◆ Cath : Left Main CAD....CABG

# *COPD: Marker for Cardiovascular Dis*

## ◆ COPD pts

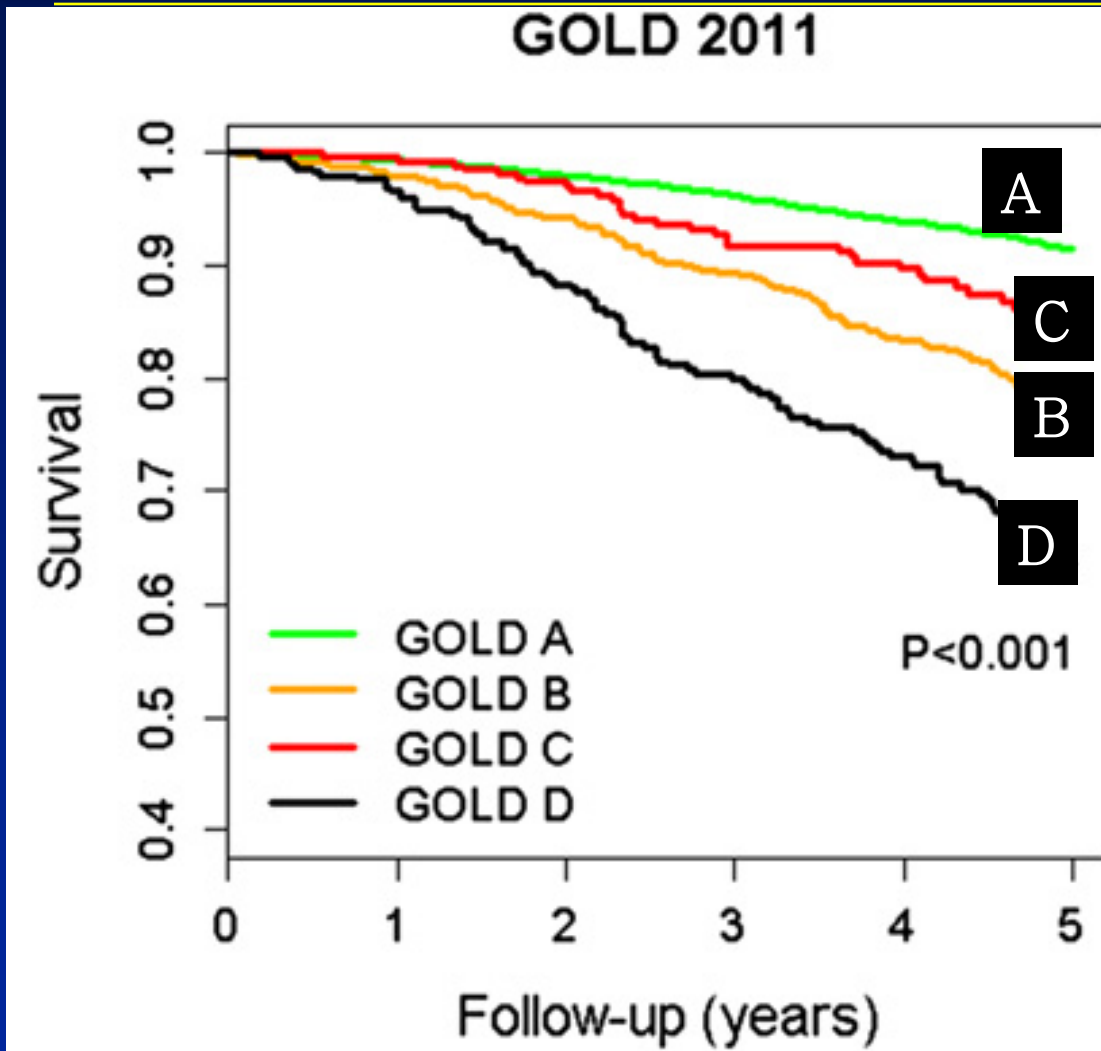
- *CV Disease: Meta-Analysis and Systematic Review*
  - Lancet Respir Med 2015; 3:631
- *Compared to the rate of peers without COPD in the general population – 2 to 5 fold higher rates of*
  - ◆ Ischemic heart disease
  - ◆ Arrhythmias
  - ◆ Heart failure
- **Death: Twice as likely to die of CV disease as of COPD**

Huiart, L. et al. Chest 2005;128:2640-2646

# *Lethal LABA/LAMA inhalers?*

- ◆ CV Safety of Inhaled Long-acting Bronchodilators in COPD JAMA Int Med 2013; 173: 1175-84
- ◆ Ontario Pharmacy Database, case-control
- ◆ Dx of COPD, age>65, New prescription for
  - *LABA – salmeterol or formoterol or LAMA antimuscarinic (tiotrop)*
- ◆ ED/hospitalization for CV event (ACS, CHF)
  - *Increased risk, 15-30%, mainly in first 2-3 wks*
  - *No difference for LABA vs LAMA*
  - *How to explain?*

# GOLD 2011 vs 2007



## ◆ Group B

➤ *Mild-mod obstruction*

➤ *Dyspnea – prominent*

## ◆ Higher mortality than Gp C

➤ *Despite better FEV1*

## ◆ Died of CAD, HF and lung cancer

# Safety of LABA/LAMA inhalers?

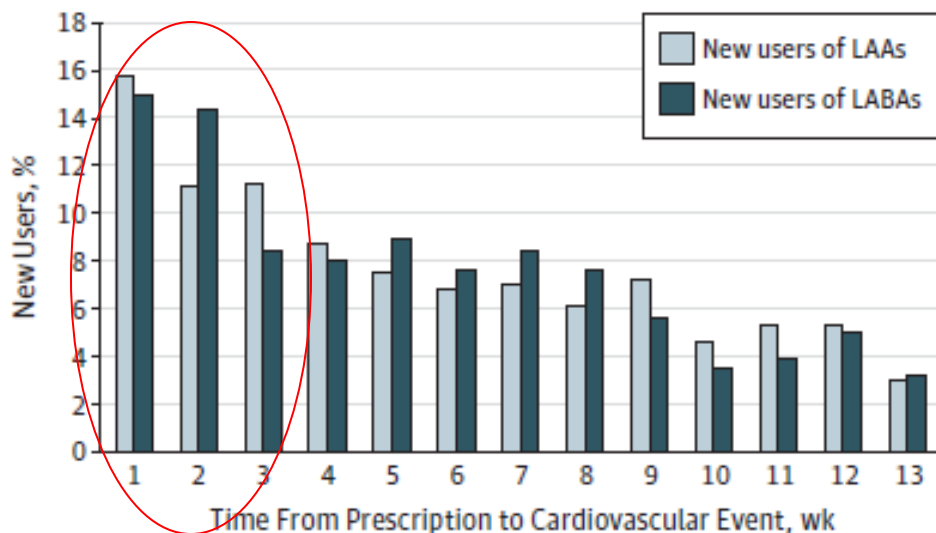
## Original Investigation

### Cardiovascular Safety of Inhaled Long-Acting Bronchodilators in Individuals With Chronic Obstructive Pulmonary Disease

Andrea Gershon, MD, MS; Ruth Croxford, MSc, PStat; Andrew Calzavara, MSc; Teresa To, PhD; Matthew B. Stanbrook, MD, PhD; Ross Upshur, MD, MSc; Thérèse A. Stukel, PhD

*JAMA Intern Med.* 2013;173(13):1175-1184.

Figure. Percentage of Individuals Experiencing Various Durations of Time From Receipt of an Inhaled Long-Acting  $\beta$ -Agonist (LABA) or Long-Acting Anticholinergic (LAA) to a Cardiovascular Event



1. Rapid CV effects?
  2. More likely, misdiagnosis of CAD/CHF as COPD worsening
    - 50% spirometry
    - Dual dx – tricky
- ◆ Large RCTs – no adverse CV effects

# *COPD and Cardiovascular Disease*



European Journal of Heart Failure (2012) 14, 348–350  
doi:10.1093/eurjhf/hfs022

EDITORIAL

## **Chronic obstructive pulmonary disease: a slowly progressive cardiovascular disease masked by its pulmonary effects?**

Frans H. Rutten\* and Arno W. Hoes

### ◆ **Beta-blockers in COPD pts with CAD**

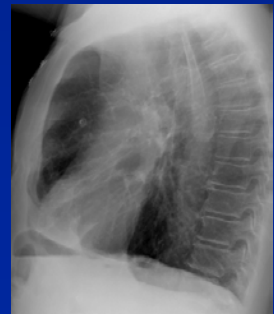
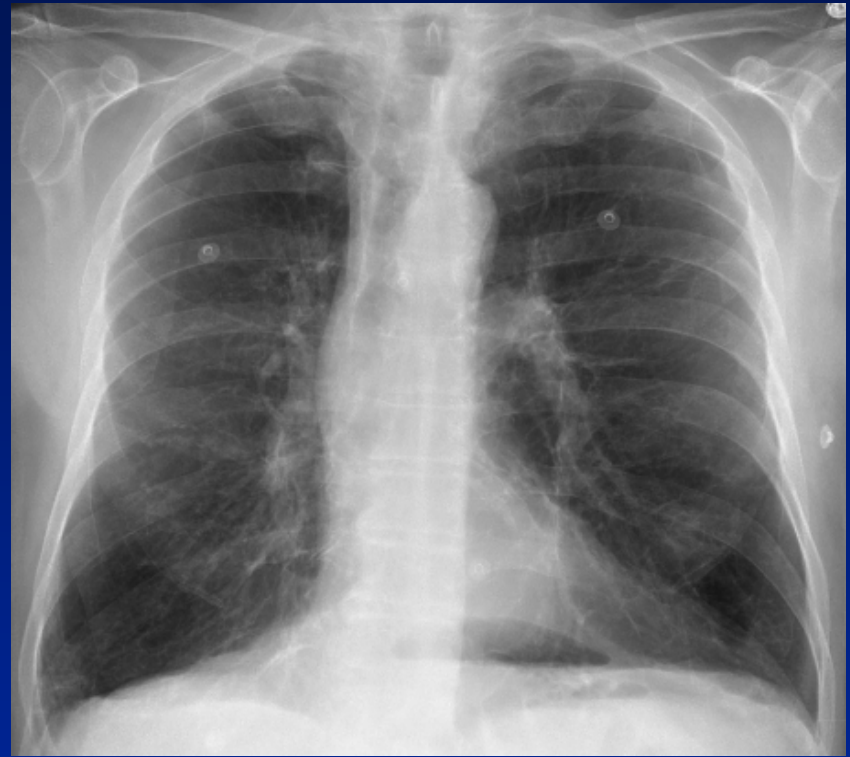
- *Markedly underprescribed*
- *COPD esp on no BB associated with worse outcomes in MI, CAD, CHF*





# Acute COPD Management

- ◆ 67 yo man with >100 pk-yr
- ◆ 1<sup>st</sup> admission 2/03
  - *COPD Exacerbation*
- ◆ FEV1 0.65L
  - *23% predicted*
- ◆ Treatment options?
- ◆ What about death and dyspnea?
  - *Will COPD kill him?*
  - *What is his ICU prognosis if he lands in MICU?*



# *Bacterial Infection in COPD?*

## ◆ Standard explanation of COPD exacerbation

➤ *Increase in bacterial load*

## ◆ Recent revision

➤ *Acute exacerbations correlate strongly with new isolates*

- *S. pneumoniae, Moraxella, H. influenza*
- *Pseudomonas*

# Antibiotics in Acute COPD?

## ◆ Hospitalized pts - YES

### ➤ *Early antibiotics (cohort study)*

◆ Rothberg, M. B. et al. JAMA 2010;303:2035-2042.

### ➤ *Reduced risk of:*

◆ Mech ventilation, In-hospital mortality, Readmission w/in 30 d

### ➤ *Regardless of change in sputum*

## ◆ Outpatients

### ➤ *Anthonisen criteria – Dyspnea, Sputum Amount, Sputum Purulence*

### ➤ *If Sputum change – YES*

## ◆ Duration – 5-10 days

## ◆ Agent: almost any, exc if MDR risk

## ◆ Decreased mortality (RR=0.87) regardless of sputum increase

# Systemic Steroids = Targeted

- ◆ **Mildly ill – mortality risk ~1% - PO predn ok**
  - *Prednisone = IV steroids?*
  - *JAMA June, 2010:– retrospective, acute COPD, non-ICU*
    - ◆ 92% IV steroids...Matched the 8% treated PO
    - ◆ Oral steroids –pts did No Worse...99% survival
  - *Regimen? – Standard 2 wk taper*
    - *JAMA May, '13 - RCT, pred 40 mg/d, 14d=5 d*
- ◆ **Prednisone in ICU? – ERJ 2014 – don't bother**
  - *Open-label pred vs placebo, hypercap RF, no Diff.*
- ◆ **Moderate-severely ill – mortality 10-20%**
  - *IV methylprednisolone -  $\leq 500$  mg/d*
    - *Am J Respir Crit Care Med 2014.189:1052-1064*

# *COPD admission: Alternative Dx?*

## ◆ Occult PE

- *Only if atypical flare – no sputum/infection*
- *PE-CT showed PE in 25% of cases*

## ◆ CHF or CAD – as alternative or simultaneously

- *BNP or nt-proBNP, Troponin*
  - ◆ Every COPD admission

# *COPD and the Advance Directive*

- ◆ **67 y. o. man w/ COPD, FEV1 0.6 L**
  1. *You will never get extubated?*
  2. *You may get extubated, but won't survive hospitalization?*
  3. *You are likely to survive the ICU and hospital, but will need post-acute care?*
  4. *You are likely to survive ICU and be discharged to home?*

# Humility re: Severe COPD

## Severe COPD Myths

- ◆ Poor QOL
- ◆ High mortality in ICU
- ◆ Difficult to extubate
  
- ◆ Mech ventilation is burdensome and feared
- ◆ Predictable course
- ◆ Die of COPD

## Reality

- ◆ Compared to ?
- ◆ Lowest mort 20-25%
- ◆ Easier than ARDS, etc
  
- ◆ 96% said Yes, Again
  - *Wildman MJ (UK ICUs). Thorax. 2009;64:128-32*
- ◆ Unpredictable
- ◆ 2-3x more CV deaths



# *The Real Meaning of ICU*

- ◆ ICU = Intensive Clarification Unit
- ◆ Preparation is rare
- ◆ Emergent discussions are difficult
- ◆ Futility as a basis for limiting care?
  - *Prediction at outset is inaccurate*
    - ◆ Most intubated pts (75-85%) are going to survive
  - *48-72 hr re-evaluation*
- ◆ Prognosis - Trajectory of disease
  - *Frailty, functional status, exacerbations*



# *COPD and the Advance Directive*

- ◆ 67 y. o. man w/ COPD, FEV1 0.6 L, good ex tolerance, no exacerbations
  1. *He will never get extubated*
  2. *He may get extubated, but won't survive hospitalization*
  3. *He is likely to survive the ICU and hospital, but will need post-acute care*
  4. *He survived intubation and the ICU, and was discharged home*

# *COPD and the Advance Directive*

- ◆ 71 y. o. man w/ COPD, FEV1 0.6 L, 4 yr later, after 3 exac in past yr
- ◆ Prognosis Now?
  - *BODE score – high ... + Exacerbations*
- ◆ He survived the ICU and was discharged to rehab
- ◆ Died 6 mos later, 4.5 yrs after the initial discussion

# *Interstitial Lung Disease*

- ◆ Questions for From the Internist
- ◆ Elderly patients – not just a referral
  - *Biopsy vs no biopsy?*
  - *Empiric steroids vs No empiric steroids?*
  - *Death from interstitial disease, or with it?*

# Interstitial Disease – Cases

## ◆ Dyspnea in the dining room

## ◆ Crackles on preop exam

➤ *Is it interstitial disease, and if so, cause?*

➤ *Will he die with the interstitial disease, or of it?*

## ◆ Dyspnea in a patient with known pulmonary fibrosis

➤ *It's interstitial lung disease progression, right?*



# *Dyspnea in the Dining Room*

- ◆ **84 yo woman referred with dyspnea in the past year**
  - *Moved back to MA from Fla*
  - *Subtly increasing shortness of breath, w/ longer recovery, on walking to the dining*
  - *Mild dry cough*
  - *Exam – fine crackles lower ½ of chest*
  - *Spirometry – FVC 85% predicted*
  - *CT –interstitial disease*
  - *FVC: 2.5L .....2.3L 2 yr later , more SOB*

# *Interstitial Disease – the other 10-15%*

## ◆ **Inflammatory disorders**

- *Granulomatous – Sarcoidosis*
- *Pneumonia-like – BOOP*
  - ◆ Bronchiolitis obliterans-organizing pneumonia
- *Vasculitic – Wegener's (ANCA-associated vasc.)*

## ◆ **Exposure-related**

- *Drugs*
  - ◆ Amiodarone
  - ◆ Nitrofurantoin
- *Environmental - Hypersensitivity pneumonitis*
  - Mold, Pigeons

## ◆ **(Idiopathic pulmonary fibrosis - UIP etc.)**

# *Biopsy in Interstitial Disease*

- ◆ **Clinical data, chest CT, PFTs**
  - *IPF Clinic, only 85-90% accurate*
- ◆ **Thoracoscopic biopsy - VATS**
  - *Much better tolerated, mortality <0.5% if done early when well*
- ◆ **Might defer if**
  - *Multiple other medical problems esp CAD*
  - *Incidentally detected*

# ILD Treatment: Can't we do Something?

## ◆ Inflammatory element

➤ *Steroids? Azathioprine? NAC?*

## ◆ ILD + Pulm HTN

➤ *PDE5 inhibitors – Sildenafil?*

➤ *Endothelin antagonists – Bosentan?*



# *Interstitial Lung Disease*

## ◆ **First – admit ignorance**

### ➤ *Pathogenesis*

◆ Original paradigm - Inflammation

◆ Current paradigm – Injury, disordered repair

## ◆ **Treatment: Mainly non-steroidal**

➤ *GERD mgt – Early-bird eating, Wedge, PPI bid*

➤ *Observation – many die with ILD, not of it*

## ◆ **Targeted agents: pirfenidone, nintedanib?**



# ILD Treatment: Less is More

## ◆ Am Thoracic Soc (and others) Guidelines, 2015

• *Am J Respir Crit Care Med.* 192; e3–e19, Jul 15, 2015

➤ ~~Steroids? Azathioprine? NAC?~~

➤ *Strong Recommendation Against Steroids*

## ◆ ILD + Pulm HTN

➤ ~~PDE5 inhibitors – Sildenafil?~~

➤ ~~Endothelin antagonists – Bosentan?~~

➤ *Strong Recommendation Against Pulm HTN meds*

## ◆ Targeted agents – pirfenidone, nintedanib

➤ *Conditional Recommendation For*

# Pirfenidone - antifibrotic

## ◆ RCT, *NEJM*, May 2014

### ➤ *Mild-moderate pulmonary fibrosis (IPF)*

◆ FVC 50-90% predicted

### ➤ *Outcomes*

◆ Less loss of lung fcn

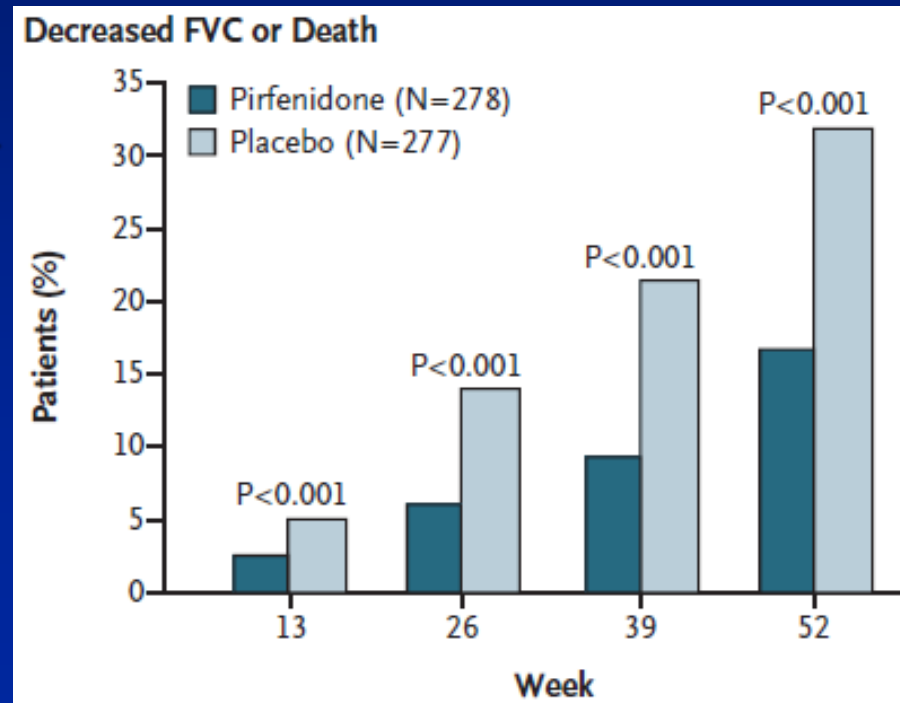
◆ Lower mortality

● 3.6 vs 5.1%

### ➤ *Adverse effects*

◆ Photosensitivity

◆ GI upset, fatigue



# *Nintedanib – Tyr kinase inhibitor*

## ◆ RCTs, including *NEJM*, May 2014

### ➤ *Mild-moderate pulmonary fibrosis (IPF)*

◆ FVC  $\geq 50\%$  predicted

### ➤ *Outcomes*

◆ Less loss of lung fcn ~100 ml less per yr

◆ Not proven - lower mortality (5.5 vs 7.8%), fewer acute exac

### ➤ *Adverse effects*

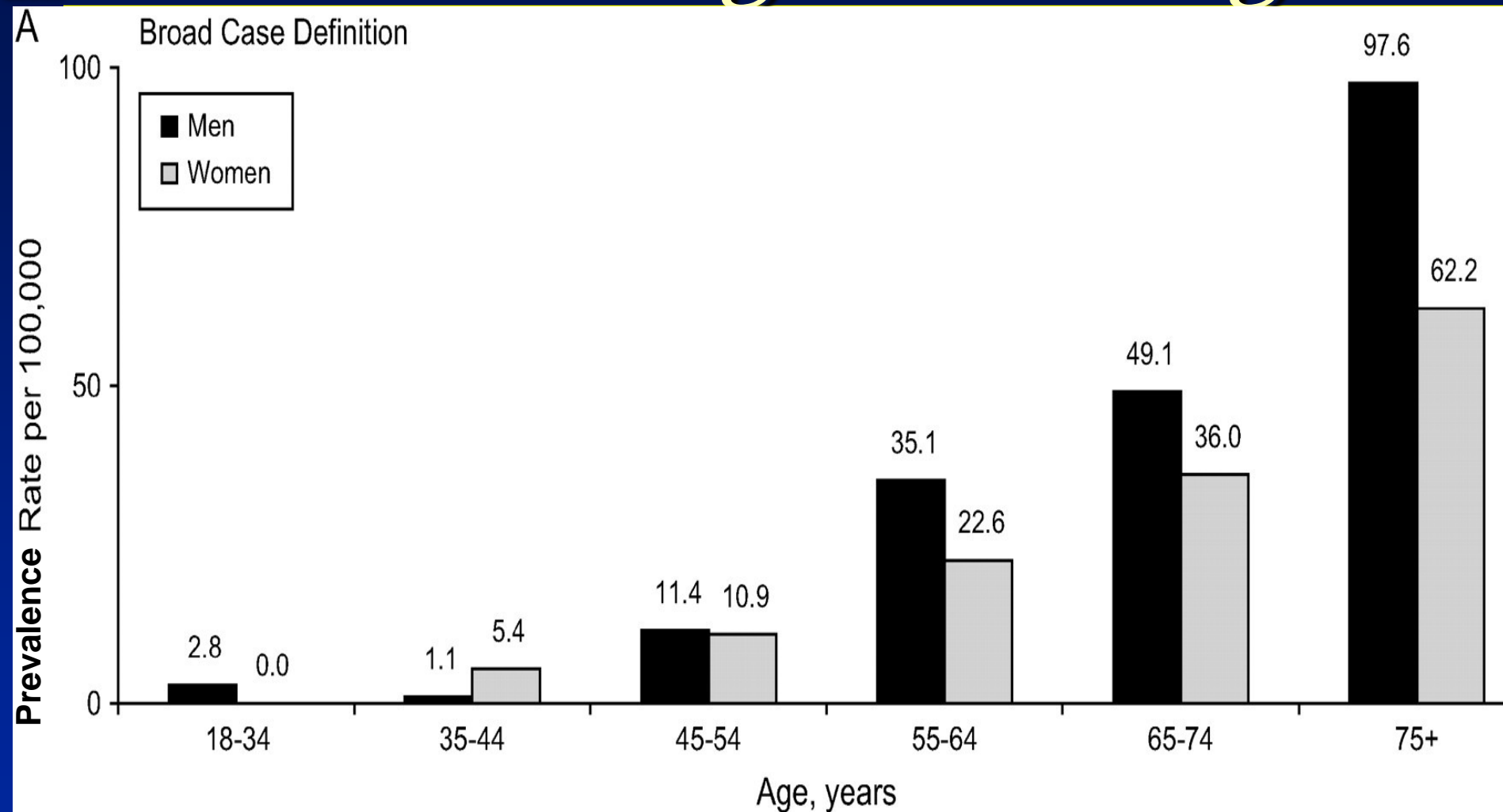
◆ Diarrhea, nausea

# Interstitial Lung Disease #2

- ◆ 72 yo retired executive
- ◆ Preop for prostate resection
- ◆ Lung exam – crackles
- ◆ CT chest
- ◆ PFTs
  - *FVC 75% predicted*
  - *Ex oximetry*
    - ◆ 96% at rest and after 3 min walking



# Interstitial Lung Dis and Age

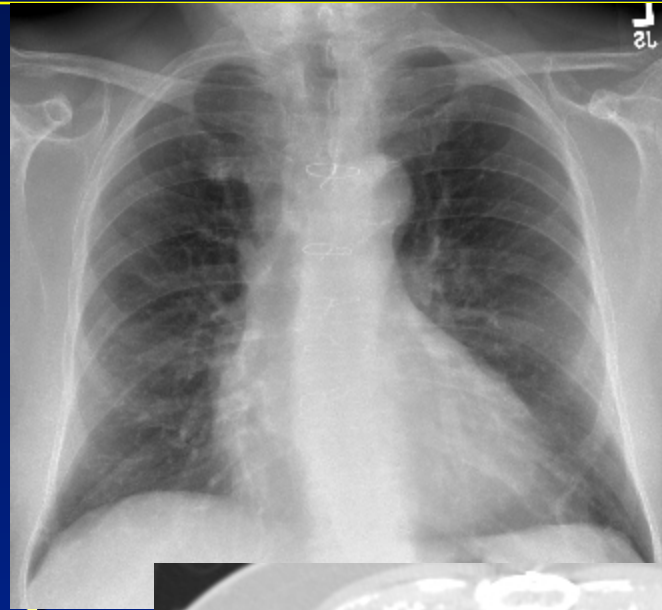


Raghu, G, et al *Am J Respir Crit Care Med* 2006;174,810-816



# ILD #3: Known ILD, new SOB

- ◆ Retired teacher, no exposures
- ◆ Distant smoking
- ◆ Repeat spirometry
  - *FVC 2.2L, 65% pred*
- ◆ Stable for >2 yrs
- ◆ Now dyspnea for the past 3-6 mos



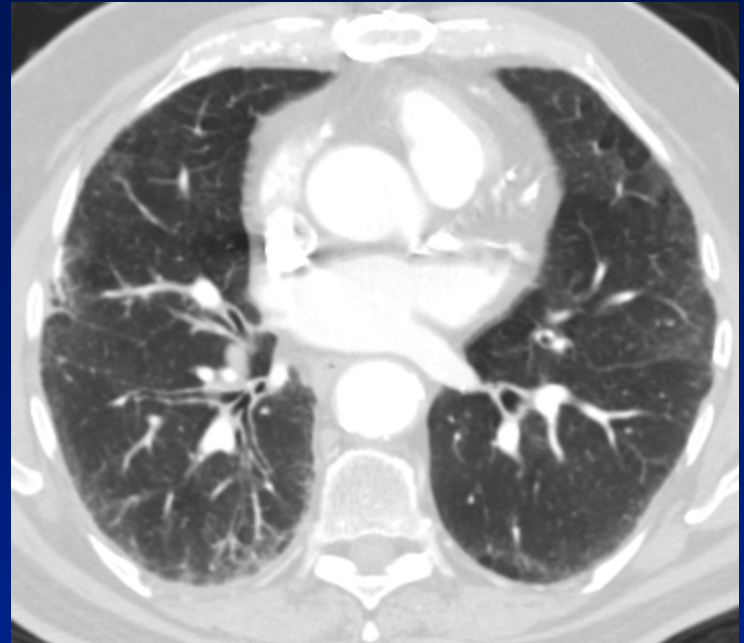
# *Interstitial Lung Disease*

- ◆ **Dyspnea in a patient with interstitial disease - not always the crackles....**
  - *IPF with progression*
  - *CAD, CHF*
  - *Pulmonary embolism*
  - *Pulmonary HTN*
  - *Lung cancer*



# 81 yo man with ILD, new SOB

- ◆ FVC 2.2L, 65% pred.
  - *Stable PFT*
- ◆ Cardiac cath
  - *Severe 3 vessel CAD*



# Conclusions: COPD

## ◆ Severity and Prognosis

- *Uncertainty and Dangerous Myths*
- *FEV1 + Functional Status (BODE score) + Exacerbations*

## ◆ 1<sup>st</sup> inhaler – long-acting anti-muscarinic

## ◆ Get w/ Guidelines – Spirometry ... [CAD?]

## ◆ Recurrent exacerbations

- *Triple inhaler therapy, caution on azithro, magic pills*
- *Not always COPD – Bronchiectasis, CAD, CHF*

## ◆ Acute exacerbation

- *Rationale for steroids + antibiotics*
- *Consider other causes – PE, CHF, CAD*

# Conclusions: Interstitial lung disease

- ◆ Look for the treatable/reversible alternative diagnoses
  - *Vasculitis? BOOP?*
  - *Hypersensitivity pneumonitis/drugs?*
- ◆ Recurrent injury
  - *GERD mgt, NOT steroids*
- ◆ Idiopathic pulm fibrosis (IPF)
  - *Prostate CA paradigm...in some cases*
  - *New good treatments – eg pirfenidone*
  - *ILD w/ dyspnea – could be CV disease?*

