COPD and Early Interception of Lung Cancer

George Washko MD
Division of Pulmonary and Critical Care Medicine
Brigham and Women’s Hospital
Screening for Lung Cancer and Finding Disease
Disclosures

• **Consultancies**: GlaxoSmithKline, Boehringer Ingelheim, Genentech, PulmonX

• **Quantitative Imaging Solutions**: Consulting group and software development for data management

• **Grants**: NIH, Boehringer Ingelheim (characterization of parenchymal disease in smokers), BTG, Janssen

• **Spouse**: Works for Biogen which is developing therapies for pulmonary fibrosis
How to leverage LDCT data?

• The majority of patients undergoing screening will not have cancer

• What other clinically actionable data is in the image?

• How can disease detection inform lung cancer screening?
Chronic Bronchitis

Emphysema
Broad range of disability for any FEV₁
COPD = \sum \text{comorbidities}
Applications of Imaging

- Airway Disease
- Parenchymal Disease
- Vascular Disease
- Extra-Pulmonary
Bronchiectasis, AECOPD and Inflammation in COPD

(AJRCCM 2004; 170:400-407)

- 54 Patients with COPD
- Mean FEV1 38%
- HRCT
- Self reported AECOPD by diary
- Bronchiectasis associated with higher levels of inflammatory cytokines and prolonged recovery
Bronchiectasis and mortality in COPD

- Prevalence of bronchiectasis 57% (cohort n=201)
- Bronchiectasis associated with increased risk of death HR 2.54

Martinez-Garcia, et al. AJRCCM 2013
Quantification of emphysema on chest CT

NETT Results: Mortality
Upper-lobe disease and low exercise capacity

Probability of death

P = 0.005
RR = 0.47

High-risk patients excluded

NEJM 348:2059-73, May 22, 2003
Decline in Lung Function

- 279 Patients with COPD & CT
- Multiple logistic regression demonstrated that rapid decliners were independently associated with emphysema severity

Nishimura, et al. AJRCCM 2012; 185:44-52
Smoking Related Lung Disease

Emphysema/COPD  ↔  Overlap  ↔  Pulmonary Fibrosis

Academic Radiology 2010
NEJM 2011
Figure 3. Mortality Rates by ILA Status for the Framingham Heart Study, AGES-Reykjavik, COPDGene, and ECLIPSE Studies

**Framingham Heart Study**
- HR (95% CI), 2.7 (1.1-6.5); P = .03
- Mortality, %
- No. at risk
  - ILA: 177, 176, 171, 170, 107
  - No ILA: 1370, 1367, 1364, 1361, 1022

**AGES-Reykjavik Study**
- HR (95% CI), 1.3 (1.2-1.4); P < .001
- Mortality, %
- No. at risk
  - ILA: 378, 365, 343, 328, 304
  - No ILA: 3216, 3177, 3124, 3044, 2956

**COPDGene Study**
- HR (95% CI), 18 (1.1-2.8); P = .01
- Mortality, %
- No. at risk
  - ILA: 156
  - No ILA: 1173

**ECLIPSE Study**
- HR (95% CI), 1.4 (1.1-2.0); P = .02
- Mortality, %
- No. at risk
  - ILA: 156
  - No ILA: 528

Putman et al. JAMA 2016; 315(7):672-81.
Cardiac Dysfunction
Biventricular Morphology
**COPDGene**

- 262 smokers from National Jewish Health

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**Figure 1:** The right ventricle (blue) and left ventricle (red) in three subjects with a cardiac model fitted to the surface of the heart using volumetric non-contrast CT scan. A subject with Gold 0 disease and with an RV/LV ratio of 0.5, RVSP of 20 and no evidence of ventricular dysfunction (A), A subject with Gold 3 disease an RV/LV ratio of 0.8, RV dilation, elevated RVSP of 47 (B), and a subject with Gold 2 disease with LV dilation and ejection fraction of 35%.
Self reported physician diagnosed outcomes

(A) RVSP

Model:
RV Volume, Age, Gender;
RV Volume * Gender

Area under ROC curve = 0.7692

(B) RV Failure

Model:
RV Volume, Age, Gender;
Age * RV Volume

Area under ROC curve = 0.7600

(C) LV Failure (EF < 55%)

Model:
LV Volume, BMI, Gender;
LV Volume * Gender;
BMI * Gender

Area under ROC curve = 0.7274

(D) CHF

Model:
Total Ventricular Volume, BMI

Area under ROC curve = 0.8008
Cardiac Morphology and Response to Beta Blockers

Bhatt et al, AJRCCM 2017
Body Composition

FEV1 35% Predicted

FEV1 35% Predicted
Body Composition – Multisite Assessment
Mid Thigh Muscle Cross Sectional Area

N=142

Independent covariates:

- Age
- Sex
- BMI
- FEV1
- DLCO
- PaO2 and PaCO2

**TABLE 3. PREDICTORS OF MORTALITY: MULTIVARIATE ANALYSIS**

<table>
<thead>
<tr>
<th></th>
<th>Hazard Ratio</th>
<th>95% CI</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MTCSA$_{CT}$ &lt; 70 cm$^2$</td>
<td>3.68</td>
<td>1.52–8.09</td>
<td>0.0038</td>
</tr>
<tr>
<td>FEV$_1$ &lt; 50% predicted</td>
<td>4.78</td>
<td>1.12–20.34</td>
<td>0.0342</td>
</tr>
</tbody>
</table>

*Definition of abbreviations: CI = confidence interval; MTCSA$_{CT}$ = midthigh muscle cross-sectional area obtained by CT scan.*

Marquis et al AJRCCM 2002
Bone Mineral Density

N=3321 current and ex-smokers in COPDGene

Low volumetric bone mineral density (vBMD)

- 58% of all subjects
- 84% of very subjects with very severe COPD

Males had greater risk of low vBMD (-2.5 SD below young adult mean by QCT)

Males with more vertebral fractures

Jaramillo et al. Annals of ATS 2015
Informing Patient Care

- Identification of patients at high risk for adverse events/poor outcomes
- Opportunity for multidisciplinary care coordination
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Questions?
1. Biphasic CT Acquisition
   Inspiration CT (HU)

2. Image Processing
   (Segmentation and Spatial Alignment)
   Joint Density Histogram of Aligned CT Images

3. Classification Model
   - fSAD
   - Normal
   - Emphysema

Expiration CT (HU)

Spatial Visualization


Slide courtesy of M. Han