



COPD: What's New with Diagnosis and Treatment?

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Learning Objectives

- Describe best practices for the diagnosis of COPD
- Compare various treatment options to determine the best choice for an individual patient
- Appraise the latest evidence for diagnosis and management of COPD to determine if a practice change is warranted.

Epidemiology

- COPD projected to be the third leading cause of death worldwide by 2020¹
 - Cause of death of 3 million people 2012
 - 6% of all death globally
- Fifth leading cause of disability
- Chronic obstructive pulmonary disease accounts for 3.2% of all physician office visits annually²²

Quality of life³³

- Cross-sectional, prospective, observational study of 100 patients in Poland
- Quality of life higher in
 - Younger patients
 - Patients with higher levels of education
- No impact of gender, smoking, weight

COPD and Suicide

- COPD patients are 1.9 times more likely to commit suicide than people without COPD²⁹

The GOLD Method for Diagnosis

- Consensus opinion based upon literature
- Utilizes both spirometry and symptom assessment

GOLD Guidelines

- Global Initiative for Chronic Obstructive Lung Disease
- Initiated in 1998 by National Heart, Lung and Blood Institute
- Focus attention on the management and prevention of COPD

GOLD Guidelines

- Expert consensus document
- Diverse areas of interest- socioeconomics to education
- PubMed search of relevant literature for each update
- Most current recommendations published Nov 2018
 - Literature current through July 2018

Diagnosis

- History and physical exam findings should prompt consideration of spirometry
- Spirometry required for diagnosis
 - FEV₁/ FVC ratio of <0.70 with appropriate clinical context

Diagnosis

- Dyspnea
 - Progressive over time
 - Typically worse with exercise
 - Persistent
- Chronic cough
 - Productive of sputum not required for diagnosis, though sputum production in any pattern suggestive
- Recurrent respiratory infections
- Exposure to risk factors
- Family history of COPD

Risk Factors for COPD in US

- Tobacco smoke
 - Greater mortality than non-smokers²
- Pipe, Cigar and Marijuana smoke³
- Environmental smoke exposure⁴
- Occupational exposures⁵
- Genetic factors
- Asthma
- History of severe infections
- Poor lung development esp. associated with low birth weight

Marijuana and COPD³⁹

- Increases risk of COPD
- Few long term studies exist
- Occurs by increasing forced vital capacity
 - Rather than decrease in FEV₁
 - Likely due to acute bronchodilator effects
- Increased risk of bullae formation and barotrauma

Low birth weight and COPD⁴⁰

- Review of 16 studies of 69,365 individuals
- Increased risk of COPD with
 - Tobacco exposure in utero and early life
 - Low birth weight
 - Asthma as child

Socioeconomic Risk Factors

■ Indoor air pollution

- Women particularly who are exposed to wood burning in poorly vented dwellings⁵

■ Poverty^{6,7}

- Higher risk of developing
 - Unclear if pollutant exposure, poor nutrition or increased infection risk is the cause

Should we screen patients with risk factor?

- Probably not
 - History and physical examination findings should prompt spirometry
 - Tobacco use, alone, for instance shouldn't prompt screening
- Most groups do not recommend
 - ACP, GOLD, USPSTF

Diagnosis of COPD

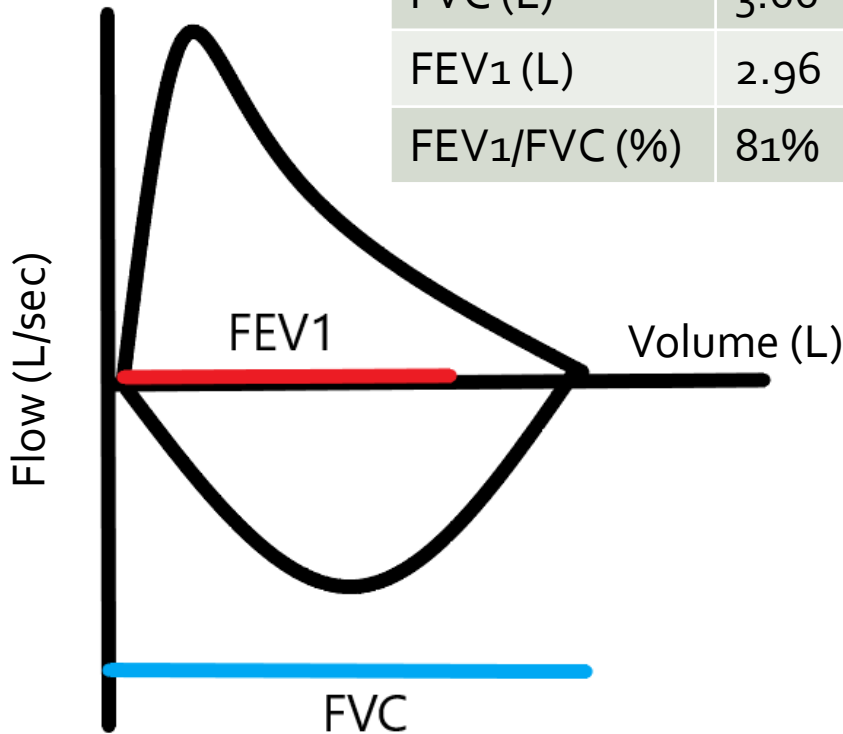
- Assess with spirometry ($FEV_1/FVC < 0.7$)
- Determine grade with GOLD 1-4 Classification
- Determine ABCD score

Spirometry Review

- Forced vital capacity (FVC)
 - Total volume of air exhaled during a maximal forced expiration effort
- Forced expiratory volume in 1 second (FEV1)
 - Volume of air exhaled in the first second after a maximal inhalation
- FEV1/ FVC ratio
 - Percentage of FVC expired in one second

Spirometry Review

	Predicted	Best	% of Predicted
FVC (L)	3.66	3.14	86%
FEV ₁ (L)	2.96	2.12	72%
FEV ₁ /FVC (%)	81%	68%	



Spirometry

- Useful, but not sufficient alone
- Useful for characterizing airflow limitation
- Does not correlate with impairment ^{9, 10}
- Perform to categorize patient COPD severity from an airflow perspective

Spirometry

	Category	FEV ₁
GOLD 1	Mild	FEV ₁ ≥ 80% Predicted
GOLD 2	Moderate	50% ≤ FEV ₁ ≤ 80% Predicted
GOLD 3	Severe	30% ≤ FEV ₁ ≤ 50% Predicted
GOLD 4	Very Severe	FEV ₁ ≤ 30% Predicted

Post Bronchodilator Measurements in Patients with FEV₁/FVC < 0.70

Diagnosis of COPD

- Assess with spirometry ($FEV_1/FVC < 0.7$)
- Determine grade with GOLD 1-4 Classification
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Symptom Severity Assessment

- COPD Assessment Test (CAT) Recommended¹¹
 - Includes dyspnea symptoms and others
 - Likert style (0-5) questions addressing
 - Cough
 - Mucus production
 - Chest tightness
 - Breathlessness with exercise
 - Activity limitation
 - Confidence in leaving home
 - Sleep
 - Energy
 - Total Score 0-40

ABCD Assessment Tool

	CAT < 10	CAT ≥ 10
0-1 exacerbations, 0 hospital admissions	A	B
More than 2 exacerbations or more than 1 hospital admission	C	D

GOLD 1-4 and ABCD

- Why does this matter?
 - Guides therapy
 - Provides a way to monitor disease progression
 - May help studies clarify treatment effectiveness

After the diagnosis

- Screen patients once for alpha-1 antitrypsin deficiency⁸
 - Less than 20% normal is suggestive of deficiency

Treatment- Goals

- Reduce hospitalizations
- reduce exacerbations
- decrease dyspnea
- improve quality of life
- slow disease progression
- reduce mortality

Treatment Strategy

- Reduce Risk
 - Tobacco cessation counseling
- Implement initial treatment
- Assess symptoms and exacerbations
- Review inhaler technique
- Escalate or de-escalate as needed
- Consider pulmonary rehabilitation, nutrition, psychosocial support
 - Improves symptoms, but underutilized²²

Smoking Cessation

- Important first line treatment recommendation
- Remember to use pharmacotherapy as well as structured support
- Spirometry with lung age may help encourage cessation⁴¹

Smoking Demographics³⁴

- Data from the 2011 U.S. National Health and Wellness Survey (n = 50,000).
- In 2011, 18% of US adults were current smokers
 - 27% of current smokers were attempting to quit
- Current smokers more likely to:
 - Be poor
 - Be non-Hispanic white
 - Have less education
 - Be uninsured
 - Demonstrate fewer health conscious behaviors like regular exercise, vaccination

Rural Tobacco Use in Adolescents³¹

- National Youth Tobacco Survey data from 2011-2014
- Adults and adolescents in rural areas more likely to be tobacco users
 - E-cigarette use increasing everywhere (0.82% of youth age 11-17 in 2011, 8.62% in 2014)
 - Cigarette taxes, advertisement exposure and location predict adolescent smoking
- May see less urban-rural disparity with e-cigarette use

Tobacco cessation and Social Determinants³⁰

- Homeless smokers in Boston April 2014-July 2014 (N=306)
- Subsistence difficulties defines as difficulty finding shelter, food, clothing, wash space, bathroom facility
- Increased subsistence difficulty associated with more perceived barriers to quitting smoking
 - No association with cessation readiness or confidence
 - Less likely to remain abstinent once quit (OR=0.33)

Smoking cessation prescriptions³²

- National Ambulatory Medical Care Survey data from 2007 to 2012
- Average prescription rate of smoking cessation medication (varenicline, bupropion or NRT) over 5 years = 3.64%
- Hispanic race and depression = higher prescription rates
 - Driven by high rate of bupropion prescription

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Bronchodilators

- Beta 2 Agonists and Anti-muscarinics
- Improve quality of life
- Decrease annual rate of FEV₁ decline
- Decrease number of exacerbations

Beta 2 Agonists

- Short acting last 4-6 hours, long acting 12 hours
- Adverse effects: Tachycardia, Hypokalemia
- No association between beta2-agonist use and increased mortality with COPD¹²⁻¹⁴

Common Medications

Generic Name	Trade Name	Class
Levalbuterol	Xopenex	Short acting beta agonist
Albuterol		Short acting beta agonist
Terbutaline	Brethine	Short acting beta agonist
Arformoterol	Brovana	Long acting beta agonist
Formoterol	Foradil	Long acting beta agonist
Indacaterol	Arcapta	Long acting beta agonist
Olodaterol	Striverdi	Long acting beta agonist
Salmeterol	Serevent	Long acting beta agonist

Antimuscarinics

- Block bronchoconstriction effects on smooth muscles
- Adverse effects: Dry mouth, urinary symptoms?
- Tiotropium improves health status, symptoms, effectiveness of pulmonary rehabilitation and reduce exacerbations and hospitalizations¹⁶⁻¹⁸

Common Medications

Generic Name	Trade Name	Class
Ipratropium bromide	Atrovent	Short acting antimuscarinic
Aclidinium bromide	Tudorza	Long acting antimuscarinic
Glycopyrrolate	Seebri	Long acting antimuscarinic
Tiotropium	Spiriva	Long acting antimuscarinic
Umeclidinium	Incruse Ellipta	Long acting antimuscarinic

Methylxanthines

- Narrow therapeutic window
- Adverse effects common
- Monitoring needed
- If trying, should discontinue if no improvement in several weeks of therapy

Phosphodiesterase 4 inhibitor

- Patients with severe or refractory symptoms
- Decreases exacerbations
- No improvement in quality of life or overall symptoms

Common Medications

Generic Name	Trade Name	Class
Aminophylline		Methylxanthine
Theophylline		Methylxanthine
Roflumilast	Daliresp	Phosphodiesterase 4 inhibitor

Combination Medications

Medication #1	Medication #2	Medication #3	Trade Name
Salbutamol	Ipratropium bromide		Combivent, DuoNeb
Formoterol	Glycopyrrolate		Brevespi Aerosphere
Indacaterol	Glycopyrrolate		Utibron
Vilanterol	Umeclidinium		Anoro Ellipta
Olodaterol	Tiotropium		Stiolto Respimat
Formoterol	Budesonide		Symbicort
Formoterol	Mometasone		Dulera
Salmeterol	Fluticasone		Advair
Vilanterol	Fluticasone furoate		Breo Ellipta
Fluticasone	Umeclidinium	Vilanterol	Trelegy

Inhaled Steroids and Pneumonia²³

- Review of 43 studies
- Typical patient was male, mean age of 63 with 40 pack year smoking history and FEV₁ less than 50% predicted
- Increase noted in non fatal pneumonia events with use of fluticasone or budesonide alone or in combination with a long acting beta agonist
 - OR= 1.78, 95% CI 1.50-2.12
- Increase in pneumonia, though no change in mortality as a result

Initial Treatment Recommendations

	CAT < 10	CAT ≥ 10
0-1 exacerbations, 0 hospital admissions	A: Bronchodilator (short or long acting)	B: Long acting bronchodilator (antimuscarinic or beta 2 agonist)
More than 2 exacerbations or more than 1 hospital admission	C: Long acting anti-muscarinic	D: 1) Long acting antimuscarinic 2) If highly symptomatic- Long acting antimuscarinic and long acting beta agonist 3) If high eosinophils, inhaled corticosteroid and long acting beta agonist

Initial Treatment Recommendations- Example

	CAT < 10	CAT ≥ 10
0-1 exacerbations, 0 hospital admissions	A: Albuterol	B: Salmeterol (Serevent) or Tiotropium (Spiriva)
More than 2 exacerbations or more than 1 hospital admission	C: Tiotropium (Spiriva)	D: 1) Tiotropium (Spiriva) 2) Vilanterol/Umeclidinium (Anoro Ellipta) 3) Formoterol/budesonide (Symbicort)

Treatment Strategy

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Inhaler Technique Matters

- Incorrect technique may be more than 53%⁴²
- Incorrect technique associated with higher symptoms score, increased cough, worse FEV₁⁴²
- Patients may make errors up to 20% of the time with inhaler⁴³
 - Of 60 expected doses, patient actually received 34 correctly on average in one study⁴³

Treatment Follow Up

- If initial treatment is working- continue it
- If treatment is not working, clarify
 - Dyspnea increased?
 - Increased exacerbations?
 - Both?
- Remember to vaccinate

Dyspnea- Escalating Treatment

- LAMA or LABA
 - Add the other agent
- LAMA and LABA
 - Switch inhaler device, molecule or treat other causes of dyspnea
- LABA and ICS
 - Add LAMA
- LAMA, LABA and ICS
 - Switch inhaler device, molecule or treat other causes of dyspnea

Dyspnea- De-escalating Treatment

- LABA and ICS
 - LABA and LAMA
- LAMA, LABA and ICS
 - LABA and LAMA

Exacerbations- Escalating Treatment

- LAMA or LABA
 - LABA and LAMA
 - LABA and ICS
- LAMA and LABA
 - Add ICS
 - Consider roflumilast if $FEV_1 < 50\%$ and chronic bronchitis
 - Consider azithromycin for 1 year in daily smokers
- LABA and ICS
 - Add LAMA
- LAMA, LABA and ICS
 - Consider roflumilast if $FEV_1 < 50\%$ and chronic bronchitis
 - Consider azithromycin for 1 year in daily smokers

Exacerbations- De-escalating Treatment

- LABA and ICS
 - Add LAMA and remove ICS
- LAMA, LABA and ICS
 - Remove ICS

Medication side effects³⁸

- COPD medications may increase risk of diabetes
- Analysis of 15,287 patients with COPD free of diabetes at baseline
 - 6.3% of population diagnosed with new onset diabetes during study
- Increased risk if individual using inhaled corticosteroids alone or in combination with statins or statins and antidepressants

COPD and Lung Cancer²⁰

- Meta-analysis of COPD associated with 5 year overall survival of lung cancer
 - Articles published before September 30, 2017
 - 29 studies, 70,111 patients
- Presence of COPD indicates poor survival for patients with lung cancer

Oxygen Therapy²⁵

- Oxygen does improve dyspnea and fatigue for those with moderate hypoxia
- Does ambulatory oxygen help patients who otherwise don't meet criteria for long term oxygen therapy?
 - Four studies of 331 participant
 - No clear evidence to suggest that mortality or exercise capacity improve

Treatment Strategy

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Pulmonary rehabilitation

- Strength and endurance training
- Educational, nutritional and psychosocial support
- Improves symptoms
- Improves exercise tolerance
- Very underutilized even in areas where readily available

Pulmonary Rehabilitation and Social Determinants²⁶

- Pulmonary rehabilitation adherence is generally low
- Study of adherence rates by social determinants found that
 - Low adherence increased with limited functional capacity and current smoking
 - Less than 35% of sessions attended
 - Moderate adherence increased with socioeconomic disadvantage
 - 35-85% of sessions attended
 - High adherence in groups with higher socioeconomic standing, non-smokers and higher functional capacity

Potential Biomarker²¹

- 17 patients enrolled in study to isolate circulating pulmonary cells in peripheral blood
 - 6/17 had cells whereas no healthy volunteers had cells
 - Increased circulating pulmonary cells suggested increased severity of COPD
- Potential biomarker for severity?

Managing Exacerbations

- Acute worsening of respiratory symptoms requiring additional therapy
 - Mild- Treated with short acting bronchodilators only
 - Moderate- Add antibiotics and/ or oral corticosteroids
 - Severe- Add hospitalization or visit to ER
- Most (80%) can be managed on outpatient basis⁸

Interventions that Reduce Exacerbation Frequency

- Long acting beta 2 agonists
- Long acting antimuscarinics
- Long acting beta 2 agonists combined with inhaled corticosteroids
- Triple therapy (LABA, LAMA and ICS)
- Roflumilast
- Vaccines
- Long term macrolide therapy
- Smoking cessation
- Lung rehabilitation

Does Heliox help exacerbations?²⁴

- Heliox has low density which may decrease work of breathing
- Four studies reviewed (1997-2000)
 - Data obtained for 69 patients
 - Not significant change noted in FEV₁ or FVC when heliox used
- Insufficient evidence to justify use of Heliox. May benefit from additional studies in avoidance of mechanical ventilation

Prolonged antibiotics for COPD²⁸

- RCT of hospitalized patients with COPD
 - Inclusion criteria
 - Greater than 10 pack year history, more than 1 exacerbation in the prior year
 - Control group (n=154)
 - Acute treatment of steroids and antibiotics
 - Study group (n=147)
 - 500mg/ day for 3 days of azithromycin plus 250mg BID for 3 months
 - Azithromycin group
 - Longer time to first re-hospitalization
- Azithromycin as a prolonged course may reduce re-hospitalization

Length of Stay and Readmission³⁵

- Observational study of 33,558 veterans admitted to 130 VA hospitals 2008-2011
- Increased length of stay in hospital increases patient risk for readmission, not association at hospital level

Do residents make a difference?³⁷

- Orlando community teaching hospital patients
January 2011-2014
- 1419 patients, 306 on teaching service, 1113 on
non-teaching service
- Teaching service
 - Lower cost per patient
 - Shorter length of stay
 - Less consultant use
 - No change in mortality or readmission

Medicaid Expansion Impact³⁶

- Does having access to care through Medicaid increase diagnosis rates?
- 2011-2015 Behavioral Risk Factor Surveillance System data
- 521,622 respondents
 - Diagnosis of COPD did not change with expansion
 - Lack of health insurance decreased from 32% to 21%, diagnosis of COPD was unchanged
 - Diagnosis of COPD= 7% in Medicaid expansion states, 8% in non-expansion states

Do we follow GOLD?¹⁹

- Retrospective chart review from 2 community clinics (n=101 patients)
 - No use of validated measures of dyspnea such as CAT
 - Only 21% had formal spirometry done
 - OF those with spirometry 31.5% were incorrectly diagnosed with COPD
 - Varied therapies not following GOLD guidelines
 - 42% of patients who qualified on long acting muscarinic inhalers

Questions?

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