


COPD UPDATES FROM GOLD REPORT 2022


AND THERAPEUTIC PERSPECTIVES RELATIVE TO PRIMARY CARE

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WHAT IS COPD

- **Definition**
 - Now one of the 3 most common causes of the death world wide
 - Projected to increase with older generations
 - A chronic, progressive, often treatable disease that reduces the lungs ability to move air into or out of the lungs, or further alter the ability of oxygen to reach the blood.
- **From a primary care perspective**
 - Causes
 - Management



CONTRIBUTING FACTORS

- **Genetics**
 - Alpha-1 antitrypsin – inhibits serine proteases affecting elastin in lung tissues
 - Matrix metalloproteinase 12 (MMP-12) , glutathione S-transferase
 - Nrf2 – regulate antioxidants
 - Gender
- **Lung Growth / Development**
- **Environmental Exposures**
 - Tobacco / marijuana / inhalants
 - Occupational fumes / chemicals
 - Wood / coal / biomass burning
- **Infections or other lung injury**

PATHOGENESIS

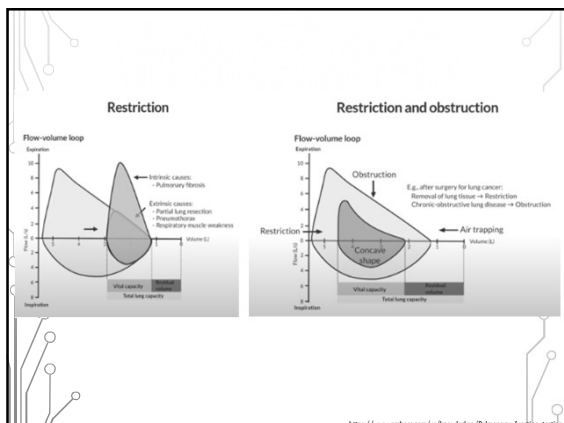
- Inflammatory process (outside cause or inside dysregulation)
 - Oxidative stress
 - Inflammatory cells
 - Inflammatory mediators shown to be increased in COPD patients
 - Induce structural changes
 - Fibrotic changes
 - Limits small airways

PATHOGENESIS

- Inflammation, fibrosis, exudates
- 1. Airflow limitations
 - Reduce FEV1 and FEV1/FVC ratio
 - Peripheral airway traps gasses and cause hyperinflation
 - Changes in ability to move gas in or out
- 2. Gas exchange
 - Less movement of gasses
 - Limited ventilation by muscle impairment or drive
 - Reduced alveolar surface area or capillary diffusion distance – VA/Q = Ventilation perfusion ratio
- Mucus Hypersecretion (not all)
 - More goblet cells with enlarged submucosal glands
 - Many changes are due to epidermal growth factor receptor
- Pulmonary Hypertension (not all)
 - Vascular remodeling, increased smooth muscle

CHRONIC OBSTRUCTIVE PULMONARY DISEASE

<https://annietseng.net/work/pathology/>



CHEST X-RAY

- Not generally useful in diagnosis of COPD.
- Does help rule out alternative diagnosis
 - Identify other consolidations, infections, lung cancers, fibrotic changes, fluid accumulations
 - Pleural/cardiac abnormalities, costal margin changes,
 - Also could help show progression over time.

DIAGNOSIS ESTABLISHED

- Grade of severity
- Choosing therapies

Spirometrically confirmed diagnosis

→

Assessment of airflow limitation

→

Assessment of symptoms/risk of exacerbations

Post-bronchodilator
 $FEV_1/FVC < 0.7$

	FEV ₁ (% predicted)
GOLD 1	≥ 80
GOLD 2	50-79
GOLD 3	30-49
GOLD 4	< 30

Exacerbation history
 ≥ 2
 or
 ≥ 1 leading to hospital admission
 or
 0 or 1 (not leading to hospital admission)

C	D
A	B

mMRC 0-1	mMRC ≥ 2
CAT < 10	CAT ≥ 10

Symptoms

GRADING SCALES

- mMRC
 - Quickly evaluate a change in breathing status
- CAT Score
 - 8 question evaluation of symptom control
 - Each question scale 0 – 5
- St George's Respiratory Questionnaire (SGRQ)
 - 14 question evaluation
 - >25 is generally cut off for poorly controlled

MMRC EVAL

- Quick evaluation
- Easy to place into GOLD Category
- Score of 0-1 = A or C
- Score >2 = B or D

Description of Breathlessness	Grade	Score
I only get breathless with strenuous exercise	0	None
I get short of breath when hurrying on level ground or walking up a slight hill	1	Slight
On level ground, I walk slower than people of the same age because of breathlessness, or have to stop for breath when walking at my own pace.	2	Moderate
I stop for breath after walking about 100 yards or after a few minutes on level ground.	3	Severe
I am too breathless to leave the house or I am breathless when dressing.	4	Very severe

CAT SCORE

How is your COPD? Take the COPD assessment test™ (CAT)

The questionnaire will help you and your healthcare professional measure the impact COPD (Chronic Obstructive Pulmonary Disease) is having on your well-being and daily life. Your answers, and the scores, can be used by you and your healthcare professional to help improve the management of your COPD and get the greatest benefit from treatment.

For each item below, place a mark (X) in the box that best describes you currently. Be sure to only select one response for each question.

Example: I am very happy I am very sad

Score

I never cough I cough all the time

I have no phlegm (mucus) in my chest at all My chest is completely full of phlegm (mucus)

My chest does not feel tight at all My chest feels very tight

When I walk up a hill or one flight of stairs I am not breathless When I walk up a hill or one flight of stairs I am very breathless

I am not limited doing any activities at home I am very limited doing activities at home

I am confident leaving my home despite my lung condition I am not at all confident leaving my home because of my lung condition

I sleep soundly I don't sleep soundly because of my lung condition

I have lots of energy I have no energy at all

Total score

- More in-depth
- Score of <10
 - = A or C
- Score >10
 - = B or D

PREVENTATIVE MEASURES OF EXACERBATION

- Smoking
 - Greatest contributor to risk in developing or worsening COPD worldwide.
 - E-Cigarettes
- Avoid other Irritants
 - Fumes, chemicals, allergens, etc.
- Pharmacologic intervention
 - Bronchodilators, inflammatory mediators
- Inhaler technique
- Vaccination
 - Flu, Covid-19, Pneumococcal
- Exercise

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MEDICATION CHOICE

- Bronchodilators by Beta Sympathomimetic Nerve Modulation
 - SABA
 - LABA
- Muscarinic Antagonists
 - LABA
 - LAMA
- Inhaled Corticosteroid

≥ 2 moderate exacerbations or ≥ 1 leading to hospitalization	Group C LAMA	Group D LAMA or LAMA + LABA* or ICS + LABA**	*Consider if ICS exacerbations (e.g. CAT ≥ 20) **Consider (Table 3.3B)
0 or 1 moderate exacerbations (not leading to hospital admission)	Group A A Bronchodilator	Group B A Long Acting Bronchodilator (LABA or LAMA)	
	mMRC 0-1, CAT < 10	mMRC ≥ 2, CAT ≥ 10	

10/18/22, A. 3. GOLD REPORT 2022

BETA

- 1 heart / 2 lungs
- Selective vs Non-selective
- COPD Drugs = agonist = relax smooth muscle
- Heart drugs = antagonist = block message to increase heart rate
- *** At high enough dose even selective drugs are non-selective

BETA EFFECTS

- If reactive airway, will have greater change in FEV1
- SABA
 - Best response by nebulizer
 - Lasts a maximum of 4 to 6 hours
 - Ex: Albuterol
 - Frequent dosing in stable disease not recommended due to higher chance to have beta 1 overflow.
- LABA
 - Lasts 12-24 hours or longer
 - Formoterol / salmeterol – 12 hours
 - Olodaterol / vilanterol – once daily
 - Preferred over frequent SABA use
 - May use supplemental SABA with less risk for overflow

LABA SIDE EFFECTS

- Sinus tachycardia or rhythm disturbances if over used
 - Increase beta 1 stimulation
- Worsened somatic tremor
- Hypotensive symptoms – vasodilation from smooth muscle relaxation
- Hypokalemia – worse with thiazides

MUSCARINIC ANTAGONIST

- Block bronchoconstriction from acetylcholine receptors on M3 muscarinic on airway smooth muscles
- Block inhibitory M2 receptors on vagal induced bronchoconstriction
 - Can help cough
- Long acting formulations bind to M3 longer than M2
- SAMA
 - Ipratropium, oxitropium
- LAMA
 - Tiotropium, Umeclidinium – once daily
 - Glycopyrrolate
 - Adclidinium – twice daily
- Multiple studies show LAMA to be better at reducing exacerbation risk as a monotherapy compared to LABA

LAMA SIDE EFFECTS

- Poorly Absorbed so low systemic side effects
- Mostly Dry Mouth
- Ipratropium – sometimes a metallic taste
- If nebulized solution can reach eye, increased risk of acute glaucoma

INHALED CORTICOSTEROIDS

- Most studies have found that using ICS a monotherapy does not improve morbidity or mortality
 - In the TORCH trials was found to have higher mortality than placebo and combination therapies.
- Benefit of treatment is highly dependent on if or the extent to which symptoms are related to a reactive airway

ICS SIDE EFFECTS

- Oral candidiasis
- Upper and lower respiratory infections
- Pneumonia
- Sore throat / voice changes / cough
- Arthralgias / musculoskeletal pain

COMBINATION THERAPIES

- LABA/LAMA
 - Several studies have found this combination reduce exacerbation risk to a greater extent than LABA/ICS in most cases.
 - LABA + LAMA is not a purely additive response; however better than either monotherapy
 - Lower dose twice daily dose has shown greater reduction of symptoms than monotherapies or once daily dosing strategies

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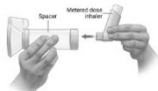

COMBINATION THERAPIES

- LABA/ICS
 - LABA can assist in ICS action and improve response when delivered together
 - Higher eosinophil counts could predict this as a more effective therapy
 - Moderate and severe COPD can show more effect in improving FEV1 and reducing exacerbation frequency and overall risk.
 - However; has not shown significant effect on all-cause mortality in clinical trials.

- STRONG SUPPORT -	- CONSIDER USE -	- AGAINST USE -
<ul style="list-style-type: none"> History of hospitalization(s) for exacerbations of COPD[#] ≥ 2 moderate exacerbations of COPD per year[#] Blood eosinophils >300 cells/µL History of, or concomitant, asthma 	<ul style="list-style-type: none"> 1 moderate exacerbation of COPD per year[#] Blood eosinophils 100-300 cells/µL 	<ul style="list-style-type: none"> Repeated pneumonia events Blood eosinophils <100 cells/µL History of mycobacterial infection

ADMINISTRATION CHOICES

- Metered Dose Inhaler
 - Soft mist inhaler
- Nebulizer
- Dry Powder inhaler
 - Capsules
- Spacers

SINGLE-DOSE DPIs		MULTI UNIT DOSE DPI
Aerolizer	Handihaler	Disalizer
Tandemhaler	Flexhaler	Orbitas Turbuhaler

<https://www.gilead.com/>

INEFFECTIVE MEDICATION

- Check Technique
 - DPI vs MDI
- Check Adherence
 - Taking it as directed
 - Refill history
- Pre-treat with SABA
- Consider alternative cause
 - GERD – Cough
 - SOB – cardiovascular, carbon monoxide, anemia
 - ACEI / ARB related cough

ADDITIONAL THERAPIES


- Methylxanthines
 - Theophylline – not recommended unless other bronchodilators are unavailable
- Oral steroids
 - 5-7 day recommendation during acute exacerbation
- Antitussive agents
 - Benzonatate
 - Dextromethorphan
 - Insufficient evidence to say they offer any benefit
- Phosphodiesterase 4 inhibitors
 - Roflumilast
 - Relaxes smooth muscles in airways by increasing cAMP
 - Augment therapy option if frequent exacerbations while on LABA/LAMA/ICS therapy
 - Especially if eosinophils <100/mcL or FEV1 <50% expected values

ADDITIONAL THERAPIES

- Mucolytics
 - N-Acetylcysteine, carbosysteine
 - Last 12 hours
 - May reduce risk of exacerbation in some populations – thicker mucus tendencies
- Antibiotics
 - Azithromycin or erythromycin
 - Short term therapy can resolve current exacerbation depending on cause
 - Long term therapy can reduce exacerbation
 - Increased risk of bacterial resistance and auditory side effects
- Supplemental Oxygen
 - Long-term use has shown to increase survival of severe patients with chronically poor oxygenation

ADDITIONAL THERAPIES

- **Pulmonary rehab**
 - 6-8 weeks
 - Personalized goals and exercises
 - Walking, incentive spirometry, blowing up balloons
 - Evidence is strongest in moderate to severe disease
 - Strong recommendation for supervised care with use of feedback (or biofeedback i.e. pedometer, phone apps)
 - Education alone has only low to moderate benefit
- **Nutritional Support**
 - Reducing weight on chest
 - Low BMI patients associated with worse outcomes
 - Improving supplementation in malnourished
 - Antioxidant supplementation (Vit C, E, Zinc, Selenium)
 - No evidence Vitamin D had any impact



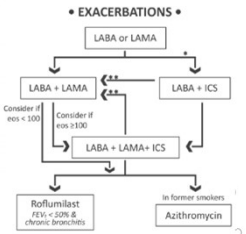
NEWER THERAPIES

- **Antibody therapies**
 - Benralizumab – Anti IL-5 receptor alpha antibody
 - Mepolizumab – Anti IL-5 antibody
 - Reduce eosinophilic activation/proliferation/signaling
 - Studies showed 15-20% reduction in severe exacerbations
 - However not dose dependent and did not relate to laboratory eosinophil count.
 - Further studies needed
 - May find a place in very select population where eosinophil counts are chronically high and have frequent exacerbations or high risk

SUMMARY OF CARE

- **Diagnosis**
- **Initial GOLD Assessment**
- **Management**
- **Review Status**
- **Adjust Therapies**

• EXACERBATIONS •



eos = blood eosinophil count (cells/ μ l)
 * Consider if eos \geq 300 or eos \geq 100 AND \geq 2 moderate exacerbations / 1 hospitalization
 ** Consider de-escalation of ICS or switch if pneumonia, inappropriate original indication or lack of response to ICS

RESOURCES

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