State of the Art: COPD in 2020

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B. Celli Disclaimer

No stocks or ownership in any company.

No Tobacco funds

Advisory boards: GSK, B.I., Astra Zeneca, Novartis, Pulmonx, Chiesi, Menarini.

Member of the Scientific and Executive Committee of GOLD
Agenda

• Describe the COPD landscape in the World
• Smoking, still a problem, but not the only one. The rise of e-injury!
• There are several “natural courses” to develop COPD
• Provide a practical approach to initiate and modify pharmacotherapy in patients with COPD.
• Review the tools available for patients on maximal therapy who remain functionally impaired
• Conclusions
Agenda

• Describe the COPD landscape in the World
www.GBD
Accessed 2/2020

Annual % change 1990-2013
Death 100K persons

Communicable

Injuries
Percent of deaths: 5.36
Annual % change = -1.01
Burden of COPD
Absolute numbers 1990 to 2016

WWW.GBD. Accessed July 2019 (Courtesy Dr. Sundeep Salvi)
Globally 65% Nonsmoking COPD
India 80% Nonsmoking COPD

Tobacco Smoking

SDI: Socio-Demographic Index

www.GBD. Accessed July 2019 (Courtesy Dr. Sundeep Salvi)
Agenda

• Smoking, still a problem, but not the only one. The rise of e-injury!
Smoking: much better but still a problem
E cigarettes

Vaping

Sales in USA in 2018 $ 4.2 billions
EVALI

Electronic Vaping Lung Injury

Harnett K et al NEJM 2020;382:766
E cigarettes

Vaping

Delivers 2 to 10 times the nicotine of regular e-cigarette

Barrington-Trimmings J and Leventhal A NEJM 2018; 379:1099
Juul Pod Mod.
A Juul's pod cartridge resembles a USB drive.
Agenda

- There are several “natural courses” to develop COPD
Course of Lung Function

Determinants of loss

Current smoking
Male
Emphysema
Low BMI
Lower CC16 levels
Higher FEV$_1$

No pharmacological therapy
Exacerbations
Pollution
Poverty

Lange P et al NEJM 2015;372:2
Course of Lung Function

Determinants of gain

Lange P et al NEJM 2015;372:2
Agenda

• Provide a practical approach to initiate and modify pharmacotherapy in patients with COPD.
Bronchodilator responsiveness in COPD

Tashkin D et al  ERJ 2008;31:742
Bronchodilator responsiveness in COPD

FEV$_1$, but not FVC response

Tashkin D et al. ERJ 2008;31:742
St George’s is 3.1 better than placebo and better than baseline

92 ml difference from placebo

25% reduction in exacerbations

TORCH: DB, R, PC, 3 year trial. 6000 patients comparing F, S, SF, P
Outcome: Primary: Mortality   Secondary: FEV1, QoL, Exacerbations

Pneumonia Risk in TORCH

- Older than 55 years
- Lower BMI < 25 Kg/m²
- FEV₁ < 50 % predicted
- Previous exacerbations

Crim C et al ERJ 2009;34:341
UPLIFT: DB, R, PC, 4 year trial. 6000 patients. Tio vs Usual care
Outcome: Primary: FEV1 decline  Secondary: QoL, AE, Mortality

St George’s is 3.3 units better than placebo and better than baseline

110 ml difference from placebo

16% reduction in exacerbations

Tashkin D et al NEJM 2008;359:1543
How to approach?
**Diagnosis**

FEV₁/FVC < 0.7

<table>
<thead>
<tr>
<th>Grade</th>
<th>FEV₁ (% pred.)</th>
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<tbody>
<tr>
<td>1</td>
<td>≥80</td>
</tr>
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<td>50-79</td>
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<td>30-49</td>
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**Assessment of airflow limitation**
Diagnosis

Assessment of airflow limitation

Assessment of symptoms/risk of exacerbations

Exacerbation history

FEV₁/FVC < 0.7

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mMRC 0-1
CAT < 10
CCQ < 1

mMRC 2+
CAT 10+
CCQ 1+

2 or more
1 or more hospitalization

0 or 1
(no hospitalization)
GOLD 2019: **Initial** Pharmacological Treatment

### INITIAL PHARMACOLOGICAL TREATMENT

<table>
<thead>
<tr>
<th>Group C</th>
<th>Group D</th>
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<tbody>
<tr>
<td><strong>≥ 2 moderate exacerbations or ≥ 1 leading to hospitalization</strong></td>
<td><strong>LAMA or LAMA + LABA</strong> or <strong>ICS + LABA</strong></td>
</tr>
<tr>
<td><strong>ΛAMA</strong></td>
<td><strong>A Long-acting Bronchodilator (LABA or LAMA)</strong></td>
</tr>
<tr>
<td><strong>mMRC 0-1 CAT &lt; 10</strong></td>
<td><strong>mMRC ≥ 2 CAT ≥ 10</strong></td>
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Group A

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<td><strong>A Bronchodilator</strong></td>
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Group B

- **ICS**=inhaled corticosteroid; **LABA**=long-acting beta₂-adrenergic agonist; **LAMA**=long-acting muscarinic antagonist.
- *Consider if highly symptomatic (eg, CAT > 20)*
- †Consider if eosinophils ≥ 300

GOLD 2019: FOLLOW-UP PHARMACOLOGICAL TREATMENT

1. IF RESPONSE TO INITIAL TREATMENT IS APPROPRIATE, MAINTAIN IT.
2. IF NOT: ✓ Consider the predominant treatable trait to target (dyspnea or exacerbations)
   - Use exacerbation pathway if both exacerbations and dyspnea need to be targeted
   ✓ Place patient in box corresponding to current treatment and follow indications
   ✓ Assess response, adjust, and review
   ✓ These recommendations do not depend on the ABCD assessment at diagnosis

**DYSPNEA**

**EXACERBATIONS**

*Consider if eosinophils ≥ 300 cells/µL or ≥ 100 cells/µL + ≥ 2 moderate exacerbations or 1 hospitalized exacerbation.
†Consider de-escalation of ICS or switch if pneumonia, inappropriate original indication, or lack of response.
Exacerbations predictors: Post hoc analysis of budesonide in 3 RC COPD trials

Data from 3 RC trials of: B/F versus F alone who had eosinophils measured

N = 4153 patients

FEV$_1$ = 1 L  38% pred

Outcomes:
Exacerbations
FEV$_1$
QoL

Bafadhel M et al Lancet RM 2018;6:117
Make diagnosis and grade risk factors

Initiate Therapy
Supervise inhaler technique and
Check adherence

FEV₁

Symptoms (Dyspnea) and Exacerbations

LAMA

Celli B and Wedzicha J NEJM 2019;381:1257
Make diagnosis and grade risk factors

FEV<sub>1</sub>

Symptoms (Dyspnea) and Exacerbations

Emphysema features
Hyperinflation
Eosinophils <100 cells/µL

Asthmatic features
Wheeze, allergies
Eosinophils >100 cells/µL

LAMA

Initiate Therapy
Supervise inhaler technique and
Check adherence

Celli B and Wedzicha J NEJM 2019;381:1257
Symptoms (Dyspnea) and Exacerbations

FEV₁

Emphysema features
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Eosinophils < 100 cells/µL

Asthmatic features
Wheeze, allergies
Eosinophils > 100 cells/µL

LAMA

Symptom persistence

LAMA+

LABA

Make diagnosis and grade risk factors

Initiate Therapy
Supervise inhaler technique
and
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Celli B and Wedzicha J NEJM 2019;381:1257
Symptoms (Dyspnea) and Exacerbations

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LAMA

Symptom persistence
LAMA+
LABA

LABA+ICS

Make diagnosis and grade risk factors
Initiate Therapy
Supervise inhaler technique and
Check adherence

Check for ICS side effects
If important discontinue and consider alternatives

Celli B and Wedzicha J NEJM 2019;381:1257
LAMA

Triple (LAMA + LABA + ICS)

Continued lack of control

LAMA + LABA

Symptom persistence

Emphysema features
Hyperinflation
Eosinophils <100 cells/µL

Asthmatic features
Wheezing, allergies
Eosinophils >100 cells/µL

Frequent and/or severe exacerbations

LABA+ICS

Make diagnosis and grade risk factors

Initiate Therapy

Supervise inhaler technique and Check adherence

Check for ICS side effects

If important discontinue and consider alternatives

Celli B and Wedzicha J NEJM 2019;381:1257
Symptoms (Dyspnea) and Exacerbations

FEV$_1$

- Emphysema features
  - Hyperinflation
  - Eosinophils <100 cells/µL

- Asthmatic features
  - Wheezing, allergies
  - Eosinophils >100 cells/µL

LAMA

- Symptom persistence

LAMA + LABA

- Continued lack of control

Triple (LAMA + LABA + ICS)

- Frequent and/or severe exacerbations

Check for persistent eosinophilia
If present, consider biologicals

(PDE4i, macrolides, NAC, Xanthines)

Check for ICS side effects
If important, discontinue and consider alternatives

Make diagnosis and grade risk factors

Initiate Therapy
Supervise inhaler technique and Check adherence

Celli B and Wedzicha J NEJM 2019;381:1257
Agenda

• Review the tools available for patients on maximal therapy who remain functionally impaired
Along with 31 RCT’s included in the 2006 Cochrane Review, the authors included 34 additional RCT’s with a grand total of 3,822 participants.

“We found statistically and clinically significant improvements in important domains of health related quality of life, including dyspnea, fatigue, emotional function and mastery as well as in the 6 MWD, a test of functional capacity.”
Hyperinflation in a 63 year old man with mMRC dyspnea of 3

FEV₁ = 32 %
FRC = 192 %
DLCO = 49 %
Endobronchial Valves (EBV)

- Zephyr (Pulmonx)
  - silicone based mounted in a nitinol stent one way valve
- Spiration (Olympus)
  - 6 Nitinol struts and polyurethane umbrella shape unidirectional valve
Endobronchial Valves for Emphysema without Interlobar Collateral Ventilation

Karin Klooster, Nick H.T. ten Hacken, M.D., Ph.D., Jorine E. Hartman, Ph.D., Huib A.M. Kerstjens, M.D., Ph.D., Eva M. van Rikxoort, Ph.D., and Dirk-Jan Slebos, M.D., Ph.D.

A Primary Outcomes in the Intention-to-Treat Population

- **FEV**
  - EBV (N=34)
  - Control (N=34)
  - P=0.002

- **FVC**
  - EBV (N=34)
  - Control (N=34)
  - P=0.005

- **6MWD**
  - EBV (N=34)
  - Control (N=34)
  - P<0.001

- **SGRQ Score**
  - EBV (N=24)
  - Control (N=33)
  - P<0.001
Conclusions

• COPD is an important health problem worldwide
• Although cigarettes remain an important cause, this is not so for the majority of countries in the world
• E-cigarettes are a major problem requiring some regulation
• Well applied pharmacotherapy works
• In patients with persistent symptoms consider rehabilitation
• Check for emphysema and hyperinflation for potential LVR
• A nihilistic approach is not justified!
“If it were not for the great variability among individuals, medicine might as well be a science and not an art”

William Osler