Management of Stable COPD

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Definition

GOLD

Airflow limitation

- not fully reversible
- progressive
- abnormal inflammatory response to noxious particles or gases

Definition contd..

ATS

Airflow limitation due to chronic bronchitis or emphysema

- generally progressive
- airway hyperreactivity
- partially reversible

Airflow Limitation Reversibility

	ATS	ERS	GOLD
↑ in FEV1	> 200ml		> 200ml
↑in FEV1 %	> 12	> 10	> 12

Consider COPD if

Chronic cough	Present intermittently or every day Often present throughout the day seldom only nocturnal
Sputum	Any pattern of chronic sputum production
Dyspnoea	Progressive (worsens over time) Persistent (present every day) Worse on exercise Worse during respiratory infections
H/o Exposure	Tobacco smoke occupational dusts and chemicals,smoke from home cooking and heating fuels

4 components of COPD management

- Assess and monitor disease
- Reduce risk factors
- Manage stable COPD
- Manage exacerbations

Diagnosis

- Symptoms + spirometry
- Management of COPD largely symptom driven
- Only an imperfect relationship between the degree of airflow limitation and symptoms

Measurement of Airflow Limitation

Spirometry

- Gold standard for diagnosis and assessment of COPD
- Postbronchodilator FEV1 < 80% of predicted value + FEV1/FVC < 70% - confirms airflow limitation that is not fully reversible
- FEV1/FVC more sensitive
  FEV1/FVC < 70% - early sign of airflow limitation when FEV1 remains normal (≥ 80% predicted)

Measurement of Airflow Limitation

If spirometry unavailable

- PEF good substitute if spirometry not available
  In COPD PEF may underestimate degree of airways obstruction
- Prolongation of FET > 6 sec → crude guide to FEV1/FVC ratio < 50%
- 6 minute walking test performed by measuring distance covered in 6 minutes when patient walks at his/her own speed (under physician supervision)
- can be performed at the primary care level

Bronchodilator reversibility testing

- To help rule out a diagnosis of asthma
- To establish a patient's best attainable lung function
- To gauge a patient's prognosis.

Post BDR FEV1 → more reliable prognostic marker than pre-BDR FEV1

IPPB study→ degree of bronchodilator response inversely related to rate of FEV1 decline in COPD patients

Bronchodilator reversibility testing

- To assess potential response to treatment

Significant ↑ in FEV1 → more likely to benefit from bronchodilators and glucocorticosteroids

↑ in FEV1 not significant → may still benefit from long-term bronchodilator therapy

Bronchodilator reversibility testing

- 400 ug ß2-agonist / 80 ug anticholinergic / the two combined
- FEV1 30-45 mts after bronchodilator given

Results

↑ in FEV1 > 200 ml

> 12% above pre-bronchodilator FEV1

Measurement of Airflow Limitation

- Ratio of inspiratory to total lung capacity - an independent risk factor for mortality in patients with COPD*
- This ratio may be a better assessment tool than FEV1
- Inspiratory capacity and lung volumes may better reflect the functional response and the improvement of symptoms and exercise tolerance induced by bronchodilator agents

Am J Respir Crit Care Med 2005;171:591–597

BODE index

- BODE index (Body mass index, airflow Obstruction, Dyspnea, and Exercise capacity) - a stronger predictor than FEV1 of the risk of hospitalization and death among patients with COPD '
- Might provide useful prognostic information

' *N Engl J Med* 2004;350:1005–12
' *Chest* 2005;128:3810–16

Exercise testing

- Functional exercise capacity - the strongest correlate of physical activity in daily life
- Recommended for more comprehensive evaluation of severity and response to treatment
- Endurance shuttle test - sensitive test for detecting changes in exercise capacity induced by bronchodilators ' and rehabilitation

' *Am J Respir Crit Care Med* 2005;172:1517–22

ABG

- FEV1 < 40% predicted
- Clinical signs of respiratory failure
- Right heart failure

Radiology

CXR

Signs of hyperinflation

- flattened diaphragm on lateral CXR
- ↑ in volume of retrosternal air space

Hyperlucency of lungs

Rapid tapering of vascular markings

HRCT chest

- If diagnosis doubtful
- If a surgical procedure such as bullectomy or lung volume reduction contemplated

α-1 antitrypsin deficiency screening

- COPD at a young age (< 45 years)
- strong family history

- serum α-1 antitrypsin <15-20 % of normal value - highly suggestive of homozygous α-1 AT deficiency

Classification of Severity

Stage	Characteristics
0: At Risk	. normal spirometry . chronic symptoms (cough, sputum production)
I: Mild COPD	. FEV1/FVC < 70% . FEV1 ≥80% predicted ± chronic symptoms (cough, sputum production)
II: Moderate COPD	. FEV1/FVC < 70% . 50% ≤FEV1 < 80% predicted . ± chronic symptoms (cough, sputum production)
III: Severe COPD	. FEV1/FVC < 70% . 30% ≤FEV1 < 50% predicted . ± chronic symptoms (cough, sputum production)
IV: Very Severe	. FEV1/FVC < 70% . FEV1 < 30% predicted or FEV1 < 50% predicted + chronic respiratory failure

Ongoing monitoring and assessment

- Monitor disease progression and development of complications (JVP,pitting ankle edema s/o RVF), symptoms of hypercapnia (bounding pulse, warm extremities, flaps and tremulousness) & hypoxia (tremors, restlessness, mental obtundation and cyanosis)

  Spirometry - if increase in symptoms or a complication

- Monitor pharmacotherapy and other medical Rx

- Monitor exacerbation
  ↑ sputum volume / dyspnea / purulent sputum

- Monitor Comorbidities
  LVF, Ca bronchus, PTB, sleep apnea,

Reduce risk factors

- Quit Smoking
- Elimination or reduction of exposures to various substances in the workplace
- ↓ exposure to indoor / outdoor pollution

General measures

- (1) avoiding open burning of crop residue
  (2) use of water to suppress dust
  (3) wearing masks at work place in areas of dust generation
- use of smokeless 'chullahs'
- Substitution of solid fuels with LPG or electricity is the best approach

Strategies to Quit Smoking

1. ASK : *EVERY* patient at *EVERY* clinic visit
2. ADVISE : To quit
3. ASSESS : Determine willingness to quit
4. ASSIST : Aid the patient in quitting – provide practical counseling ,pharmacotherapy and social support
5. ARRANGE : Schedule follow-up contact

Pharmacotherapy for smoking cessation

- Pharmacotherapy - when counseling not sufficient to help patients quit smoking
- Nicotine replacement therapy (nicotine gum, inhaler, nasal spray, transdermal patch,sublingual tablet, or lozenge)
  ↑ long-term smoking abstinence rates
- Bupropion , nortriptyline - ↑ long-term quit rates
- Clonidine - use limited by side effects

Pharmacotherapy for smoking cessation

Quit rates

- Placebo 6%
- NRT and behavioural therapy 9%
- Bupropion (6-9 wks) 18% at 1 yr

Treatment Options

Pharmacologic therapy

- Bronchodilators
- Glucocorticosteroids
- Vaccines
- Alpha-1 antitrypsin augmentation therapy
- Antibiotics
- Mucolytics
- Antioxidants
- Immunoregulators
- Antitussives
- Vasodilators
- Respiratory Stimulants
- Narcotics
- Others

Non-pharmacologic

- Pulmonary rehabilitation
- Oxygen
- Ventilatory support
- Surgery
  - Bullectomy
  - Lung Volume Reduction Surgery (LVRS)
  - Lung Transplantation

General principles

- None of the existing medications shown to modify long-term decline in lung function
- Smoking cessation and continuous long-term oxygen treatment only pharmacologic interventions that modify natural history of COPD
- Stepwise increase in treatment
- Treatment response variable

Bronchodilators

- Bronchodilator medications are central to symptom management in COPD
- Inhaled therapy preferred
- Choice between ß2-agonist, anticholinergic, theophylline, or combination therapy depends on availability and individual response in terms of symptom relief and side effects
- Bronchodilators prescribed on an as-needed or on a regular basis to prevent or reduce symptoms

Bronchodilators contd..

- DRCs using FEV1 relatively flat with all classes of bronchodilators
- All categories of bronchodilators ↑ exercise capacity in COPD, without necessarily improving FEV1
- Improve emptying of lungs, ↓ dynamic hyperinflation at rest and during exercise
- Improve exercise performance
- Does not modify the decline of function or prognosis of the disease

Bronchodilators contd..

- Long-acting inhaled bronchodilators are more effective and convenient, but more expensive
- Combining bronchodilators may improve efficacy and decrease the risk of side effects compared to increasing the dose of a single bronchodilator

ß2-agonists

Relax airway smooth muscle by stimulating ß2-adrenergic receptors, which ↑ c-AMP

Oral therapy slower in onset & more side effects

- Resting sinus tachycardia
- Tremor
- Hypokalemia
- O_2 consumption ↑

} show tachyphylaxis

Therapy at Each Stage of COPD

New (2003)	0: At Risk	I: Mild	II: Moderate	III: Severe	IV: Very Severe
Avoidance of risk factor(s); influenza vaccination					
	Add short-acting bronchodilator when needed				
		Add regular treatment with one or more long-acting bronchodilators *Add* rehabilitation			
			Add inhaled glucocorticosteroids if repeated exacerbations		
				Add long-term oxygen if chronic respiratory failure *Consider* surgical treatments	

ß2-agonists

Drug	Inhaler(ug)	Duration of Action (hrs)
Short-acting		
Fenoterol	100-200 (MDI)	4-6
Salbutamol	100, 200 (MDI & DPI)	4-6
Terbutaline	400, 500 (DPI)	4-6
Long-acting		
Formoterol	4.5–12 (MDI & DPI)	12+
Salmeterol	25-50 (MDI & DPI)	12+

Anticholinergics

Drug	Inhaler (ug)	Duration of Action (hrs)
Anticholinergics		
Short-acting		
Ipratropium bromide	20, 40 (MDI)	6-8
Oxitropium bromide	100 (MDI)	7-9
Long-acting		
Tiotropium	18 (DPI)	+24
Combination		
Fenoterol/Ipratropium	200/80 (MDI)	6-8
Salbutamol/Ipratropium	75/15 (MDI)	6-8

Glucocorticosteroids

- Regular inhaled glucocorticosteroids does not modify long-term decline of FEV1

Appropriate for

- Symptomatic COPD patients with an FEV1 < 50% predicted (*Stage III:Severe COPD* and *Stage IV: Very Severe COPD*) and
- Repeated exacerbations

Glucocorticosteroids

- Reduce the frequency of exacerbations[2]
- Inhaled glucocorticosteroid combined with a long-acting B-agonist is more effective than the individual components
- Long-term treatment with oral glucocorticosteroids is not recommended in COPD

2 Lancet 2003; 361:449-56
Cochrane Database Syst Rev 2004;3:CD003794

Drug	Inhaler	Solution for	Oral
Beclomethasone	**50-400 (MDI & DPI)**	**0.2-0.4**	
Budesonide	**100, 200, 400**	**(DPI)**	**0.20, 0.25, 0.5**
Fluticasone	**50-500 (MDI & DPI)**		
Triamcinolone	**100 (MDI)**	**40**	
Combination			
Formoterol/Budesonide	**4.5/80, 160 (DPI)**		
	(9/320) (DPI)		
Salmeterol/Fluticasone	**50/100, 250, 500 (DPI)**		
	25/50, 125, 250 (MDI)		
Systemic glucocorticosteroids			
Prednisone			**5-60 mg (Pill)**
Methyl-prednisolone	**10-2000 mg**		**4, 8, 16 mg (Pill)**

Glucocorticosteroids

- long-term inhaled steroids reduce mortality from all causes in patients with COPD

Thorax 2005;60:992–997

Tiotropium

- Tiotropium, a long-acting anticholinergic agent,reduces frequency of exacerbations & use of health care resources in patients with moderate to severe COPD

Ann Intern Med 2005;143:317–26

Theophylline

- Oral theophylline only if inhaled treatments have failed to provide adequate relief
- All studies that have shown efficacy of theophylline in COPD were done with slow-release preparations
- Addition of theophylline to ß2-agonists or anticholinergics may produce additional improvements in lung function and health status
- Combination of salbutamol with theophylline in a single tablet not recommended

Phosphodiesterase Inhibitors

- In moderate to severe COPD, long-term roflumilast improves FEV1 and other lung function parameters
- Reduces the rate of mild exacerbations
- Cilomilast maintains pulmonary function, improves health status, and reduces the rate ofCOPD exacerbations
- Cilomilast reduces the number of CD8 T cells in the airway mucosa of patients with COPD

Lancet 2005;365:167–175

Statins

- statins used for cardiovascular diseases and the metabolic syndrome may have antiinflammatory effects in the lung

Chest 2005;128:574S

Vaccination

- Influenza vaccines can reduce serious illnessand death in COPD patients by about 50% [1]
- Vaccines containing killed or live, inactivated viruses are recommended and should be given once (in autumn)or twice (in autumn and winter) each year
- Pneumococcal vaccine containing 23 virulent serotypes used but sufficient data lacking [2]

1 *N Engl J Med* 1994; 331:778-84
2 *N Engl J Med* 1986; 315:1318-27

α-1 Antitrypsin Augmentation Therapy

- Young patients with severe hereditary alpha-1 antitrypsin deficiency and established emphysema
- very expensive,
- not widely available
- not recommended for COPD unrelated to alpha-1 antitrypsin deficiency

Antibiotics

- Prophylactic, continuous use of antibiotics → no effect on the frequency of COPD exacerbations
- Antibiotics not recommended other than for treating infectious exacerbations of COPD and other bacterial infections

Mucolytics

- Mucolytic(mucokinetic, mucoregulator) agents (ambroxol, erdosteine, carbocysteine, iodinated glycerol)
- Few patients with viscous sputum may benefit from mucolytics '
- Overall benefits very small
- Regular use not recommended

' *Cochrane Database Syst Rev* 2000; 2:

Antioxidant agents

- N-acetylcysteine - shown to reduce frequency of exacerbations and could have a role in treatment of recurrent exacerbations
- Routine use not yet recommended

Anti TNF-α Ab

- Infliximab - no clinically beneficial effects in a small group of patients with mild to moderate COPD

Antitussives

- Cough, although sometimes a troublesome symptom in COPD, has a significant protective role
- Regular use of antitussives contraindicated in stable COPD

Vasodilators

- Inhaled nitric oxide can worsen gas exchange because of altered hypoxic regulation of ventilation-perfusion balance
- Nitric oxide contraindicated in stable COPD

Other drugs

Narcotics (morphine)

- Effective for treating dyspnea in COPD patients with advanced disease.
- Benefits may be limited to a few sensitive subjects

Others

Nedocromil, leukotriene modifiers not adequately tested in COPD

Respiratory stimulants

- No evidence that almitrine improves survival or quality of life
- Almitrine not recommended for regular use in stable COPD patients
- Doxapram not recommended in stable COPD

Components of pulmonary rehabilitation programs

- Exercise training
  - simple corridor exercise training
- Nutrition counseling
- Education

Home-based RMET

- Home-based ***tube breathing*** leads to significant improvement of endurance exercise capacity, a reduction in perception of dyspnea, and an improvement in quality of life in patients with moderate-to-severe COPD

Chest 2006;129:886-92

Oxygen therapy

- Long-term oxygen (>15 hours /day) to patients with chronic respiratory failure increase survival
- Also have a beneficial impact on exercise capacity , hemodynamics, hematologic characteristics, lungmechanics and mental state
- Long-term home oxygen therapy improved survival in a selected group of COPD patients with severe hypoxaemia (arterial PaO2 less than 55 mm Hg (8.0 kPa)'
- Did not improve survival in patients with mild to moderate hypoxaemia or in those with only arterial desaturation at night

'*Cochrane Database Syst Rev* 2005;4:CD001744

Oxygen therapy

Indications

Stage IV: Very Severe COPD with

- PaO2 ≤ 55 mm Hg or SaO2 ≤ 88% ± hypercapnia
- PaO2 55– 60 mm Hg or SaO2 89%, if e/o pulmonary hypertension, peripheral edema s/o CCF, or polycythemia (hematocrit > 55%)

Goal

- To ↑ the baseline PaO2 to at least 60 mm Hg at rest and/or
- To produce SaO2 at least 90%

Noninvasive mechanical ventilation

- No convincing evidence that this therapy has a role in the management of stable COPD
- Some patients with chronic hypercapnia may benefit but no randomized controlled study

Bullectomy

- Normal or minimally reduced diffusing capacity, absence of significant hypoxemia, and evidence of regional reduction in perfusion with good perfusion in the remaining lung - likely benefit from surgery
- Pulmonary hypertension, hypercapnia, and severe emphysema - not absolute contraindications
- Bulla should occupy 50% or more of the hemithorax and produce definite displacement of the adjacent lung

Lung Volume Reduction Surgery (LVRS)

- Improves exercise capacity in predominant upper lobe emphysema and a low post rehabilitation exercise capacity
- May improve global health status in patients with heterogeneous emphysema
- Improved diaphragm function may contribute to functional improvement after LVRS
- LVRS increased diaphragm length → lower motor unit firing rates and reduced breathing effort → improved quality of life and exercise performance