

Management of chronic heart failure associated with chronic pulmonary disease

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**Prof. Luigi Tavazzi
GVM Hospitals of Care and Research
Cotignola, Italy**

Chronic Obstructive Pulmonary Disease Definition

A “disease with some significant extrapulmonary effects that may contribute to the severity in individual patients. Its pulmonary component is characterized by airflow limitation that is not fully reversible and frequently progressive due to an abnormal inflammatory response of the lung to noxious particles or gases”.

**The Global Initiative for Chronic Obstructive Lung Disease.
<http://www.goldcopd.org>**

Definition of heart failure

HF is a clinical syndrome in which patients have the following features:

- Symptoms typical of HF
(breathlessness at rest or on exercise, fatigue, tiredness, ankle swelling)

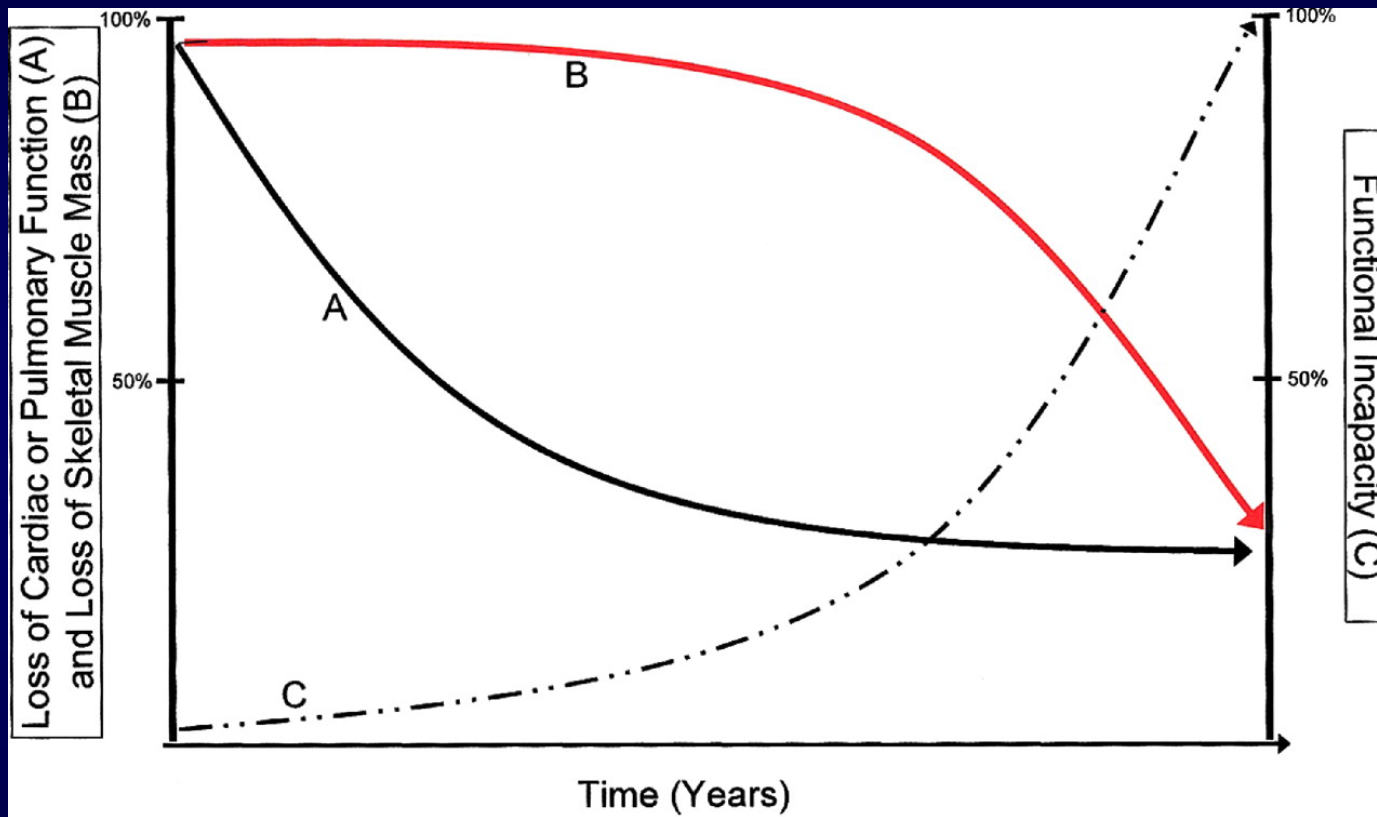
and

- Signs typical of HF
(tachycardia, tachypnoea, pulmonary rales, pleural effusion, raised jugular venous pressure, peripheral oedema, hepatomegaly)

and

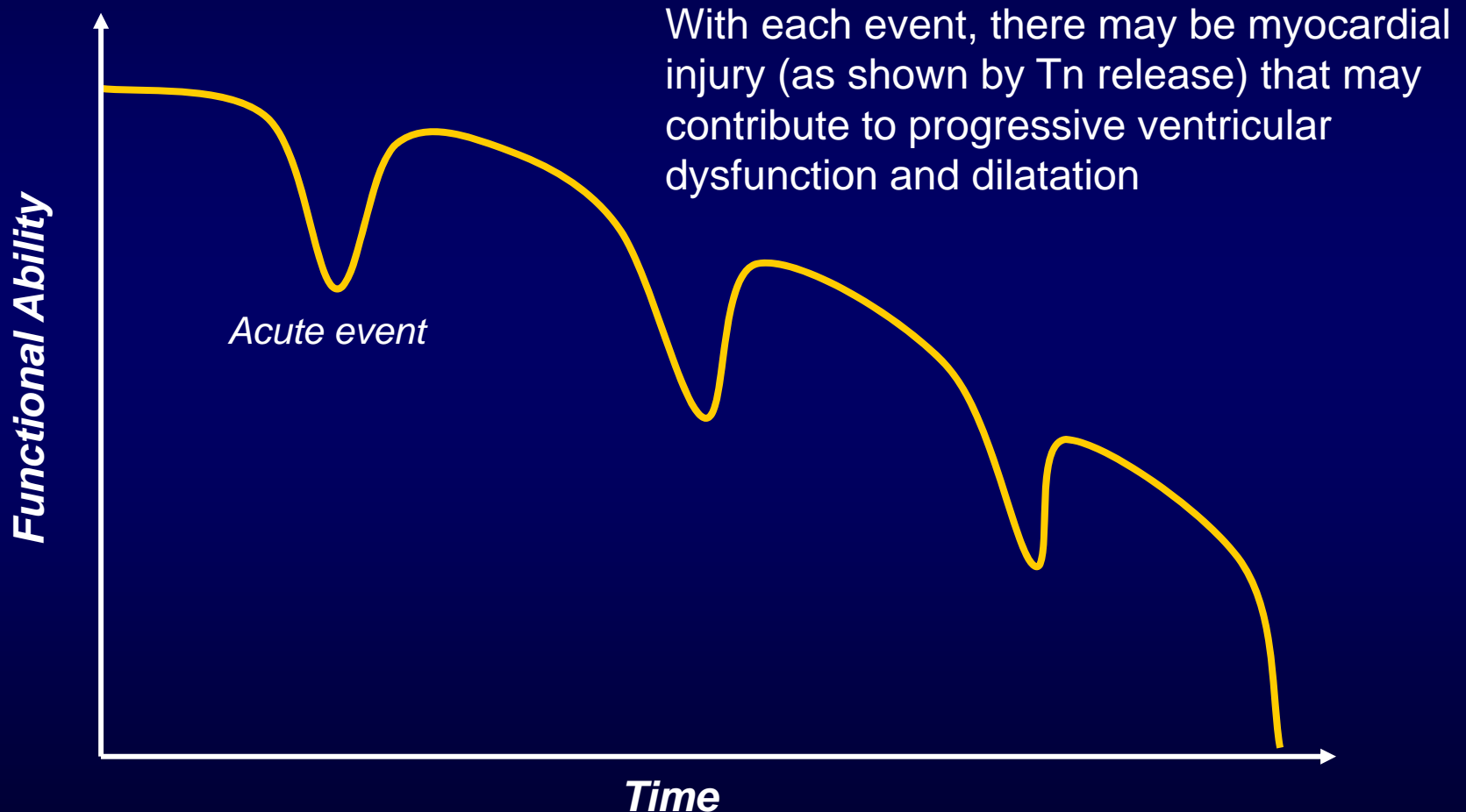
- Objective evidence of a structural or functional abnormality of the heart at rest
(cardiomegaly, third heart sound, cardiac murmurs, abnormality on the echocardiogram, raised natriuretic peptide concentration)

Progression of CHF and COPD



Le Jemtel, T. H. et al. J Am Coll Cardiol 2007;49:171-180

Acute Exacerbations May Contribute to the Progression of Heart Failure



Chronic Heart Failure and COPD

US Epidemiology:

- 14 milion have COPD
- 5 milion have CHF

Prevalence of COPD in HF patients

- No study has systematically examined pulmonary function in patients with stable HF
- Reported prevalence (42 studies):
 - 11-52% in North American cohorts
 - 9-41% in European cohorts
 - increases until ~75 yrs and declines thereafter
 - seems higher in HF with preserved LVEF (5/16 studies)

Prevalence of HF in COPD patients

- ~ 20% in 3 studies (settings: 1 Emergency Dept, 1 regional hospital network, 1 community)
- No ECHO evidence of isolated right HF

THEN

patients with COPD and suspected HF must be considered to have LV dysfunction until proven otherwise

- In 18 reports prevalence of LV systolic dysfunction (low EF) ranges from 10% to 46%

Cor Pulmonale and COPD

- Proportion of COPD patients developing cor pulmonale is surprisingly uncertain. Variability in prevalence rates among studies is huge
- In general
 - isolated RV failure is very rare
 - magnitude of PH is modest
 - severe resting PH is uncommon
 - higher prevalence with exercise

Development of Pulmonary Hypertension over time in COPD patients

- 131 COPD patients underwent 2 right heart catheterization a mean of 6.8 years apart
- Initial evaluation:
 - no resting PH
 - 57% exercise-induced PH
- Second evaluation:
25% resting (mild) PH (most with exercise-induced PH at the first examination)

Pulmonary hypertension in hypoxemic lung disease

Pulmonary vasoconstriction caused by:

- alveolar hypoxia
- acidemia
- hypercarbia
- inflammation
- distortion by parenchymal changes
- increased CO and blood viscosity

Pulmonary vascular remodelling caused by:

- Nitric oxide
- Endothelin
- Serotonin
- Hypoxia inducible factor 1
- Inflammation

COPD and inflammation

- **Systemic inflammation markers correlate with the presence and severity of COPD and risk for hospitalization and death.**
- **Inflammation is a determinant of atherothrombosis.**
- **Ischemic heart disease is a leading (but unrecognized) cause of death in COPD, cardiovascular death accounting for ~50% of all COPD deaths.**

CHF and inflammation

- A systemic chronic inflammation (CRP, interleukins, fibrinogen TNF_α) is present in CHF
- RCTs targeting different inflammation pathways (anti TNF_α , antiendothelins, statins) performed in CHF were unsuccessful

Muscle atrophy and fatigue in CHF and COPD

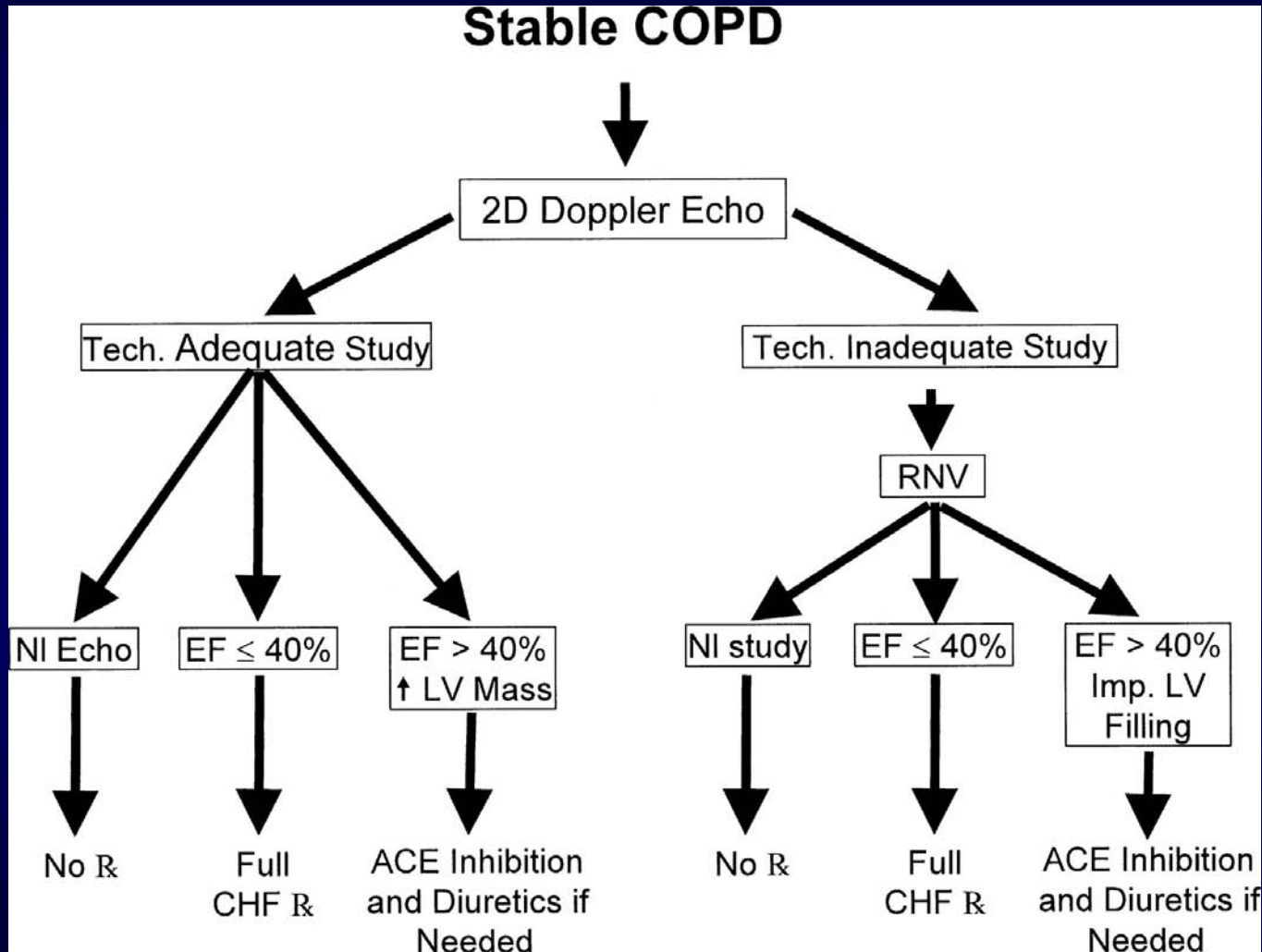
Low level systemic inflammation, increased oxidative stress and muscle disuse contribute, in both CHF and COPD, to:

- reduce protein synthesis**
- accelerate protein degradation**
- lead to skeletal muscle atrophy**

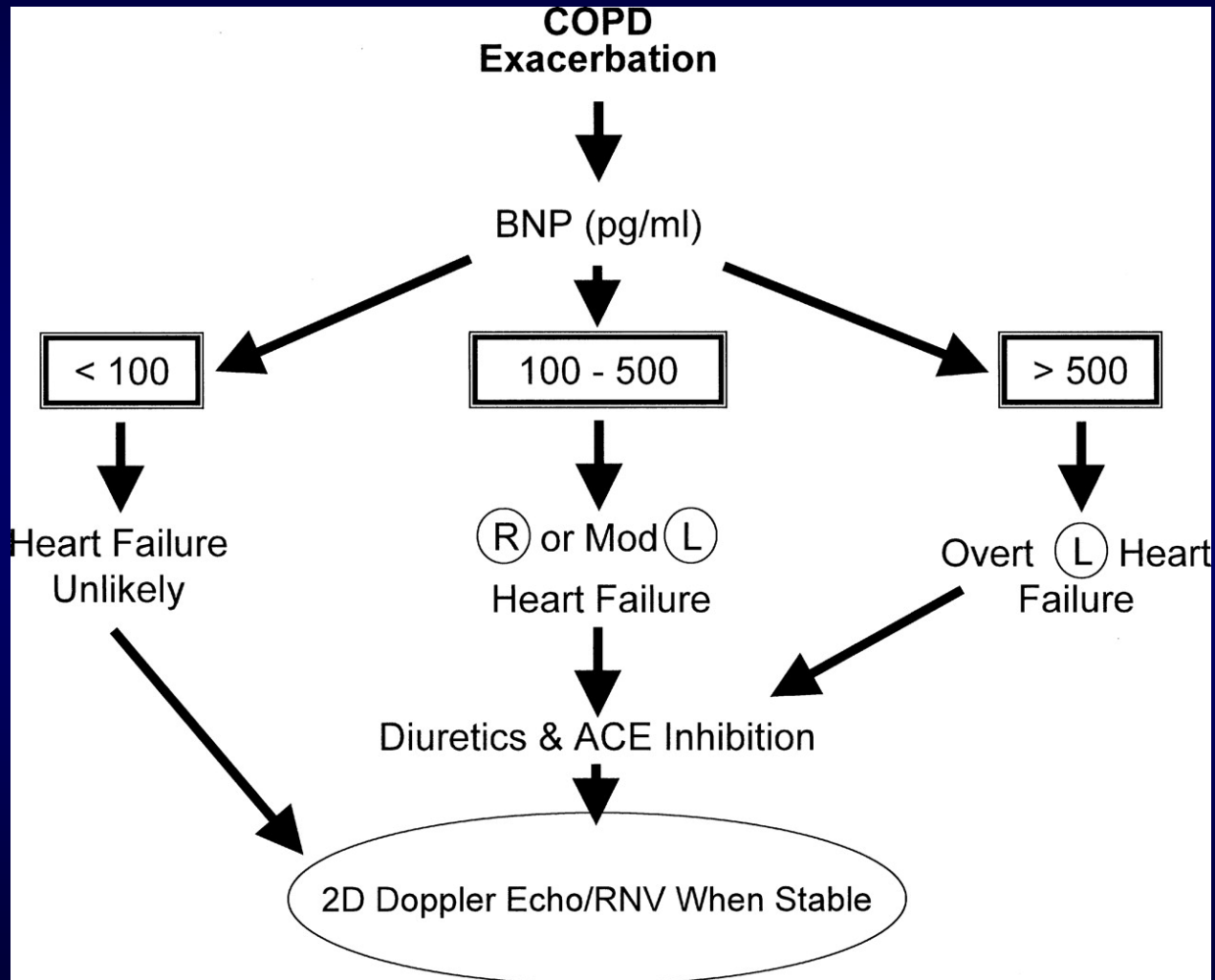
Pitfalls in diagnosing COPD in patients with HF

- In *decompensated HF*: airflow obstruction is common (airway compression and obstruction, bronchial hyperaposisiveness)
- In *stable HF*: restrictive ventilatory defects predominate (interstitial fibrosis, muscle weakness, cardiomegaly, pulmonary congestion)
- Few HF patients perform spirometry

Evaluation of Heart Failure in stable COPD patients



Evaluation of Heart Failure During COPD Exacerbation



**Diagnosing HF
with preserved LVEF in COPD**

No established criteria

Therapeutic approach in CHF and COPD: Beta-blockade

- β -blockers are underused in CHF patients with definite or suspected COPD due to concern of respiratory deterioration. These patients were excluded from the RCTs in CHF
- Selective B1 blockade does not worsen FEV1 and does not attenuate B2 agonist-induced bronchodilatation, though selectivity may be lost at highest doses and B-receptor polymorphisms or receptor exposure rate may individually affect the response to both β -agonists and blockers
- **Benefits of B1 blockade far outweigh the risks in CHF-COPD patients**

Therapeutic approach in CHF and COPD: Beta-blockade

- Non-selective BB attenuates B2 agonist-induced bronchodilatation, but does not affect the rate of hospitalization for COPD exacerbation (3 studies)
- In both CHF and COPD patients the acute administration of BBs worsens the clinical status (worsening the pump function of the heart and the airway responsiveness respectively), with time and slow up-titration this converts into benefit
- **The current Guidelines on CHF recommend BB in all patients with coexistent COPD and CHF**

Therapeutic approach in CHF and COPD: Beta-blockade

- A meta analysis of 5 single dose and 6 longer-duration trials of B2 agonists underline their adverse cardiovascular effects in COPD patients
- B2 agonists are associated with an increased risk for CHF (OR 3.4) and all-cause mortality in CHF patients
- The concomitant use of β -blockers and B2 agonists has not been assessed in clinical trials
- **The adverse effects of B2 agonists are likely to be exacerbated in patients with coexistent CHF and COPD**

Therapeutic approach in CHF and COPD

RAA system modulation

May lower cardiovascular risk,
preventing lung injury and skeletal
muscle atrophy (by IGF-1)

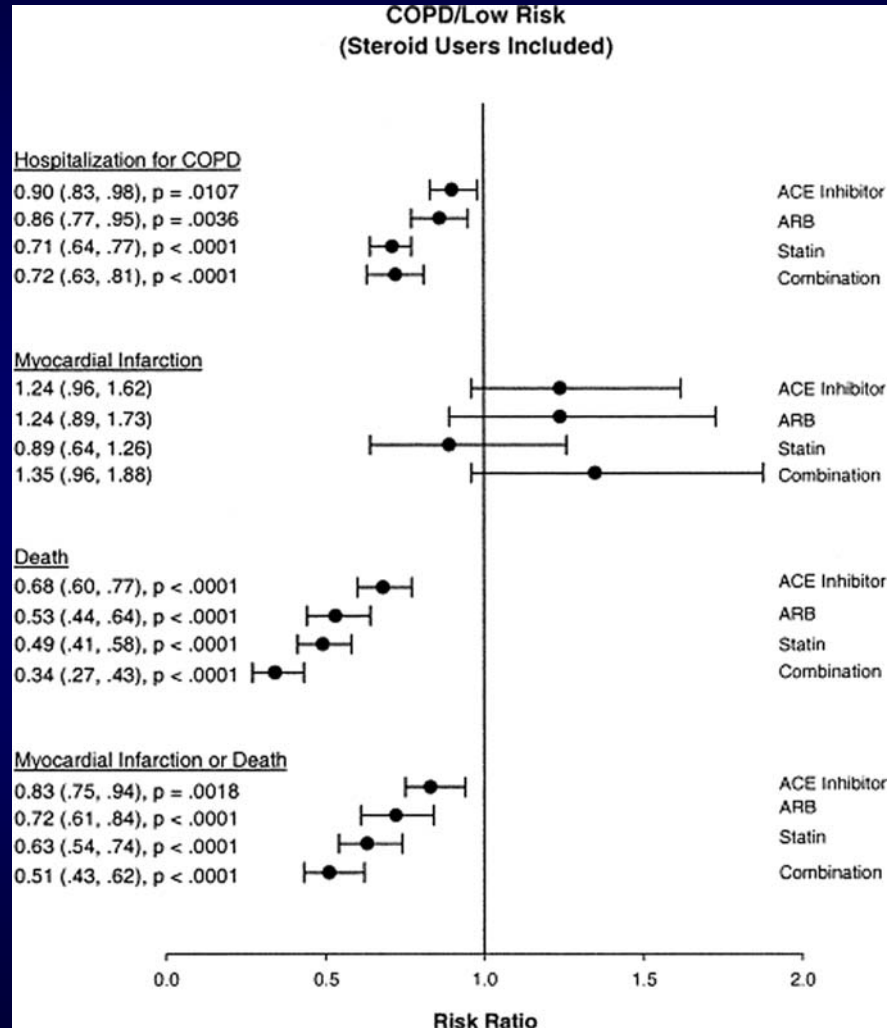
Therapeutic approach in CHF and COPD

Statins

Appeared beneficial in small studies and post-hoc analyses in both CHF and COPD.

Large RCTs in CHF did not confirm benefit (CORONA, GISSI-HF).
RCTs in COPD are missing

Canadian database Statin therapy in COPD



Therapeutic approach in CHF and COPD

Gherlin

A novel GH-releasing peptide has been shown to reduce muscle atrophy and improve functional capacity in both CHF and COPD