Quando il Cuore fa la Pimadonna

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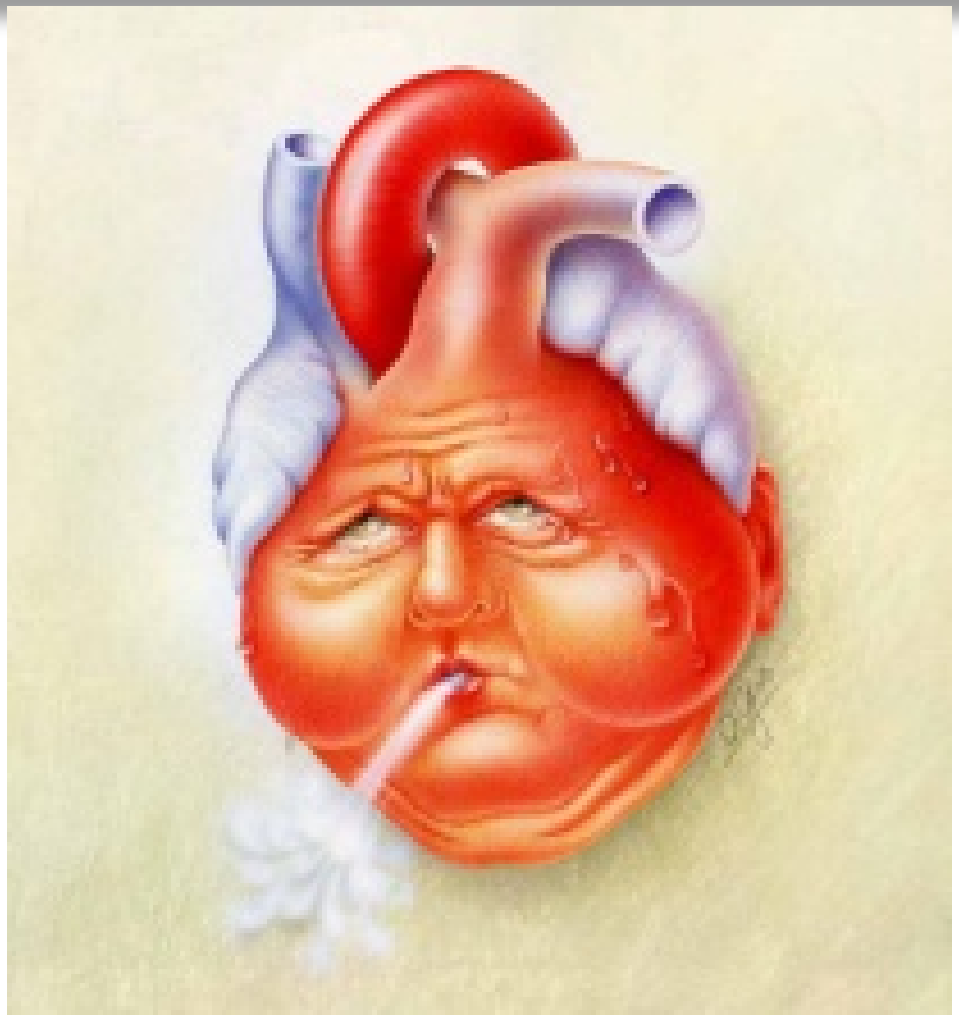
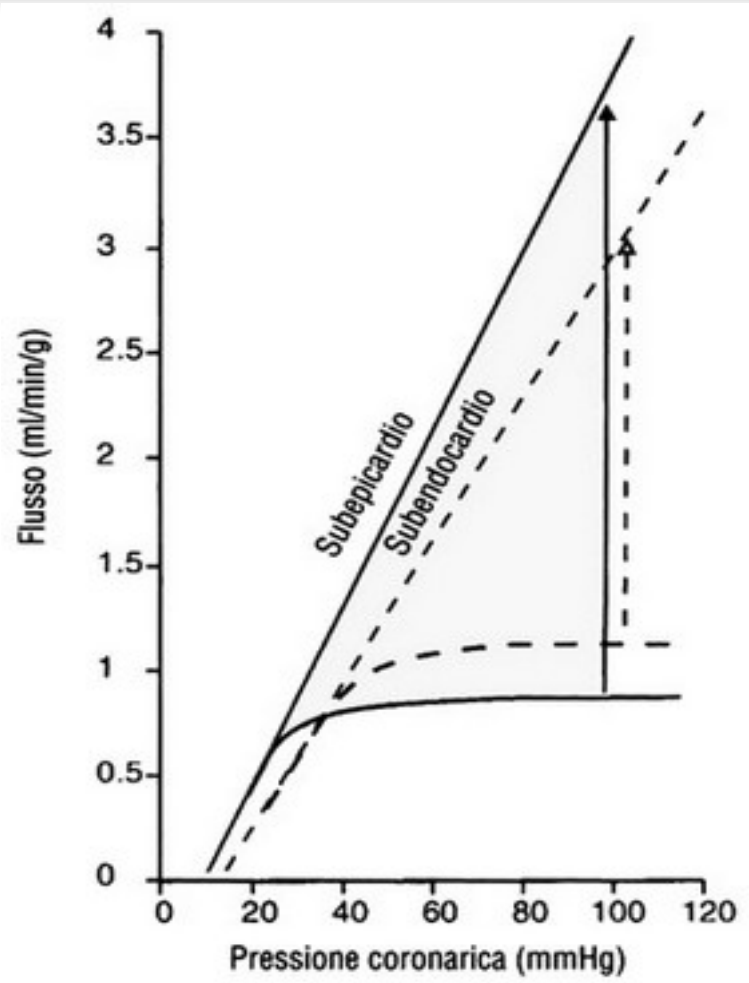
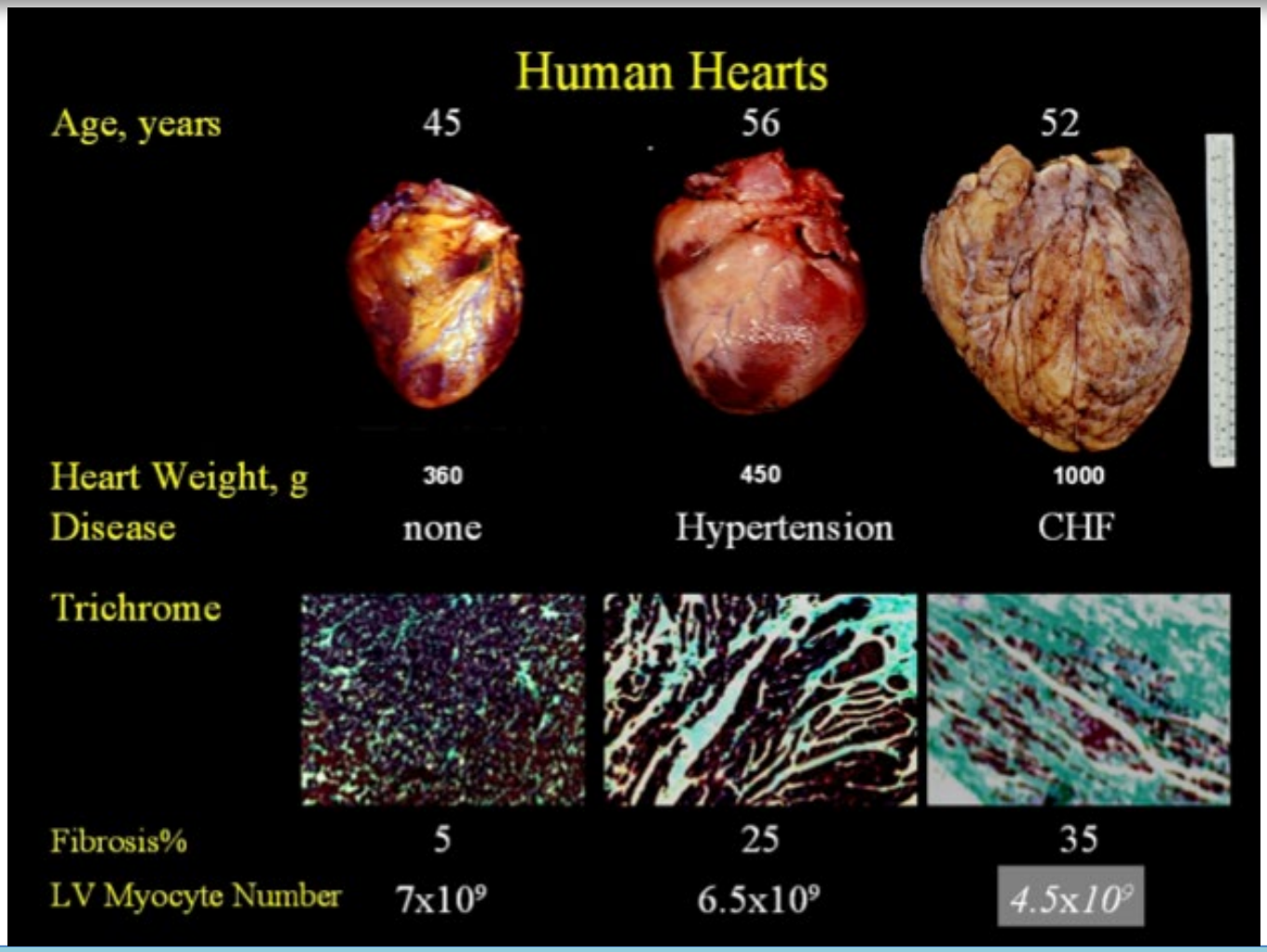
ASST Santi Paolo e Carlo
Milano

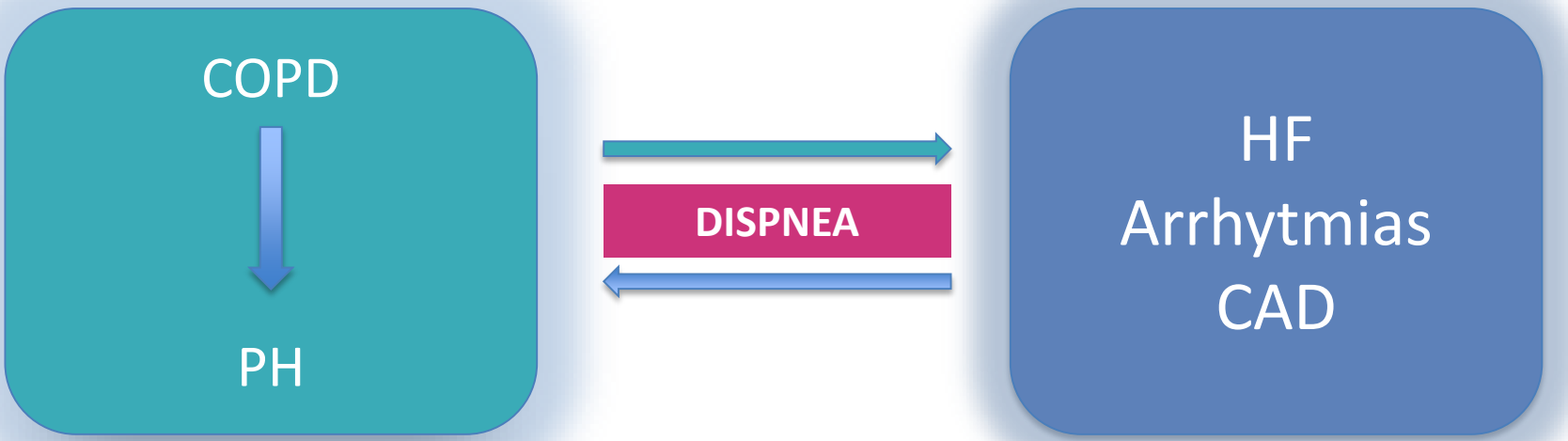


Riserva coronarica




Human Hearts
Age, years
45
56
52
Heart Weight, g
360
450
1000
Disease
none
Hypertension
CHF
Trichrome
Fibrosis%
5
25
35
LV Myocyte Number
7x10⁹
6.5x10⁹
4.5x10⁹

Meccanismo che regola il rapporto tra COPD, PH e HF/Arrythmias/CAD



COPD and Heart Failure

► The prevalence of systolic or diastolic heart failure in COPD patients ranges from 20 to 70%, and its annual incidence between 3-4%. Incident heart failure is a significant and independent predictor of all-cause mortality.

► Unrecognized heart failure may mimic or accompany acute COPD; 40% of COPD patients that are mechanically ventilated because of hypercapnic respiratory failure have evidence of left ventricular dysfunction.

► There is no evidence that chronic heart failure should be treated differently in the presence of COPD. Treatment with $ß_1$-blockers improves survival in heart failure and is recommended. However, $ß_1$-blockers are often not prescribed in COPD despite available evidence showing that their use in COPD is safe. Selective $ß_1$-blockers should be used.

► Acute heart failure should be treated according to usual heart failure guidelines since there is no evidence to support an alternative management strategy. Noninvasive ventilation added to conventional therapy improves outcomes for patients with either hypercapnic respiratory failure due to an exacerbation of COPD as well as heart failure with acute pulmonary edema.

COPD and Ischaemic Heart Diseases

► Ischaemic heart disease should be considered in all COPD patients depending on their risk factor profile. The cardiovascular risk may be assessed by the global risk calculator, which can be found on the US National Heart Blood Lung Institute website and treatment initiated based on the current recommendations.

► During acute COPD exacerbations, there is an increased risk of myocardial damage in patients with concomitant ischemic heart disease. Patients who demonstrate abnormal cardiac troponins in isolation are at increased risk of adverse outcomes including short-term (30day) and long-term mortality.

► The treatment of ischaemic heart disease should be according to guidelines irrespective of the presence of COPD and vice versa.

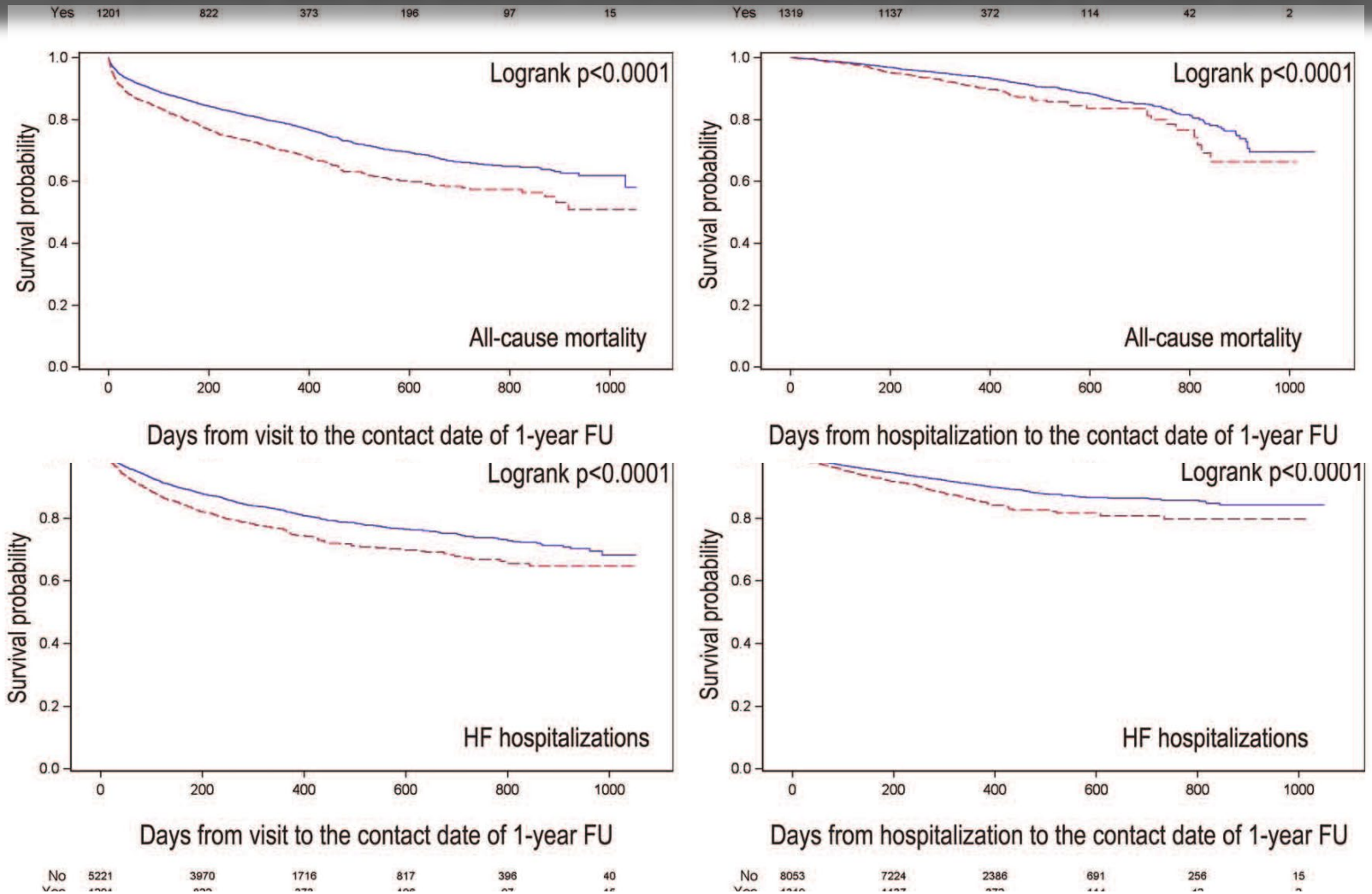
COPD and Arrythmias

► Cardiac arrhythmias are common in COPD and vice versa. Atrial fibrillation is frequent and directly associated with FEV_1.

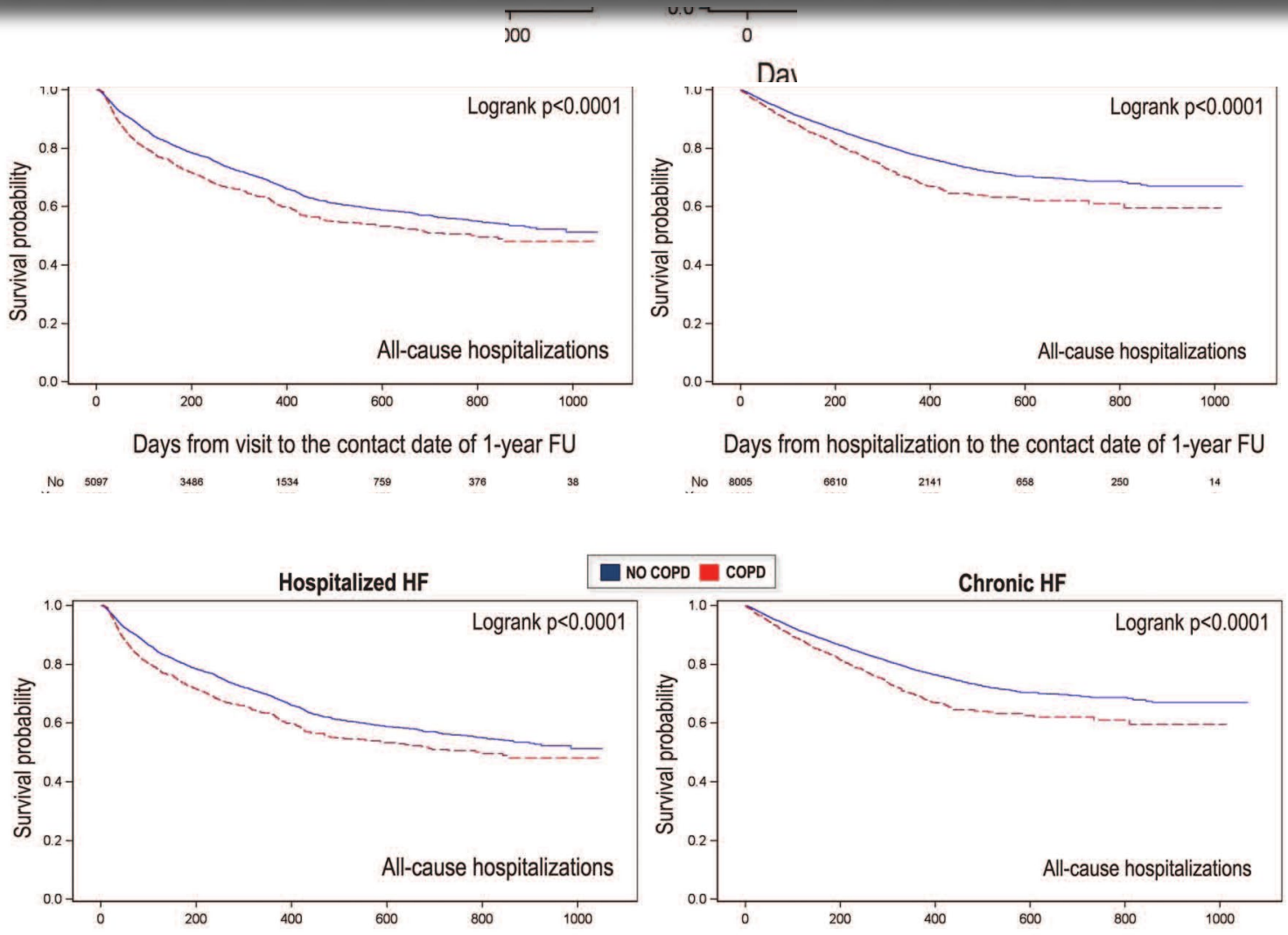
► In COPD patients presenting with severe worsening dyspnoea, associated atrial fibrillation is frequently documented, and it may be either a trigger or a consequence of an acute exacerbation episode.

► The presence of atrial fibrillation does not alter the treatment of COPD. Bronchodilators have been previously described as potentially pro-arrhythmic agents however, available evidence suggests an overall acceptable safety profile for long-acting $beta_2$-agonists, anticholinergic drugs (and inhaled corticosteroids). Nevertheless, caution is advised when using short-acting $beta_2$-agonists and theophylline, which may precipitate AF and make control of the ventricular response rate difficult.

Kaplan–Meier curves for all clinical outcomes in hospitalized and chronic heart failure (HF) patients with and without chronic obstructive pulmonary disease (COPD).



Kaplan–Meier curves for all clinical outcomes in hospitalized and chronic heart failure (HF) patients with and without chronic obstructive pulmonary disease (COPD).

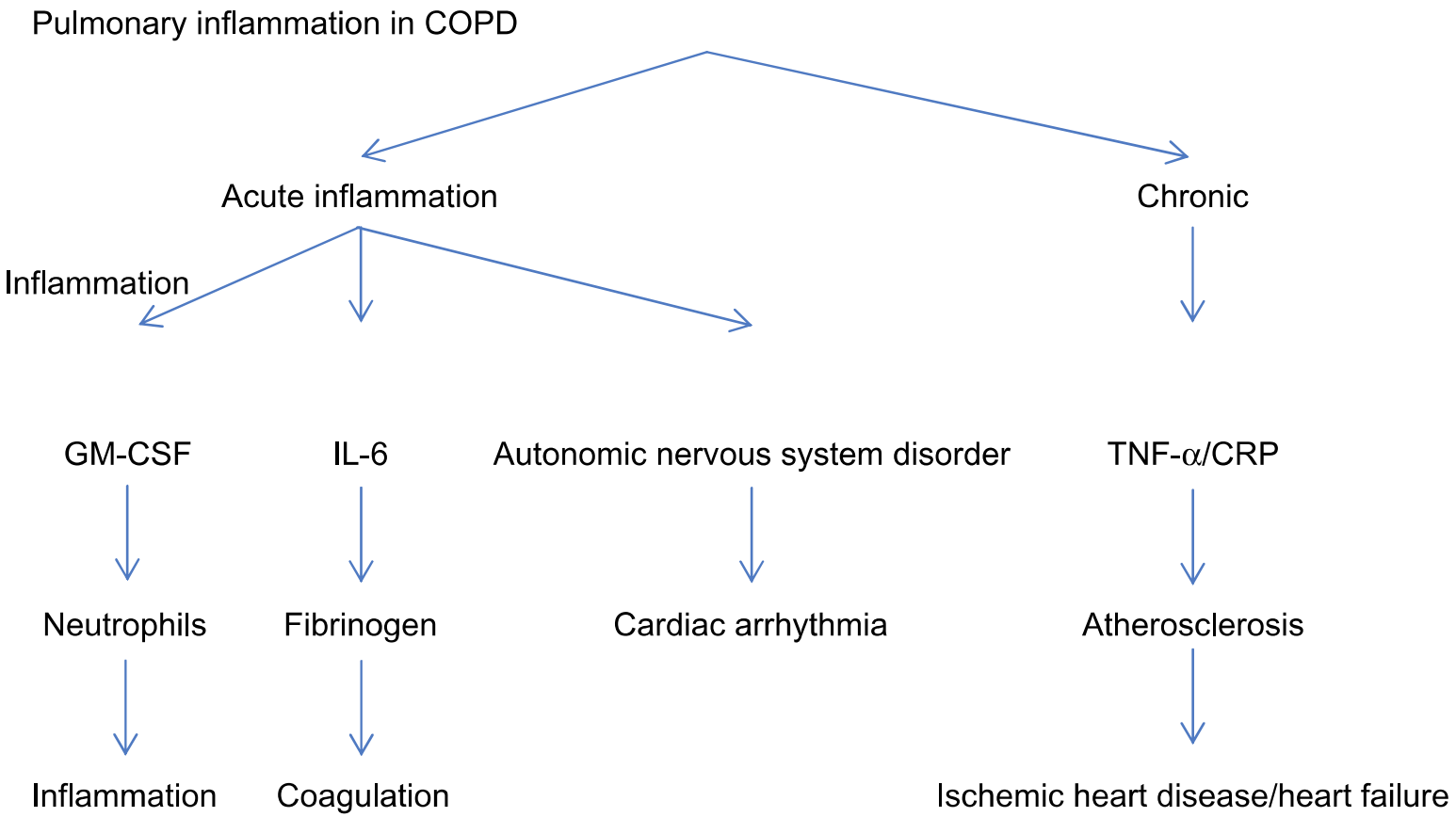


One-year event rate by chronic obstructive pulmonary disease (COPD) status and Cox multivariable analysis of the association between COPD and clinical outcomes

	Hospitalized heart failure				Chronic heart failure			
	COPD ($n = 1262$)	No COPD ($n = 5237$)	Adjusted HR (95% CI)	*P*-value	COPD ($n = 1290$)	No COPD ($n = 7890$)	Adjusted HR (95% CI)	*P*-value
All-cause mortality (%)	34.7	25.6	1.12 (0.97–1.29)	0.109	11.2	7.7	1.04 (0.82–1.30)	0.755
CV mortality (%)	22.5	15.6	1.24 (1.07–1.45)	0.005	5.7	4.1	1.04 (0.77–1.42)	0.783
All-cause hospitalization (%)	49.7	43.1	1.16 (1.04–1.29)	0.008	36.4	26.6	1.26 (1.13–1.41)	<0.001
HF hospitalization (%)	31.5	24.6	1.22 (1.05–1.42)	0.009	17.0	11.5	1.37 (1.17–1.60)	<0.001
All-cause mortality or HF hospitalization (%)	54.5	44.2	1.12 (1.00–1.26)	0.046	25.1	17.6	1.06 (0.90–1.25)	0.489

Heart J of HF 2018

Lung inflammation in chronic obstructive pulmonary disease may contribute to the appearance of cardiovascular events.



De Miguel Diez X .et al, International Journal of COPD 2013

Dispnea Cardiogena

- Scompenso cardiaco
- Ischemia (anche come equivalente anginoso)
- Aritmie

MALATTIE DEL CIRCOLO POLMONARE

- Embolia polmonare
- Ipertensione polmonare

Segni e sintomi dello Scompenso

Symptoms	Signs
Typical	More specific
Breathlessness Orthopnoea Paroxysmal nocturnal dyspnoea Reduced exercise tolerance Fatigue, tiredness, increased time to recover after exercise Ankle swelling	Elevated jugular venous pressure Hepatojugular reflux Third heart sound (gallop rhythm) Laterally displaced apical impulse
Less typical	Less specific
Nocturnal cough Wheezing Bloated feeling Loss of appetite Confusion (especially in the elderly) Depression Palpitations Dizziness Syncope Bendopnea[53]	Weight gain (>2 kg/week) Weight loss (in advanced HF) Tissue wasting (cachexia) Cardiac murmur Peripheral oedema (ankle, sacral, scrotal) Pulmonary crepitations Reduced air entry and dullness to percussion at lung bases (pleural effusion) Tachycardia Irregular pulse Tachypnoea Cheyne Stokes respiration Hepatomegaly Ascites Cold extremities Oliguria Narrow pulse pressure

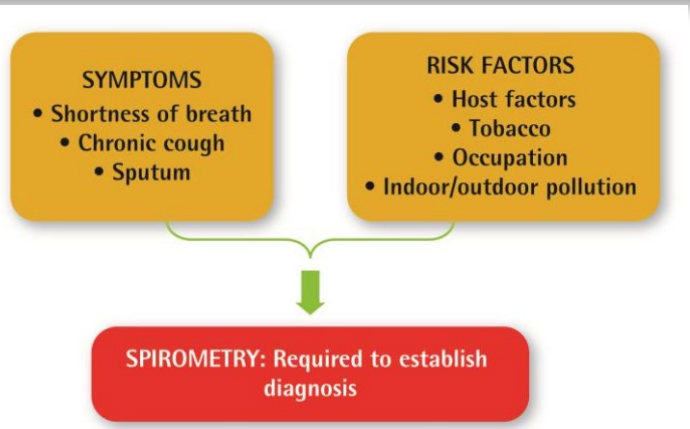


Table 2.2. Other causes of chronic cough

Intrathoracic

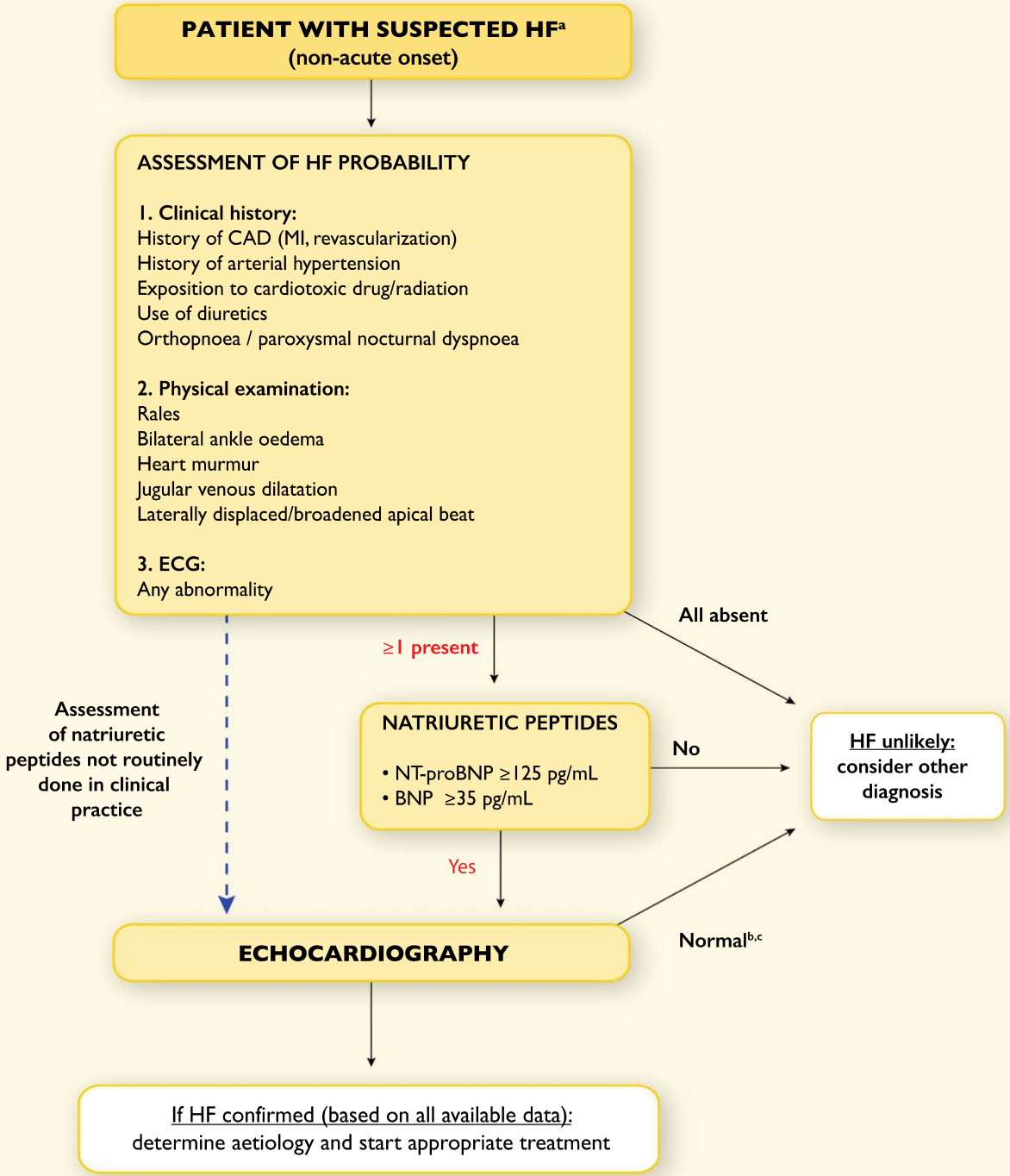
- Asthma
- Lung cancer
- Tuberculosis
- Bronchiectasis
- Left heart failure
- Interstitial lung disease
- Cystic fibrosis
- Idiopathic cough

Extrathoracic

- Chronic allergic rhinitis
- Post nasal drip syndrome (PNDS)
- Upper Airway Cough Syndrome (UACS)
- Gastroesophageal reflux
- Medication (e.g. ACE inhibitors)

Cause di HF

DISEASED MYOCARDIUM		
Ischaemic heart disease	Myocardial scar	
	Myocardial stunning/hibernation	
	Epicardial coronary artery disease	
	Abnormal coronary microcirculation	
	Endothelial dysfunction	
Toxic damage	Recreational substance abuse	Alcohol, cocaine, amphetamine, anabolic steroids.
	Heavy metals	Copper, iron, lead, cobalt.
	Medications	Cytostatic drugs (e.g. anthracyclines), immunomodulating drugs (e.g. interferons monoclonal antibodies such as trastuzumab, cetuximab), antidepressant drugs, antiarrhythmics, non-steroidal anti-Inflammatory drugs, anaesthetics.
	Radiation	
Immune-mediated and inflammatory damage	Related to infection	Bacteria, spirochaetes, fungi, protozoa, parasites (Chagas disease), rickettsiae, viruses (HIV/AIDS).
	Not related to infection	Lymphocytic/giant cell myocarditis, autoimmune diseases (e.g. Graves' disease, rheumatoid arthritis, connective tissue disorders, mainly systemic lupus erythematosus), hypersensitivity and eosinophilic myocarditis (Churg–Strauss).
Infiltration	Related to malignancy	Direct infiltrations and metastases.
	Not related to malignancy	Amyloidosis, sarcoidosis, haemochromatosis (iron), glycogen storage diseases (e.g. Pompe disease), lysosomal storage diseases (e.g. Fabry disease).
Metabolic derangements	Hormonal	Thyroid diseases, parathyroid diseases, acromegaly, GH deficiency, hypercortisolaemia, Conn's disease, Addison disease, diabetes, metabolic syndrome, phaeochromocytoma, pathologies related to pregnancy and peripartum.
	Nutritional	Deficiencies in thiamine, L-carnitine, selenium, iron, phosphates, calcium, complex malnutrition (e.g. malignancy, AIDS, anorexia nervosa), obesity.
Genetic abnormalities	Diverse forms	HCM, DCM, LV non-compaction, ARVC, restrictive cardiomyopathy (for details see respective expert documents), muscular dystrophies and laminopathies.
ABNORMAL LOADING CONDITIONS		
Hypertension		
Valve and myocardium structural defects	Acquired	Mitral, aortic, tricuspid and pulmonary valve diseases.
	Congenital	Atrial and ventricular septum defects and others (for details see a respective expert document).
Pericardial and endomyocardial pathologies	Pericardial	Constrictive pericarditis Pericardial effusion
	Endomyocardial	HES, EMF, endocardial fibroelastosis.
High output states		Severe anaemia, sepsis, thyrotoxicosis, Paget's disease, arteriovenous fistula, pregnancy.
Volume overload		Renal failure, iatrogenic fluid overload.
ARRHYTHMIAS		
Tachyarrhythmias		Atrial, ventricular arrhythmias.
Bradyarrhythmias		Sinus node dysfunctions, conduction disorders.


PATIENT WITH SUSPECTED HF[a]
(non-acute onset)
ASSESSMENT OF HF PROBABILITY
1. Clinical history:
History of CAD (MI, revascularization)
History of arterial hypertension
Exposition to cardiotoxic drug/radiation
Use of diuretics
Orthopnoea / paroxysmal nocturnal dyspnoea
2. Physical examination:
Rales
Bilateral ankle oedema
Heart murmur
Jugular venous dilatation
Laterally displaced/broadened apical beat
3. ECG:
Any abnormality
All absent
≥1 present
Assessment of natriuretic peptides not routinely done in clinical practice
NATRIURETIC PEPTIDES
• NT-proBNP ≥125 pg/mL
• BNP ≥35 pg/mL
No
HF unlikely: consider other diagnosis
Yes
ECHOCARDIOGRAPHY
Normal[b,c]
If HF confirmed (based on all available data):
determine aetiology and start appropriate treatment

Cause di innalzamento di NT pro BNP

Cardiac	Heart failure Acute coronary syndromes Pulmonary embolism Myocarditis Left ventricular hypertrophy Hypertrophic or restrictive cardiomyopathy Valvular heart disease Congenital heart disease Atrial and ventricular tachyarrhythmias Heart contusion Cardioversion, ICD shock Surgical procedures involving the heart Pulmonary hypertension
Non-cardiac	Advanced age Ischaemic stroke Subarachnoid haemorrhage Renal dysfunction Liver dysfunction (mainly liver cirrhosis with ascites) Paraneoplastic syndrome Chronic obstructive pulmonary disease Severe infections (including pneumonia and sepsis) Severe burns Anaemia Severe metabolic and hormone abnormalities (e.g. thyrotoxicosis, diabetic ketosis)

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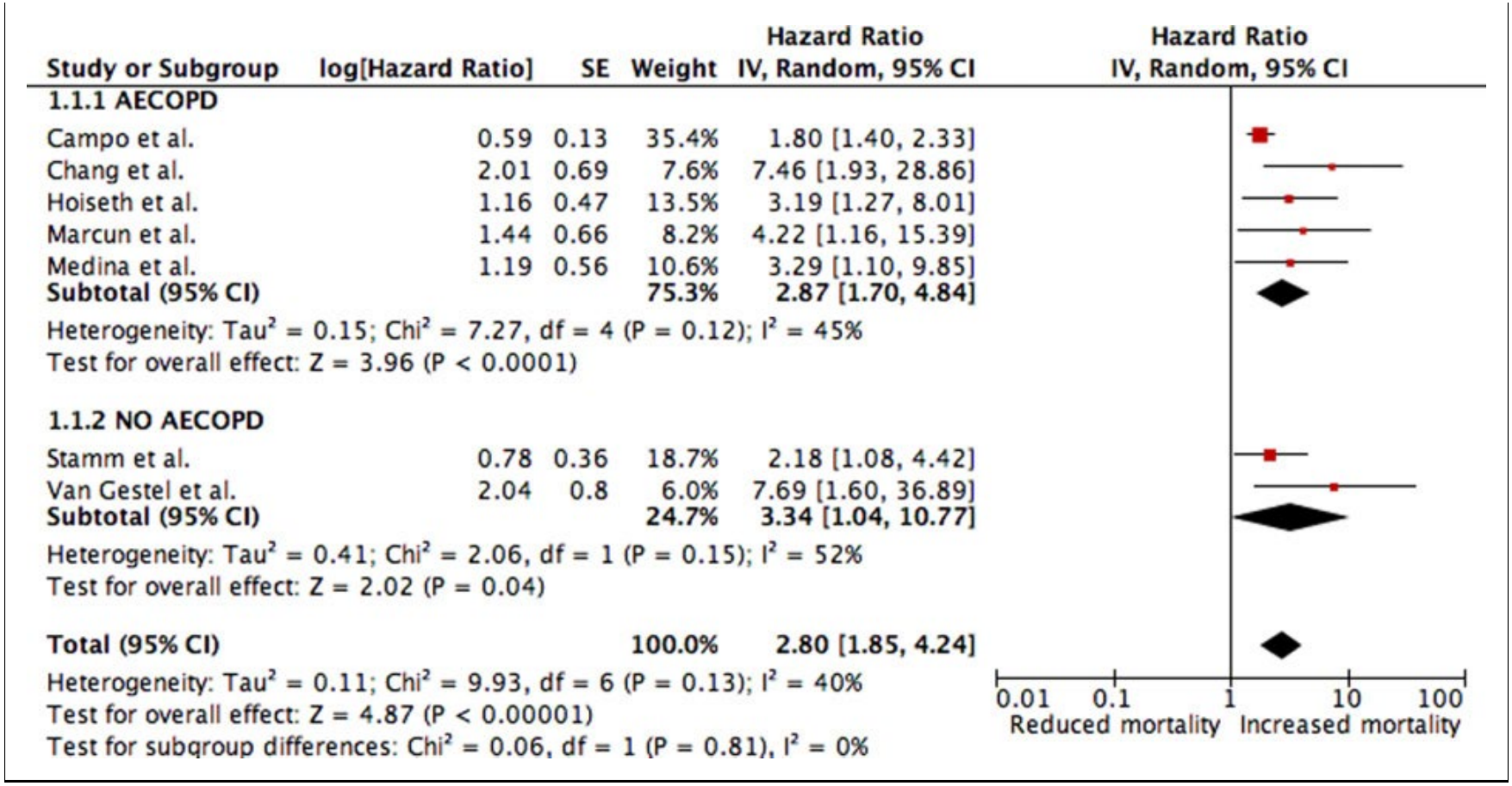
Relationship between NT-proBNP above the cut-off and all-cause mortality.



Pavasini R. et al Chronic Respiratory Disease2017

Definition of heart failure with preserved (HFpEF), mid-range (HFmrEF) and reduced ejection fraction (HFrEF)

Type of HF		HFrEF	HFmrEF	HFpEF
CRITERIA	1	Symptoms ± Signs[a]	Symptoms ± Signs[a]	Symptoms ± Signs[a]
	2	LVEF <40%	LVEF 40–49%	LVEF ≥50%
	3	–	1. Elevated levels of natriuretic peptides[b]; 2. At least one additional criterion: a. relevant structural heart disease (LVH and/or LAE), b. diastolic dysfunction (for details see Section 4.3.2).	1. Elevated levels of natriuretic peptides[b]; 2. At least one additional criterion: a. relevant structural heart disease (LVH and/or LAE), b. diastolic dysfunction (for details see Section 4.3.2).

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Typical demographics and co-morbidities associated with heart failure with preserved ejection fraction

Advanced age
Arterial hypertension
Atrial fibrillation
Female gender
Kidney dysfunction
Metabolic syndrome
Obesity
Physical deconditioning
Pulmonary disease (e.g. COPD)
Pulmonary hypertension
Sleep apnoea

Importance of co-morbidities in patients with heart failure

1. interfere with the diagnostic process of HF (e.g. COPD as a potentially confounding cause of dyspnoea).[390, 391]
2. aggravate HF symptoms and further impair quality of life.[391, 392]
3. contribute to the burden of hospitalizations and mortality,[393] as the main cause of readmissions at 1 and 3 months.[394]
4. may affect the use of treatments for HF (e.g. renin–angiotensin system inhibitors contra-indicated in some patients with severe renal dysfunction or beta-blockers relatively contra-indicated in asthma).[395, 396]
5. evidence base for HF treatment is more limited as co-morbidities were mostly an exclusion criterion in trials; efficacy and safety of interventions is therefore often lacking in the presence of co-morbidities.
6. drugs used to treat co-morbidities may cause worsening HF (e.g. NSAIDs given for arthritis, some anti-cancer drugs).[397]
7. interaction between drugs used to treat HF and those used to treat co-morbidities, resulting in lower efficacy, poorer safety, and the occurrence of side effects (e.g. beta-blockers for HFrEF and beta-agonists for COPD and asthma).[391, 395, 396]

Acute coronary syndrome.
Tachyarrhythmia (e.g. atrial fibrillation, ventricular tachycardia).
Excessive rise in blood pressure.
Infection (e.g. pneumonia, infective endocarditis, sepsis).
Non-adherence with salt/fluid intake or medications.
Bradyarrhythmia.
Toxic substances (alcohol, recreational drugs).
Drugs (e.g. NSAIDs, corticosteroids, negative inotropic substances, cardiotoxic chemotherapeutics).
Exacerbation of chronic obstructive pulmonary disease.
Pulmonary embolism.
Surgery and perioperative complications.
Increased sympathetic drive, stress-related cardiomyopathy.
Metabolic/hormonal derangements (e.g. thyroid dysfunction, diabetic ketosis, adrenal dysfunction, pregnancy and peripartum related abnormalities).
Cerebrovascular insult.
Acute mechanical cause: myocardial rupture complicating ACS (free wall rupture, ventricular septal defect, acute mitral regurgitation), chest trauma or cardiac intervention, acute native or prosthetic valve incompetence secondary to endocarditis, aortic dissection or thrombosis.

Markers of worse prognosis in patients with heart failure

Demographic data	Older age, male sex, low socio-economic status.
Severity of heart failure	Advanced NYHA Class, longer HF duration, reduced peak oxygen consumption, high VE-VCO_2 slope, Cheyne–Stoke ventilation, short 6-minute walking distance, reduced muscle strength, poor quality of life.
Clinical status	High resting heart rate, low blood pressure, clinical features of fluid overload (both pulmonary congestion and peripheral oedema, jugular venous dilatation, hepatomegaly), clinical features of peripheral hypoperfusion, body wasting, frailty.
Myocardial remodeling and severity of heart dysfunction	Low LVEF, LV dilatation, severe diastolic LV dysfunction, high LV filling pressure, mitral regurgitation, aortic stenosis, LV hypertrophy, left atrial dilatation, RV dysfunction, pulmonary hypertension, dyssynchrony, vast area of hypo/akinesis, wide QRS complex, presumed inflammation or infiltration on CMR, inducible ischaemia and poor viability on imaging.
Biomarkers of neurohormonal activation	Low sodium, high natriuretic peptides, high plasma renin activity, high aldosterone and catecholamines, high endothelin-1, high adrenomedullin, high vasopressin.
Other biomarkers	Markers of renal function, inflammationatory markers, cardiac stress markers, cardiac damage markers, metabolic markers, collagen markers, markers of organ damage/dysfunction.
Genetic testing (see section 5.10.1)	Certain mutations in inherited cardiomyopathies associated with high-risk of sudden cardiac death or rapid HF progression.
Cardiovascular co-morbidities	Atrial fibrillation, ventricular arrhythmia, non-revascularizable coronary artery disease, previous stroke/TIA, peripheral arterial disease.
Non-cardiovascular co-morbidities	Diabetes, anaemia, iron deficiency, COPD, renal failure, liver dysfunction, sleep apnoea, cognitive impairment, depression.
Non-adherence	Non-adherence with recommended HF treatment.
Clinical events	HF hospitalization, aborted cardiac arrest, ICD shocks.

L’ipertensione polmonare moderata è spesso presente sia nell’interstiziopatia polmonare severa sia nella BPCO severa mentre l’ipertensione polmonare severa in queste situazioni è rara. L’ipertensione polmonare severa è spesso presente invece nella sindrome combinata enfisema/fibrosi dove l’ipertensione polmonare ha una elevatissima prevalenza.

Definizione di PH

Definition	Characteristics[a]	Clinical group(s)[b]
PH	PAPm ≥25 mmHg	All
Pre-capillary PH	PAPm ≥25 mmHg PAWP ≤15 mmHg	1. Pulmonary arterial hypertension 3. PH due to lung diseases 4. Chronic thromboembolic PH 5. PH with unclear and/or multifactorial mechanisms
Post-capillary PH	PAPm ≥25 mmHg PAWP >15 mmHg	2. PH due to left heart disease 5. PH with unclear and/or multifactorial mechanisms
Isolated post-capillary PH (Ipc-PH)	DPG <7 mmHg and/or PVR ≤3 WU[c]	
Combined post-capillary and pre-capillary PH (Cpc-PH)	DPG ≥7 mmHg and/or PVR >3 WU[c]	

DPG = Diastolic Pressure Gradient (PAP diastolica – PAWP media)

PVR = Resistenze Vascolari Polmonari

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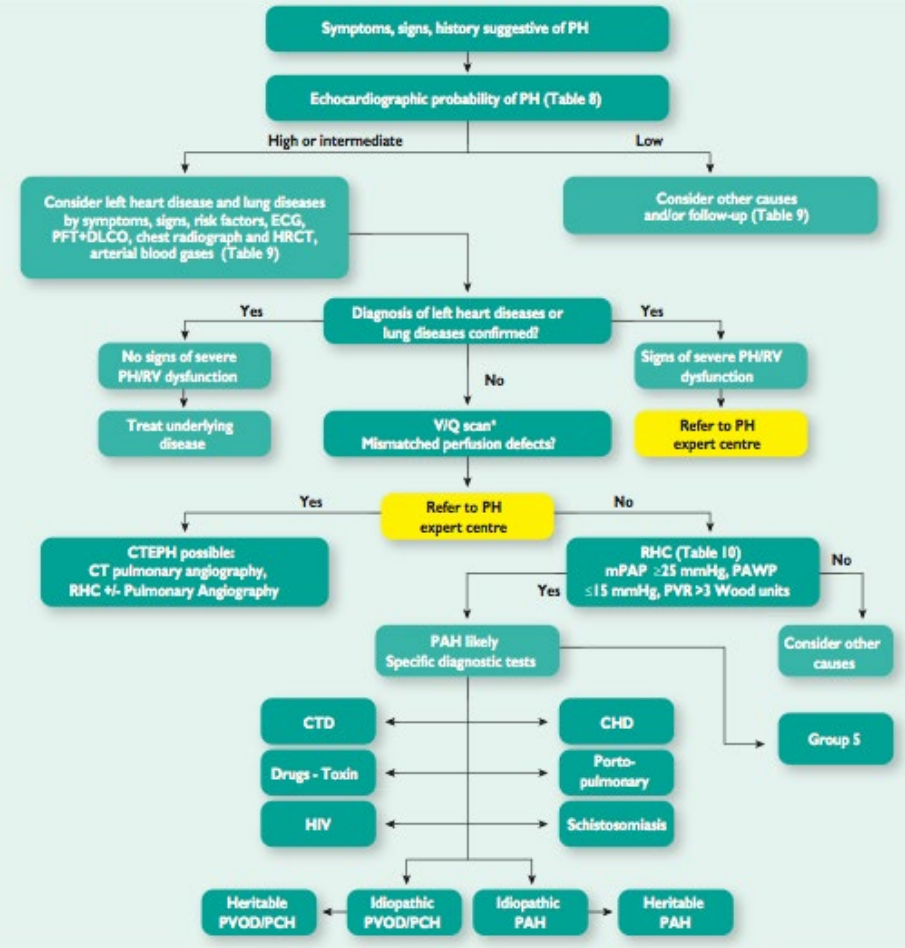
The severity of PH is usually poorly associated with the severity of the underlying lung disease. The most common indicators for the presence of PH in these patients are a disproportionally low DLCO and a low pCO2.

Algoritmo diagnostico



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Classificazione della PH

1. Pulmonary arterial hypertension

- 1.1 Idiopathic
- 1.2 Heritable
  - 1.2.1 BMPR2 mutation
  - 1.2.2 Other mutations
- 1.3 Drugs and toxins induced
- 1.4 Associated with:
  - 1.4.1 Connective tissue disease
  - 1.4.2 Human immunodeficiency virus (HIV) infection
  - 1.4.3 Portal hypertension
  - 1.4.4 Congenital heart disease (Table 6)
  - 1.4.5 Schistosomiasis

1'. Pulmonary veno-occlusive disease and/or pulmonary capillary haemangiomatosis

- 1'.1 Idiopathic
- 1'.2 Heritable
  - 1'.2.1 EIF2AK4 mutation
  - 1'.2.2 Other mutations
- 1'.3 Drugs, toxins and radiation induced
- 1'.4 Associated with:
  - 1'.4.1 Connective tissue disease
  - 1'.4.2 HIV infection

1''. Persistent pulmonary hypertension of the newborn

2. Pulmonary hypertension due to left heart disease

- 2.1 Left ventricular systolic dysfunction
- 2.2 Left ventricular diastolic dysfunction
- 2.3 Valvular disease
- 2.4 Congenital / acquired left heart inflow/outflow tract obstruction and congenital cardiomyopathies
- 2.5 Congenital /acquired pulmonary veins stenosis

3. Pulmonary hypertension due to lung diseases and/or hypoxia

- 3.1 Chronic obstructive pulmonary disease
- 3.2 Interstitial lung disease
- 3.3 Other pulmonary diseases with mixed restrictive and obstructive pattern
- 3.4 Sleep-disordered breathing
- 3.5 Alveolar hypoventilation disorders
- 3.6 Chronic exposure to high altitude
- 3.7 Developmental lung diseases (Web Table III)

4. Chronic thromboembolic pulmonary hypertension and other pulmonary artery obstructions

- 4.1 Chronic thromboembolic pulmonary hypertension
- 4.2 Other pulmonary artery obstructions
  - 4.2.1 Angiosarcoma
  - 4.2.2 Other intravascular tumors
  - 4.2.3 Arteritis
  - 4.2.4 Congenital pulmonary arteries stenoses
  - 4.2.5 Parasites (hydatidosis)

5. Pulmonary hypertension with unclear and/or multifactorial mechanisms

- 5.1 Haematological disorders: chronic haemolytic anaemia, myeloproliferative disorders, splenectomy
- 5.2 Systemic disorders: sarcoidosis, pulmonary histiocytosis, lymphangioleiomyomatosis, neurofibromatosis
- 5.3 Metabolic disorders: glycogen storage disease, Gaucher disease, thyroid disorders
- 5.4 Others: pulmonary tumoral thrombothic microangiopathy, fibrosing mediastinitis, chronic renal failure (with/without dialysis), segmental pulmonary hypertension

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Haemodynamic classification of pulmonary hypertension due to lung disease

Terminology	Haemodynamics (right heart catheterization)
COPD/IPF/CPFE without PH	PAPm <25 mmHg
COPD/IPF/CPFE with PH	PAPm ≥25 mmHg
COPD/IPF/CPFE with severe PH	PAPm >35 mmHg, or PAPm ≥25 mmHg in the presence of a low cardiac output (CI <2.5 L/min, not explained by other causes)

IPF = Fibrosi polmonare idiopatica
CPFE = Fibrosi ed enfisema polmonari Idiopatici

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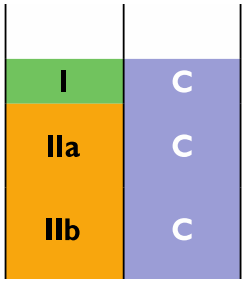
Recommendations for pulmonary hypertension due to lung diseases

Recommendations	Class[a]	Level[b]
Echocardiography is recommended for the non-invasive diagnostic assessment of suspected PH in patients with lung disease	I	C
Referral to an expert centre is recommended[d] in patients with echocardiographic signs of severe PH and/or severe right ventricular dysfunction	I	C
The optimal treatment of the underlying lung disease, including long-term O_2 therapy in patients with chronic hypoxaemia, is recommended in patients with PH due to lung diseases	I	C
Referral to PH expert center should be considered for patients with signs of severe PH/severe RV failure for individual-based treatment	IIa	C
RHC is not recommended for suspected PH in patients with lung disease, unless therapeutic consequences are to be expected (e.g. lung transplantation, alternative diagnoses such as PAH or CTEPH, potential enrolment in a clinical trial)	III	C
The use of drugs approved for PAH is not recommended in patients with PH due to lung diseases	III	C

Recommendations for diagnostic tests in patients with heart failure

Right heart catheterization with a pulmonary artery catheter:

- is recommended in patients with severe HF being evaluated for heart transplantation or mechanical circulatory support;
- should be considered in patients with probable pulmonary hypertension assessed by echocardiography in order to confirm pulmonary hypertension and its reversibility before the correction of valve/structural heart disease;
- may be considered in order to adjust therapy in patients with HF who remain severely symptomatic despite initial standard therapies and whose haemodynamic status is unclear.



Recommendations for right heart catheterization in pulmonary hypertension

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Recommendations	Class[a]	Level[b]	Ref.[c]
RHC is recommended to confirm the diagnosis of pulmonary arterial hypertension (group 1) and to support treatment decisions	I	C	
In patients with PH, it is recommended to perform RHC in expert centres (see section 12) as it is technically demanding and may be associated with serious complications	I	B	69
RHC should be considered in pulmonary arterial hypertension (group 1) to assess the treatment effect of drugs (Table 16)	IIa	C	
RHC is recommended in patients with congenital cardiac shunts to support decisions on correction (Table 24)	I	C	
RHC is recommended in patients with PH due to left heart disease (group 2) or lung disease (group 3) if organ transplantation is considered	I	C	
When measurement of PAWP is unreliable, left heart catheterization should be considered to measure LVEDP	IIa	C	
RHC may be considered in patients with suspected PH and left heart disease or lung disease to assist in the differential diagnosis and support treatment decisions	IIb	C	
RHC is indicated in patients with CTEPH (group 4) to confirm the diagnosis and support treatment decisions	I	C	

Suggested assessment and timing for the follow-up of patients with pulmonary arterial hypertension

	At baseline	Every 3–6 months[a]	Every 6–12 months[a]	3–6 months after changes in therapy[a]	In case of clinical worsening
Medical assessment and determination of functional class	+	+	+	+	+
ECG	+	+	+	+	+
6MWT/Borg dyspnoea score	+	+	+	+	+
CPET	+		+		+[e]
Echo	+		+	+	+
Basic lab[b]	+	+	+	+	+
Extended lab[c]	+		+		+
Blood gas analysis[d]	+		+	+	+
Right heart catheterization	+		+[f]	+[e]	+[e]

I PARAMETRI VALUTABILI CON IL CPET SONO:

	Determinazione non invasiva	Determinazione invasiva
Lavoro	Work rate	
Risposta Metabolica	VO2, VCO2, RER,	
	SOGLIA ANAEROBICA (AT)	Lattato
Risposta Cardiovascolare	HR, ECG, BP, polso di O2	
Risposta Ventilatoria	VE, Vt, FR, Riserva respiratoria	
Scambi Gassosi	SaO2, VE/VCO2, VE/VO2 PETO2, PETCO2, Vd/Vt	PaO2, P(A-a)O2
Equilibrio acido-base		pH, PaCO2, HCO3-
Sintomi	dispnea, fatica, dolore toracico	

Pattern di risposta al TCP

PARAMETRI	COPD	ILD	PVD	CHF	OBESITY	DECONDITIONATED
VO2 Max / Peak	1 decreased	1 decreased	1 decreased	1 decreased	1 decreased for actual, normal for ideal weight	1 decreased
AT	1 normal 2 decreased 3 indeterminated	1 normal 2 decreased	1 decreased	1 decreased	1 normal	1 normal 2 decreased
PEAK HR	1 decreased 2 normal in mild	1 decreased	1 normal 2 slightly decreased	1 variable 2 normal in mid	1 normal 2 slightly decreased	1 normal 2 slightly decreased
O2 PULSE	1 normal 2 decreased	1 normal 2 decreased	1 normal 2 decreased	1 decreased	1 normal	1 decreased
(VE/MVV) %	1 increased	1 normal 2 increased	1 normal 2 increased	1 normal 2 decreased	1 normal 2 increased	1 normal
VE/VCO2 (at AT)	1 increased	1 increased	1 increased	1 increased	1 normal	1 normal
Vd/Vt	1 increased	1 increased	1 increased	1 increased	1 increased	1 normal
PaO2	1 variable	1 decreased	1 decreased	1 normal	1 normal, may increase	1 normal
P(A-a) O2	1variable 2 usually increased	1 increased	1 increased	1 usually normal	1 may decrease	1 normal

Betabloccanti

WHY?

To improve symptoms, reduce the risk of HF hospitalization and increase survival.

IN WHOM AND WHEN?

Indications:

1. Potentially all patients with stable mild or moderate systolic HF (LVEF <40%) (NYHA Class II-III).
2. First-line treatment, along with an ACE-I and an MRA, in patients with stabilized HF; start as early as possible in the course of disease.
3. Patients with severe HF also benefit from beta-blockers but treatment should be started under the care of a specialist.

Contra-indications:

1. Second- or third-degree AV block (in the absence of a permanent pacemaker).
2. Critical limb ischaemia.
3. Asthma (relative contra-indication): if cardio-selective beta-blockers are indicated, asthma is not necessarily an *absolute* contra-indication, but these medications should only be used under close medical supervision by a specialist, with consideration of the risks for and against their use[223,224]; COPD is not a contra-indication.
4. Known allergic reaction/other adverse reaction (drug-specific).

Cautions/seek specialist advice:

1. Severe (NYHA Class IV) HF.
2. Current or recent (<4 weeks) exacerbation of HF (e.g. hospital admission with worsening HF), heart block, or heart rate <50 bpm.
3. If persisting signs of congestion, hypotension (systolic <90 mmHg), raised jugular venous pressure, ascites, marked peripheral oedema - try to relieve congestion and achieve 'euvolaemia' before starting a beta-blocker.
4. Drug interactions to look out for (because of risk of bradycardia/atrioventricular block):
   - Verapamil, diltiazem (should be discontinued).[b]
   - Digoxin.
   - Amiodarone.
   - Ivabradine.

WHICH BETA-BLOCKER AND WHAT DOSE? - See Table 7.2

Bisoprolol: starting dose 1.25 mg *o.d.*, target dose 10 mg *o.d.*
Carvedilol: starting dose 3.125 mg *b.i.d.*, target dose 25 mg *b.i.d.*
Metoprolol succinate (CR/XL): starting dose 12.5–25 mg *o.d.*, target dose 200 mg *o.d.*
Nebivolol: starting dose 1.25 mg *o.d.*, target dose 10 mg *o.d.*

WHERE?

- In the community in stable patients (NYHA Class IV/patients with severe HF and those with a current/recent exacerbation should be referred for specialist advice).
- In patients hospitalized with worsening HF – after stabilizing, relieving congestion, and, if possible, restoring 'euvolaemia' (but ideally before discharge).
- Other exceptions–see 'Cautions/seek specialist advice'.

HOW TO USE?

- Start with a low dose in a stable condition (see Table 7.2).
- Double the dose at not less than 2-week intervals (slower up-titration may be needed in some patients).
- Aim for target dose (see above) or, failing that, the highest tolerated dose (remember: some beta-blocker is better than no beta-blocker).
- Monitor heart rate, blood pressure, and clinical status (symptoms, signs–especially signs of congestion, body weight).
- A specialist HF nurse may assist with education of the patient, follow-up (in person or by telephone), and dose up-titration.
- When to stop up-titration, reduce dose, stop treatment–see PROBLEM SOLVING.

PROBLEM SOLVING

Worsening symptoms or signs (e.g. increasing dyspnoea, fatigue, oedema, weight gain):

- If increasing congestion, increase dose of diuretic or halve dose of beta-blocker (if increasing diuretic dose does not work).
- If marked fatigue (or bradycardia–see below), halve dose of beta-blocker (rarely necessary); review patient in 1–2 weeks; if not improved, seek specialist advice.
- If serious deterioration, halve dose of beta-blocker or stop this treatment (rarely necessary); seek specialist advice.

Low heart rate:

- If <50 bpm and worsening symptoms, halve dose of beta-blocker, or, if severe deterioration, stop beta-blocker (rarely necessary).
- Review need for other heart rate-slowing drugs (e.g. digoxin, amiodarone, diltiazem, or verapamil[b]).
- Arrange electrocardiogram to exclude heart block.
- Seek specialist advice.

Asymptomatic low blood pressure:

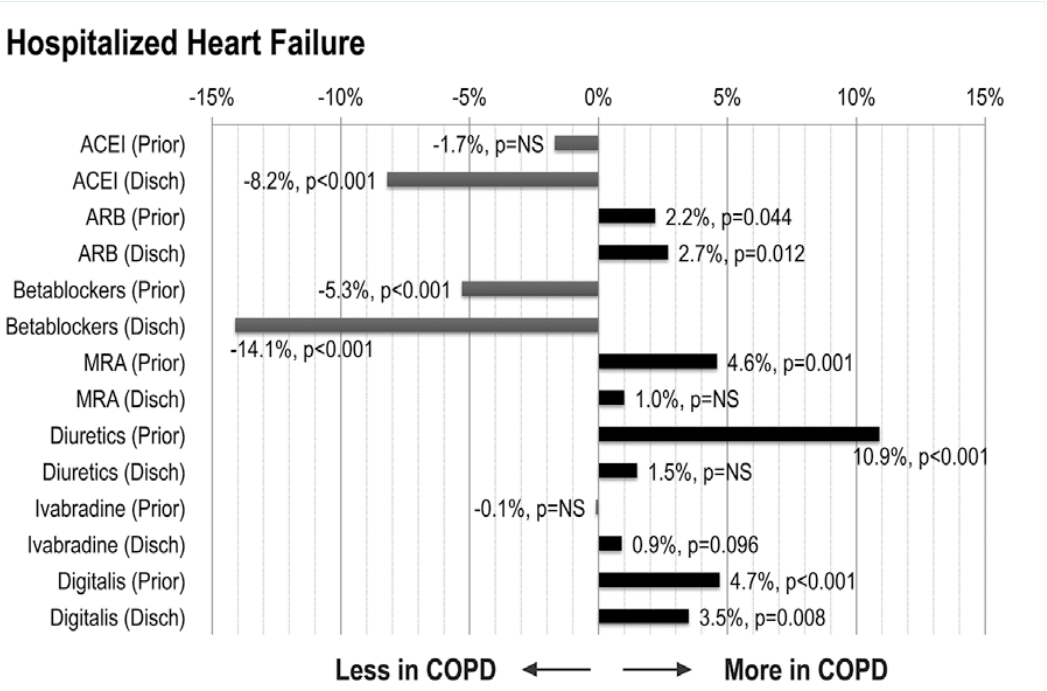
- Does not usually require any change in therapy.

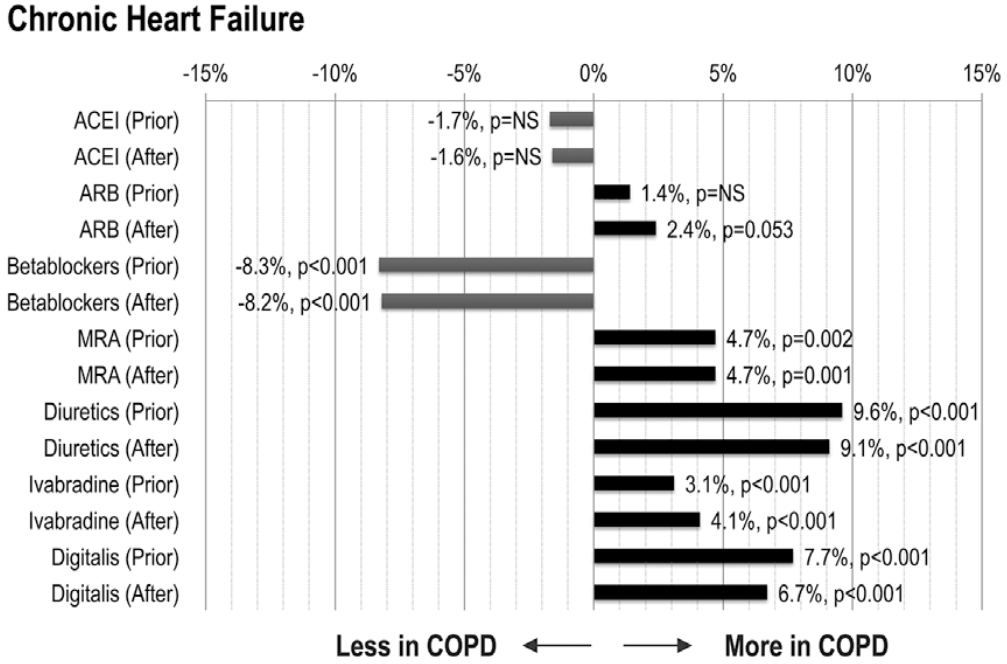
Symptomatic hypotension:

- If dizziness, light headedness, or confusion and a low blood pressure, reconsider need for nitrates, calcium-channel blockers[b], and other vasodilators and reduce/stop, if possible.
- If no signs or symptoms of congestion, consider reducing diuretic dose.
- If these measures do not solve problem, seek specialist advice.

ADVICE TO PATIENT

- Explain expected benefits (see WHY?) and mention possibility of temporary adverse effects.
  - Treatment is given to improve symptoms, to prevent worsening of HF leading to hospital admission, and to increase survival.
  - Symptomatic improvement may develop slowly after starting treatment, sometimes taking 3–6 months or longer.
  - Temporary symptomatic deterioration may occur during initiation or up-titration phase; in the long term beta-blockers improve well-being.
- Advise patient to report deterioration (see PROBLEM SOLVING) and that deterioration (tiredness, fatigue, breathlessness) can usually be easily managed by adjustment of other medication; patients should be advised not to stop beta-blocker therapy without consulting the physician.
- During initiation or up-titration phase to detect and to treat potential deterioration early, patients should be encouraged to weigh themselves daily (after waking, before dressing, after voiding, before eating) and to increase their diuretic dose should their weight increase, persistently (>2 days), by >1.5–2.0 kg/day.

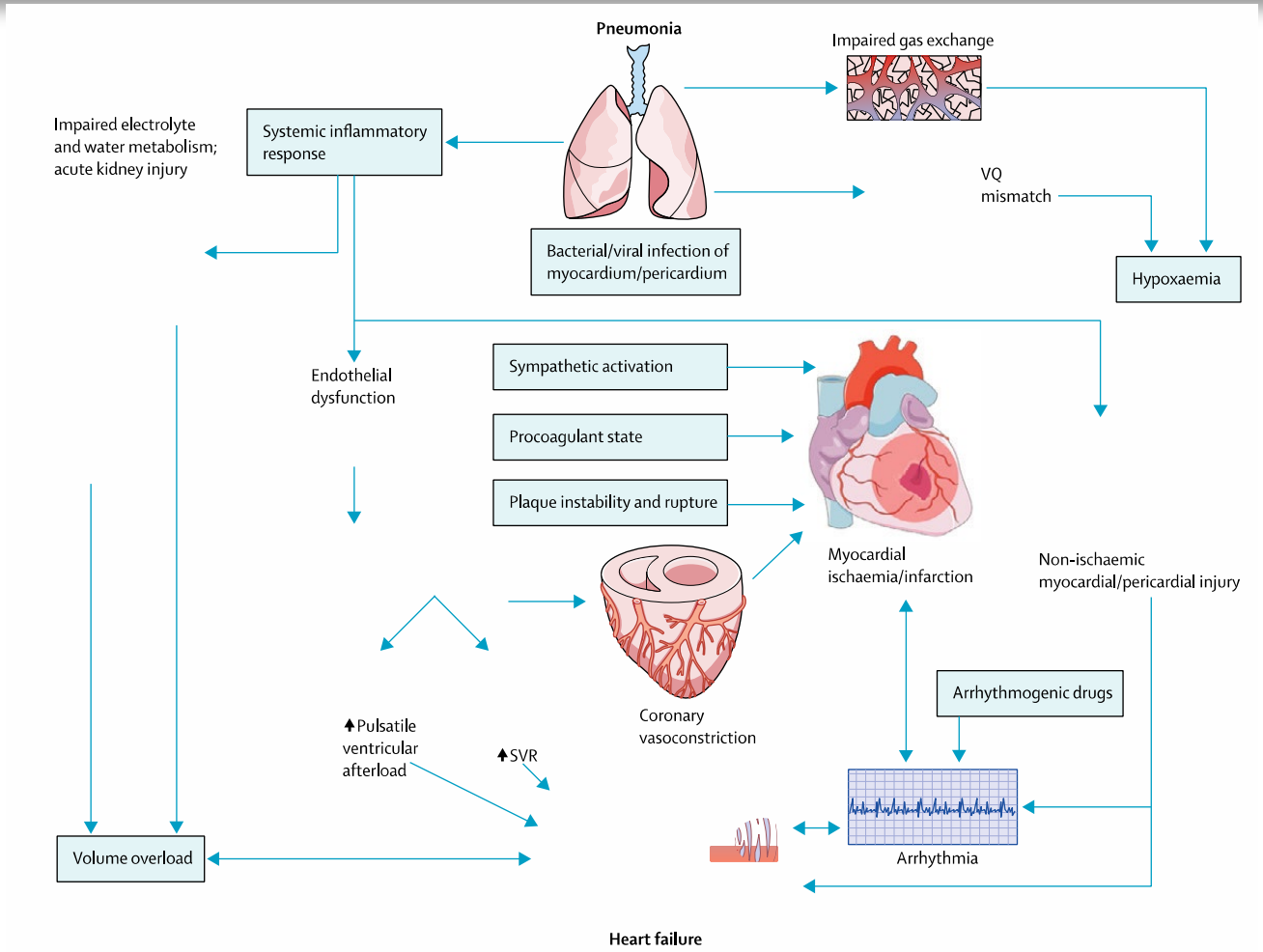




Cardiovascular treatments of hospitalized and chronic heart failure patients according to the presence or absence of chronic obstructive pulmonary disease at study entry

Eu Heart J of HF 2018

Rapporto tra polmonite e SCC



Corrales-Medina FV et al Lancet 2013

Conclusioni

Malattie polmonari, scompenso e cardiopatia ischemica sono strettamente collegati tra di loro avendo alla base elementi comuni quale il fattore di rischio fumo, l'eziologia legata all'infiammazione/immunità e la condivisione, che cuore e polmone hanno, dello spazio all'interno della gabbia toracica. Il legame più significativo tra queste patologie sta nello sviluppo di ipertensione polmonare che condiziona in modo serio la relazione tra i due organi. Importante è la sinergia tra i gestori del paziente affetto da queste comorbidità per ottenere i migliori risultati nella gestione della diagnostica differenziale e per ottimizzare la terapia che per entrambe le patologia deve essere piena ed efficace.

ASSOCIAZIONE - ONLUS

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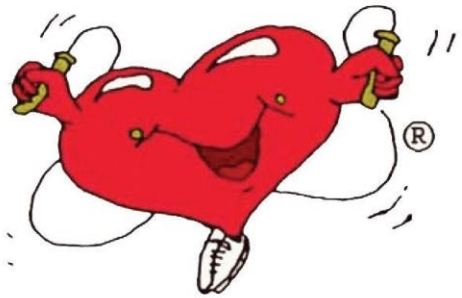


www.gruppocuorenuovo.it

Cardiovascular treatments of hospitalized and chronic heart failure patients according to the presence or absence of chronic obstructive pulmonary disease at study entry

	Hospitalized heart failure			Chronic heart failure		
	COPD ($n = 1334$)	No COPD ($n = 5586$)	*P*-value	COPD ($n = 1322$)	No COPD ($n = 8087$)	*P*-value
ACEi (Ent, %)	49.4	51.1	0.281	62.7	64.4	0.239
ACEi (Disch, %)	56.6	64.7	<0.001	65.4	67.0	0.246
ARB (Ent, %)	15.2	13.0	0.044	23.6	22.2	0.246
ARB (Disch, %)	17.0	14.3	0.012	26.1	23.7	0.053
BB (Ent, %)	51.0	56.3	<0.001	77.0	85.3	<0.001
BB (Disch, %)	62.8	76.9	<0.001	81.6	89.8	<0.001
MRA (Ent, %)	38.1	33.5	0.001	57.0	52.3	0.002
MRA (Disch, %)	55.4	54.4	0.53	62.9	58.2	0.001
Diuretics (Ent, %)	72.8	61.9	<0.001	87.7	78.1	<0.001
Diuretics (Disch, %)	84.5	83.0	0.199	90.6	81.5	<0.001
2nd Diuretic (Ent, %)	7.9	5.5	<0.001	13.3	9.6	<0.001
2nd Diuretic (Disch, %)	10.8	9.2	0.095	15.9	10.8	<0.001
Ivabradine (Ent, %)	1.2	1.3	0.803	8.5	5.4	<0.001
Ivabradine (Disch, %)	3.9	3.0	0.096	11.9	7.8	<0.001
Digitalis (Ent, %)	22.8	18.1	<0.001	27.9	20.2	<0.001
Digitalis (Disch, %)	27.4	23.9	0.008	28.6	21.9	<0.001
Statins (Ent, %)	42.3	42.0	0.835	58.9	57.0	0.207
Statins (Disch, %)	54.4	59.3	0.001	62.2	60.1	0.142
Amiodarone (Ent, %)	10.0	9.4	0.483	13.8	13.6	0.854
Amiodarone (Disch, %)	13.4	14.3	0.403	14.6	13.8	0.444
CCB (Ent, %)	18.9	14.5	<0.001	12.9	11.1	0.052
CCB (Disch, %)	18.1	14.7	0.003	12.6	11.2	0.161

Web Table 4.4 Diagnostic tests for specific causes of heart failure with preserved ejection fraction

Genetic testing (e.g. for ATTR amyloidosis and HCM; see also section 5.10.1)
Bence-Jones proteinuria (AL amyloidosis)
99mTc-DPD scintigraphy (wild-type transthyretrin amyloidosis)
Eosinophilia, IL-2 receptor, ACE (sarcoidosis)
Hs troponin, CK, CK-MB (myocarditis)
Borellia burgdorferi IgM (borreliosis)
HIV serology (HIV cardiomyopathy)
Tryponosoma cruzi serology (Chagas disease)
Serum ferritin, genetic testing (haemochromatosis)
Alpha-galactosidase activity in leucocytes (Fabry disease)
Eosinophilia (Löffler endomyocarditis)

1. Eisenmenger's syndrome

Includes all large intra- and extra-cardiac defects which begin as systemic-to-pulmonary shunts and progress with time to severe elevation of PVR and to reversal (pulmonary-to-systemic) or bidirectional shunting; cyanosis, secondary erythrocytosis, and multiple organ involvement are usually present.

2. PAH associated with prevalent systemic-to-pulmonary shunts

- Correctable[a]
- Non-correctable

Includes moderate to large defects; PVR is mildly to moderately increased, systemic-to-pulmonary shunting is still prevalent, whereas cyanosis at rest is not a feature.

3. PAH with small/coincidental defects[b]

Marked elevation in PVR in the presence of small cardiac defects (usually ventricular septal defects <1 cm and atrial septal defects <2 cm of effective diameter assessed by echo), which themselves do not account for the development of elevated PVR; the clinical picture is very similar to idiopathic PAH. Closing the defects is contra-indicated.

4. PAH after defect correction

Congenital heart disease is repaired, but PAH either persists immediately after correction or recurs/develops months or years after correction in the absence of significant postoperative haemodynamic lesions.

Up to 60% of patients with severe left ventricular (LV) systolic dysfunction and up to 70% of patients with heart failure with preserved ejection fraction may present with PH. PH can be found in virtually all patients with severe symptomatic mitral valve disease and in up to 65% of those with symptomatic aortic stenosis.

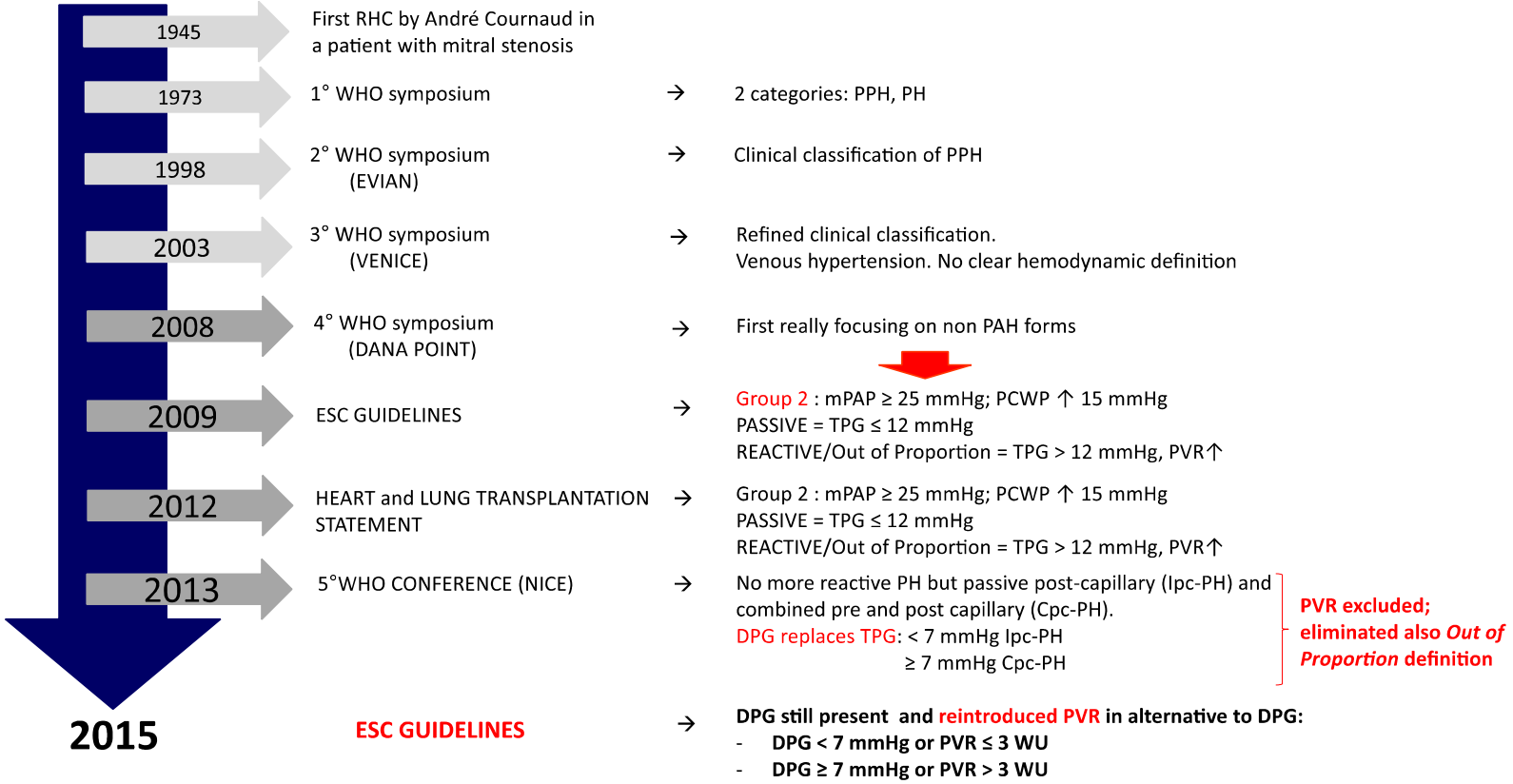
Phase II and III clinical trials performed in patients with heart failure with mid-range ejection fraction and heart failure with preserved ejection fraction

Trial	Intervention	Major inclusion criteria	Mean follow-up	Primary endpoints
PEP-CHF[320]	Perindopril vs placebo.	LV wall motion index ≥1.4 (corresponding to LVEF ≥40%), symptomatic HF treated with diuretic, diastolic dysfunction in echocardiography, age ≥70 y.	2.1 y	No difference in combined all-cause mortality or cardiovascular hospitalization (36% vs 37%, *P* =0.35).
I-PRESERVE [318]	Irbesartan vs placebo.	LVEF ≥45%, NYHA III–IV with corroborative evidence, or NYHA II with HF hospitalization in recent 6 months, age ≥60 y.	4.1 y	No difference in combined all-cause mortality or HF hospitalization (24% vs 25%, *P* =0.54).
CHARM-Preserved[319]	Candesartan vs placebo.	LVEF >40%, NYHA II–IV, history of cardiac hospitalization.	3.0 y	Trend towards a reduction in combined cardiovascular mortality or HF hospitalization by 11% (22% vs 24%, unadjusted *P* =0.12, adjusted *P* =0.051).
Aldo-DHF[330]	Spironolactone vs placebo.	LVEF ≥50%, NYHA II–III, peak VO_2 ≤25 mL/min/kg, diastolic dysfunction on echocardiography or atrial fibrillation, age ≥50 y.	1.0 y	Reduction in E/e' by – 1.5 (*P* < 0.001) No change in peak VO_2 (*P* =0.81).
TOPCAT[310]	Spironolactone vs placebo.	LVEF ≥45%, ≥1 HF sign, ≥1 HF symptom, HF hospitalization within recent 12 months, or BNP ≥100 pg/mL or NT-proBNP ≥360 pg/mL, age ≥50 y.	3.3 y	No difference in combined cardiovascular death, aborted cardiac arrest, or HF hospitalization (19% vs 20%, *P* =0.14).
SENIORS[173]	Nebivolol vs placebo.	HF confirmed as HF hospitalization in recent 12 months and/or LVEF ≤35% in recent 6 months, age ≥70 y, 36% with LVEF >35%.	1.8 y	Reduction in combined all-cause mortality or cardiovascular hospitalization by 14% (31% vs 35%, *P* =0.04).
DIG-PEF[323]	Digoxin vs placebo.	HF with LVEF >45%, sinus rhythm.	3.1 y	No difference in combined HF mortality or HF hospitalization (21% vs 24%, *P* =0.14)
PARAMOUNT[309]	Sacubitril/ valsartan vs valsartan.	HF with LVEF ≥45%, NYHA II-III, NT-proBNP >400 pg/mL.	12 w	Reduction in NT-proBNP: ratio of change sacubitril/ valsartan 0.77, 95% CI 0.64–0.92 (*P* =0.005).
RELAX[311]	Sildenafil vs placebo.	HF with LVEF ≥45%, NYHA II-IV, peak VO_2 <60% of reference values, NT-proBNP >400 pg/mL or high LV filling pressures.	24 w	No change in peak VO_2 (*P* =0.90).

PH con LHD (gruppo 2)

In a retrospective analysis performed in a large PH centre, LHD was identified as the cause of PH in 36% of all patients referred for evaluation, of which 55% had ‘passive’ PH, defined as a TPG ,12 mmHg.

Changes in group2 definition and wording over time from first right heart catheterization (RHC) to our days



Guazzi M, Curr Heart Fail Rep 2016.

Examples of key factors suggestive of group 2 pulmonary hypertension

Clinical presentation	Echocardiography	Other features
Age >65 years	Structural left heart abnormality • Disease of left heart valves • LA enlargement (>4.2 cm) • Bowing of the IAS to the right • LV dysfunction • Concentric LV hypertrophy and/or increased LV mass	ECG • LVH and/or LAH • AF/Afib • LBBB • Presence of Q waves
Symptoms of left heart failure	Doppler indices of increased filling pressures • Increased E/e' • >Type 2–3 mitral flow abnormality	Other imaging • Kerley B lines • Pleural effusion • Pulmonary oedema • LA enlargement
Features of metabolic syndrome	Absence of • RV dysfunction • Mid systolic notching of the PA flow • Pericardial effusion	
History of heart disease (past or current)		
Persistent atrial fibrillation		

Left Heart PH Diastolic Pulmonary Gradient

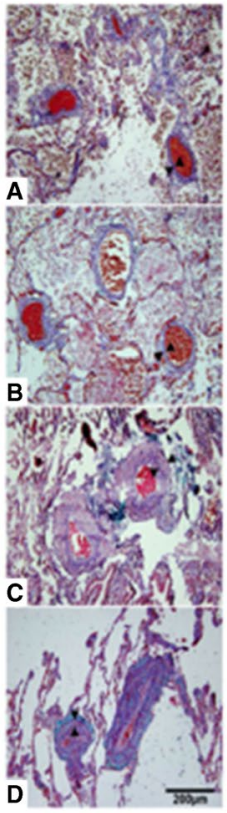
Left Heart PH
Diastolic Pulmonary
Gradient

3 mmHg

5 mmHg

13 mmHg

Idiopathic PAH

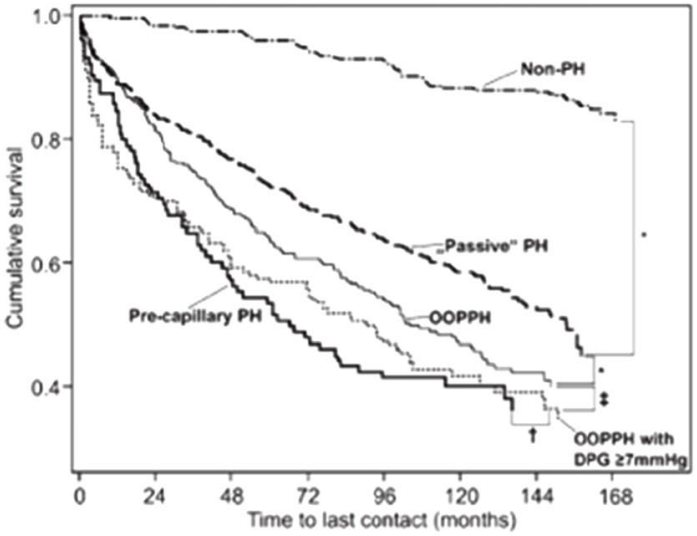


Normal
(passive)

Abnormal

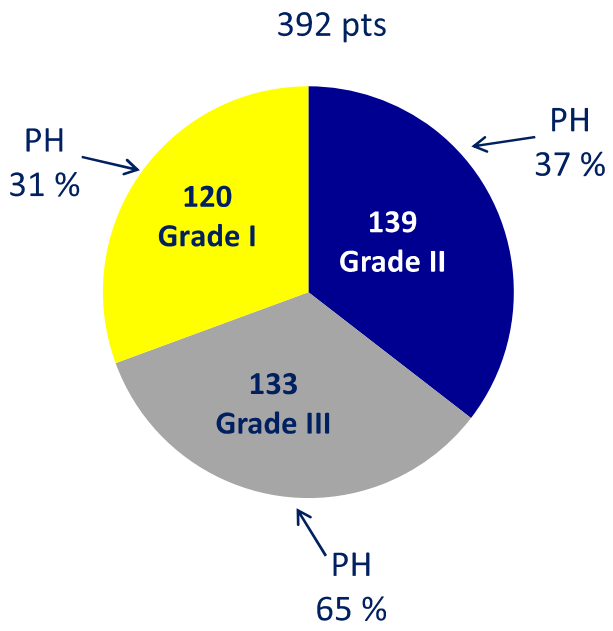
Precapillary/
Postcapillary

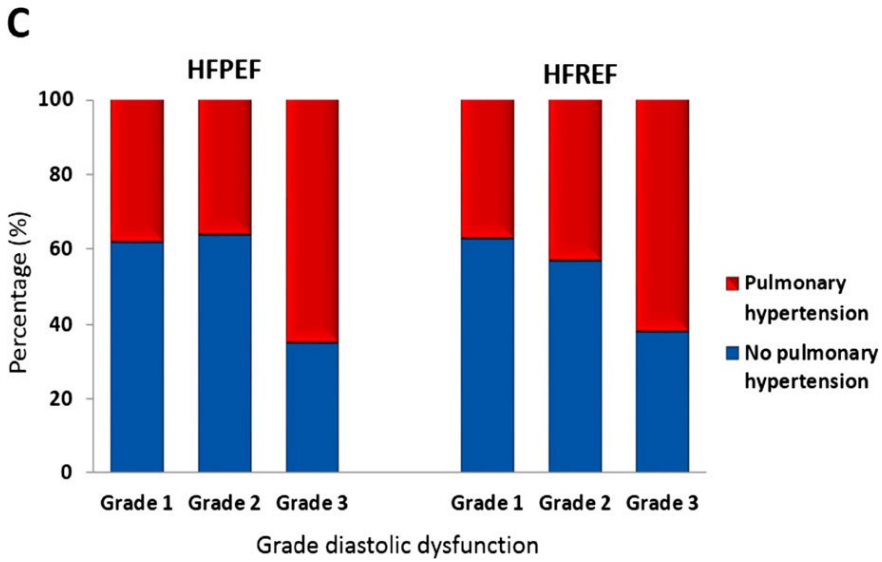
Precapillary



Guazzi M. Curr Heart Fail Rep 2016

Interaction between diastolic dysfunction and PH in a group of elderly HF patients





54% of entire population with PH, TPG > 12 mmHg

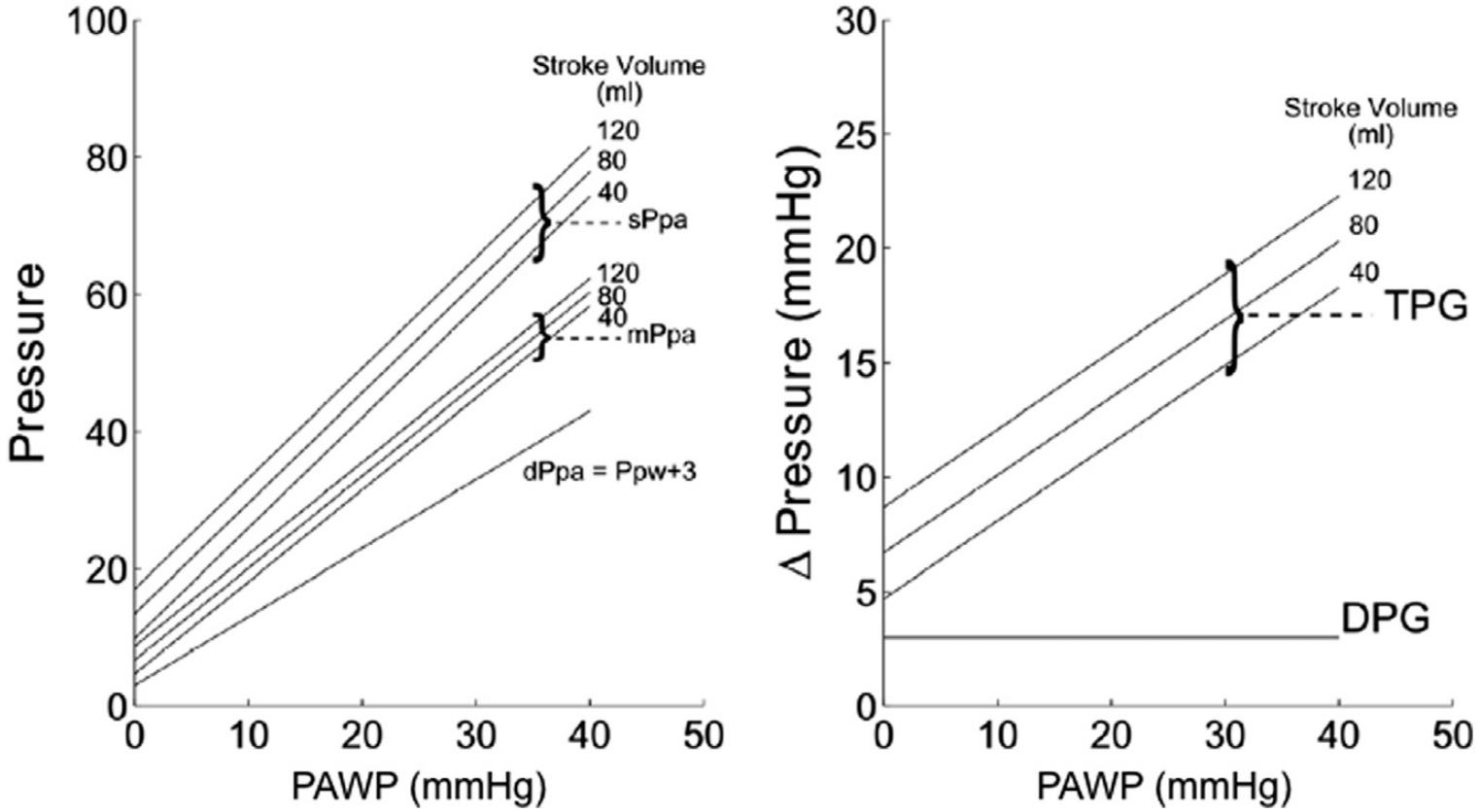
Guazzi M Curr Heart Fail Rep 2016

Proposta per una classificazione della PH-LHD

Terminology	PAWP	Diastolic PAP – PAWP
Isolated post-capillary PH	>15 mm Hg	<7 mm Hg
Combined post-capillary and pre-capillary PH	>15 mm Hg	≥7 mm Hg

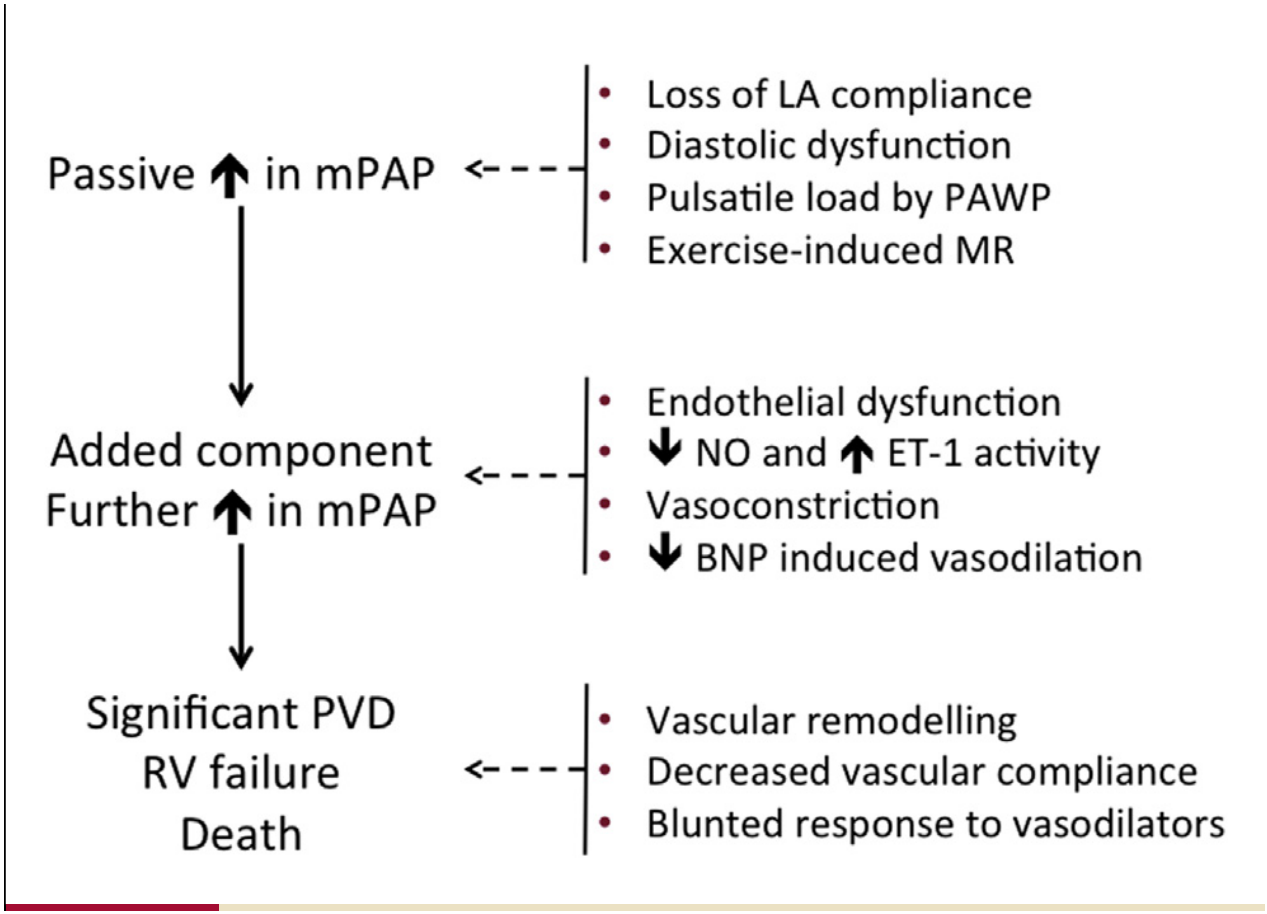
Vachiéry JL et al. JACC 2013

Effect of PAWP and SV on Pulmonary pressure



Vachiéry JL et al. JACC 2013

Pulmonary Hypertension due to Left Heart Diseases



Vachiéry JL et al. JACC 2013

Peak tricuspid regurgitation velocity (m/s)	Presence of other echo 'PH signs'[a]	Echocardiographic probability of pulmonary hypertension
≤2.8 or not measurable	No	Low
≤2.8 or not measurable	Yes	Intermediate
2.9–3.4	No	
2.9–3.4	Yes	High
>3.4	Not required	

PAH

ACCF/AHA stages of heart failure

A	At high risk for HF but without structural heart disease or symptoms of HF.
B	Structural heart disease but without signs or symptoms of HF.
C	Structural heart disease with prior or current symptoms of HF.
D	Refractory HF requiring specialized interventions.

Class I	No limitation of physical activity. Ordinary physical activity does not cause undue breathlessness, fatigue, or palpitations.
Class II	Slight limitation of physical activity. Comfortable at rest, but ordinary physical activity results in undue breathlessness, fatigue, or palpitations.
Class III	Marked limitation of physical activity. Comfortable at rest, but less than ordinary physical activity results in undue breathlessness, fatigue, or palpitations.
Class IV	Unable to carry on any physical activity without discomfort. Symptoms at rest can be present. If any physical activity is undertaken, discomfort is increased.

Practical guidance on the use of mineralocorticoid receptor antagonists in patients with heart failure with reduced ejection fraction

WHY?

To improve symptoms, reduce the risk of HF hospitalization and increase survival.

IN WHOM AND WHEN?

Indications:

1. Potentially all patients with persisting symptoms (NYHA Class II–IV) and an LVEF ≤35% despite treatment with an ACE-I (or ARB) and a beta-blocker.

Contra-indications:

1. Known allergic reaction/other adverse reaction (drug-specific).

Cautions/seek specialist advice:

1. Significant hyperkalaemia (K+ >5.0 mmol/L).[b]
2. Significant renal dysfunction (creatinine >221 μmol/L [>2.5 mg/dL] or eGFR <30 mL/min/1.73 m^2).[b]
3. Drug interactions to look out for:
   - o K+ supplements/ K+-sparing diuretics (e.g. amiloride and triamterene; beware combination preparations with furosemide).
   - o ACE-Is/ARBs/renin inhibitors.[c]
   - o NSAIDs.[d]
   - o Trimethoprim/trimethoprim-sulfamethoxazole.
   - o 'Low-salt' substitutes with a high K+ content.
   - o strong CYP3A4 inhibitors, e.g. ketoconazole, itraconazole, nefazodone, telithromycin, clarithromycin, ritonavir, and nelfinavir (when eplerenone used).

WHICH MRA AND WHAT DOSE? - see Table 7.2

Eplerenone: starting dose 25 mg *o.d.*, target dose 50 mg *o.d.*
Spironolactone: starting dose 25 mg *o.d.*, target dose 50 mg *o.d.*

WHERE?

In the community or in the hospital.
Exceptions—see 'Cautions/seek specialist advice'.

HOW TO USE?

- Check renal function and electrolytes (particularly K+).
- Start with a low dose (see above).
- Consider dose up-titration after 4–8 weeks.
- Check blood chemistry at 1 and 4 weeks after starting/increasing dose and at 8 and 12 weeks; 6, 9, and 12 months; 4-monthly thereafter.
  - o If K+ rises above 5.5 mmol/L or creatinine rises to 221 μmol/L (2.5 mg/dL)/eGFR <30 mL/min/1.73 m^2, halve dose and monitor blood chemistry closely.
  - o If K+ rises to >6.0 mmol/L or creatinine to >310 μmol (3.5 mg/dL) eGFR <20 mL/min/1.73 m^2, stop MRA immediately and seek specialist advice.
- A specialist HF nurse may assist with education of the patient, follow-up (in person or by telephone), biochemical monitoring, and dose up-titration.

PROBLEM SOLVING

Worsening renal function/hyperkalaemia:

- See HOW TO USE?
- The main concern is hyperkalaemia (>6.0 mmol/L); although this was uncommon in RALES and EMPHASIS-HF, it has been seen more commonly in clinical practice.
- Conversely, a high-normal K+ level may be desirable in patients with HF, especially if they are taking digoxin.
- It is important to avoid other K+-retaining drugs (e.g. K+-sparing diuretics such as amiloride and triamterene) and nephrotoxic agents (e.g. NSAIDs[d]).
- The risk of hyperkalaemia and renal dysfunction when an MRA is given to patients already taking both an ACE-I and ARB is higher than when an MRA is added to just an ACE-I or ARB given singly; this triple combination of an ACE-Is, ARB and MRA is NOT recommended (see recommendations below).
- Some 'low-salt' substitutes have a high K+ content.
- Male patients treated with spironolactone may uncommonly develop breast discomfort or gynaecomastia (switching to eplerenone should be considered).

ADVICE TO PATIENT

- Explain expected benefits (see WHY?).
  - o Treatment is given to improve symptoms, to prevent worsening of HF leading to hospital admission, and to increase survival.
  - o Symptomatic improvement occurs within a few weeks to a few months of starting treatment.
- Avoid NSAIDs[d] not prescribed by a physician (i.e. purchased over-the-counter) and salt substitutes high in K+.
- If diarrhoea/vomiting occurs or there is infection with fever leading to intense sweating patients should be aware the risk of dehydration and electrolyte imbalance, they should contact the physician/nurse.

Practical guidance on the use of angiotensin-converting enzyme inhibitors (or angiotensin II receptor blockers) in patients with heart failure with reduced ejection fraction[a]

WHY?

To improve symptoms and exercise capacity, reduce the risk of HF hospitalization and increase survival.

IN WHOM AND WHEN?

Indications:

1. Potentially all patients with HF and an LVEF <40%.
2. First-line treatment (along with a beta-blockers and an MRA) in patients with HF NYHA Class II–IV, start as early as possible in the course of disease.
3. ACE-Is are also of benefit in patients with asymptomatic LV systolic dysfunction (NYHA Class I).

Contra-indications:

1. History of angioedema.[b]
2. Known bilateral renal artery stenosis.
3. Pregnancy/risk of pregnancy.
4. Known allergic reaction/other adverse reaction (drug-specific).

Cautions/seek specialist advice:

1. Significant hyperkalaemia (K+ >5.0 mmol/L).
2. Significant renal dysfunction (creatinine >221 μmol/L [>2.5 mg/dL] or eGFR <30 mL/min/1.73 m^2).
3. Symptomatic or severe asymptomatic hypotension (systolic blood pressure <90 mmHg).
4. Drug interactions to look out for:
   - o K+ supplements/ K+-sparing diuretics, e.g. amiloride and triamterene (beware combination preparations with furosemide).
   - o MRAs.
   - o Renin inhibitors[c].
   - o NSAIDs[d].
   - o Trimethoprim/trimethoprim-sulfamethoxazole.
   - o 'Low-salt' substitutes with a high K+ content.

WHICH ACE-INHIBITOR AND WHAT DOSE? – see also Table 7.2

Captopril: starting dose 6.25 mg *t.i.d.*, target dose 50 mg *t.i.d.*
Enalapril: starting dose 2.5 mg *b.i.d.*, target dose 20 mg *b.i.d.*
Lisinopril: starting dose 2.5–5.0 mg *o.d.*, target dose 20–35 mg *o.d.*
Ramipril: starting dose 2.5 mg *o.d.*, target dose 10 mg *o.d.*
Trandolapril: starting dose 0.5 mg *o.d.*, target dose 4 mg *o.d.*

WHERE?

- In the community in stable patients (NYHA Class IV/patients with severe HF and those with a current/recent exacerbation should be referred for specialist advice).
- In patients hospitalized with worsening HF – after stabilizing, relieving congestion, and, if possible, restoring 'euvolaemia' (but ideally before discharge).
- Other exceptions – see 'Cautions/seek specialist advice'.

HOW TO USE?

- Check renal function and electrolytes.
- Start with a low dose (see Table 7.2).
- Double the dose at not less than 2-week intervals in the community. More rapid dose up-titration may be carried out in patients in hospital or who are otherwise closely monitored, tolerability permitting.
- Aim for target dose (see above) or, failing that, the highest tolerated dose (remember: some ACE-I (or ARB) is better than no ACE-I).
- Re-check blood chemistry (urea/BUN, creatinine, K+) 1–2 weeks after initiation and 1–2 weeks after final dose titration.
- Monitor blood chemistry 4 monthly thereafter.
- When to stop up-titration, reduce dose, stop treatment–see PROBLEM SOLVING.
- It is very rarely necessary to stop an ACE-I (or ARB), and clinical deterioration is likely if treatment is withdrawn. Ideally, specialist advice should be sought before treatment discontinuation.
- A specialist HF nurse may assist with education of the patient, follow-up (in person or by telephone), biochemical monitoring and dose up-titration.

PROBLEM SOLVING

Asymptomatic low blood pressure:

- Does not usually require any change in therapy.

Symptomatic hypotension:

- Dizziness/light headedness is common and often improves with time–patients should be reassured.
- Reconsider need for nitrates, calcium-channel blockers,[e] and other vasodilators and reduce dose/stop, if possible.
- If no signs or symptoms of congestion, consider reducing diuretic dose.
- If these measures do not solve problem, seek specialist advice.

Cough:

- Cough is common in patients with HF, many of whom have smoking-related lung disease.
- Cough is also a symptom of pulmonary oedema, which should be excluded when a new worsening cough develops.
- ACE-I-induced cough does not always require treatment discontinuation.
- When a troublesome cough does develop (e.g. one stopping the patient from sleeping) and can be proved to be due to ACE-inhibition (i.e. recurs after ACE-I withdrawal and re-challenge), substitution of an ARB is recommended.

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RESEARCH ARTICLE

Characteristics, treatments and 1-year prognosis of hospitalized and ambulatory heart failure patients with chronic obstructive pulmonary disease in the European Society of Cardiology Heart Failure Long-Term Registry

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