Heart failure

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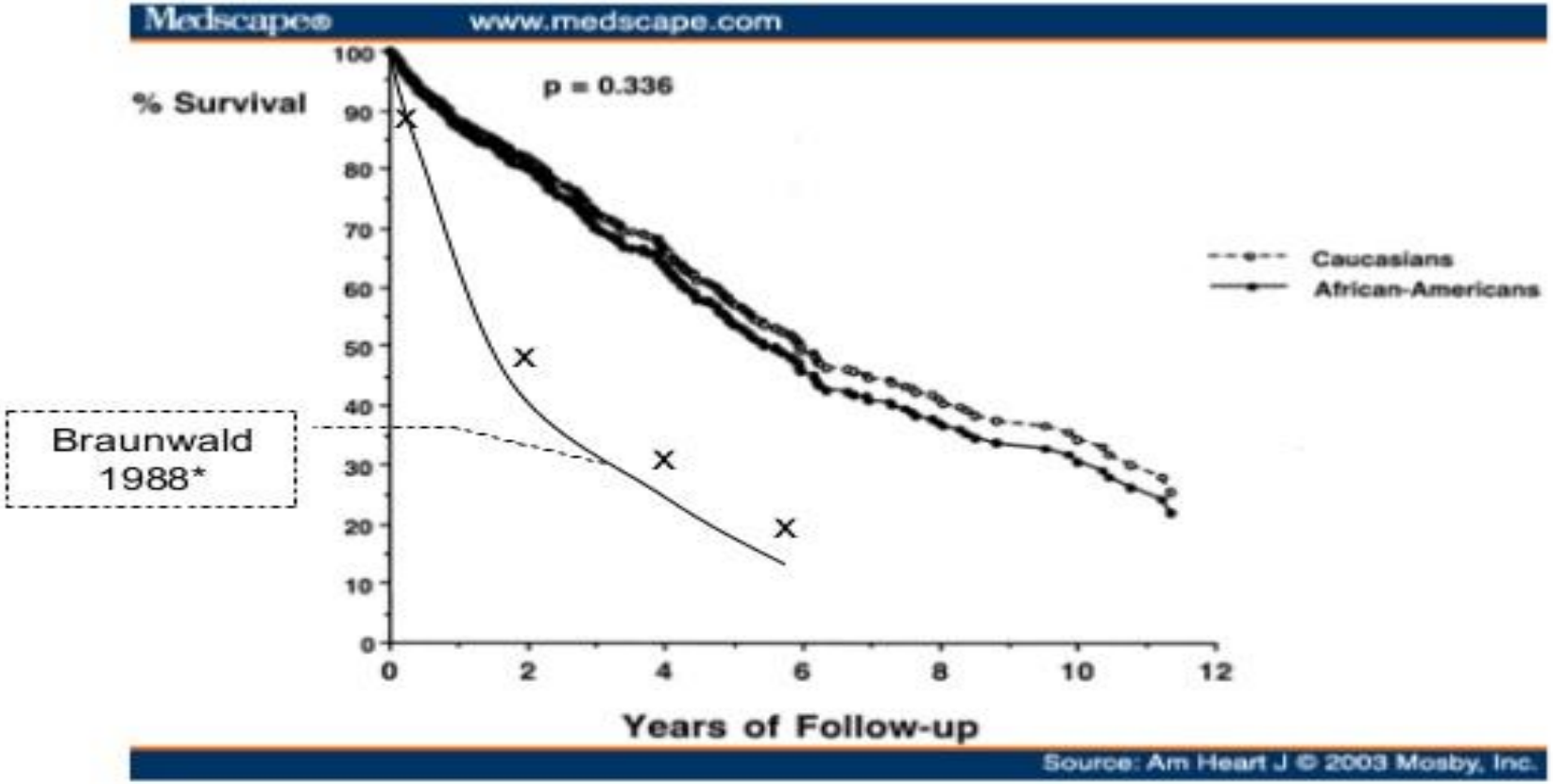
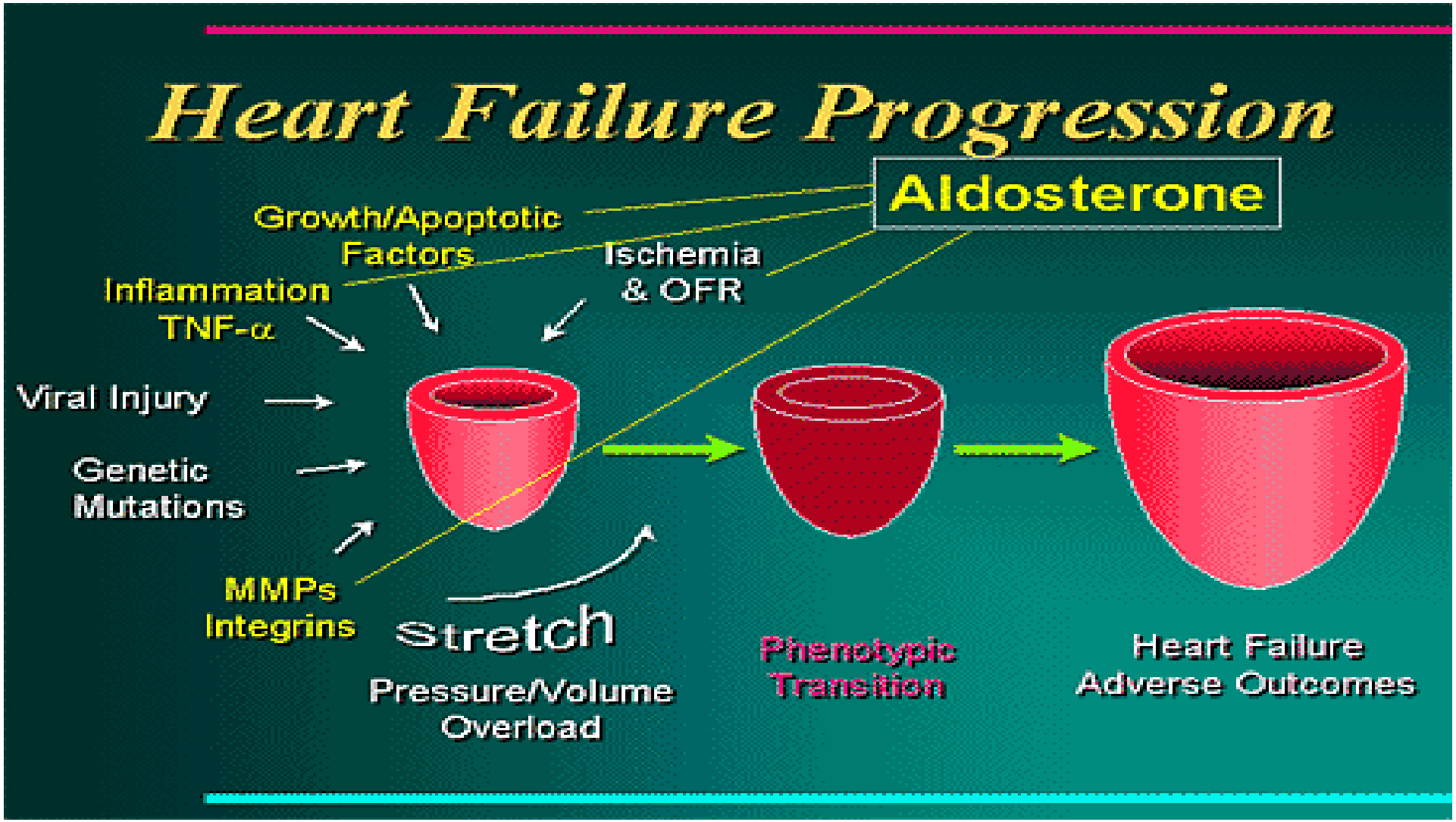
Definition

- The pathophysiological process in which the heart is unable to meet the metabolic requirements of tissue in oxygen and substrate

Survival rates after CHF

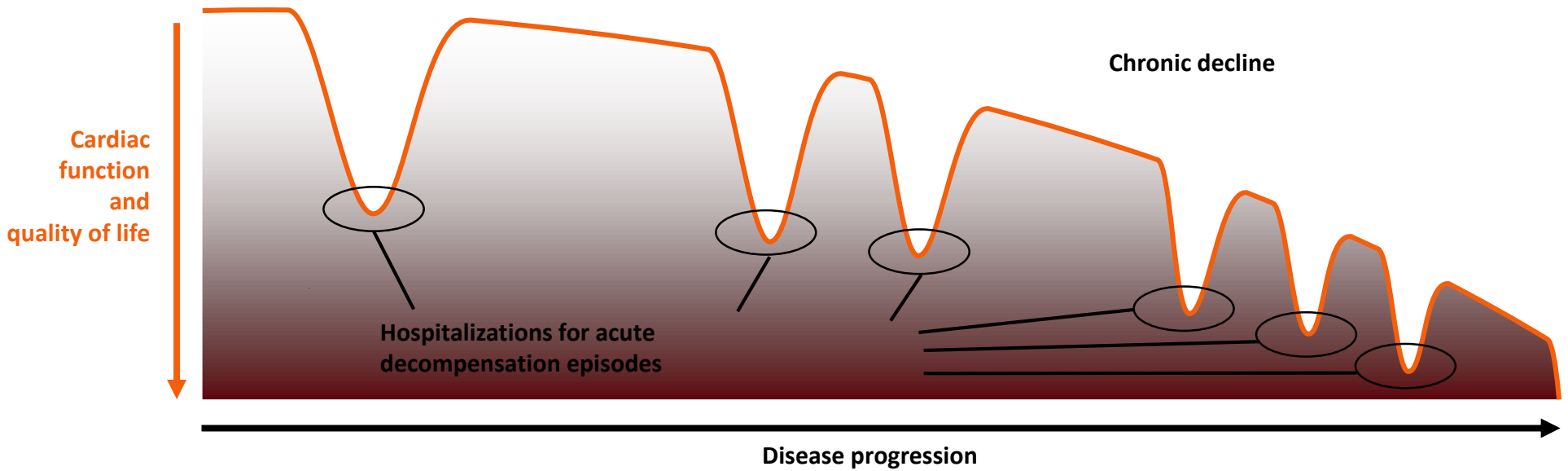
(effect of medical therapy)




Heart Failure Progression
Aldosterone
Growth/Apoptotic Factors
Ischemia & OFR
Inflammation TNF-α
Viral Injury
Genetic Mutations
MMPs Integrins
stretch
Pressure/Volume Overload
Phenotypic Transition
Heart Failure Adverse Outcomes

HF is a chronic condition interspersed with acute episodes

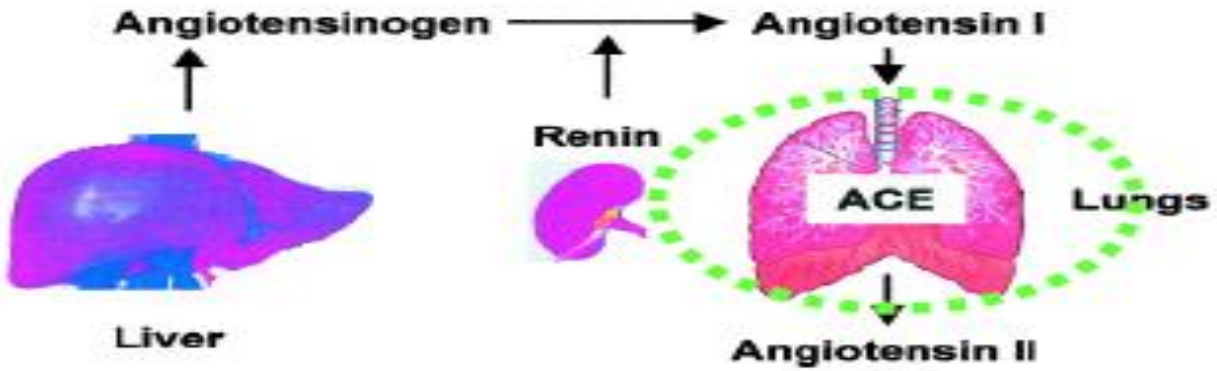
- Increasing frequency of acute events with disease progression leads to high rates of hospitalization and increased risk of mortality[1–5]



Adapted from Gheorghiade et al. 2005[2]

HF=heart failure

1. Ahmed et al. Am Heart J 2006;151:444–50; 2. Gheorghiade et al. Am J Cardiol 2005;96:11G–17G
3. Gheorghiade, Pang. J Am Coll Cardiol 2009;53:557–73; 4. Holland et al. J Card Fail 2010;16:150–6
5. Muntwyler et al. Eur Heart J 2002;23:1861–6



Blood vessel
Vasoconstriction
SMC hypertrophy
Superoxide generation
Endothelin secretion
Monocyte activation
Inflammatory cytokines
Reduced fibrinolysis

Kidney
Sodium and water retention
Efferent arteriolar vasoconstriction
Glomerular and interstitial fibrosis

Heart
Cellular hypertrophy
Myocyte apoptosis
Myocardial fibrosis
Inflammatory cytokines
Coronary vasoconstriction
Positive inotropy
Proarrhythmia

Adrenal gland
Aldosterone secretion

Brain
Vasopressin secretion
Sympathetic activation

2016 Guidelines for the diagnosis and treatment of acute and chronic heart failure

European Heart Journal (2016) **37**, 2129-2200

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Definition of heart failure

With preserved (HFpEF), mid-range (HFmrEF) and reduced ejection fraction (HFrEF)

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

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Aetiologies of heart failure (1)

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	

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Aetiologies of heart failure (2)

DISEASED MYOCARDIUM *(cont'd)*		
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), hyper-sensitivity 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.

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Aetiologies of heart failure (3)

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.

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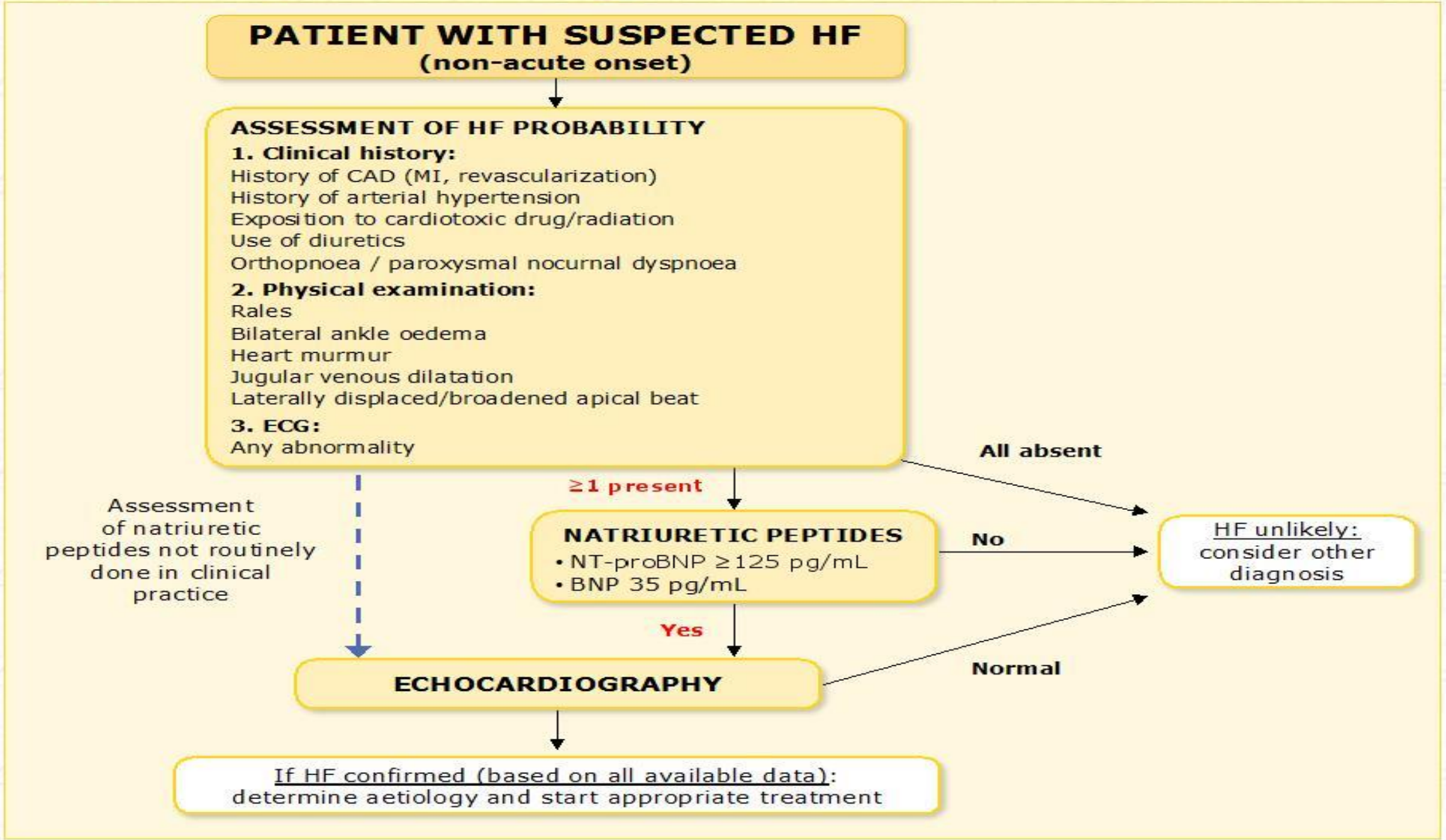
Symptoms and signs typical of heart failure

Symptoms	Signs
Typical	**More spécific**
• 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	• 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

Diagnostic algorithm for a diagnosis of heart failure of non-acute onset



Classification of Heart Failure: ACC/AHA Stage vs NYHA Class

ACC/AHA Heart Failure Stage	NYHA Functional Class
A. At risk for heart failure but without structural heart disease or symptoms	None
B. Structural heart disease but without heart failure	I. Asymptomatic
C. Structural heart disease with prior or current heart failure symptoms	II. Symptomatic with moderate exertion III. Symptomatic with minimal exertion
D. Refractory heart failure requiring specialized interventions	IV. Symptomatic at rest

Hunt SA et al. *Circulation*. 2001;104:2996-3007.
Farrell MH et al. *JAMA*. 2002;287:890-897.

Diagnostic tests

Diagnostic tests in patients with heart failure (1)

Recommendations	Class	Level
The following diagnostic tests are recommended/should be considered for initial assessment of a patient with newly diagnosed HF in order to evaluate the patient's suitability for particular therapies, to detect reversible/treatable causes of HF and co-morbidities interfering with HF:		
– haemoglobin and WBC, – sodium, potassium, urea, creatinine (with estimated GFR), – liver function tests (bilirubin, AST, ALT, GGTP), – glucose, HbA1c, – lipide profile, – TSH, – ferritin, TSAT = TIBC,	I	C
– natriuretic peptides.	IIa	C
Additional diagnostic tests aiming to identify other HF aetiologies and co-morbidities should be considered in individual patients with HF when there is a clinical suspicion of a particular pathology (see Full Text Table 3.4 on HF aetiologies).	IIa	C

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Diagnostic tests in patients with heart failure (2)

Recommendations	Class	Level
A 12-lead ECG is recommended in all patients with HF in order to determine heart rhythm, heart rate, QRS morphology, and QRS duration, and to detect other relevant abnormalities. This information is needed to plan and monitor treatment.	I	C
Exercise testing in patients with HF:		
– is recommended as a part of the evaluation for heart transplantation and/or mechanical circulatory support (cardiopulmonary exercise testing);	I	C
– should be considered to optimize prescription of exercise training (preferably cardiopulmonary exercise testing);	IIa	C
– should be considered to identify the cause of unexplained dyspnoea (cardiopulmonary exercise testing);	IIa	C
– may be considered to detect reversible myocardial ischaemia.	IIa	C
Chest radiography (X-ray) is recommended in patients with HF to detect/exclude alternative pulmonary or other diseases, which may contribute to dyspnoea. It may also identify pulmonary congestion/oedema and is more useful in patients with suspected HF in the acute setting.	I	C

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Prevention

Prevent or delay the development of overt heart failure or prevent death before the onset of symptoms (1)

Recommendations	Class	Level
Treatment of hypertension is recommended to prevent or delay the onset of HF and prolong life.	I	A
Treatment with statins is recommended in patients with or at high-risk of CAD whether or not they have LV systolic dysfunction, in order to prevent or delay the onset of HF and prolong life.	I	A
Counselling and treatment for smoking cessation and alcohol intake reduction is recommended for people who smoke or who consume excess alcohol in order to prevent or delay the onset of HF.	I	C
Treating other risk factors of HF (e.g. obesity, dysglycaemia) should be considered in order to prevent or delay the onset of HF.	IIa	C
Empagliflozin should be considered in patients with type 2 diabetes in order to prevent or delay the onset of HF and prolong life.	IIa	B
ACE-I is recommended in patients with asymptomatic LV systolic dysfunction and a history of myocardial infarction in order to prevent or delay the onset of HF and prolong life.	I	A

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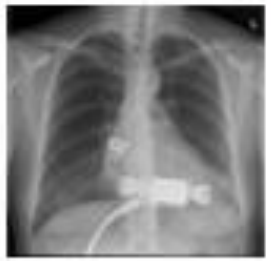
Treatment of chronic heart failure

Palliative Drugs **Neurohormonal Drugs** **Devices** **ARNI**

Pre-1980 | 1980s | 1990s | 2000s | 2010s | 2014



Sensing Devices

Digitalis
Diuretics

ACE-I

ICDs
β-Blockers

CRT, CRT-D
MR-Antagonists
Ivabradine

ARNI

Pharmacological treatments in patients with symptomatic (NYHA Class II-IV) heart failure with reduced ejection fraction

Recommendations	Class	Level
An ACE-I is recommended, in addition to a beta-blocker, for symptomatic patients with HFrEF to reduce the risk of HF hospitalization and death.	I	A
A beta-blocker is recommended, in addition an ACE-I, for patients with stable, symptomatic HFrEF to reduce the risk of HF hospitalization and death.	I	A
An MRA is recommended for patients with HFrEF, who remain symptomatic despite treatment with an ACE-I and a beta-blocker, to reduce the risk of HF hospitalization and death.	I	A

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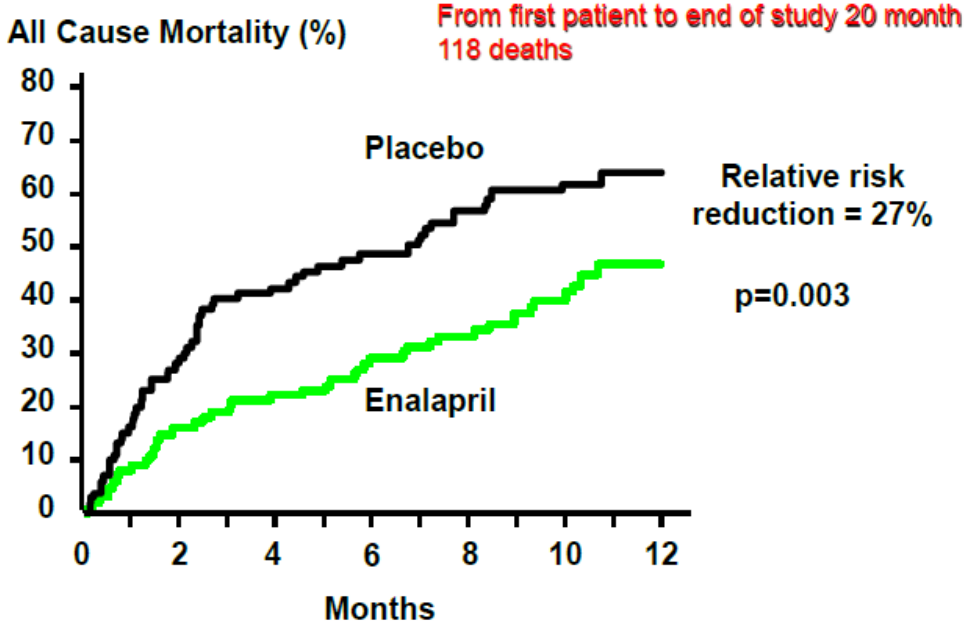
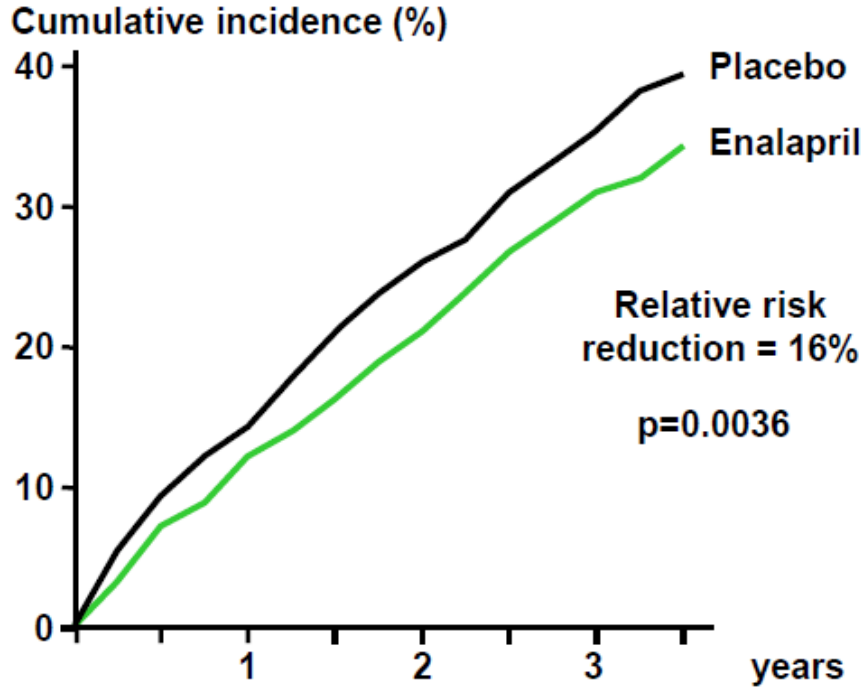
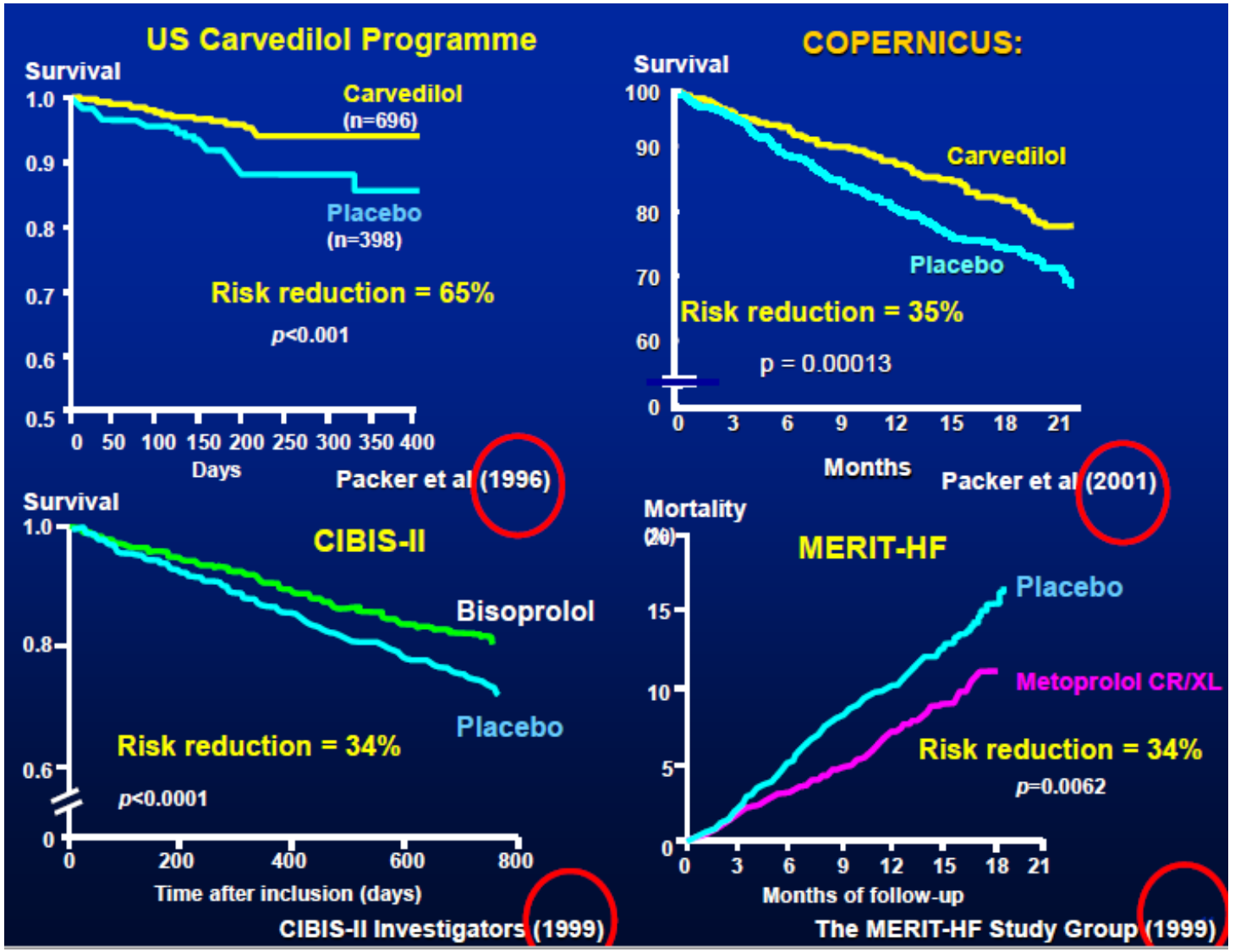
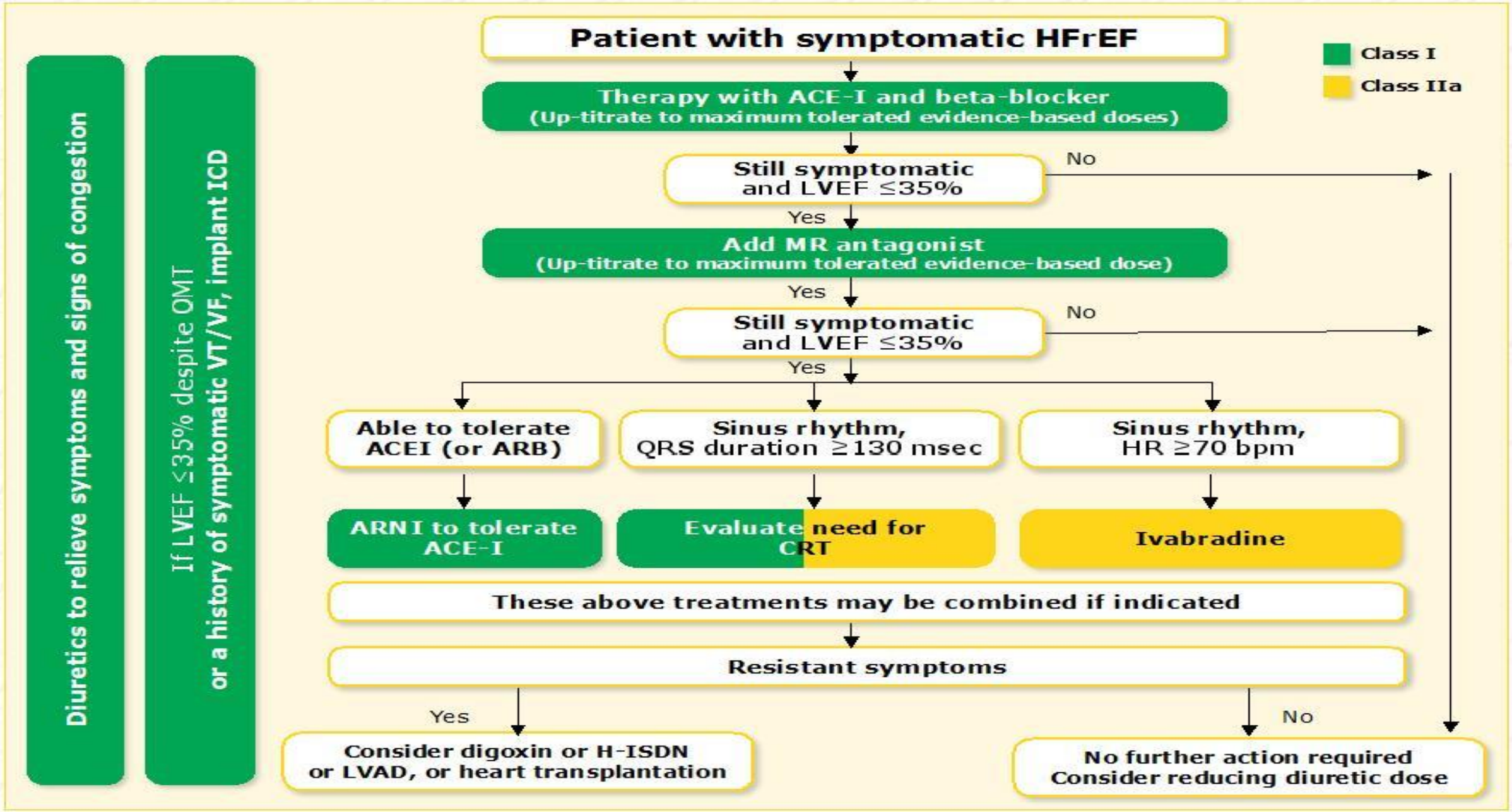
253 patients in NYHA class IV
Randomized to placebo/enalapril
From first patient to end of study 20 month
118 deaths






US Carvedilol Programme
Survival
1.0
0.9
0.8
0.7
0.6
0.5
Carvedilol
(n=696)
Placebo
(n=398)
Risk reduction = 65%
p<0.001
0 50 100 150 200 250 300 350 400
Days
Packer et al (1996)
COPERNICUS:
Survival
100
90
80
70
60
0
Carvedilol
Placebo
Risk reduction = 35%
p = 0.00013
0 3 6 9 12 15 18 21
Months
Packer et al (2001)
Survival
CIBIS-II
1.0
0.8
0.6
0
Bisoprolol
Placebo
Risk reduction = 34%
p<0.0001
0 200 400 600 800
Time after inclusion (days)
CIBIS-II Investigators (1999)
Mortality
(%)
MERIT-HF
20
15
10
5
0
Placebo
Metoprolol CR/XL
Risk reduction = 34%
p=0.0062
0 3 6 9 12 15 18 21
Months of follow-up
The MERIT-HF Study Group (1999)

Therapeutic algorithm for a patient with symptomatic heart failure with reduced ejection fraction



Cardiac resynchronization therapy implantation in patients with heart failure (1)

Recommendations	Class	Level
CRT is recommended for symptomatic patients with HF in sinus rhythm with a QRS duration ≥150 msec and LBBB QRS morphology and with LVEF ≤35% despite OMT in order to improve symptoms and reduce morbidity and mortality.	I	A
CRT should be considered for symptomatic patients with HF in sinus rhythm with a QRS duration ≥150 msec and non-LBBB QRS morphology and with LVEF ≤35% despite OMT in order to improve symptoms and reduce morbidity and mortality.	IIa	B
CRT is recommended for symptomatic patients with HF in sinus rhythm with a QRS duration of 130–149 msec and LBBB QRS morphology and with LVEF ≤35% despite OMT in order to improve symptoms and reduce morbidity and mortality.	I	B
CRT may be considered for symptomatic patients with HF in sinus rhythm with a QRS duration of 130–149 msec and non-LBBB QRS morphology and with LVEF ≤35% despite OMT in order to improve symptoms and reduce morbidity and mortality.	IIb	B

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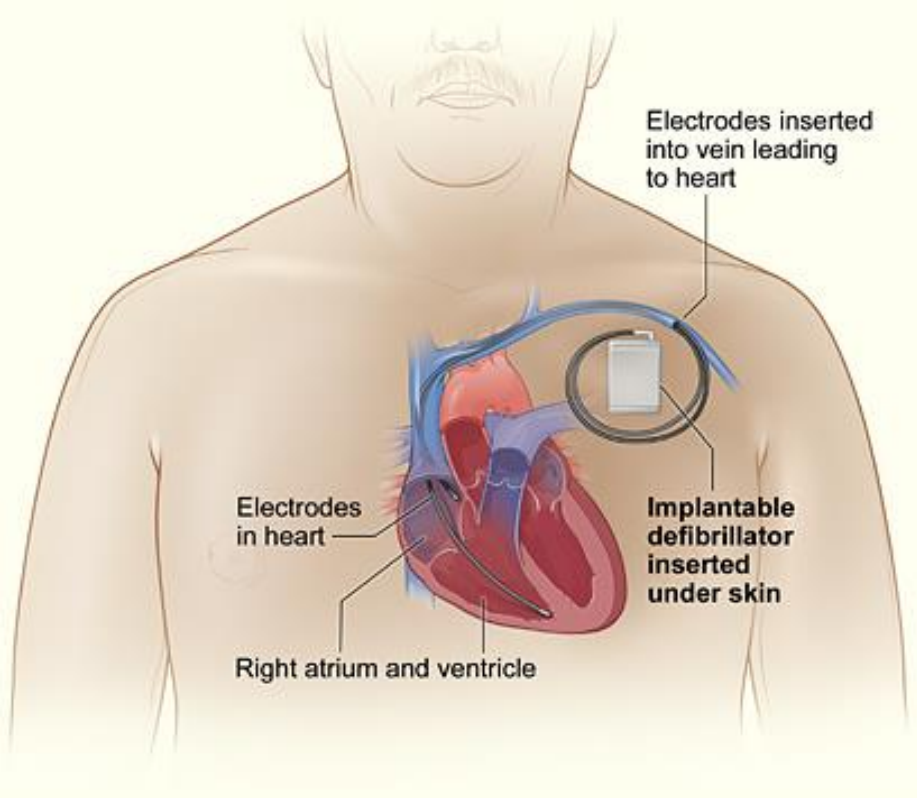
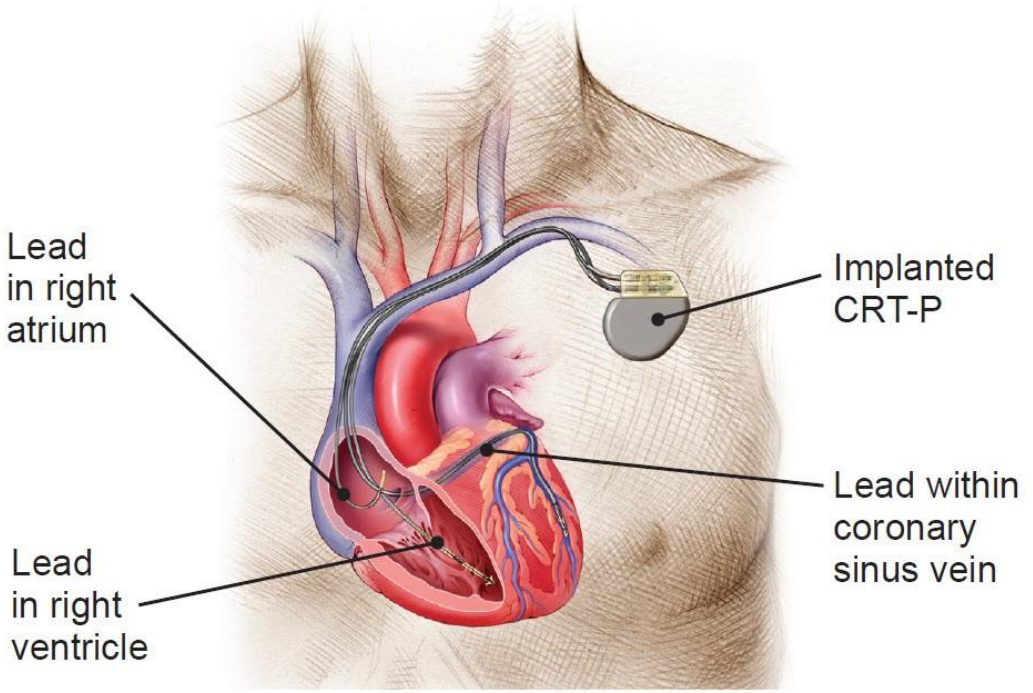
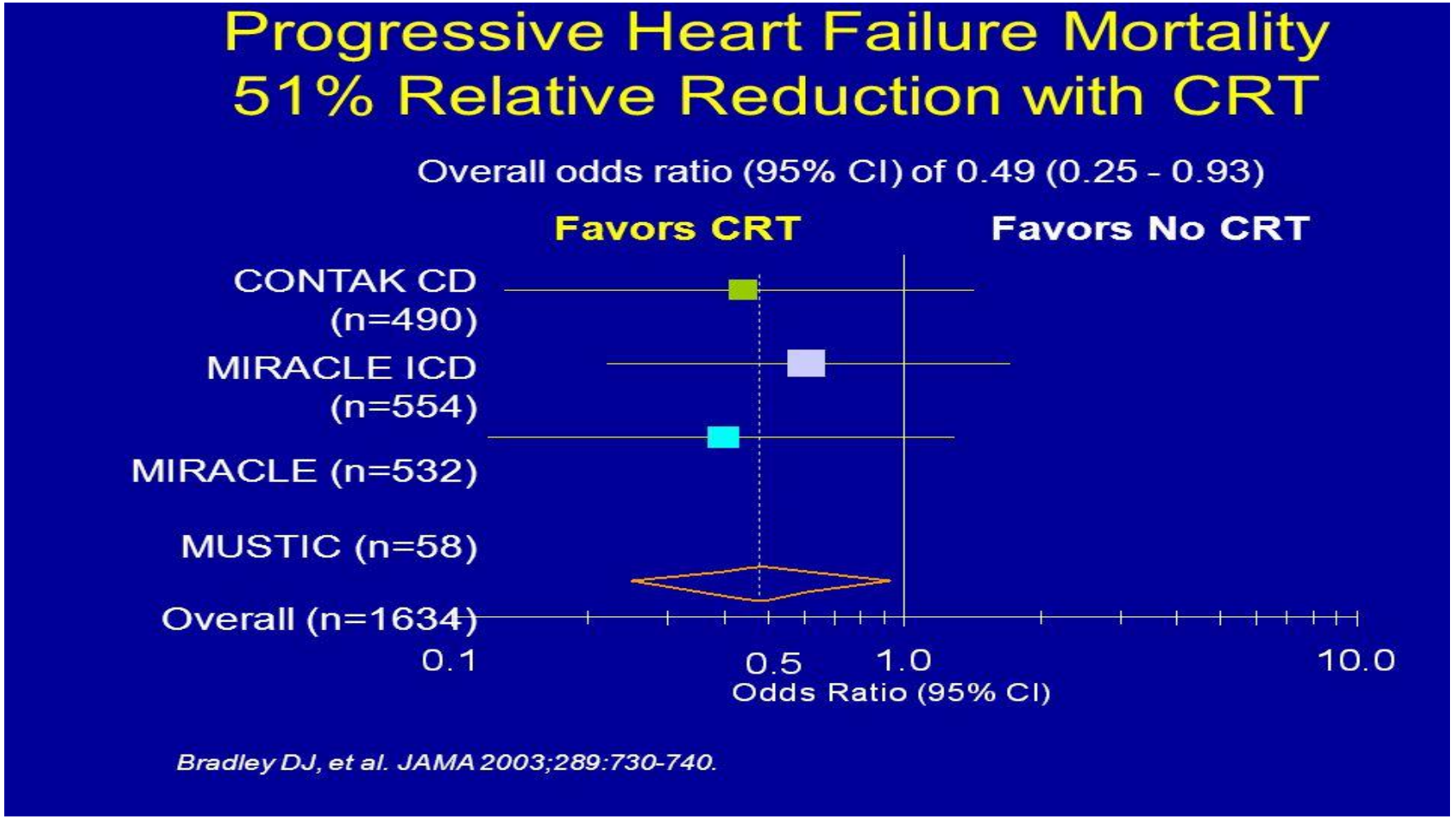

Electrodes inserted into vein leading to heart
Electrodes in heart
Implantable defibrillator inserted under skin
Right atrium and ventricle

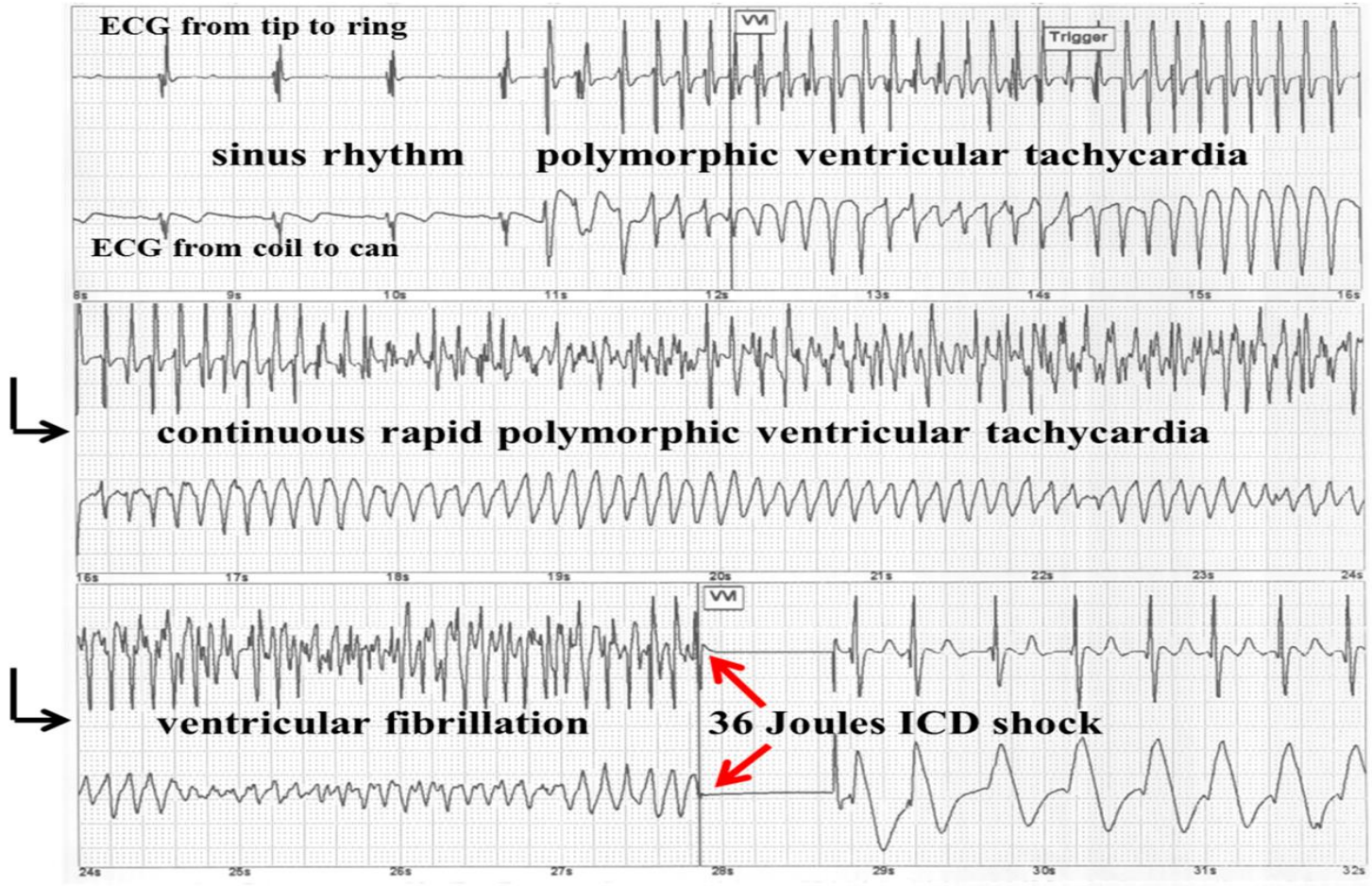

Lead in right atrium
Implanted CRT-P
Lead within coronary sinus vein
Lead in right ventricle

Progressive Heart Failure Mortality
51% Relative Reduction with CRT



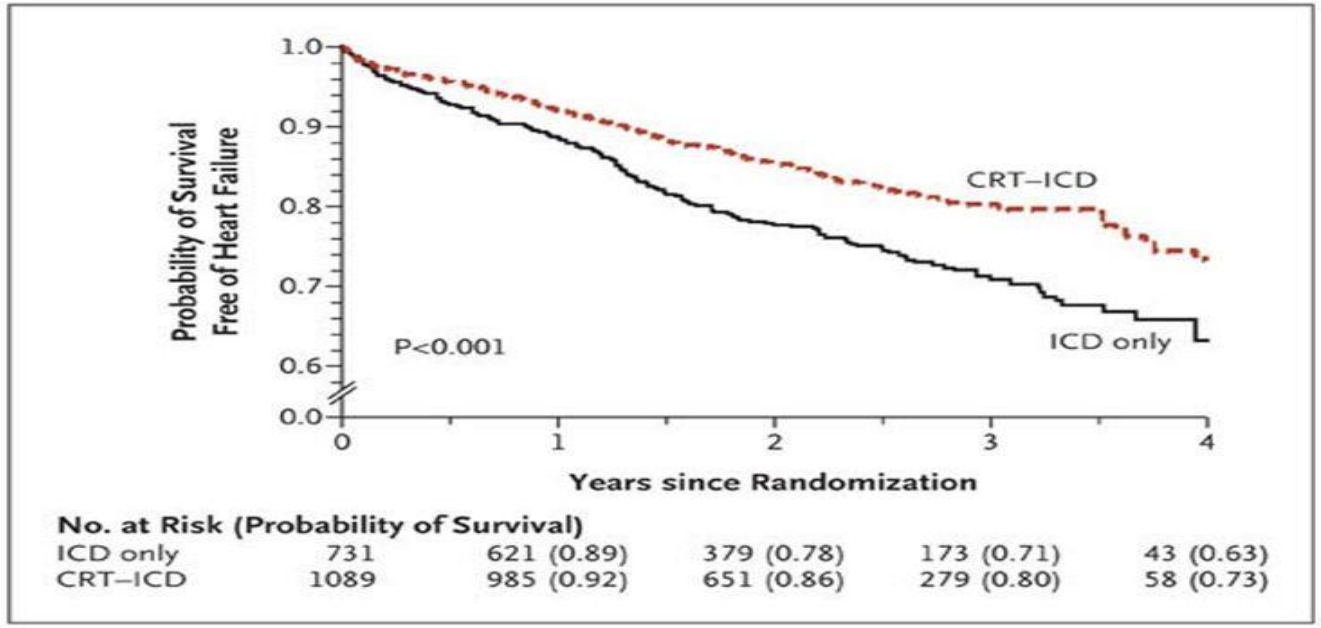
Bradley DJ, et al. JAMA 2003;289:730-740.

CRT-D


ECG from tip to ring
VVI
Trigger
sinus rhythm
polymorphic ventricular tachycardia
ECG from coil to can
8s 9s 10s 11s 12s 13s 14s 15s 16s
continuous rapid polymorphic ventricular tachycardia
16s 17s 18s 19s 20s 21s 22s 23s 24s
VVI
ventricular fibrillation
36 Joules ICD shock
24s 25s 26s 27s 28s 29s 30s 31s 32s

CRT-D

Kaplan-Meier Estimates of the Probability of Survival Free of Heart Failure



No. at Risk (Probability of Survival)

ICD only	731	621 (0.89)	379 (0.78)	173 (0.71)	43 (0.63)
CRT–ICD	1089	985 (0.92)	651 (0.86)	279 (0.80)	58 (0.73)

Moss AJ et al. N Engl J Med 2009;361:1329-1338

Co-morbidities

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).
2. Aggravate HF symptoms and further impair quality of life.
3. Contribute to the burden of hospitalizations and mortality, as the main cause of readmissions at 1 and 3 months.
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).
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).
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).

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Acute heart failure

Factors triggering acute heart failure

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 chemo-therapeutics).
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.

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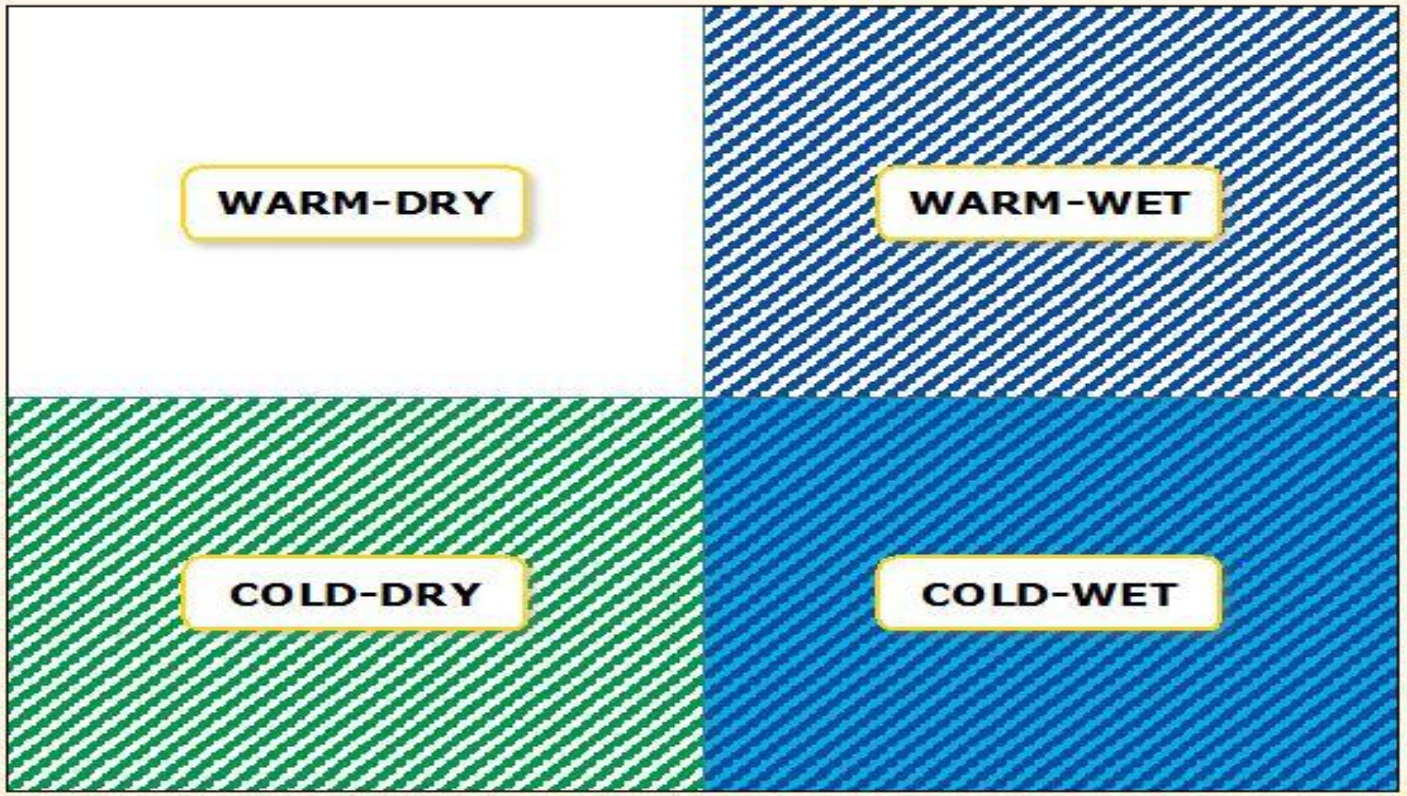
Clinical profiles of patients with acute heart failure based on the presence/absence of congestion and/or hypoperfusion

CONGESTION (−)

CONGESTION (+)
Pulmonary congestion
Orthopnoea/paroxysmal nocturnal dyspnoea
Peripheral (bilateral) oedema
Jugular venous dilatation
Congested hepatomegaly
Gut congestion, ascites
Hepatojugular reflux

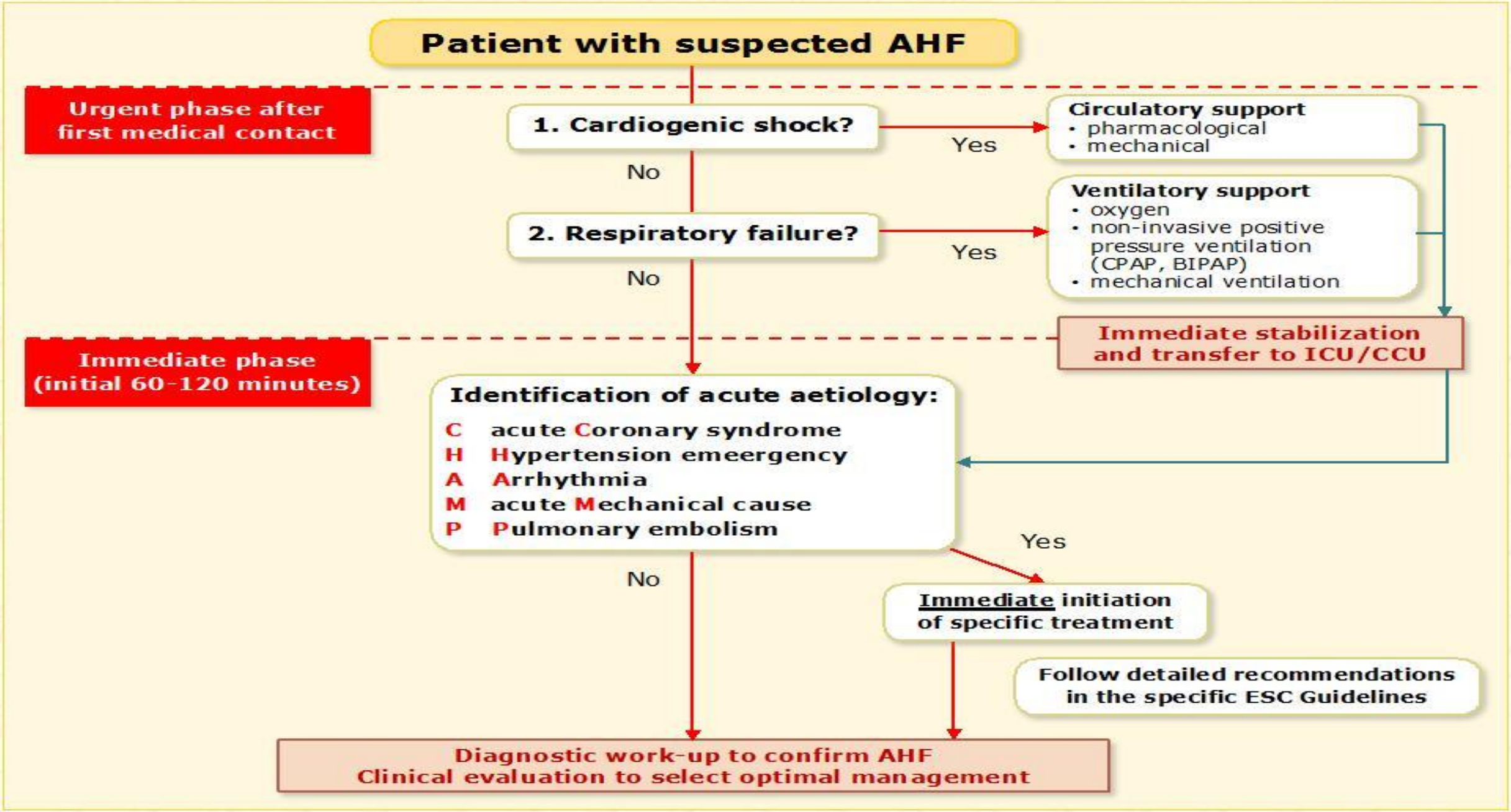
HYPOPERFUSION (−)



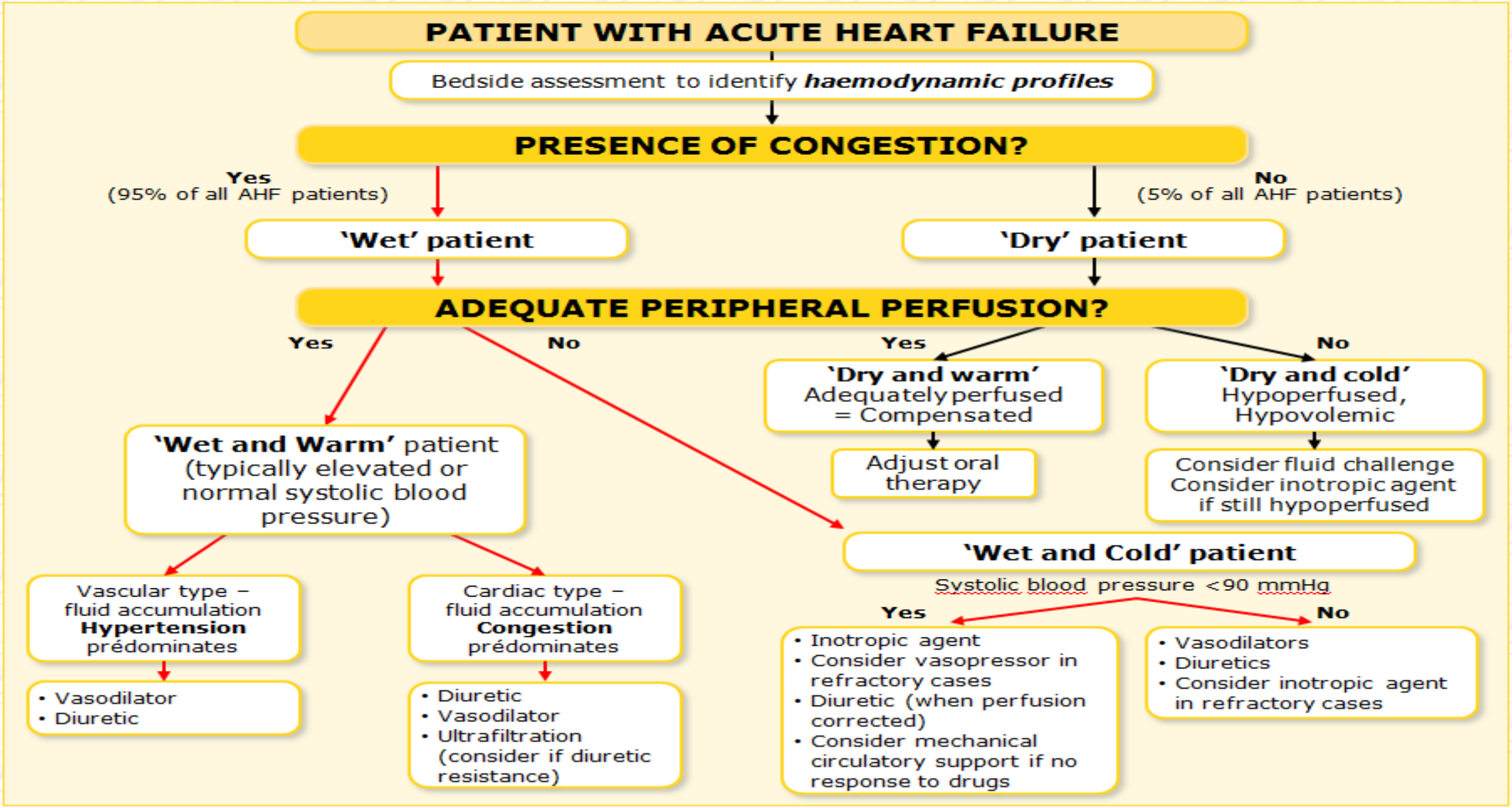
HYPOPERFUSION (+)
Cold sweated extremities
Oliguria
Mental confusion
Dizziness
Narrow pulse pressure

Hypoperfusion is not synonymous with hypotension, but often hypoperfusion is accompanied by hypotension

Initial management of a patient with acute heart failure



Management of patients with acute heart failure based on clinical profile during an early phase



Causes of elevated concentrations of natriuretic peptides

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. thyro-toxicosis, diabetic ketosis)

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Mechanical circulatory support

Terms describing various indications for mechanical circulatory support

Bridge to decision (BTD)/ Bridge to bridge (BTB)	Use of short-term MCS (e.g. ECLS or ECMO) in patients with cardiogenic shock until haemodynamics and end-organ perfusion are stabilized, contra-indications for long-term MCS are excluded (brain damage after resuscitation) and additional therapeutic options including long-term VAD therapy or heart transplant can be evaluated.
Bridge to candidacy (BTC)	Use of MCS (usually LVAD) to improve end-organ function in order to make an ineligible patient eligible for heart transplantation.
Bridge to transplantation (BTT)	Use of MCS (LVAD or BiVAD) to keep patient alive who is otherwise at high risk of death before transplantation until a donor organ becomes available.
Bridge to recovery (BTR)	Use of MCS (typically LVAD) to keep patient alive until cardiac function recovers sufficiently to remove MCS.
Destination therapy (DT)	Long-term use of MCS (LVAD) as an alternative to transplantation in patients with end-stage HF ineligible for transplantation or long-term waiting for heart transplantation.

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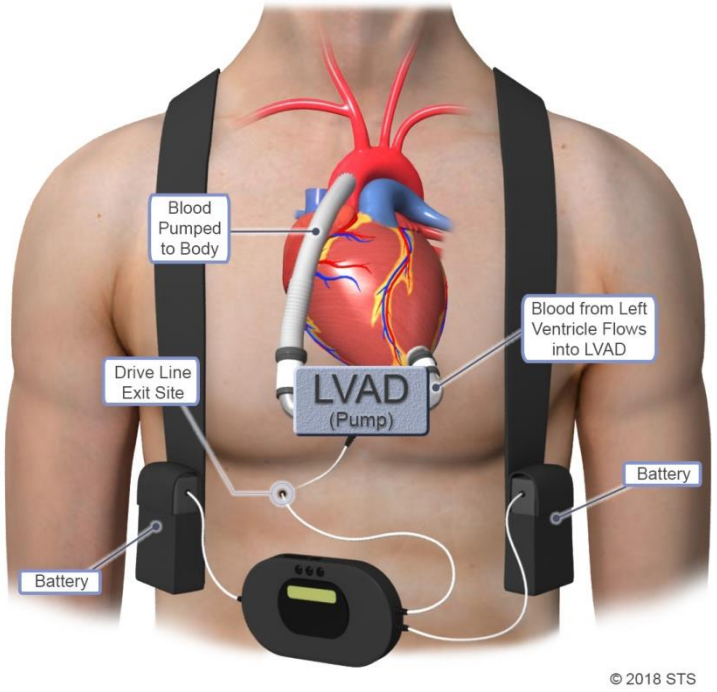
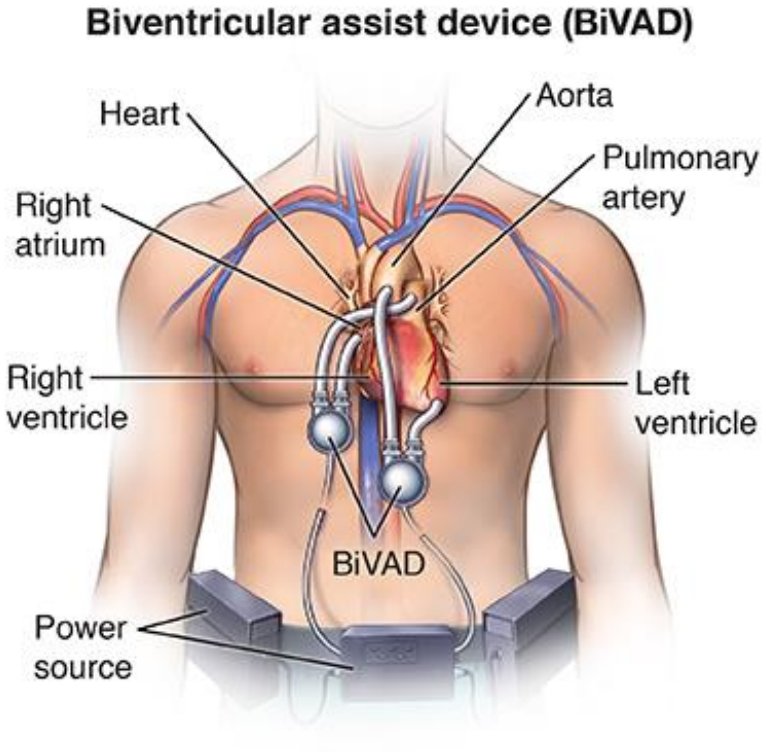
Mechanical circulatory support





Heart transplantation

Heart transplantation:
indications and contra-indications

Patients to consider	End-stage HF with severe symptoms, a poor prognosis, and no remaining alternative treatment options. Motivated, well informed, and emotionally stable. Capable of complying with the intensive treatment required postoperatively.
Contra-indications	Active infection. Severe peripheral arterial or cerebrovascular disease. Pharmacologically irreversible pulmonary hypertension (LVAD should be considered with a subsequent reevaluation to establish candidacy). Cancer (a collaboration with oncology specialists should occur to stratify each patient as to their risk of tumour recurrence). Irreversible renal dysfunction (e.g. creatinine clearance <30 mL/min). Systemic disease with multi-organ involvement. Other serious co-morbidity with poor prognosis. Pre-transplant BMI >35 kg/m^2 (weight loss is recommended to achieve a BMI <35 kg/m^2). Current alcohol or drug abuse. Any patient for whom social supports are deemed insufficient to achieve compliant care in the outpatient setting.

Dos and don’ts

To do and not to do messages from the Guidelines (1)

Recommendations	Class	Level
Cardiac imaging in patients with suspected or established heart failure		
TTE is recommended for the assessment of myocardial structure and function in subjects with suspected HF in order to establish a diagnosis of either HFrEF, HFmrEF or HFpEF.	I	C
TTE is recommended for the assessment of LVEF in order to identify patients with HF who would be suitable for evidence-based pharmacological and device (ICD, CRT) treatment recommended for HFrEF.	I	C
Aiming to prevent or delay the development of overt heart failure or prevent death before the onset of symptoms		
Treatment of hypertension is recommended to prevent or delay the onset of HF and prolong life.	I	A
ACE-I is recommended in patients with asymptomatic LV systolic dysfunction and a history of myocardial infarction in order to prevent or delay the onset of HF and prolong life.	I	A
Beta-blocker is recommended in patients with asymptomatic LV systolic dysfunction and a history of myocardial infarction, in order to prevent or delay the onset of HF and prolong life.	I	B

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To do and not to do messages from the Guidelines (2)

Recommendations	Class	Level
Pharmacological treatments indicated in patients with symptomatic heart failure with reduced ejection fraction		
An ACE-I is recommended, in addition to a beta-blocker, for symptomatic patients with HFrEF to reduce the risk of HF hospitalization and death.	I	A
A beta-blocker is recommended, in addition to an ACE-I, for patients with stable, symptomatic HFrEF to reduce the risk of HF hospitalization and death.	I	A
An MRA is recommended for patients with HFrEF, who remain symptomatic despite treatment with an ACE-I and a beta-blocker, to reduce the risk of HF hospitalization and death.	I	A
Other pharmacological treatments recommended in selected patients with symptomatic heart failure with reduced ejection fraction		
Diuretics are recommended in order to improve symptoms and exercise capacity in patients with signs and/or symptoms of congestion.	I	B
Sacubitril/valsartan is recommended as a replacement for an ACE-I to further reduce the risk of HF hospitalization and death in ambulatory patients with HFrEF who remain symptomatic despite optimal treatment with an ACE-I, a beta-blocker and an MRA.	I	B

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To do and not to do messages from the Guidelines (3)

Recommendations	Class	Level
Treatments (or combinations of treatments) that may cause harm in patients with symptomatic (New York Heart Association Class II–IV) heart failure with reduced ejection fraction		
Diltiazem or verapamil are not recommended in patients with HFrEF, as they increase the risk of HF worsening and HF hospitalization.	III	C
The addition of an ARB (or a renin inhibitor) to the combination of an ACE-I and an MRA is not recommended in patients with HF, because of the increased risk of renal dysfunction and hyperkalaemia.	III	C
Implantable cardioverter-defibrillator in patients with heart failure		
Secondary prevention An ICD is recommended to reduce the risk of sudden death and all-cause mortality in patients who have recovered from a ventricular arrhythmia causing haemodynamic instability, and who are expected to survive for >1 year with good functional status.	I	A

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To do and not to do messages from the Guidelines (4)

Recommendations	Class	Level
Implantable cardioverter-defibrillator in patients with heart failure *(cont'd)*		
Primary prevention An ICD is recommended to reduce the risk of sudden death and all-cause mortality in patients with symptomatic HF (NYHA Class II–III), and an LVEF ≤35% despite ≥3 months of OMT, provided they are expected to survive substantially longer than 1 year with good functional status, and they have:		
• IHD (unless they have had an MI in the prior 40 days)	I	A
• DCM	I	B
ICD implantation is not recommended within 40 days of an MI as implantation at this time does not improve prognosis.	III	A
Cardiac resynchronization therapy implantation in patients with heart failure		
CRT is recommended for symptomatic patients with HF in sinus rhythm with a QRS duration ≥150 msec and LBBB QRS morphology and with LVEF ≤35% despite OMT in order to improve symptoms and reduce morbidity and mortality.	I	A

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To do and not to do messages from the Guidelines (5)

Recommendations	Class	Level
Cardiac resynchronization therapy implantation in patients with heart failure *(cont'd)*		
CRT is recommended for symptomatic patients with HF in sinus rhythm with a QRS duration of 130–149 msec and LBBB QRS morphology and with LVEF ≤35% despite OMT in order to improve symptoms and reduce morbidity and mortality.	I	B
CRT rather than RV pacing is recommended for patients with HFrEF regardless of NYHA Class who have an indication for ventricular pacing and high degree AV block in order to reduce morbidity. This includes patients with atrial fibrillation (see Section 10.1).	I	A
CRT is contra-indicated in patients with a QRS duration <130 msec.	III	A
Not-recommended treatments of co-morbidities in patients with heart failure		
Adaptive servo-ventilation is not recommended in patients with HFrEF and a predominant central sleep apnoea because of an increased all-cause and cardiovascular mortality.	III	B
Thiazolidinediones (glitazones) are not recommended in patients with HF, as they increase the risk of HF worsening and HF hospitalization.	III	A
NSAIDs or COX-2 inhibitors are not recommended in patients with HF, as they increase the risk of HF worsening and HF hospitalization.	III	B

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To do and not to do messages from the Guidelines (6)

Recommendations	Class	Level
Regarding diagnostic measurements in patients with suspected acute heart failure		
Upon presentation a measurement of plasma natriuretic peptide level (BNP, NT-proBNP or MR-proANP) is recommended in all patients with acute dyspnoea and suspected AHF to help in the differentiation of AHF from non-cardiac causes of acute dyspnoea.	I	A
The management of patients with acute heart failure – pharmacotherapy		
Intravenous loop diuretics are recommended for all patients with AHF admitted with signs/symptoms of fluid overload to improve symptoms. It is recommended to regularly monitor symptoms, urine output, renal function and electrolytes during use of i.v. diuretics.	I	C
In patients with new-onset AHF or those with chronic, decompensated HF not receiving oral diuretics the initial recommended dose should be 20–40 mg i.v. furosemide (or equivalent); for those on chronic diuretic therapy, initial i.v. dose should be at least equivalent to oral dose.	I	B
It is recommended to give diuretics either as intermittent boluses or a continuous infusion, and the dose and duration should be adjusted according to the patients' symptoms and clinical status.	I	B

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To do and not to do messages from the Guidelines (7)

Recommendations	Class	Level
The management of patients with acute heart failure – pharmacotherapy *(cont'd)*		
Inotropic agents are not recommended unless the patient is symptomatically hypotensive or hypoperfused because of safety concern.	III	A
Regarding management of patients with cardiogenic shock		
In all patients with suspected cardiogenic shock, immediate ECG and echocardiography are recommended.	I	C
All patients with cardiogenic shock should be rapidly transferred to a tertiary care centre which has a 24/7 service of cardiac catheterization, and a dedicated ICU/CCU with availability of short-term mechanical circulatory support.	I	C
Regarding oral evidence-based disease-modifying therapies in patients with acute heart failure		
In case of worsening of chronic HFrEF, every attempt should be made to continue evidence-based, disease-modifying therapies, in the absence of haemodynamic instability or contra-indications.	I	C

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To do and not to do messages from the Guidelines (7)

Recommendations	Class	Level
Exercise, multidisciplinary management, and monitoring of patients with heart failure		
It is recommended that regular aerobic exercise is encouraged in patients with HF to improve functional capacity and symptoms.	I	A
It is recommended that regular aerobic exercise is encouraged in stable patients with HFrEF to reduce the risk of HF hospitalization.	I	A
It is recommended that patients with HF are enrolled in a multidisciplinary care management programme to reduce the risk of HF hospitalization and mortality.	I	A

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Thank you