Gruppo di ricerca geriatrica

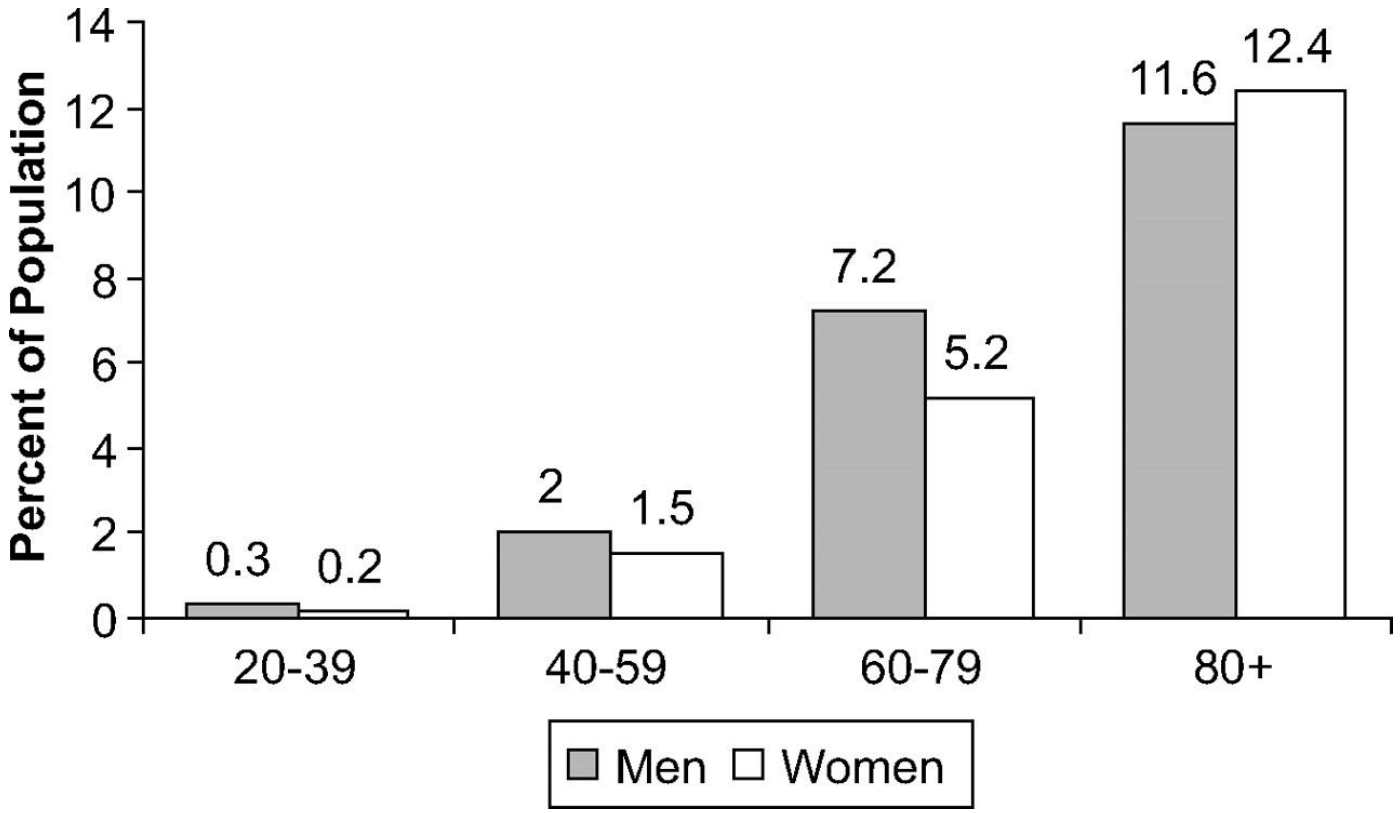
Journal Club

13 Febbraio 2008

Fattori condizionanti la sopravvivenza nel paziente con scompenso di cuore

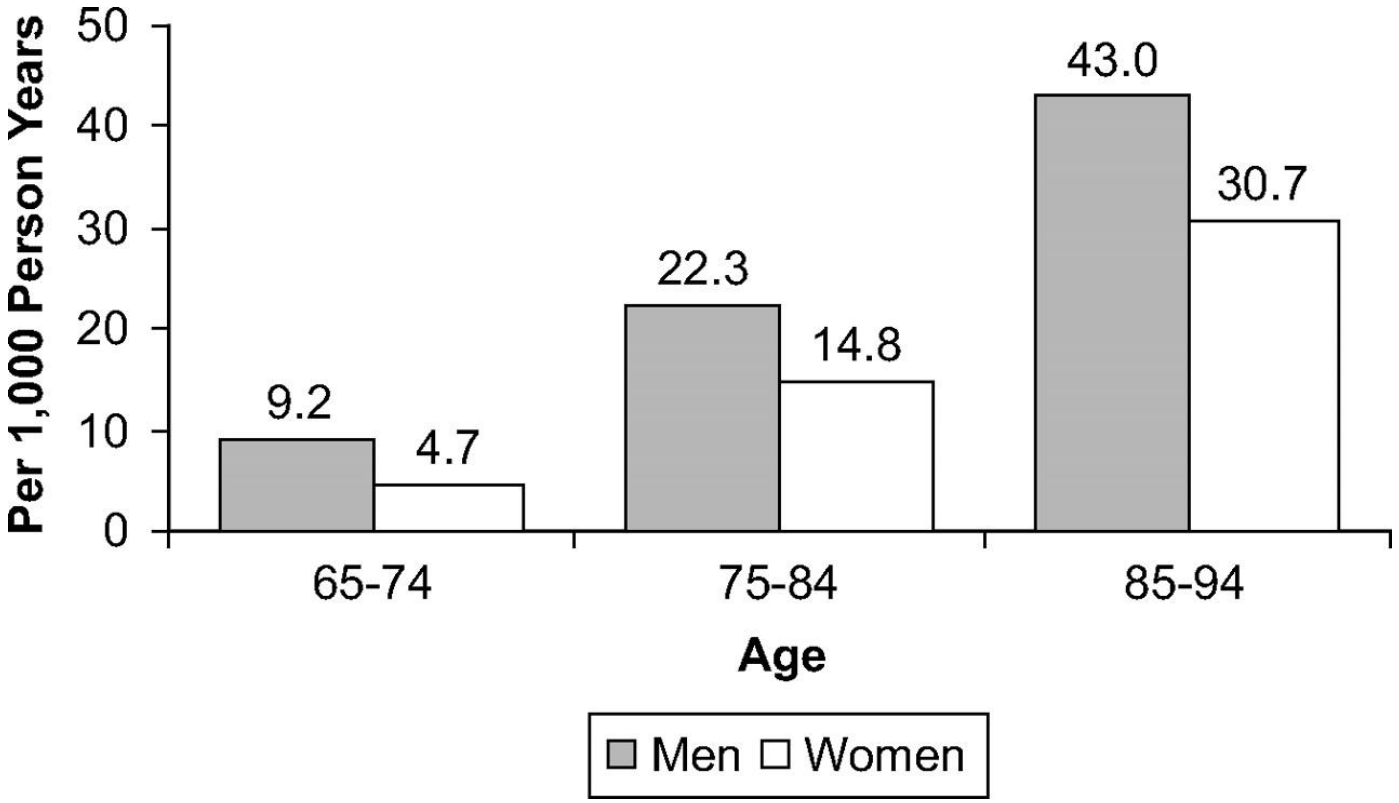
Intissar Sleiman

Prevalence of heart failure by sex and age (NHANES:1999-2004)



Circulation 2007

Incidence of heart failure by age and sex (FHS 1980-2003)



Circulation, 2007

European Heart Journal (2008) 29, 2388–2442
doi:10.1093/eurheartj/ehn309

ESC GUIDELINES

ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2008‡

The Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2008 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association of the ESC (HFA) and endorsed by the European Society of Intensive Care Medicine (ESICM)

Table 3 Definition of heart failure

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

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

  and
- **Signs typical of heart failure**
  (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)

Table 4 Common clinical manifestations of heart failure

Dominant clinical feature	Symptoms	Signs
Peripheral oedema/congestion	Breathlessness Tiredness, fatigue Anorexia	Peripheral oedema Raised jugular venous pressure Pulmonary oedema Hepatomegaly, ascites Fluid overload (congestion) Cachexia
Pulmonary oedema	Severe breathlessness at rest	Crackles or rales over lungs, effusion Tachycardia, tachypnoea
Cardiogenic shock (low output syndromes)	Confusion Weakness Cold periphery	Poor peripheral perfusion SBP <90 mmHg Anuria or oliguria
High blood pressure (hypertensive heart failure)	Breathlessness	Usually raised BP, LV hypertrophy, and preserved EF
Right heart failure	Breathlessness Fatigue	Evidence of RV dysfunction Raised JVP, peripheral oedema, hepatomegaly, gut congestion

Table 5 Classification of heart failure

• **New onset**	First presentation Acute or slow onset
• **Transient**	Recurrent or episodic
• **Chronic**	Persistent Stable, worsening, or decompensated

Table 6 Classification of heart failure by structural abnormality (ACC/AHA), or by symptoms relating to functional capacity (NYHA)

ACC/AHA stages of heart failure		**NYHA functional classification**	
Stage of heart failure based on structure and damage to heart muscle		**Severity based on symptoms and physical activity**	
Stage A	At high risk for developing heart failure. No identified structural or functional abnormality; no signs or symptoms.	**Class I**	No limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, or dyspnoea.
Stage B	Developed structural heart disease that is strongly associated with the development of heart failure, but without signs or symptoms.	**Class II**	Slight limitation of physical activity. Comfortable at rest, but ordinary physical activity results in fatigue, palpitation, or dyspnoea.
Stage C	Symptomatic heart failure associated with underlying structural heart disease.	**Class III**	Marked limitation of physical activity. Comfortable at rest, but less than ordinary activity results in fatigue, palpitation, or dyspnoea.
Stage D	Advanced structural heart disease and marked symptoms of heart failure at rest despite maximal medical therapy.	**Class IV**	Unable to carry on any physical activity without discomfort. Symptoms at rest. If any physical activity is undertaken, discomfort is increased.

ACC = American College of Cardiology; AHA = American Heart Association. Hunt SA *et al. Circulation* 2005;**112**:1825–1852.
The Criteria Committee of the New York Heart Association. Nomenclature and Criteria for Diagnosis of Diseases of the Heart and Great Vessels. 9th ed. Little Brown & Co; 1994. pp 253–256.

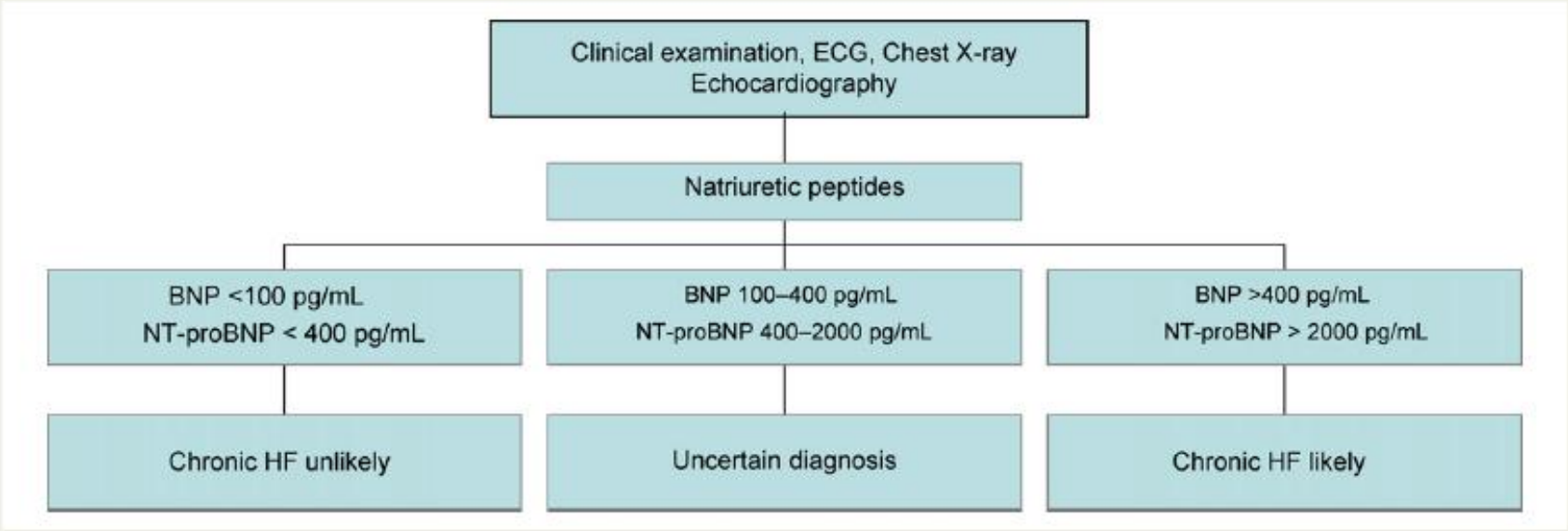


Figure 1 Flow chart for the diagnosis of HF with natriuretic peptides in untreated patients with symptoms suggestive of HF.

Table 11 Diagnostic assessments supporting the presence of heart failure

Assessment	Diagnosis of heart failure	
	Supports if present	Opposes if normal or absent
Compatible symptoms	++	++
Compatible signs	++	+
Cardiac dysfunction on echocardiography	+++	+++
Response of symptoms or signs to therapy	+++	++
ECG		
Normal		++
Abnormal	++	+
Dysrhythmia	+++	+
Laboratory		
Elevated BNP/NT-proBNP	+++	+
Low/normal BNP/NT-proBNP	+	+++
Hyponatraemia	+	+
Renal dysfunction	+	+
Mild elevations of troponin	+	+
Chest X-ray		
Pulmonary congestion	+++	+
Reduced exercise capacity	+++	++
Abnormal pulmonary function tests	+	+
Abnormal haemodynamics at rest	+++	++

+ = some importance; ++ = intermediate importance; +++ = great importance.

Peculiarità del paziente anziano

- Di malattia
- Di terapia
- Di prognosi

Peculiarità del paziente anziano

- ✓ **Di malattia**

HYPERTENSIVE HYPERTROPHIC CARDIOMYOPATHY OF THE ELDERLY

ERIC J. TOPOL, M.D., THOMAS A. TRAILL, M.R.C.P., AND NICHOLAS J. FORTUIN, M.D.

Abstract Using echocardiography, we identified 21 patients with a syndrome that included severe concentric cardiac hypertrophy, a small left ventricular cavity, and supernormal indexes of systolic function without concurrent medical illness or ischemic heart disease. Thirteen of the patients presented with dyspnea or chest pain. All patients studied had a history of hypertension and were compared with normotensive controls matched for age and sex. The patients were elderly (mean age, 73.3 years), predominantly female (16 patients), and mostly black (15 patients). Their cardiac function was characterized by excessive left ventricular emptying (ejection fraction on two-dimensional echocardiography [patients vs. controls], 79±4 vs. 59±5 per cent, P<0.001) and abnormal diastolic function as manifested by a prolonged early diastolic filling period (279±25 vs. 160±45 msec, P<0.001) and reduced peak diastolic dimension increase (11±4 vs. 16±5 cm per second, P<0.05). In spite of the clinical presentation of heart failure, all of 9 patients receiving either beta-receptor antagonists or calcium-channel blocking agents obtained symptomatic relief, whereas 6 of 12 patients receiving vasodilator medications had severe hypotensive reactions, including one death. We conclude that this unique subset of hypertensive patients has a clinical syndrome that warrants recognition and tailored management.

NEJM, 1985

Table 1. Demographic Characteristics and Medical History

Characteristic	Systolic Function		p*	No LVEF Assessment
	Preserved (n = 26,322)	Reduced (n = 25,865)		(n = 45,607)
Age (yrs, mean ± SD)	73.9 ± 13.2	69.8 ± 14.4	<0.0001	72.8 ± 14.1
Women (%)	62	40	<0.0001	51
Admission at academic center (%)	30	35	<0.0001	33
Medicare/Medicaid insurance (%)	80	73	<0.0001	81
African American (%)	17	22	<0.0001	22
Hypertension, CAD, or diabetes (%)	91	88	<0.0001	92
Hypertension (%)	77	69	<0.0001	72
CAD (%)	50	59	<0.0001	61
Diabetes mellitus (%)	45	40	<0.0001	46
Chronic renal insufficiency (%)	26	26	0.98	35
History of heart failure (%)	63	72	<0.0001	86
Prior myocardial infarction (%)	24	36	<0.0001	33
COPD or asthma (%)	31	27	<0.0001	33
Cardiac valvular disease (%)	21	22	0.13	24
Peripheral vascular disease (%)	17	17	0.33	19
Ventricular tachycardia (%)	3	11	<0.0001	10

*Comparison between preserved and reduced systolic function groups.
CAD = coronary artery disease; COPD = chronic obstructive pulmonary disease; LVEF = left ventricular ejection fraction.

JACC, 2006

Table 2. Clinical Presentation

Characteristic	Systolic Function		p*	No LVEF Assessment (n = 45,607)
	Preserved (n = 26,322)	Reduced (n = 25,865)		
Admission to ED or observation unit (%)	79	75	<0.0001	79
Admission to intensive care unit (%)	14	18	<0.0001	12
Peripheral edema (%)	69	63	<0.0001	65
Rales (%)	69	67	0.0002	67
Systolic BP >140 mm Hg (%)	61	44	<0.0001	46
Systolic BP (mm Hg, mean ± SD)	152.5 ± 32.7	138.9 ± 30.9	<0.0001	140.9 ± 32.5
Systolic BP ≤90 mm Hg (%)	1	4	<0.0001	4
Diastolic BP (mm Hg, mean ± SD)	78.7 ± 20.6	80.0 ± 20.4	<0.0001	76.0 ± 19.7
Initial serum Cr (mg/dl, mean ± SD)	1.7 ± 1.5	1.6 ± 1.3	0.0281	1.9 ± 1.8
Serum Cr >2 mg/dl (%)	17	18	0.57	24
BUN (mg/dl, mean ± SD)	29.3 ± 19.3	30.2 ± 19.8	<0.0001	34.5 ± 22.5
Heart rate (beats/min, mean ± SD)	86.8 ± 22.0	92.9 ± 22.7	<0.0001	86.7 ± 20.7
Dyspnea at rest (%)	34	34	0.19	35
Atrial fibrillation on first ECG (%)	21	17	<0.0001	20

*Comparison between preserved and reduced systolic function groups.
BP = blood pressure; BUN = blood urea nitrogen; Cr = creatinine; ECG = electrocardiogram; ED = emergency department; LVEF = left ventricular ejection fraction.

JACC, 2006

Table 6. Clinical Outcomes During Hospitalization

Outcome	Systolic Function			
	Preserved (n = 26,322)	Reduced (n = 25,865)	p*	No LVEF Assessment (n = 45,607)
Mortality (%)	2.8	3.9	<0.0001	4.8
Length of hospitalization (days, median [interquartile range])	4.9 [3.1–7.6]	5.0 [3.2–8.1]	<0.0001	3.8 [2.3–6.1]
Admitted to ICU (%)	18.9	24.7	<0.0001	15.3
Length of ICU/CCU stay (days, median [interquartile range])	2.7 [1.4–4.9]	3.0 [1.6–5.1]	<0.0001	2.0 [1.0–3.8]
Weight loss >10 lbs (%)	79.8	80.7	0.0298	75.8
	26.9	30.4	<0.0001	23.2
Asymptomatic at discharge (%)	55	55	0.21	51

*Comparison between preserved and reduced systolic function groups.
CCU = coronary care unit; ICU = intensive care unit; LVEF = left ventricular ejection fraction.

JACC, 2006

Table 1. Characteristics of Patients.*

Characteristic	Reduced Ejection Fraction (<40%) (N=1570)	Preserved Ejection Fraction (>50%) (N=880)	P Value
Mean LVEF — %	25.9	62.4	<0.001
Age — yr	71.8 ± 12	75.4 ± 11.51	<0.001
Male sex — no. (%)	983 (62.6)	302 (34.3)	<0.001
Coronary artery disease or ischemia — no. (%)	764 (48.7)	312 (35.5)	<0.001
Hypertension — no. (%)	772 (49.2)	485 (55.1)	0.005
Hyperlipidemia — no. (%)	350 (22.3)	136 (15.5)	<0.001
Diabetes — no. (%)	611 (38.9)	279 (31.7)	<0.001
Cerebrovascular accident or transient ischemic attack — no. (%)	229 (14.6)	133 (15.1)	0.72
Angina — no. (%)	440 (28.0)	201 (22.8)	0.005
Ever smoked — no. (%)	754 (48.0)	322 (36.6)	<0.001
Currently smoking — no. (%)	271 (17.3)	106 (12.0)	<0.001
Peripheral vascular disease — no. (%)	236 (15.0)	92 (10.5)	<0.001
Atrial fibrillation — no. (%)	370 (23.6)	280 (31.8)	<0.001
Cancer — no. (%)	182 (11.6)	105 (11.9)	0.80
COPD — no. (%)	207 (13.2)	156 (17.7)	0.002
Prior myocardial infarction — no. (%)	612 (39.0)	146 (16.6)	<0.001
Prior CABG — no. (%)	203 (12.9)	51 (5.8)	<0.001
Prior PCI — no. (%)	48 (3.1)	16 (1.8)	0.07
Peptic ulcer disease — no. (%)	94 (6.0)	74 (8.4)	0.02
Hepatitis or cirrhosis — no. (%)	20 (1.3)	16 (1.8)	0.28
Dementia — no. (%)	76 (4.8)	49 (5.6)	0.43
Hemoglobin <10 g/dl — no. (%)	155 (9.9)	186 (21.1)	<0.001
Mean systolic blood pressure — mm Hg	146	156	<0.001
Mean respiratory rate — breaths/min	26	26	0.17
Serum sodium <136 mmol/liter — no. (%)	362 (23.1)	209 (23.8)	0.70
Serum creatinine >150 mmol/liter — no. (%)	296 (18.9)	195 (22.2)	0.95
Dialysis — no. (%)	18 (1.1)	9 (1.0)	0.78

* Plus–minus values are means ±SD. LVEF denotes left ventricular ejection fraction, COPD chronic obstructive pulmonary disease, CABG coronary-artery bypass grafting, and PCI percutaneous coronary intervention.

NEJM, 2006

Table 3. In-Hospital Care, Complications, and Outcomes.

Variable	Reduced Ejection Fraction (<40%) (N=1570)	Preserved Ejection Fraction (>50%) (N=880)	P Value
	no. (%)		
In-hospital care			
Cardiologist as primary physician	527 (33.6)	217 (24.7)	<0.001
Consultation with a cardiologist	687 (43.8)	328 (37.3)	0.002
Sodium restricted	1069 (68.1)	539 (61.2)	<0.001
Fluid restricted	216 (13.8)	113 (12.8)	0.52
Weight recorded on >50% of hospital days	301 (19.2)	154 (17.5)	0.31
Complications			
Atrial fibrillation or flutter	116 (7.4)	64 (7.3)	0.92
Hypotension	94 (6.0)	30 (3.4)	0.005
Cardiac arrest	36 (2.3)	11 (1.2)	0.07
Cardiogenic shock	16 (1.0)	2 (0.2)	0.03
Acute coronary syndrome (myocardial infarction or unstable angina)	81 (5.2)	38 (4.3)	0.35
Renal failure	437 (27.8)	235 (26.7)	0.55
Bilevel positive airway pressure or continuous positive airway pressure	124 (7.9)	57 (6.5)	0.20
Mechanical ventilation	94 (6.0)	28 (3.2)	0.002
Readmission to coronary care unit or intensive care unit	77 (4.9)	29 (3.3)	0.06
Assessment for heart transplantation at admission	7 (0.4)	4 (0.5)	0.98
Outcomes			
30-Day mortality	112 (7.1)	47 (5.3)	0.08
1-Yr mortality	400 (25.5)	195 (22.2)	0.07
30-Day readmission for heart failure*	73 (4.9)	38 (4.5)	0.66
1-Yr readmission for heart failure*	240 (16.1)	114 (13.5)	0.09
30-Day mortality or readmission for heart failure	182 (11.6)	83 (9.4)	0.10
1-Yr mortality or readmission for heart failure	566 (36.0)	274 (31.1)	0.01

* Readmission rates were calculated for the 2339 patients who survived the index admission: 1493 with reduced ejection fraction and 846 with preserved ejection fraction.

NEJM, 2006

Diastolic Heart Failure or FH with normal ejection fraction

More likely to be older, female, and hypertensive

Less likely to have had a prior myocardial infarction or to be receiving an angiotensin converting enzyme inhibitor or angiotensin II receptor blocker.

Lower in-hospital mortality but similar ICU and hospital length of stay.

Peculiarità del paziente anziano

- ✓ **Di terapia**

Treatment for patients with heart failure and preserved ejection fraction

Control of systolic and diastolic hypertension

Control of ventricular rate in patients with atrial fibrillation

Control of pulmonary congestion and peripheral edema with diuretics

Coronary revascularization in patients with CHD in whom ischemia is judged to have an adverse effect on diastolic function

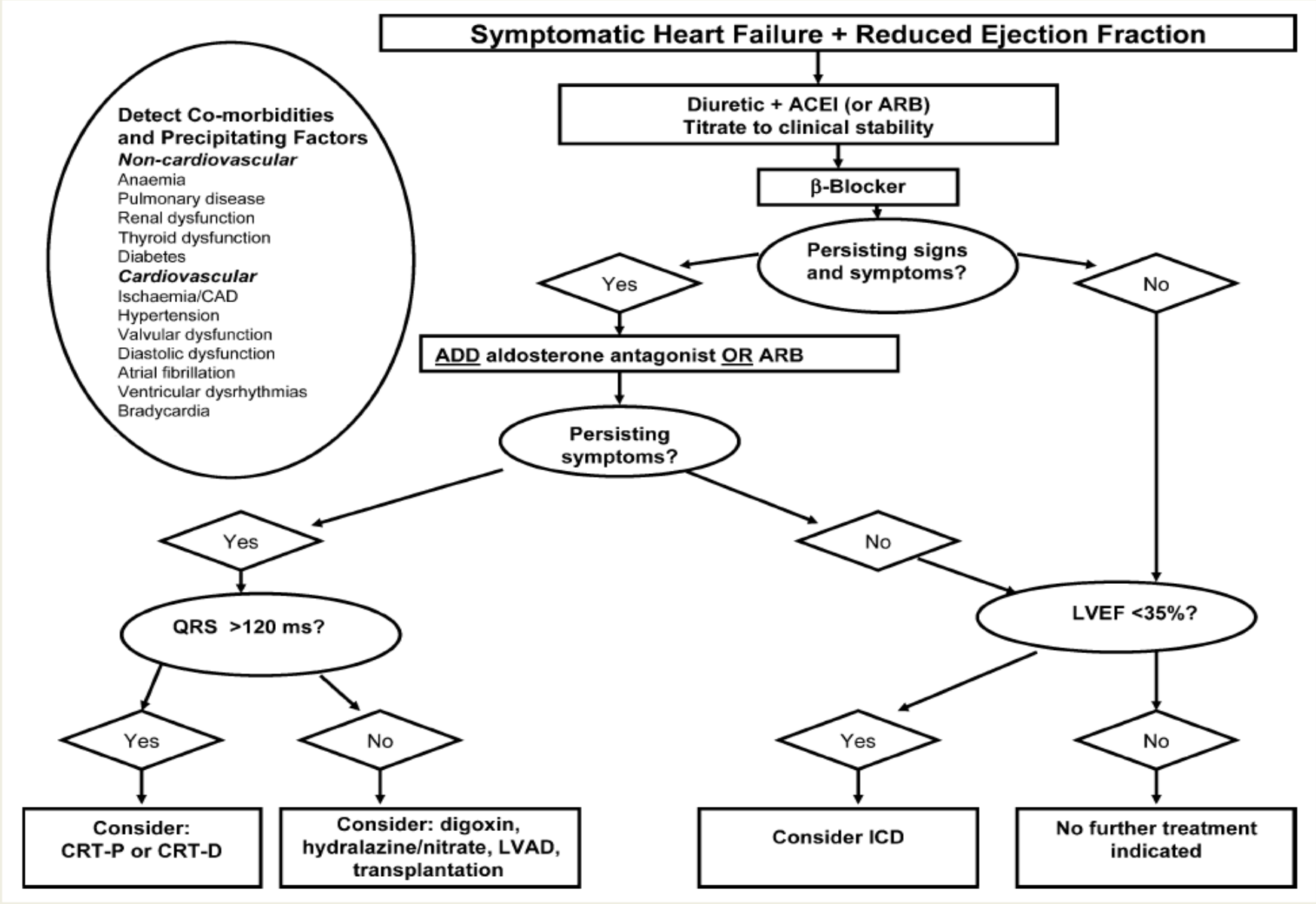


Figure 2 A treatment algorithm for patients with symptomatic heart failure and reduced ejection fraction.

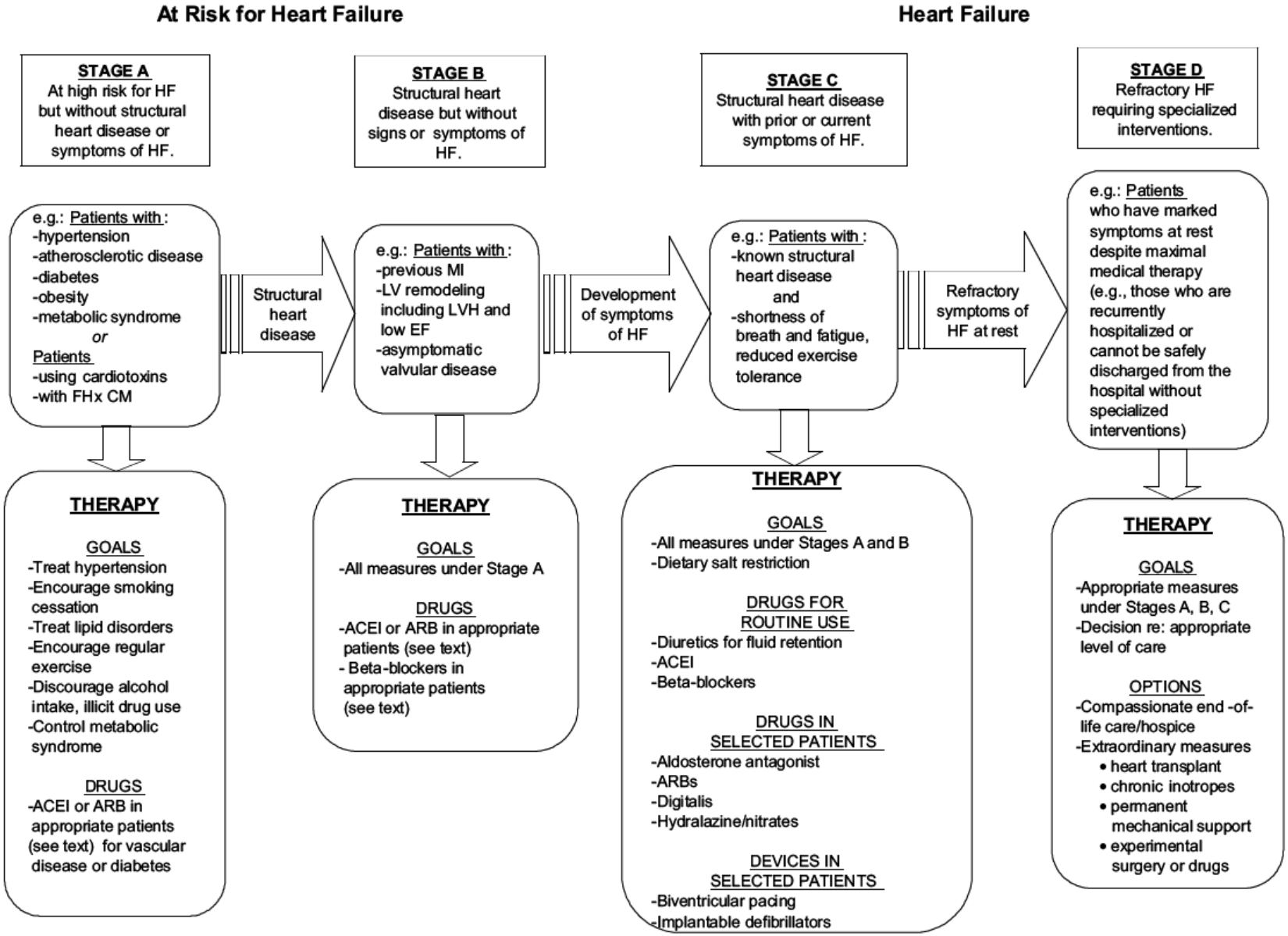


Figure 1. Stages in the development of heart failure/recommended therapy by stage. FHx CM indicates family history of cardiomyopathy; ACEI, angiotensin converting enzyme inhibitors; and ARB, angiotensin receptor blocker.

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Drug Treatment of Chronic Heart Failure in the Elderly

Gregor Leibundgut, Matthias Pfisterer and *Hans-Peter Brunner-La Rocca*

Cardiology, University Hospital Basel, Basel, Switzerland

Drugs Aging, 2007

Table I. Differences between elderly and younger patients (adapted from Bulpitt[17])

Major differences	Minor differences
Physiological alterations in very old age general: weight loss, lower cholesterol cardiovascular: lower heart rate, reduced heart rate response to exercise, lower blood pressure[18]	Reduced metabolism, particularly renal function and volume of distribution (usually manageable by modification of drug dosage and schedule)[25]
Risk assessment (and possibly therapeutic goals) different overweight and hypertension associated with better survival[19]	Individual flexibility reduced scepticism about therapy lifestyle changes more difficult
Presence of dementia[20] survival no longer primary goal involvement of relatives and institutions	Strategies of long-term survival less relevant (e.g. diabetes mellitus, risk factors)
Co-morbidities[21] and resultant co-medication increased risk of drug interactions and adverse effects as a result of polypharmacy[22] may limit therapeutic options	Increased time needed (e.g. for visits, explanations)[26]
Reduction of reserves and compensatory mechanisms (e.g. orthostatic dysregulation)	Positive selection how do patients who develop heart failure in old age differ from those who developed heart failure earlier?
Less studied[11,23,24] women diastolic dysfunction (heart failure with preserved left-ventricular systolic function)	End-of-life preferences may differ[27]

Table II. Evidence level for chronic heart failure therapy relative to age

Treatment	Age group	
	<75y	≥75y
Reduced systolic function; LVEF ≤40%		
ACE inhibitors	++++	++[a,b]
ARBs	++++	++[a]
β-Adrenoceptor antagonists	++++	+++[a,b]
Aldosterone receptor antagonists	+++	++[a]
Preserved systolic function; LVEF >(40–)50%		
ACE inhibitors[c]	++[d]	+
ARBs[c]	++[d]	+
β-Adrenoceptor antagonists	++[a]	+
Aldosterone receptor antagonists	–	–

a Evidence from subgroup analysis.

b Evidence from retrospective analysis of large cohorts.

c Primarily involving reduction in re-hospitalisation for heart failure.

d Evidence from one RCT with limited positive effects.

ARBs = angiotensin II type 1 receptor antagonists (angiotensin receptor blockers); **LVEF** = left-ventricular ejection fraction; **RCT** = randomised controlled trial; **+** indicates evidence from subgroup analysis with limited positive effects; **++** indicates evidence from subgroup analysis, retrospective analysis of large cohorts, or one RCT with limited positive effects; **+++** indicates evidence from one large positive RCT; **++++** indicates evidence from several large positive RCTs; – indicates no outcome data available.

Drugs Aging, 2007

Drug treatment of chronic heart failure in elderly patients is, in principle, identical to that in younger patients. However, drug treatment in elderly patients requires more careful monitoring, adjustments to therapy ……..Given the low use of recommended drugs in elderly patients, multidisciplinary approaches may be particularly useful in this regard.

Drugs Aging, 2007

DEFEAT Heart Failure: Assessment and Management of Heart Failure in Nursing Homes Made Easy

Ali Ahmed, MD, MPH, FACC, FAHA, Linda Jones, MN, CRNP, and Clare I. Hays, MD

Heart failure (HF) in older adults presents challenges that are different in many ways than those for younger adults. Diagnosis of HF in older adults can be delayed due to attributing early symptoms to normal changes of aging or, in the setting of a normal ejection fraction, failing to appreciate diastolic heart failure. Moreover, treatment of HF in the elderly is often complicated by comorbidities and polypharmacy. The long-term care setting can present even more challenges, yet can be made easy by following a simple mnemonic **DEFEAT**-HF. After making a clinical **D**iagnosis and determining the **E**tiology, **F**luid volume must be assessed to achieve euvolemia, and **E**jection fr**A**ction must be determined to guide **T**herapy. **(J Am Med Dir Assoc 2008; 9: 383–389)**

Keywords: Chronic heart failure; nursing home; assessment; management

JAMDA, 2008

D Diagnosis Make a clinical diagnosis of heart failure before ordering any test, especially an echocardiogram. A normal ejection fraction in a patient without a clinical diagnosis may confound the diagnosis process. If a clinical diagnosis is already made or patient had hospitalization due to heart failure, check how the diagnosis was established.

E Etiology Hypertension and myocardial infarction are the two most common causes. Expect multiple causes in elderly heart failure patients in the long-term care setting. Continued treatment of risk factors such as high blood pressure and myocardial ischemia is important to prevent disease progression.

F Fluid volume Single most important physical examination. Best assessed by estimating jugular venous pressure in the neck. External jugular veins are very useful if their limitations are appreciated. Being superficial veins they are subject to external pressure or internal obstruction. Thus a distended external jugular vein without visible pulsation should not generally be used to estimate venous pressure.

EA Ejection frAction Single most important test after a clinical diagnosis of heart failure has been made. It is a marker of prognosis (generally patients with lower ejection fraction have a poorer prognosis) and a guide to therapy.

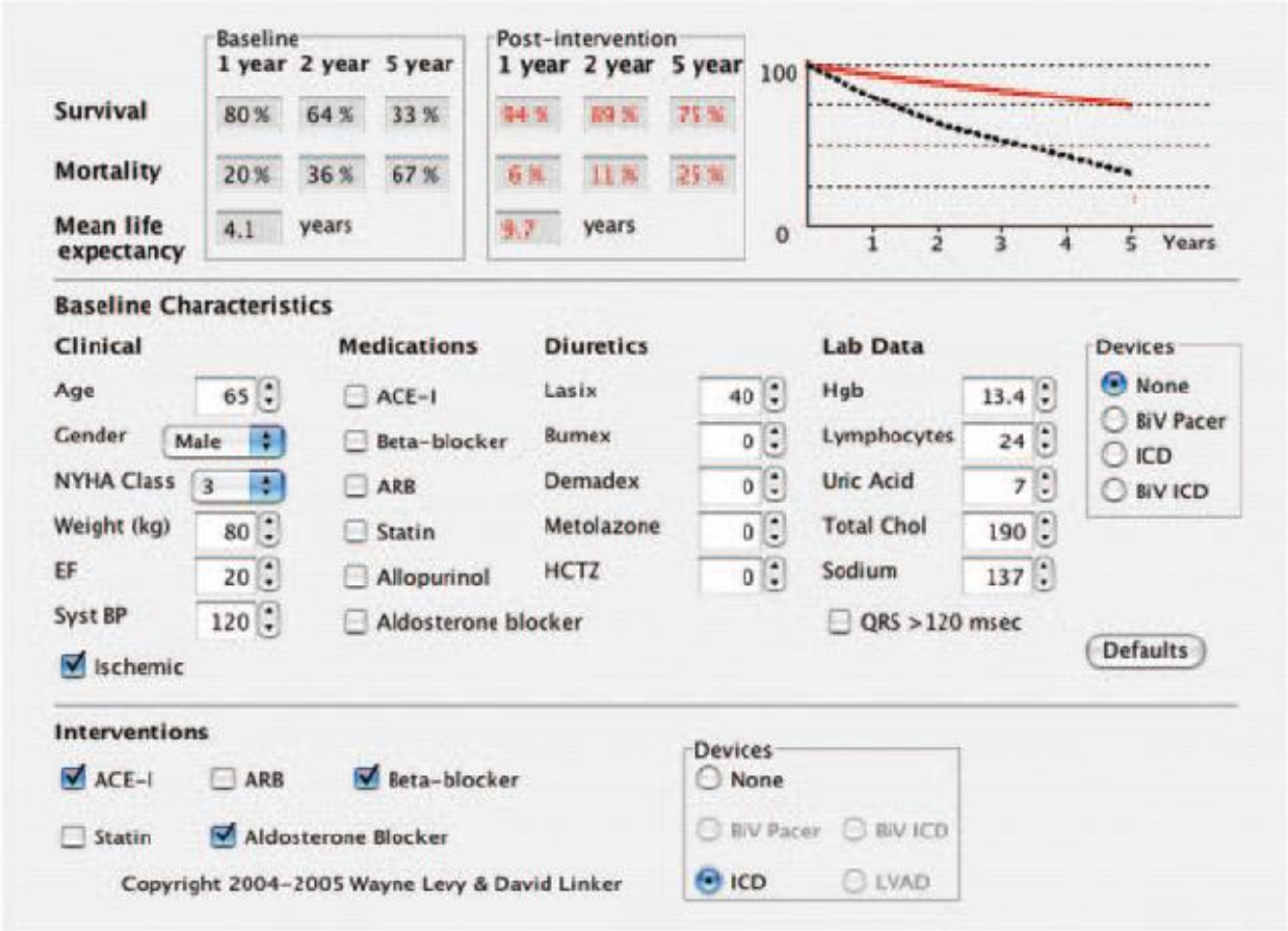
T Treatment Heart failure therapy can be divided into symptom-relieving and life-prolonging therapies. The two most important life-prolonging therapies for heart failure patients with low ejection fraction (45%) are ACE inhibitors (or an ARB if intolerant to ACE inhibitor) and beta-blockers (those approved for use in heart failure and shown to reduce mortality, namely metoprolol extended release and carvedilol). Survival benefit of these drugs in diastolic heart failure has not yet been proven. All symptomatic heart failure patients with fluid volume overload should be treated with a diuretic and once euvolemia is achieved the lowest possible dose should be used to maintain euvolemia in conjunction with salt and fluid restriction. Digitalis in low doses (0.125 mg or less per day) should be used to reduce symptoms and risk of hospitalization. In patients who cannot tolerate beta-blockers at low dosages, digitalis can also reduce mortality.

JAMDA, 2008

HF in the long-term care setting is a complex syndrome, the management of which can be challenging. …..Guidelines provide little specific information for HF patients in the long-term care setting. However, familiarity with a major national guideline may provide a foundation on which HF treatment in the long-term care setting can be individualized.

JAMDA, 2008

The seattle Heart failure model



Circulation 2006

Peculiarità del paziente anziano

- ✓ **Di prognosi**

Table 17 Conditions associated with a poor prognosis in heart failure

Demographics	Clinical	Electrophysiological	Functional/ exertional	Laboratory	Imaging
Advanced age*	**Hypotension***	**Tachycardia** **Q waves**	**Reduced work, low peak VO_2***	**Marked elevation of BNP/NT pro-BNP***	**Low LVEF***
Ischaemic aetiology*	**NYHA functional class III–IV***	**Wide QRS***		**Hyponatraemia***	
Resuscitated sudden death*	**Prior HF hospitalization***	**LV hypertrophy** **Complex ventricular arrhythmias***		**Elevated troponin*** **Elevated biomarkers, neurohumoral activation***	
Poor compliance	Tachycardia	Low heart rate variability Atrial fibrillation	Poor 6 min walk distance	Elevated creatinine/BUN	Increased LV volumes
Renal dysfunction	Pulmonary rales	T-wave alternans	High VE/VCO_2 slope	Elevated bilirubin Anaemia	Low cardiac index
Diabetes	Aortic stenosis		Periodic breathing	Elevated uric acid	High LV filling pressure
Anaemia	Low body mass index				Restrictive mitral filling pattern, pulmonary hypertension
COPD	Sleep-related breathing disorders				Impaired right ventricular function
Depression					

* = powerful predictors.

Long-term Survival in Elderly Patients Hospitalized for Heart Failure

14-Year Follow-up From a Prospective Randomized Trial

Bao C. Huynh, MD, PharmD; Aleksandr Rovner, MD; Michael W. Rich, MD

Table 3. Multivariate Predictors of Mortality

Predictor	Regression Coefficient	HR (95% CI)	*P* Value*
Age, per 5 y	0.13	1.14 (1.03-1.26)	.01
Serum sodium <135 mEq/L	0.51	1.67 (1.19-2.32)	.003
CAD	–0.41	1.51 (1.16-1.95)	.002
Dementia	–0.70	2.02 (1.13-3.61)	.02
PVD	–0.55	1.74 (1.20-2.52)	.004
SBP, per 10 mm Hg	–0.05	0.95 (0.92-0.98)	.004
SUN, per 10 mg/dL (3.57 mmol/L)	0.18	1.20 (1.12-1.29)	<.001

Abbreviations: CAD, coronary artery disease; CI, confidence interval; HR, hazard ratio; PVD, peripheral vascular disease; SBP, systolic blood pressure; SUN, serum urea nitrogen.

*Cox regression χ^2 statistics.

Arch Intern Med 2006

Table 5. Median Survival and Mortality According to the Number of Prognostic Factors

Risk Factors	No.	Median Survival (95% CI), d	Mortality, No. (%)			*P* Value*
			6 mo	1 y	5 y	
0-1	89	1652 (1386-1918)	7 (7.9)	8 (9.0)	51 (57.3)	<.001
2-3	153	789 (579-999)	15 (9.8)	34 (22.2)	121 (79.1)	
≥4	37	152 (84-220)	22 (59.5)	27 (73.0)	37 (100)	

Abbreviation: CI, confidence interval.
*$P<.001$ for each risk class comparison.

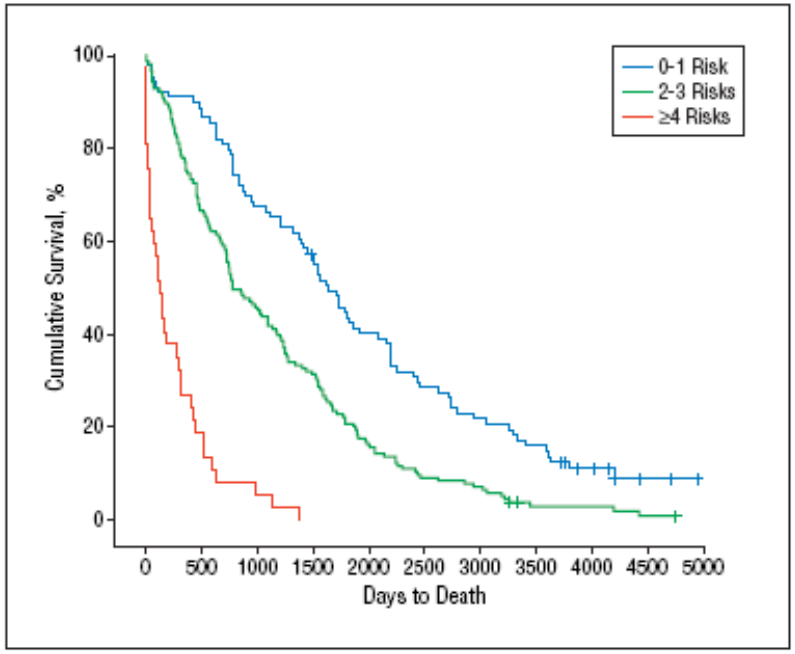


Figure 3. Probability of survival based on number of prognostic risk factors (log-rank $\chi^2=127.63$; $P<.001$).

Arch Intern Med 2006

Circulation
Heart Failure
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Learn and Live

Discordant Short- and Long-Term Outcomes Associated With Diabetes in Patients With Heart Failure: Importance of Age and Sex: A Population Study of 5.1 Million People in Scotland

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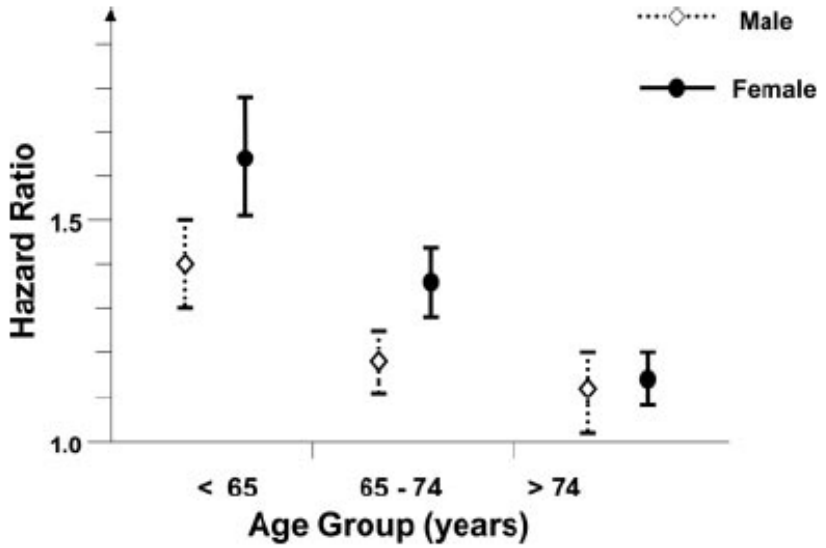

Figure 4. Adjusted risk of death at 5 years in men and women (diabetics compared with nondiabetics). Patients who died in the first 30 days were excluded.

Circ Heart Fail, 2008

Depression and Major Outcomes in Older Patients With Heart Failure

Association Based on Cox Regression Analysis of Groups of Risk With 6-Month Mortality in 800 Hospitalized Elderly Patients*

Characteristic†	No. of Patients/No. of Events	Crude Analysis		Adjusted Analysis‡	
		RR	95% CI	RR	95% CI
No HF and no depression	353/14	1.0	Reference	1.0	Reference
No HF and yes depression	361/23	1.9	0.9-4.0	1.8	0.8-4.3
Yes HF and no depression	47/7	3.2	1.0-10.3	3.1	1.0-10.4
Yes HF and yes depression	39/8	6.9	2.6-18.3	5.8	2.1-16.6
Disability in BADL	143/22	2.8	1.6-4.9	2.2	1.1-4.6
Serum albumin <3.5 g/dL	112/16	2.4	1.3-4.4	2.0	0.9-4.1
APACHE score >5	76/14	3.3	1.7-6.2	2.3	1.1-5.0

*RR indicates relative risk; CI, confidence interval; HF, heart failure; BADL, basic activities of daily living; and APACHE, Acute Physiology and Chronic Health Evaluation.

†Variables failing to qualify for entering the multivariate regression model were age, male sex, cognitive impairment, anemia (hemoglobin level <8 g/dL), diabetes mellitus, chronic obstructive pulmonary disease, and gastrointestinal diseases.

‡Adjusted for potential confounders (disability in BADL, serum albumin levels <3.5 g/dL, and APACHE score >5).

Arch Intern Med, 2002

Short-Term Survival in Elderly Patients Hospitalized for Heart Failure: the Role of Diabetes and newly Recognized Hyperglycemia.

Table 1: Characteristics of 340 Hospitalized Elderly Patients with Heart Failure According to their Glycemic Status

Patients	Without History of Diabetes and Normal Glycemic Values Mean ± SD n=204	With History of Diabetes Mean ± SD n=101	P^A	Without History of Diabetes and Abnormal Glucose Values Mean ± SD n=35	P^B	P^C
Age, Years	79.2 (± 8.0)	78.9 (± 8.3)	.7	77.6 (± 7.7)	.2	.4
Gender (male), n (%)	80 (39.2 %)	37 (36.6 %)	.3	19 (54.3%)	.06	.05
Mini-Mental State Examination Score (0-30)	25.3 (± 5.4)	24.6 (± 4.8)	.2	23.6 (± 6.1)	.09	.3
Preadmission Barthel Index (0-100)	90.7 (± 16.5)	85.7 (± 22.4)	.02	83.6 (± 22.9)	.02	.6
Charlson Index (0-33)	4.8 (± 1.3)	5.0 (± 1.5)	.1	5.1 (± 1.5)	.2	.8
APS Score (0-33)	2.7 (± 3.1)	3.2 (± 3.3)	.1	3.5 (± 3.8)	.1	.6
Left Ventricular Ejection Fraction*	58.9 (± 19.9)	59.3 (± 19.3)	.9	57.7 (± 19.5)	.7	.7

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JAGS, 2009 In press

Serum- Glycemia (mg/dl)	92.8 (± 13.3)	133.1(± 51.2)	*.000*	143.9 (± 17.2)	*.000*	*.2*
Serum-Cholesterol (mg/dl)	193.0 (± 51.1)	186.4 (± 52.2)	*.2*	191.9 (± 42.2)	*.8*	*.5*
Serum- Albumin (g/dl)	4.0 (± 0.7)	3.8 (± 0.6)	*.01*	3.8 (± 0.5)	*.05*	*.8*
Serum- Creatinine (mg/dl)	1.1 (± 0.7)	1.3 (± 0.8)	*.6*	1.2 ± 1.0)	*.5*	*.9*
Serum- Urea (mg/dl)	25.8 (± 11.4)	28.8 (± 13.1)	*.04*	26.7 (± 10.6)	*.6*	*.3*
Sodium (mmol/l)	138.5 (± 4.6)	137.6 (± 5.2)	*.2*	137.0 (± 4.5)	*.5*	*.7*
Troponin I, ng/ ml	0.39 (± 1.34)	0.40 (± 1.32)	*.3*	0.42 (± 1.35)	*.6*	*.4*
Heart Rate, beats/min	85 (± 19.0)	83 (± 18.0)	*.6*	98 (± 21.0)	*.02*	*.02*
Systolic blood pressure, mm Hg	153 (± 35)	159 (± 38)	*.6*	157 (± 37)	*.7*	*.6*
NYHA [†] Class III-IV n (%)	123 (60.3)	63 (62.4)	0.4	25 (71.4)	*.1*	*.2*
Comorbidity						
Anemia[‡], n (%)	86 (42.2)	42 (41.6)	*.9*	17 (48.6)	*.4*	*.4*
Hypertension, n (%)	190 (93.0)	94 (93.0)	*.9*	30 (85.7)	*.1*	*.1*
Previous Myocardial Infarction, n (%)	129 (63.0)	68 (67.3)	*.4*	25 (71.4)	*.4*	*.8*
Valve Disease n (%)	18 (8.8)	11 (10.9)	*.5*	4 (11.4)	*.6*	*.9*
Atrial Fibrillation n (%)	67 (32.8)	39 (38.6)	*.3*	8 (22.9)	*.1*	*.04*
Chronic Obstructive Pulmonary Disease n (%)	31 (15.2)	12 (11.9)	*.4*	6 (17.1)	*.6*	*.3*

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Number of Drugs at Admission	5.4 (± 2.3)	6.5 (± 3.0)	*.001*	6.6 (± 2.6)	*.01*	*.9*
Length of Stay in Hospital (days)	6.0 (± 2.6)	7.1 (± 4.3)	*.007*	6.5 (± 4.1)	*.3*	*.5*

A= comparisons between patients without history of diabetes and normal glycemic values vs. patients with history of diabetes.

B= comparisons between patients without history of diabetes and normal glycemic values vs. patients with history of diabetes and abnormal glucose values.

C= comparisons between patients with history of diabetes vs. patients without history of diabetes and abnormal glucose values.

* Report of Left Ventricular Ejection Fraction was available in 287 patients.

† NYHA= New York Heart Association class

‡ Anemia as defined by a haemoglobin concentration < 13.5 g/dl in men and < 12 g/dl in women.

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Table 2: Factors Associated with 3 Month Mortality in a Group of 340 Elderly Patients with Heart Failure According to Glycemic Status

	N/events	Unadjusted	Adjusted*
		RR (95% C.I.)	*RR (95% C.I.)*
Moderate to Severe Dementia (Mini-Mental State Examination Score <18)	121/16	3.4 (1.3-8.7)	3.1 (1.2-7.8)
Acute Physiology Score† (> 4)	78/11	3.8 (1.7- 8.4)	1.8 (1.1-7.4)
Without history of Diabetes and normal glycemic value	204/11	1.0-Ref	1.0-Ref
With history of Diabetes	101/10	1.8 (0.8-4.1)	1.4 (0.5-4.4)
Without history of Diabetes and abnormal glucose value	35/7	3.6 (1.4-9.3)	2.7 (1.0-9.4)

Univariate analysis and multiple logistic regressions were applied to identify factors statistically associated with 3 month mortality.

* Variables associated to 3 month mortality and not entered in multivariate Cox proportional hazards model were: age (80+), gender, number of drugs, hyponatraemia, serum albumin, and left ventricular ejection fraction.

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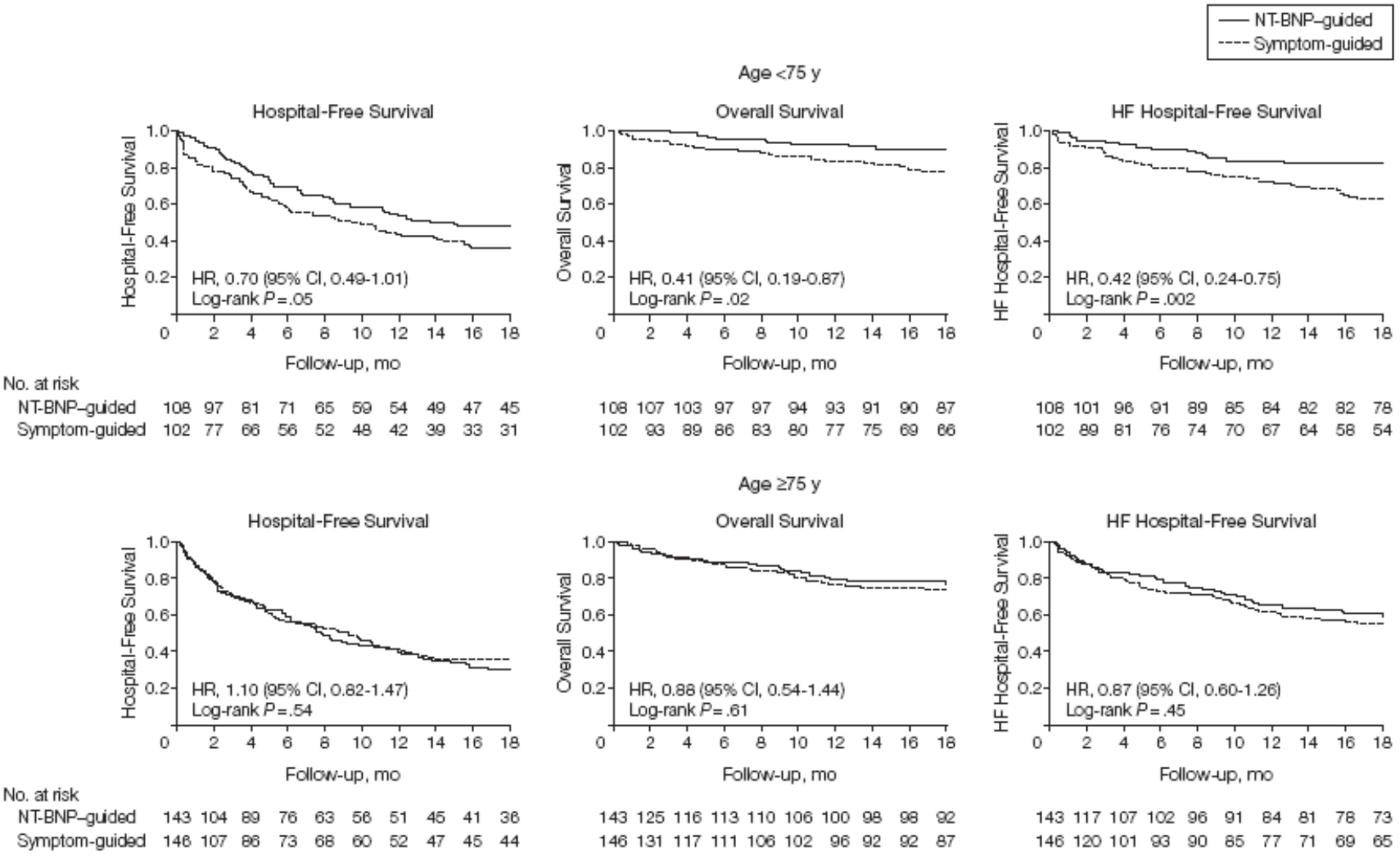

The differences between treatment groups were observed only in younger but not older patients. NT-BNP indicates N-terminal brain natriuretic peptide; CI, confidence interval; HF, heart failure; HR, hazard ratio.

JAMA 2009

In conclusion, the time course of heart failure therapy is gradual, composed of up titration of medications, reassessment of patient symptoms and signs, clinician persistence and patience, and obtaining BNP levels. There are no easy answers and no simple solutions in the search for a single biomarker for diagnosis, prognosis, and treatment of heart failure.

JAMA, 2009