Overview of Heart Failure

Classification, aetiologies, assessments and biomarkers

Dr Yung Chi Yui
Ruttonjee Hospital

NATIONAL BESTSELLER

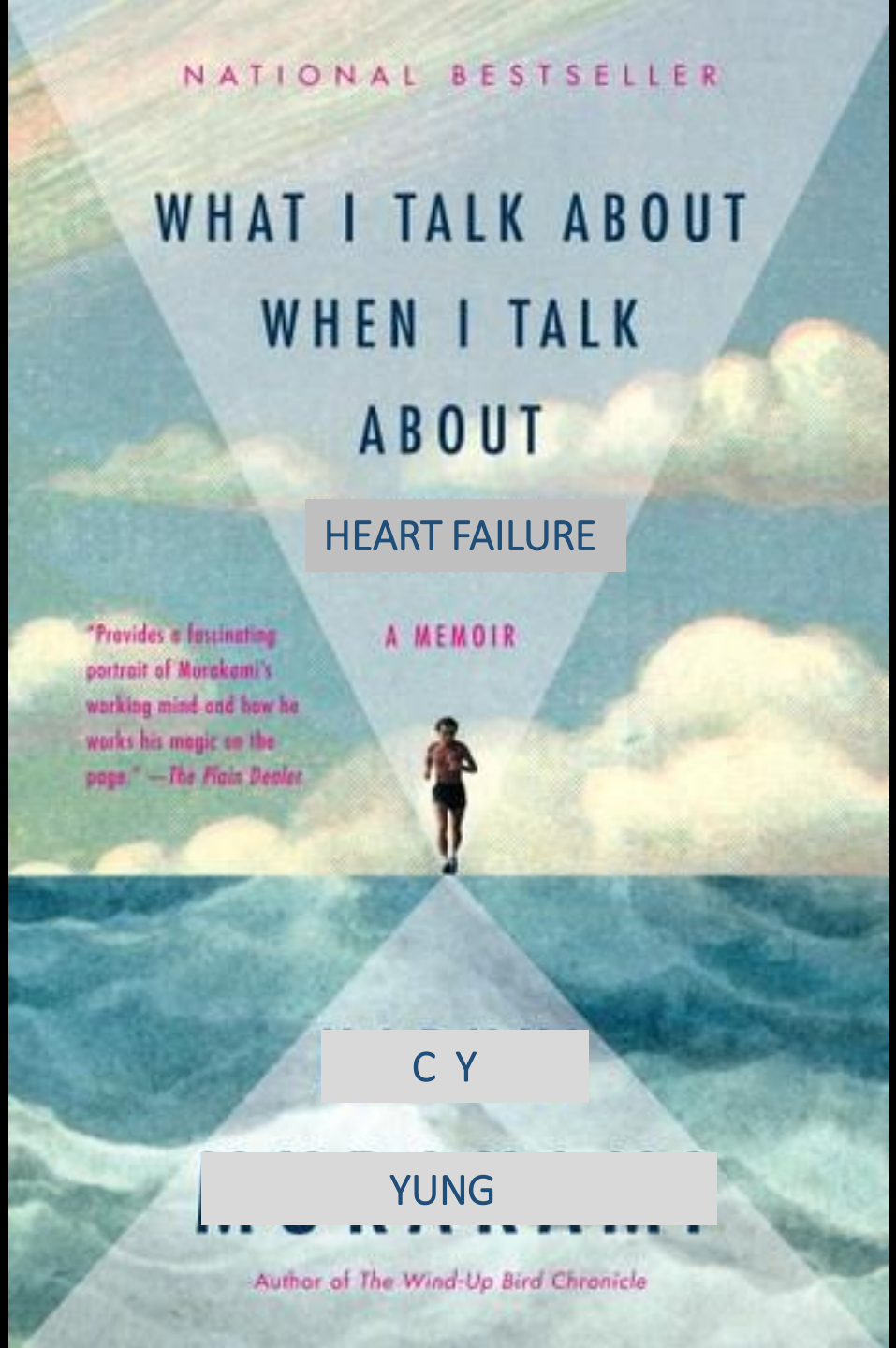
WHAT I TALK ABOUT WHEN I TALK ABOUT RUNNING

A MEMOIR

"Provides a fascinating portrait of Murakami's working mind and how he works his magic on the page." —*The Plain Dealer*

HARUKI MURAKAMI

Author of *The Wind-Up Bird Chronicle*


NATIONAL BESTSELLER
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HEART FAILURE
A MEMOIR
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C Y
YUNG
Author of The Wind-Up Bird Chronicle

Definition

- ACC guideline

HF is a **complex clinical syndrome** that results from any structural or functional impairment of ventricular **filling or ejection** of blood

- ESC guideline

HF is a **clinical syndrome** characterized by typical symptoms (e.g. breathlessness, ankle swelling and fatigue) that may be accompanied by signs (e.g. elevated jugular venous pressure, pulmonary crackles and peripheral oedema) caused by a structural and/or functional cardiac abnormality, resulting in a **reduced cardiac output** and/or **elevated intracardiac pressures** at rest or during stress.

Definition

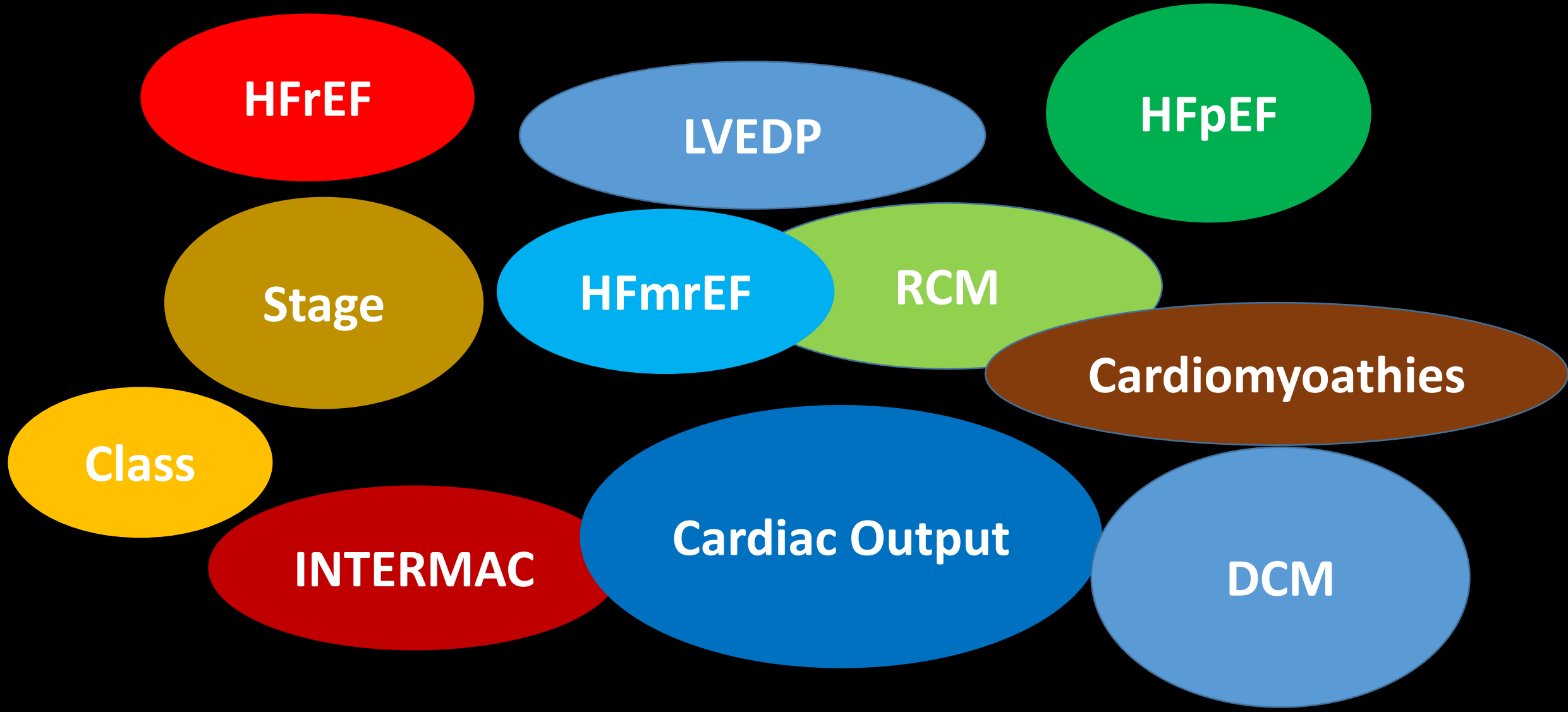
- ACC guideline

HF is a **complex cli** m any structural or functiona blood

- ESC

HF i g. breati panied by signs (e y crackles and peripheral oedema) or functional cardiac abnormality, resulting in a **reduced cardiac output** and/or **elevated intracardiac pressures** at rest or during stress.

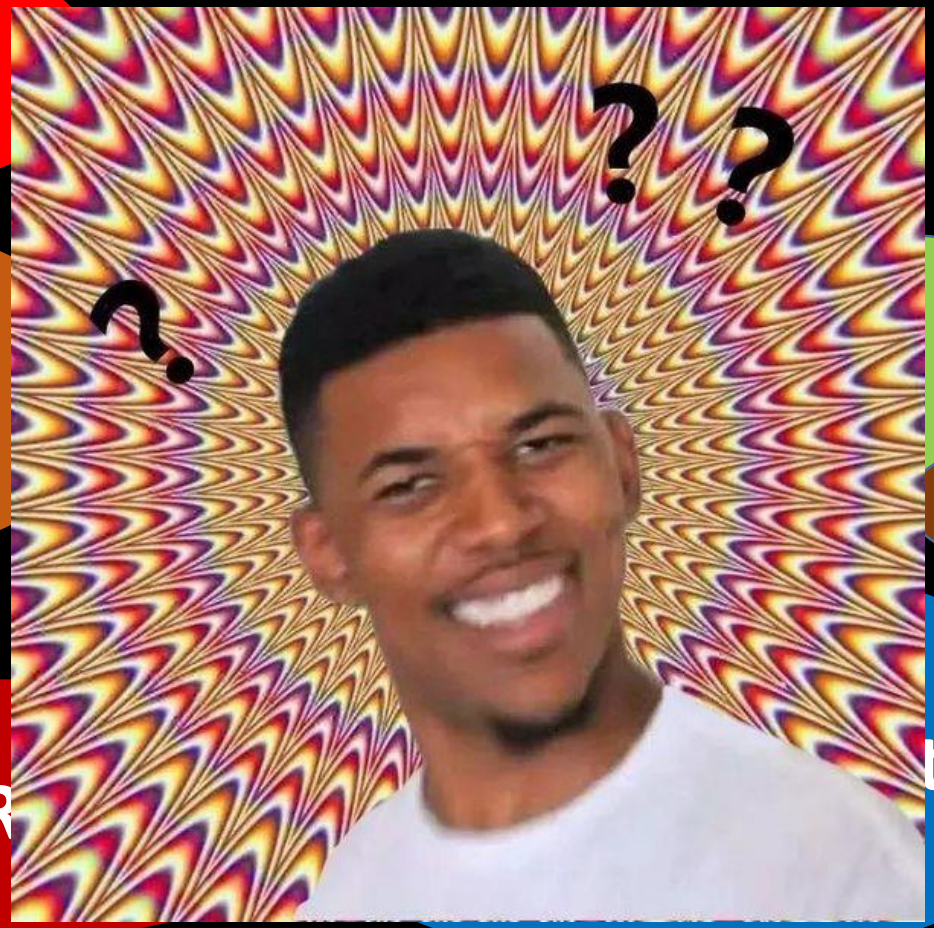
HF is NOT a diagnosis !


HFrEF
LVEDP
HFpEF
Stage
HFmrEF
RCM
Cardiomyoathies
Class
INTERMAC
Cardiac Output
DCM

HFrEF

HFpEF

Stage



Cardiomyoathies

Class

INTER

DCM

Things You Must Know

- HF with reduced EF (HFrEF LVEF<40%) Vs HF with preserved EF (HFpEF LVEF>40%)
- Stage and Class (+/- INTERMAC)

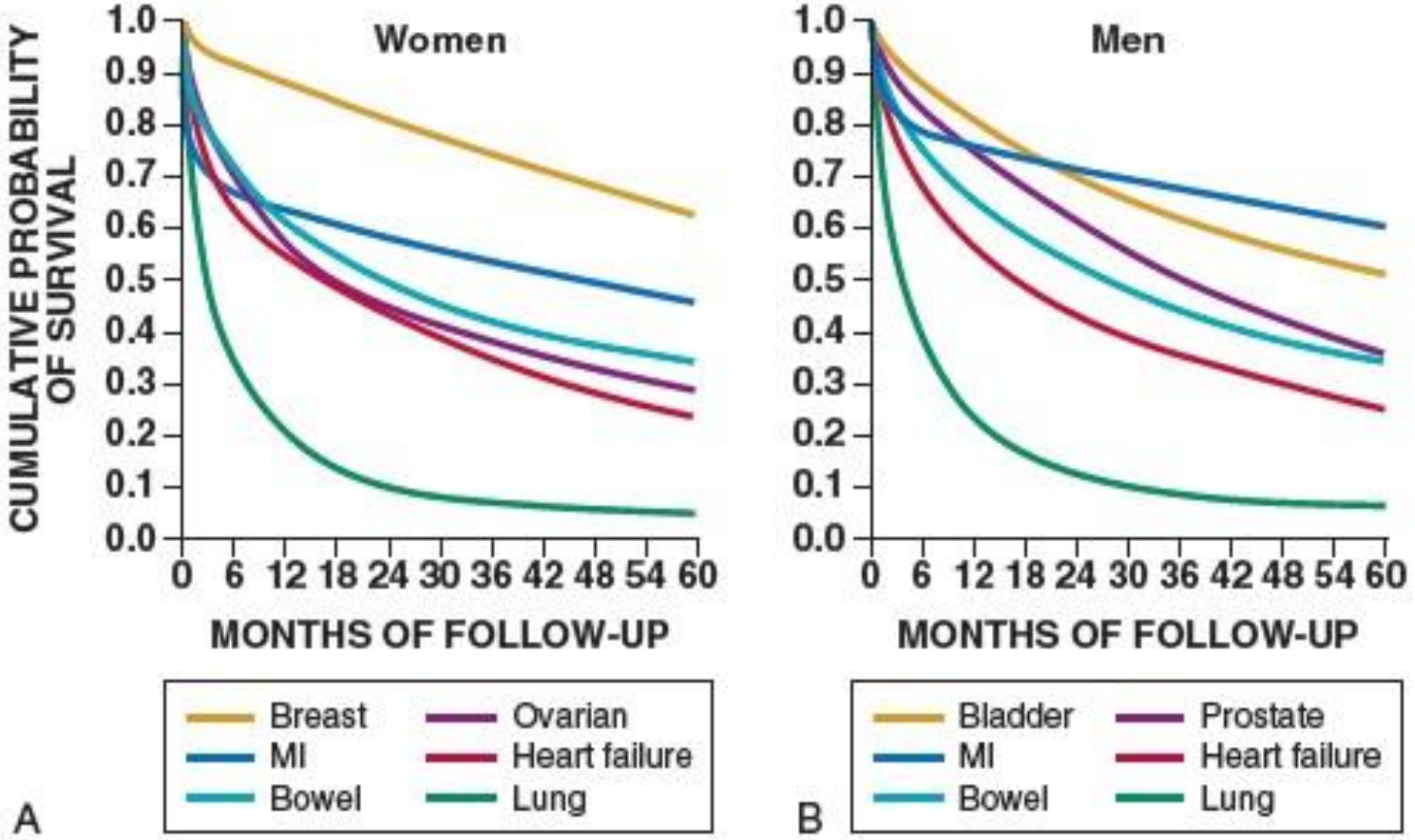


FIGURE 25.1 Survival in HF patients compared to cancer. Five-year survival following a first admission to any Scottish hospital in 1991 for heart failure, myocardial infarction (MI), and the four most common sites of cancer specific to men and women. (Modified from Stewart S, MacIntyre K, Hole DJ, et al. More 'malignant' than cancer? Five-year survival following a first admission for heart failure. Eur J Heart Fail 2001;3:315-22.)

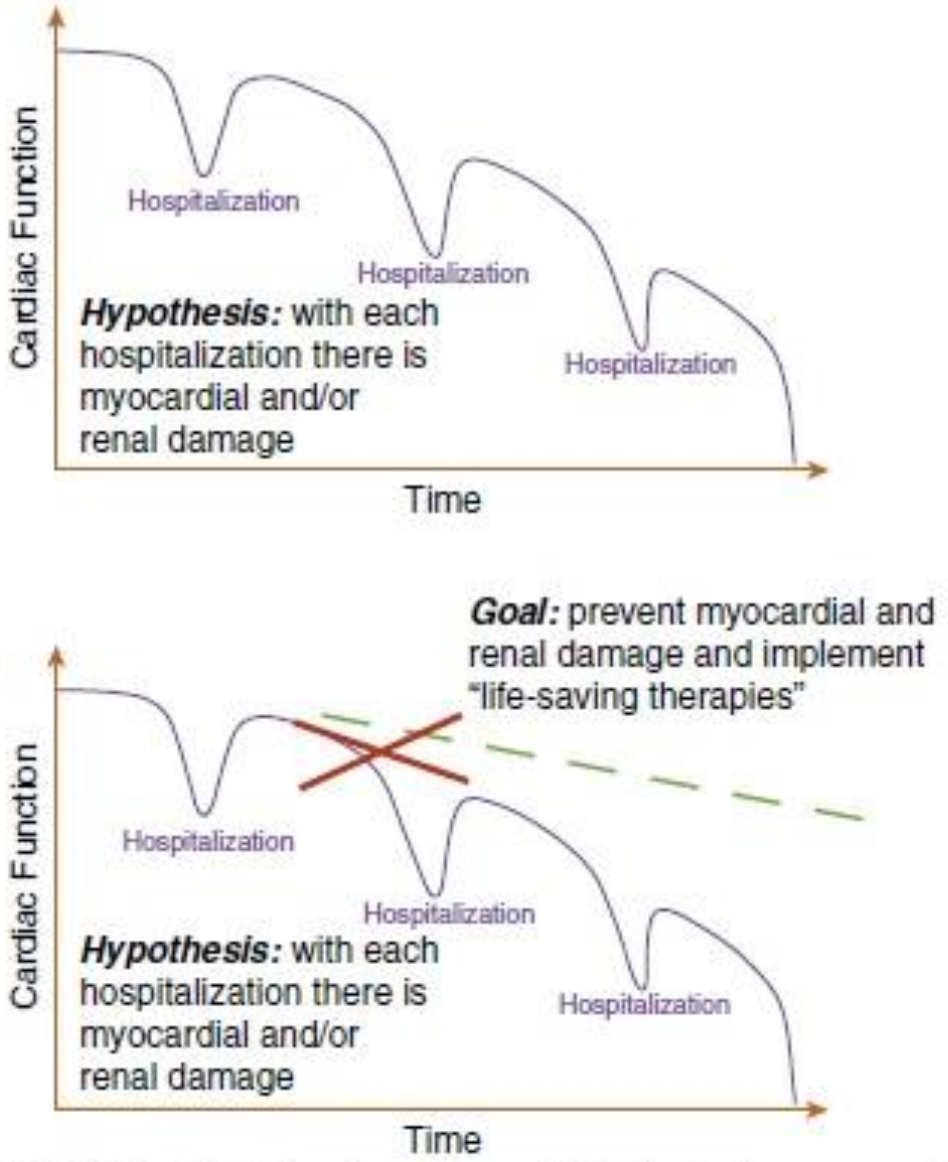


Fig. 36.6 (A) Contribution of each hospitalization to the progression of heart failure. (B) Potential impact of halting organ injury during an acute heart failure hospitalization. (Modified from Gheorghiade M, De Luca L, Fonarow GC, et al. Pathophysiologic targets in the early phase of acute heart failure syndromes. *Am J Cardiol.* 2005;96[6A]:11G–17G.)

TABLE 21.1 American College of Cardiology/American Heart Association (ACC/AHA) Stages of Heart Failure (HF) Compared to the New York Heart Association (NYHA) Functional Classification

ACC/AHA STAGES		NYHA FUNCTIONAL CLASSIFICATION	
A	At high risk for HF but without structural heart disease or symptoms of HF.	None	
B	Structural heart disease but without signs or symptoms of HF.	I	No limitation of physical activity. Ordinary physical activity does not cause symptoms of HF.
C	Structural heart disease with prior or current symptoms of HF.	I	No limitation of physical activity. Ordinary physical activity does not cause symptoms of HF.
		II	Slight limitation of physical activity. Comfortable at rest, but ordinary physical activity results in symptoms of HF.
		III	Marked limitation of physical activity. Comfortable at rest, but less than ordinary activity causes symptoms of HF.
D	Refractory HF requiring specialized interventions.	IV	Unable to carry on any physical activity without symptoms of HF, or symptoms of HF at rest.

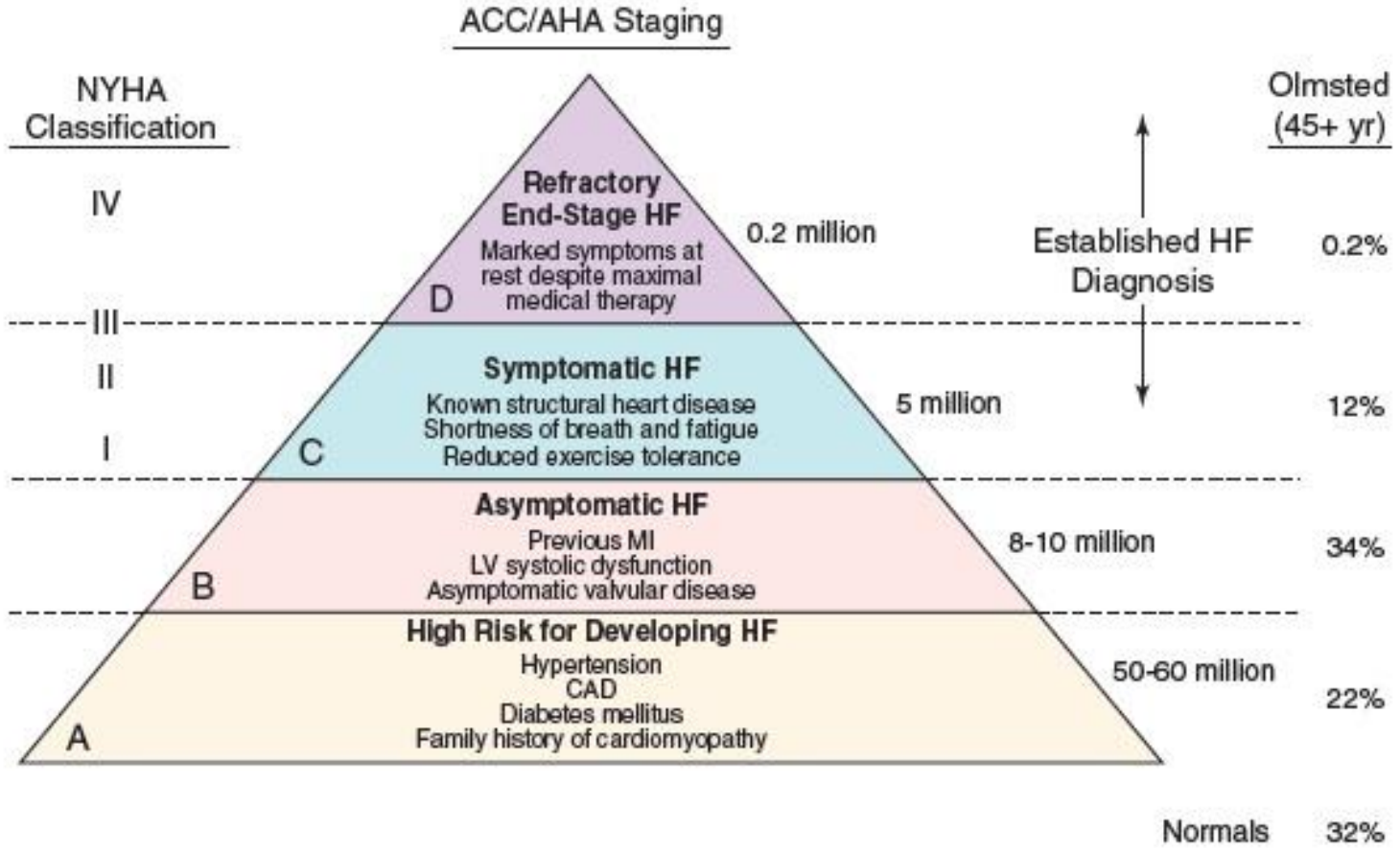


FIGURE 25.3 Stages of heart failure (HF) and prevalence of stages (data from the Olmstead County Epidemiology Study). Patients with stage A HF are at high risk for HF but do not have structural heart disease or symptoms of HF. This group includes patients with hypertension, diabetes, coronary artery disease (CAD), previous exposure to cardiotoxic drugs, or a family history of cardiomyopathy. Patients with stage B HF have structural heart disease but have no symptoms of HF. This group includes patients with left ventricular (LV) hypertrophy, previous myocardial infarction (MI), LV systolic dysfunction, or valvular heart disease, all of whom would be considered to have New York Heart Association (NYHA) Class I symptoms. Patients with stage C HF have known structural heart disease and current or previous symptoms of HF. Their symptoms may be classified as NYHA Class I, II, or III. Patients with stage D HF have refractory symptoms of HF at rest despite maximal medical therapy, are hospitalized, and require specialized interventions or hospice care. All such patients would be considered to have NYHA Class IV symptoms. AHA. American Heart Association; ACC, American College of Cardiology. (Modified from Ammar KA, Jacobsen SJ, Mahoney DW, et al. Prevalence and prognostic significance of heart failure stages: application of the American College of Cardiology/American Heart Association heart failure staging criteria in the community. Circulation 2007;115:1563-70.)

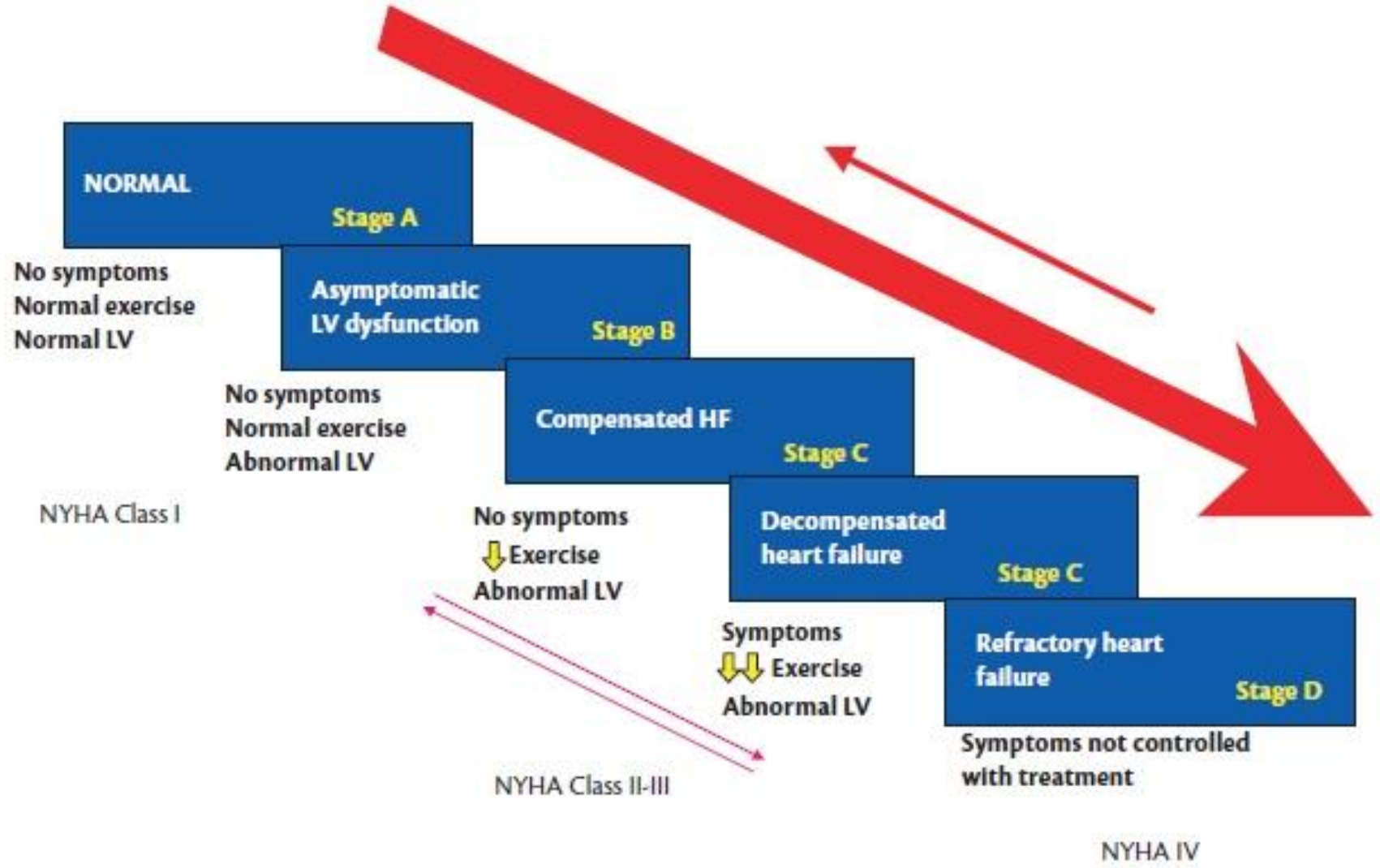


Fig. 1.2 Schematic depiction of the progression of heart failure using the ACC/AHA Guidelines for the Evaluation and Management of Heart Failure in the Adult. This adaptation superimposes NYHA functional class on the stages to emphasize that stages A and B represent asymptomatic conditions.

Adapted from Hunt SA, Baker DW, Chin MH, Cinquegrani MP, Feldmanmd AM, Francis GS, et al. ACC/AHA Guidelines for the Evaluation and Management of Chronic Heart Failure in the Adult: Executive Summary A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Revise the 1995 Guidelines for the Evaluation and Management of Heart Failure).

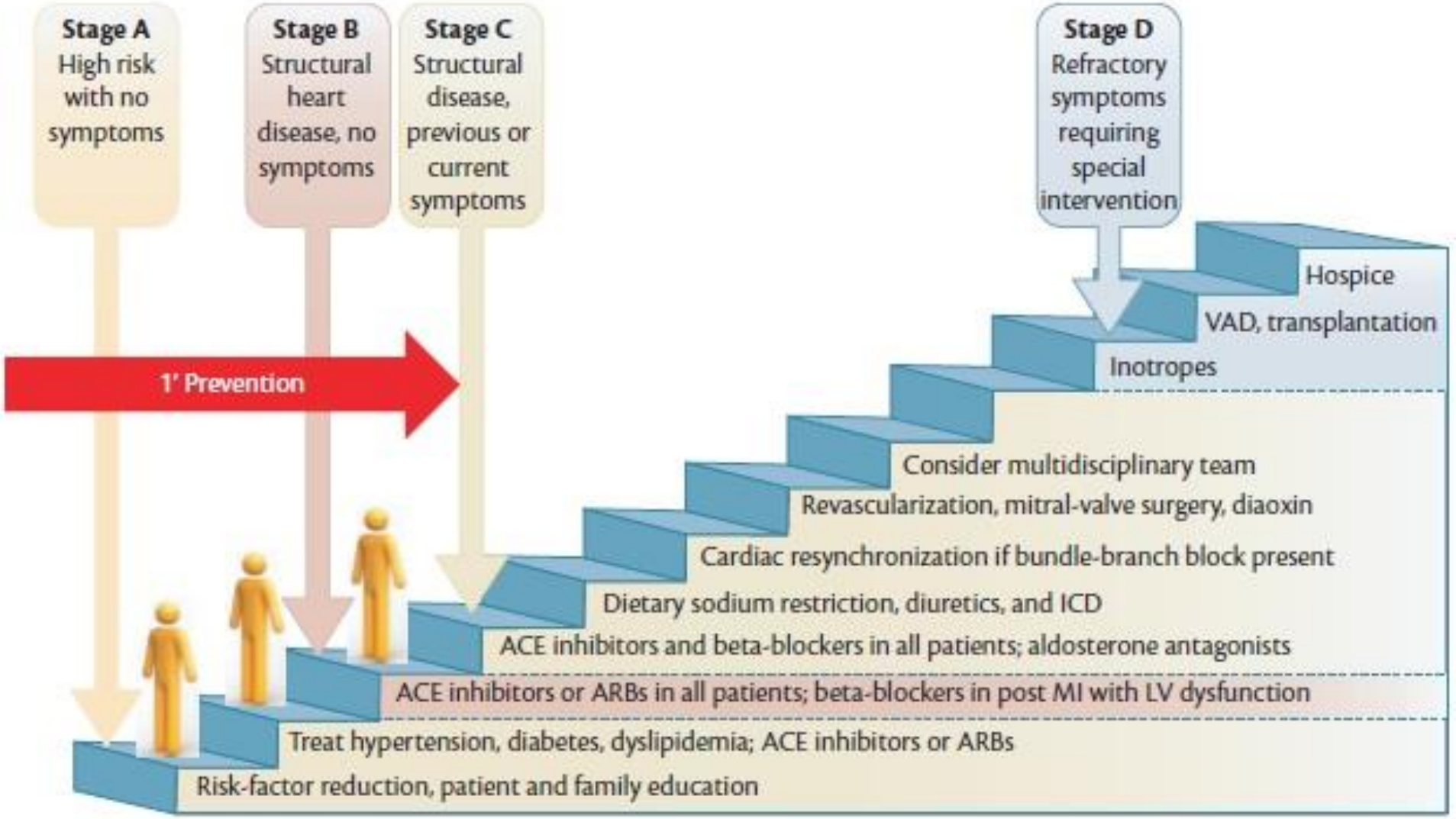
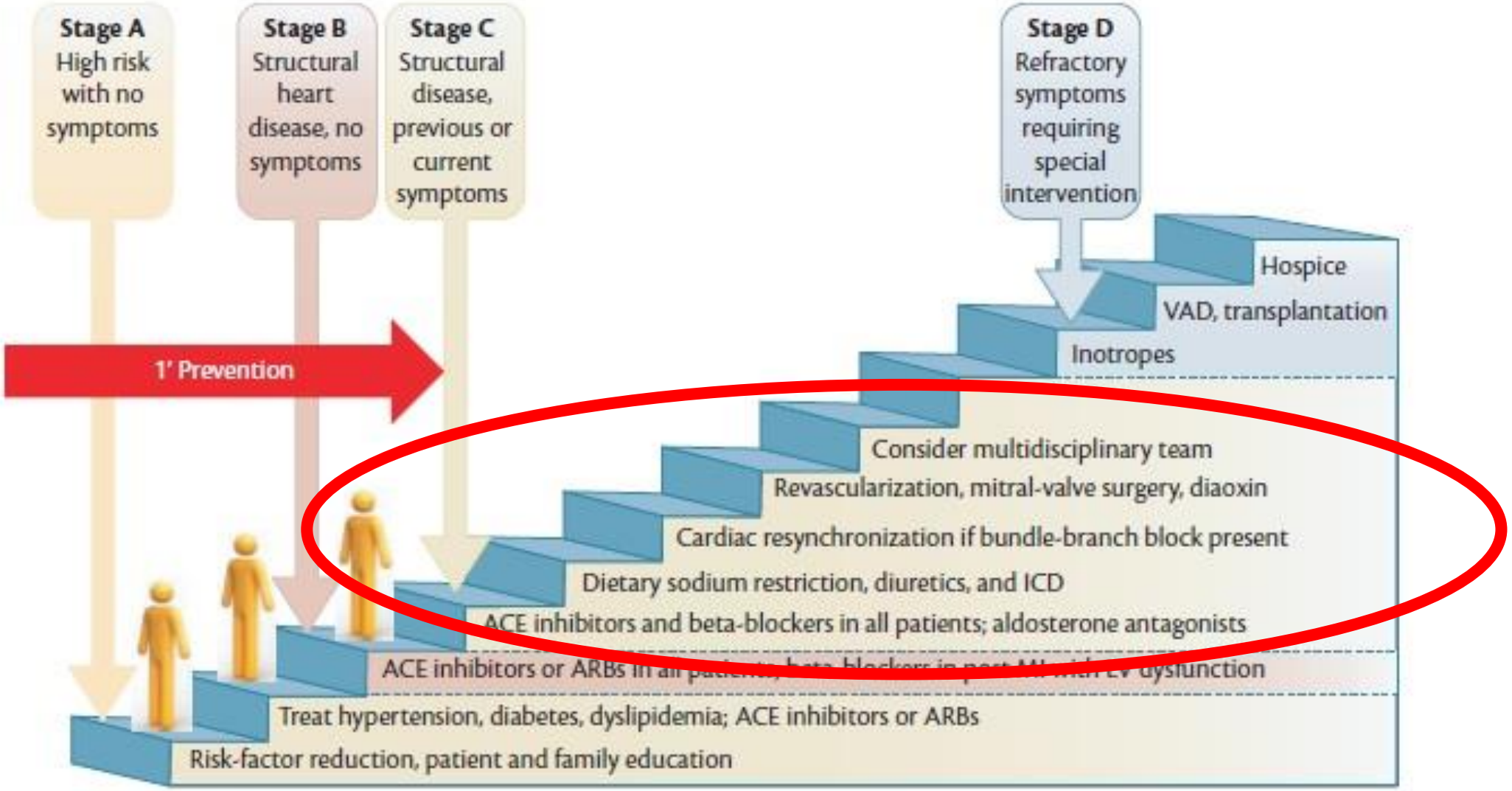


Fig. 1.3 Opportunities to prevent heart failure in AHA/ACC stages A and B.
Adapted from Jessup M, Brozena S. Heart failure. N Engl J Med 2003;348(20):2007–18.



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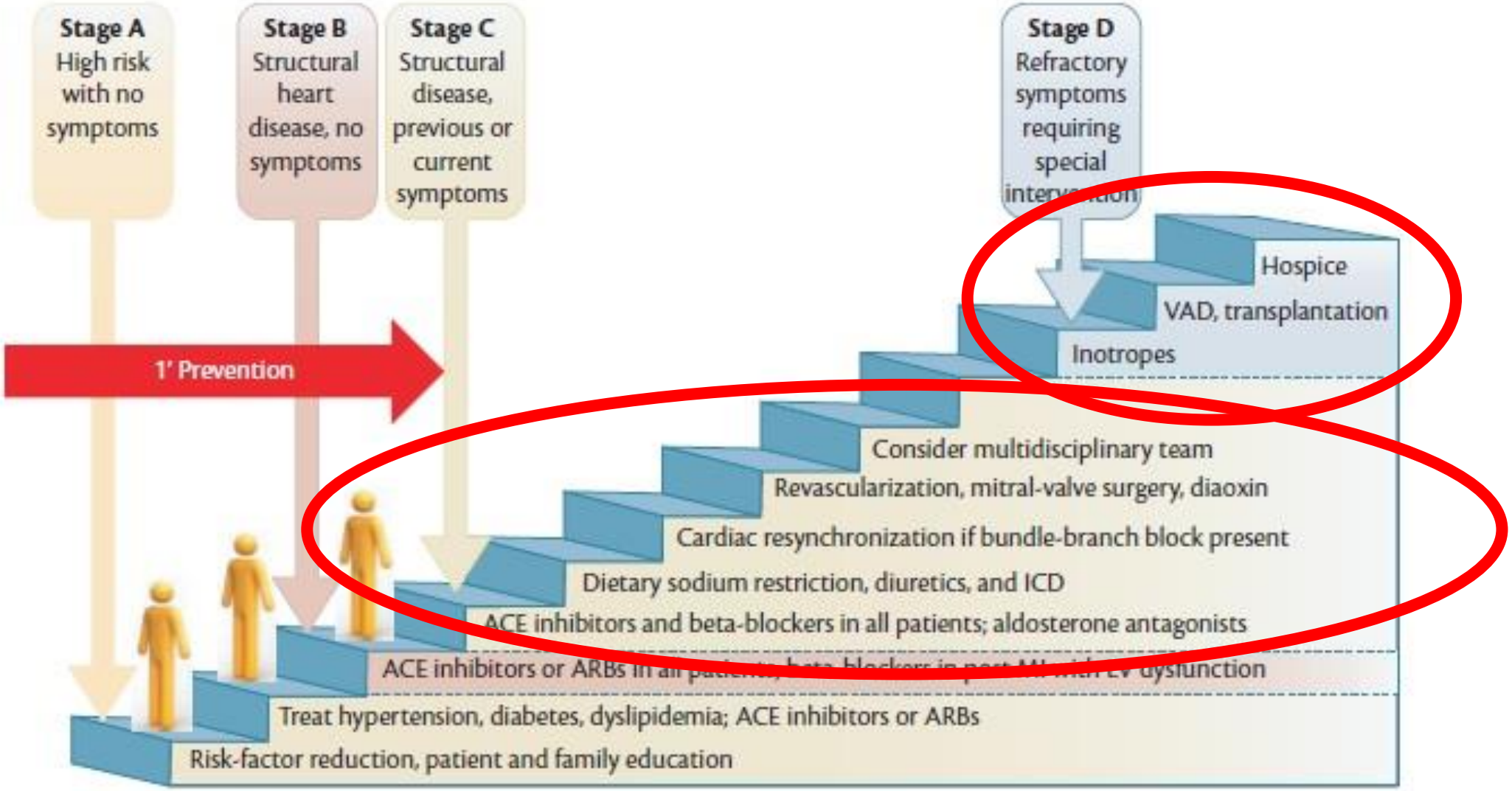

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Box 1.1 Clinical features useful for the identification of patients with stage D heart failure[55]

- Repeated (≥2) hospitalizations or Emergency Department visits for heart failure in the past year
- Progressive deterioration in renal function—e.g., rise in blood urea nitrogen (BUN) and creatinine
- Weight loss without other cause (e.g., cardiac cachexia)
- Intolerance to angiotensin converting enzyme (ACE) inhibitors due to hypotension and/or worsening renal function
- Intolerance to β-blockers due to worsening heart failure or hypotension
- Frequent systolic blood pressure <90 mmHg
- Persistent dyspnea with dressing or bathing requiring rest
- Inability to walk one block on the level ground due to dyspnea or fatigue
- Recent need to escalate diuretics to maintain volume status, often reaching daily furosemide equivalent dose >160 mg/day and/or use of supplemental metolazone therapy
- Progressive decline in serum sodium, usually to <133 mEq/L
- Frequent ICD shocks

55. Yancy CW, Jessup M, Bozkurt B. 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Circulation 2013;128(16):e240–327.

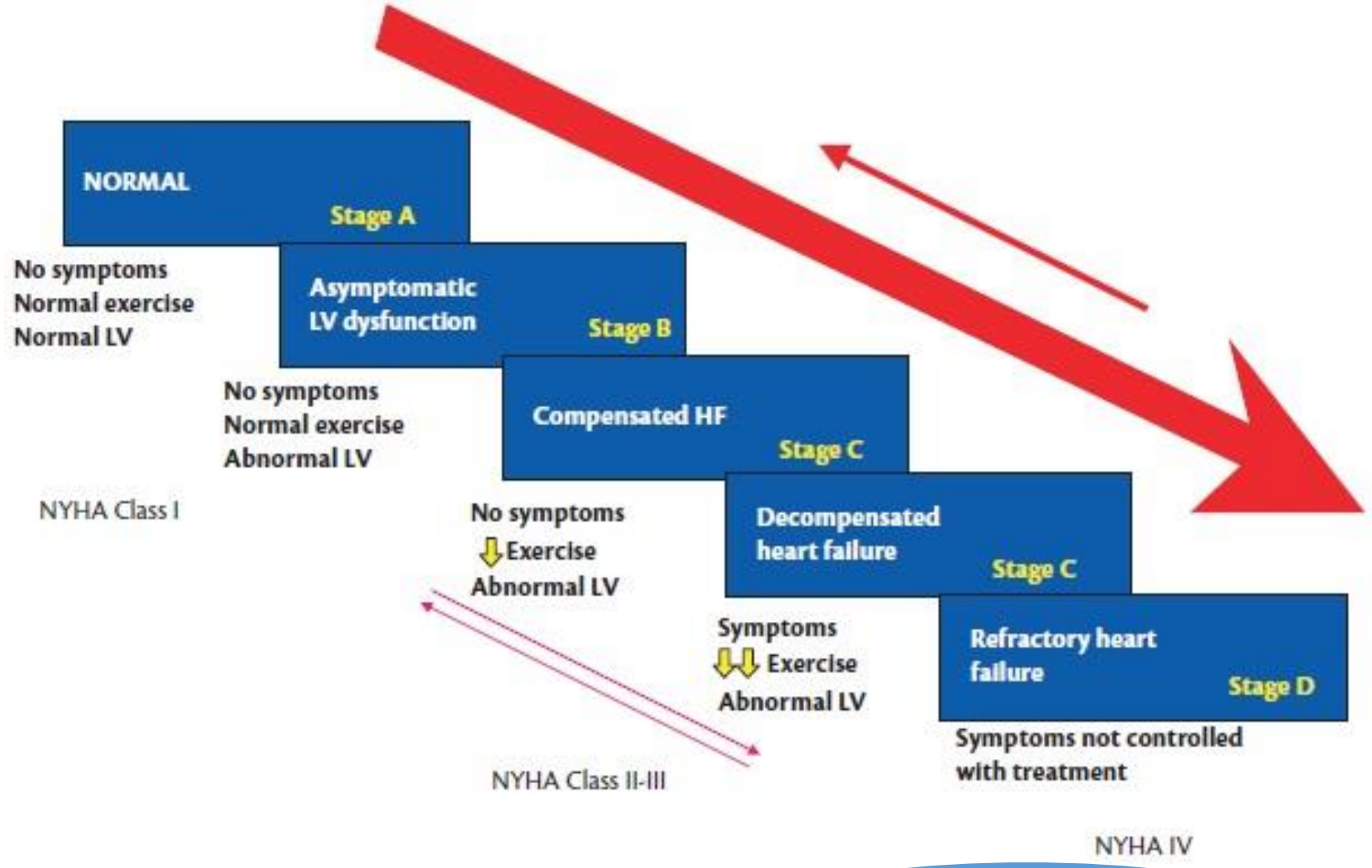

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Table 1.1 INTERMACS criteria which further discriminate patients with advanced heart failure beyond NYHA class

INTERMACS level	NYHA class	Shorthand
1	IV	"Crash and burn"
2	IV	"Sliding fast" on inotropes
3	IV	"Stable" on continuous inotropes
4	Ambulatory IV	Symptoms at rest
5	Ambulatory IV	"Housebound" Comfortable at rest, symptoms with minimal activity
6	IIIB	"Walking wounded" Meaningful activity limited
7	III	Advanced class III

Adapted from reference 115 (Stevenson LW, Pagani FD, Young JB, et al. INTERMACS profiles of advanced heart failure: the current picture. J Heart Lung Transplant 2009;28(6):535–41.)

Stages and Classes

- Functional class changes day to day but not stages
- Patients with NYHA I-II have better prognosis
- Beware of ‘true Class I’
- Identify stage D patients
- Preventing patients progress to stage C and D

Symptoms and signs

- History if of paramount importance
- Physical exam may not be ‘too accurate’ in making diagnosis (accuracy ~50-70%)
- Essential for monitoring day to day change in haemodynamic status

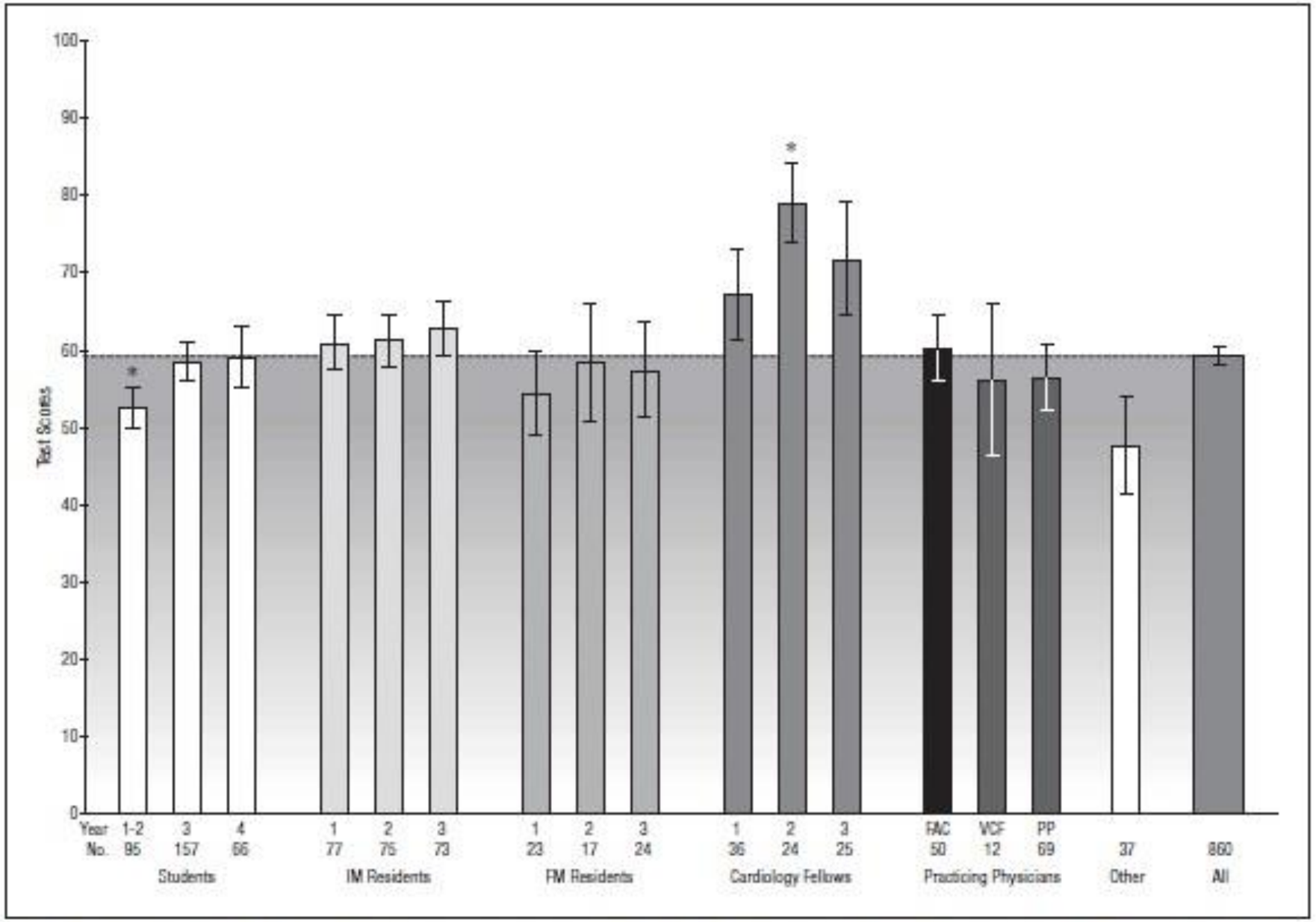


Figure 1. Mean test scores for cardiac examination competency by training level. The dotted horizontal line indicates the mean score for all participants (59.24). The mean score for full-time faculty (FAC) was not significantly different from that of medical students, internal medicine (IM) residents, family medicine (FM) residents, or other practicing physicians (volunteer clinical faculty [VCF] and private practice [PP]). Mean scores were improved in third- and fourth-year students compared with first- and second-year students ($P=.003$), but they did not improve thereafter. Asterisk indicates $P=.045$. Error bars represent 95% confidence intervals.

Competency in Cardiac Examination Skills in Medical Students, Trainees, Physicians, and FacultyA Multicenter Study
Jasminka M. Vukanovic-Criley, MD; Stuart Criley, MBA; Carole Marie Warde, MD; John R. Boker, PhD;
Lempira Guevara-Matheus, MD; Winthrop Hallowell Churchill, MD; William P. Nelson, MD; John Michael Criley, MD et al Arch Int Med 2006,166:610-616

Table 1. Criteria of CHF.*

MAJOR CRITERIA
Paroxysmal nocturnal dyspnea or orthopnea
Neck-vein distention
Rales
Cardiomegaly
Acute pulmonary edema
S_3 gallop
Increased venous pressure ->16 cm of water
Circulation time ≥25 sec
Hepatojugular reflux
MINOR CRITERIA
Ankle edema
Night cough
Dyspnea on exertion
Hepatomegaly
Pleural effusion
Vital capacity ↓ ⅓ from maximum
Tachycardia (rate of ≥120/min)
MAJOR OR MINOR CRITERION
Weight loss ≥4.5 kg in 5 days in response to treatment

*For establishing a definite diagnosis of congestive heart failure in this study, 2 major or 1 major & 2 minor criteria had to be present concurrently.

TABLE 28-8 Sensitivity, Specificity, and Predictive Accuracy of Symptoms and Signs for Diagnosing Heart Failure

SYMPTOMS OR SIGNS	SENSITIVITY (%)	SPECIFICITY (%)	PREDICTIVE ACCURACY (%)
Exertional dyspnea	66	52	23
Orthopnea	21	81	2
Paroxysmal	33	76	26
History of edema	23	80	22
Resting heart rate	7	99	6
Rales	13	91	21
Third heart sound	31	95	61
Jugular venous distention	10	97	2
Edema (on examination)	10	93	3

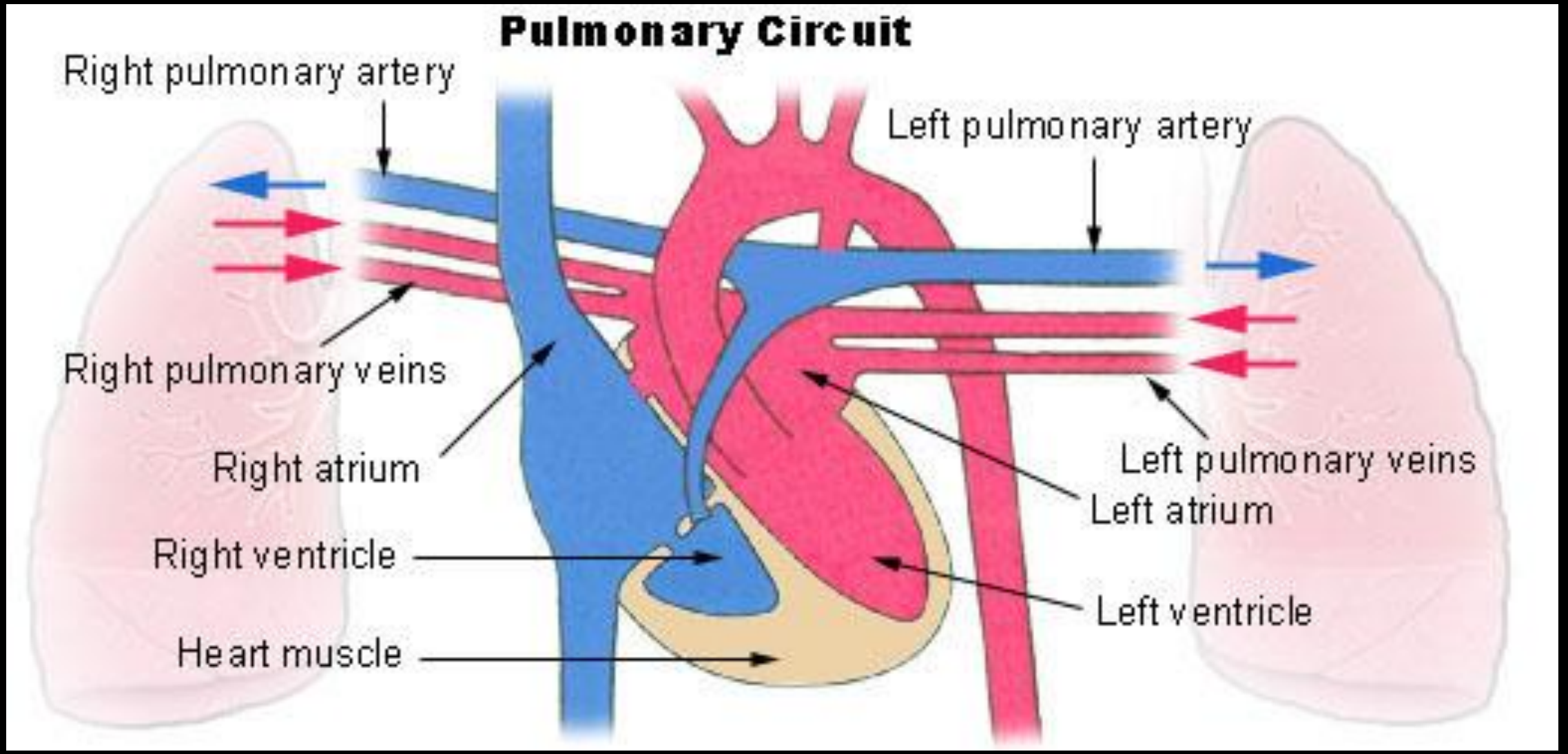
From Harlan WR, Oberman A, Grimm R, et al: Chronic congestive heart failure in coronary artery disease: clinical criteria. Ann Intern Med 86:133–138, 1977.

TABLE 28-7 Utility of Components of History and Physical Examination in Detecting Pulmonary Capillary Wedge Pressure >22 mm Hg

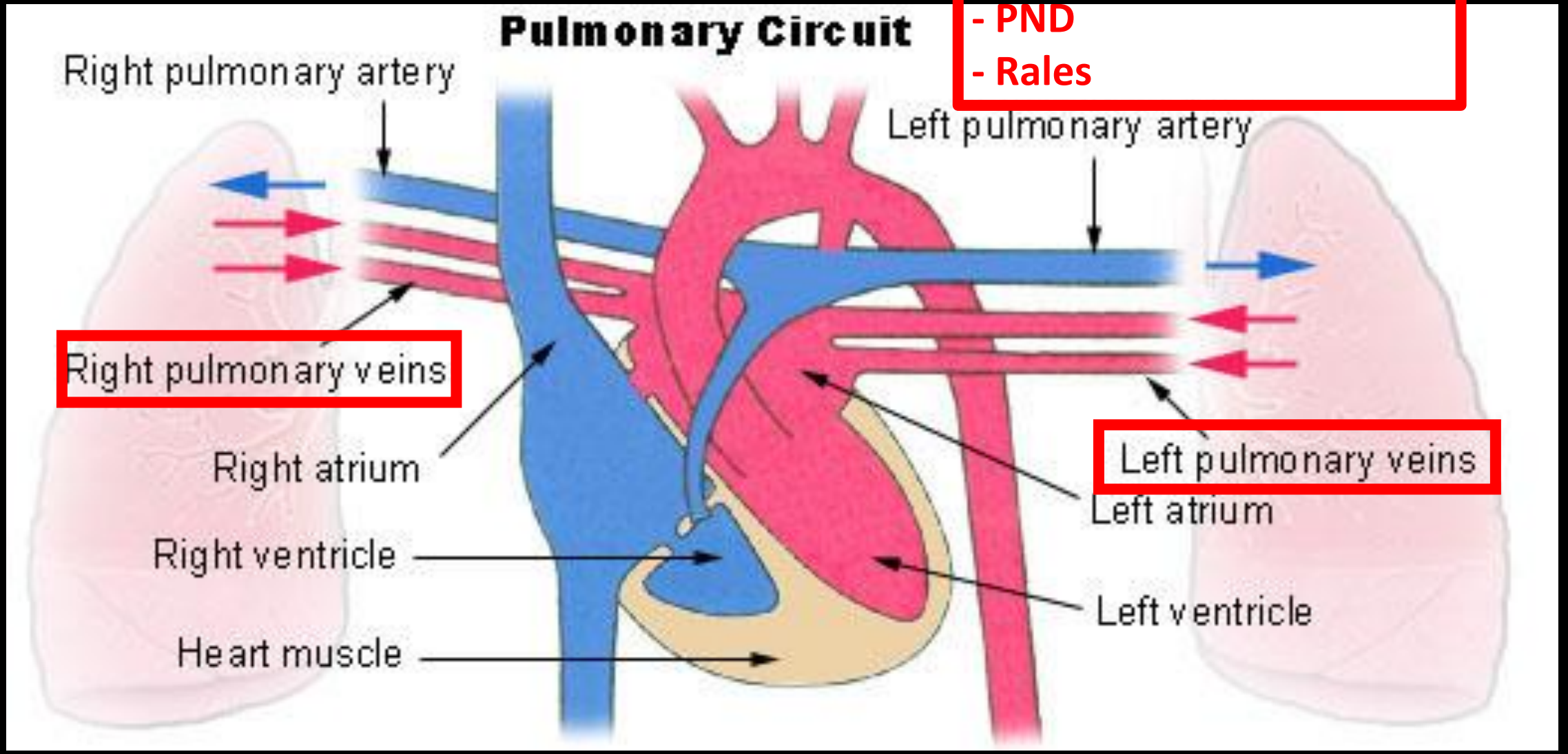
			Predictive Value		*Likelihood Ratio*	
FINDING	**SENSITIVITY**	**SPECIFICITY**	**POSITIVE**	**NEGATIVE**	**POSITIVE**	**NEGATIVE**
Rales (≥⅓ lung field)	15	89	69	38	1.32	1.04
S_3	62	32	61	33	0.92	0.85
Ascites (≥ moderate)	21	92	81	40	2.44	1.15
Edema (≥2+)	41	66	67	40	1.20	1.11
Orthopnea (≥2 pillow)	86	25	66	51	1.15	1.80
Hepatomegaly (>4 fb)	15	93	78	39	2.13	1.09
Hepatojugular reflux	83	27	65	49	1.13	1.54
JVP ≥12 mm Hg	65	64	75	52	1.79	1.82
JVP <8 mm Hg	4.3	81	28	33	0.23	0.85

fb, Fingerbreadths; *JVP*, jugular venous pressure.

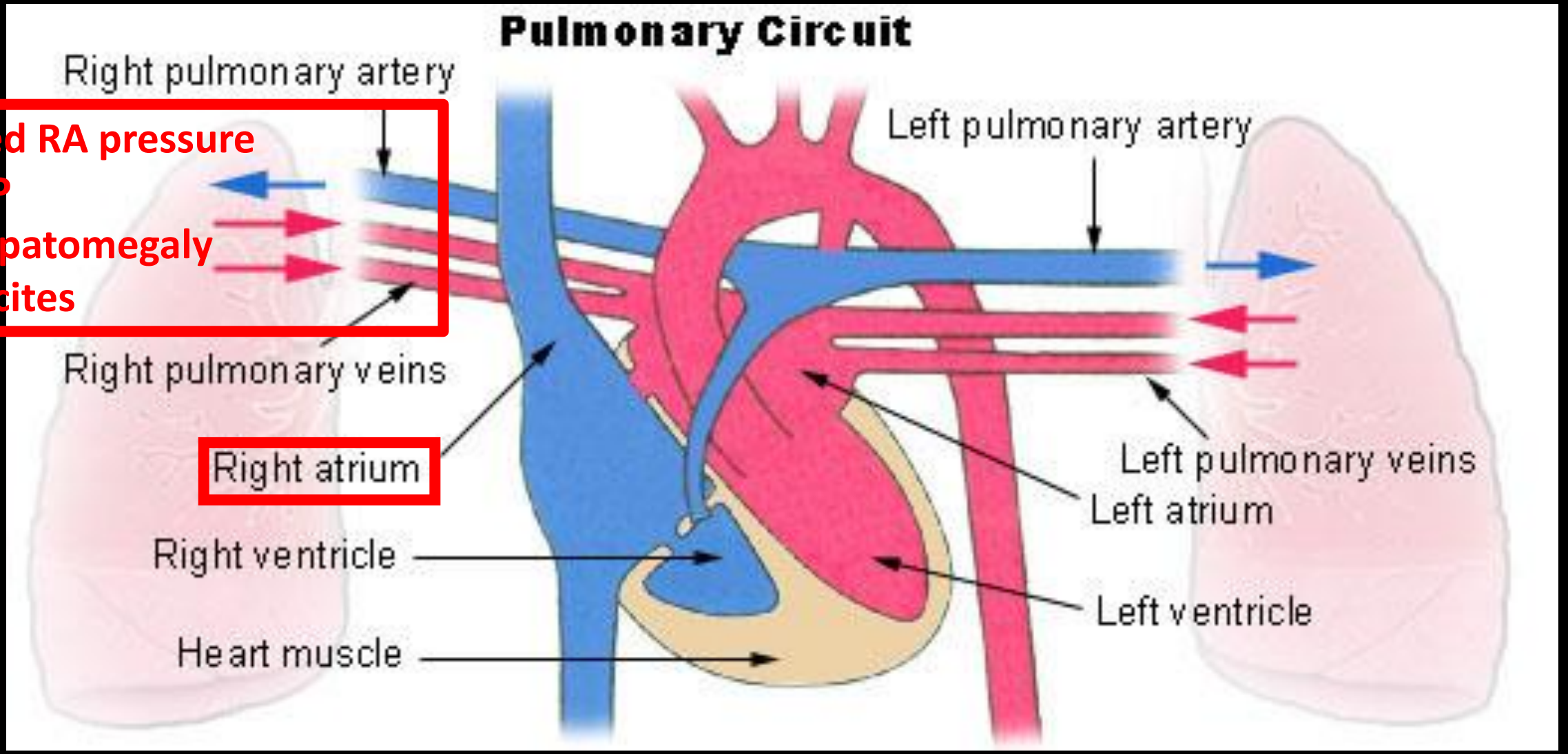
Modified from Drazner MH, Hellkamp AS, Leier CV, et al: Value of clinician assessment of hemodynamics in advanced heart failure: the escape trial. Circ Heart Fail 1:170–177, 2008.


Pulmonary Circuit
Right pulmonary artery
Left pulmonary artery
Right pulmonary veins
Right atrium
Left pulmonary veins
Left atrium
Right ventricle
Left ventricle
Heart muscle

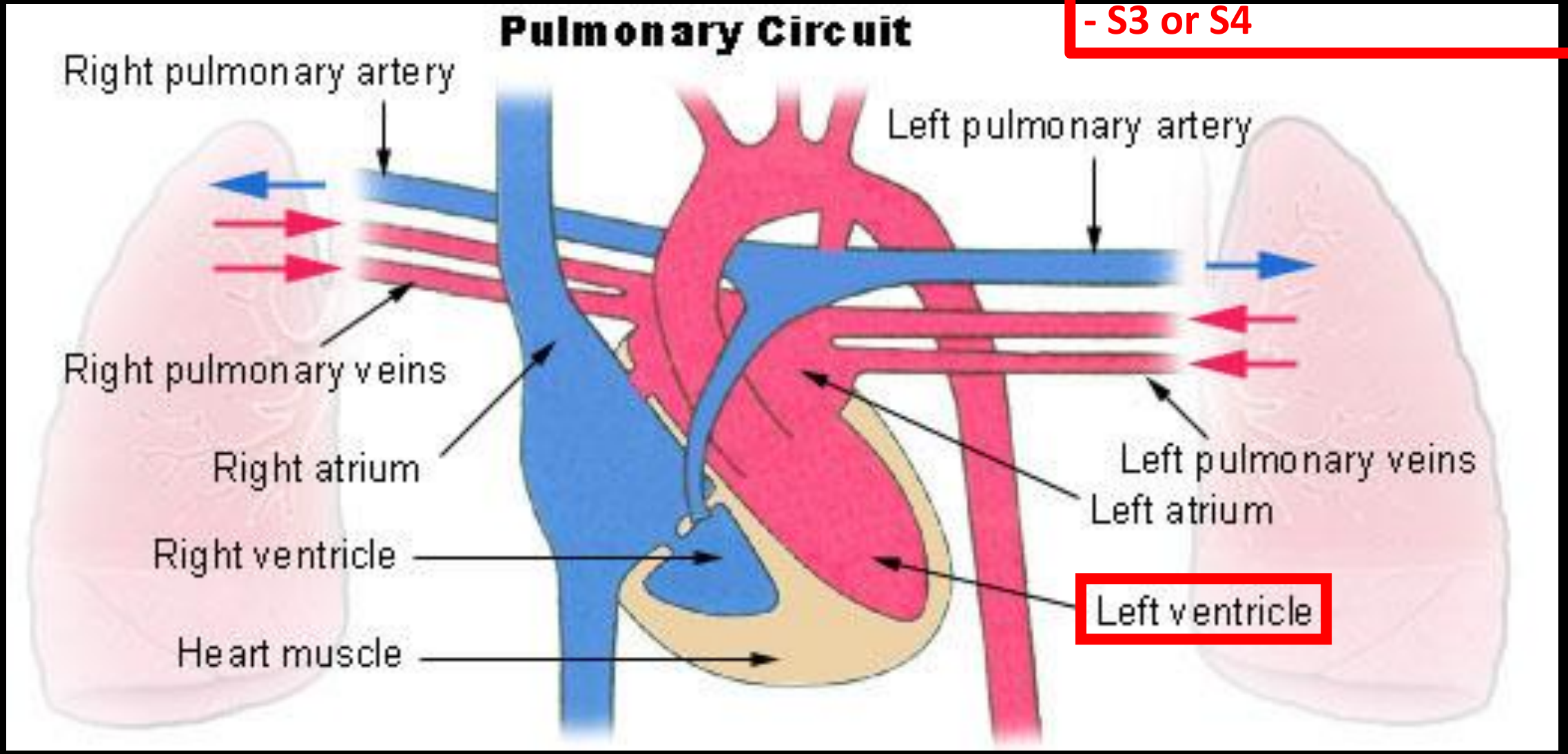
Raised PV pressure
- orthopnea
- PND
- Rales



Raised RA pressure
- **JVP**
- **Hepatomegaly**
- **Ascites**



Raised LVEDP/Vol overload
- S3 or S4



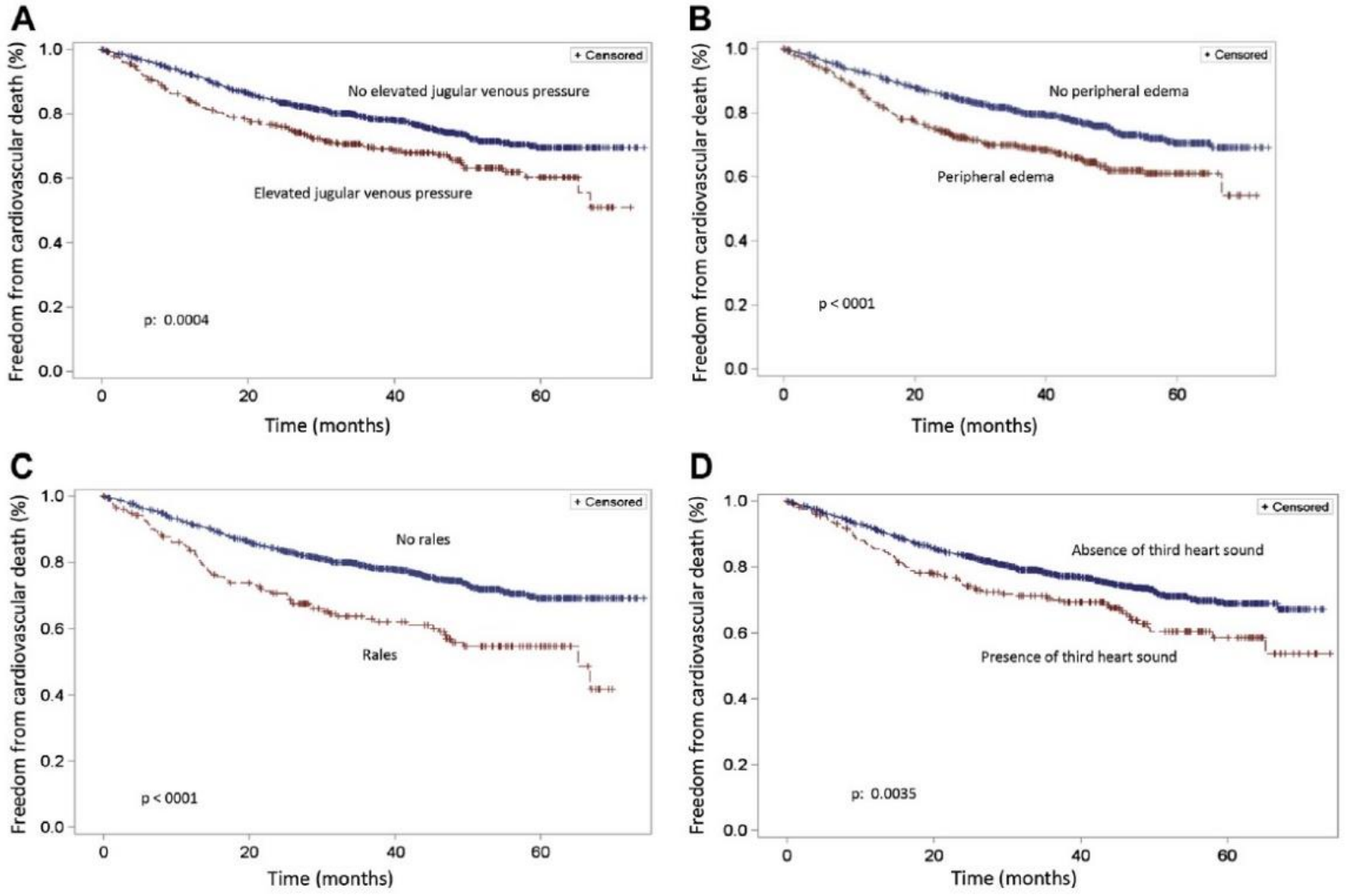
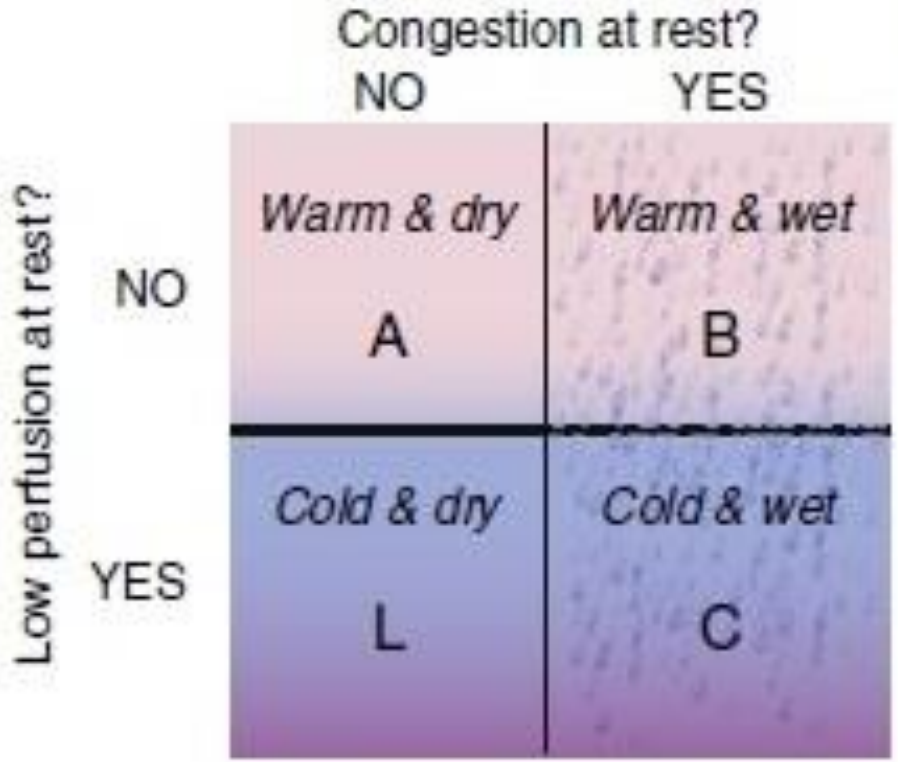


Figure 1 **Kaplan-Meier Estimates of Death From Cardiovascular Causes (Primary Outcome)**

Kaplan-Meier analysis of event-free survival for the primary endpoint (cardiovascular mortality) according to the presence **(red)** or absence **(blue)** of elevated jugular venous pressure **(A)**, peripheral edema **(B)**, rales **(C)**, and third heart sound **(D)**. Comparisons were performed by log-rank tests.

TWO-MINUTE ASSESSMENT OF HEMODYNAMIC PROFILE



Evidence for congestion

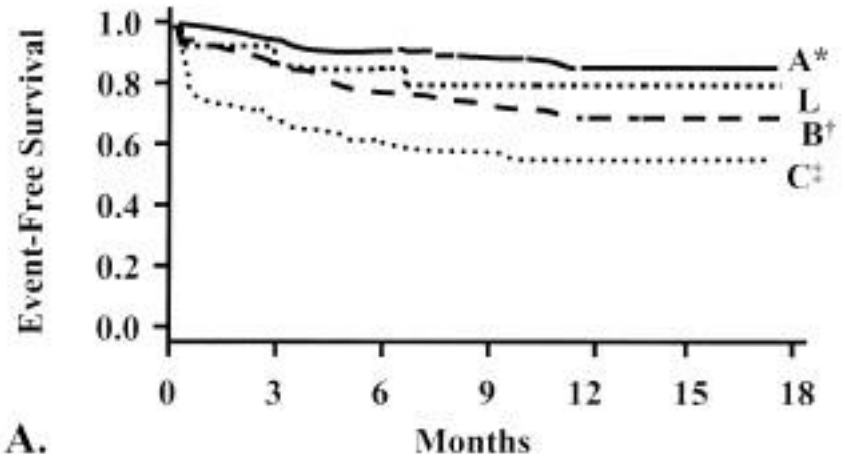
Orthopnea
Elevated jugular venous pressure
Bendopnea

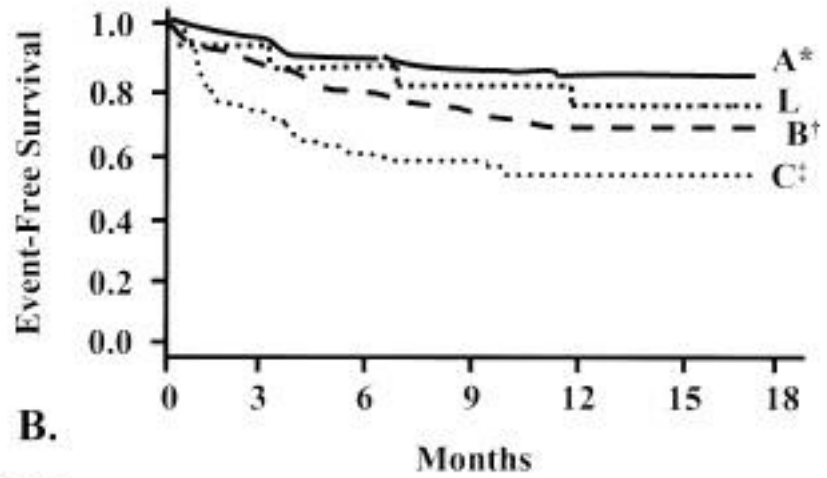
Rales (rarely)
New S3
Hepatomegaly
Ascites
Edema (more common in older patients)
Valsalva square wave

Evidence for low perfusion

Narrow auscultated pulse pressure
Cool extremities
May be sleepy, obtunded
Suspect from ACEI/ARB hypotension
Progressive oliguria

Norhia JACC 2003





NO. AT RISK							
Profile A	123	117	111	106	101	91	75
Profile B	222	193	167	153	140	122	106
Profile C	91	49	49	45	43	39	30
Profile L	16	15	15	14	13	13	9

Figure 2. Kaplan-Meier survival curves according to the clinical profiles. The end points were one-year mortality **(Panel A)** and one-year mortality plus urgent transplantation **(Panel B)**. In both **panels**, profile C conferred the worst outcomes, followed by profile B, which was worse than profile A. Profile L had too few patients for meaningful statistical analysis. **Panel A:** *$p = 0.002$ for profile A versus profile B, †$p = 0.008$ for profile B versus profile C, ‡$p < 0.001$ for profile A versus profile C. **Panel B:** *$p = 0.002$ for profile A versus profile B, †$p = 0.005$ for profile B versus profile C, ‡$p < 0.001$ for profile A versus profile C.

Norhia JACC 2003

Is our assessment of **‘congestion’** accurate?
And what do they mean?

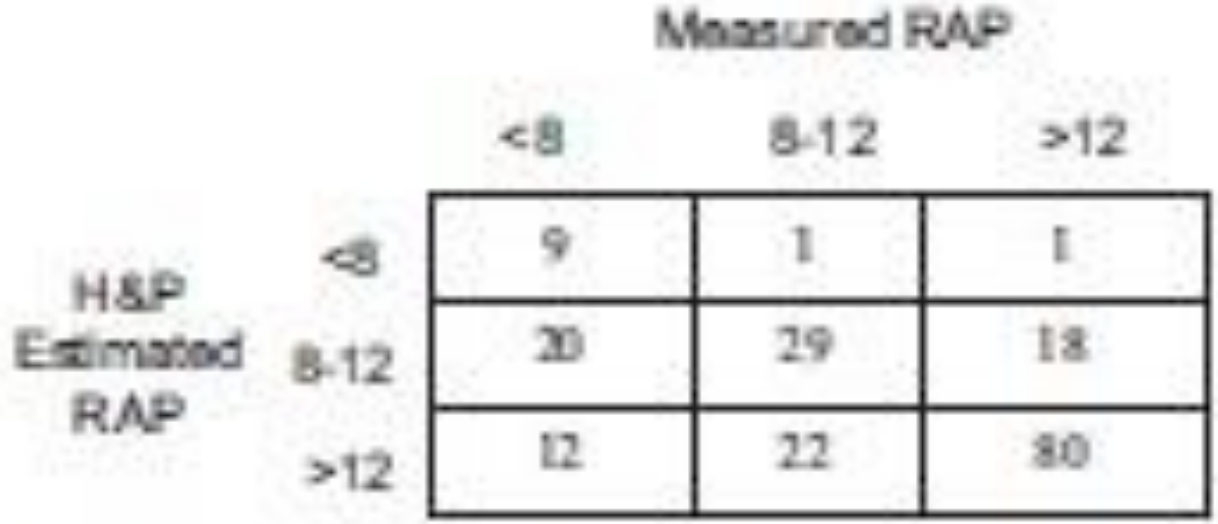


Figure 1. Number of patients stratified by their estimated RAP by H&P examination (vertically) and their measured RAP by right heart catheterization (horizontally).

Drazner Circ HF 2003

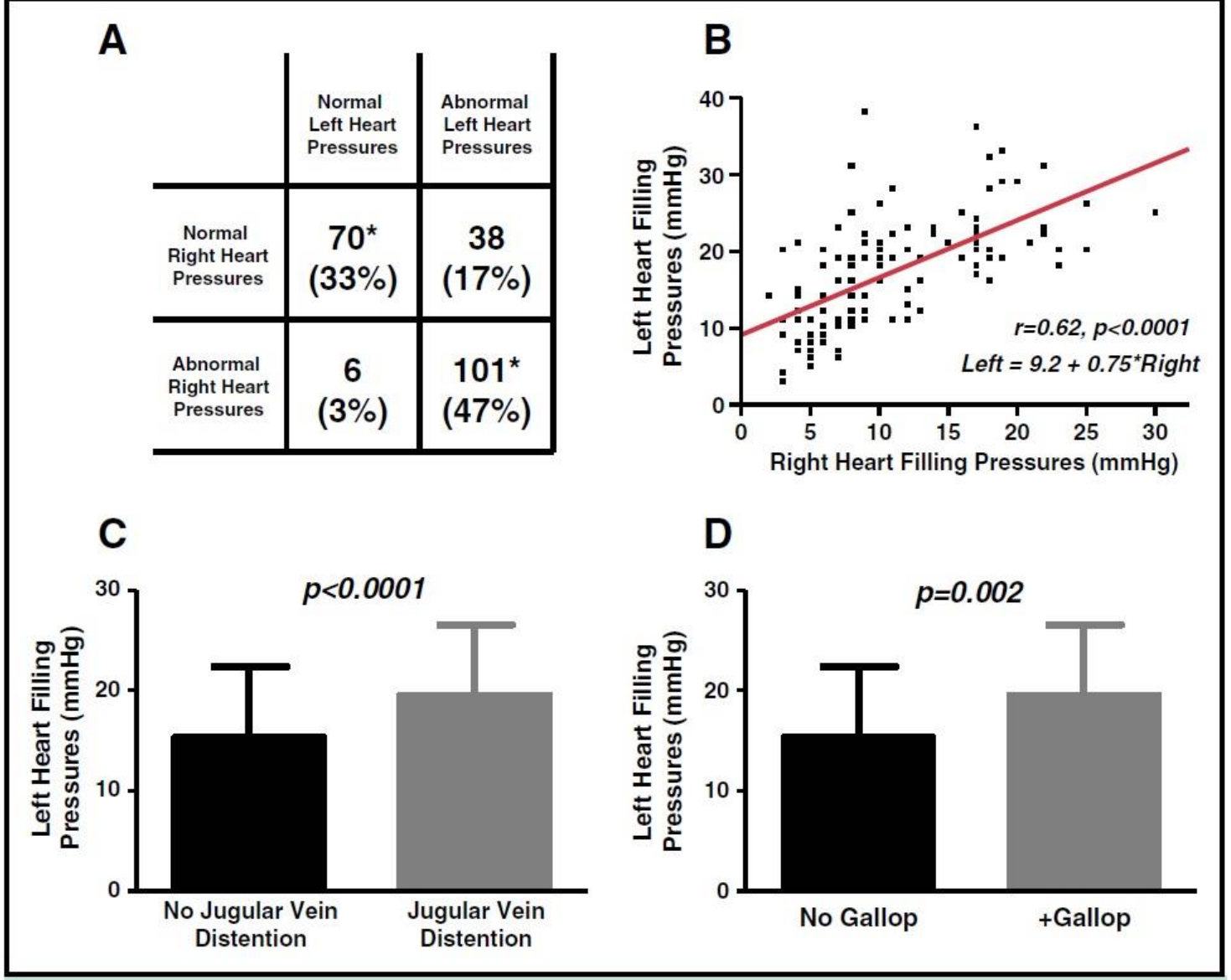
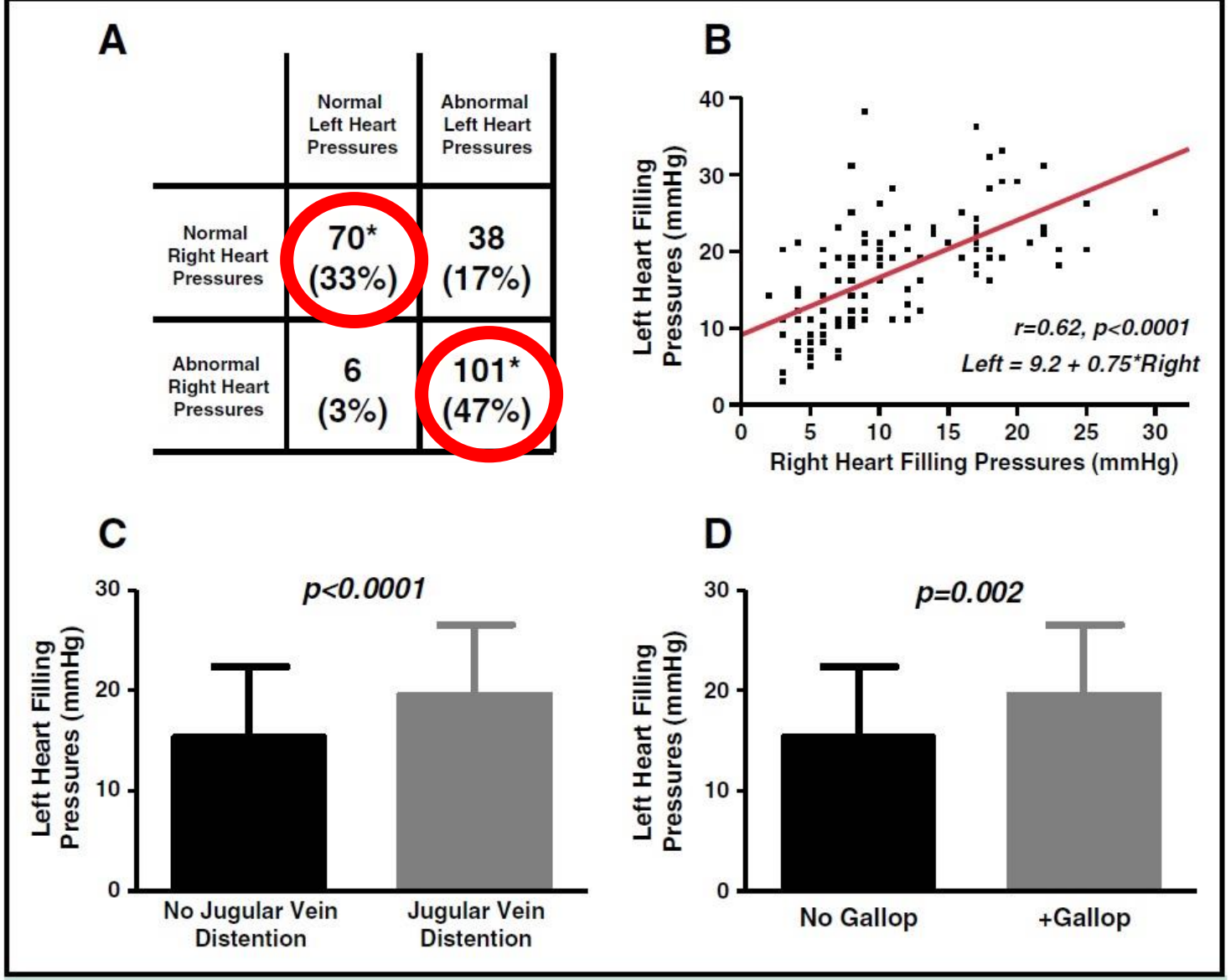


Figure (**A**) Left- and right-sided filling pressures determined at catheterization were concordantly normal or abnormal (asterisks) 80% of the time, and (**B**) were significantly correlated with one another. (**C, D**) Left heart pressures were significantly higher in patients deemed to have jugular venous distention or with gallop sounds (S3 and/or S4).

Bedside Assessment of Cardiac Hemodynamics: The Impact of Noninvasive Testing and Examiner Experience
Borlaug 2011 AJM



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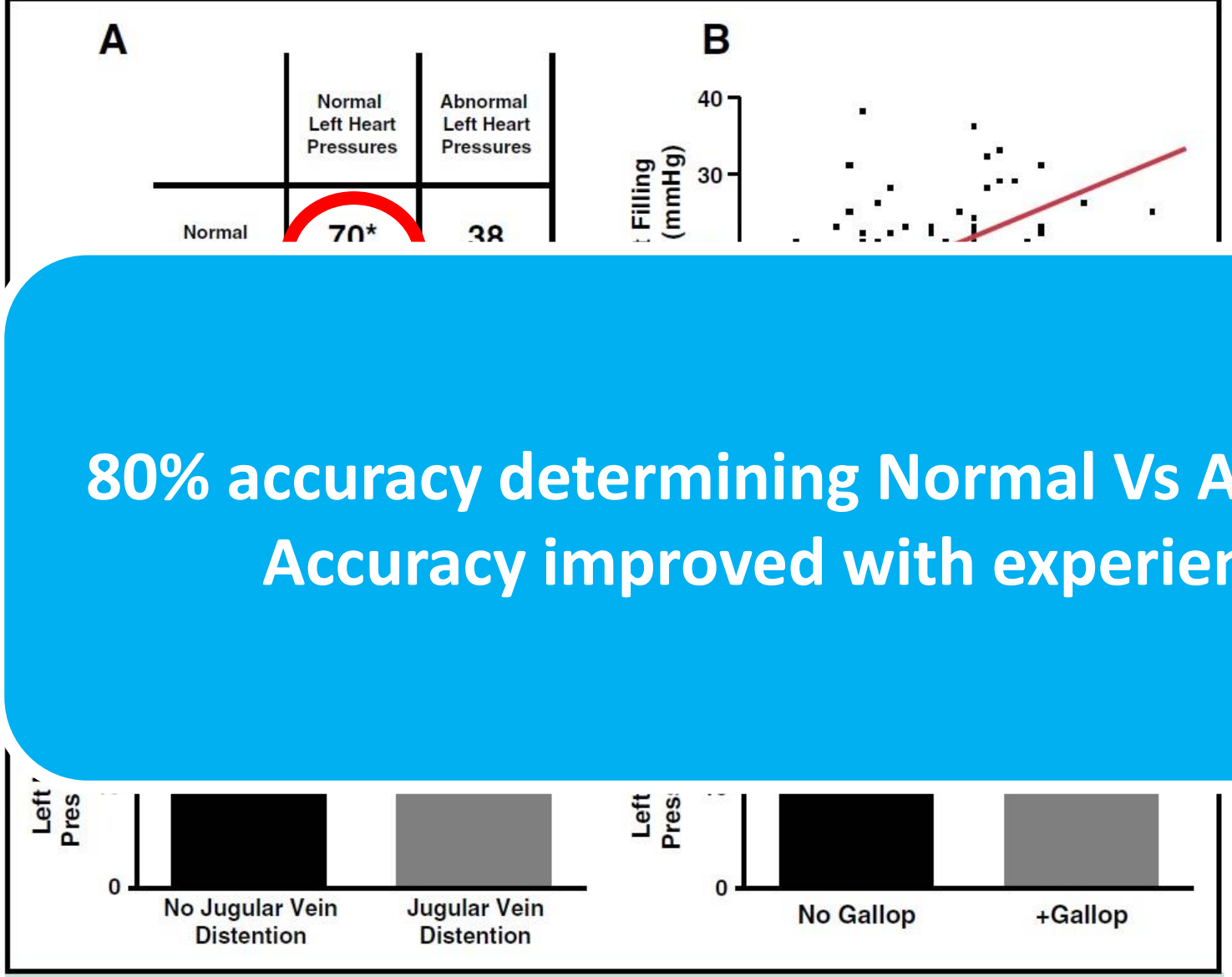


80% accuracy determining Normal Vs Abnormal
Accuracy improved with experience

Figure (**A**) Left- and right-sided filling pressures determined at catheterization were concordantly normal or abnormal (asterisks) 80% of the time, and (**B**) were significantly correlated with one another. (**C, D**) Left heart pressures were significantly higher in patients deemed to have jugular venous distention or with gallop sounds (S3 and/or S4).

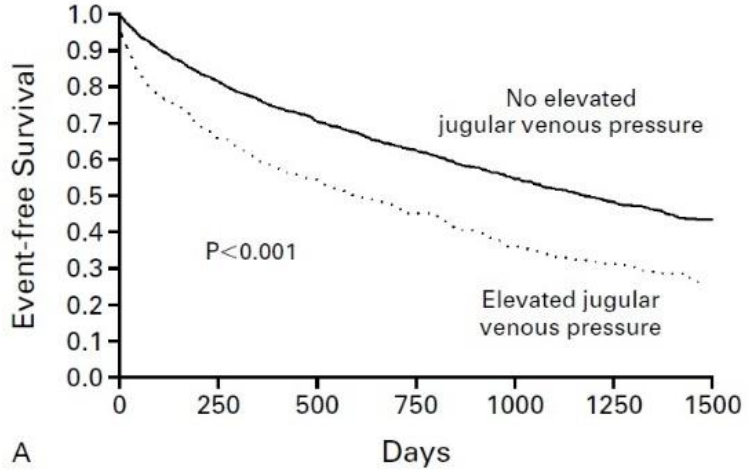
Bedside Assessment of Cardiac Hemodynamics: The Impact of Noninvasive Testing and Examiner Experience
Borlaug 2011 AJM

Table 3. Test Characteristics for Computerized Heart Sound Detection*

		LVEDP >15 mm Hg	LVEF <50%	BNP >100 pg/mL
S_3				
	Sensitivity	41 (26-58)	52 (31-73)	32 (20-46)
	Specificity	92 (80-98)	87 (76-94)	92 (78-98)
	Positive predictive value	81 (58-95)	57 (34-78)	85 (62-97)
	Negative predictive value	65 (53-76)	84 (73-92)	48 (36-60)
	Accuracy	69 (58-78)	78 (68-86)	56 (45-67)
S_4				
	Sensitivity	46 (31-63)	43 (23-66)	40 (26-54)
	Specificity	80 (66-90)	72 (59-82)	78 (61-90)
	Positive predictive value	66 (46-82)	34 (18-54)	72 (52-87)
	Negative predictive value	64 (51-76)	79 (66-88)	47 (34-60)
	Accuracy	64 (54-74)	64 (54-74)	55 (44-66)
S_3 and/or S_4				
	Sensitivity	68 (52-82)	74 (52-90)	57 (42-70)
	Specificity	73 (59-85)	64 (52-76)	72 (55-86)
	Positive predictive value	68 (52-82)	42 (26-58)	75 (59-87)
	Negative predictive value	73 (59-85)	88 (75-95)	53 (38-67)
	Accuracy	71 (61-80)	67 (56-76)	63 (52-73)

Abbreviations: BNP, B-type natriuretic peptide; LVEDP, left ventricular end-diastolic pressure; LVEF, left ventricular ejection fraction.

*Data are presented as percentage (95% confidence interval).



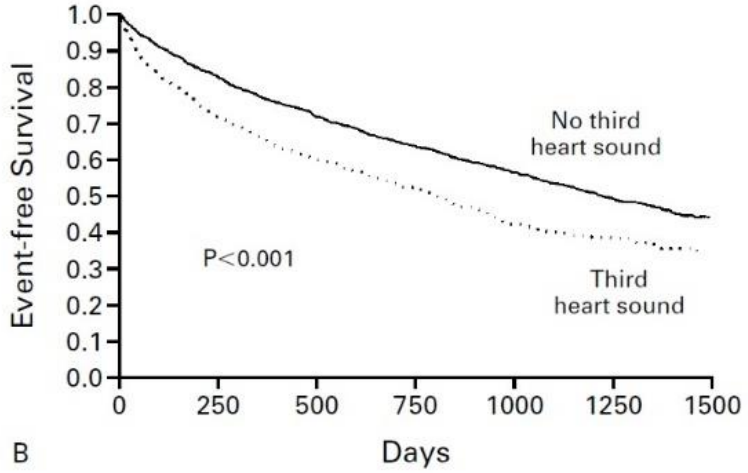
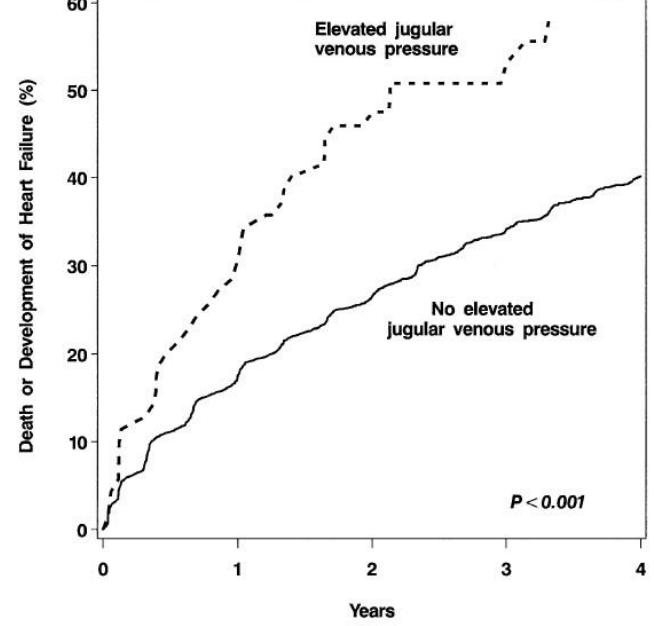


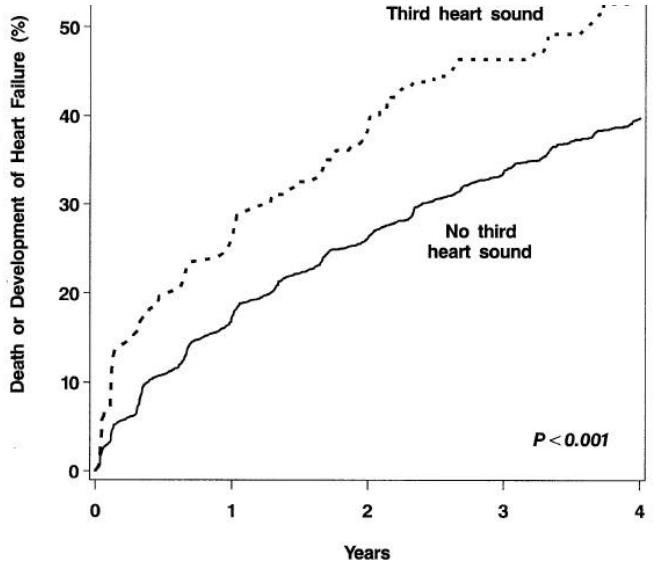
Figure 1. Kaplan–Meier Analysis of Event-free Survival According to the Presence or Absence of Elevated Jugular Venous Pressure (Panel A) and a Third Heart Sound (Panel B).

The end point was a composite of death or hospitalization for heart failure. In Panel A, the 280 patients with elevated jugular venous pressure were significantly more likely than the 2199 patients without elevated jugular venous pressure to reach the composite end point (P<0.001 by the log-rank test). In Panel B, the 597 patients with a third heart sound were significantly more likely than the 1882 patients without a third heart sound to reach the composite end point (P<0.001 by the log-rank test).



No. at risk

Elevated pressure	70	49	34	21	6
No elevated pressure	4032	3322	2442	1359	567



No. at risk

Third heart sound	209	154	113	65	35
No third heart sound	3893	3217	2362	1315	539

azner NEJM 2001
azner AJM 2003

Does JVP correlate with LVEDP?

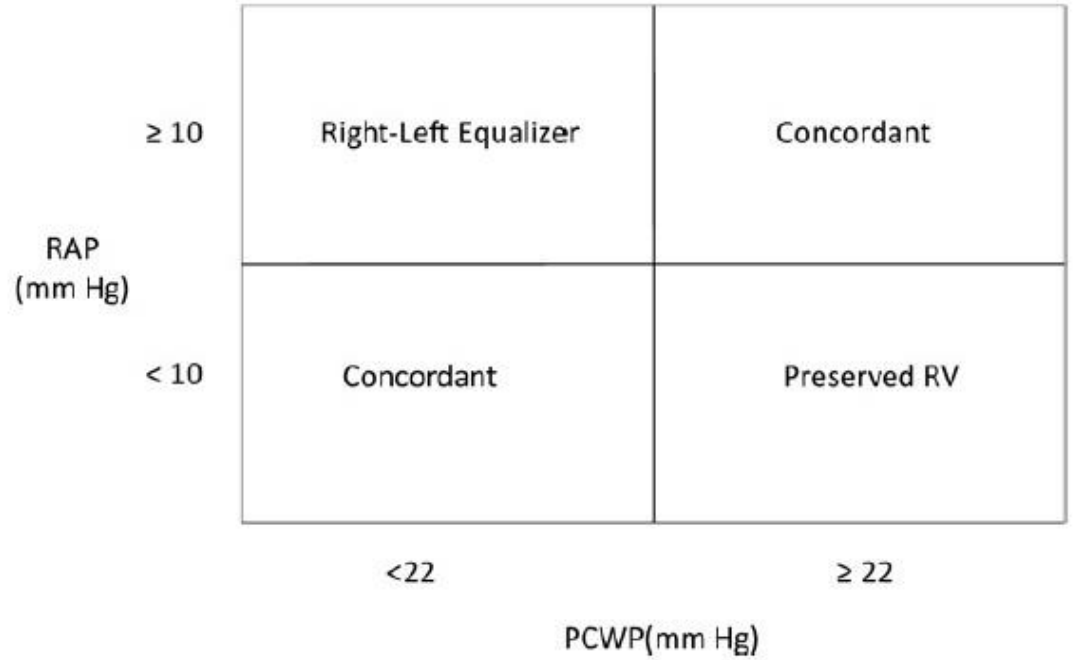


Figure 1 Hemodynamics profiles characterized by right atrial pressure (RAP) and pulmonary capillary wedge pressure (PCWP). Arbitrary thresholds for elevated RAP (≥10 mm Hg) and PCWP (≥22 mm Hg) were used. Concordant profiles are those in which RAP and PCWP were both elevated or both not elevated. A "right–left" equalizer pattern was characterized as elevated RAP and not elevated PCWP. A "preserved RV" pattern was characterized as elevated PCWP and not elevated RAP.

Table 1 Rates of Concordance of RAP and PCWP[a] Within Three Time Eras Over 14 Years

	Off inotropes		On inotropes	
Time era	*N*	Concordance	*N*	Concordance
1993 to 1998	1,626	74%	464	71%
1998 to 2002	1,369	72%	550	76%
2003 to 2007	1,084	73%	365	79%
		$p = 0.4$ for order		$p = 0.006$

[a]RAP was classified as elevated when ≥10 mm Hg and PCWP when ≥22 mm Hg. RAP and PCWP were classified as concordant when both were elevated or both were not elevated.

Drazner Circ HF 2013

Summary

- Presence of S3 and raised JVP correlates worse outcome
- Clinical assessment of JVP largely reflects RA pressure
- Raised RAP correlates with high LVEDP ~3/4 of time
- If in doubt, further means e.g. echo or cath would be needed

Aetiologies

Adapted from Oxford Textbook of Heart Failure, OUP 2011

Table 4.1 Causes of heart failure and the common modes of presentation

Cause	Examples of presentations
CHD	Myocardial infarction Chronic ischaemia Arrhythmias
Hypertension	Heart failure with preserved systolic function 'Burnt out' hypertensive cardiomyopathy Malignant hypertension/acute pulmonary oedema
Valve disease	Primary valvular disease e.g. endocarditis Secondary valvular disease e.g. functional regurgitation Congenital valvular disease
Arrhythmias	Incessant atrial arrhythmias Ventricular arrhythmias
Dilated cardiomyopathy	Idiopathic Inherited (familial) Peripartum Toxins: alcohol, cocaine, iron, copper
Congenital heart disease	Corrected transposition of great arteries Repaired tetralogy of Fallot Ebstein's anomaly
Infective	Viral myocarditis Chagas' disease HIV Lyme disease
Iatrogenic	Anthracyclines Abstruzimab
Infiltrative	Amyloid Sarcoid Neoplastic
Storage disorders	Haemochromatosis Fabry's disease Glycogen storage diseases
Endomyocardial disease	Radiotherapy Endomyocardial fibrosis Carcinoid
Pericardial disease	Calcification Infiltrative
Metabolic	Endocrine disease Nutritional disease (thiamine deficiency, selenium deficiency) Autoimmune disease
Neuromuscular disease	Friedreich's ataxia Muscular dystrophy
High-output	Anaemia Thyrotoxicosis A-V fistulae Paget's disease

Table 4.2 Aetiology of heart failure in contemporary randomized clinical trials and major registries

Study	RCT/ REG	Size	Age[a]	Male (%)	Ischaemic (%)	Nonischaemic (%)	HT (%)	IDCM (%)	Valve[b] (%)	Other (%)	Unknown (%)
SOLVD[5]	RCT	2569	61	80	71	–	–	18	–	–	–
DIG[6]	RCT	6800	64	78	70	30	9	15	–	6	–
MERIT-HF[7]	RCT	3991	64	78	66	34	–	–	–	–	–
CIBIS-II[8]	RCT	2647	61	81	50	–	–	12	–	–	38
ATLAS[9]	RCT	3192	64	79	64	35	20	28	–	6	–
RALES[10]	RCT	1663	65	73	54	46	–	–	–	–	–
Val-HeFT[11]	RCT	5010	62	80	57	–	7	31	–	5	–
COPERNICUS[12]	RCT	2289	63	80	67	–	–	–	–	–	–
COMET[13]	RCT	3029	62	80	53	–	18	–	–	–	–
COMPANION[14]	RCT	1520	67	68	56	44	–	–	–	–	–
CARE-HF[15]	RCT	813	67	73	38	–	–	–	–	–	62
GISSI-HF[16]	RCT	4574	68	77	40	–	18	34	–	3	5
SOLVD[17]	REG	6273	62	74	69	31	7	13	–	11	–
SPICE[18]	REG	9580	66	74	63	–	4	17	5	–	6
ADHERE[19]	REG	105 388	72	48	57	–	–	–	–	–	–
OPTIMIZE-HF[20]	REG	48 612	73	48	46	–	23	–	–	–	–

HT, hypertension; IDCM, idiopathic dilated cardiomyopathy; RCT, randomized clinical trial; REG, registry.

[a] Mean age in years.

[b] Valvular heart failure.

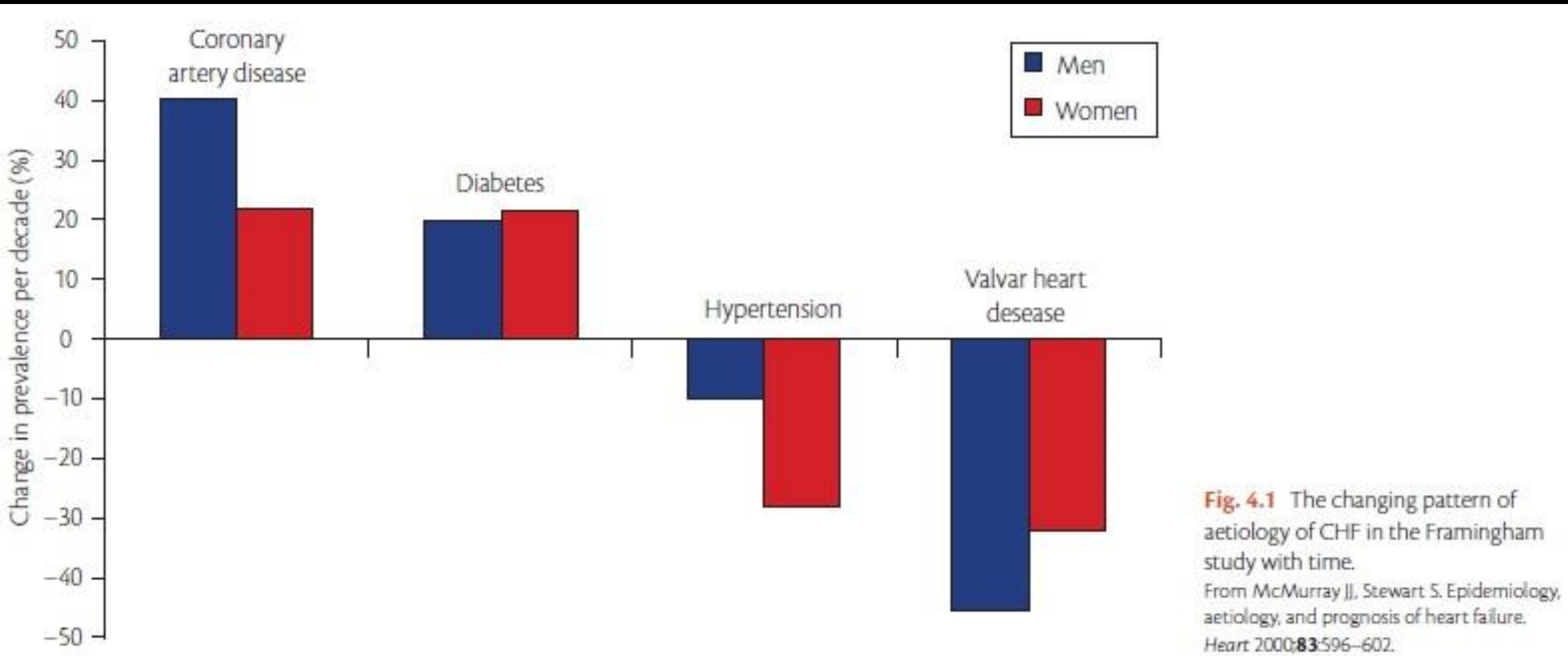


Fig. 4.1 The changing pattern of aetiology of CHF in the Framingham study with time.

From McMurray JJ, Stewart S. Epidemiology, aetiology, and prognosis of heart failure. *Heart* 2000;**83**:596–602.

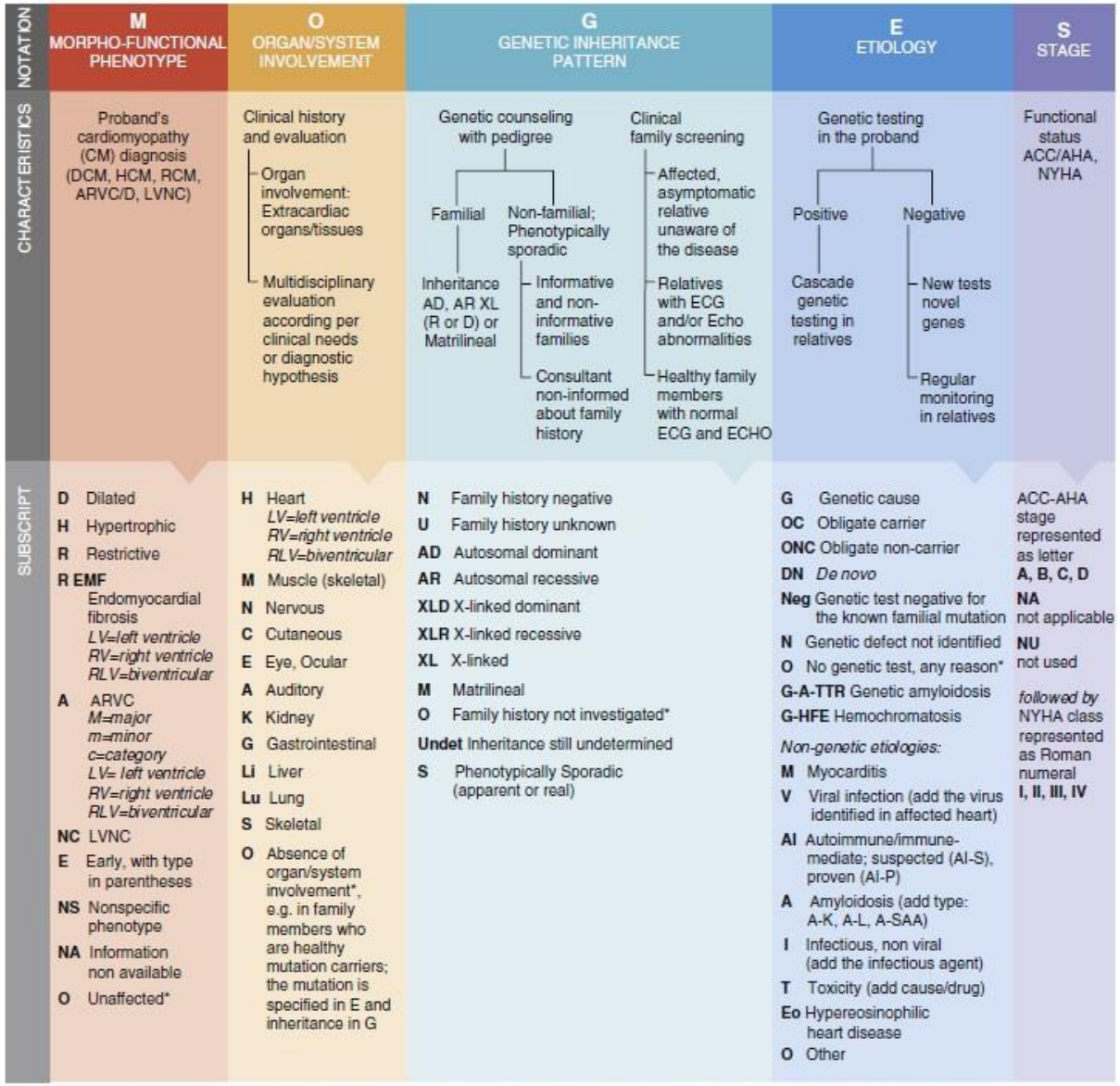


Fig. 20.1 Classification of cardiomyopathy according to MOGE(S) nosology. M, Morphofunctional phenotype; O, organ involvement; G, genetic inheritance pattern; E, etiology. (Annotation provides the description of the specific disease gene and mutation, as well as a description of nongenetic etiology). S, symptoms and functional status according to ACC/AHA staging and NYHA Class. A color code assigned to each variant can provide information about the potential role of the identified variant: affects function or probably affects function (red); variant of unknown significance (VUS) (yellow); and probably does not affect function (or probably no functional effect) or does not affect function (no functional effect) (green). DCM, Dilated cardiomyopathy. (From Arbustini E, Narula N, Tavazzi L, et al. The MOGE[S] classification of cardiomyopathy for clinicians. *J Am Coll Cardiol*. 2014;64[3]:304–318.)

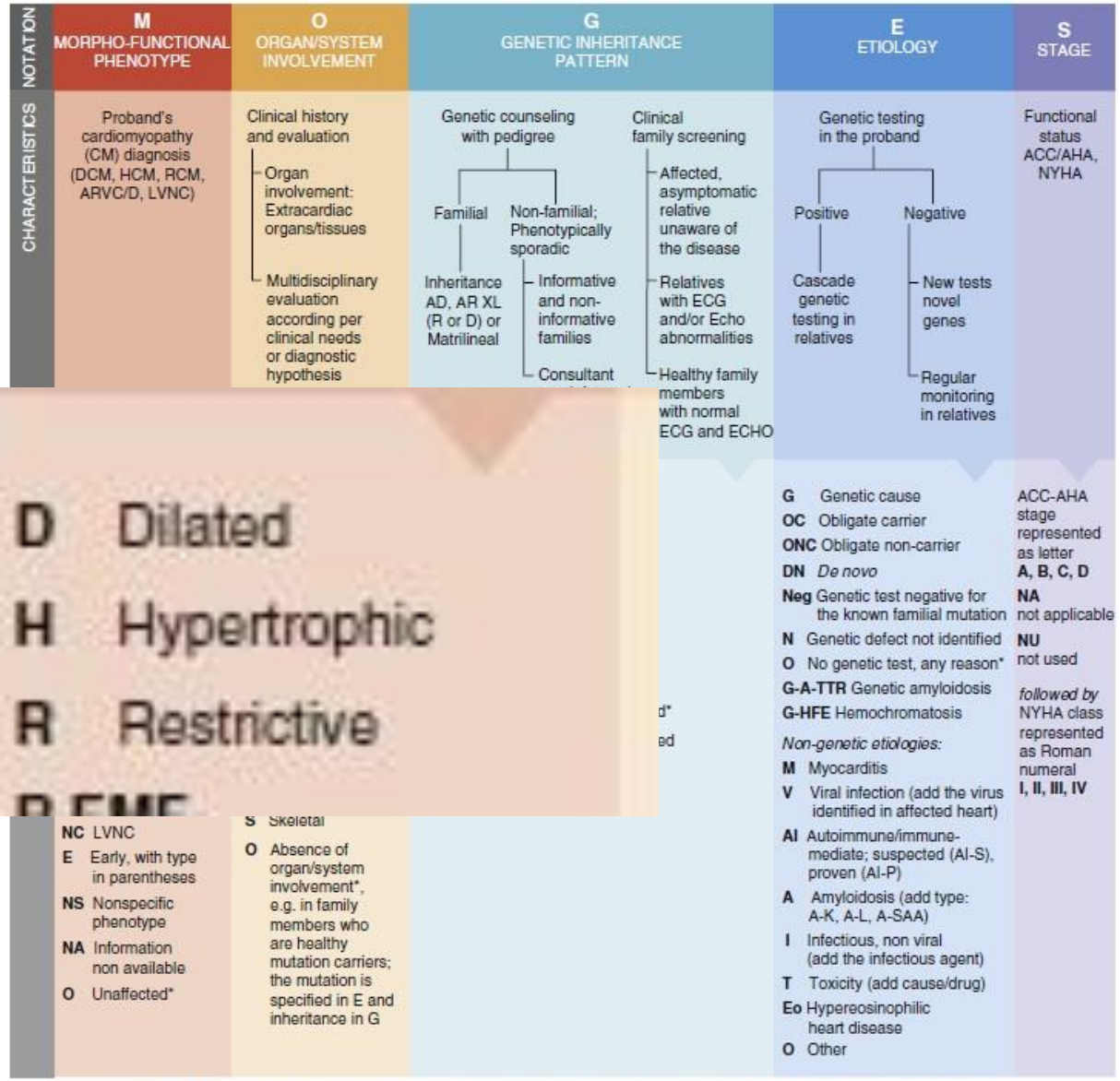


Fig. 20.1 Classification of cardiomyopathy according to MOGE(S) nosology. M, Morphofunctional phenotype; O, organ involvement; G, genetic inheritance pattern; E, etiology. (Annotation provides the description of the specific disease gene and mutation, as well as a description of nongenetic etiology). S, symptoms and functional status according to ACC/AHA staging and NYHA Class. A color code assigned to each variant can provide information about the potential role of the identified variant: affects function or probably affects function (red); variant of unknown significance (VUS) (yellow); and probably does not affect function (or probably no functional effect) or does not affect function (no functional effect) (green). DCM, Dilated cardiomyopathy. (From Arbustini E, Narula N, Tavazzi L, et al. The MOGE[S] classification of cardiomyopathy for clinicians. *J Am Coll Cardiol.* 2014;64[3]:304–318.)

Dilated Morphology

- Coronary artery disease
- Valvular heart disease
- Alcoholic heart disease
- Endocrine cause
- Recreational drugs (Cocaine, amphetamine)
- Peripartum cardiomyopathy
- Cancer treatment related
- Micronutrients deficiency
- High output heart failure
- Idiopathic

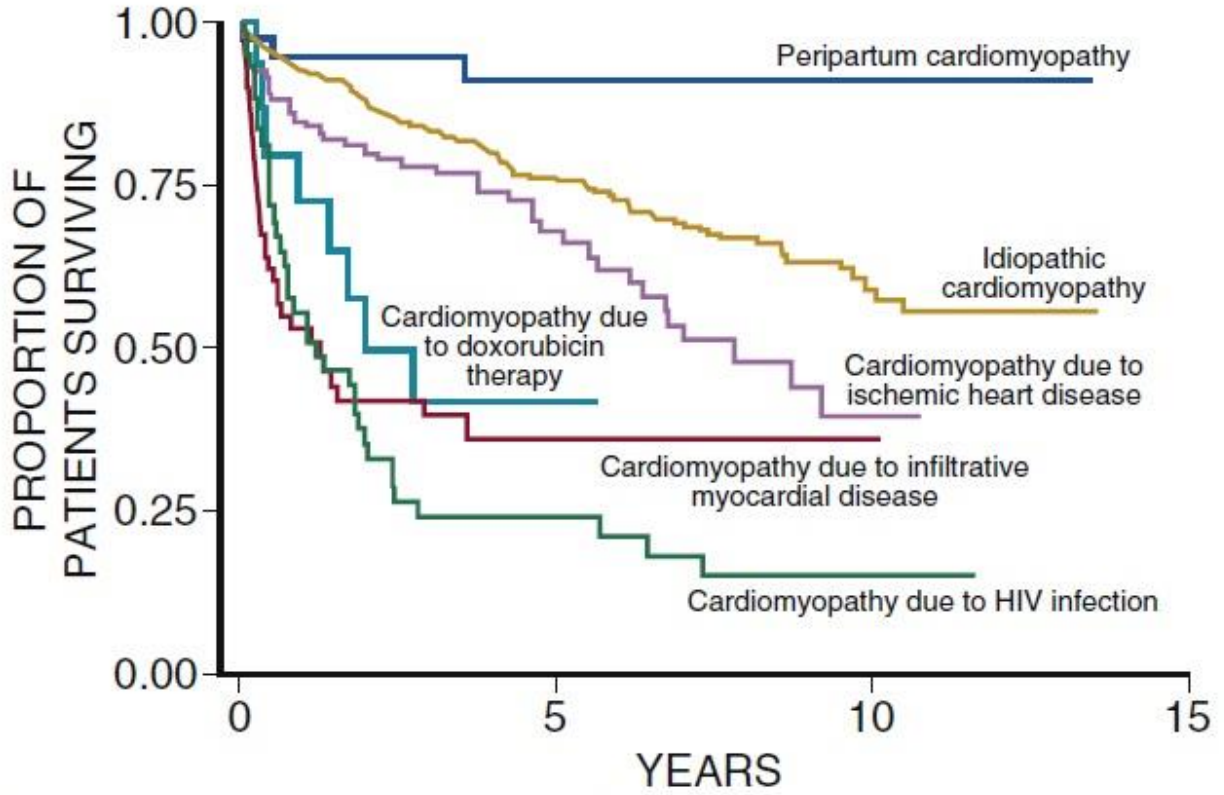


Fig. 20.9 Survival according to different etiologies of dilated cardiomyopathy. In a cohort of patients who underwent endomyocardial biopsy as part of an evaluation for heart failure due to unexplained cardiomyopathy, when compared with the patients with idiopathic cardiomyopathy, survival was significantly better in patients with peripartum cardiomyopathy and significantly worse among the patients with cardiomyopathy due to infiltrative myocardial disease, human immunodeficiency virus *(HIV)* infection, therapy with doxorubicin, and ischemic heart disease. (From Felker GM, Thompson RE, Hare JM, et al. Underlying causes and long-term survival in patients with initially unexplained cardiomyopathy. *N Engl J Med*. 2000;342[15]:1077–1084.)

Dilated Morphology

- **Coronary artery disease**
- Valvular heart disease
- Alcoholic heart disease
- Endocrine cause
- Recreational drugs (Cocaine, amph
- Peripartum cardiomyopathy
- Cancer treatment related
- Micronutrients deficiency
- High output heart failure
- Idiopathic

-Most common cause
-Must be excluded

Dilated Morphologies

- Coronary artery disease
- Valvular heart disease
- **Alcoholic heart disease**
- Endocrine cause
- Recreational drugs (Cocaine, amphet
- Peripartum cardiomyopathy
- Cancer treatment related
- Micronutrients deficiency
- High output heart failure
- Idiopathic

Related to period of binge drinking behavior (7-8 standard drinks for >5 years)

Dilated Morphology

- Coronary artery disease
- Valvular heart disease
- Alcoholic heart disease
- Endocrine cause
- Recreational drugs (Cocaine, amphe
- **Peripartum cardiomyopathy**
- Cancer treatment related
- Micronutrients deficiency
- High output heart failure
- Idiopathic

-Last month upto 5 months post-partum
-Good prognosis
-Differentials include SCAD, stress related CMP
-Counselling for breast feeding and future pregnancy

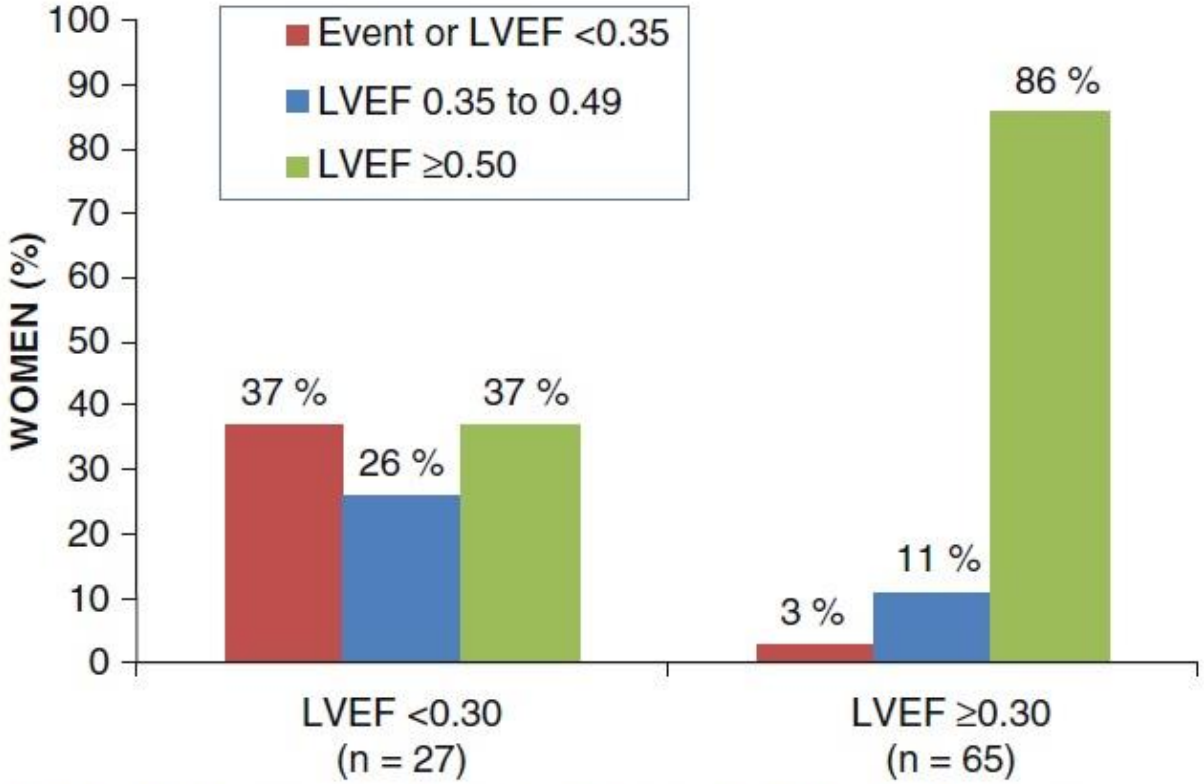


Fig. 20.11 Final status based on the initial LVEF of patients with peripartum cardiomyopathy. Comparison of status at the end of the study based on the initial LVEF. *Red column*, percentage of women with no recovery (event or final LVEF <0.35); *blue column*, percentage of women with partial recovery (final LVEF 0.35–0.49); *green column*, percentage of women with complete recovery (LVEF ≥0.50). Recovery was evident in 86% of women with a baseline LVEF ≥0.30, compared with 37% of those with an LVEF less than 0.30, p <0.001. *LVEF*, Left ventricular ejection fraction. (Modified from McNamara DM, Elkayam U, Alharethi R, et al. Clinical outcomes for peripartum cardiomyopathy in North America: results of the IPAC Study (Investigations of Pregnancy-Associated Cardiomyopathy). *J Am Coll Cardiol*. 2015;66[8]:905–914.)

Dilated Morphology

- Coronary artery disease
- Valvular heart disease
- Alcoholic heart disease
- Endocrine cause
- Recreational drugs (Cocaine, ampheta
- Peripartum cardiomyopathy
- **Cancer treatment related**
- Micronutrients deficiency
- High output heart failure
- Idiopathic

-Hx of breast cancer, lymphoma etc.
-radiation to chest wall also cause CAD, restrictive CMP, constrictive pericarditis

Dilated Morphology

- Coronary artery disease
- Valvular heart disease
- Alcoholic heart disease
- Endocrine cause
- Recreational drugs (Cocaine, ampheta
- Peripartum cardiomyopathy
- Cancer treatment related
- **Micronutrients deficiency**
- High output heart failure
- Idiopathic

-thiamine, selenium etc
-feeding problem, malabsorption

Dilated Morphology

- Coronary artery disease
- Valvular heart disease
- Alcoholic heart disease
- Endocrine cause
- Recreational drugs (Cocaine, amphetamine)
- Peripartum cardiomyopathy
- Cancer treatment related
- Micronutrients deficiency
- **High output heart failure**
- Idiopathic

- **Confirmed high output status e.g. imaging, RHC**
- **AV fistula, obesity, liver disease, etc**

Restrictive morphology

- Usually infiltrative causes
- Increase stiffness and impair ventricular filling

Restrictive morphology

- **Amyloidosis**
- Sarcoidosis
- Fabry disease
- Carcinoid disease
- Hypereosinophilic syndrome

- **Thick wall**
- **AL or TTR (familial or wild type)**
- **Asso neuropathy and autonomic dysfunction**

Restrictive morphology

- Amyloidosis
- Sarcoidosis
- **Fabry disease**
- Carcinoid disease
- Hypereosinophilic syndrome

- **Thick wall**
- **X-link inheritance**
- **Asso renal dysfunction and skin lesion**
- **Enzyme assay available for diagnosis**

Restrictive morphology

- Amyloidosis
- Sarcoidosis
- Fabry disease
- **Carcinoid disease**
- Hypereosinophilic syndrome

Usually affected right sided valves and myocardium

Restrictive morphology

- Amyloidosis
- Sarcoidosis
- Fabry disease
- Carcinoid disease
- **Hypereosinophilic syndrome**

- **High peripheral eosinophil counts**
- **Intracardiac thrombus even with preserved EF**
- **Churg-Strauss syndrome**

Hypertrophic morphology

Not all LVH are HCM

Table 3 Examples of signs and symptoms suggestive of specific diagnoses (modified from Rapezzi et al.[67])

Symptom/sign	Diagnosis
Learning difficulties, mental retardation	• Mitochondrial diseases • Noonan/LEOPARD/Costello syndrome • Danon disease
Sensorineural deafness	• Mitochondrial diseases (particularly with diabetes) • Anderson-Fabry disease • LEOPARD syndrome
Visual impairment	• Mitochondrial diseases (retinal disease, optic nerve atrophy) • TTR-related amyloidosis (cotton wool type vitreous opacities) • Danon disease (retinitis pigmentosa) • Anderson-Fabry disease (cataracts, corneal opacities)
Gait disturbance	• Friedreich's ataxia
Paraesthesia/sensory abnormalities/neuropathic pain	• Amyloidosis • Anderson-Fabry disease
Carpal tunnel syndrome	• TTR-related amyloidosis (especially when bilateral and in male patients)
Muscle weakness	• Mitochondrial diseases • Glycogen storage disorders • FHL1 mutations • Friedreich's ataxia
Palpebral ptosis	• Mitochondrial diseases • Noonan/LEOPARD syndrome • Myotonic dystrophy
Lentigines/café au lait spots	• LEOPARD/Noonan syndrome

Table 4 Electrocardiographic abnormalities suggesting specific diagnoses or morphological variants[67]

Finding	Comment
Short PR interval/pre-excitation	Pre-excitation is a common feature of storage diseases (Pompe, PRKAG2, and Danon) and mitochondrial disorders (MELAS, MERFF). A short PR interval without pre-excitation is seen in Anderson-Fabry disease.
AV block	Progressive atrioventricular conduction delay is common in mitochondrial disorders, some storage diseases (including Anderson-Fabry disease), amyloidosis, desminopathies and in patients with PRKAG2 mutations.
Extreme LVH (Sokolow score ≥50)	Extremely large QRS voltage is typical of storage diseases such as Pompe and Danon disease, but can be caused by pre-excitation alone.
Low QRS voltage (or normal voltages despite increased LV wall thickness)	Low QRS voltage in the absence of pericardial effusion, obesity and lung disease is rare in HCM (limited to cases with end-stage evolution) but is found in up to 50% of patients with AL amyloidosis and 20% with TTR amyloidosis. Differential diagnosis between HCM and cardiac amyloidosis is aided by measuring the ratio between QRS voltages and LV wall thickness.
Extreme superior ("North West") QRS axis deviation	Seen in patients with Noonan syndrome who have severe basal hypertrophy extending into the RV outflow tract.
Giant negative T wave inversion (>10 mm)	Giant negative T wave inversion in the precordial and/or inferolateral leads suggests involvement of the LV apex.
Abnormal Q waves ≥40 ms in duration and/or ≥25% of the R wave in depth and/or ≥3 mm in depth in at least two contiguous leads except aVR	Abnormally deep Q waves in the inferolateral leads, usually with a positive T wave, are associated with an asymmetrical distribution of LVH. Q waves of abnormal duration (≥40 ms) are associated with areas of replacement fibrosis.
Coved ST segment elevation in lateral chest leads	Some patients with apical or distal hypertrophy develop small apical aneurysms, sometimes associated with myocardial scarring. These may only be detectable on CMR, ventriculography or contrast echo, and are occasionally associated with ST elevation in the lateral chest leads.

AV = atrioventricular; AL = amyloid light chain; CMR = cardiac magnetic resonance; HCM = hypertrophic cardiomyopathy; LV = left ventricular; LVH = left ventricular hypertrophy; MELAS = mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes; MERFF = myoclonic epilepsy with ragged red fibres; PRKAG2 = gamma-2 subunit of the adenosine monophosphate-activated protein kinase; RV = right ventricular; TTR = transthyretin.

Table 5 Echocardiographic features that suggest specific aetiologies (modified from Rapezzi et al.[67])

Finding	Specific diseases to be considered
Increased interatrial septum thickness	Amyloidosis
Increased AV valve thickness	Amyloidosis; Anderson-Fabry disease
Increased RV free wall thickness	Amyloidosis, myocarditis, Anderson-Fabry disease, Noonan syndrome and related disorders
Mild to moderate pericardial effusion	Amyloidosis, myocarditis
Ground-glass appearance of ventricular myocardium on 2D echocardiography	Amyloidosis
Concentric LVH	Glycogen storage disease, Anderson-Fabry disease, PRKAG2 mutations
Extreme concentric LVH (wall thickness ≥30 mm)	Danon disease, Pompe disease
Global LV hypokinesia (with or without LV dilatation)	Mitochondrial disease, TTR-related amyloidosis, PRKAG2 mutations, Danon disease, myocarditis, advanced sarcomeric HCM, Anderson-Fabry disease
Right ventricular outflow tract obstruction	Noonan syndrome and associated disorders

2D = two-dimensional; AV = atrioventricular; HCM = hypertrophic cardiomyopathy; LV = left ventricular; LVH = left ventricular hypertrophy; PRKAG2 = gamma-2 subunit of the adenosine monophosphate-activated protein kinase; RV = right ventricle; TTR = transthyretin.

Biomarkers

The N-Terminal Pro-BNP Investigation of Dyspnea in the Emergency Department (PRIDE) Study

James L. Januzzi, Jr., MD, Carlos A. Ca
Aaron L. Baggish, MD, Annabel A.
Roderick Tung, MD, Renee Camer
Claudia U. Chae, MD, MPH, Donald M. Ll
Stacy Foran-Melanson, MD, Pl
Elizabeth Lee-Lewandrowski, PhD, M

ORIGINAL ARTICLE

Rapid Measurement of B-Type Natriuretic Peptide in the Emergency Diagnosis of Heart Failure

Alan S. Maisel, M.D., Padma Krishnaswamy, M.D., Richard M. Nowak, M.D., M.B.A., James McCord, M.D., Judd E. Hollander, M.D., Philippe Duc, M.D., Torbjørn Omland, M.D., Ph.D., Alan B. Storrow, M.D., William T. Abraham, M.D., Alan H.B. Wu, Ph.D., Paul Clopton, M.S., Philippe G. Steg, M.D., et al., for the Breathing Not Properly Multinational Study Investigators*

Prognostic Implications of C
N-Terminal Pro-B-Type Nat
Peptide in Patients With He

Michael R. Zile, MD,[a] Brian L. Claggett, PhD,[b] Margaret F. Prescott, PH
Milton Packer, MD,[e] Jean L. Rouleau, MD,[f] Karl Swedberg, MD,[g] Aksh
Victor C. Shi, MD,[c] Scott D. Solomon, MD[b]

ORIGINAL ARTICLE

N-Terminal Pro–B-Type Natriuretic Peptide and Long-Term Mortality Stable Coronary Heart Disease

Charlotte Kragelund, M.D., Bjørn Grønning, M.D., Lars Køber, D.M.Sc., Per Hildebrandt, D.M.Sc., and Rolf Steffensen, M.D.

ORIGINAL ARTICLE

Use of B-Type Natriuretic Peptide in the Evaluation and Management of Acute Dyspnea

Christian Mueller, M.D., André Scholer, Ph.D., Kirsten Laule-Kilian, B.Sc., Benedict Martina, M.D., Christian Schindler, Ph.D., Peter Buser, M.D., Matthias Pfisterer, M.D., and André P. Perruchoud, M.D.

TABLE 30-1 2013 ACC/AHA Heart Failure Guideline Recommendations for the Use of Biomarkers in Heart Failure

BIOMARKERS		CLASS OF RECOMMENDATION	LEVEL OF EVIDENCE
BNP or NT-proBNP	Diagnosis	I	A
	Prognosis	I	A
	Guided-therapy (chronic HF)	IIa	B
	Guided-therapy (acute HF)	IIb	C
Troponin T or I (Myocardial injury)	Prognosis	I	A
sST2, Galectin-3 (Myocardial fibrosis)	Prognosis	IIb	B for chronic A for acute

BNP, B-type natriuretic peptide; *HF,* heart failure; *sST2,* soluble ST2.

From Yancy CW, Jessup M, Bozkurt B, et al: 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association task force on practice guidelines. Circulation 128:e240–327, 2013.

BNP and NT-proBNP

- Release upon myocardial stretch
- Half life (BNP 20mins, NT-proBNP 90mins)
- 25% cleared by kidneys (upto eGFR 15ml/min)
- Correlates with NYHA functional class
- Generally higher values in HFrEF than HFpEF
- Higher baseline values in elderly in renal failure
- ARNI raises BNP but not NT-proBNP

Use

- Diagnosis of acute HF
- Diagnosis of chronic HF (as a rule out test)
- Prognosis
- Guide therapy
- Different cutoff values in different clinical situations

Falsely low

- Obesity
- Flash pulmonary edema
- Cardiac tamponade
- Pericardial constriction

TABLE 30-5 Suggested Natriuretic Peptide Cut-Points in Heart Failure

	CUTOFF VALUE	SENSITIVITY	SPECIFICITY	POSITIVE PREDICTIVE VALUE	NEGATIVE PREDICTIVE VALUE
To Exclude Acutely Decompensated HF:					
BNP	<30-50 pg/mL	97%	*	*	96%
NT-proBNP	<300 pg/mL	99%	*	*	99%
MR-proANP	<57 pmol/L	98%	*	*	97%
To Identify Acutely Decompensated HF:					
Single Cutoff Point Strategy					
BNP	<100 pg/mL	90%	76%	79%	89%
NT-proBNP	<900 pg/mL	90%	85%	76%	94%
MR-proANP	<127 pmol/L	87%	79%	67%	93%
Multiple Cut-Point Strategy					
BNP, "gray zone" approach	<100 pg/mL to exclude	90%	73%	75%	90%
	100-400 pg/mL, "gray zone"	*	*	*	*
	>400 pg/mL, to rule in	63%	91%	86%	74%
NT-proBNP, "age-stratified" approach	<450 pg/mL for age <50 years <900 pg/mL for age 50-75 years <1800 pg/mL for age >75 years	90%	84%	88%	66%
MR-proANP, "age-stratified" approach	<104 pmol/L for age <65 years 214 pmol/L for age ≥65 years	82%	86%	75%	91%
Outpatient Application					
BNP	20 pg/mL (asymptomatic)	*	*	*	96%
	or 40 pg/mL (symptomatic)	*	*	*	
NT-proBNP, "age-stratified" approaches	<125 pg/mL for age <75 years	*	*	*	98%
	<450 pg/mL for age ≥75 years	*	*	*	91%
	or				
	<50 pg/mL for age <50 years	*	*	*	98%
	<75 pg/mL for age 50-75 years	*	*	*	98%
	<250 pg/mL for age >75 years	*	*	*	93%

NT-pro BNP are very useful

NT-pro BNP is very useful

BUT

NT-pro BNP is very useful

BUT

Still not available in HA

NT-pro BNP is very useful

Sti **HA**

Take Home Messages

- HFrEF Vs HFpEF
- NYHA Classes and stages (+/-INTERMAC)
- Clinical exam provides essential information on haemodynamic status
- Identifiable causes in dilated, hypertrophic or restrictive morphologies