Assessment of left ventricular function: newer and better alternatives to the ejection fraction.

John E Sanderson
Professor of Clinical Cardiology
Department of Cardiovascular Medicine
University of Birmingham
UK

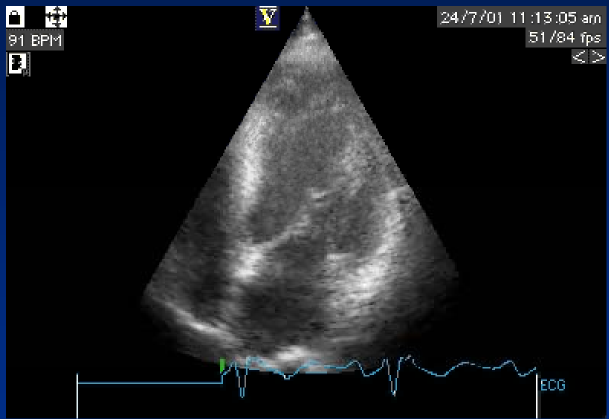
No conflict of interests

KSE 2008

UNIVERSITY OF BIRMINGHAM

LV Remodeling after AMI

1 WK

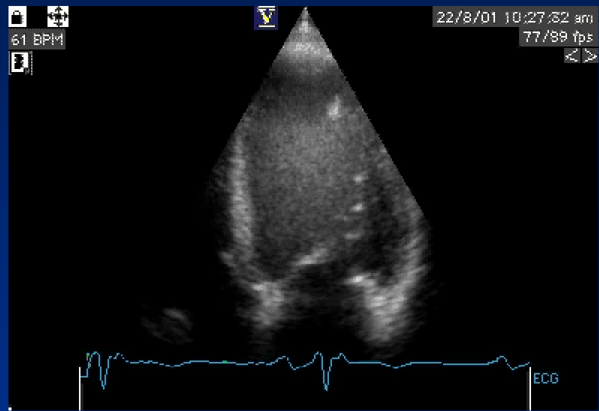


EDV 94 ml ESV 58 ml

LVDd 3.05 cm

EF 38 %

1 Month

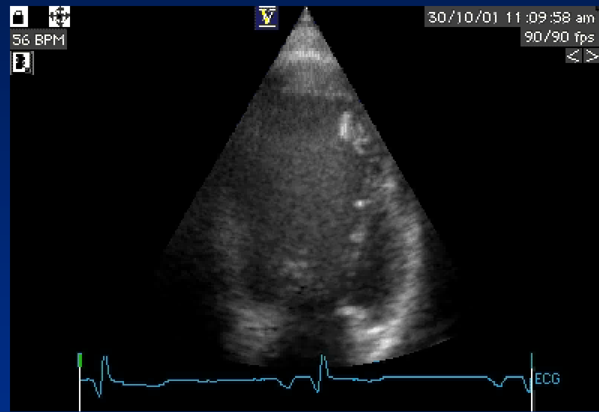


EDV 108 ml ESV 63 ml

LVDd 5.8 cm

EF 40 %

3 Months



EDV 116 ml ESV 76ml

LVDd 6.0 cm

EF 36 %

Process of Remodeling

Acute infarction (hours)

Infarct expansion (hours to days)

Global remodeling (days to months)

LVEF

- Influenced by preload, afterload, dyssynchrony and contractility.
- Measurement frequently inaccurate (often eye-balled).
- Why do we use it?

  - easy to measure

  - seems logical

  - relates to prognosis (but less well than ESV)

LVEF does not correlate with functional capacity in heart failure.

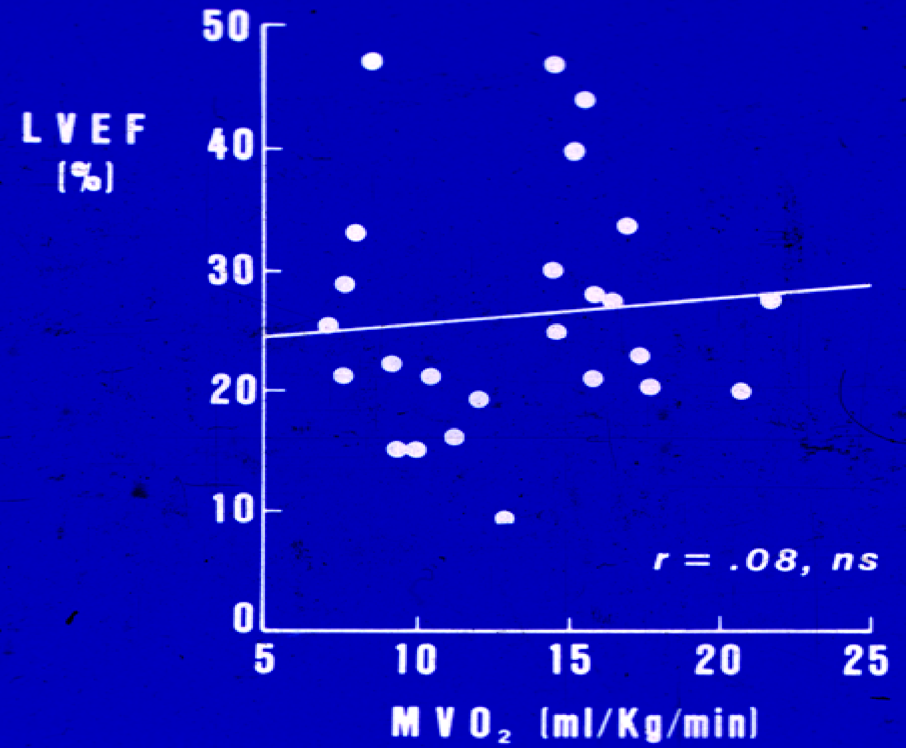
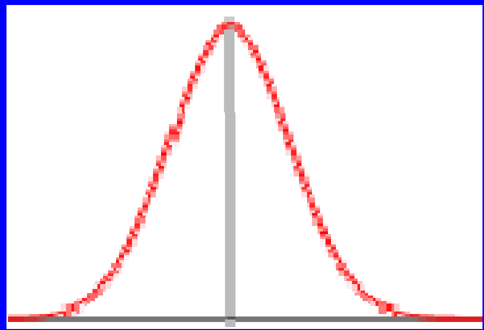


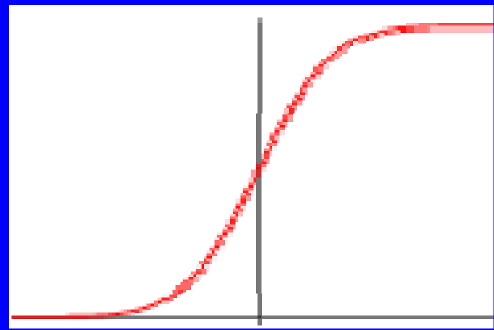
FIGURE 2. Relation between left ventricular ejection fraction (LVEF) at rest and maximal oxygen consumption (MVO_2) during exercise in patients with chronic left ventricular failure. ns = not significant.

Baker B. AM J CARDIOL. 1984;54:596

Normality plots for continuous data

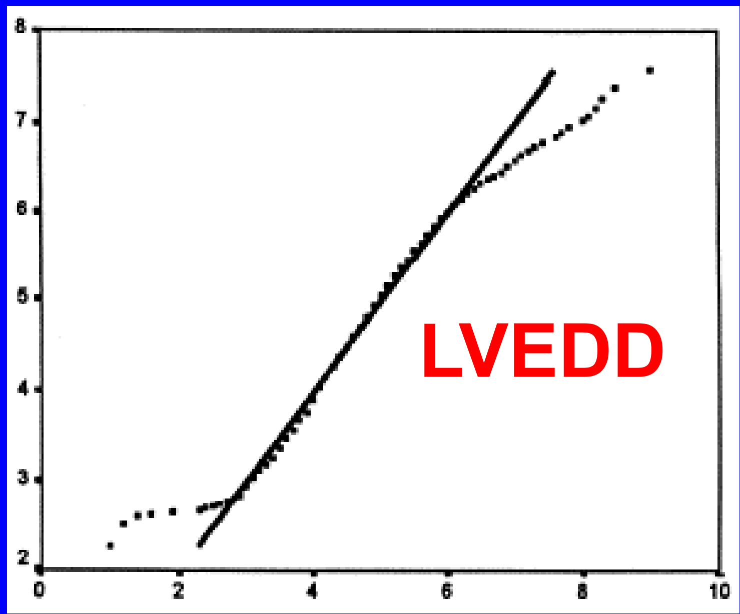
Distribution

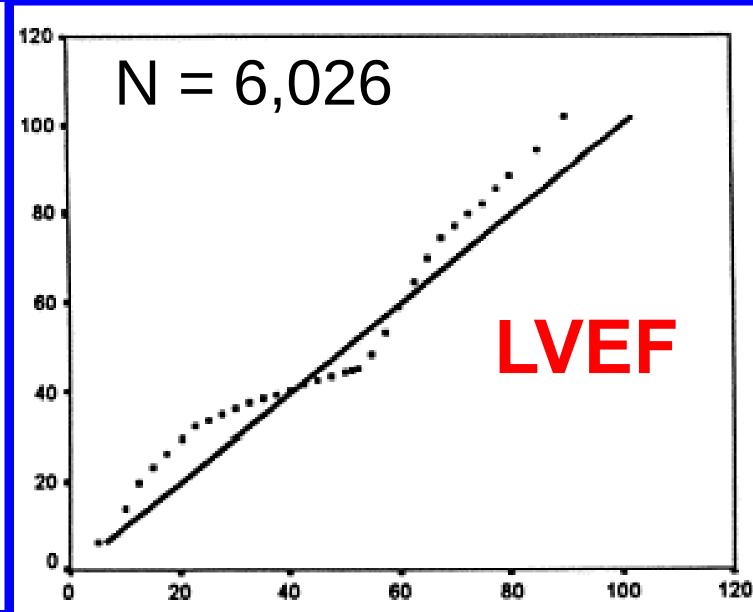




Cumulative frequency

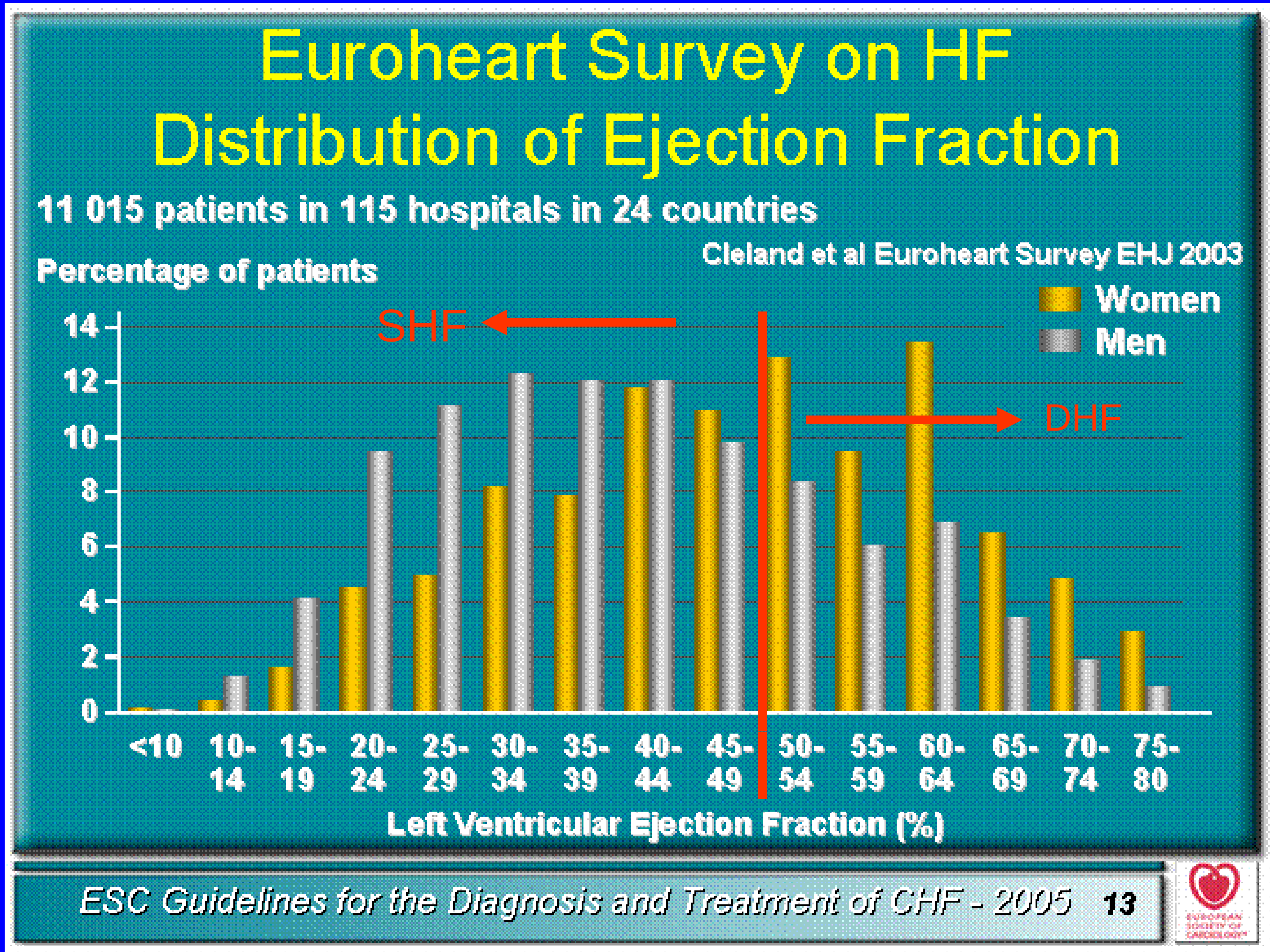
Expected normal value





Observed value

Berger AK et al, JACC 1999; 34: 1831


Euroheart Survey on HF
Distribution of Ejection Fraction
11 015 patients in 115 hospitals in 24 countries
Cleland et al Euroheart Survey EHJ 2003
Percentage of patients
Women
Men
SHF
DHF
14
12
10
8
6
4
2
0
<10
10-14
15-19
20-24
25-29
30-34
35-39
40-44
45-49
50-54
55-59
60-64
65-69
70-74
75-80
Left Ventricular Ejection Fraction (%)
ESC Guidelines for the Diagnosis and Treatment of CHF - 2005
13

Heart failure: the classical view.

- Symptoms of heart failure with reduced LVEF

=systolic heart failure

- Symptoms of heart failure with a normal LVEF

=***diastolic heart failure i.e. problem is in diastole.***

"Whats in a name? That which we call a Rose by any other name would smell as sweet." William Shakespeare

Population studies

Hogg et al JACC 2004;43:317-27

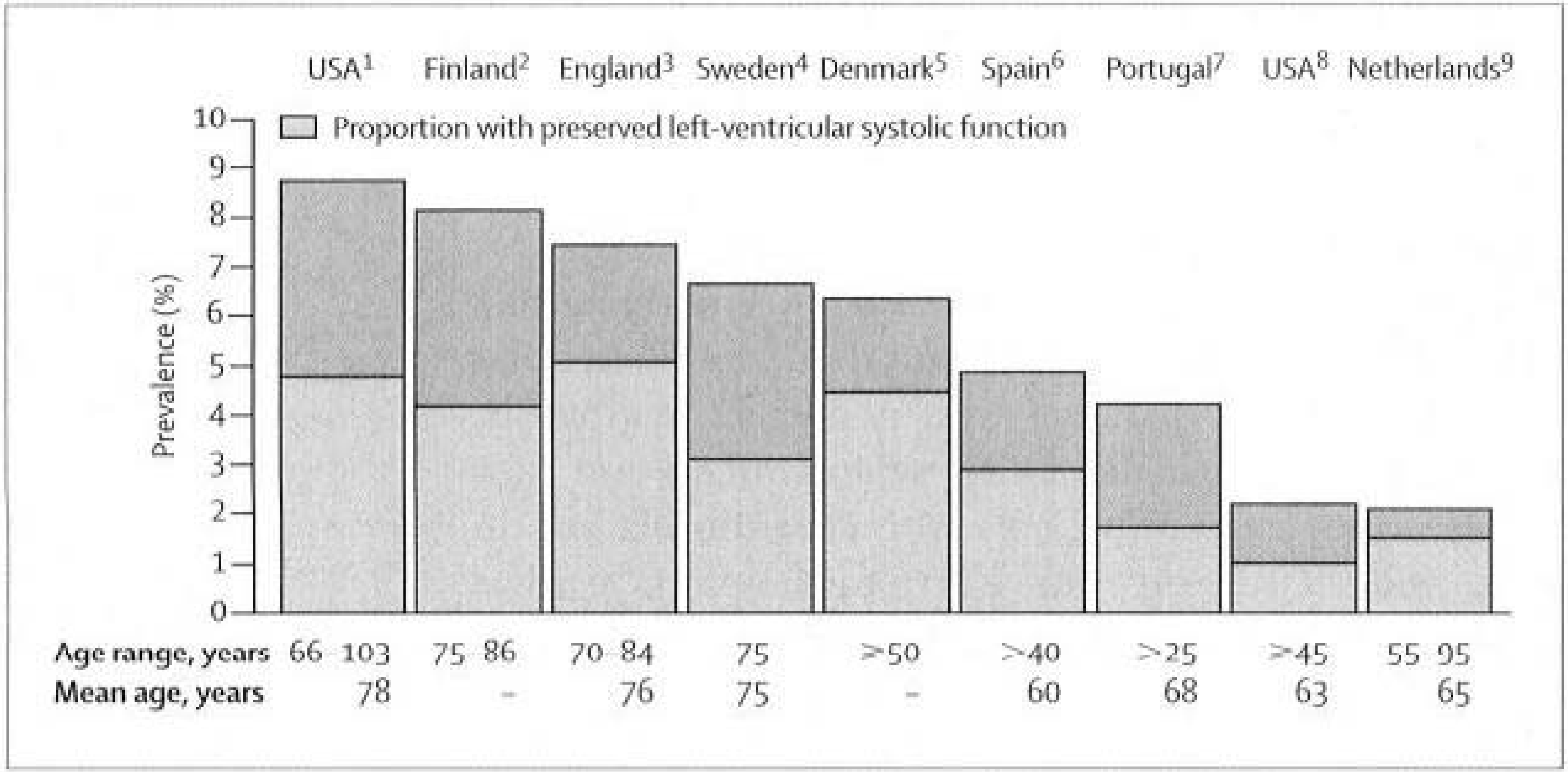


Figure 1: **Prevalence of heart failure in cross-sectional population echocardiographic studies and proportion of patients with preserved left-ventricular systolic function**

Diastolic Heart Failure in Population-Based Studies

	Diastolic Heart Failure	Systolic Heart Failure
Olmstead County (MN)[1]	43%	57%
Framingham Study[2]	51%	49%
Cardiovascular Health Study[3]	55%	45%
Strong Heart Study[4]	53%	47%

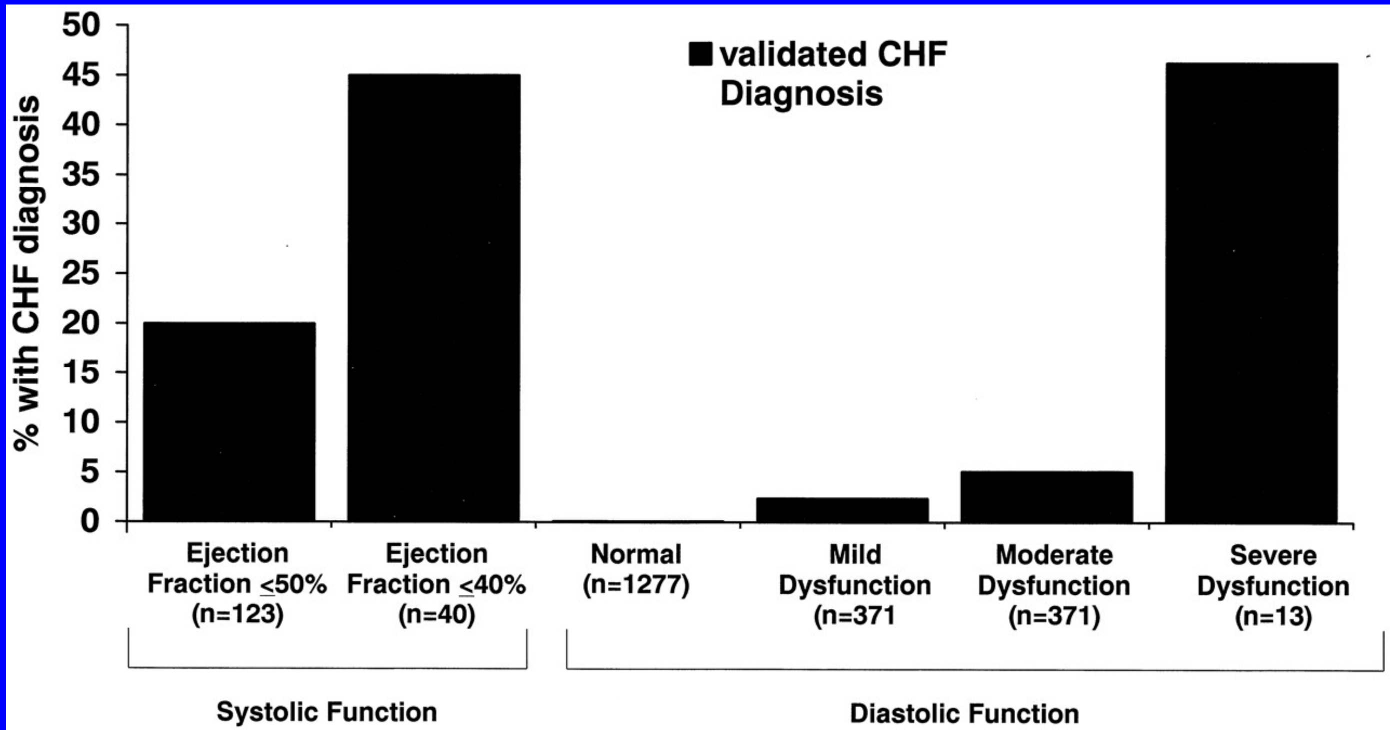
1. Senni M, Tribouilloy CM, Rodeheffer RJ, et al. Congestive heart failure in the community: a study of all incident cases in Olmsted County, Minnesota, in 1991.Circulation.1998;98:2282-9.

2. Vasan RS, Larson MG, Benjamin EJ, et al. Congestive heart failure in subjects with normal versus reduced left ventricular ejection fraction: prevalence and mortality in a population-based cohort. J Am Coll Cardiol. 1999;33:1948-55.

3. Kitzman DW, Gardin JM, Gottdiener JS, et al. Importance of heart failure with preserved systolic function in patients > or = 65 years of age. CHS Research Group. Cardiovascular Health Study. Am J Cardiol. 2001;87:413-9.

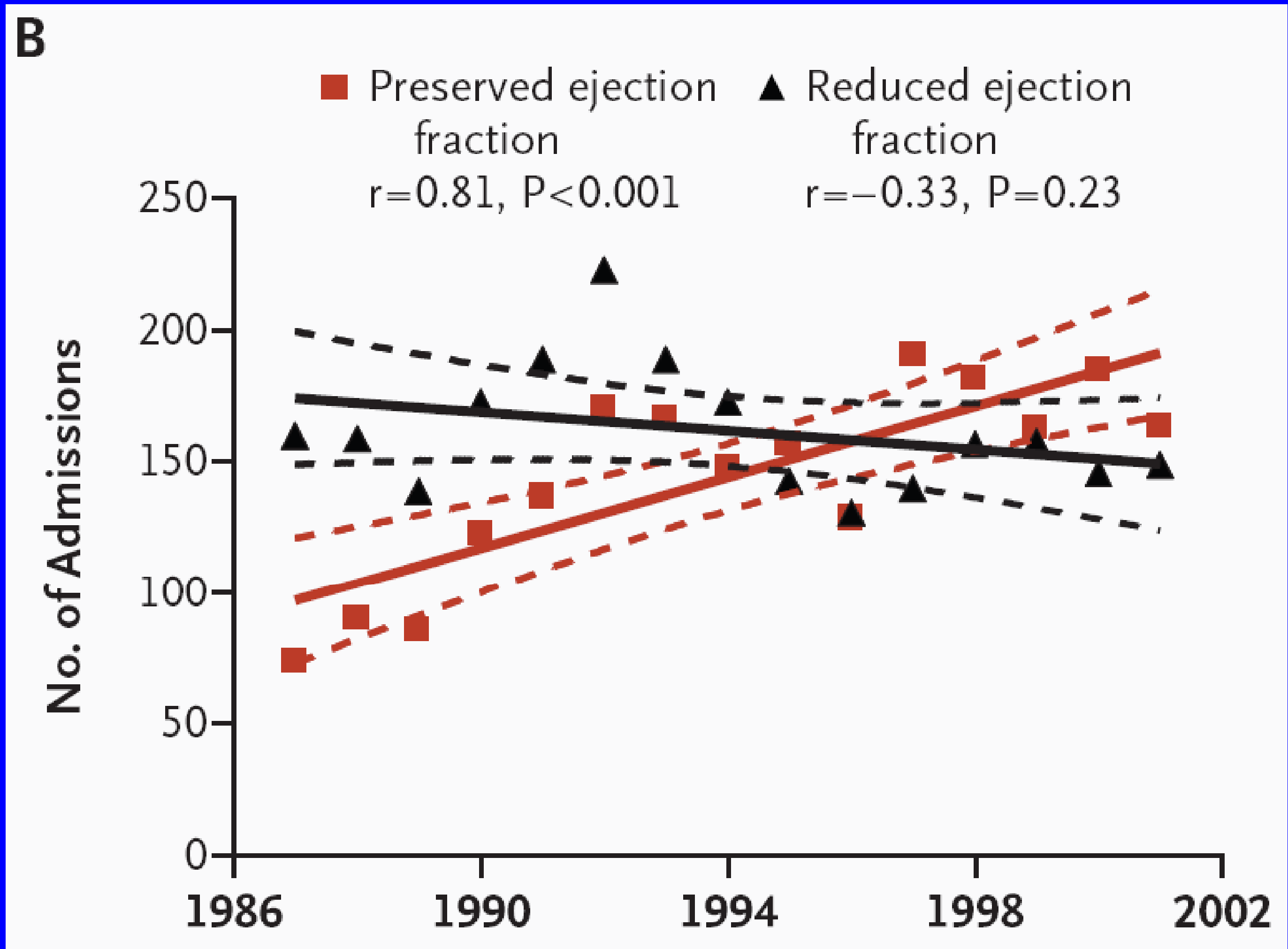
4. Devereux RB, Roman MJ, Liu JE, et al. Congestive heart failure despite normal left ventricular systolic function in a population-based sample: the Strong Heart Study. Am J Cardiol. 2000;86:1090-6.

Prevalence of heart failure in subjects in the general population with left ventricular systolic and diastolic dysfunction (Olmsted County Study, Minnesota)



Hogg, K. et al. J Am Coll Cardiol 2004;43:317-327

Changing Demography of Heart Failure



Owan TE et al. NEJM 2006

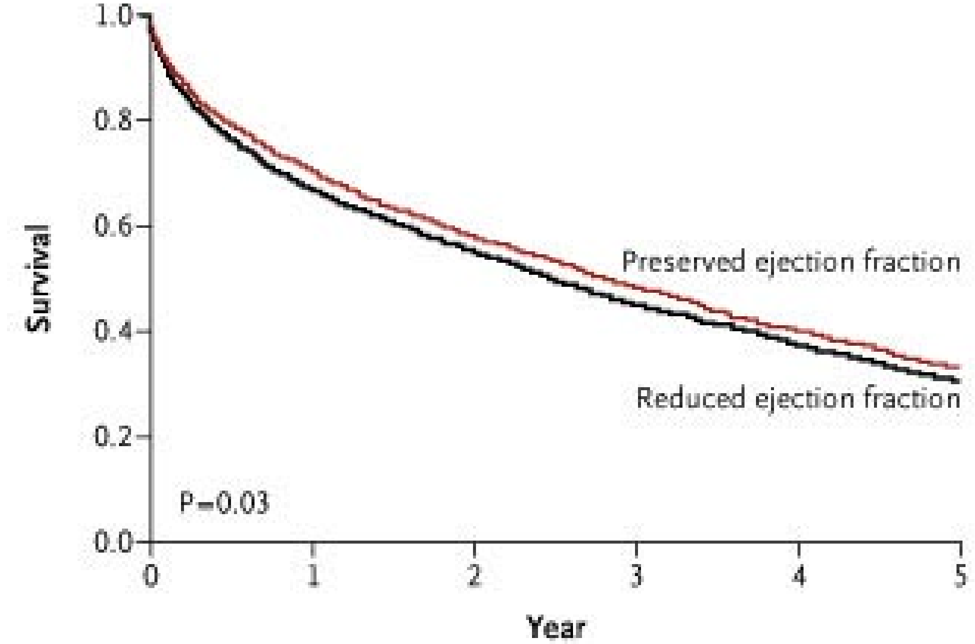
SHF VS DHF
Presenting Symptoms and Signs of Heart Failure

Table 2. Presenting Symptoms and Signs of Heart Failure.

Variable	Reduced Ejection Fraction (<40%) (N=1570)	Preserved Ejection Fraction (>50%) (N=880)	P Value
	no. (%)		
Symptoms			
Acute pulmonary edema	332 (21.1)	152 (17.3)	0.02
Dyspnea or shortness of breath	1511 (96.2)	835 (94.9)	0.11
Chest pain	399 (25.4)	212 (24.1)	0.47
Orthopnea	729 (46.4)	374 (42.5)	0.06
Syncope	27 (1.7)	10 (1.1)	0.26
Paroxysmal nocturnal dyspnea	473 (30.1)	220 (25.0)	0.007
Signs			
Bilateral ankle edema	888 (56.6)	581 (66.0)	<.001
Wheezing	302 (19.2)	173 (19.7)	0.80
Neck-vein distention	962 (61.3)	506 (57.5)	0.07
Crackles or rales on lung examination	1324 (84.3)	743 (84.4)	0.95
Hepatojugular reflux	119 (7.6)	69 (7.8)	0.82
Hepatomegaly	81 (5.2)	38 (4.3)	0.35
Presence of S3	196 (12.5)	74 (8.4)	0.002
Presence of S4	80 (5.1)	33 (3.8)	0.13
Chest radiographic signs			
Pulmonary edema	814 (51.8)	414 (47.0)	0.02
Pleural effusion	716 (45.6)	360 (40.9)	0.03

Bhatia R et al. N Engl J Med 2006;355:260-269

Kaplan-Meier Survival Curves for Patients with Heart Failure and Preserved or Reduced Ejection Fraction



No. at Risk						
Reduced ejection fraction	2424	1637	1350	1049	813	604
Preserved ejection fraction	2166	1539	1270	1001	758	574

Owan T et al. N Engl J Med 2006;355:251-259

So what are the differences between SHF vs DHF

- Symptoms similar
- Mortality similar
- Both have evidence of diastolic dysfunction
- Both have abnormalities of systolic function

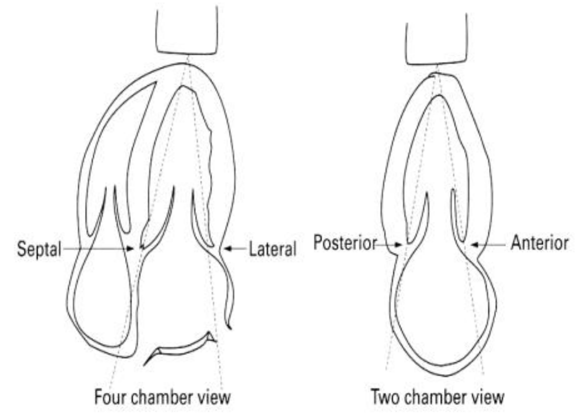
Platt versus Pickering on Hypertension 1960s

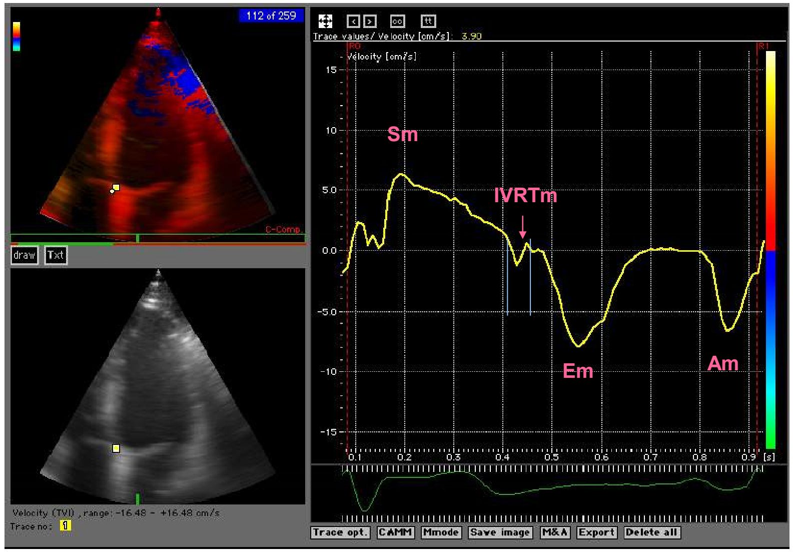
-unimodal vs bimodal.

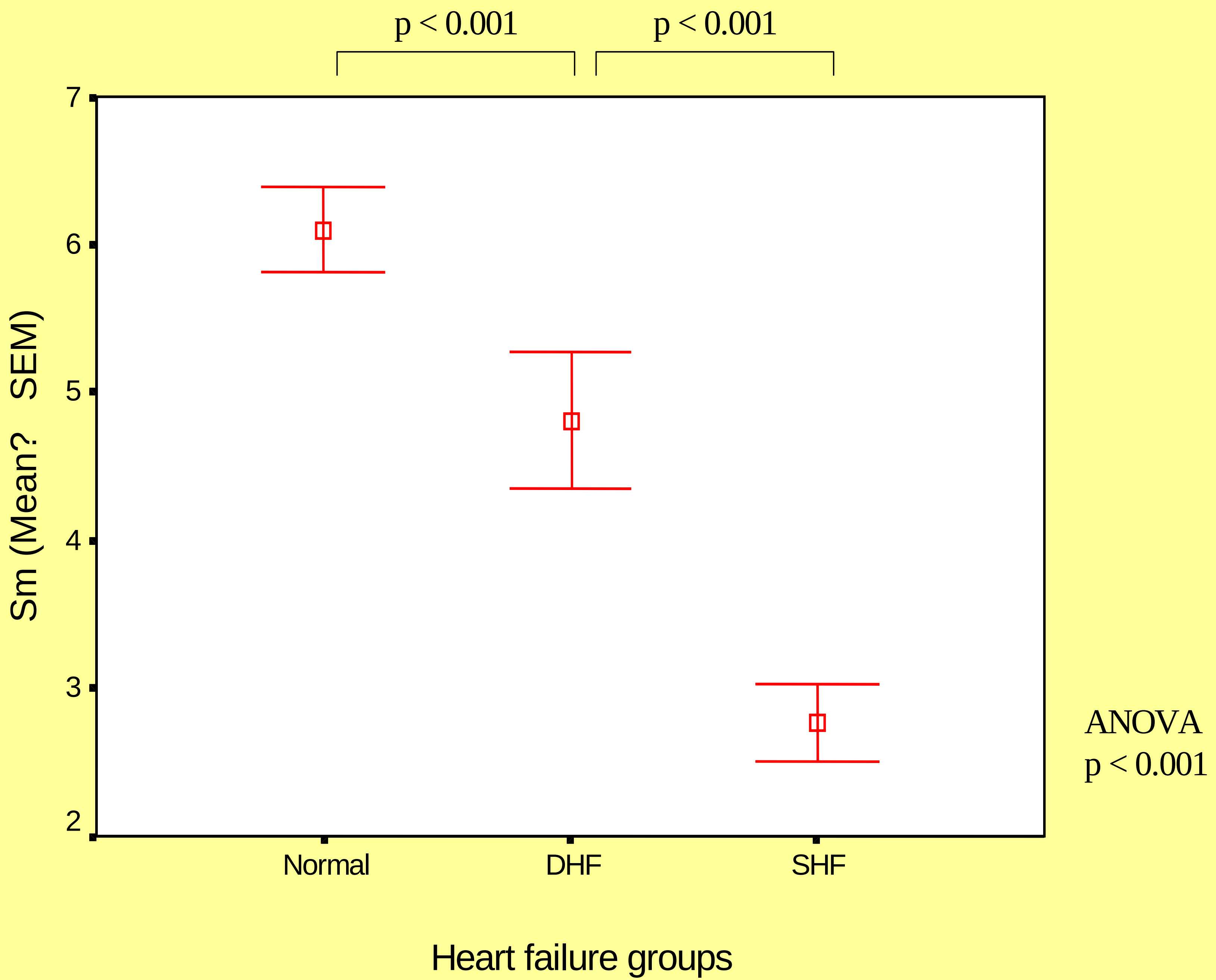
Is ventricular systolic function really normal in HFNEF? Assessment by TDI

- Yip GWK, Wang M, Ho PY, Sanderson JE. Eur J Echocardiogr 2000;2:S60

Measurement of mitral ring motion- four sites







Yip G, Wang M, Ho P Sanderson JE *Heart 2002;87:121-125*

Long axis function in 150 patients with HFNEF/DHF

(Sanderson JE, Wang M, Wang T et al Heart 2008)

	Age-matched Normals	DHF	P value
Sm (cm/s)	5.6 ± 1.0	4.5 ± 1.2	<0.0005
Em (cm/s)	5.7 ± 1.5	3.7 ± 1.6	<0.0005
E/Em (E/E’)	12 ± 3	20± 9	<0.0005
LVEF (%)	62 ± 8	53 ± 13	<0.0005

So long axis systolic function is not normal in patients with HF and "preserved" LV systolic functions.

Confirmation:

- Petrie MC et al. "Diastolic heart failure" or heart failure caused by subtle left ventricular systolic dysfunction. Heart 2002;87:29-31.
- Nikitin NP et al. Color tissue Doppler-derived long-axis left ventricular function in heart failure with preserived global systolic function. Am J Cardiol 2002;90:1174-7
- Yu CM et al. Progression of systolic abnormalities in patients with "isolated" diastolic heart failure and diastolic dysfunction. Circulation 2002;105:1195-201.
- Bruch C et al. Doppler tissue analysis of mitral annular velocities: evidence for systolic abnormalities in patients with diastolic heart failure. J Am Soc Echocardiogr 2003;16:1031-6.
- Vinereanu D et al. "Pure" diastolic dysfunction is associated with long-axis systolic function. Implications for the diagnosis and classification of heart failure. Eur J Heart Fail 2005; epub May 24.

Conclusion:

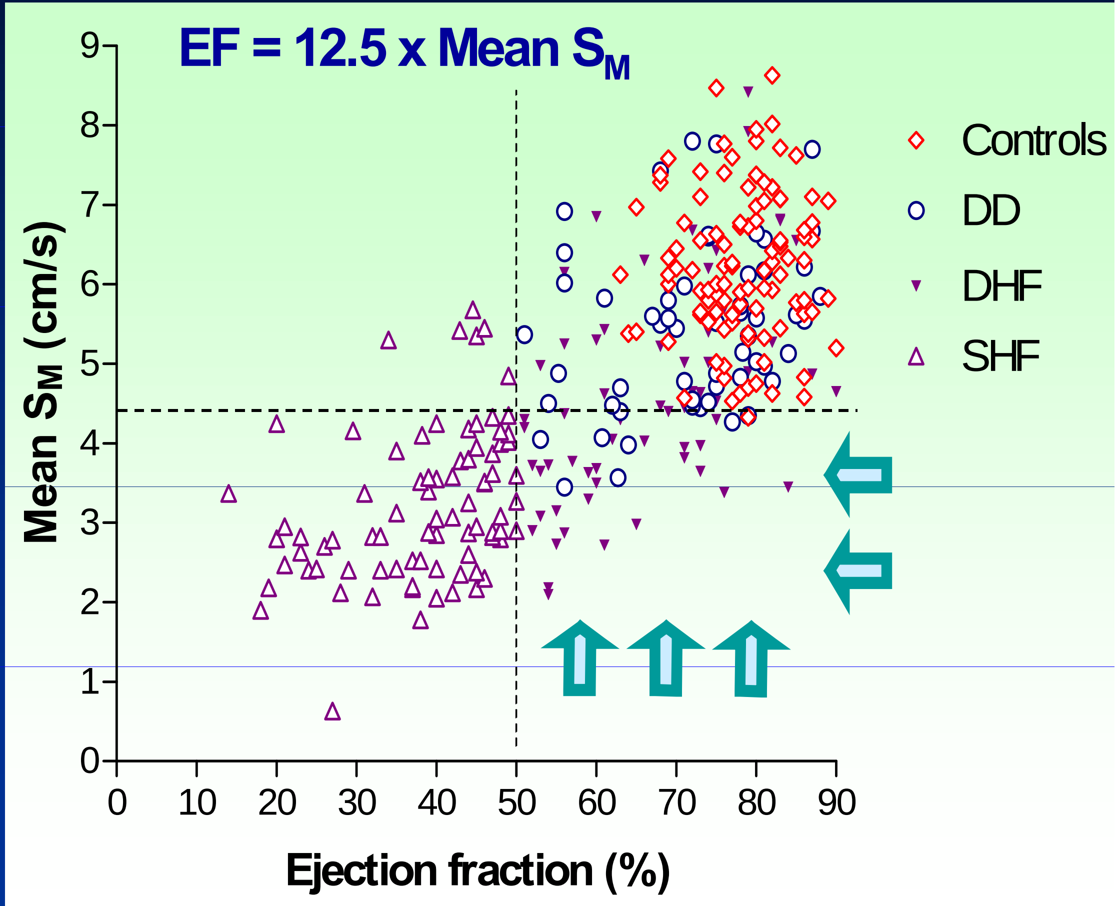
“Thus subtle abnormalities of systolic function are present in patients with heart failure and a normal left ventricular ejection fraction, and there appears to be a continuum of systolic function between those with truly normal, mildly impaired (labelled diastolic heart failure), and obviously abnormal left ventricular systolic function. Isolated diastolic dysfunction is uncommon.”

Yip G, Wang M, Zhang Y, Fung JWH, Ho P Sanderson JE Left ventricular long axis function in diastolic heart failure is reduced in both diastole and systole: time for a redefinition? *Heart 2002;87:121-125*

i.e. Systolic function is not normal despite “normal” LVEF

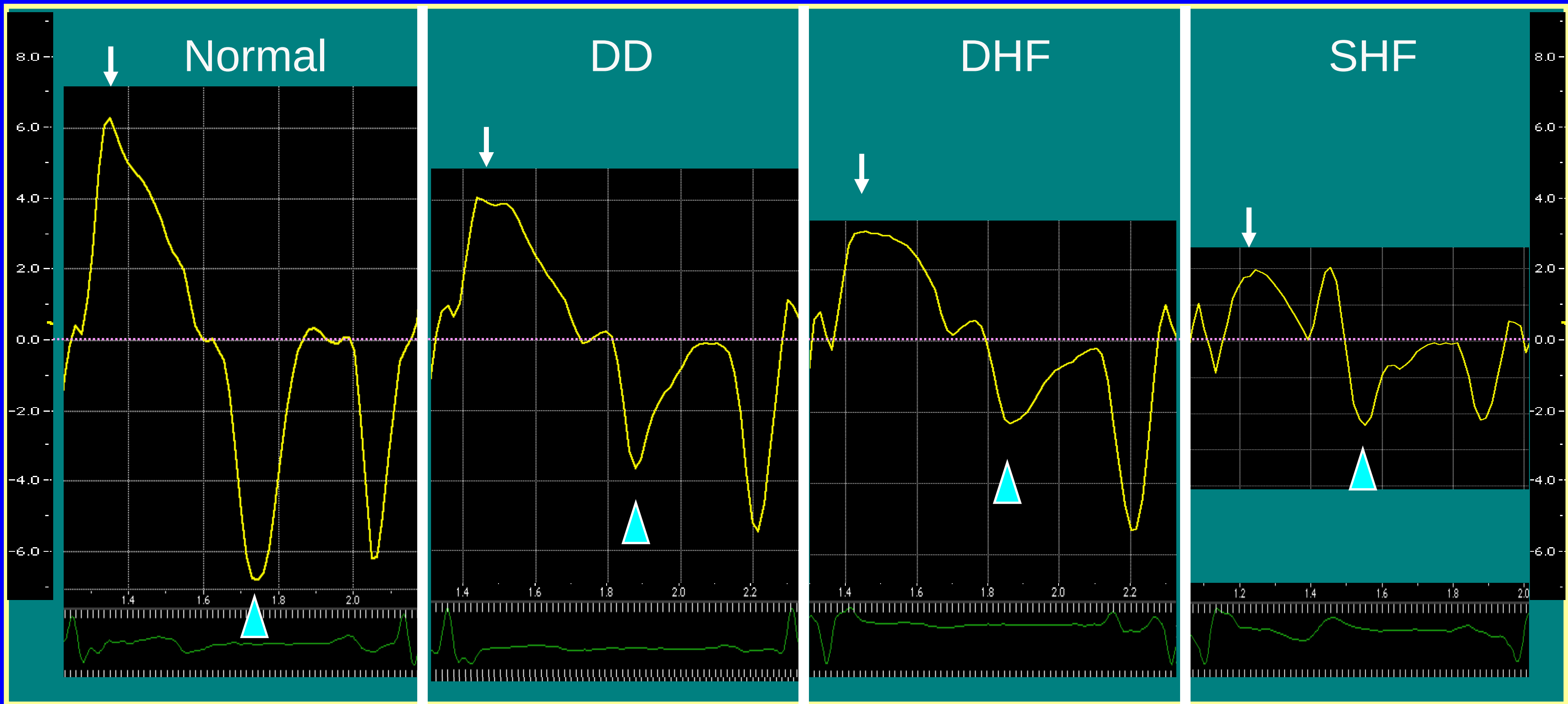
Systolic Abnormalities in Diastolic Dysfunction and Diastolic Heart Failure

- N = 339
- C = 106, DD = 68
  DHF = 73, SHF= 92
- S_M : C>DD>DHF>SHF
- Abnormal S_M is present in 52% of DHF and 14% with DD (-2SD)



Yu CM et al, Circ 2002

Systolic Abnormalities in Diastolic Dysfunction and Diastolic Heart Failure



Em : Normal > DD > DHF = SHF

Sm : Normal > DD > DHF > SHF

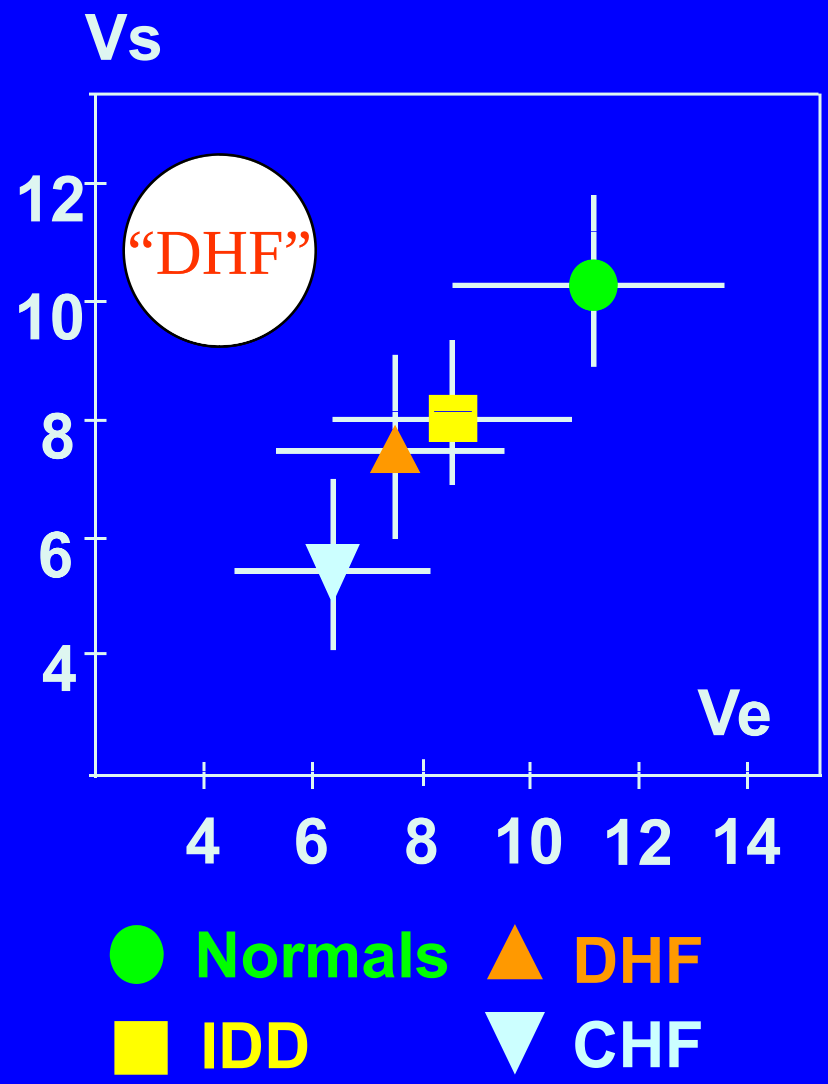
Yu CM et al, Circ 2002

LV long-axis systolic and diastolic velocities :
No evidence for "pure" diastolic dysfunction

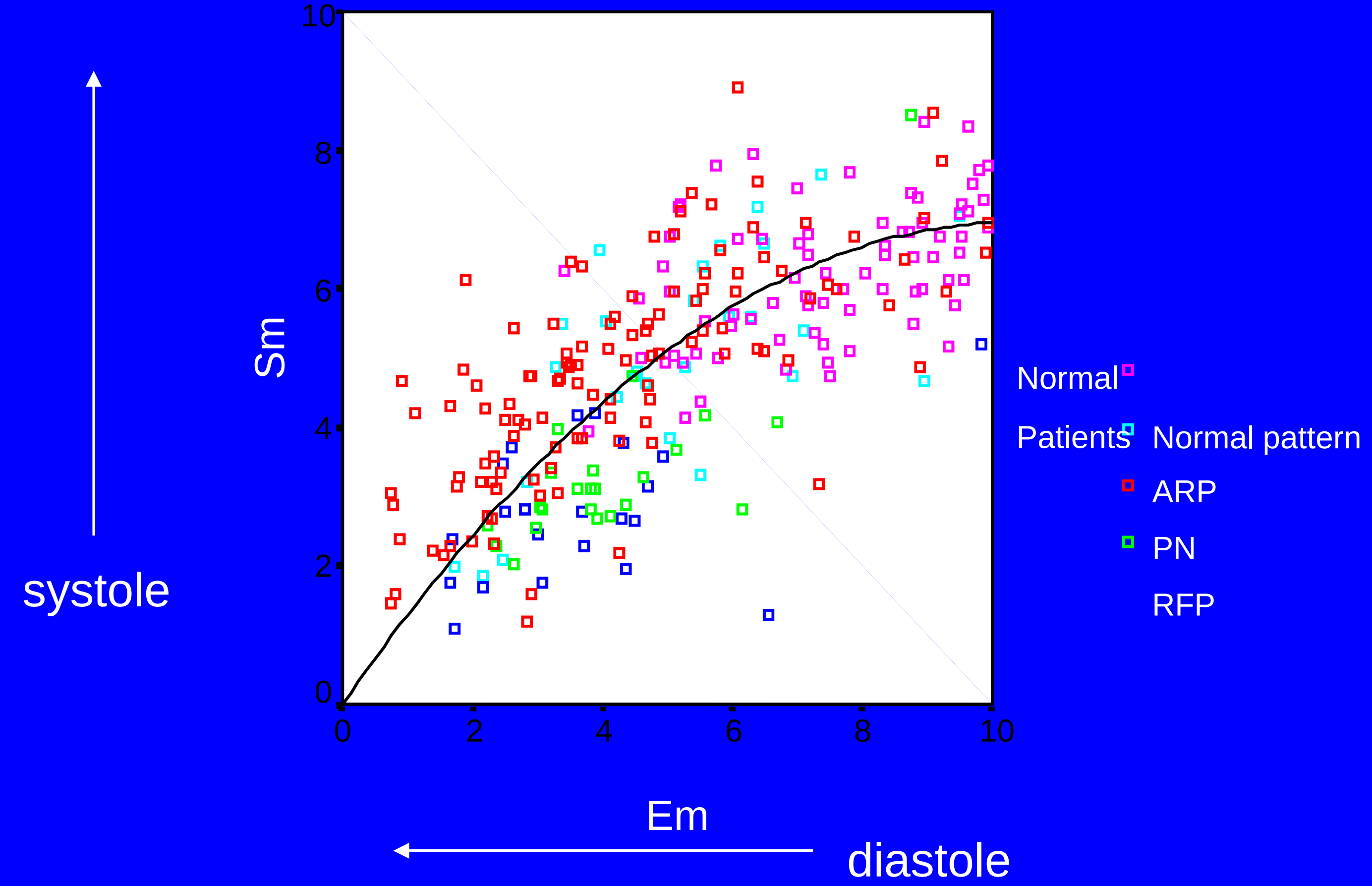
Vinereanu D,

Eur J Heart Failure

2005;7:820-828.



“So that the coming together depends on the going apart;the systole depends on the diastole; the flow depends on the ebb.” DH Lawrence

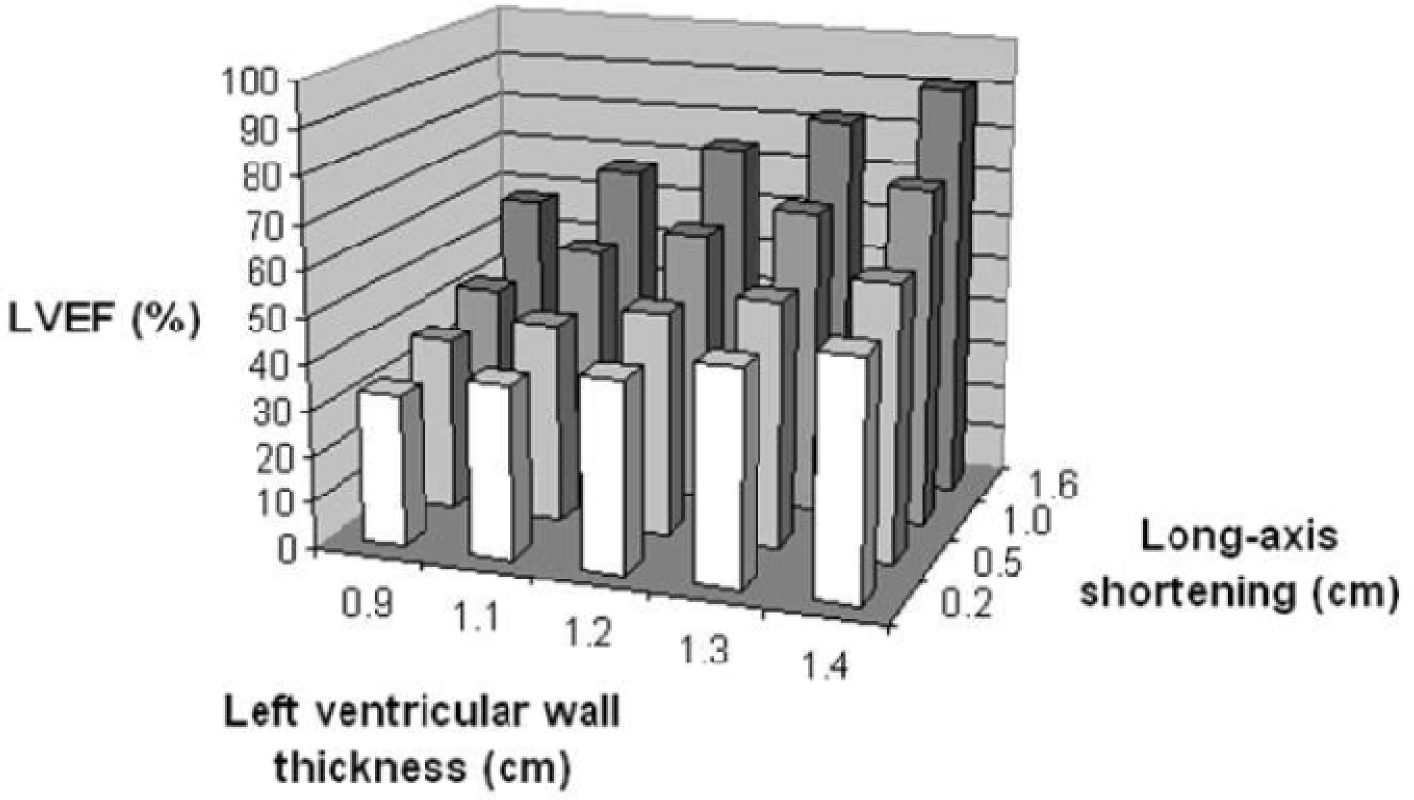


Yip G, Zhang Y, Tan P, Wang M, Ho P, Brodin L-A, Sanderson JE

Clinical Science 2002;102:515-22

Why is the ejection fraction normal?
The effect of LVH

Figure 1. Inter-relationship of LVEF, long-axis shortening & LVH



A novel mechanism of heart failure with normal ejection fraction

McIver and Townsend Heart 2008

WHY IS THE LVEF NORMAL IN HFNEF?

Apply:
Internal volume = external volume – LV wall volume

to the definition of ejection fraction:

$$\text{Ejection fraction} = \frac{\text{End-diastolic internal volume} - \text{End-systolic internal volume}}{\text{End-diastolic internal volume}}$$

which gives:

$$\text{Ejection fraction} = \frac{\text{End-diastolic external volume} - \text{End-systolic external volume}}{\text{End-diastolic external volume} - \text{LV wall volume}}$$

Thus if the external cardiac volumes remain constant, then any increase in LV wall volume must necessarily raise ejection fraction.

From : Manistry CH & Francis DP
Ejection fraction- a measure of desperation? Heart 2008

Table: comparison of clinical features of SHF and HFNEF

	HF with reduced EF (SHF)	**HF with normal EF (HFNEF)**
Gender	M>F	F>M
Age	50-60 years	60-70 years
Aetiology	Myocardial infarction; idiopathic DCM	Hypertension ± diabetes; Atrial fibrillation Transient ischaemia
Clinical progress	Persistent HF	Often episodic HF
Ventricular remodeling (increased LV volumes)	+++	0
LVH	+/-	+++
Dyssynchrony	common	? less common
Mitral inflow pattern	RFP or ARP	ARP
Peak mitral annular systolic velocity	Markedly reduced	Moderately reduced
Peak mitral annular early diastolic velocity	Markedly reduced	Moderately reduced
LA pressure	raised	raised
LA volume	increased	increased

DCM= dilated cardiomyopathy; HF= heart failure; RFP= restrictive filling pattern; ARP= abnormal relaxation pattern.

Sanderson JE Review: heart failure with a normal ejection fraction
Heart 2007;93:155-158

SHF vs HFNEF the importance of remodeling.

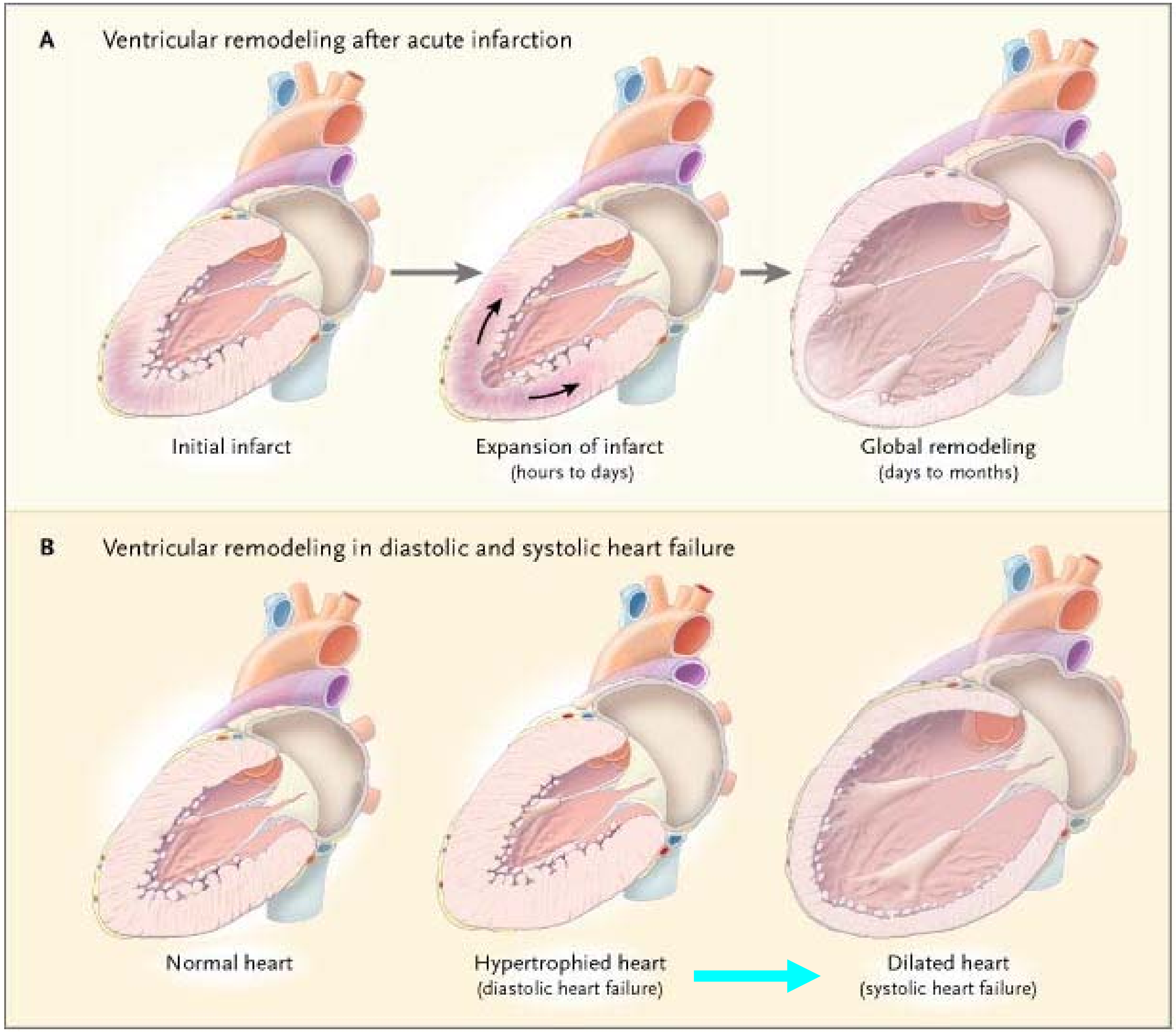


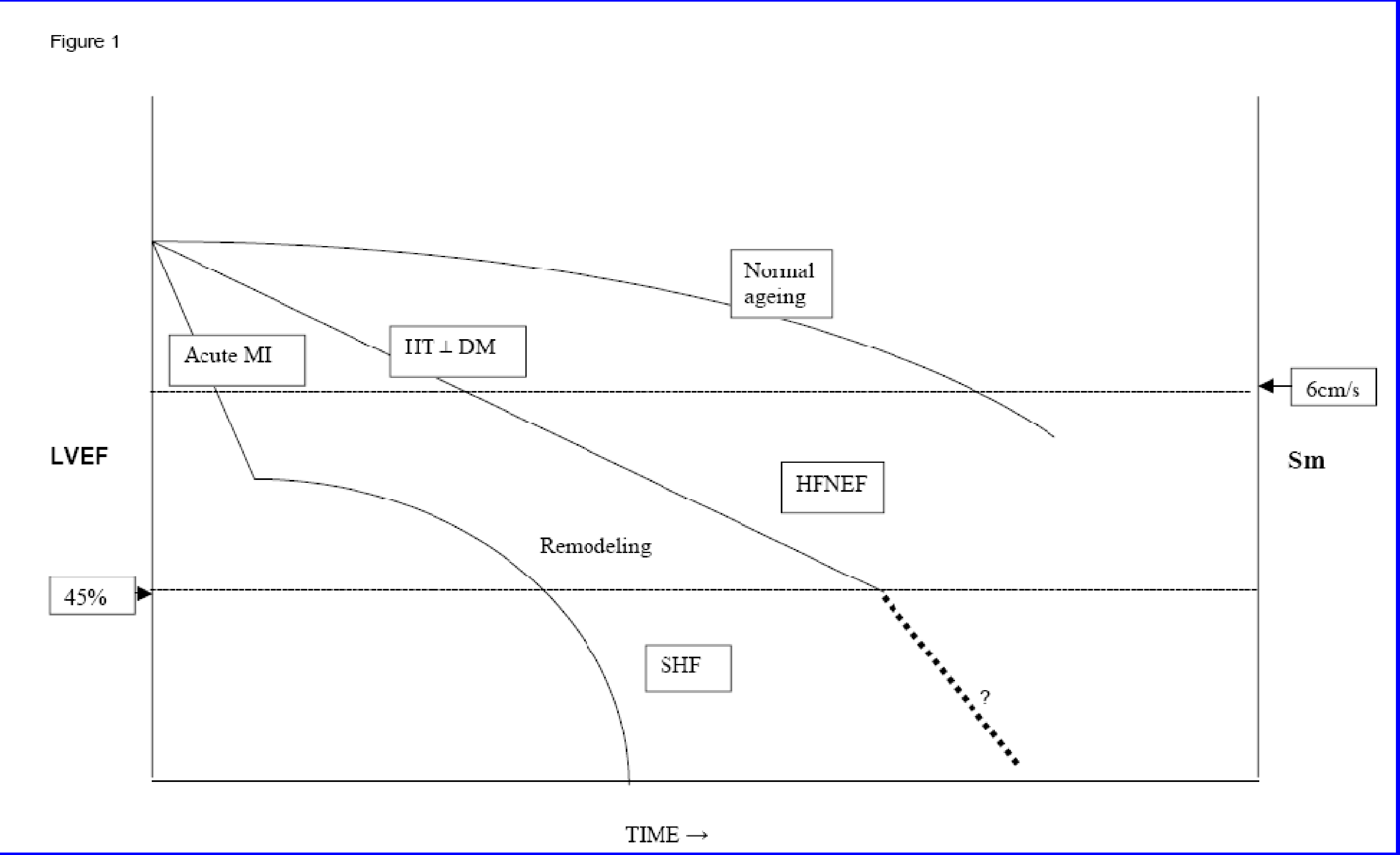
Table 1. Characteristics of Patients.*

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.

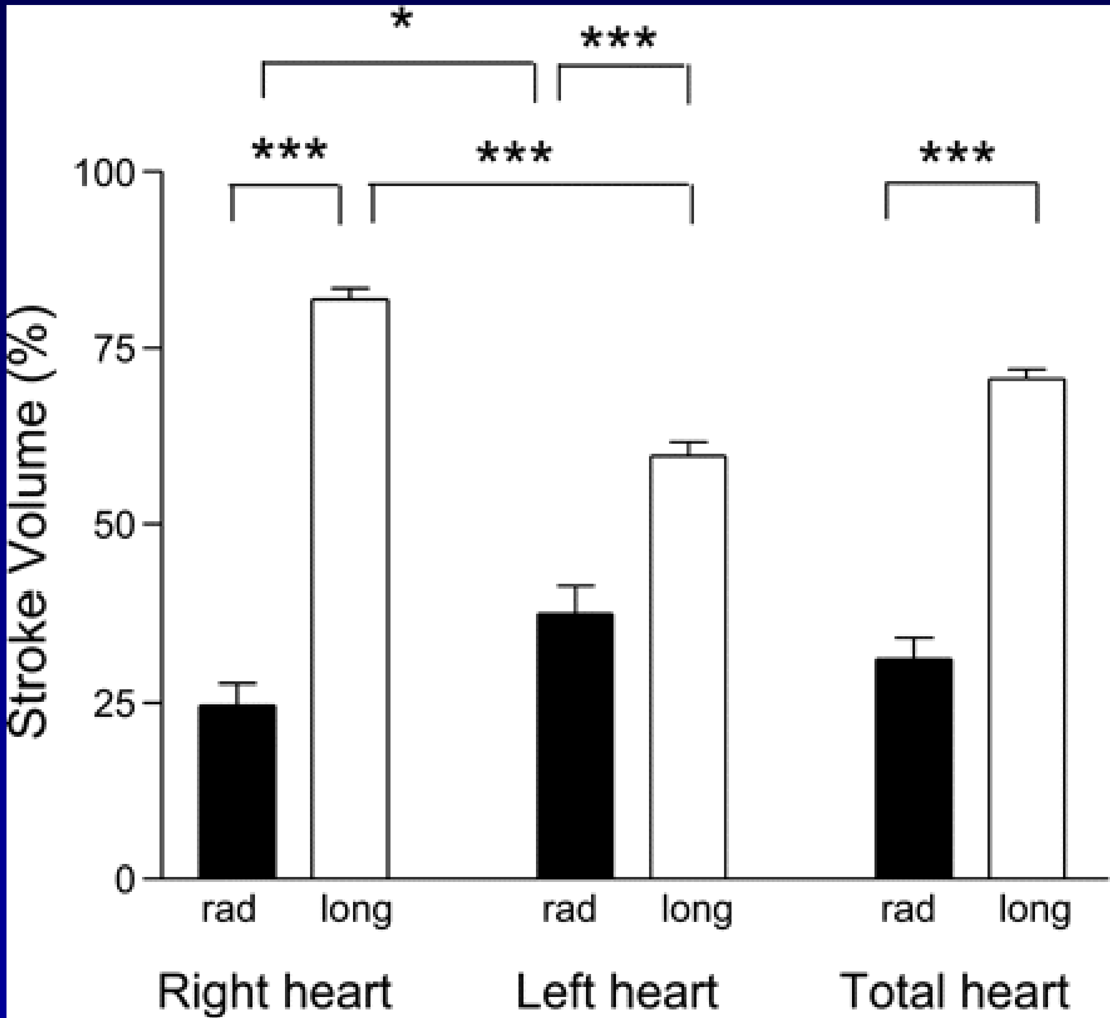
Bhatia R et al. N Engl J Med 2006;355:260-269

HEART FAILURE – PHENOTYPE RELATES TO DEGREE OF REMODELING AND AETIOLOGY

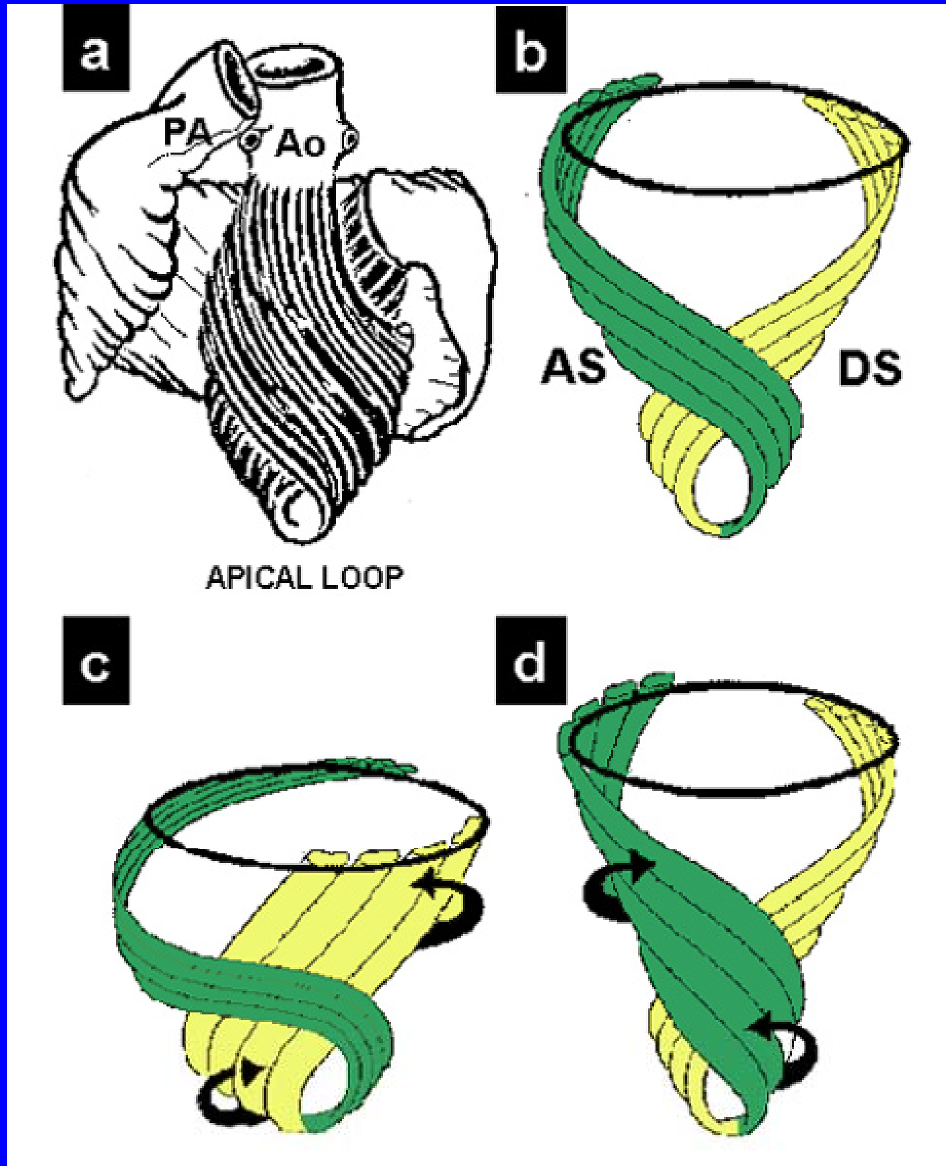


Sanderson JE Review: heart failure with a normal ejection fraction Heart 2007;93:155-158

Importance of longitudinal ventricular function.



Carlsson, M. et al. Am J Physiol Heart Circ Physiol 2007;293: H636-H644



SEQUENTIAL CONTRACTION OF THE DESCENDENT AND ASCENDENT SEGMENTS PRODUCE "SYSTOLIC VENTRICULAR FILLING"
Torrent-Guasp et al Eur J Cardiovasc Surgery 2004;25:376-386

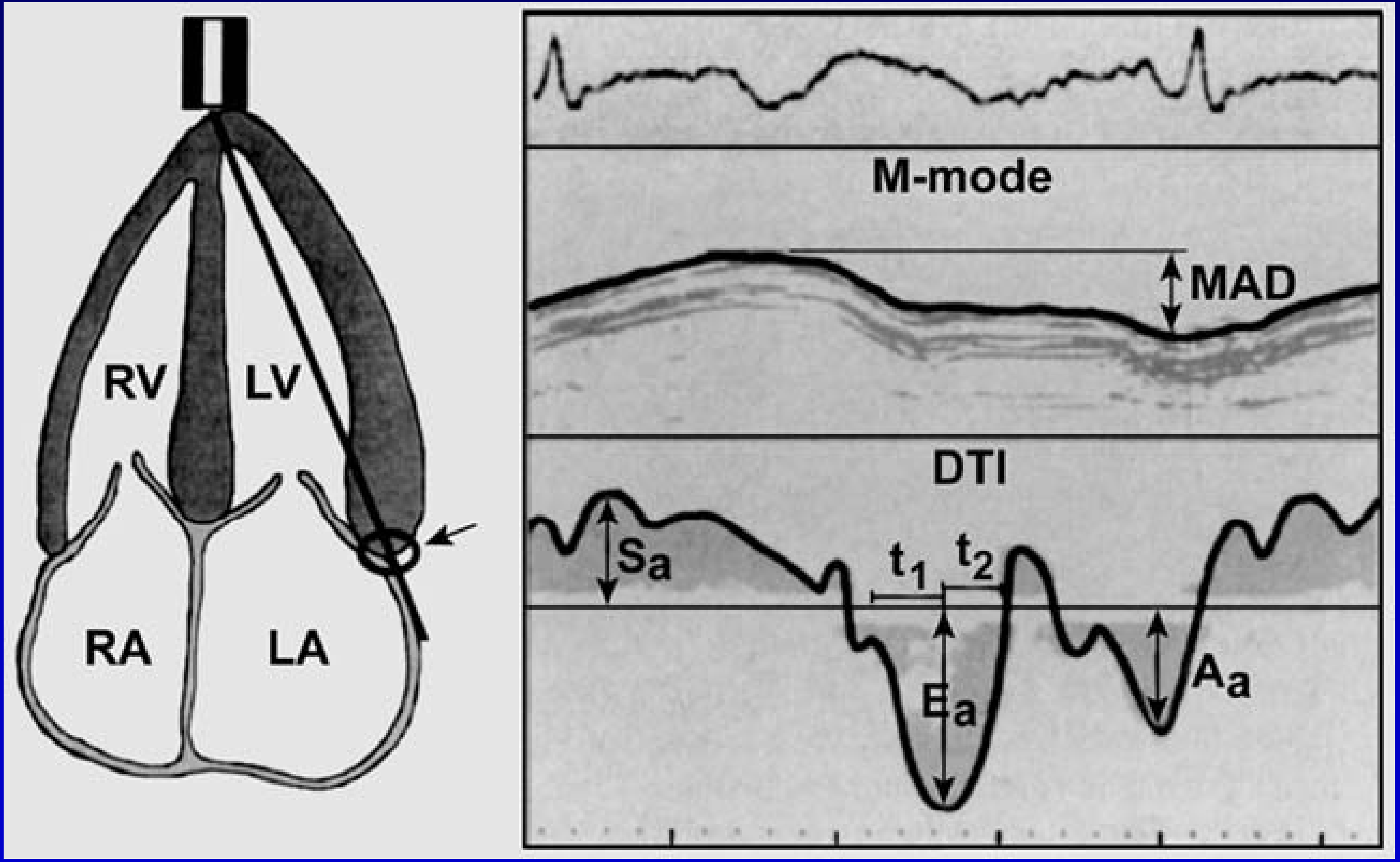
Atrioventricular plane displacement is the major contributor to left ventricular pumping in healthy adults, athletes, and patients with dilated cardiomyopathy.

Carlsson et al. Am J Physiol Heart Circ Physiol Nov 10 2006 [ePub ahead of print]

- C-MRI study

	SV mls	***AVPD mm***	***SV AVPD%***
athletes	140±4	17±1	57±2
DCM	72±7	7±1	67±4
controls	116±6	16±0	60±2

Mitral Annular Velocity
M-mode and Tissue Doppler



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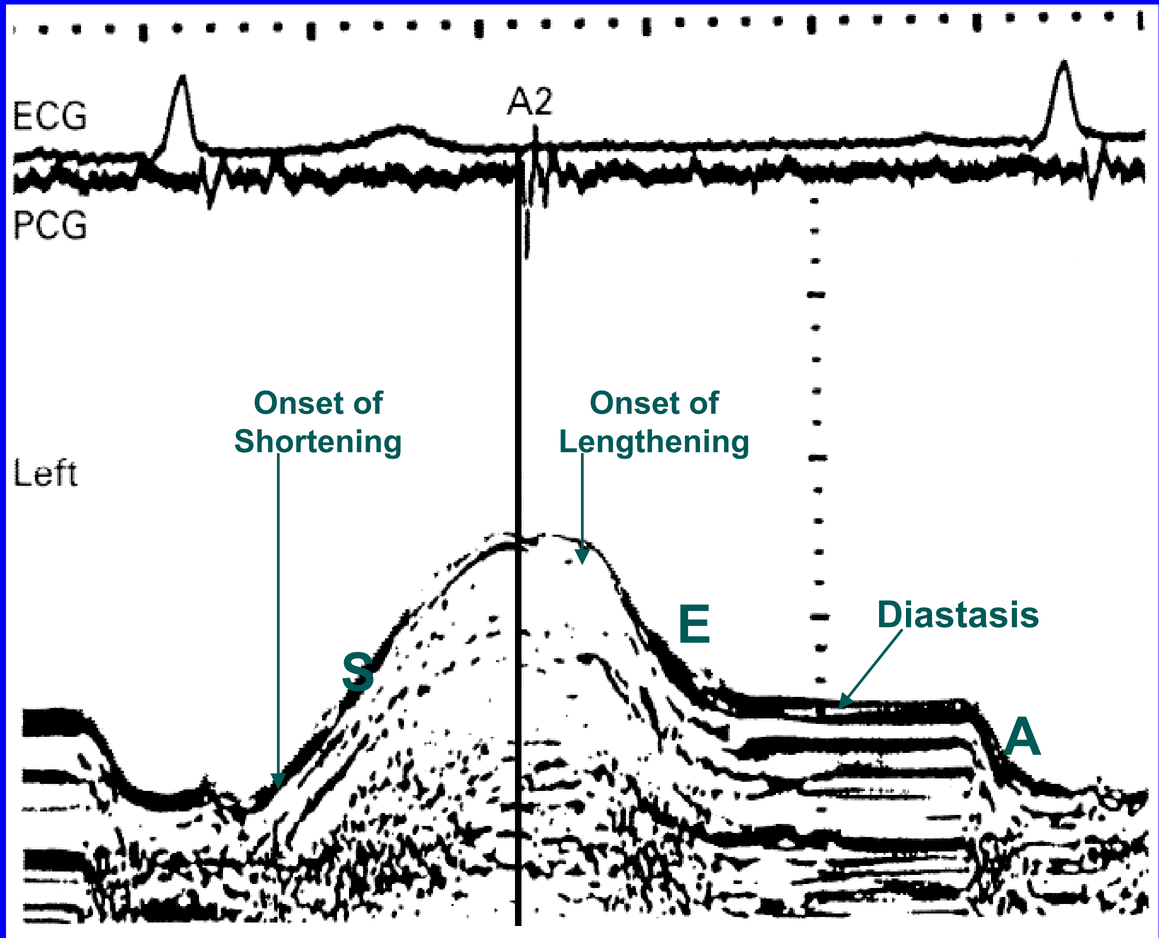
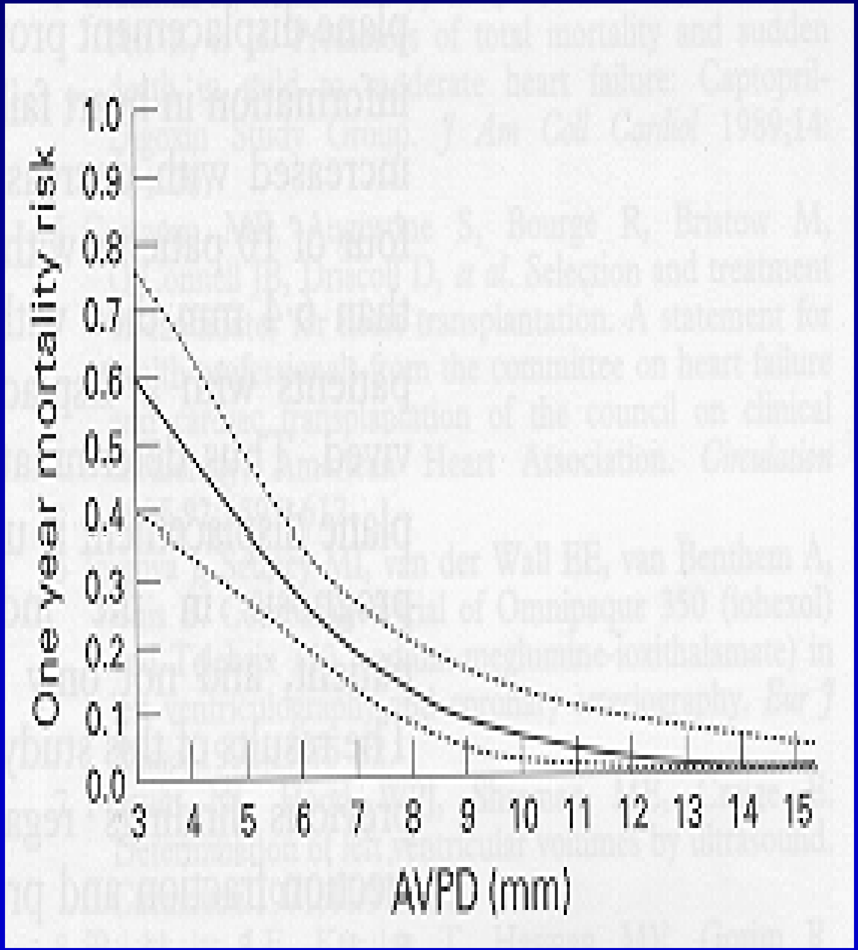
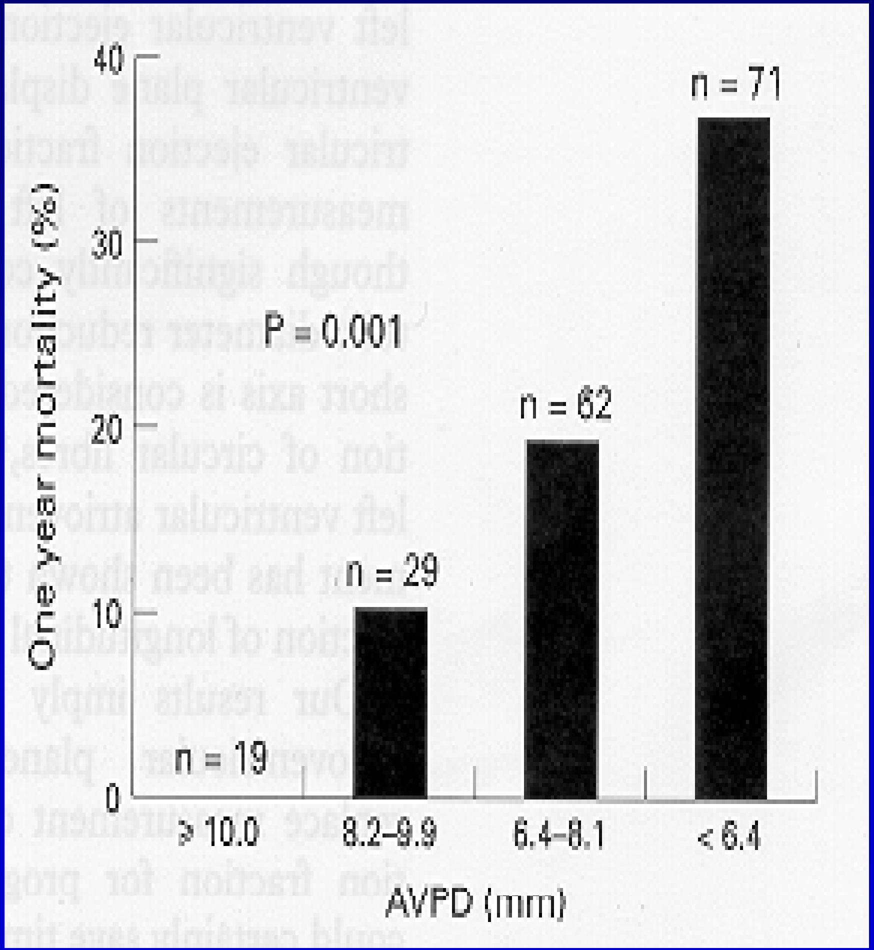
Normal Long Axis (M-mode)



Henein MY. Heart 1997;77:338-345

Long Axis in heart failure-mortality





EF (%)= (AVPD (mm) x 5.5) - 5

(**Willenheimer** et al Heart 1997;78:230-236)

Ventricular long-axis function is of major importance for long-term survival in patients with heart failure

B Grüner Sveälv, E L Olofsson and B Andersson

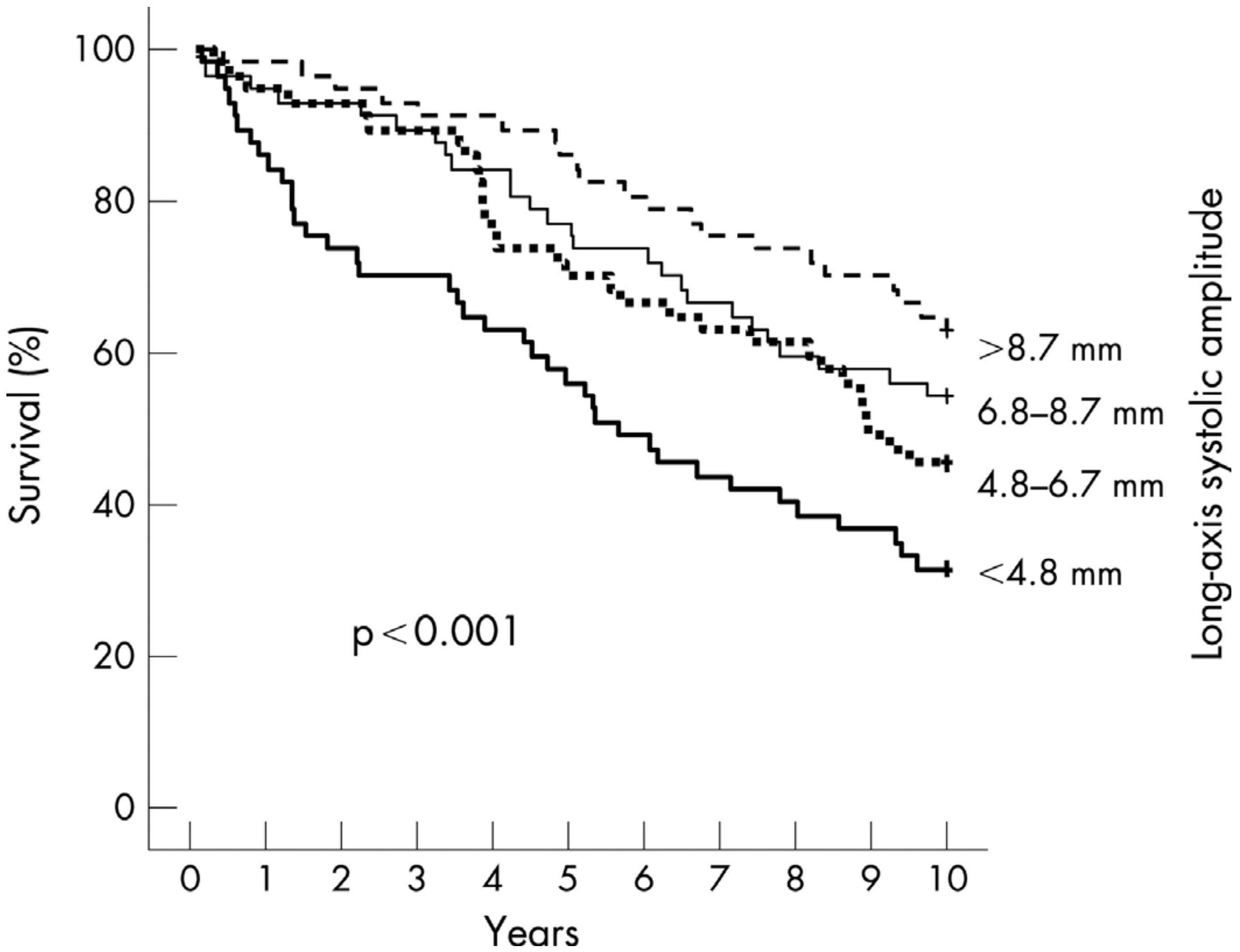
Heart 2008;94;284-289; originally published online 17 Jun 2007;
doi:10.1136/hrt.2006.106294

Table 2 Predictors of 10-year mortality in 228 patients with chronic heart failure

	Univariate association		Multivariate association	
Predictors	**p Value**	**HR (95% CI)**	**p Value**	**HR (95% CI)**
Gender	0.20	0.76 (0.50 to 1.16)	0.32	
Age	0.55	0.99 (0.97 to 1.01)	0.53	
Heart rate (bpm)	0.42	1.02 (0.97 to 1.08)	0.51	
SBP (mm Hg)	0.002	0.93 (0.89 to 0.98)	0.21	
LA (mm)	0.001	1.22 (1.08 to 1.36)	0.30	
LVEDD (mm)	<0.001	1.30 (1.20 to 1.42)	0.06	
SAX FS (%), n = 199	<0.001	0.72 (0.65 to 0.81)	0.16	
LVLAX syst ampl (mm)	<0.001	0.83 (0.77 to 0.89)	0.024	0.80 (0.66 to 0.97)
LVLAX syst vel (cm/s)	<0.001	0.71 (0.60 to 0.83)	0.12	
LVLAX EDFV (cm/s)	0.014	0.88 (0.79 to 0.97)	0.30	
RV LAX syst ampl (mm)	<0.001	0.93 (0.89 to 0.97)	0.60	
RV LAX syst vel (cm/s), n = 206	0.007	0.90 (0.84 to 0.97)	0.24	
RV LAX EDFV (cm/s)	0.001	0.88 (0.81 to 0.94)	0.09	

Univariate and multivariate Cox regression analysis of 10 years' mortality. Calculations were performed on continuous data. Changes of five units were used for age, heart rate, systolic blood pressure, left atrial dimension, left ventricular end-diastolic dimension, and short-axis fractional shortening. Remaining variables have low numeric value and changes are expressed for one unit.
EDFV, early diastolic filling velocity; LA, left atrium; LVEDD, left ventricular end-diastolic dimension; LVLAX, left ventricular long axis; RV LAX, right ventricular long axis; SAX FS, short-axis fractional shortening; SBP, systolic blood pressure.

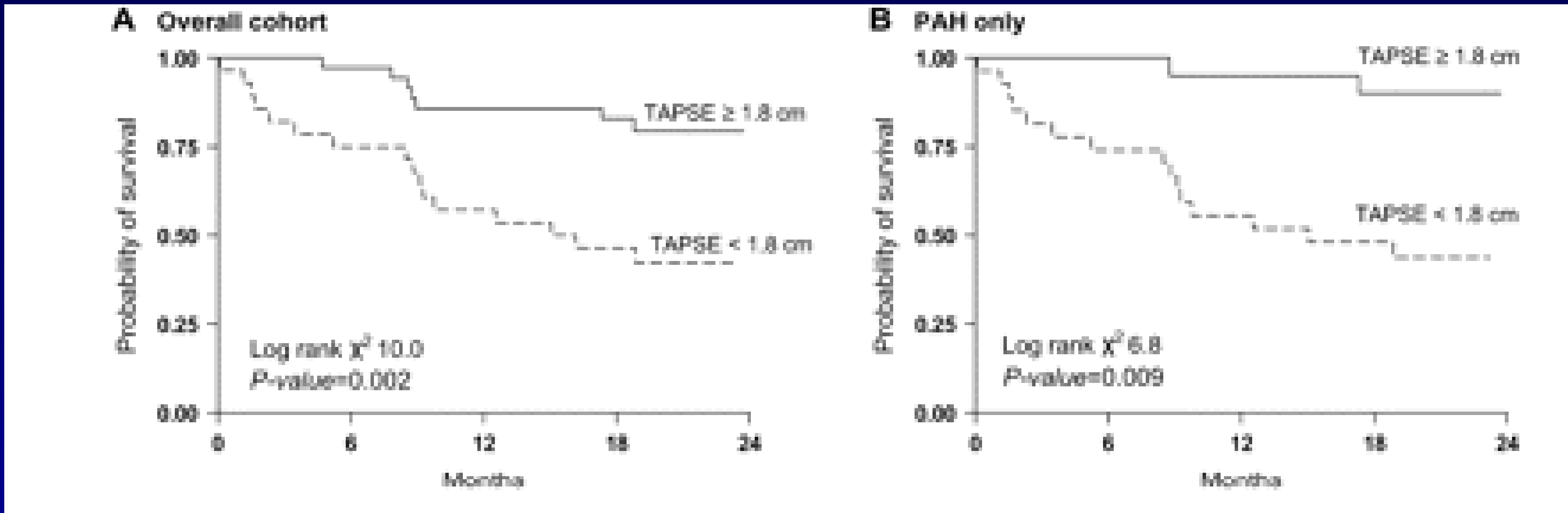
Figure 1 Survival curves are displayed for each quartile of left ventricular long-axis systolic amplitude. There was an overall difference between the curves as assessed by the log-rank test (p8.7 mm. Q3 vs Q4, hazard ratio (HR) = 0.72 (95% confidence interval 0.41 to 1.29), p = 0.27. Q2 vs Q4, HR = 0.76 (0.57 to 0.99), p = 0.049. Q1 vs Q4, HR = 0.72 (0.60 to 0.86), p



Svealv, B G. et al. Heart 2008;94:284-289

Heart ONLINE

The RV: TAPSE and survival

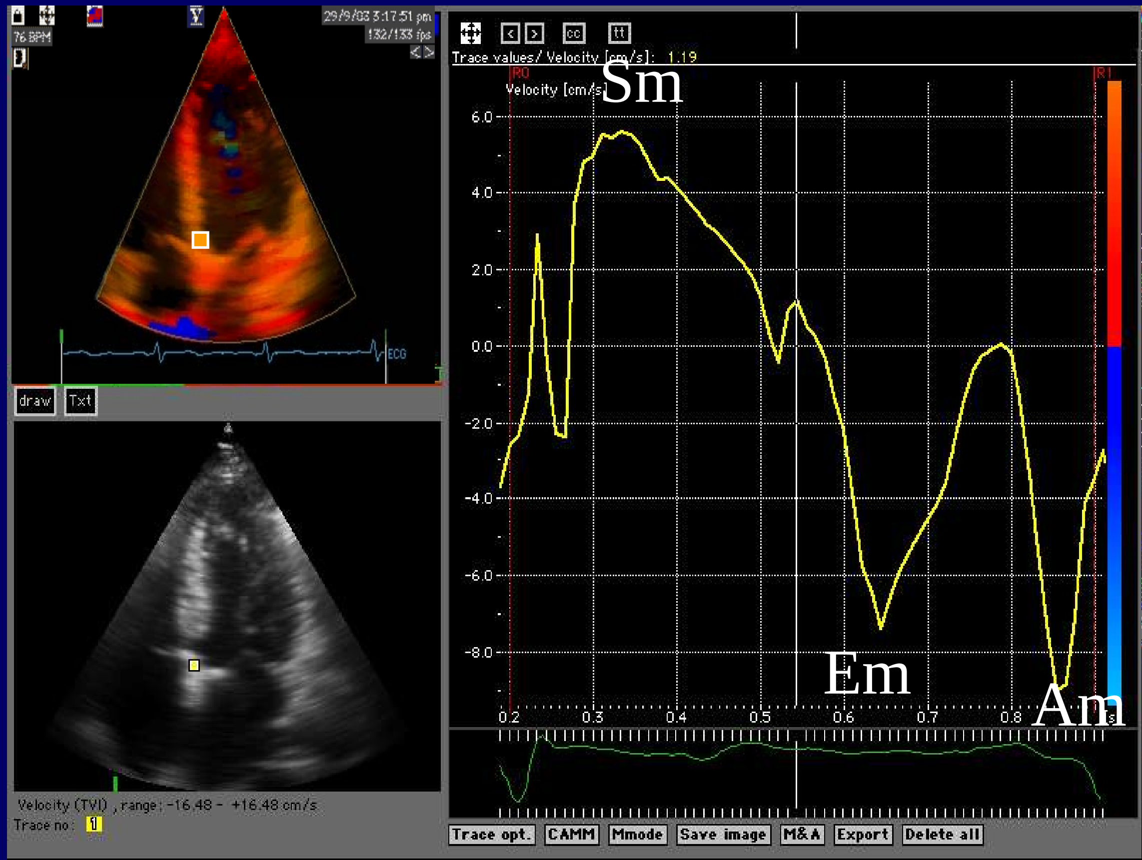


TAPSE ≥ 1.8 cm (N)	35	34	30	29	23	17	17	16	15	15
TAPSE < 1.8 cm (N)	28	21	16	13	10	30	23	18	16	13

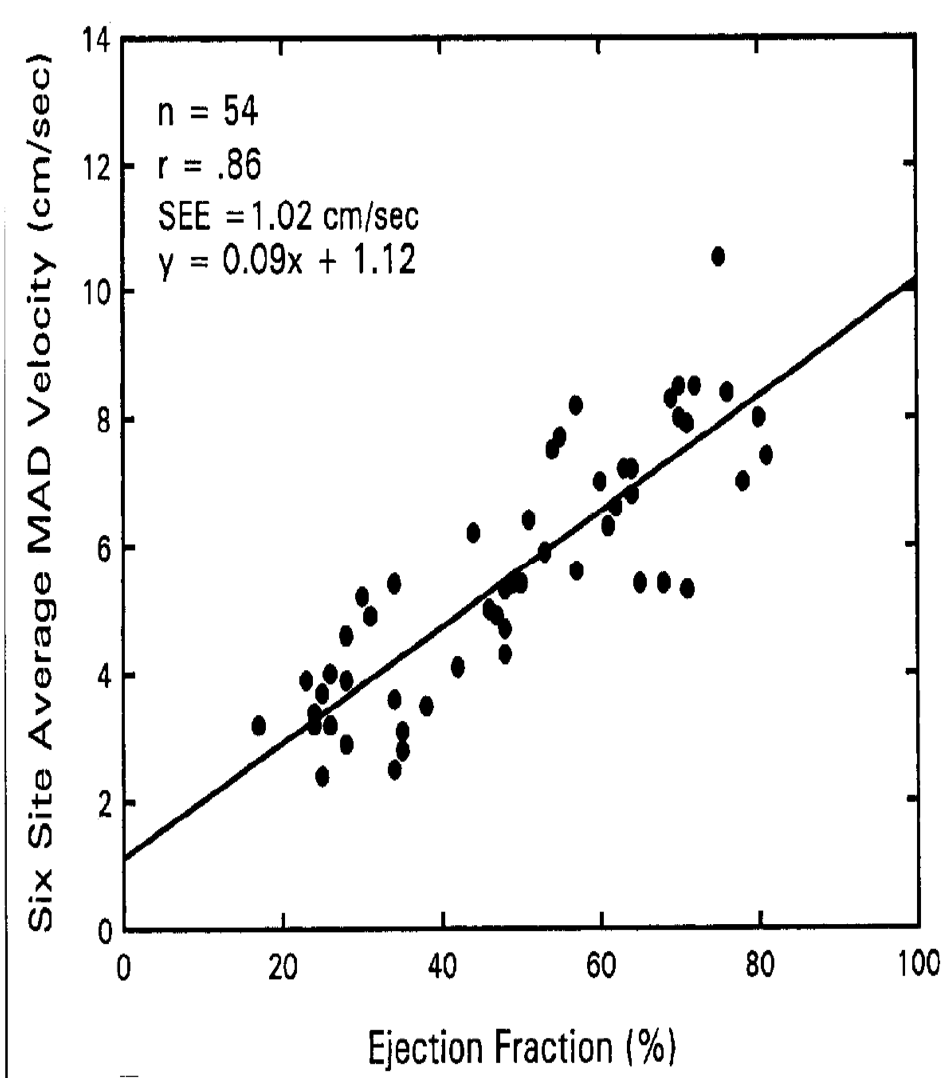
Forfia PR et al Am J Resp Crit Carae Med 2006;174:1034

Tissue Doppler Imaging
the alternative to LVEF

- Sm
- Em
- Am.



TDI in global function



- 55 pts. Aged 56 ± 15 yrs

(1 calcified annulus excluded)

- EF ≈ 8.2 (Mean Sm) + 3% & correlated well with EF from RNA

- Sm 5.4 cm/s predicts EF>50% (6 sites) sens 88%, spec 97%

Gulati VK. AJC 1996;77:979-984

TDI and SRI can detect systolic dysfunction when LVEF is normal

- DHF/HFNEF
- Hypertrophic cardiomyopathy
- HT with LVH
- Diabetes
- Valvular Heart Disease -MR and AS
- Amyloid
- Freidrich's ataxia
- Tetralogy of Fallot

Conclusion:

"Thus subtle abnormalities of systolic function are present in patients with heart failure and a normal left ventricular ejection fraction, and there appears to be a continuum of systolic function between those with truly normal, mildly impaired (labelled diastolic heart failure), and obviously abnormal left ventricular systolic function. Isolated diastolic dysfunction is uncommon."

Yip G, Wang M, Zhang Y, Fung JWH, Ho P Sanderson JE Left ventricular long axis function in diastolic heart failure is reduced in both diastole and systole: time for a redefinition? *Heart 2002;87:121-125*

Echo in Hypertension with LVH

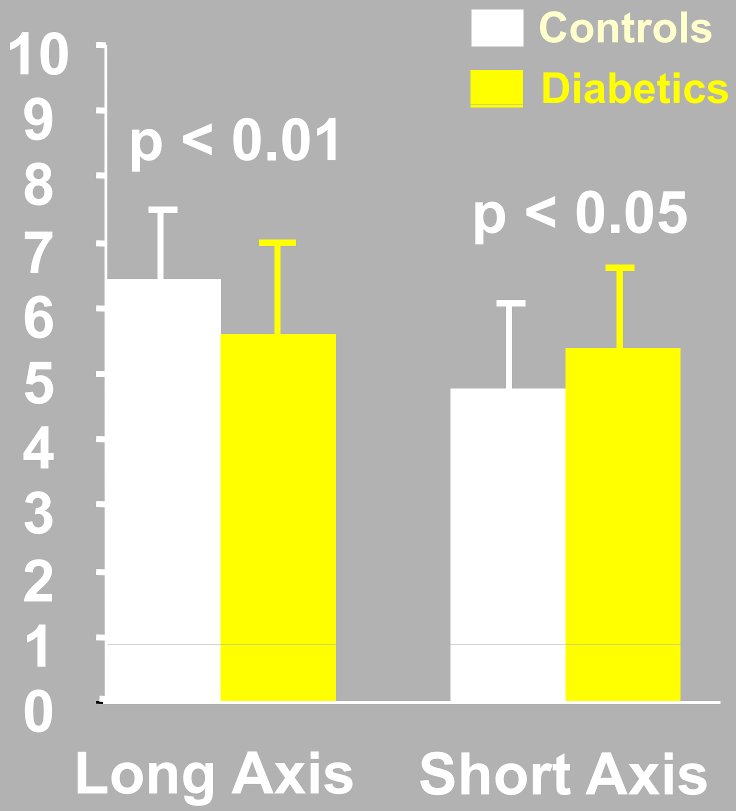
Wang et al J Hypertension 2005;23:183-191

Table 2 Echocardiographic variables in normals and patients

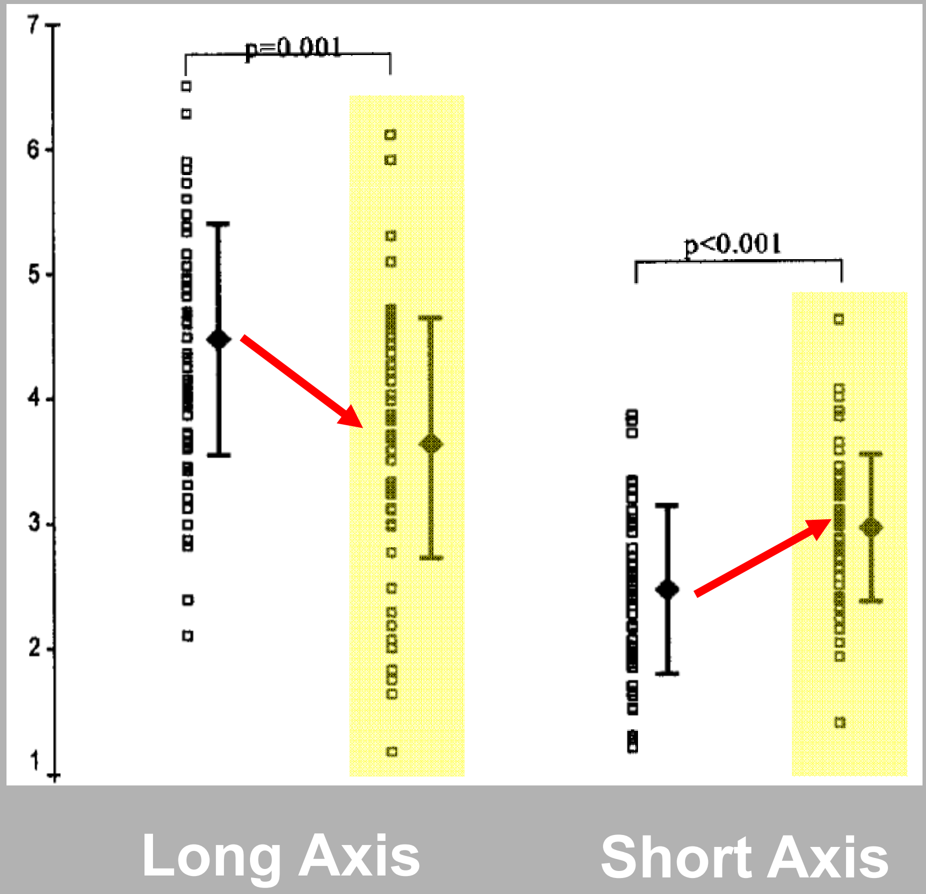
	Normals ($n = 78$)	Patients ($n = 174$)
Age (years)	62 (60–65)	62 (60–64)
Female/male (number)	44/34	84/90
Body mass index (kg/m^2)	23.9 (23.0–24.8)	23.8 (23.1–24.6)
Two-dimensional variables		
IVSd (cm)	1.13 (1.08–1.19)	1.44 (1.39–1.50)***
LVPWd cm)	1.02 (0.98–1.06)	1.30 (1.25–1.34)***
LVDd (cm)	4.57 (4.46–4.68)	5.17 (5.02–5.33)***
LVDs (cm)	2.93 (2.83–3.02)	3.69 (3.52–3.87)***
RWTI	0.45 (0.43–0.48)	0.52 (0.50–0.54)**
LADs (cm)	3.43 (3.33–3.52)	4.13 (4.02–4.24)***
LVMI (g/m^2)	127 (118–137)	240 (224–255)***
LVEF2D (%)	60.4 (58.5–62.2)	50.9 (49.1–52.7)***
FS (%)	36.2 (34.9–37.5)	29.7 (28.1–31.2)***
Tissue Doppler imaging		
Sm (cm/s)	5.89 (5.64–6.14)	4.49 (4.29–4.69)***
Em (cm/s)	6.78 (6.37–7.19)	4.14 (3.90–4.37)***
Am (cm/s)	7.59 (7.27–7.91)	6.47 (6.12–6.82)***
IVRTm (ms)	72.8 (69.1–76.6)	96.1 (92.5–99.8)*
Mitral inflow variables		
E (m/s)	0.71 (0.67–0.74)	0.75 (0.72–0.79)
A (m/s)	0.73 (0.70–0.77)	0.82 (0.79–0.86)**
DT (s)	0.19 (0.18–0.20)	0.21 (0.20–0.22)**
IVRT (s)	0.10 (0.09–0.10)	0.10 (0.10–0.11)
E/A	0.99 (0.93–1.05)	1.07 (0.97–1.18)
PN or RFP	0	30 (17%)***
Propagation velocity		
Vp (m/s)	54.9 (51.4–58.5)	40.5 (38.1–42.9)***
Left ventricular filling pressure		
E/Em	11.0 (10.3–11.7)	21.2 (19.4–23.0)***
E/Vp	1.45 (1.33–1.57)	2.02 (1.90–2.13)***

Diabetes

Systolic velocity at rest
cm/s



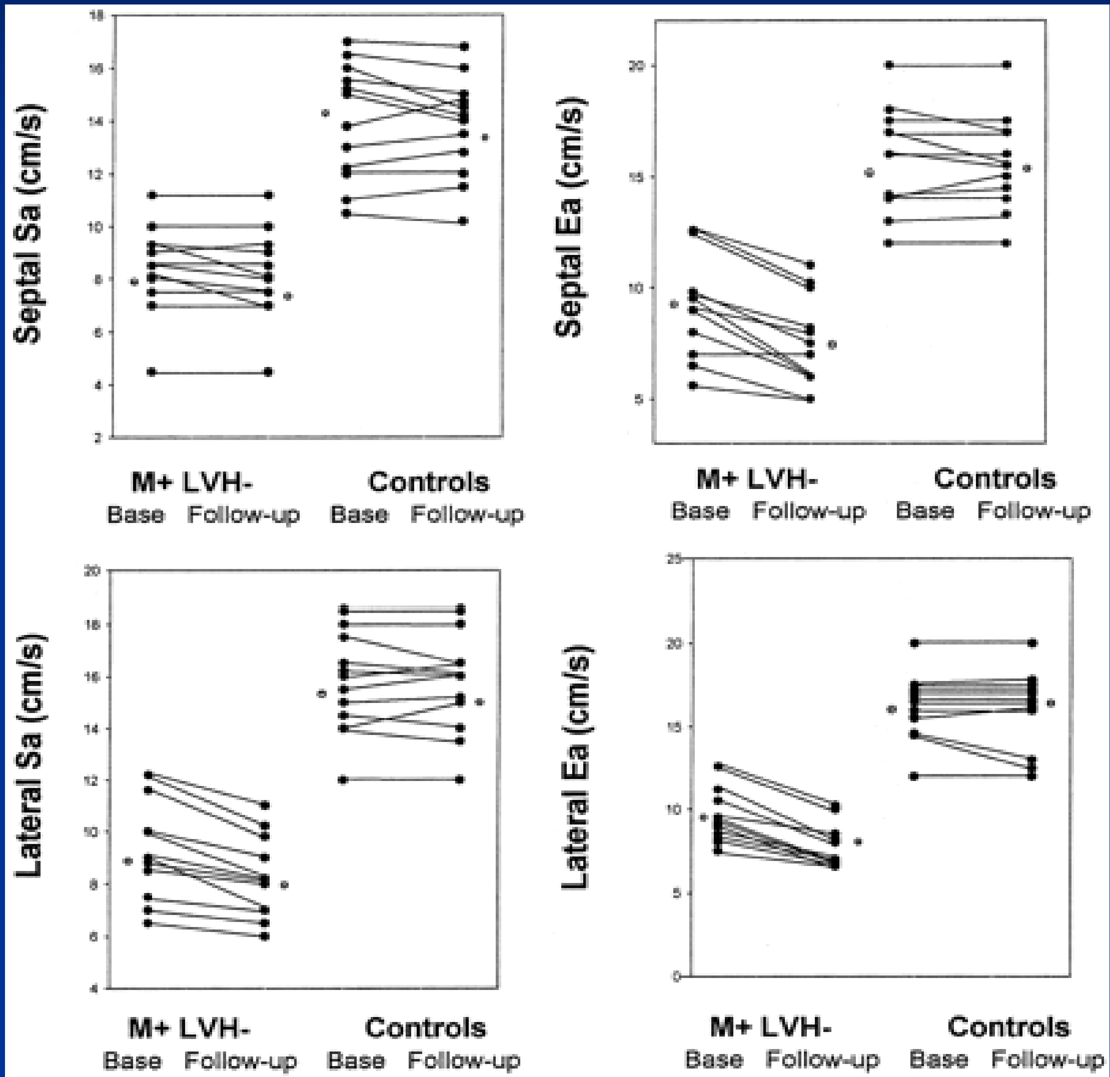
Vinereanu D et al,
Clinical Science 2003; 105: 591



Fang ZY et al,
Clinical Science 2004; 106: 53

TDI predicts the development of HCM in subjects with subclinical disease.

M+ is mutation Positive group

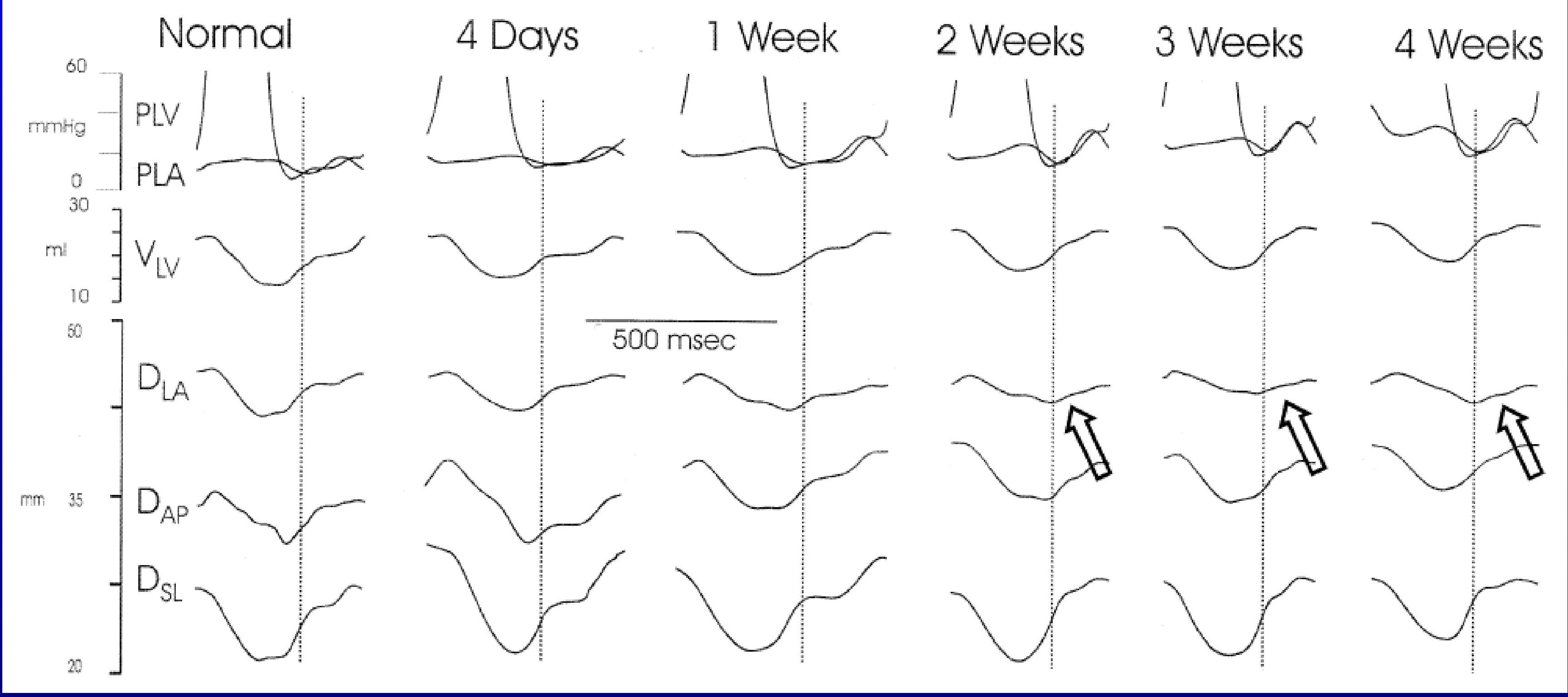


Nagueh et al Circulation 2003;108:395-398.

Diastolic Mitral Annular Velocity During the Development of Heart Failure

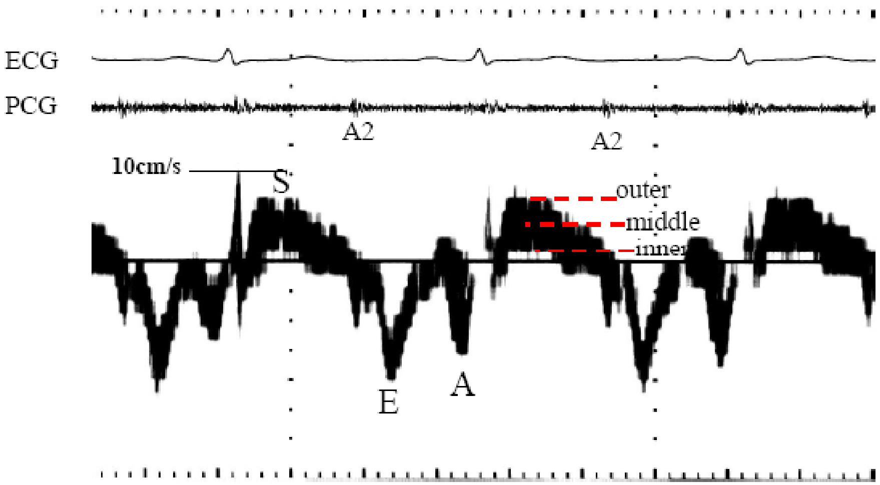
Hiroshi Hasegawa, MD, PHD, William C. Little, MD, Michiya Ohno, MD, PHD, Steffen Brucks, MD, Atsushi Morimoto, MD, PHD, Heng-Jie Cheng, MD, PHD, Che-Ping Cheng, MD, PHD

Winston-Salem, North Carolina



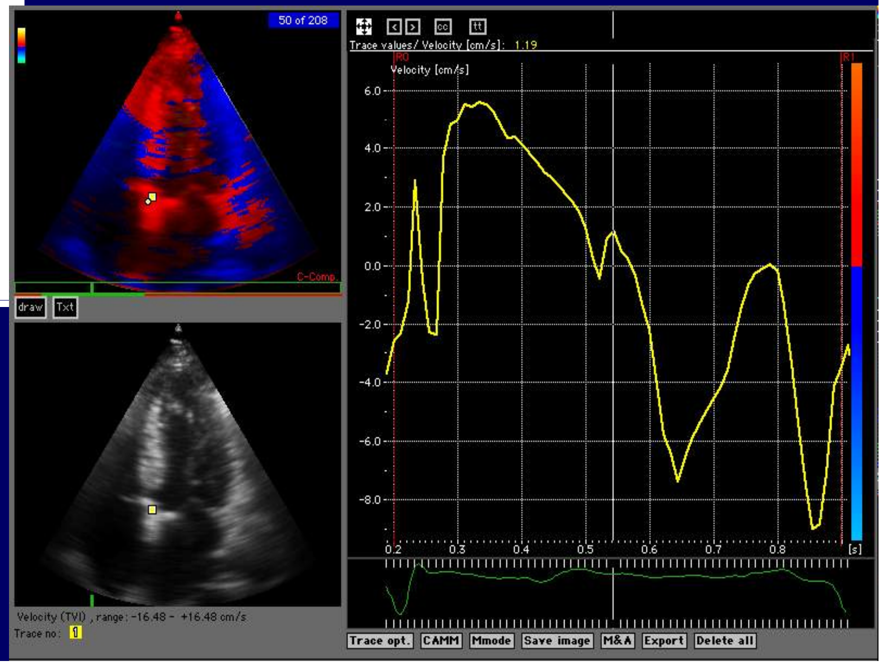
J Am Coll Cardiol 2003:41:1590-7

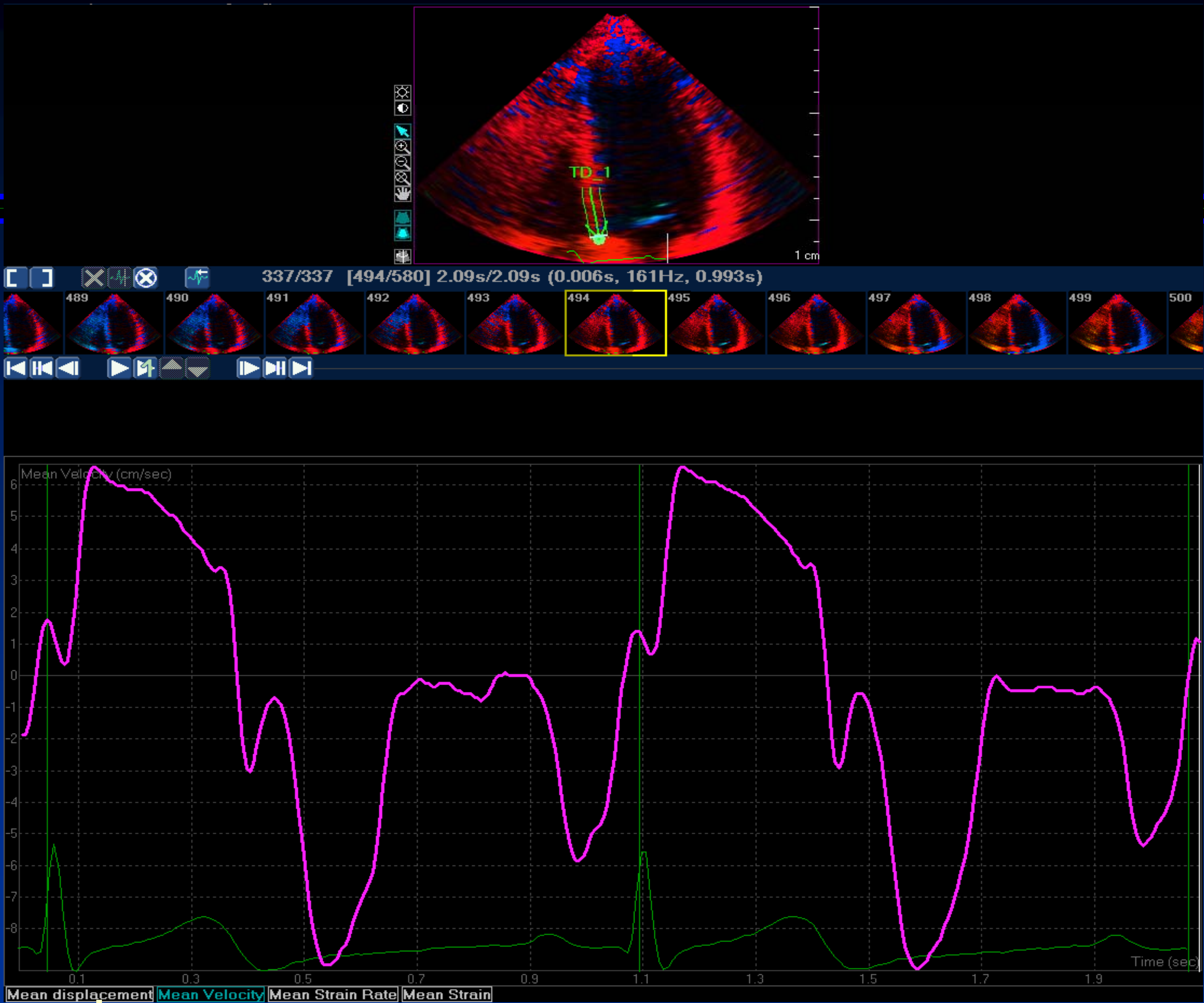
NB: PW Doppler versus Colour (offline) TDI



Chen et al Int J Cardiol 2004;97:289

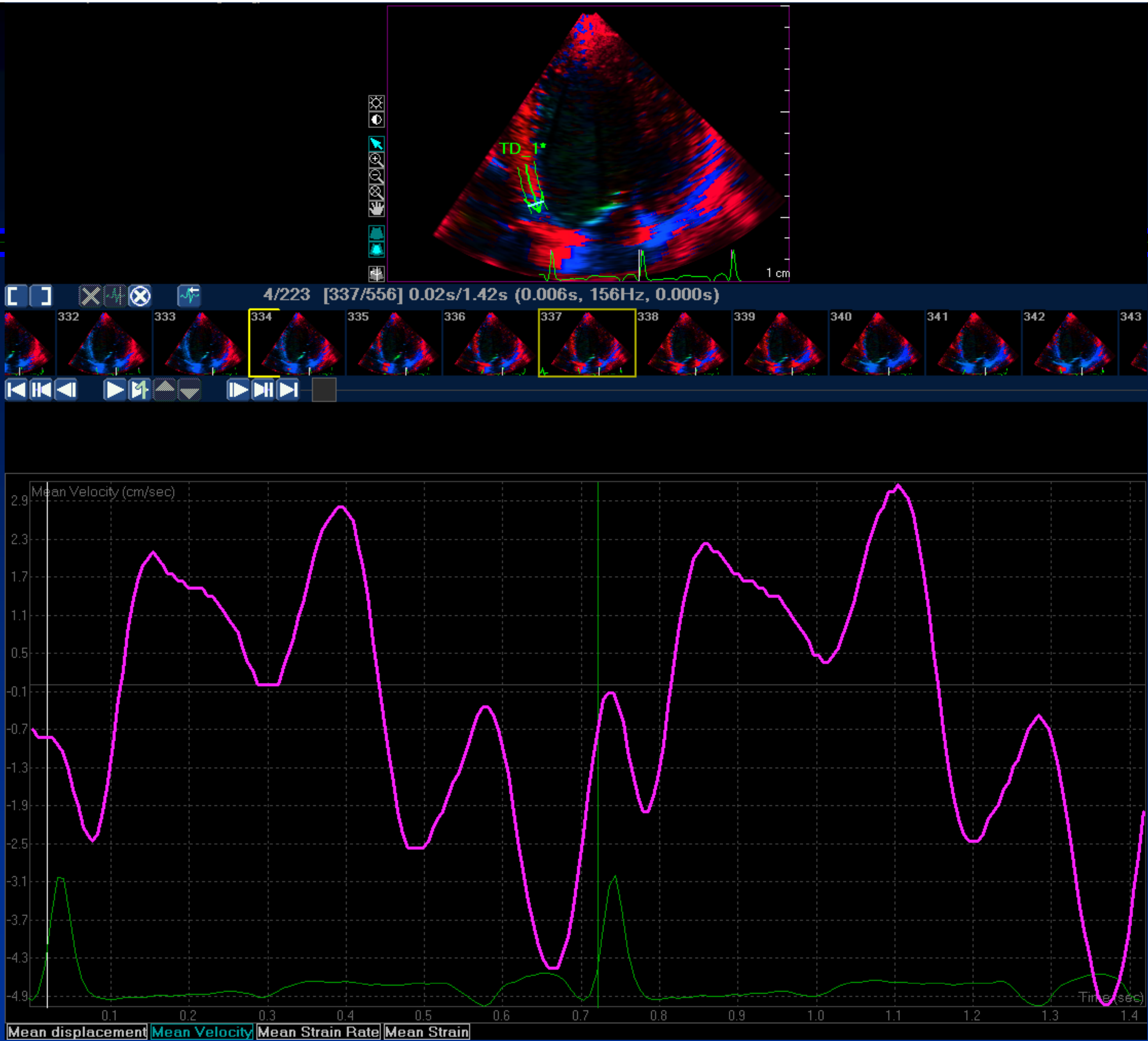
Also lateral versus septal wall?





Normal

Sm=6.6cm/s, Em=9.26cm/s



SHF

Sm=2.2cm/s, Em=2.5cm/s

STATE-OF-THE-ART PAPER

Tissue Doppler Imaging

A New Prognosticator for Cardiovascular Diseases

Cheuk-Man Yu, MD, FRCP, FRACP,* John E. Sanderson, MD, FRCP, FACC,†
Thomas H. Marwick, MD, PhD, FACC,‡ Jae K. Oh, FACC§

Table 2 Summary of Studies Which Assessed the Prognostic Importance of Tissue Doppler Imaging (TDI) Parameters in Cardiac Diseases

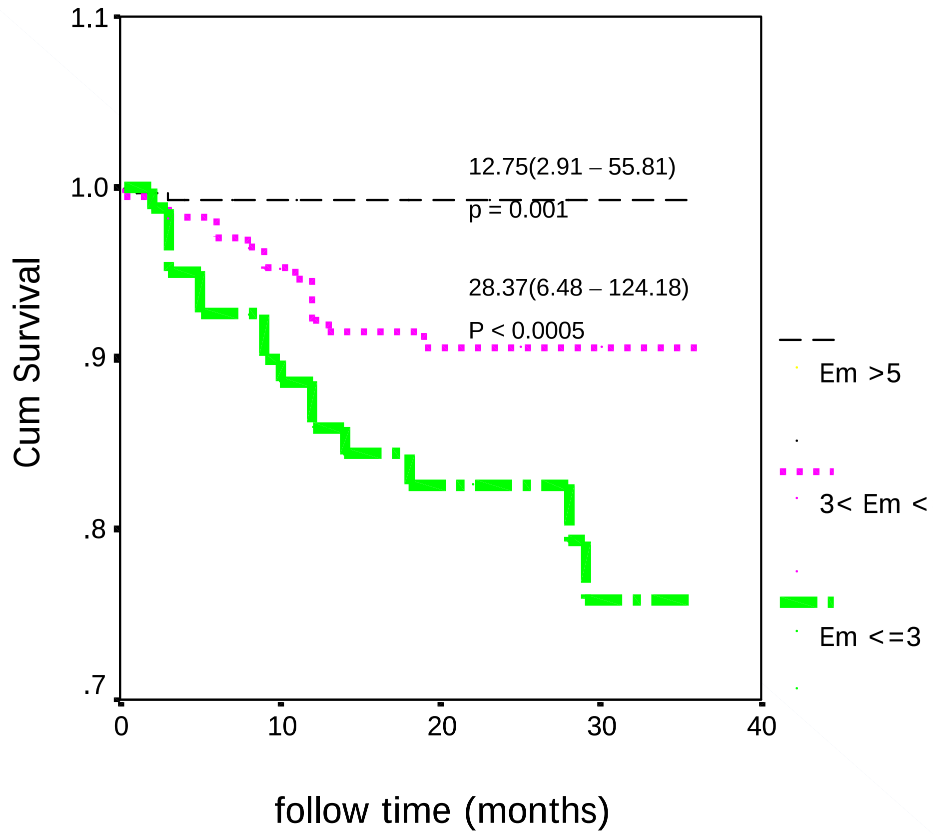
Author	Parameters	Disease Group	Sample Size	Follow-Up Duration	End Point Measure	Predictors of Event	Other Findings
1. Resting echocardiography with TDI							
Wang et al. (10)	Mean Sm, Em, Am from 4 basal LV segments	Various heart diseases	353 patients 165 controls	23 months	Mortaity	Sm ≤3 cm/s, Em <3 cm/s, Am ≤4 cm/s	Em adds independent prognostic value to clinical data and deceleration time
Richartz et al. (17)	Sa and Ea at septal and lateral mitral annulus	HF (idiopathic dilated cardiomyopathy)	40 patients 25 controls	Cross-sectional study	Acute pulmonary edema	Ea	Patients with recent onset acute pulmonary edema were associated with lower Ea than stable HF patients but had similar Sa
Wang et al. (16)	Mean Sm, Em, Am from 4 basal LV segments, E/Em	HF	182 patients	48 months	Cardiac mortality	Sm, Em, Am, E/Em	Em <3 cm/s and E/Em >15 had independent prognostic value to clinical data and deceleration time
Dokainish et al. (23)	E/Ea (Ea averaged from septal and lateral mitral annulus)	HF	116 patients	18 months	Cardiac mortality or HF hospitalization	E/Ea ≥15	E/Ea ≥15 adds independent prognostic value to BNP and ejection fraction
Yamamoto et al. (24)	E/Ea, Aa	HF	96 patients	29 months	Cardiac mortality or HF hospitalization	E/Ea ≥15, Aa ≥5 cm/s	Both E/Ea ≥15 and Aa ≤5 cm/s independently predicted a worse prognosis
Hillis et al. (27)	E/Ea	AMI	250 patients	13 months	Mortaity	E/Ea ≥15	E/Ea ≥15 has independent predictive value
Wang et al. (14)	Sm, Em, Am	Hypertension	174 patients 78 controls	19 months	Cardiac mortality	Sm, Em, Am	Em <3.5 cm/s is an independent prognosticator together with IVSd >1.4 cm
2. Stress echocardiography with TDI							
Marwick et al. (13)	Mean Sm from 6 basal LV segments	DSE for suspected CHD	576 patients	16 months	Mortaity or AMI	Sm >6 cm/s	Sm >6 cm/s predicted a lower event rate, but not wall motion score
3. Dyssynchrony assessment with TDI							
Bader et al. (58)	Maximum difference of time to onset of Sm at 4 basal LV segments	HF	104 patients	12 months	HF hospitalization	Intraventricular dyssynchrony	Intraventricular but not interventricular dyssynchrony predicted HF events
Cho et al. (60)	Ts-SD or Ts-diff from 4 basal and 4 mid LV segments	HF and QRS ≤120 ms	106 patients	17 months	Mortaity, cardiac transplantation, or HF events	Ts-SD >37 ms, Ts-diff >91 ms	Ts-SD >37 ms has sensitivity of 68% and specificity of 71%, and Ts-diff >91 ms has sensitivity of 70% and specificity of 68% to predict events
Bax et al. (65)	Septal-to-lateral wall delay in time to peak Sm	HF, received CRT	85 patients	12 months	Mortaity or HF hospitalization	Septal-to-lateral wall delay	Septal-to-lateral wall delay ≥65 ms has a sensitivity and specificity of 80% to predict clinical improvement

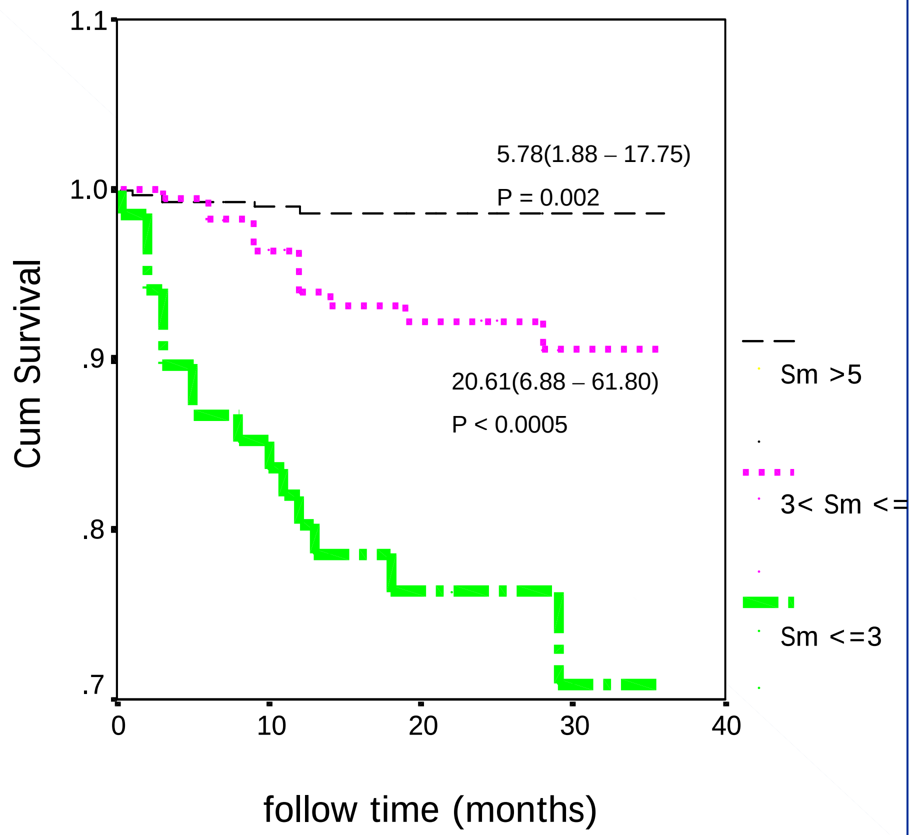
AMI = acute myocardial infarction; CHD = coronary heart disease; CRT = cardiac resynchronization therapy; DSE = dobutamine stress echocardiography; HF = heart failure; IVSd = thickness of interventricular septum at end-diastole; LV = left ventricular; Ts-diff = maximum difference in time to peak systolic velocity; Ts-SD = standard deviation of time to peak systolic velocity; other abbreviations as in Table 1.

(J Am Coll Cardiol 2007;49:1903–14)

Peak early diastolic and systolic mitral annulus velocity by TDI adds independent and incremental prognostic value.

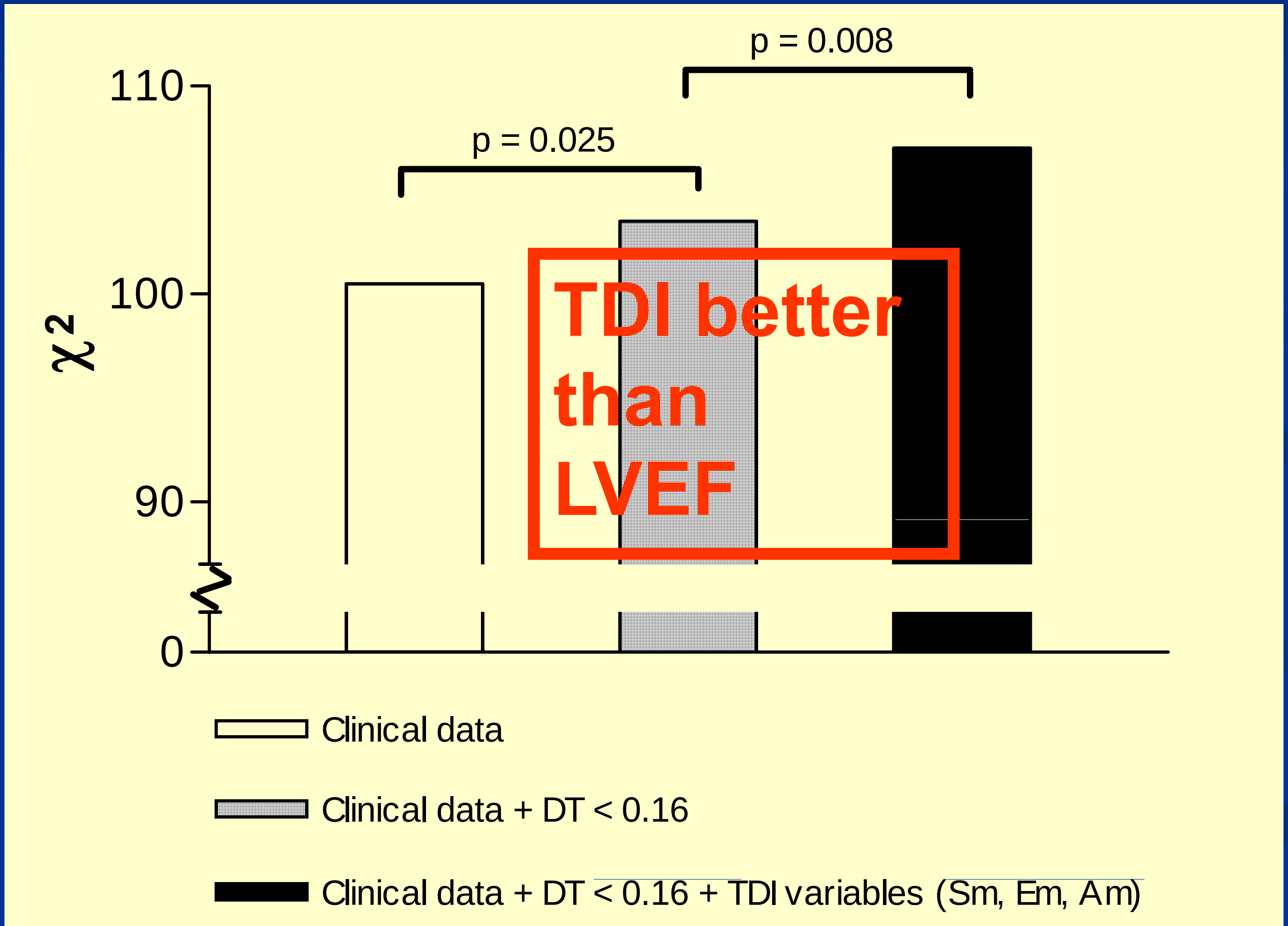
Wang M, Yip G, Wang A et al. JACC 2003;41:820-6





353 patients with cardiac disease and 165 normals.

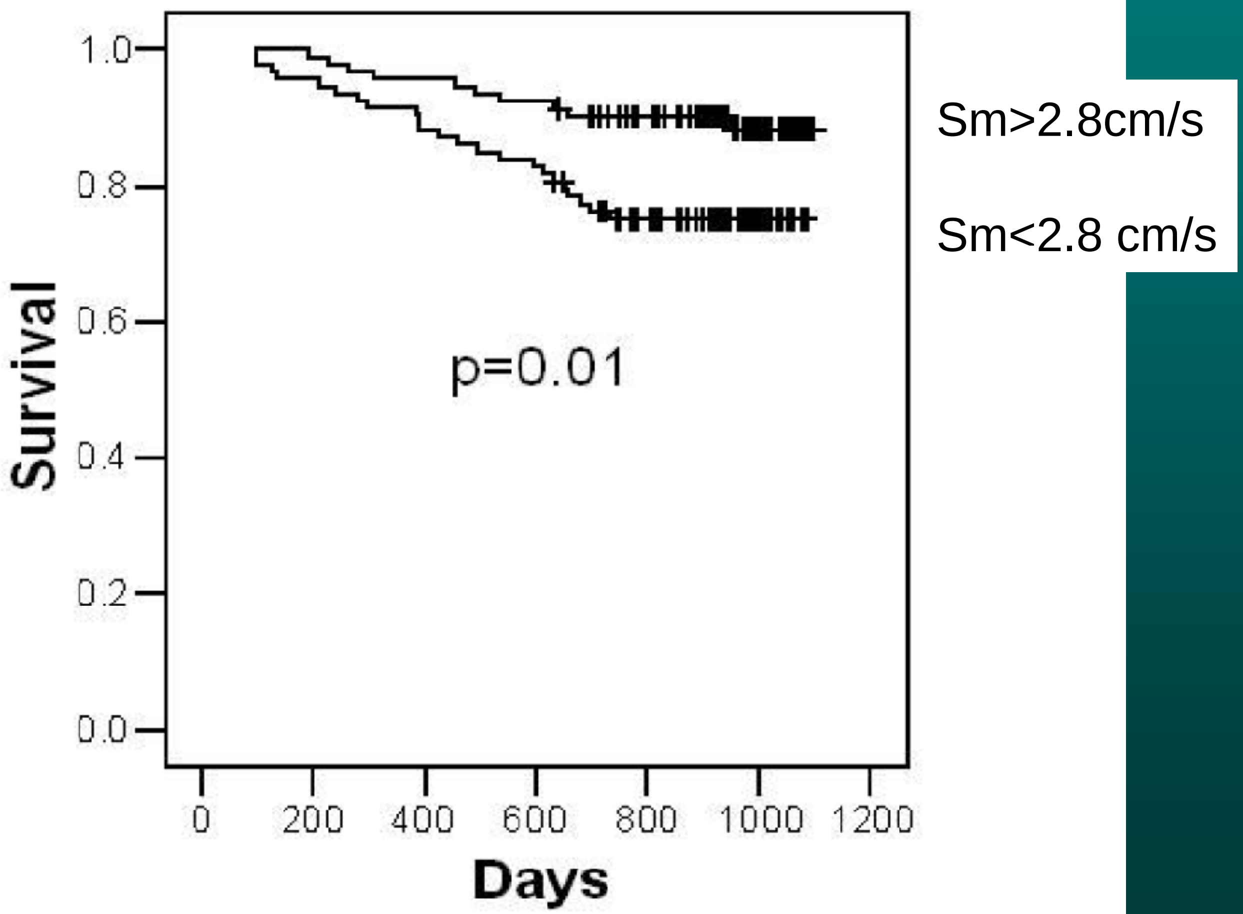
Incremental value of DT <160 s and tissue Doppler imaging variables in predicting cardiac death



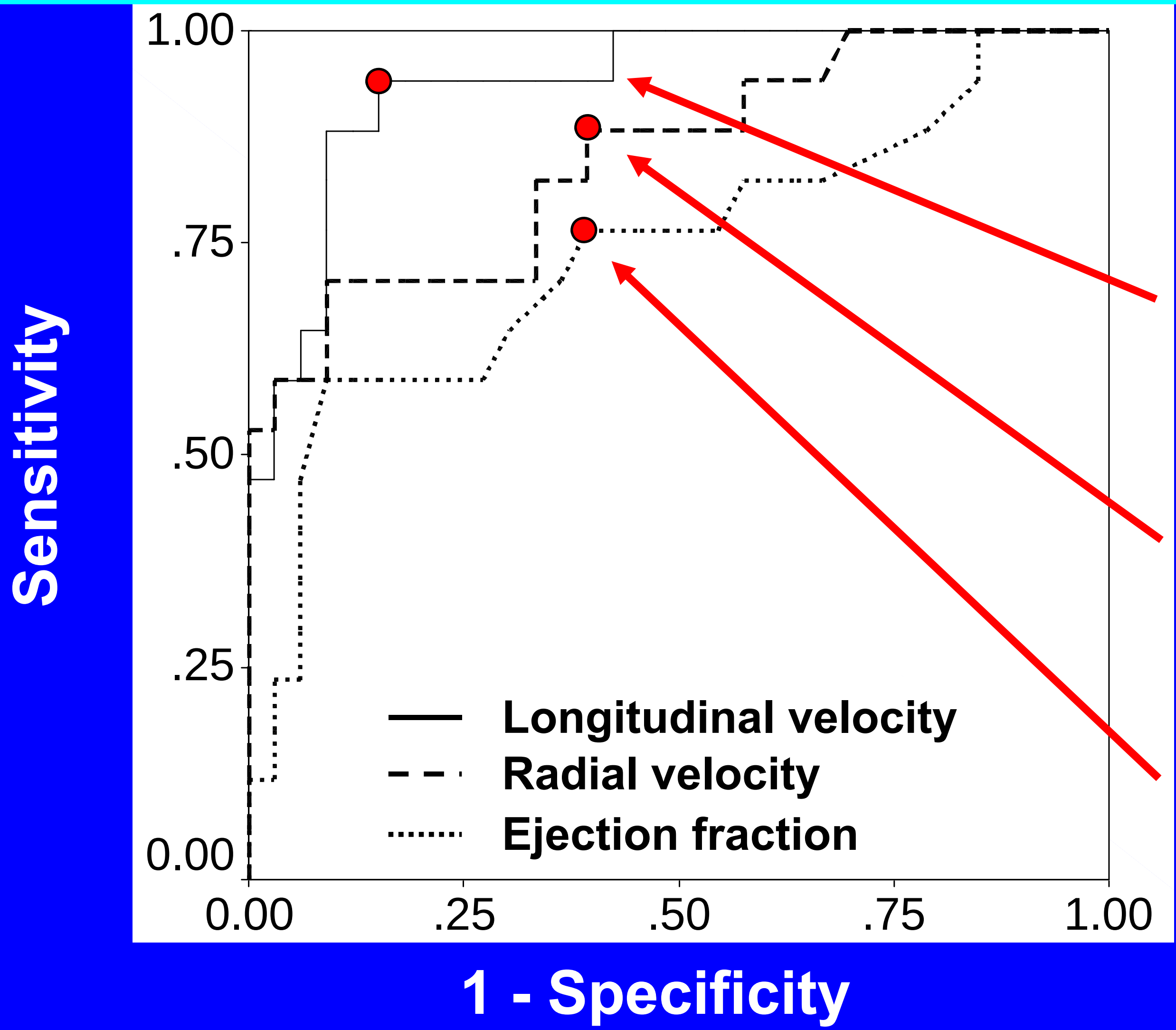
Wang M, Yip G, Wang A et al. JACC 2003;41:820-6

The prognostic value of systolic mitral annular velocity measured with Doppler tissue imaging in patients with chronic heart failure due to left ventricular systolic dysfunction

Nikolay P Nikitin, Poay Huan Loh, Ramesh de Silva, Justin Ghosh, Olga Y Khaleva, Kevin Goode, Alan S Rigby, Farqad Alamgir, Andrew L Clark and John GF Cleland



Performance of echocardiographic tests for suspected heart failure *(BNP > 88 pg/ml)*



Receiver operating characteristics

Longitudinal systolic velocity
AUC = 0.94

Radial systolic velocity
AUC = 0.85

Global ejection fraction
AUC = 0.74

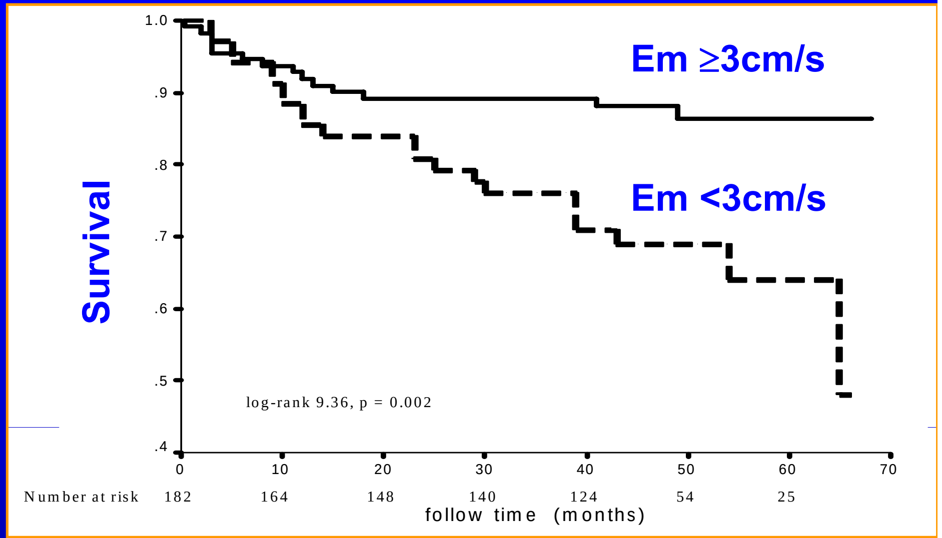
Vinereanu D et al,
Eur J Heart Failure 2005

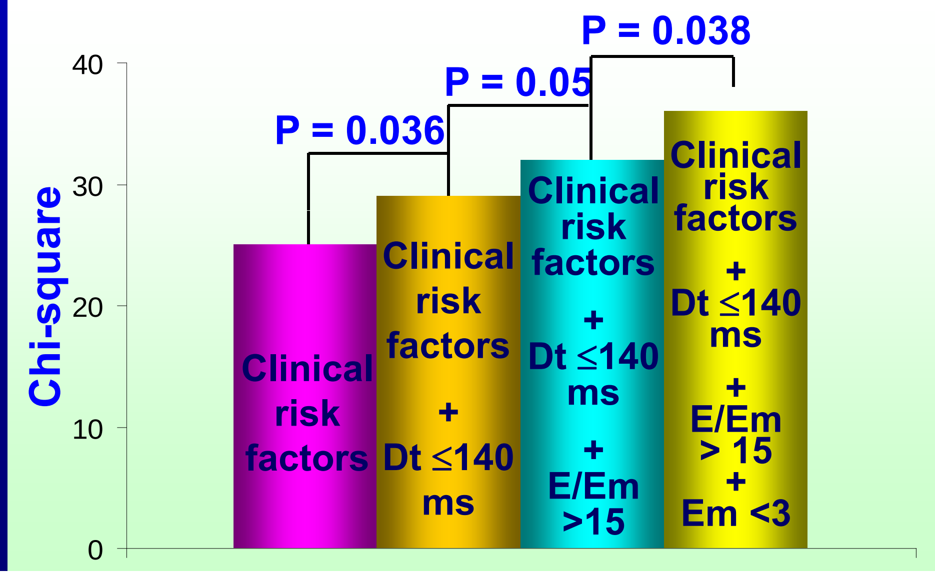
Incremental Predictive Value of Em & E/Em
in Heart Failure -
Wang M, et al, JACC 2005;45:272-7.

- 182 CHF pts with EF <50%
- Median F.U. : 48 months
- End-point : Cardiac mortality

Results :

- Em independently predicted cardiac mortality (RR = 0.61; CI = 0.45-0.82)
- Em < 3cm/s predicted mortality
- Incremental prognostic value by E/Em >15



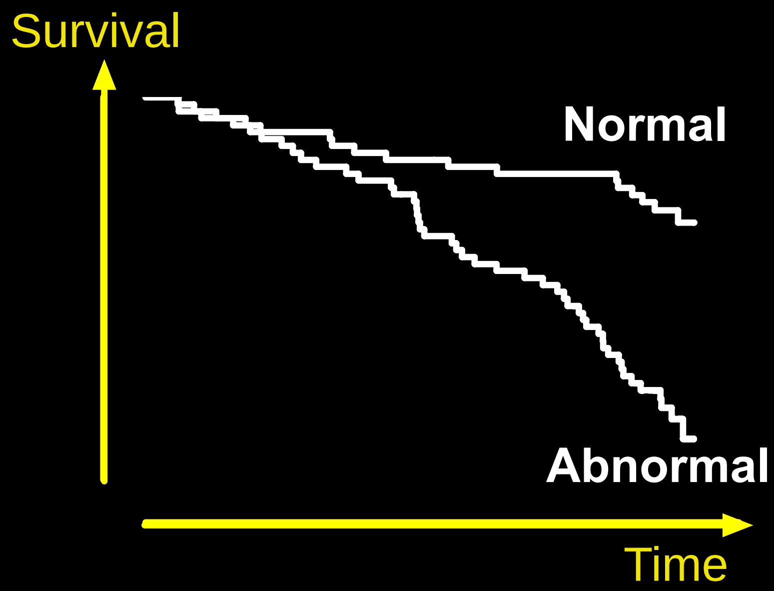


Echocardiographic Tissue Doppler Imaging Is a Powerful Independent Prognosticator of Overall Mortality in the General Population

Results From the Fourth Copenhagen City Heart Study (2002-2007)

Rasmus Mogelvang

The Copenhagen City Heart Study
& Department of Cardiology,
Gentofte University Hospital
Denmark



Presented at ACC 2008

Copenhagen City Heart Study

Gentofte Hospital

Methods

1,100 persons from the Copenhagen City Heart Study

↓

Conventional Echocardiography

&

Tissue Doppler Imaging

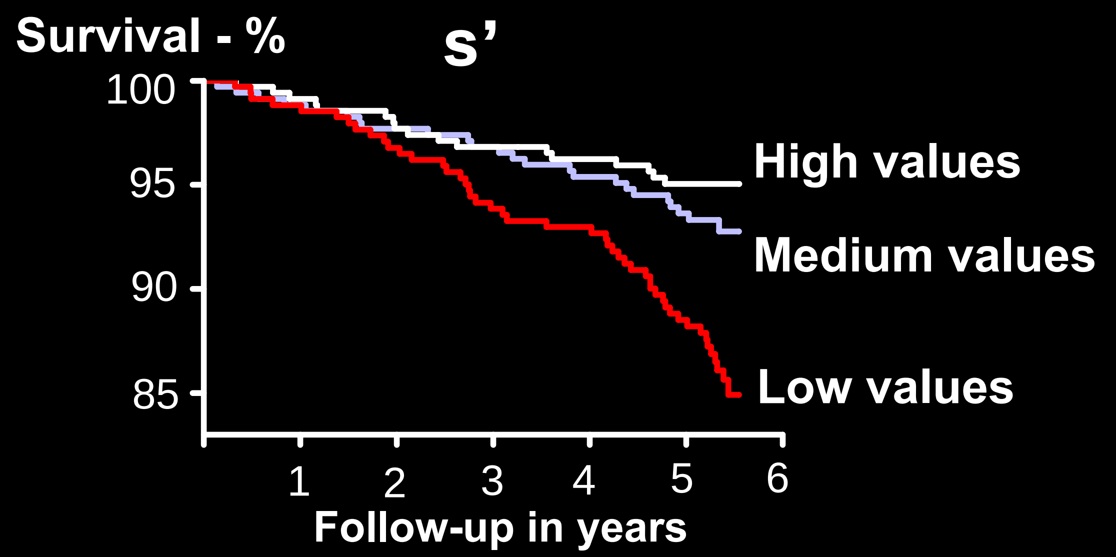
↓

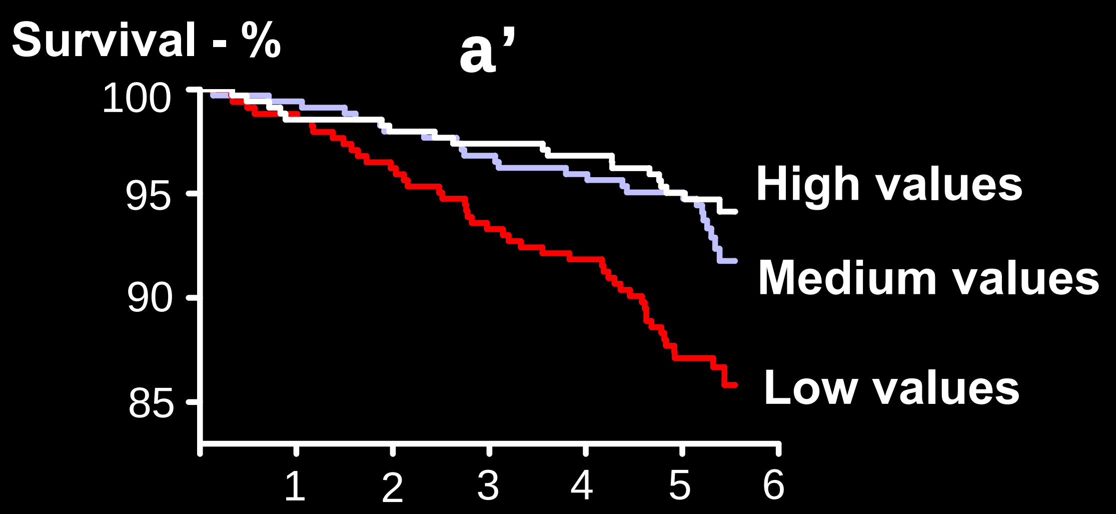
Mean Follow-up: 5.1 years

http://www.lib.utexas.edu/maps

Gentofte Hospital

Kaplan-Meier Survival Plots

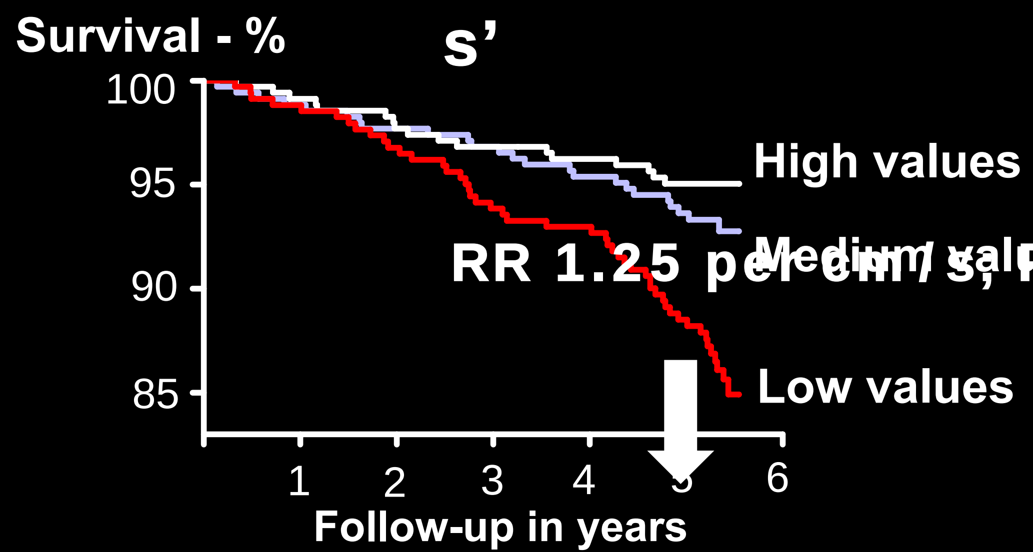




Kaplan-Meier Survival Plots

Multivariate Analysis

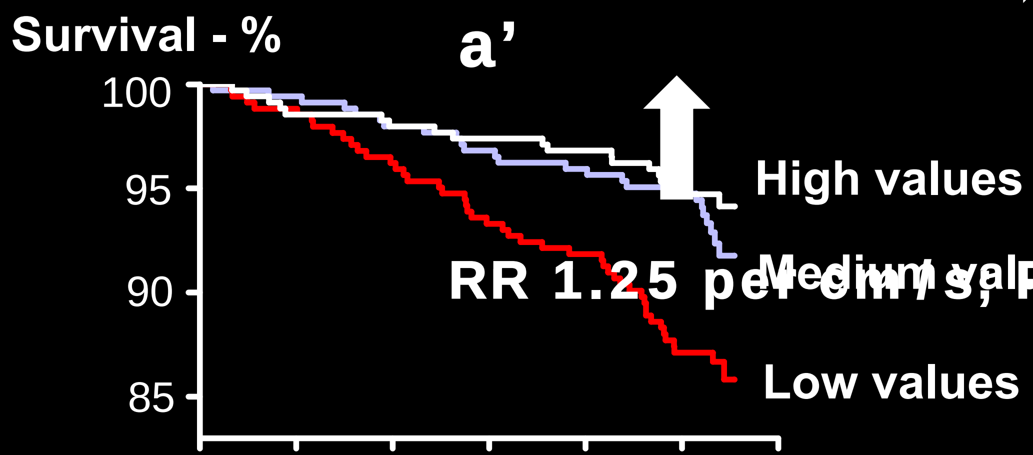
s’



RR 1.25 per cm/s; P<0.04

8 cm/s vs. 3 cm/s ➡ RR 3.0

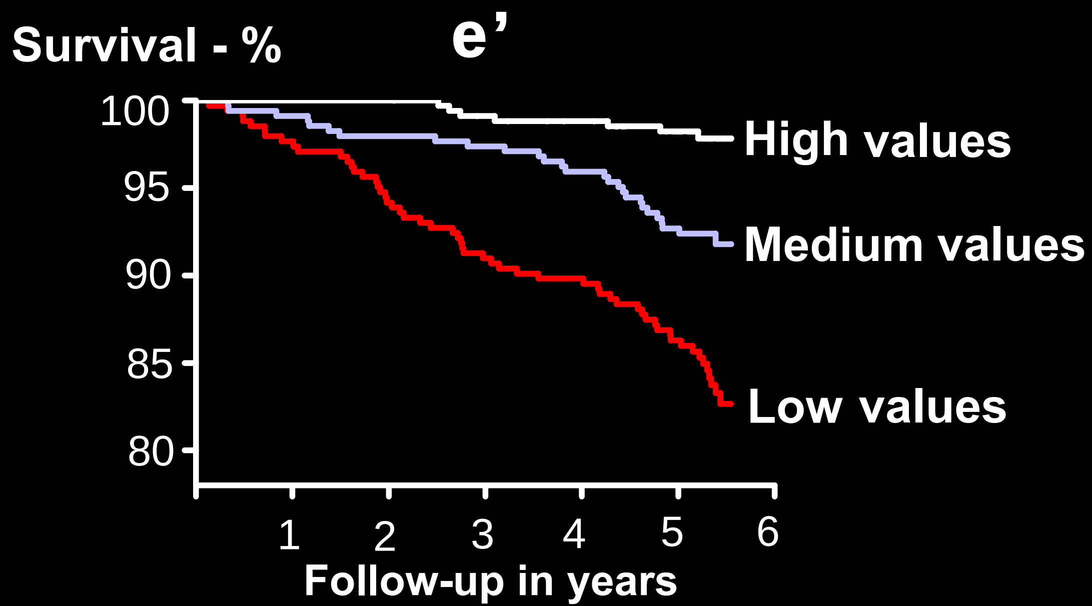
a’



RR 1.25 per cm/s; P<0.001

Gentofte Hospital

Kaplan-Meier Survival Plot for e’



Multivariate analysis ➡ **Relative Risk 1.02**
(0.90-1.16); P=0.77

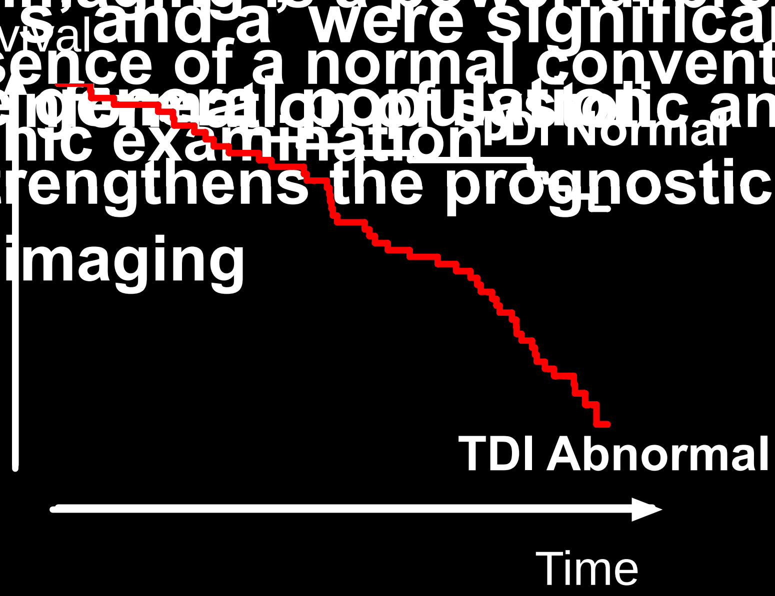
Conclusions

1. Tissue Doppler imaging is a powerful prognosticator, even in the presence of a normal conventional echocardiographic examination
2. Low values of s’ and a’ were significant predictors of death
3. Combining the information of systolic and diastolic performance strengthens the prognostic value of tissue Doppler imaging

Tissue Doppler imaging is a powerful prognosticator - even in the presence of a normal conventional echocardiographic examination

2. Low values of s’ and a’ were significant predictors of death in the general population

3. Combining the information of systolic and diastolic performance strengthens the prognostic value of tissue Doppler imaging



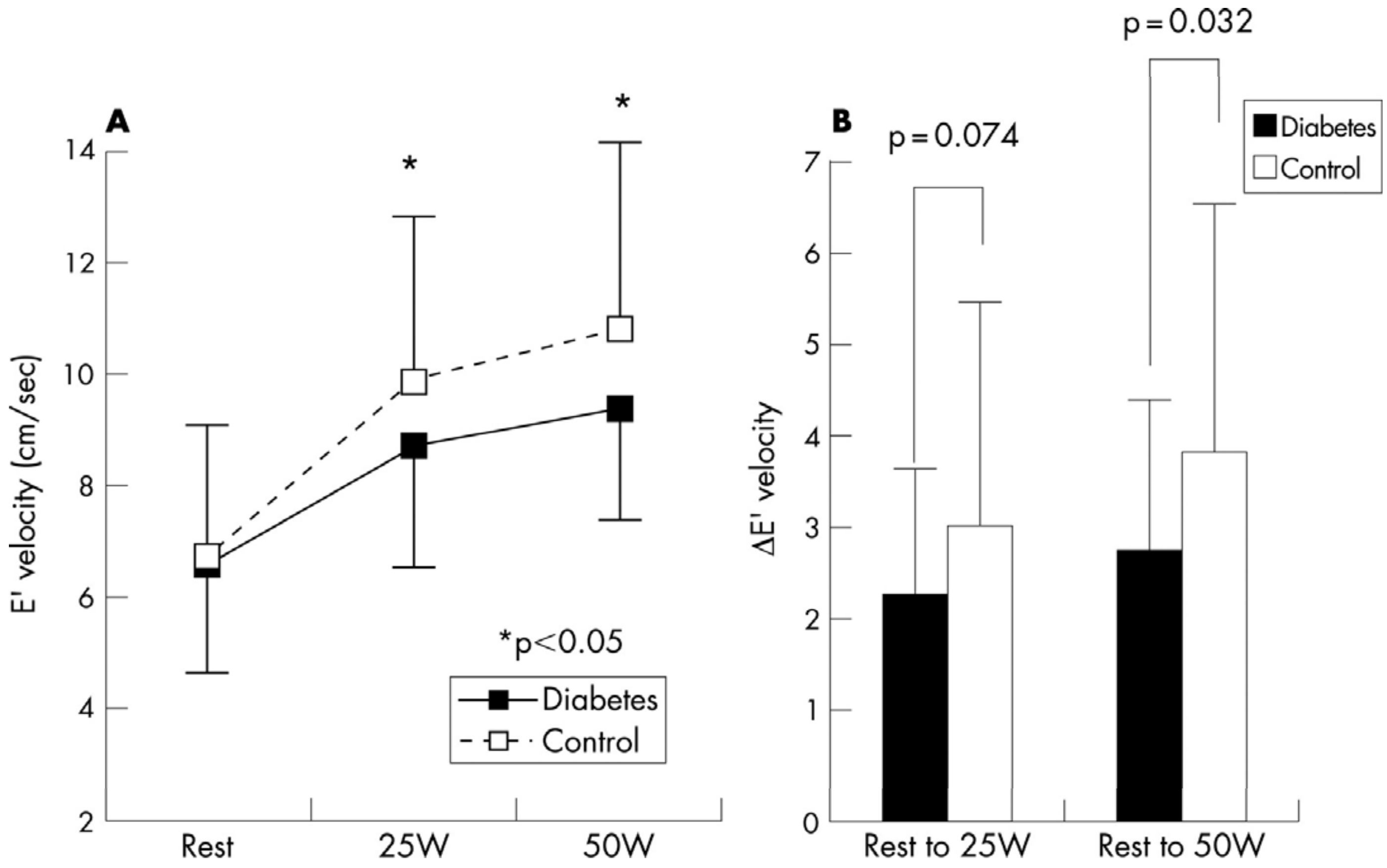
Diastolic Exercise Stress Testing

Normal Values

	Baseline	Exercise
E (cm/s)	73 ± 19	90 ± 25
A (cm/s)	69 ± 17	87 ± 22
DT (ms)	192 ± 40	176 ± 42
E' (cm/s)	12 ± 4	15 ± 5
E/E'	6.7 ± 2.2	6.6 ± 2.5

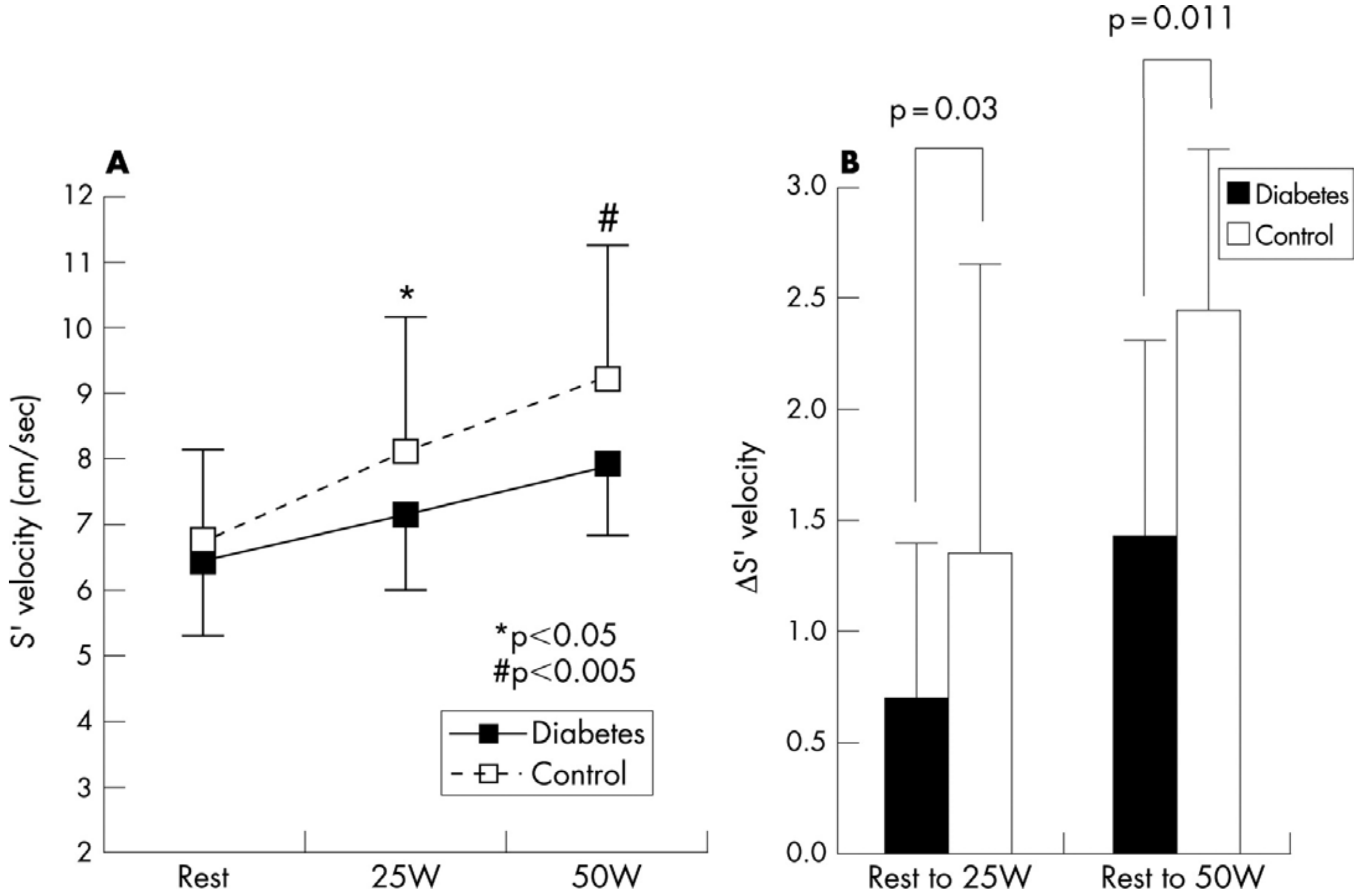
Ha J et al: AJC Jan 2003

Figure 1 Left panel: change of E' from rest to exercise. Note that an increase in E' with exercise was less pronounced in patients with diabetes. Right panel: the change of E' with exercise was significantly smaller in patients with diabetes compared with the control.



Ha, J.-W. et al. Heart 2007;93:1571-1576

Figure 2 Left panel: change of S' from rest to exercise. Note that an increase in S' with exercise was blunted in patients with diabetes. Right panel: the increment of S' with exercise was significantly smaller in patients with diabetes compared with control.



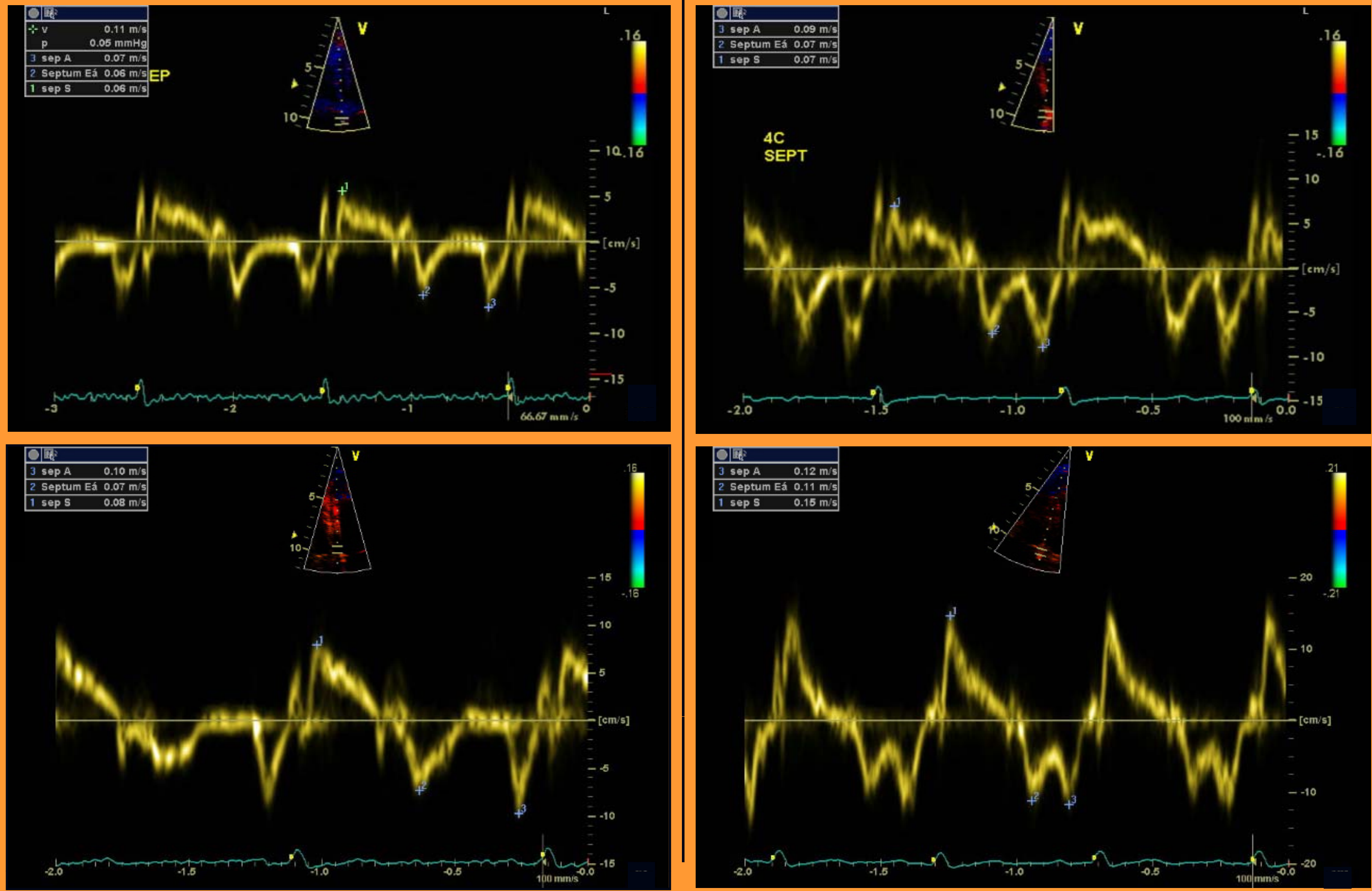
Ha, J.-W. et al. Heart 2007;93:1571-1576

Longitudinal Functional Reserve Index (LFR Index) in HFNEF

Patient, ♀ 77 years | **Control, ♀ 72 years**

Rest | Rest

Exercise | Exercise

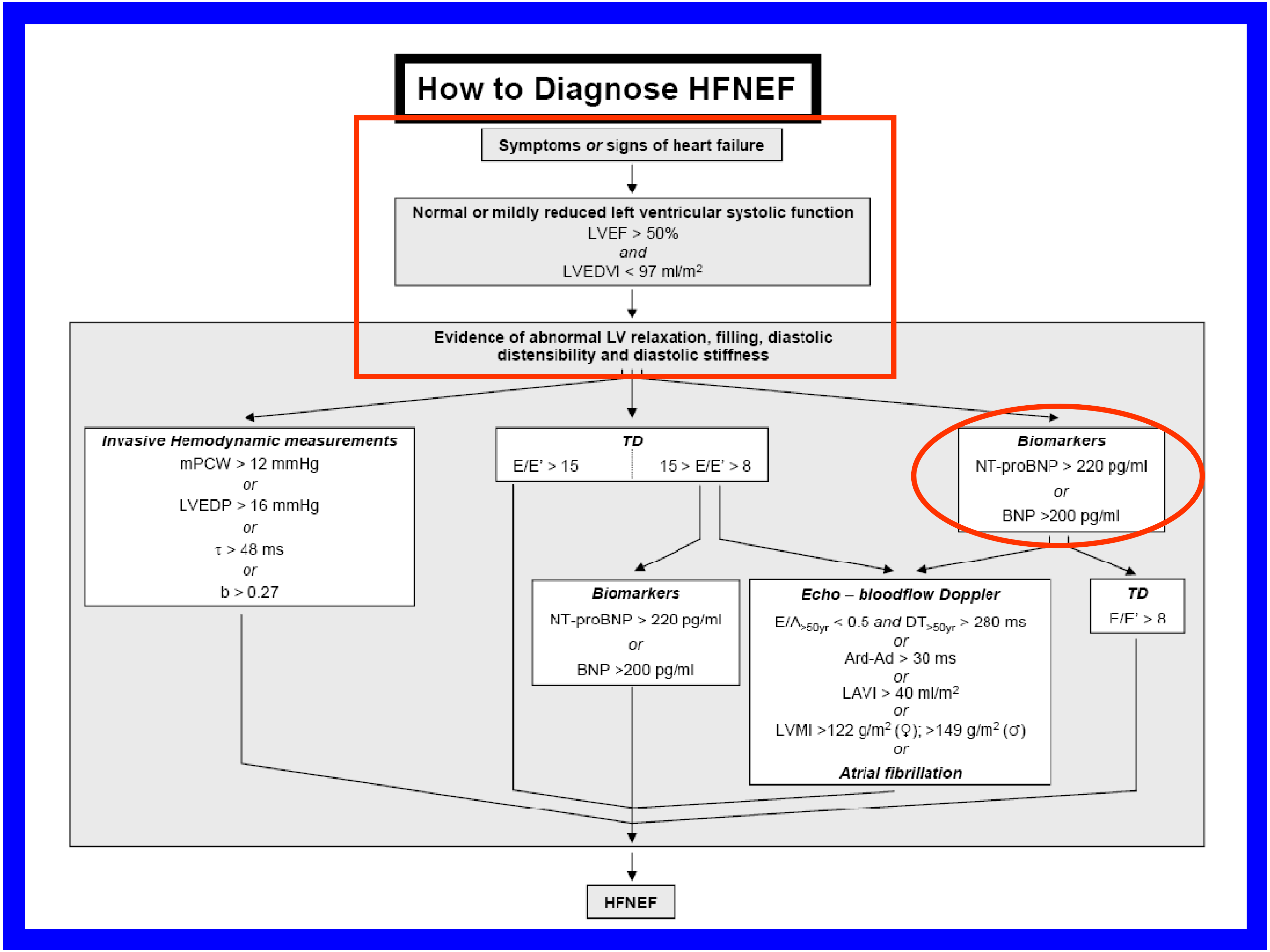


Diastolic (Systolic) LFR Index = ΔEm (or Sm) * (1-1/Em (or Sm) at rest) *

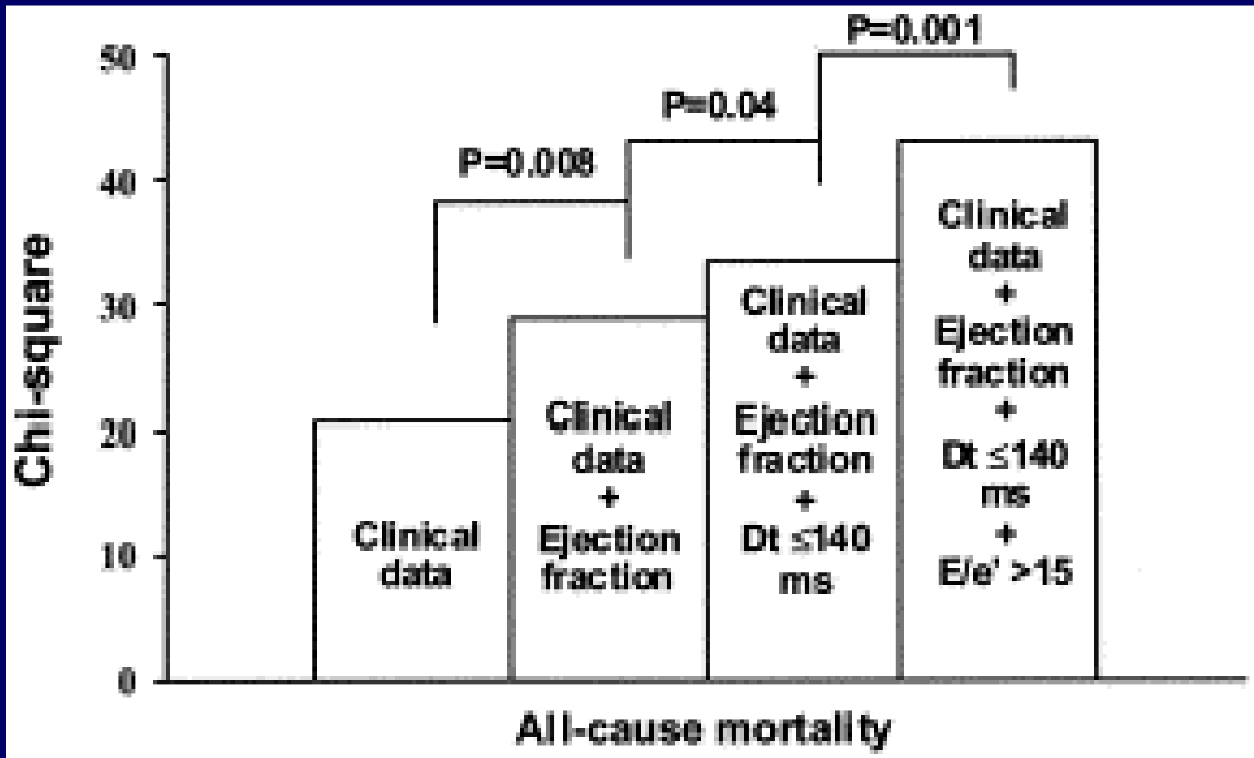
*(Ha et al., Heart 2007)

Longitudinal Functional Reserve Index (LFR Index)

Echo Results	Patients (n=39)	Controls (n=21)
Em at Rest (cm/s)	7.9±4.2	7.9±2.1
Em at Exercise (cm/s)	9.9±2.3 p=0.000	12.5±2.6
Sm at Rest (cm/s)	7.9±1.6	8.0±1.5
Sm at Exercise (cm/s)	8.9±1.9 p=0.003	10.6±2.2
Diastolic LFR Index (cm/s)	2.0±1.5 p=0.001	3.9±2.4
Systolic LFR Index (cm/s)	0.9±1.5 p=0.001	2.3±1.5


How to Diagnose HFNEF
Symptoms or signs of heart failure
Normal or mildly reduced left ventricular systolic function
LVEF > 50%
and
LVEDVI < 97 ml/m2
Evidence of abnormal LV relaxation, filling, diastolic distensibility and diastolic stiffness
Invasive Hemodynamic measurements
mPCW > 12 mmHg
or
LVEDP > 16 mmHg
or
τ > 48 ms
or
b > 0.27
TD
E/E' > 15
15 > E/E' > 8
Biomarkers
NT-proBNP > 220 pg/ml
or
BNP >200 pg/ml
Biomarkers
NT-proBNP > 220 pg/ml
or
BNP >200 pg/ml
Echo – bloodflow Doppler
E/A>50yr < 0.5 and DT>50yr > 280 ms
or
Ard-Ad > 30 ms
or
LAVI > 40 ml/m2
or
LVMI >122 g/m2 (♀); >149 g/m2 (♂)
or
Atrial fibrillation
TD
E/E' > 8
HFNEF

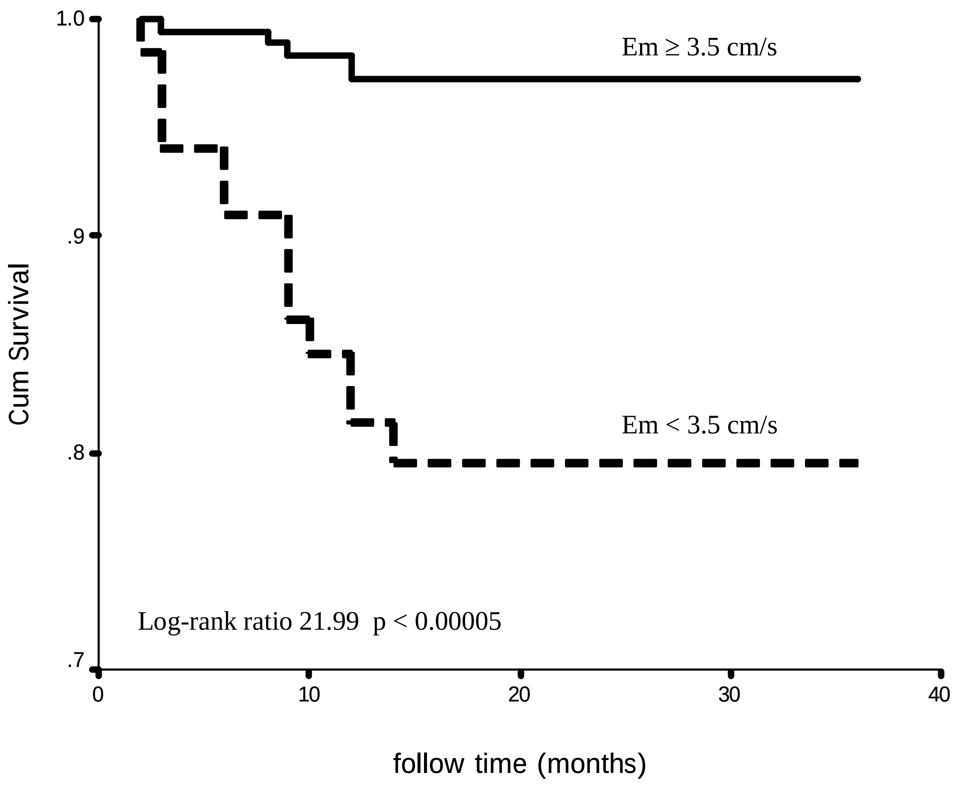
Incremental value of an E/E' ratio >15 in predicting all-cause mortality post myocardial infarction.



Hillis GS et al. J Am Coll Cardiol 2004;43:360-7

TDI provides incremental prognostic value in hypertension with LVH

Wang et al J Hypertension 2005;23:183-191



TDI Limitations

- Angle dependence
- Velocities measured from relatively fixed apex, a normal segment affected by tethering from adjacent segments (scar or ischaemic)
- Translational movement reduced by tissue auto-tracking algorithm in future
- Gradual decrease in velocity gradient from base to apex

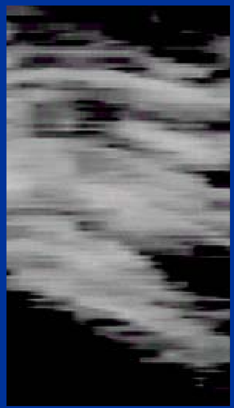
"Strain": Deformation

$$S = \frac{L - L_0}{L_0}$$

(Lagrangian)

S = +25%

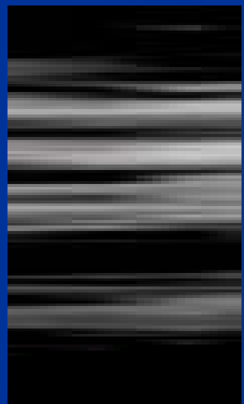
L_0



L

S = 0%

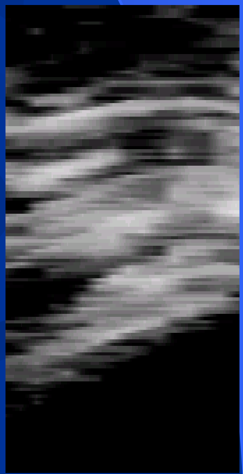
L_0



L

S = -25%

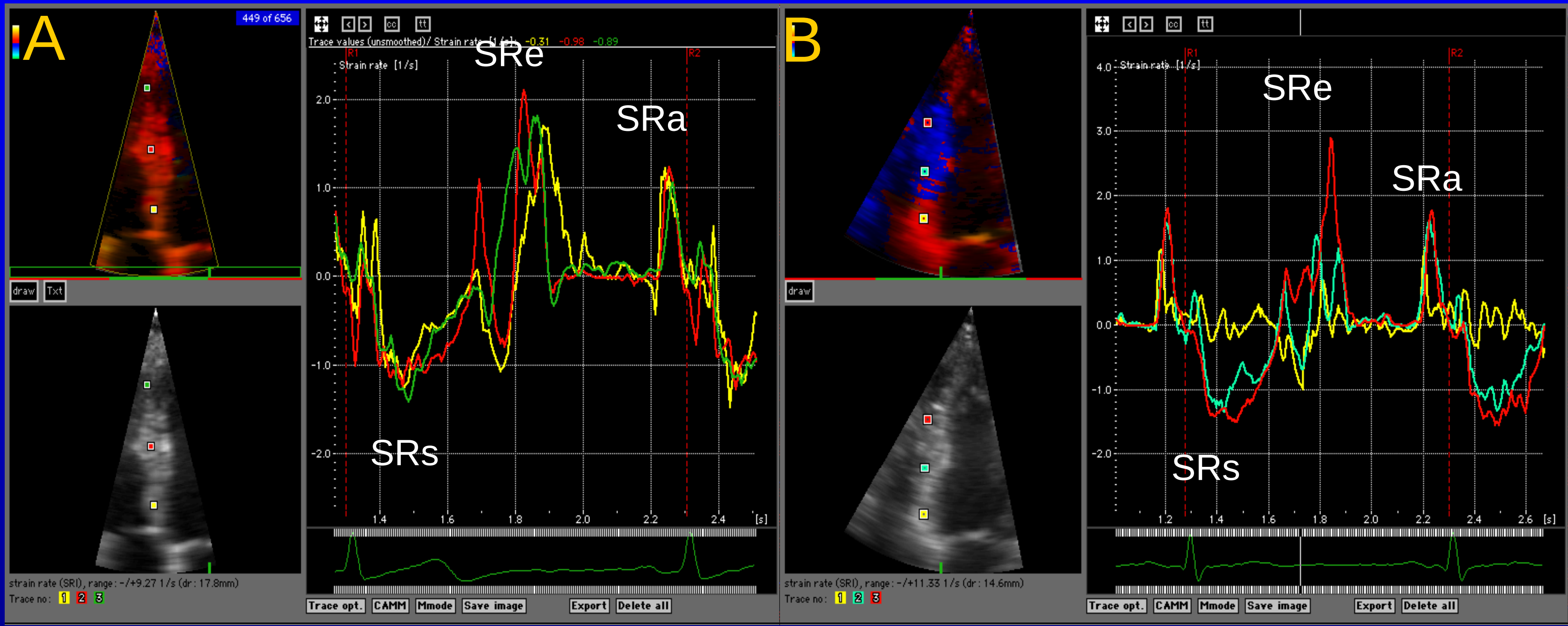
L_0



L

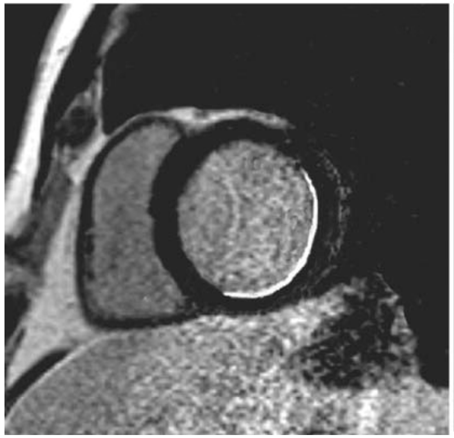
A: SRI in a normal subject.

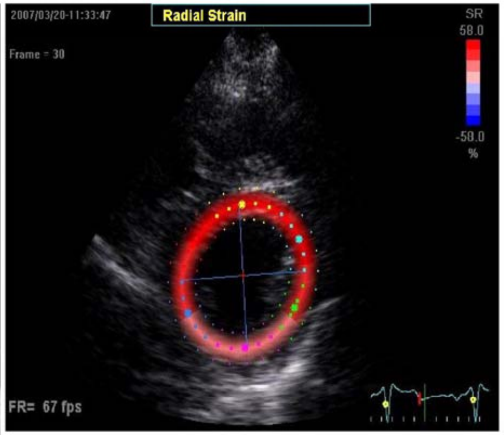
B: SRI in a transmural MI (basal IVS).

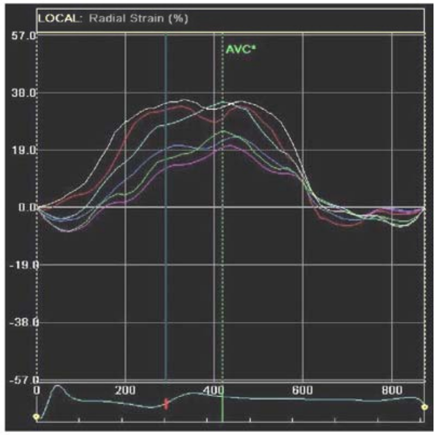


Zhang Y,Chan AKY, Yu CM, Yip GWK, Fung JWH, Lam WMM, So NM, Wang M, Wu EB, Wong JT, Sanderson JE. Strain Rate Imaging Differentiates Transmural From Non-transmural Myocardial Infarction: A Validation Study Using Delayed-enhancement Magnetic Resonance Imaging. J Am Coll Cardiol 2005;46:864-71

ceMRI and Strain Imaging in Nontransmural Infarction

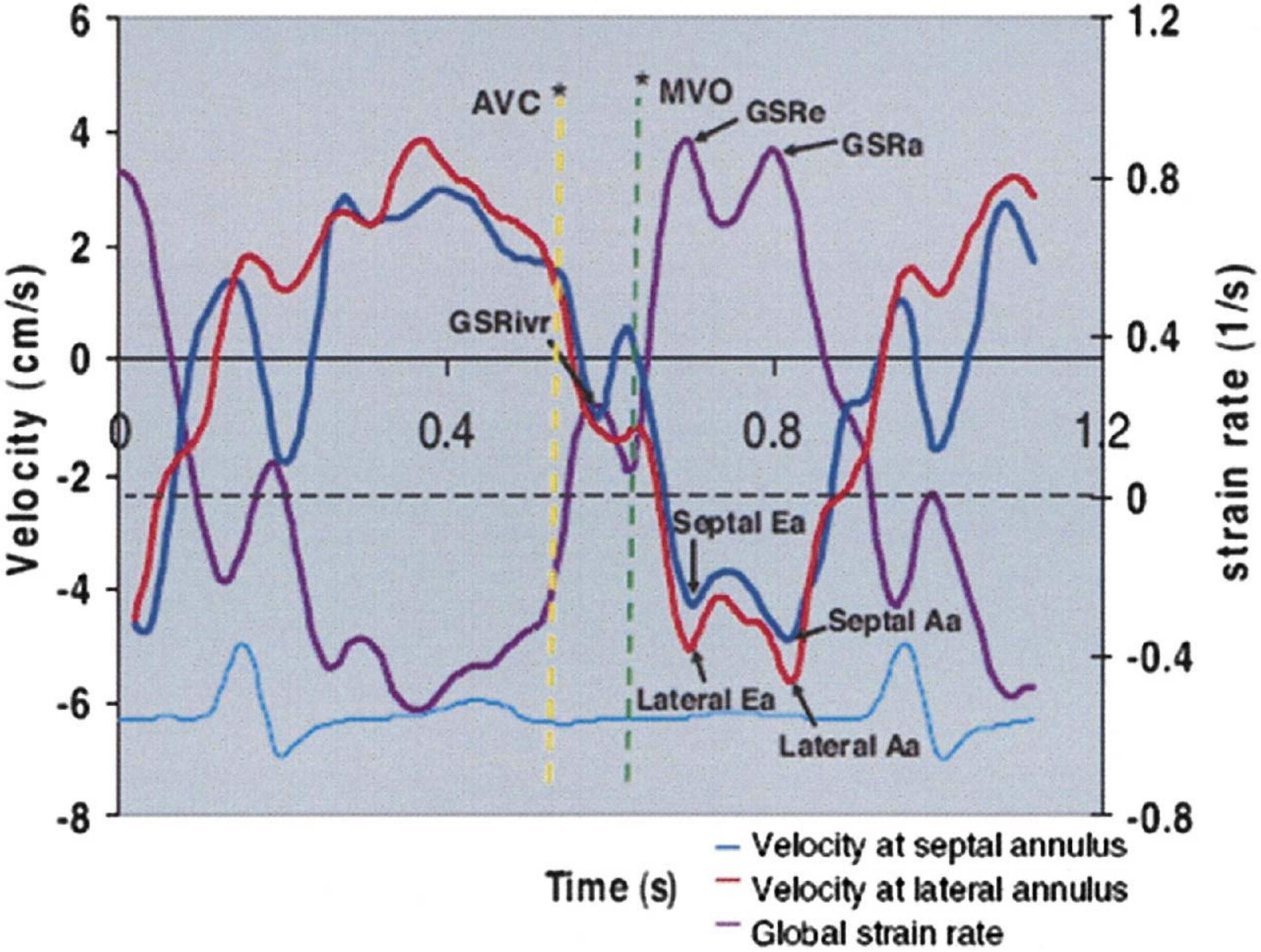






Becker, M. et al. J Am Coll Cardiol 2008;51:1473-1481

Global Strain Rate Profile



Lester, S. J. et al. J Am Coll Cardiol 2008;51:679-689

Global and Regional Myocardial Function Quantification by Two-Dimensional Strain

Application in Hypertrophic Cardiomyopathy

Karim Serri, MD, Patricia Reant, MD, Marianne Lafitte, MD, Marianne Berhouet, MD, Valerie Le Bouffos, MD, Raymond Roudaut, MD, Stephane Lafitte, MD, PHD

Pessac, France

Despite apparently normal left ventricular systolic function, all components of strain were significantly reduced in HCM. Average longitudinal, transverse, circumferential, and radial strain in patients with HCM and controls were −15.1 ± 6.2% versus −20.3 ± 5.6%, 23.3 ± 17.0% versus 27.2 ± 14.9%, −16.8 ± 7.1% versus 19.6 ± 5.2%, and 25.2 ± 13.9% versus 36.8 ± 17.2%, respectively (all $p < 0.001$). In patients with asymmetrical HCM, longitudinal septal strain was significantly lower than for other left ventricular segments combined: −9.2 ± 4.7% versus −12.7 ± 7.1% ($p = 0.001$). Average interobserver and intraobserver variabilities were 11% and 11.3%, respectively.

JACC 2006;47:1175-1181

Clinical applications

Table 3. Use of Strain (ε) and Strain Rate (SR) for Detection of Subclinical Disease of the Myocardium

Disease	Evidence
Amyloidosis	Systolic ε/SR (not S′ or E′) identified subclinical disease (24)
Friedrich ataxia	Reduction of LV (not RV), systolic ε/SR, and diastolic SR proportionate to LVH (25)
LV hypertrophy	Systolic ε/SR reduced in LVH before abnormal filling (26), systolic ε distinguished HCM and HT-LVH (27)
Tetralogy	RV-S and ε/SR reduced (28), IVA (not S′ or SR) proportionate to PR severity (29)
Senning	Reduction of systolic ε/SR in the systemic RV (30)
Valvular disease	Subclinical LV dysfunction in asymptomatic MR (31)

E′ = early diastolic tissue velocity; HCM = hypertrophic cardiomyopathy; HT-LVH = hypertensive left ventricular hypertrophy; IVA = isovolumic acceleration; LV = left ventricle/ventricular; LVH = left ventricular hypertrophy; MR = mitral regurgitation; PR = pulmonic regurgitation; RV = right ventricle/ventricular; S′ = tissue systolic velocity; SRI = strain rate image/imaging.

Marwick T JACC 2006;47:1313-1332

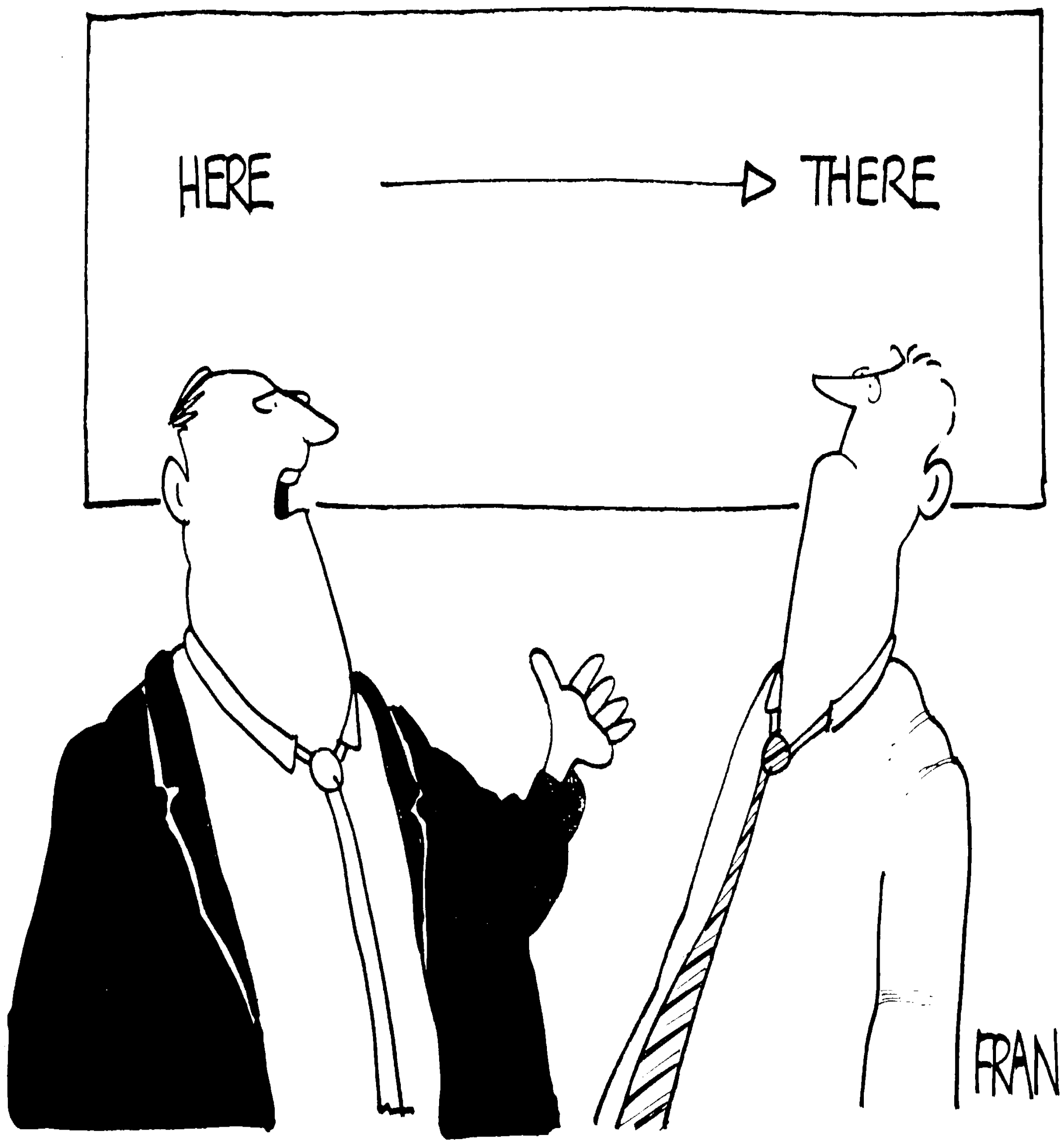
Conclusions

- For Heart Failure patients the common usage of LVEF as a measure of LV function has been a disaster.
- 50% have been excluded from clinical trials.
- Misleading Echo reports: “LVEF is normal – patient does not have heart failure”.
- TDI/SRI more accurate, reproducible and better prognostic indicator.

New classification of Heart failure

- Symptoms and signs of HF +raised BNP
- Is there LV remodelling (small vs big heart)?
- What is the mechanism underlying dysfunction?

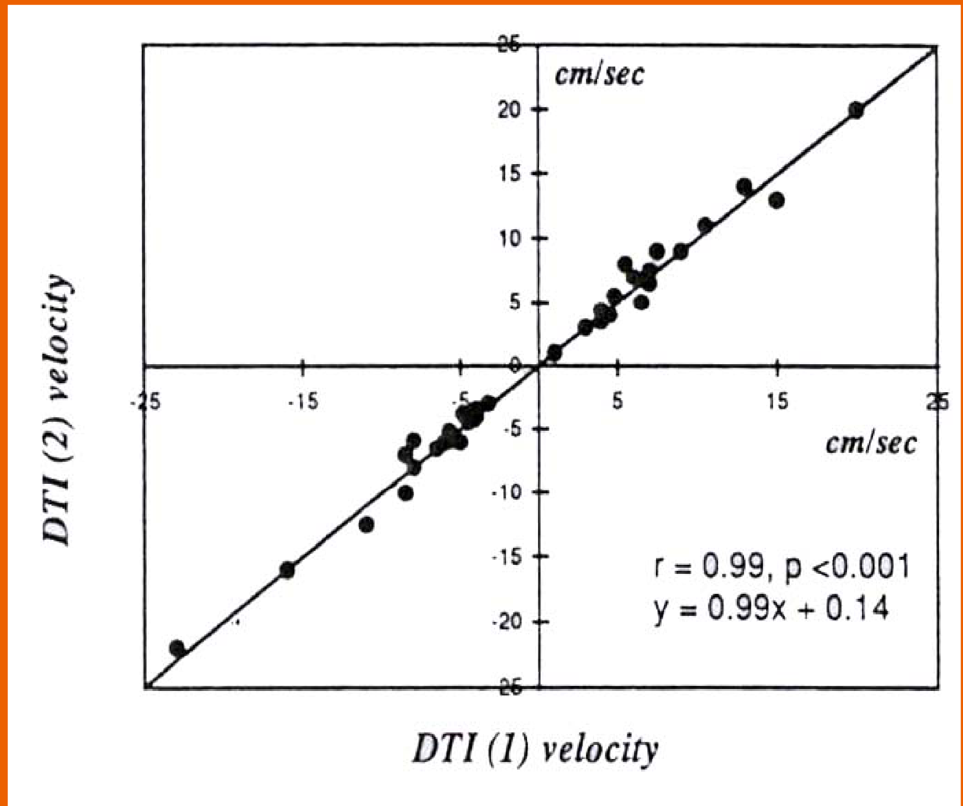
  -Systolic, diastolic, regional, dyssynchrony, valvular etc
- What is the aetiology?



"It's a simple model... but it works for me..."

Comparison of TDI and M-Mode Measurement of LV Function

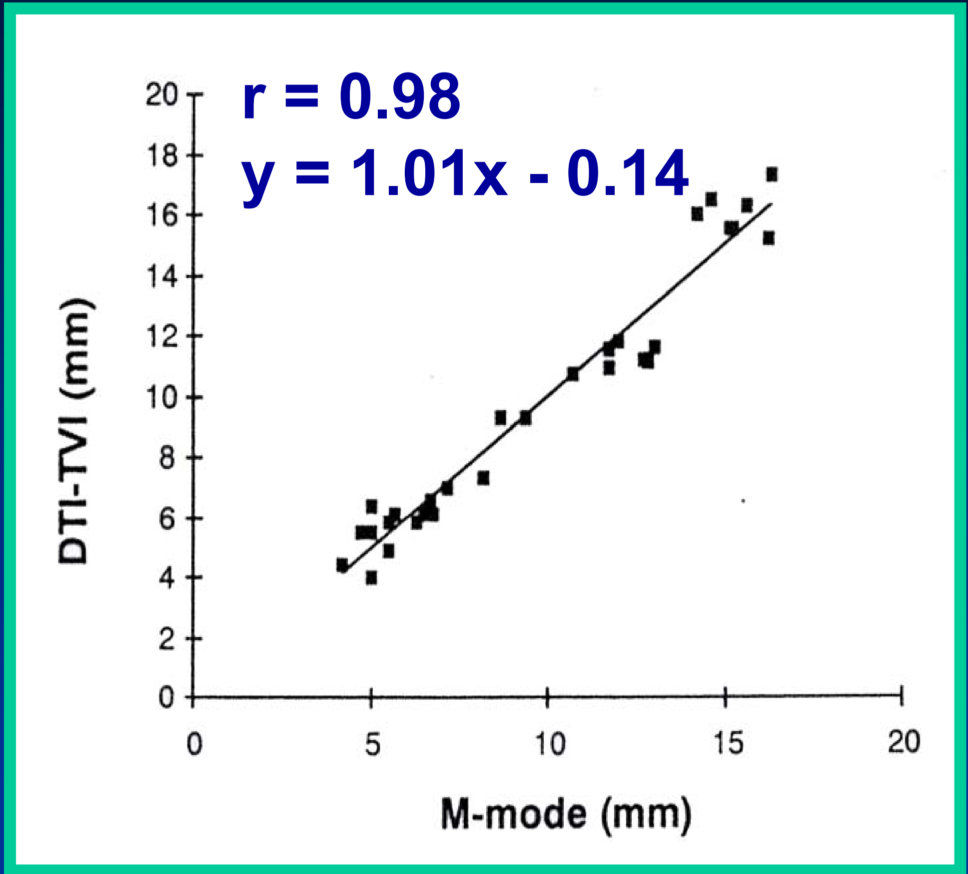
- 23 Controls & 17 patients with LVH
- Good correlation between TDI & M-Mode velocities ($r=0.95$, $p<0.001$)
- TDI had higher reproducibility then M-mode



Garcia MJ, AHJ 1996;132:648-56

Comparison of TDI and M-Mode Assessment of Mitral Annulus Displacement

- 23 Controls & 17 patients with LVH
- Apical TDI Vs M-Mode
- Velocity-time integral of TDI correlated closely with mitral annulus displacement.



Rodriguez et al, AHJ 1996;131:982-7