

# Is This Myocardial Disease Reversible or Not?

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순환기내과 최진오

# Disclosures

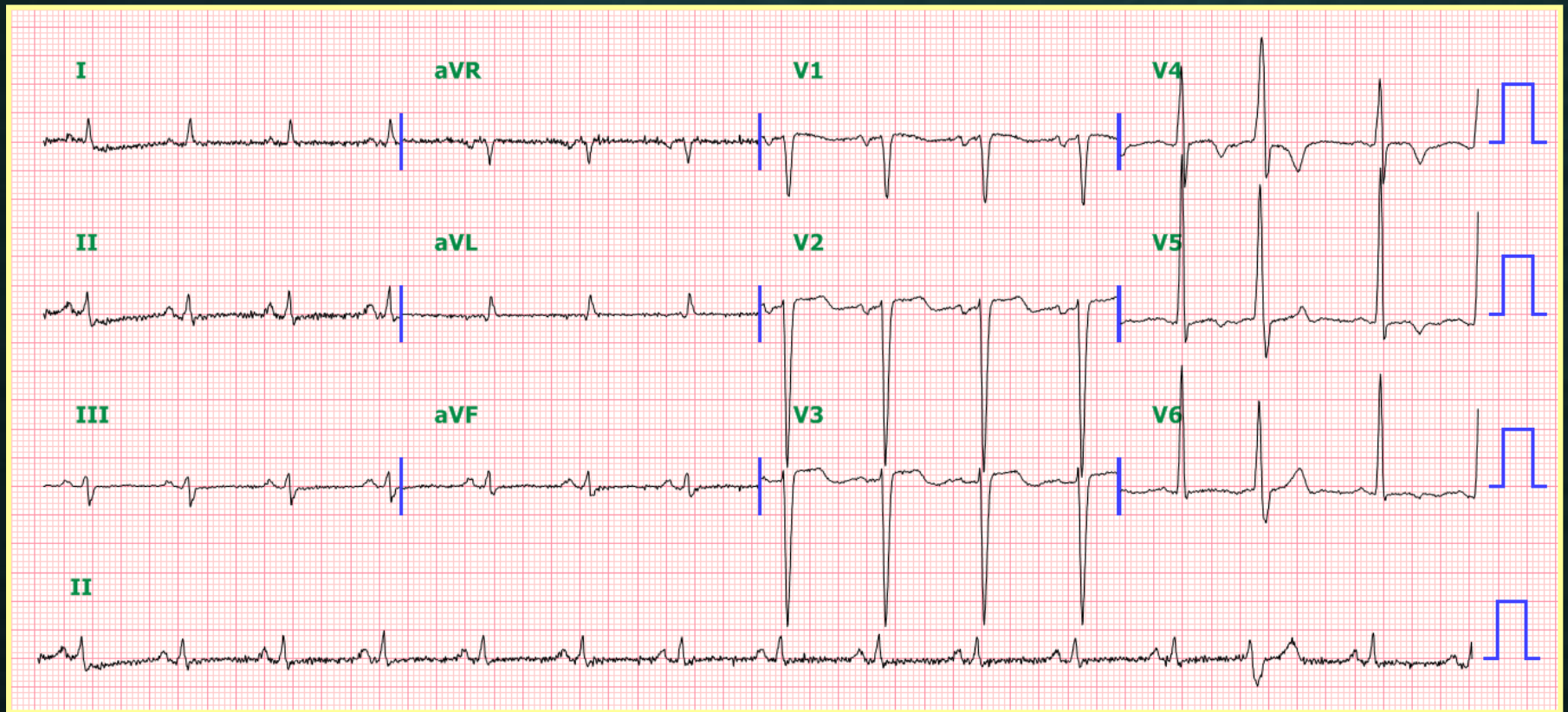
- I am not EP specialist
- I do not perform CRT or ICD procedure
- I am not going to deal with the predictors for CRT responders in this presentation
- But I would like to talk about who would undergo LV reverse remodeling (RR) with optimal medical treatment
  
- Otherwise nothing to disclose at this moment

# Aim of this presentation

- Not to provide insight about who would benefit from CRT or ICD
- But to understand LVRR occurs even in the patients with very severe symptoms and LV dysfunction
- Check possibility LVRR before device implantation

# Case

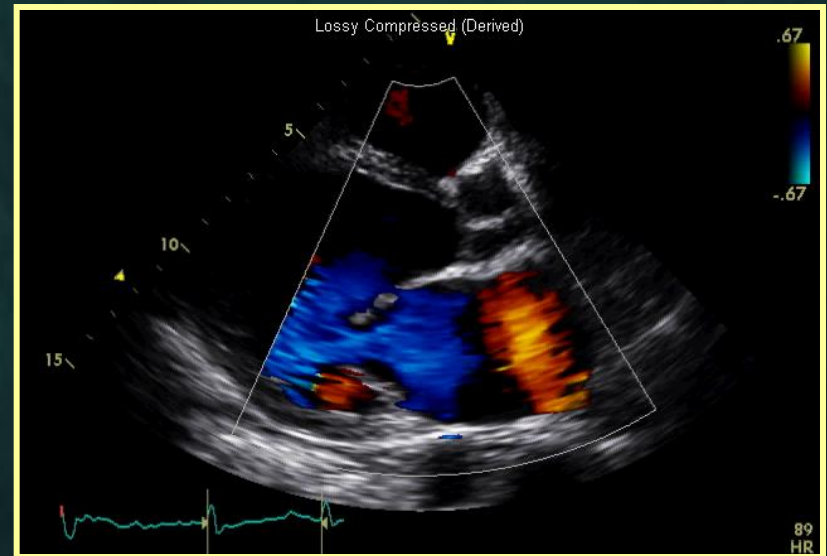
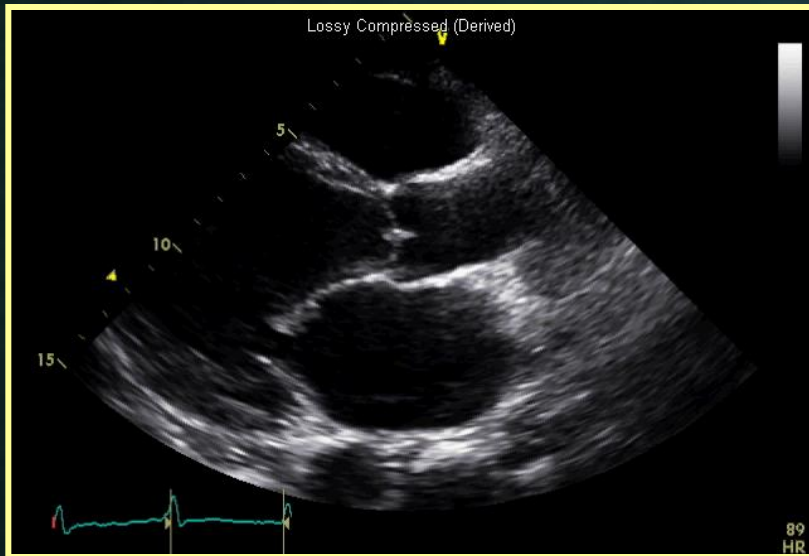
- **M/53**
- **DOE (3 month ago)**
- **Slightly improved after diuretics**
- **BP 108/74 mmHg HR 95 bpm**
- **JVP at 7cm above sternal angle**
- **Systolic mm at apex**



# CPA

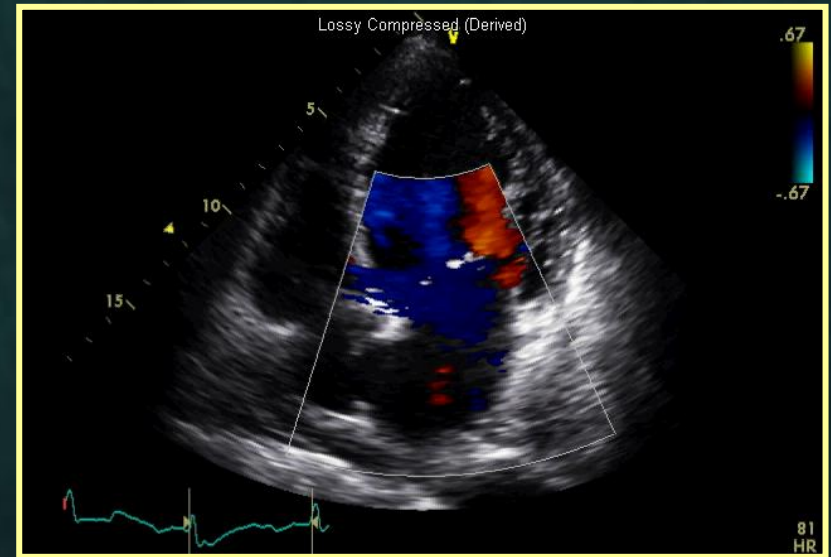
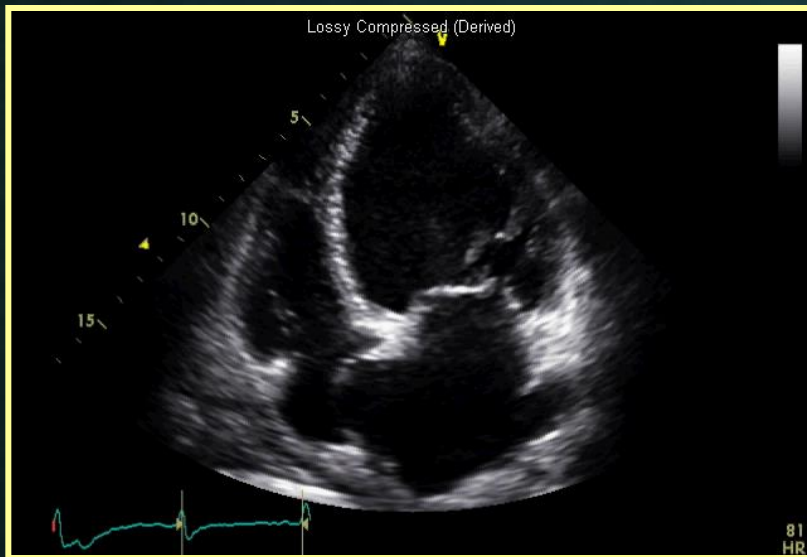


# EchoCG



**LV 75/61mm EF 23%**

# EchoCG

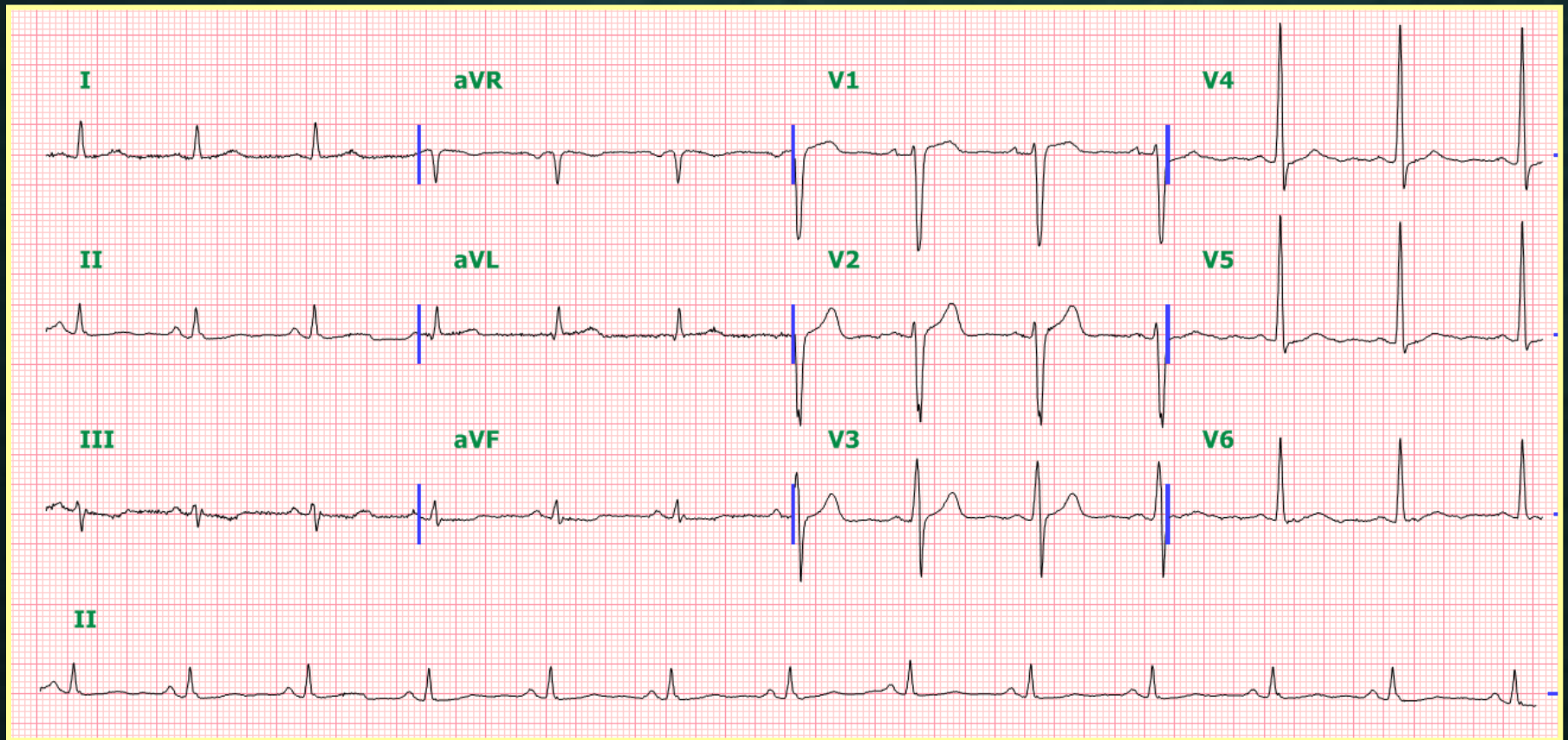


**LV 75/61mm EF 23%**



# Medical FU with following mx

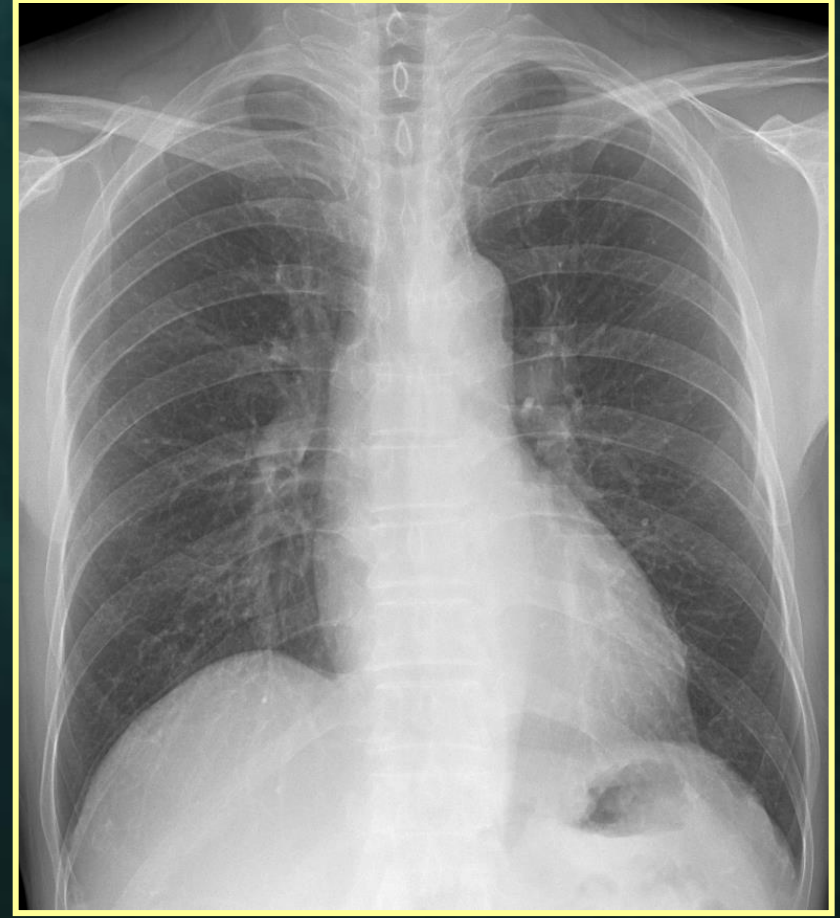
- Candesartan                      8mg                      qd
- Thiazide                            12.5mg                qd
- Spironolactone                12.5mg                qd
- Carvedilol                        12.5mg                bid



# CPA

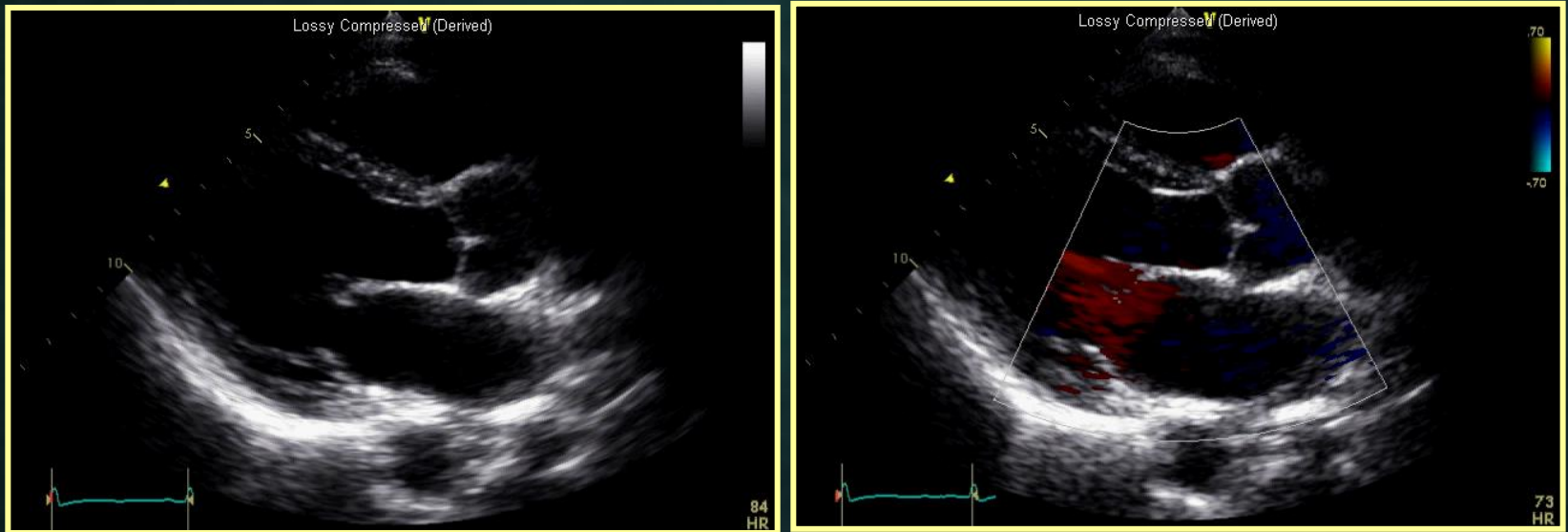


At Initial Presentation



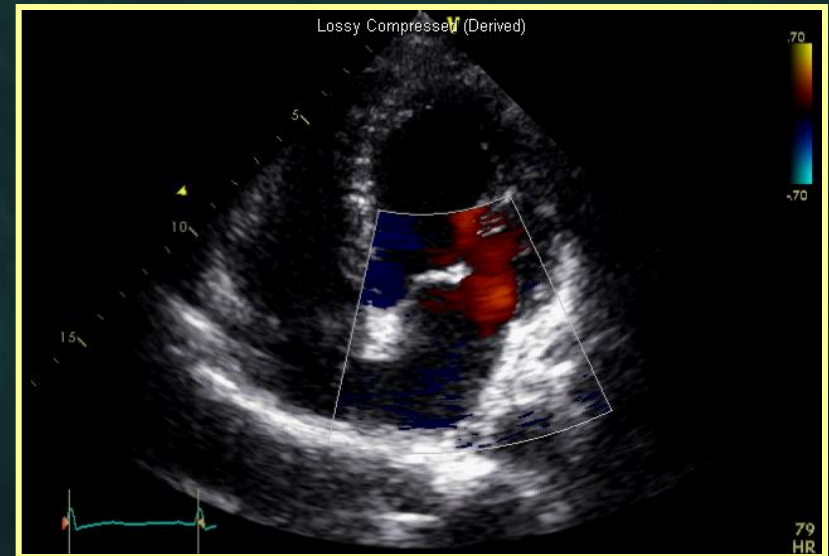
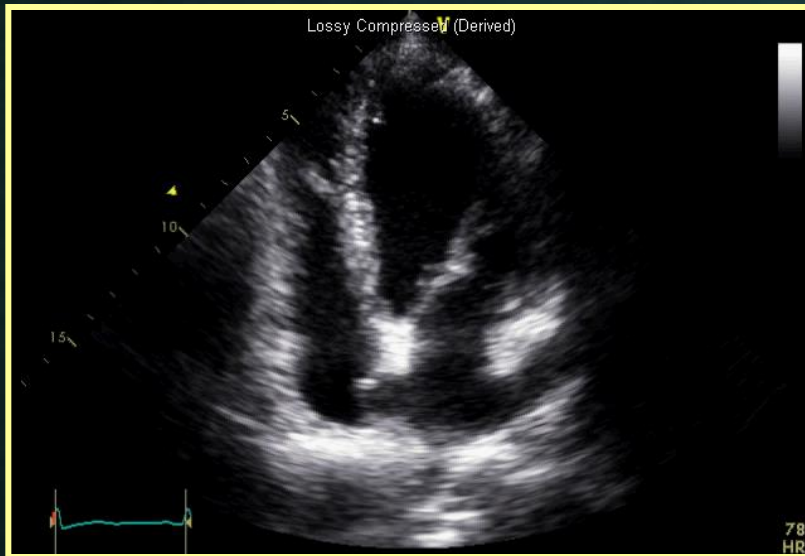
FU

# EchoCG



**LV 75/61mm EF 23% → 59/44 EF 51%**

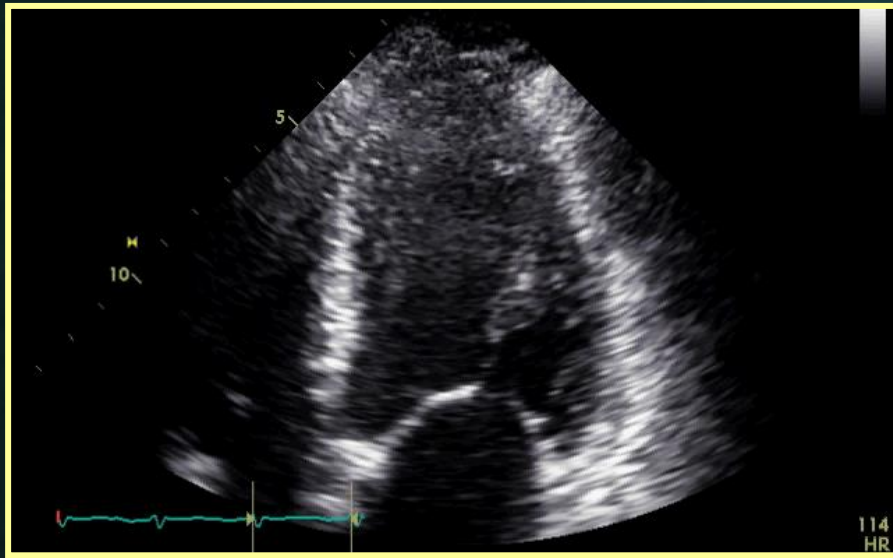
# EchoCG



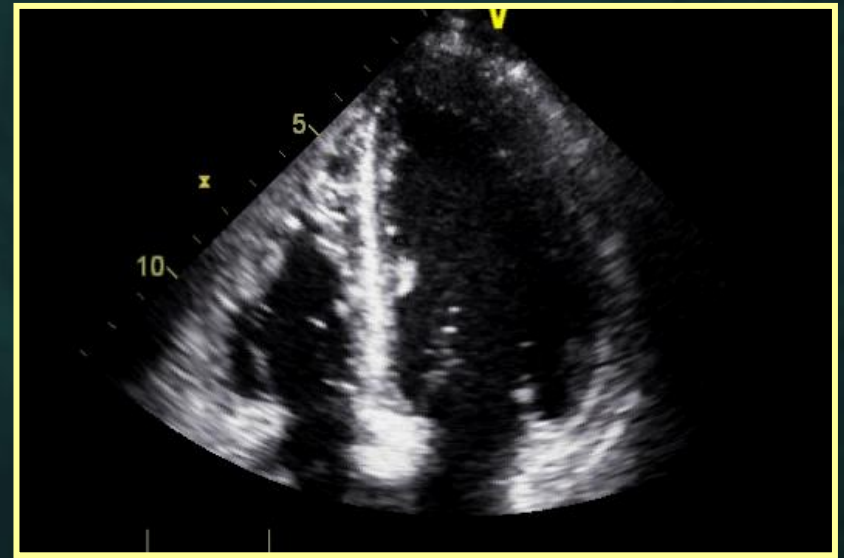
**LV 75/61mm EF 23% → 59/44 EF 51%**

# Stress-induced CMP

## Apical ballooning syndrome



At Initial Presentation



FU

# Reversible Myocardial Disease

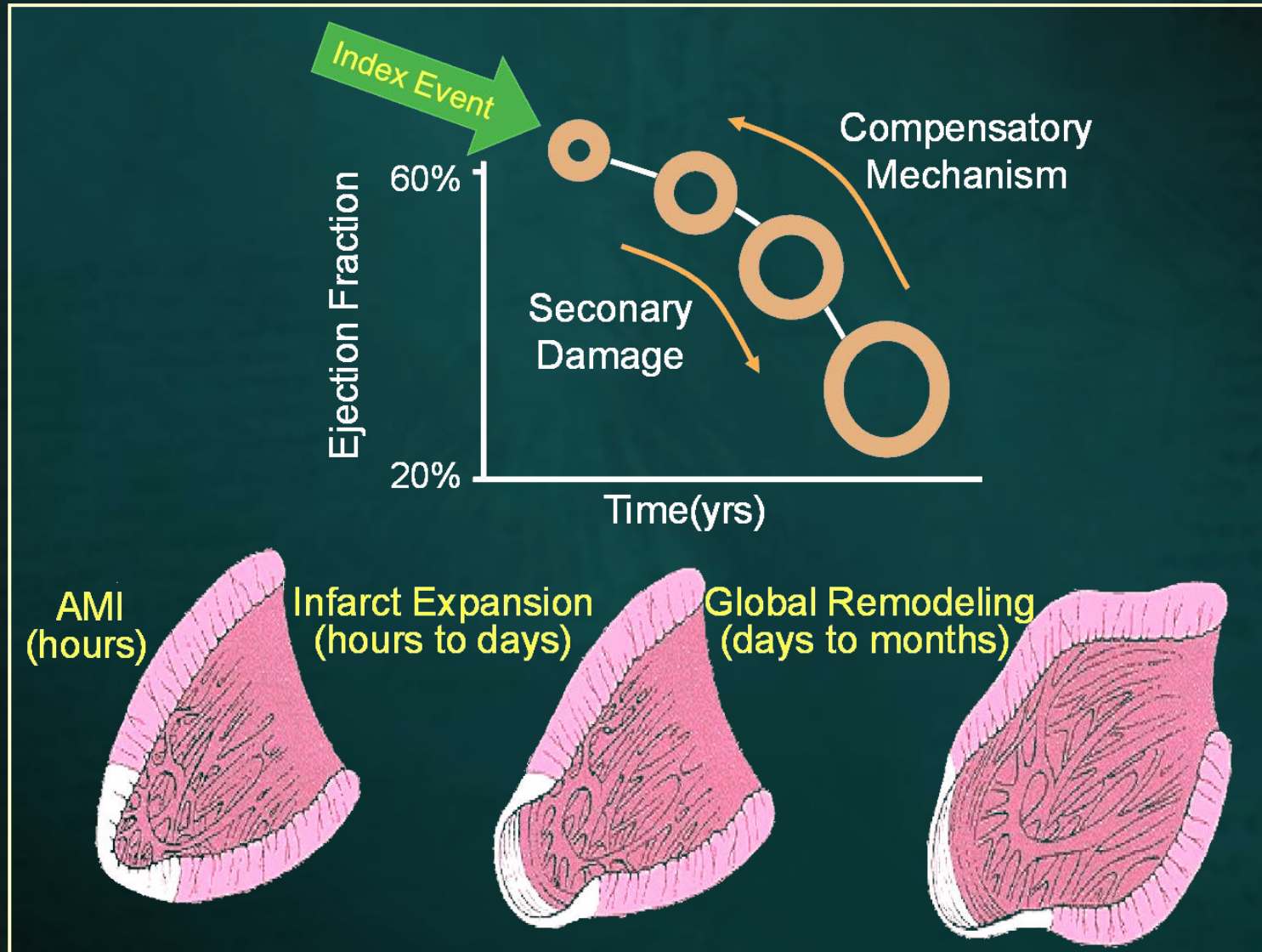
- **Stress-induced cardiomyopathy**
- **Alcoholic cardiomyopathy**
- **Peripartum cardiomyopathy**
- **Fulminant myocarditis**
- **Stunned / Hibernated myocardium**
- **Valvular heart diseases**
- **Etc**

# Reverse remodeling in Dilated CMP

Reversible DCM



# LV remodeling after AMI

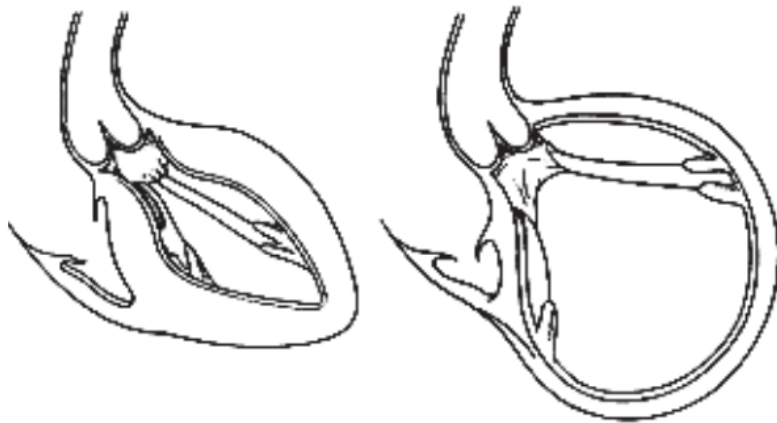


# Pathophysiology of HF

- **LV remodeling**
  - **Progressive LV dilation**
  - **Mediated by**
    - **Hemodynamic load**
    - **Neurohormonal activation**
    - **Other factors**

# LV Remodeling: more spherical

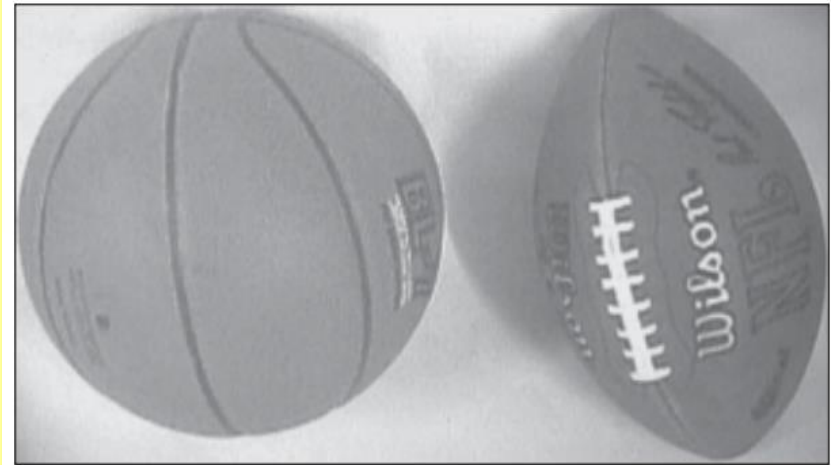
## Heart Shape



Normal  
(Ellipse)

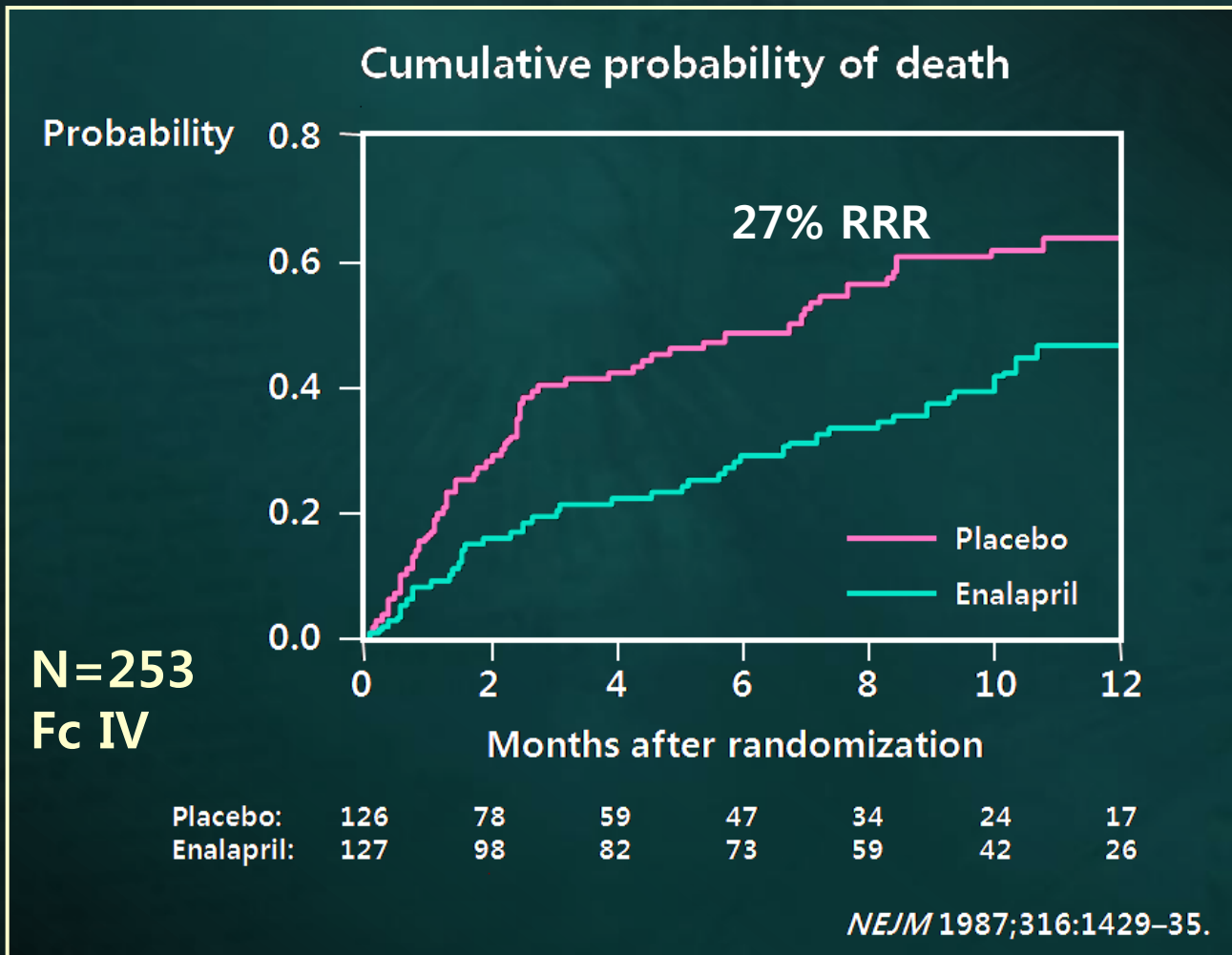
Dilated  
(shpere)

**Fig.1:** Left ventricular shape. The normal LV has an elliptical shape, with a well-defined apex. The dilated LV becomes spherical, and loses its oblique fiber angle orientation.

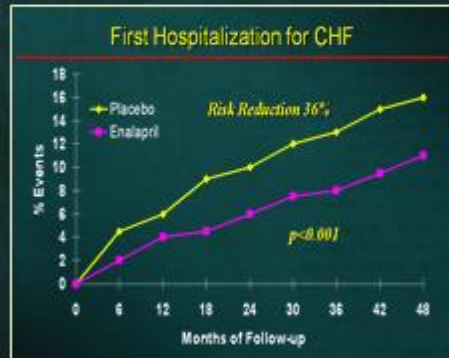
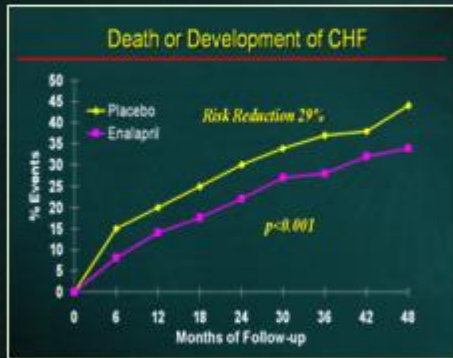


**Fig.-2:** The athletic corollary to shape changes between the normal, elliptical football and the globular, spherical basketball shape in heart failure. The surgical objective is to remake the elliptical football. (Reproduced with permission of Hisayoshi Suma, MD).

# CONSENSUS: Cooperative North Scandinavian Enalapril Survival Study



## SOLVD Prevention Trial



N=4226  
LVEF < 35%  
aSx

NEJM 1992;327:685-91

## SOLVD Treatment Trial

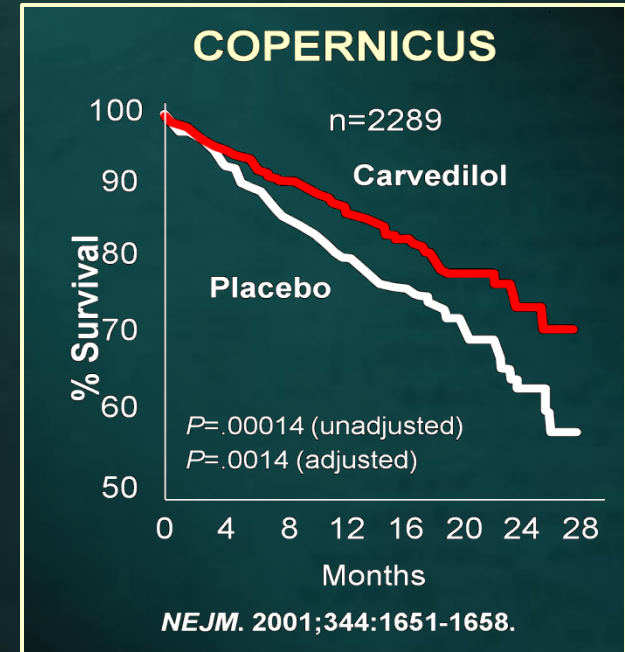
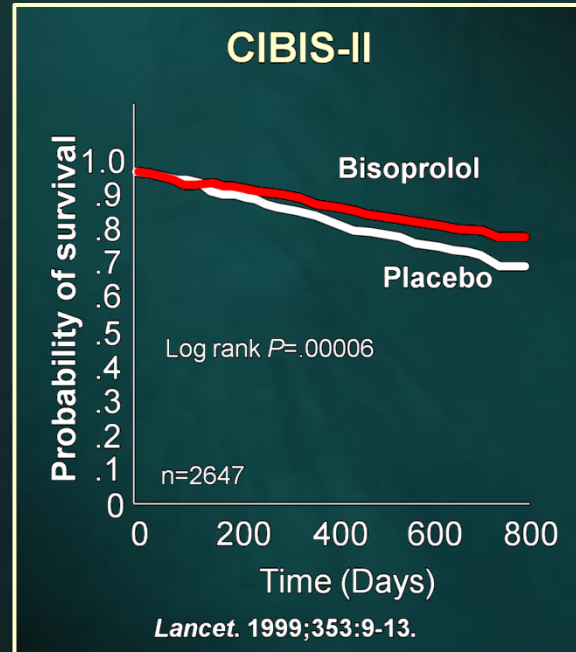
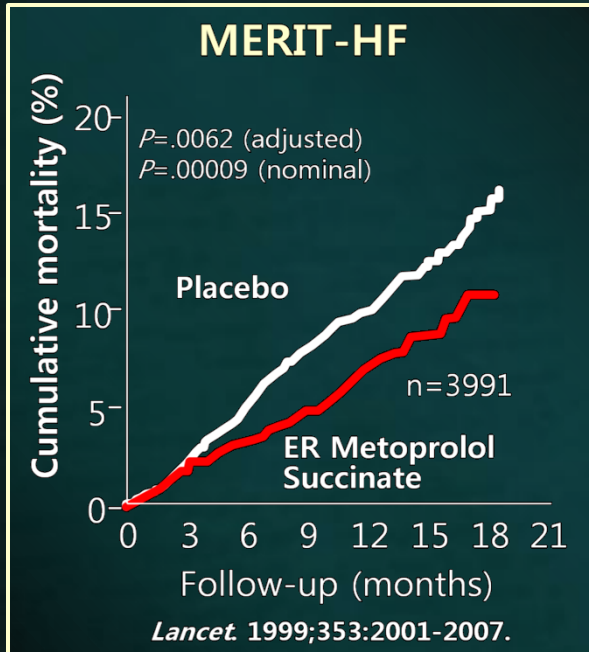


N=2569  
LVEF < 35%  
Fc II-III or IV



NEJM 1991;325:293-302

# Survival Studies with $\beta$ -Blockers in HF



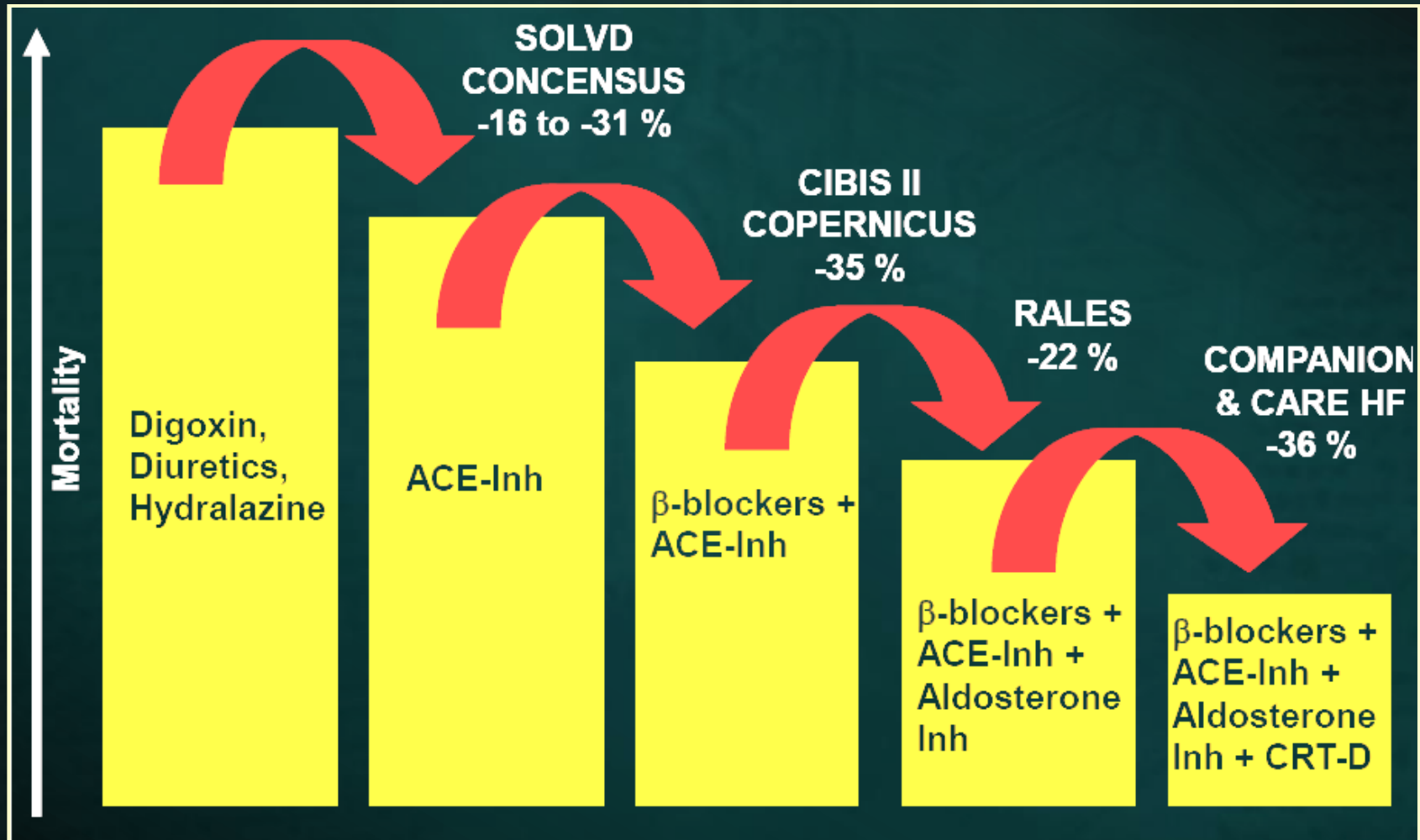
**Mortality:**

↓ **34%**

↓ **34%**

↓ **35%**

# Progression of HF Mx; Add-on Tx



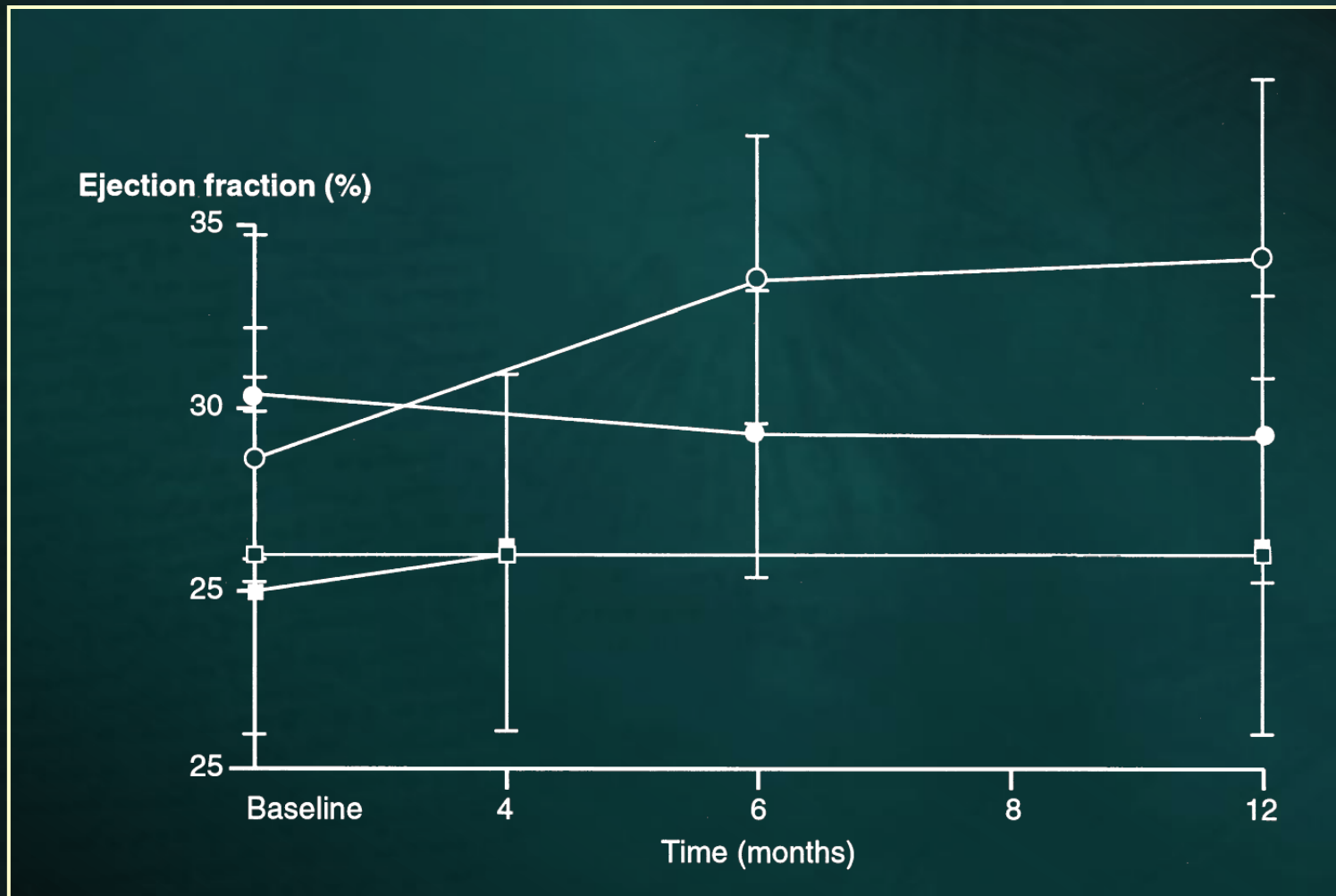
Class/Type	Specific Drug	Study Population	Impact on Mortality	Impact on Morbidity	Impact on Remodeling
Cardiac glycosides	Digoxin	HF (2)	=	? (decreased hospitalizations)	? Improved EF
Vasodilators	Hydralazine/ isosorbide dinitrate	HF (100)	+	?	Improved EF
	Prazosin	HF (100)	=	?	=
Calcium channel blockers	Diltiazem	HF (101)	-	-	?
	Felodipine	HF (102)	=	=	Short-term improved EF
Inotropic agents	Milrinone	HF (1)	-	-	?
ACE inhibitors	Captopril	Post MI (85, 103)	+	+	Improved EF; attenuation of LV dilation
	Enalapril	Post MI (104)	-	+	?
		Asymptomatic LV dysfunction, including post-MI (15)	+	+	Improved EF; attenuation of LV dilation
		HF (14, 105)	+	+	Improved EF; attenuation of LV dilation; improved ESV



Class/Type	Specific Drug	Study Population	Impact on Mortality	Impact on Morbidity	Impact on Remodeling
Beta blockers	Bisoprolol	HF (12, 86, 110)	+	+	Improved fractional shortening and decreased ESV
	Carvedilol	HF (7, 8, 111–114)	+	+	Improved EF, decreased ESV and EDV and dimensions; improved sphericity index, EF, WMI
		Post-MI (115)	+	+	Improved EF, decreased ESV and EDV; improved WMI
	Metoprolol	HF (6,10)	+	+	Improved EF, decreased LV volumes; improved LV geometry
	Propranolol	Post-MI (116)	+		Improved EF
	Timolol	Post-MI (117)	+		Improved EF

# Improvement of LV EF in HFrEF

## SOLVD and ANZ study

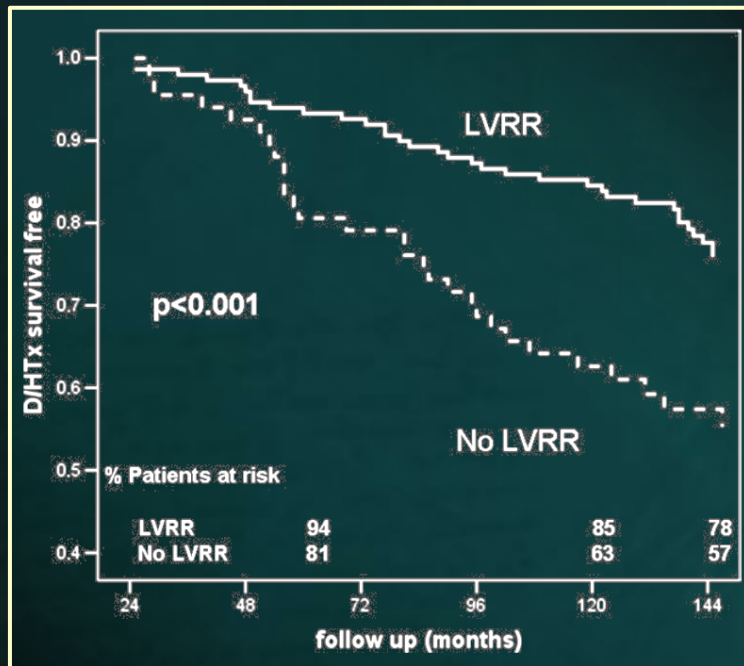


- **RAS inhibitor;**
  - **May attenuate LV dilation**
  
- **Beta blockers;**
  - **May reverse LV remodeling**

# LV Reverse remodeling (LVRR)

**LV ESV ↓ ≥ 15%**

# LVRR on GDMT



**Table 6** Incremental Prognostic Role of LVRR, NYHA Functional Classes III to IV, and Moderate to Severe MR at Mid-Term Follow-Up (Model 2)

	HR	95% CI	p Value	AUC
<b>Death/HTx</b>				0.80
Model 1*	2.02	1.48-2.76	<0.001	
LVRR	0.44	0.25-0.78	0.005	
NYHA functional class III to IV at 24 months	3.75	2.03-6.95	<0.001	
Moderate to severe MR at 24 months	1.70	1.02-2.83	0.04	
<b>Pump failure death/HTx</b>				0.77
Model 1†	1.82	1.04-3.17	0.03	
LVRR	0.24	0.07-0.84	0.03	
NYHA functional class III to IV at 24 months	6.73	2.92-15.53	<0.001	
Moderate to severe MR at 24 months	2.79	1.22-6.34	0.01	
<b>Sudden death/MVA</b>				0.69
Model 1‡	2.18	1.49-3.19	<0.001	
LVRR	0.39	0.21-0.74	0.004	
NYHA functional class III to IV at 24 months	1.13	0.41-3.12	0.80	
Moderate to severe MR at 24 months	1.50	0.80-2.79	0.20	

This may suggest a higher probability of improvement in patients with **more chances of tailoring treatment** and an increased possibility of modulating the afterload in the absence of severe, long-standing, irreversible structural abnormalities

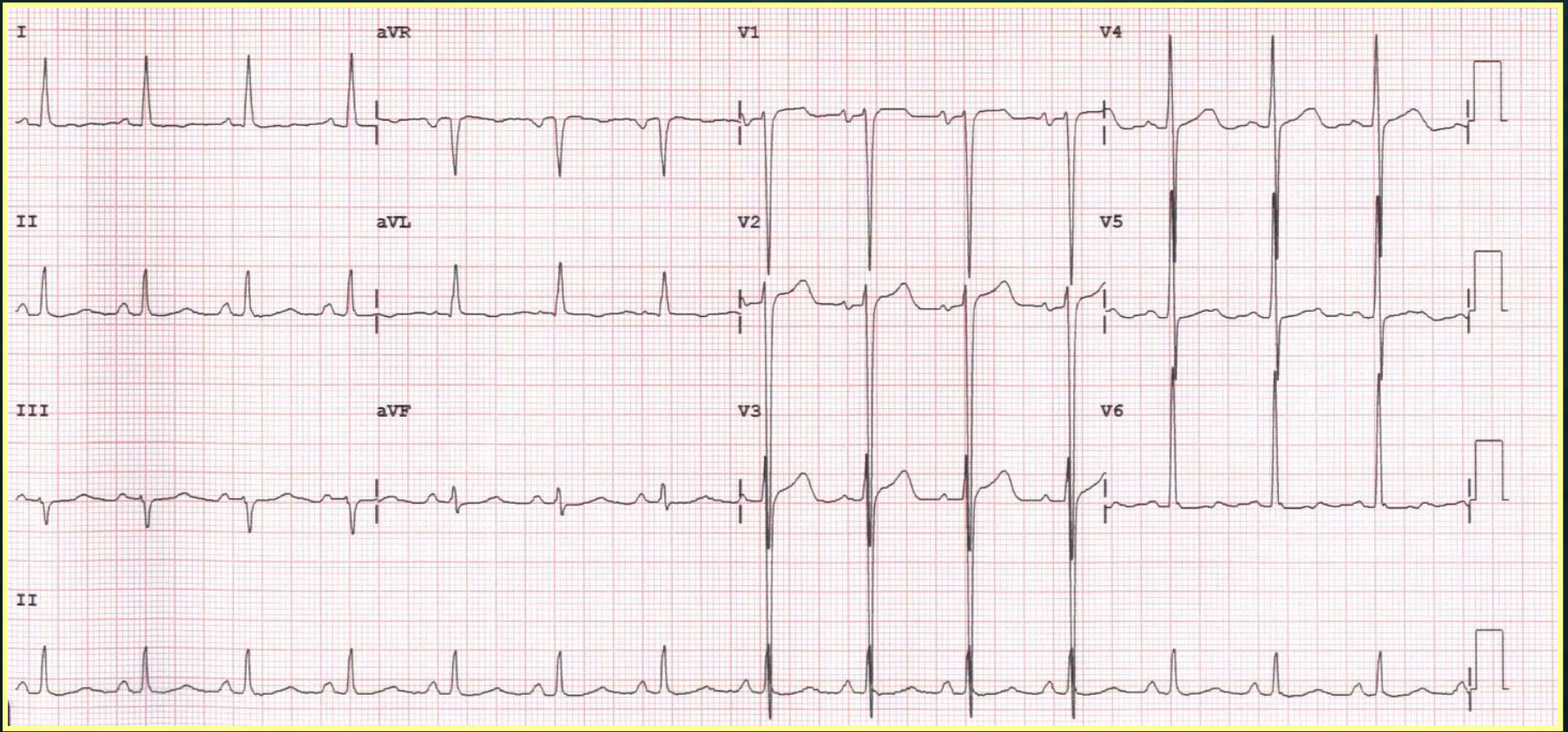
## Optimal Medical Treatment

**Table 3** Baseline Independent Predictors of LVRR at Mid-Term Follow-Up

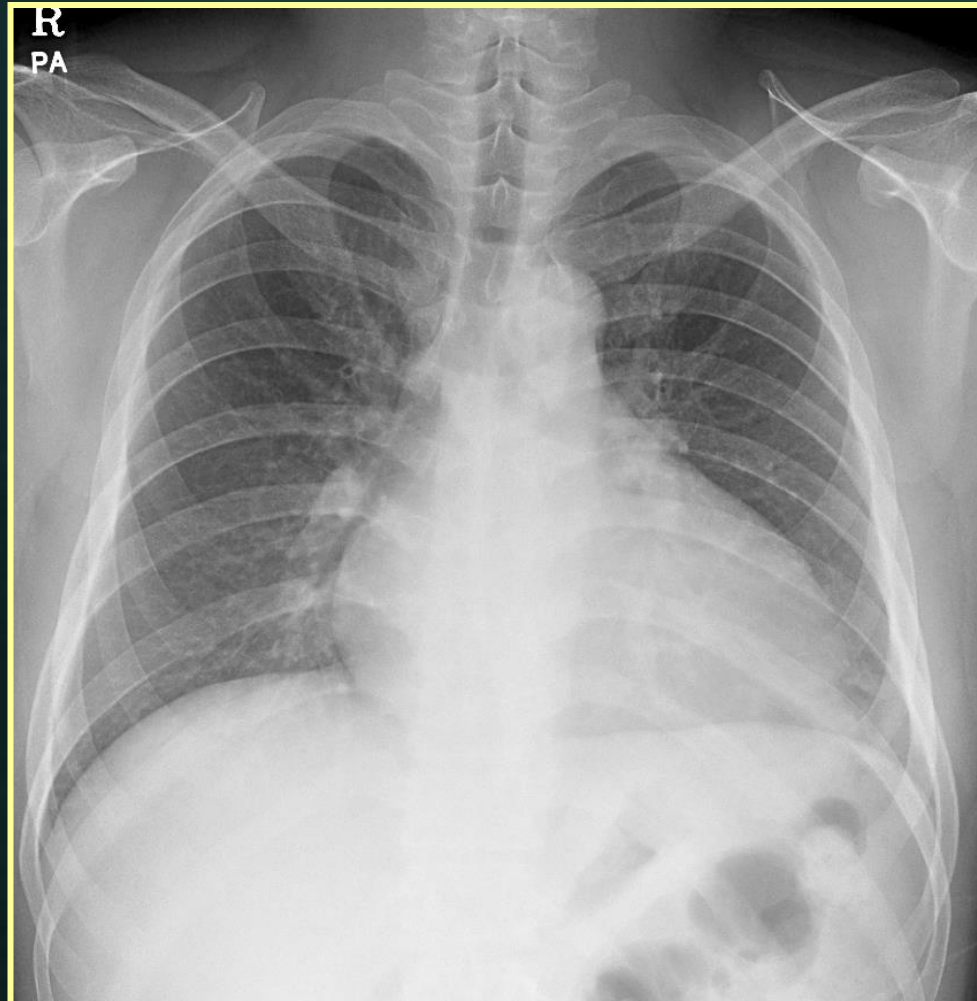
	OR	95% CI	p Value
SBP, per 10-mm Hg increase	1.23	1.01-1.53	0.047
Absence of LBBB	2.47	1.25-4.87	0.009

# Case II

- **M/32**
- **2 MA Dyspnea**
- **Orthopnea (+) and NYHA Fc IV dyspnea**
- **BP 180/120 mmHg HR 78 bpm**

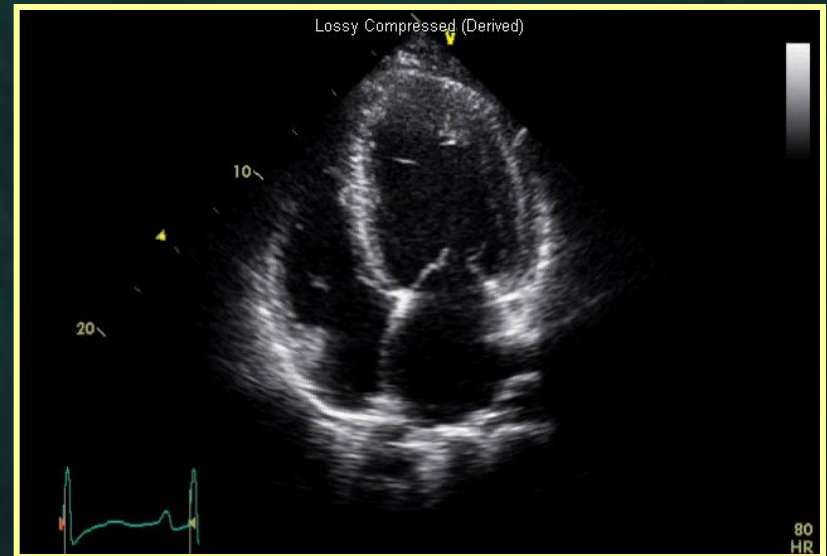
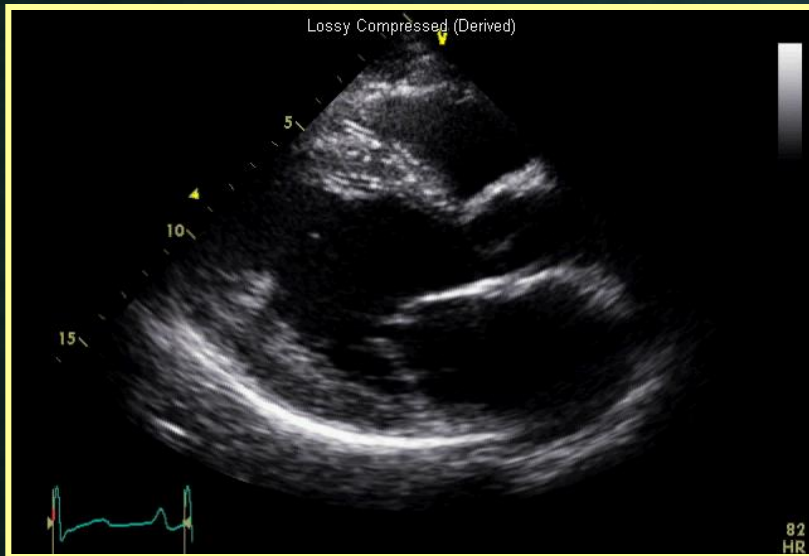


# CPA



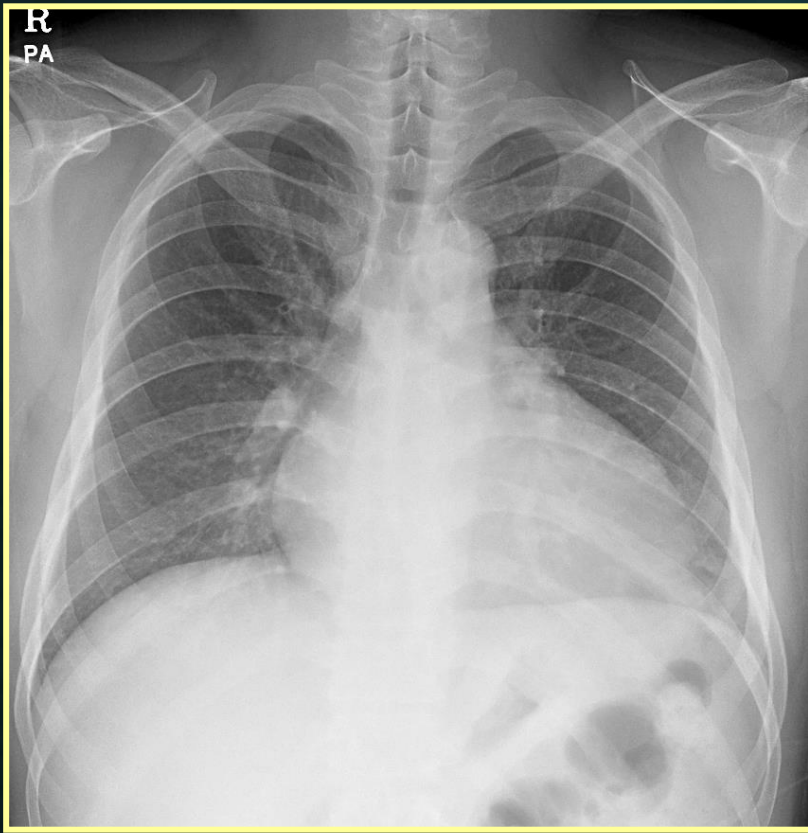


# Echo

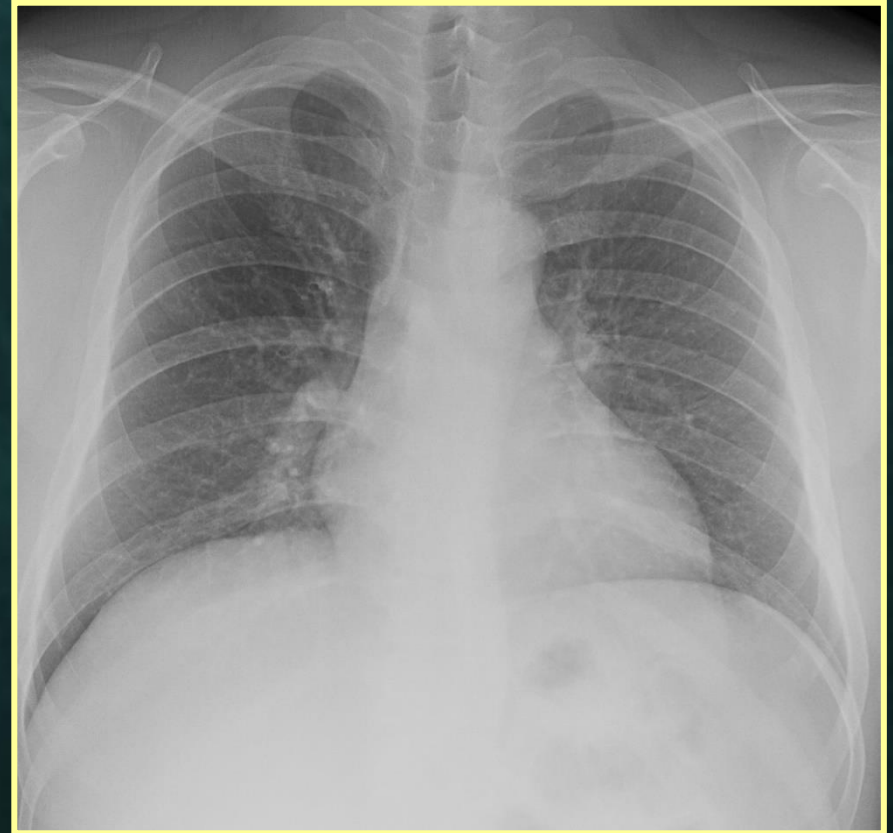


**LV 65/55 mm EF 23%**

# CPA

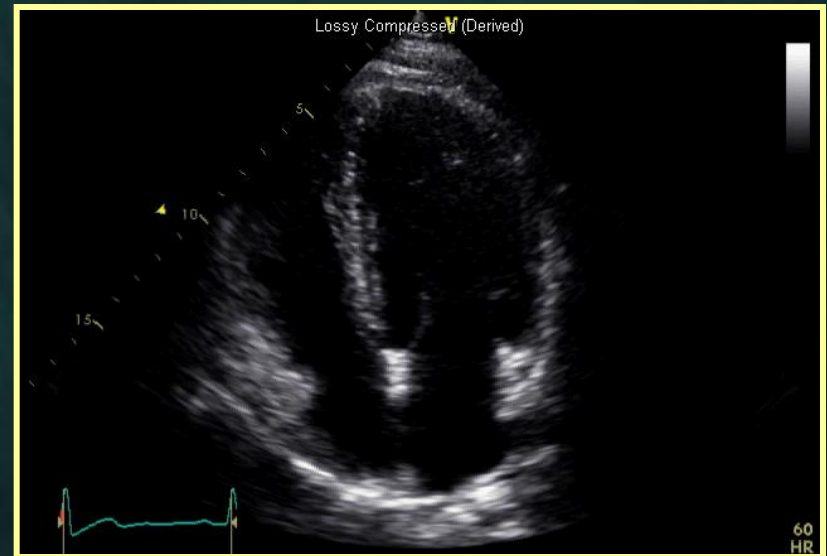
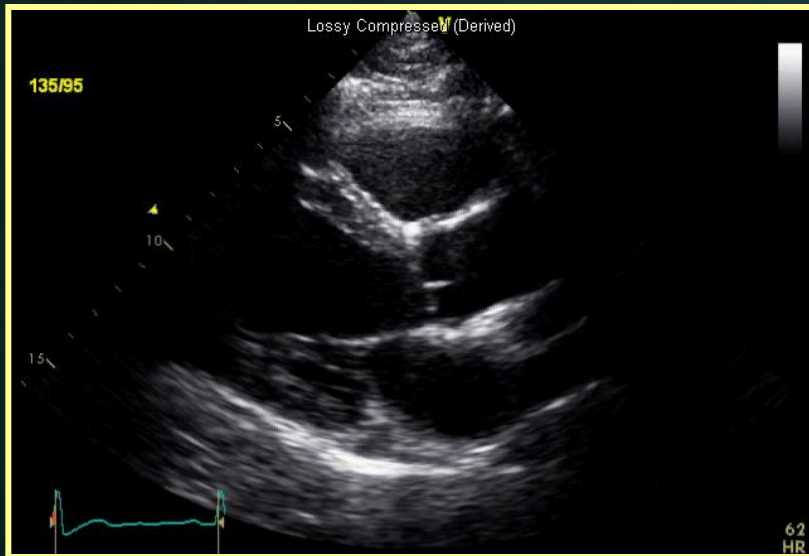


At Initial Presentation



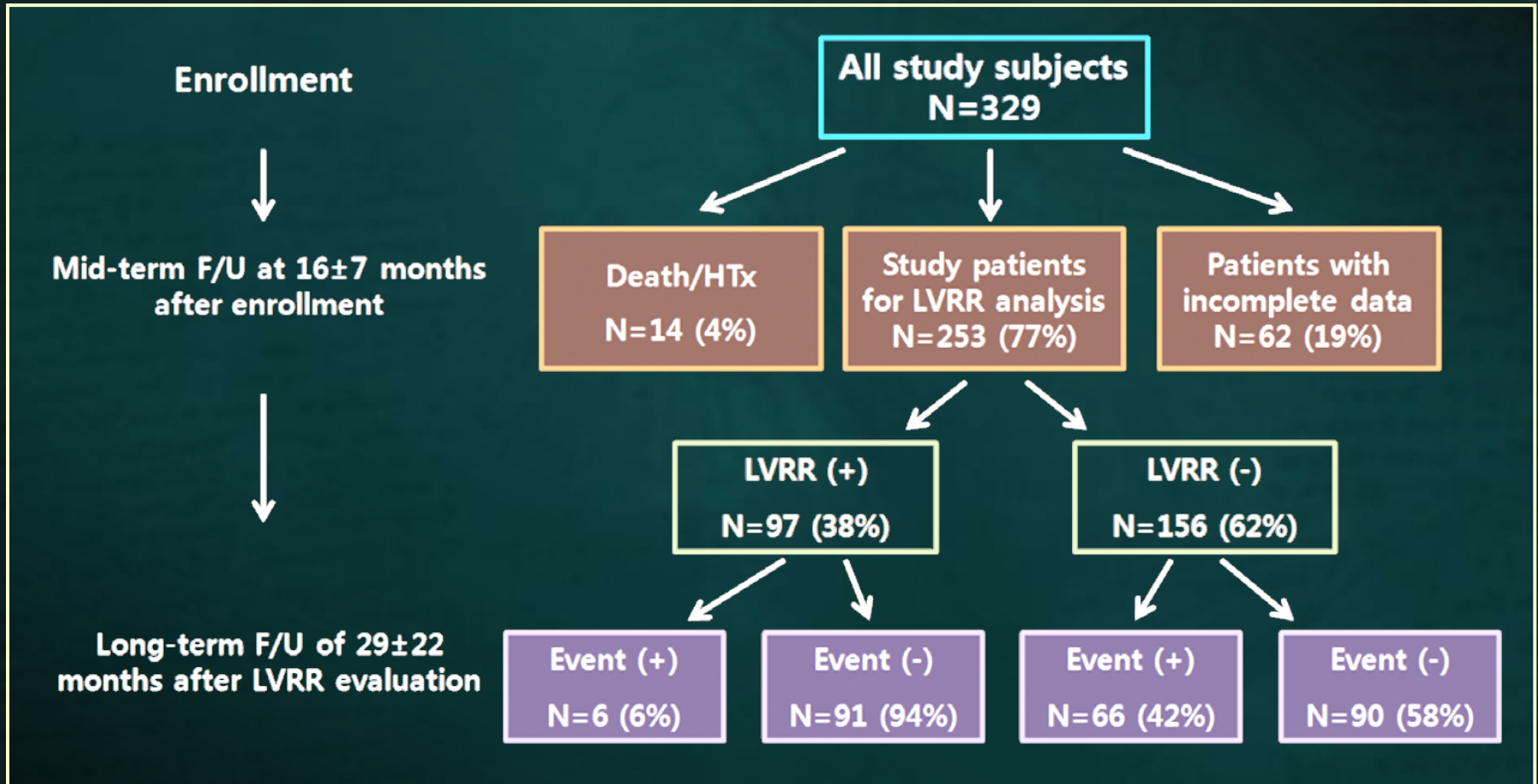
FU

# Echo



**LV 65/55 mm EF 23% → 53/24 EF 70%**

# LVRR in NICM



# LVRR in NICM

**Table 4. Results of Multivariate Baseline Independent Predictors of LVRR at Midterm Follow-up**

Variable (n=253)	OR (95% CI)	P value
SBP, per 10 mmHg increase	1.24 (1.07–1.44)	0.005
QRS duration >120 ms	0.32 (0.16–0.65)	0.002
$\beta$ -blocker	2.22 (1.17–4.22)	0.015
Log NT-proBNP at baseline	1.11 (0.72–1.80)	0.575
LVEF, per 10% increase	0.62 (0.40–0.98)	0.040
LVESD index	0.93 (0.87–0.99)	0.030

Adjusted covariates include male sex, age, SBP on admission, prolongation of QRS, use of  $\beta$ -blocker, log NT-proBNP at baseline, LVEF, LVESD index and E/e'.

# Prevalence and Clinical Predictors of Reverse Remodeling in Patients with Dilated Cardiomyopathy

Michael Arad MD<sup>1</sup>, Tamar Nussbaum MD<sup>1</sup>, Ido Blechman BA<sup>1</sup>, Micha S. Feinberg MD<sup>2</sup>, Nira Koren-Morag PhD<sup>3</sup>, Yael Peled MD<sup>1</sup> and Dov Freimark MD<sup>1</sup>

<sup>1</sup>Heart Failure Service and <sup>2</sup>Non-Invasive Cardiology Unit, Leviev Heart Institute, Sheba Medical Center, Tel Hashomer, Israel

<sup>3</sup>Division of Epidemiology, Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel

- **N=188 DCM**
- **LVRR in 50 (26%)**
- **LVRR**
  - **Less common in familial DCM and longstanding disease and prior exposure to chemoTx**
  - **More common in recent onset disease, lower initial LVEF and normal ECG**

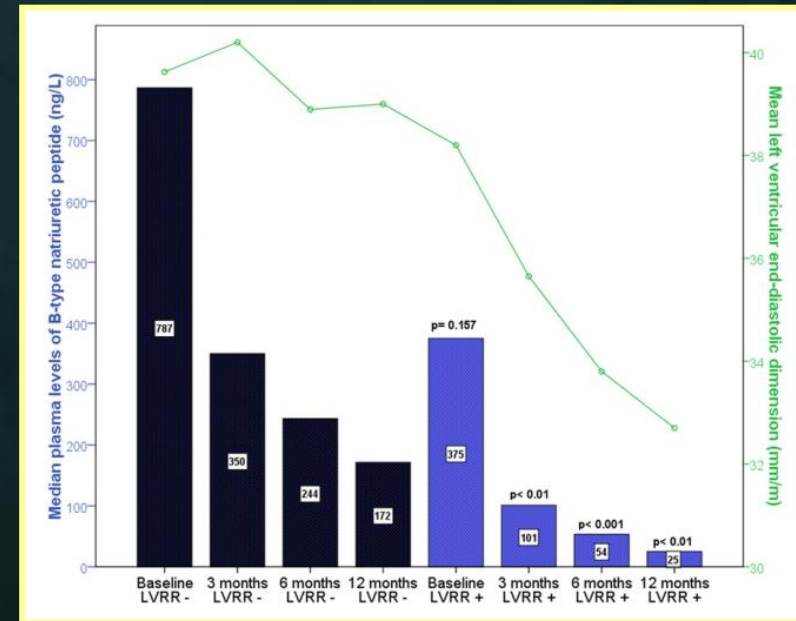
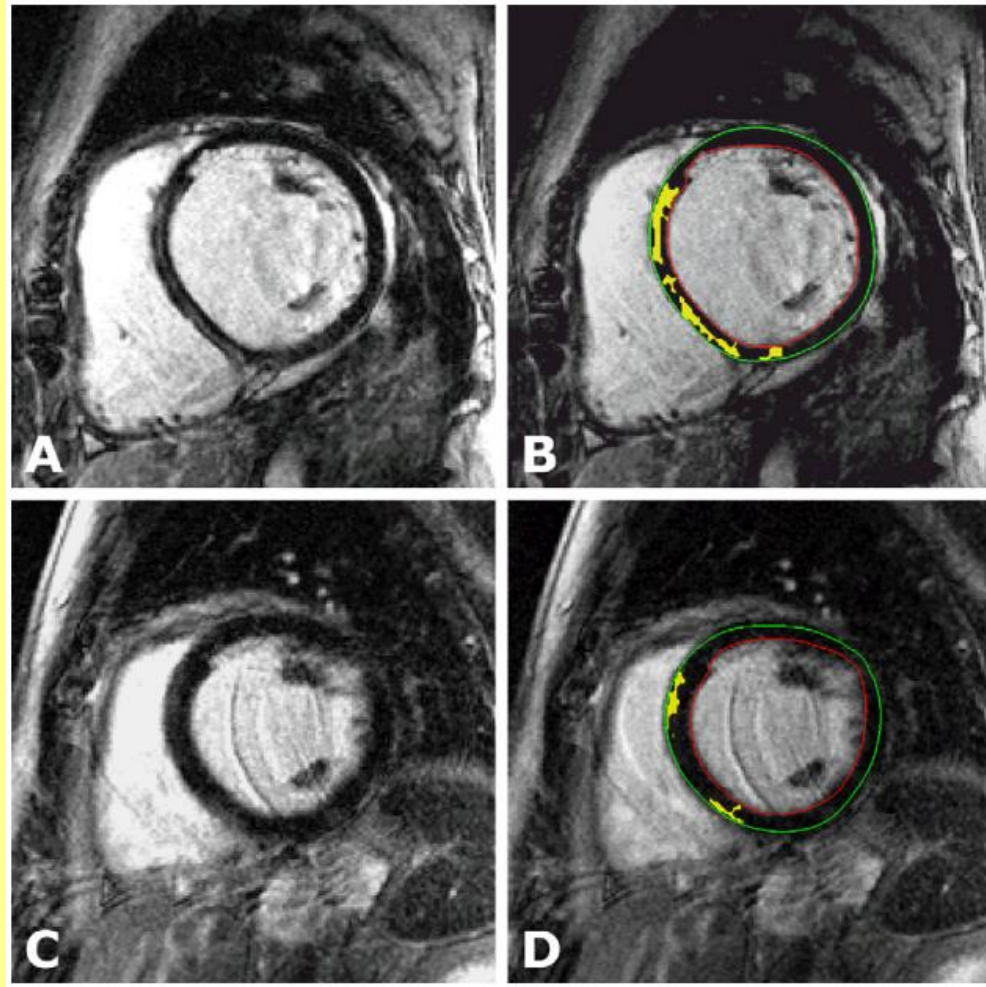
# Favorable factors for LV reverse remodeling

- High BP at presentation
- Absence of LBBB or prolonged QRS duration

## Novel Predictors of Left Ventricular Reverse Remodeling in Individuals With Recent-Onset Dilated Cardiomyopathy

Milos Kubanek, MD, PhD,\* Marek Sramko, MD,† Jana Maluskova, MD,‡ Dana Kautznerova, MD,§  
Jiri Weichet, MD, PhD,\* Petr Lupinek, MD, PhD,\* Jana Vrbska, MD,\* Ivan Malek, MD, PhD,\*  
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Prague, Czech Republic





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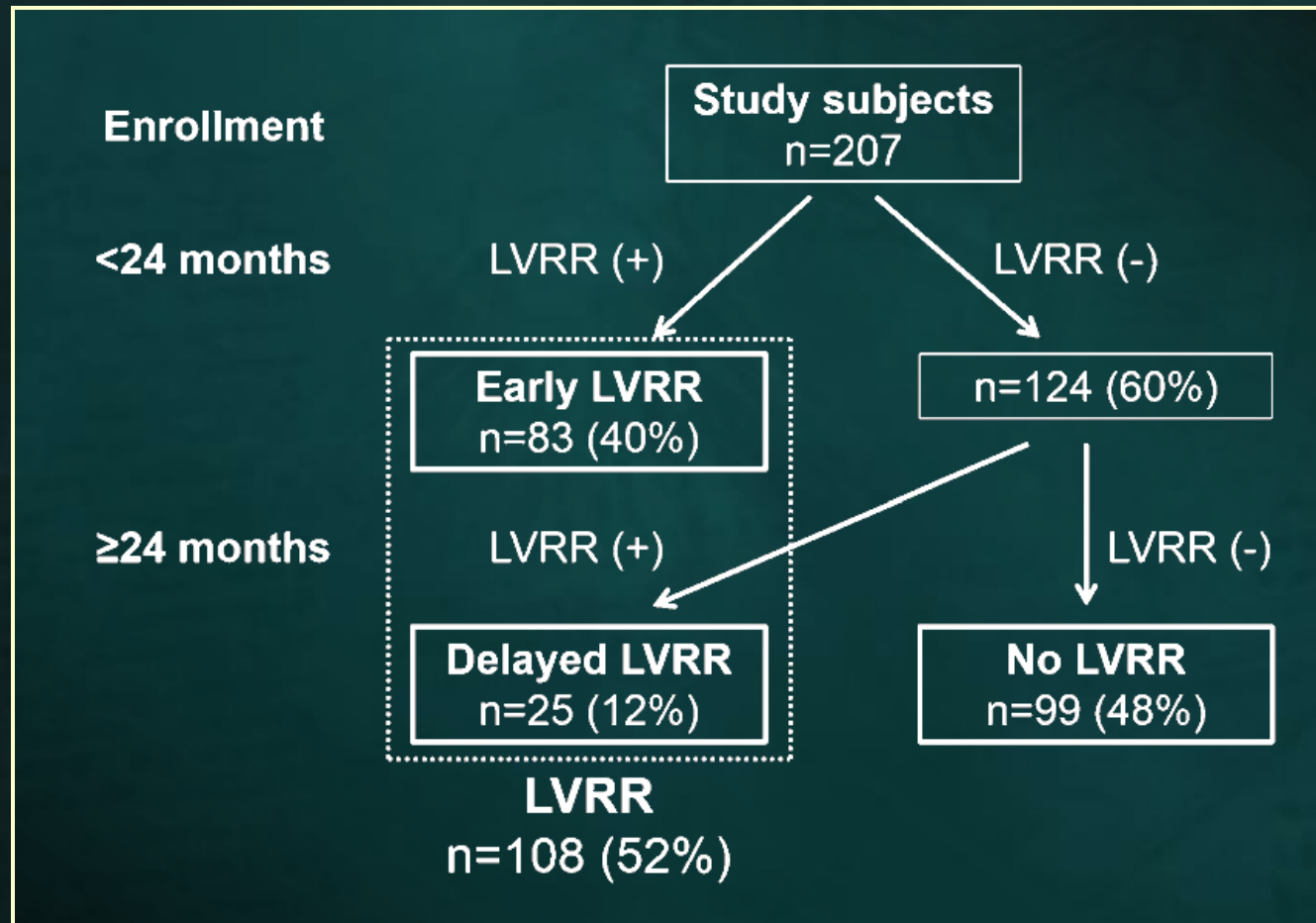
**Table 1**

### Results of Multivariate Analysis Showing the Strongest Predictors of LVRR at Baseline and 3 and 6 Months of Follow-Up

	Independent Predictors of LVRR	Odds Ratio (95% CI)	p Value
Baseline (Model 1)	1. Indexed LGE extent	0.67 (0.50–0.90)	0.008*
	2. Myocardial edema ratio (per 0.1 unit)	1.45 (1.04–2.02)	0.027*
3 Months (Model 2)	Logarithm of BNP (3 months)	0.14 (0.02–0.94)	0.042*
6 Months (Model 3)	1. LVEDD index (6 months)	0.73 (0.56–0.96)	0.014*
	2. E/E' ratio (6 months)	0.56 (0.33–0.94)	0.019*

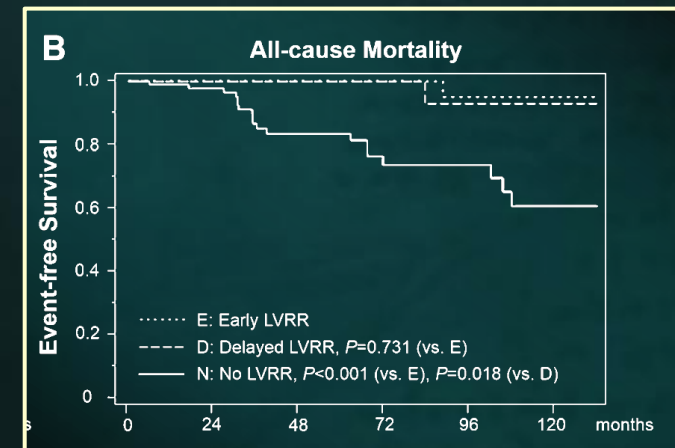
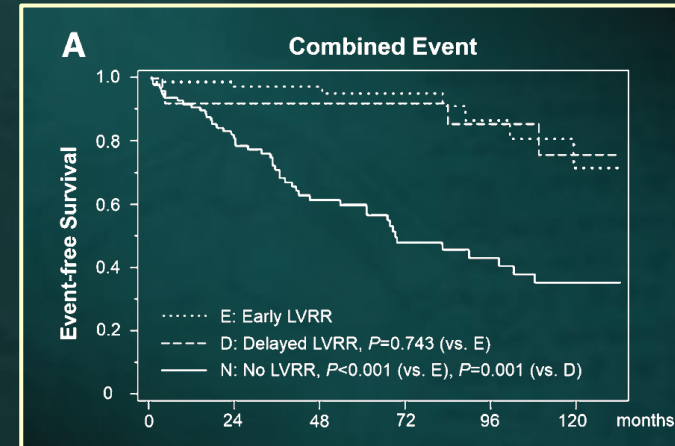
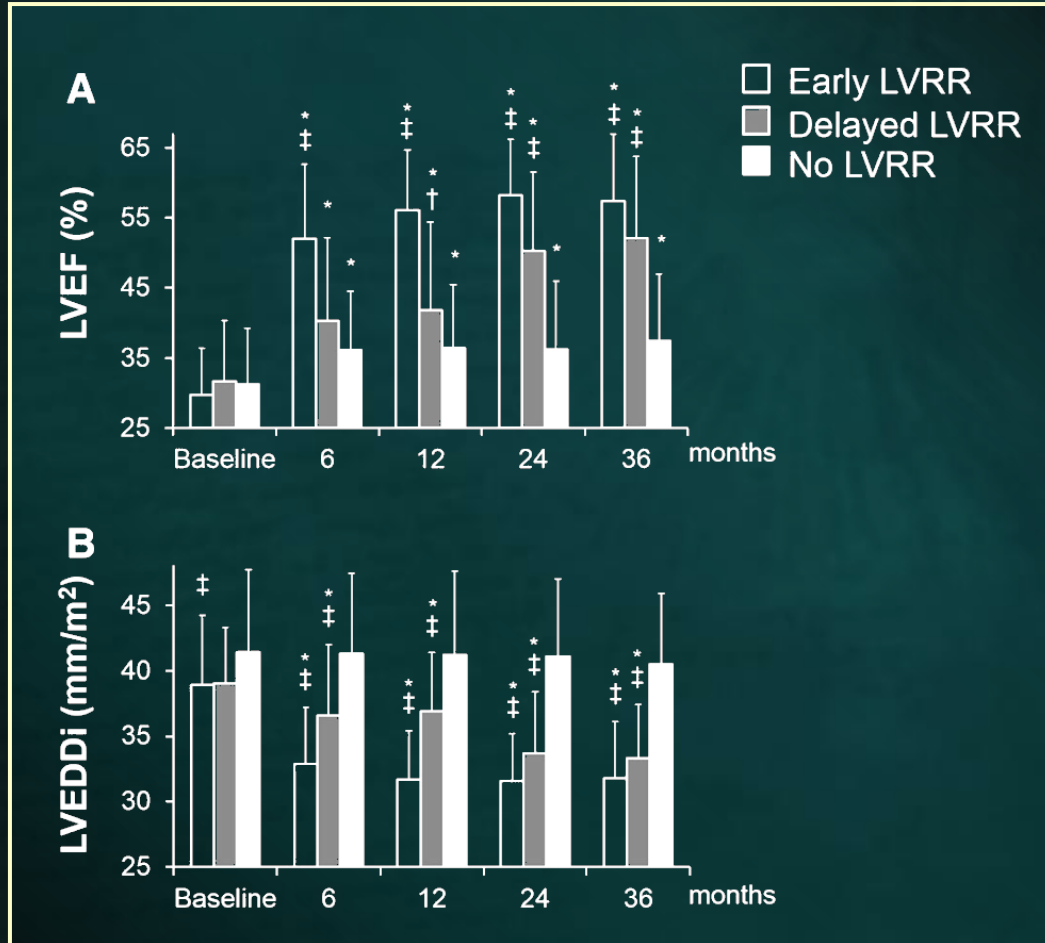
# Time course of left ventricular reverse remodeling in response to pharmacotherapy: clinical implication for heart failure prognosis in patients with idiopathic dilated cardiomyopathy

Yuki Ikeda · Takayuki Inomata · Yuichiro Iida · Miwa Iwamoto-Ishida · Takeru Nabeta · Shunsuke Ishii · Takanori Sato · Tomoyoshi Yanagisawa · Tomohiro Mizutani · Takashi Naruke · Toshimi Koitabashi · Ichiro Takeuchi · Mototsugu Nishii · Junya Ako



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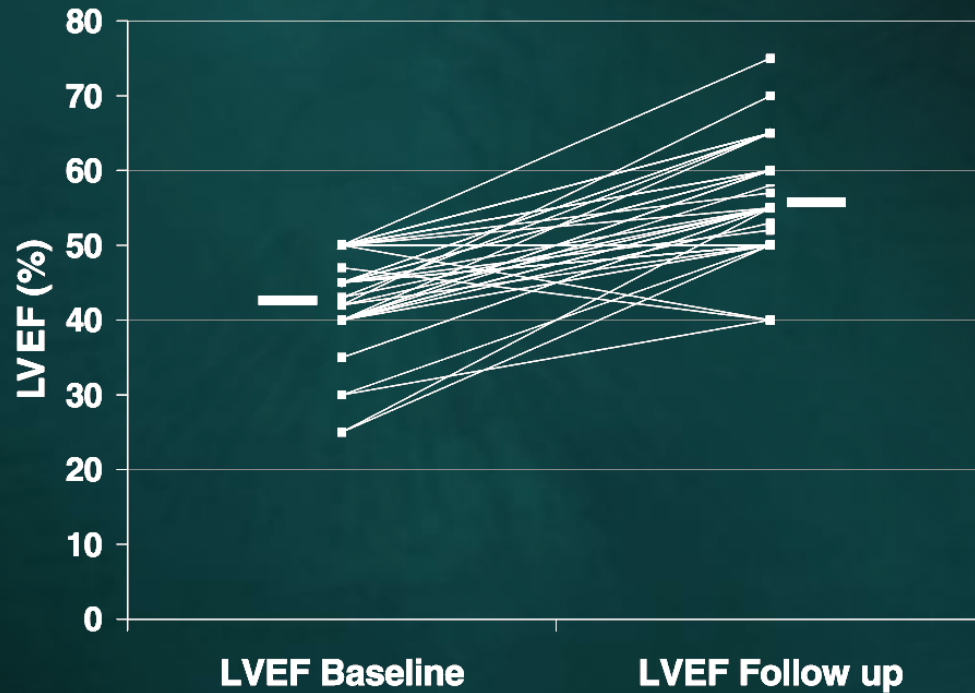
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## Reversal of Left Ventricular Dysfunction Following Ablation of Atrial Fibrillation

PHILIP J. GENTLESK, M.D., WILLIAM H. SAUER, M.D., EDWARD P. GERSTENFELD, M.D.,  
 DAVID LIN, M.D., SANJAY DIXIT, M.D., ERICA ZADO, PA-C, DAVID CALLANS, M.D., and  
 FRANCIS E. MARCHLINSKI, M.D.

From the Cardiovascular Division, Department of Medicine, Hospital of the University of Pennsylvania, Philadelphia, Pennsylvania, USA



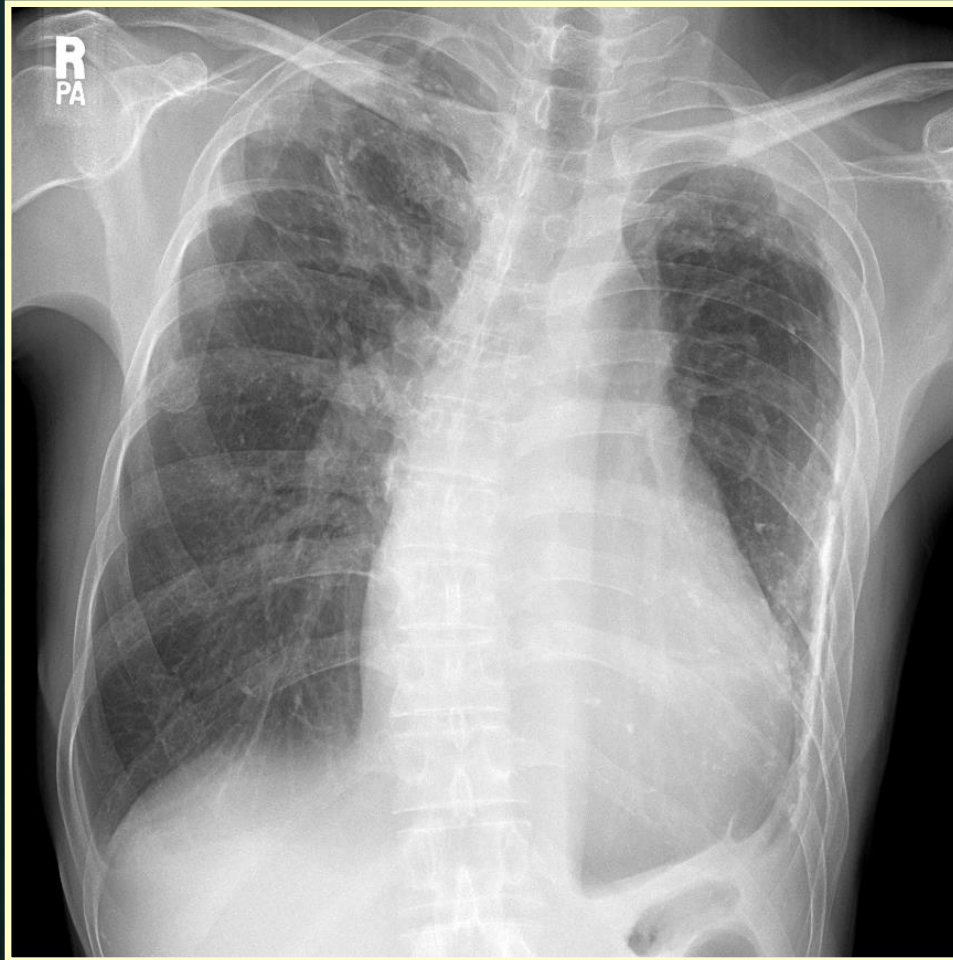
**Figure 4.** Effect of pulmonary vein isolation on left ventricular ejection fraction (LVEF) in 50 patients without coronary artery or valvular disease and with a preablation diagnosis of idiopathic cardiomyopathy. All but three patients experienced an increase in LVEF with the mean LVEF increasing from  $42 \pm 9\%$  to  $57 \pm 7\%$ ,  $P < 0.001$ .

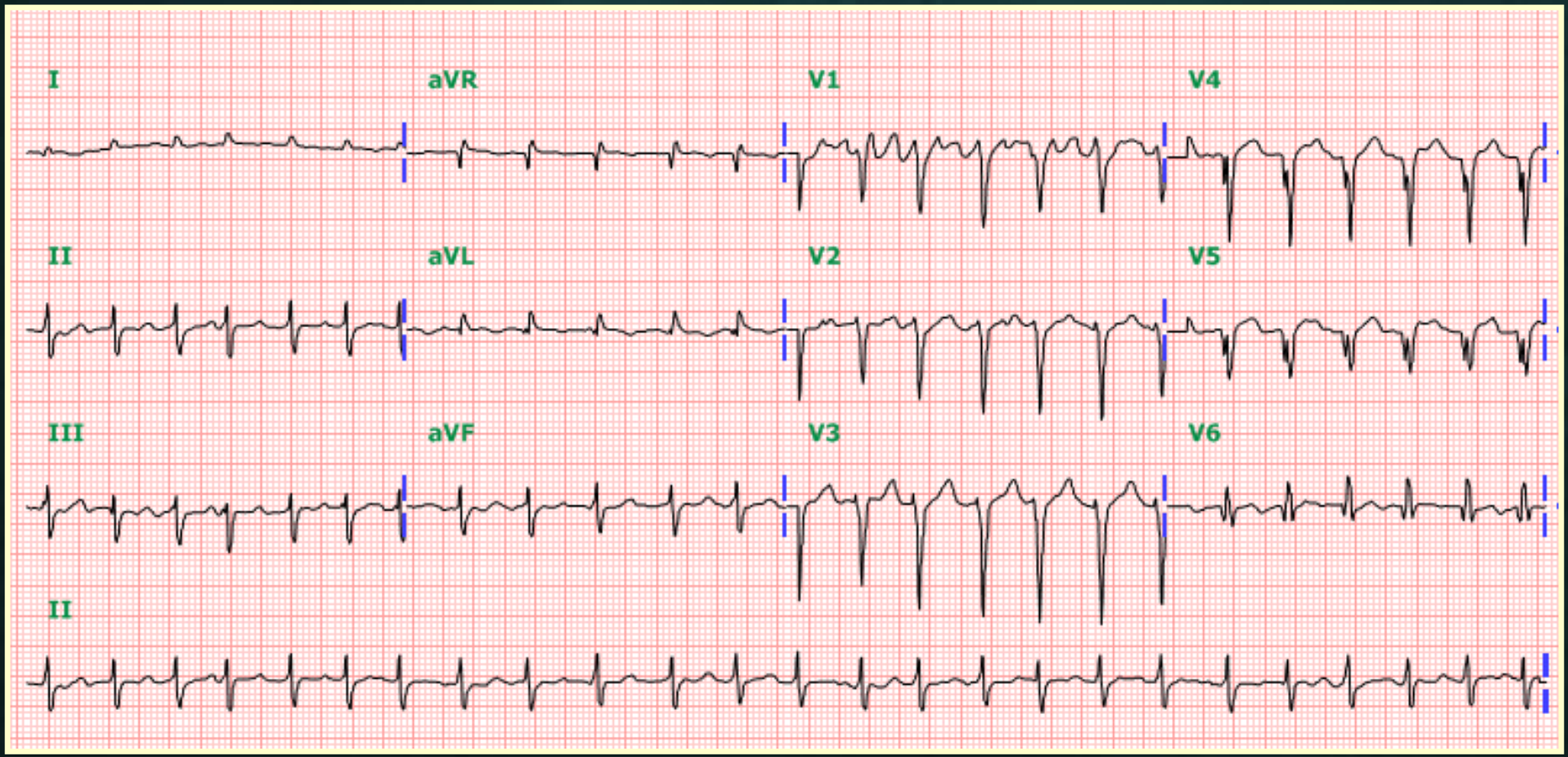
# Case III

- **M/53**
  
- **Known Tbc destroyed lung**
- **Dyspnea**
- **BP 100/82 HR 66bpm**
- **NT-proBNP 2072 pg/ml**
- **LVEDD/ESD/EF 64/50/25%, mild to moderate MR**
- **Tx plan**
  - **Candesartan + spironolactone + lasix**

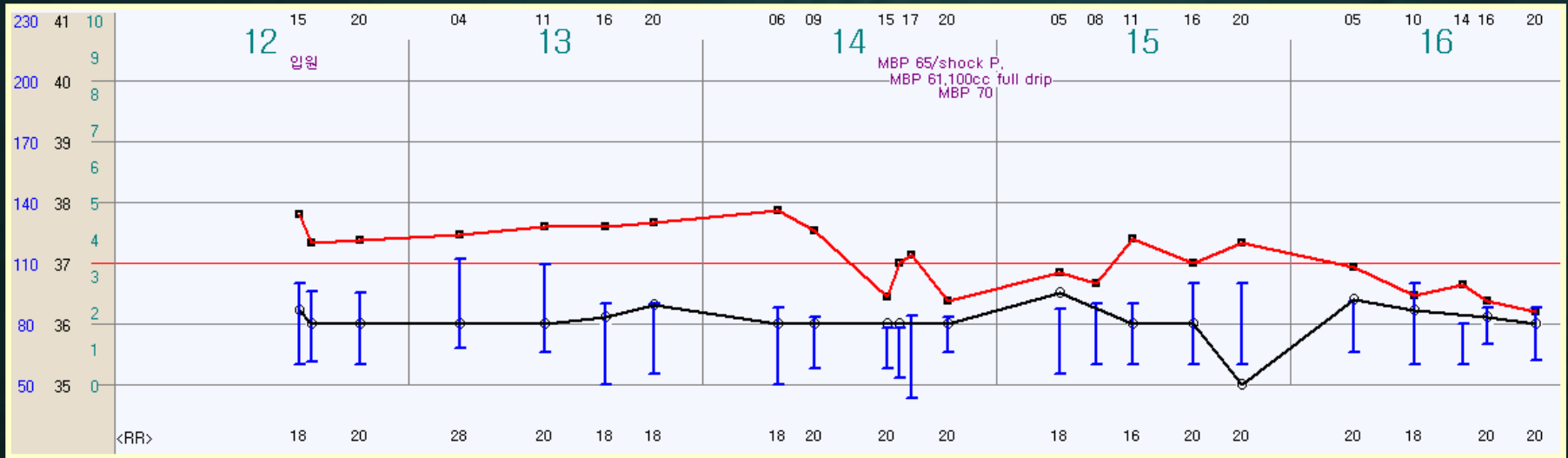
- **Symptom persist**
- **Anorexia**
- **Depressive mood**
- **BP 64/48 mmHg HR 130 bpm**

# CPA



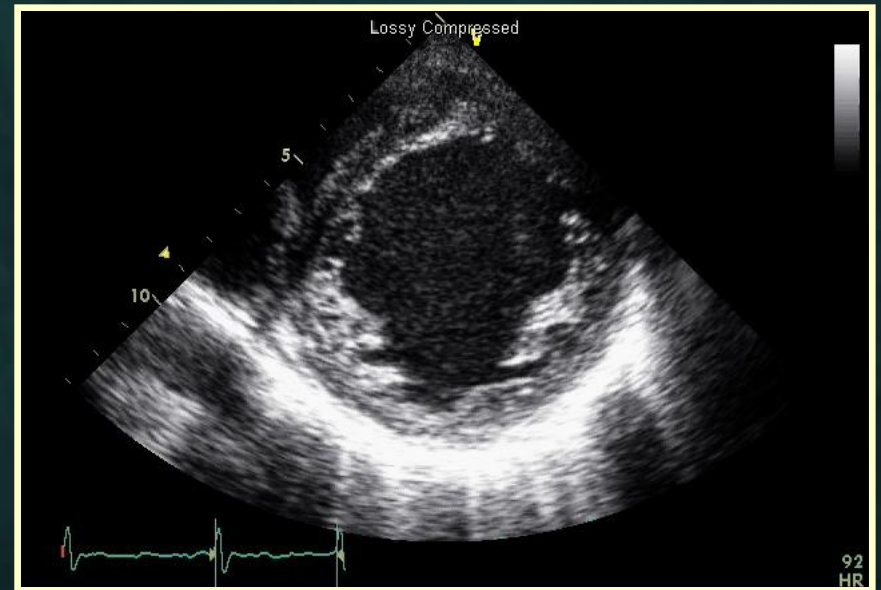
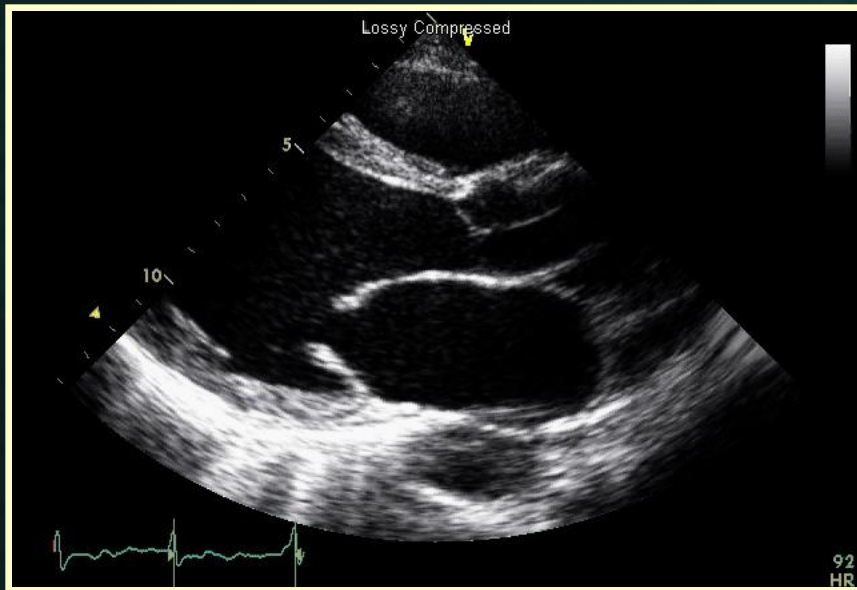


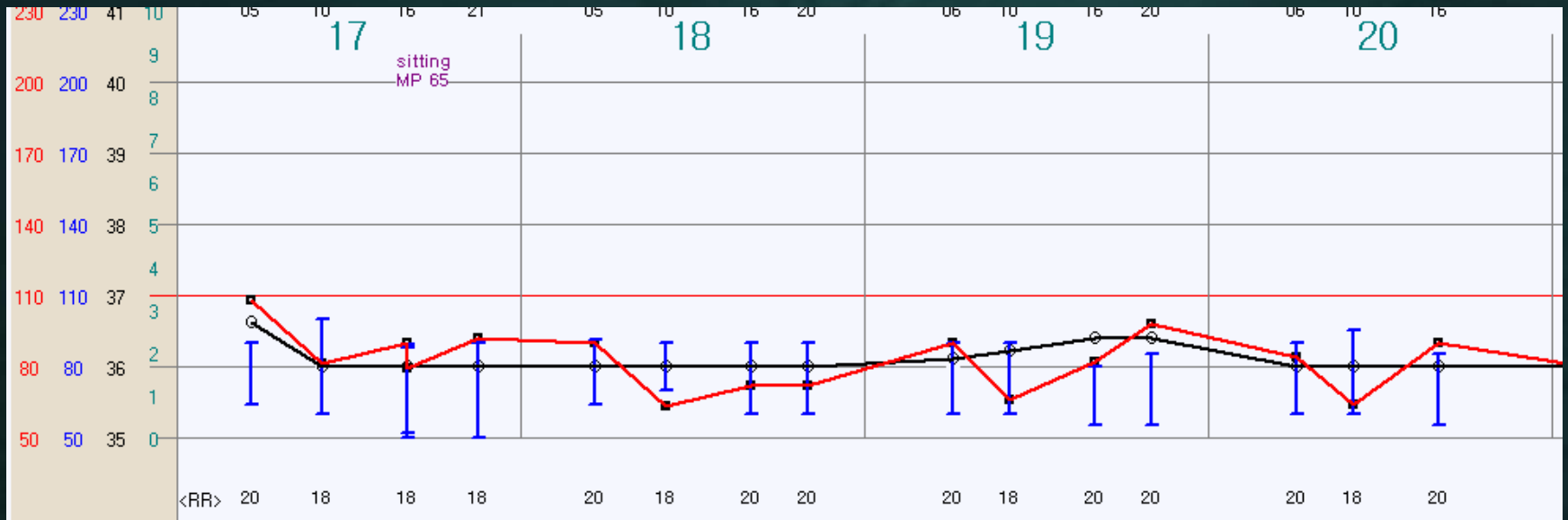




- Digoxin loading
- Furosemide dose up+Captopril 6.25 tid
- HD #4 carvedilol 3.125mg qd 추가
- NT-proBNP 6332→4769

# Echo at admission

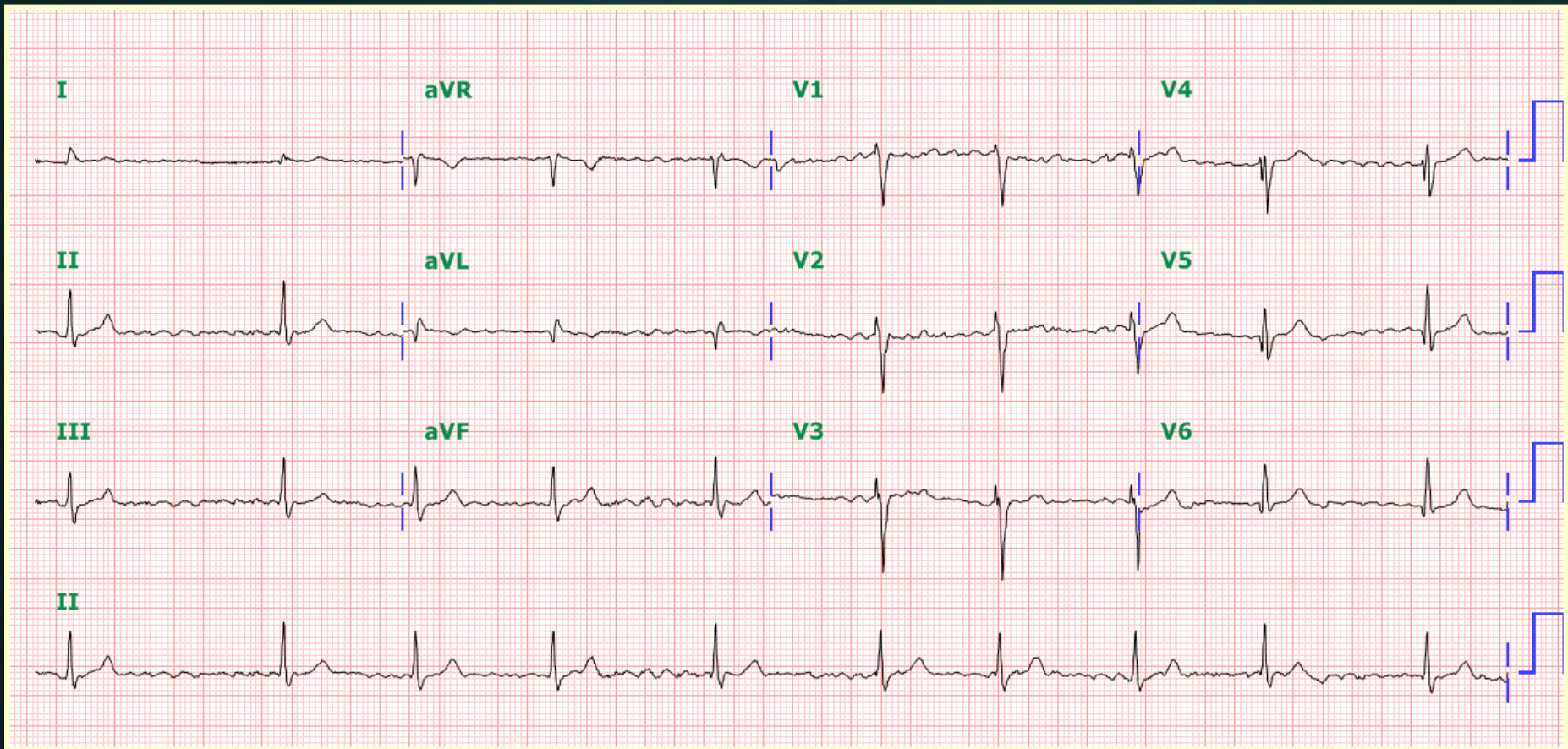




- BP 90/60 HR 70-80bpm
- Bisoprolol 1.25 qd
- Ramipril 2.5mg qd
- Furosemide 10mg qd
- Spironolactone 12.5 mg qd
- Warfarin 2mg qd
- Digoxin 0.125mg qd

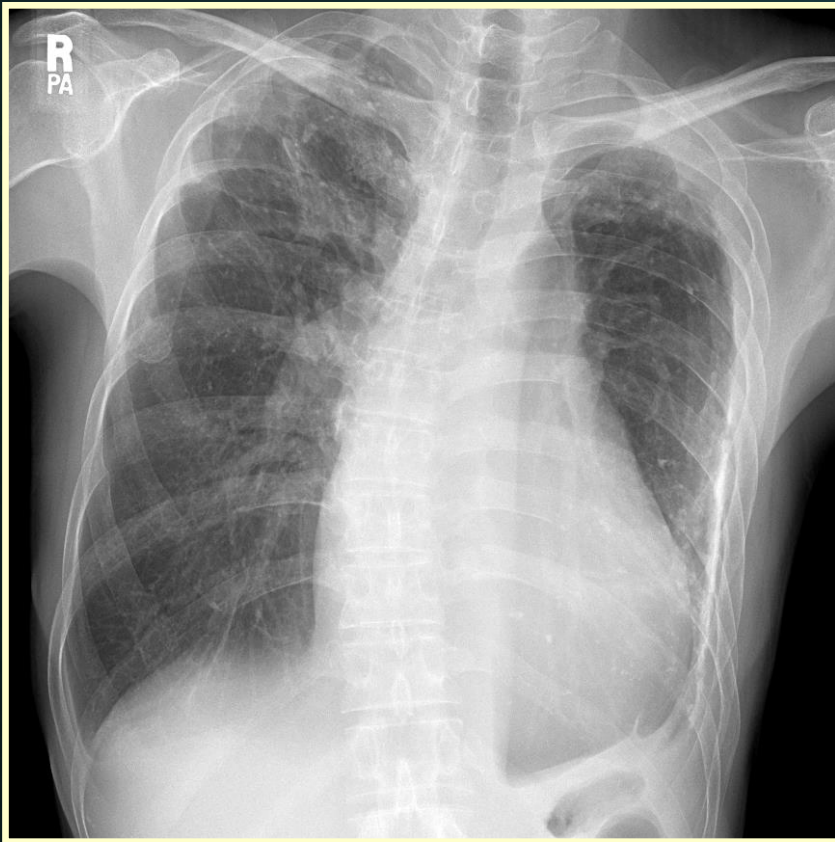
# FU

➤ Sx much improved



# CPA FU

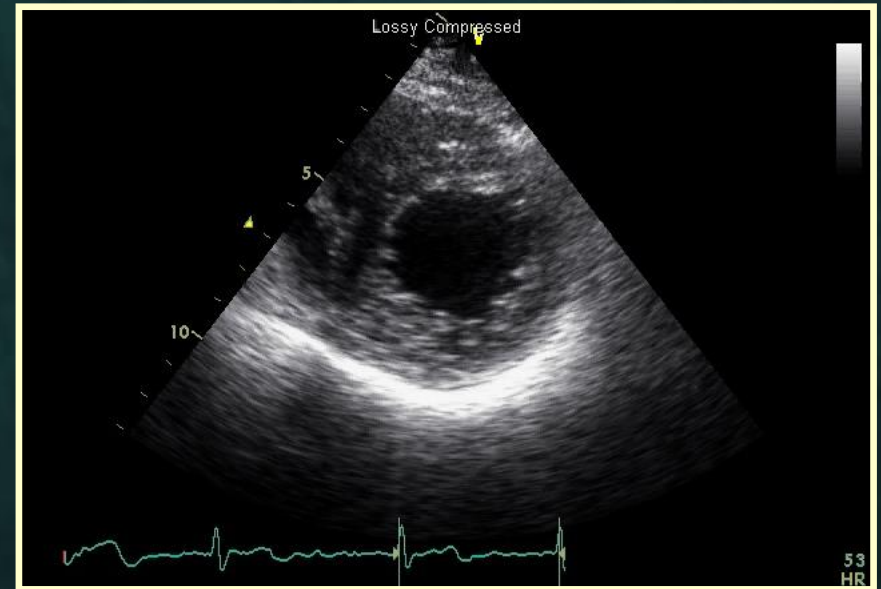
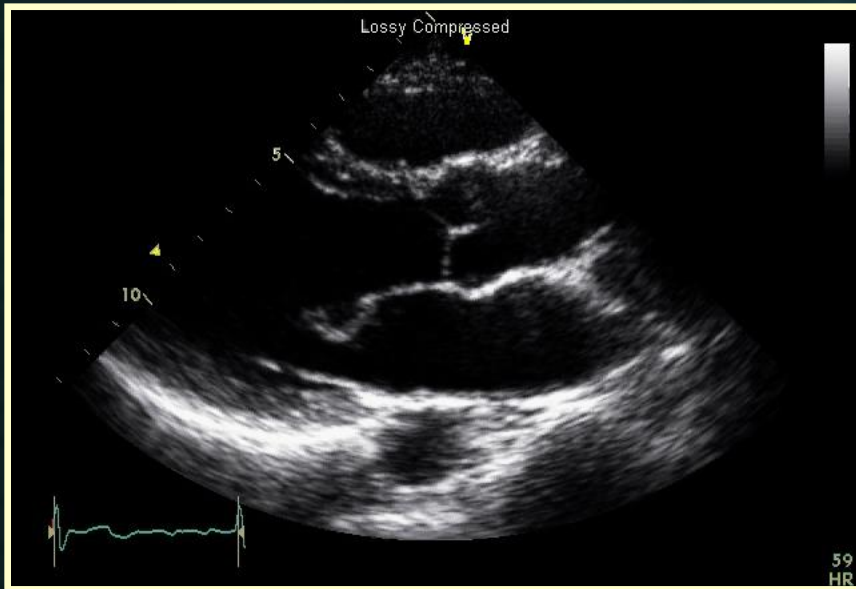
Initial



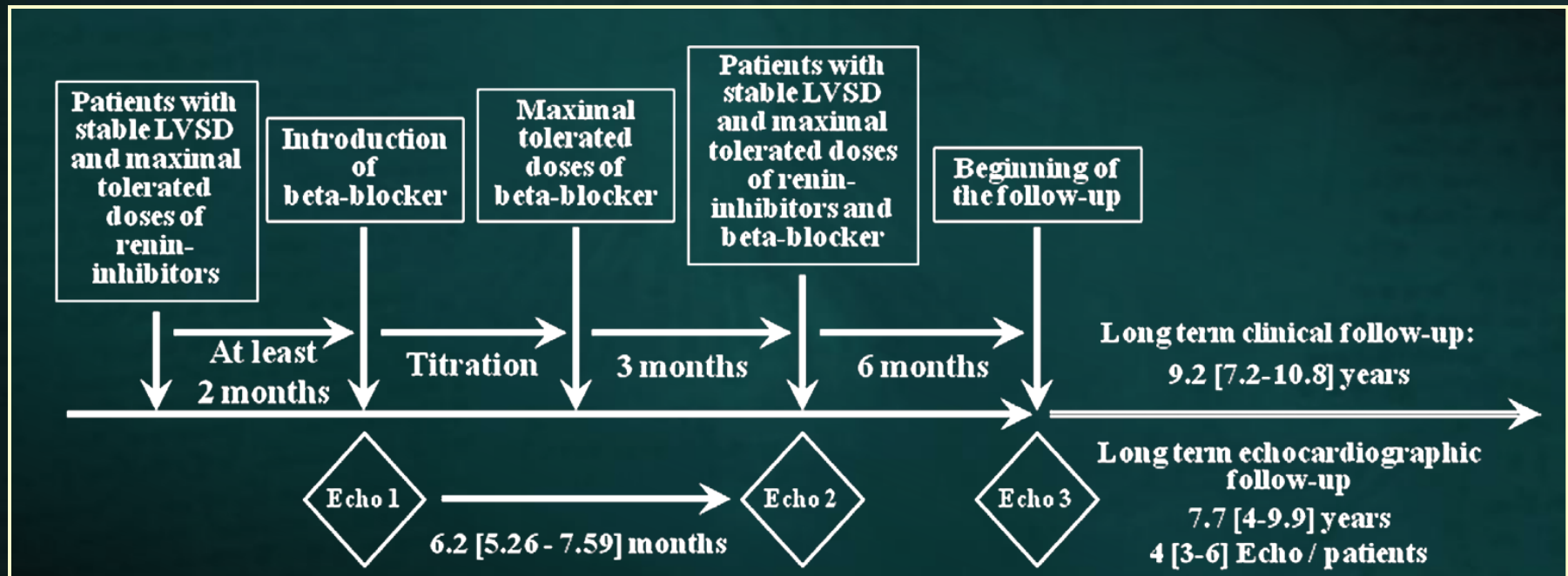
2Yr later



# 2 Year later



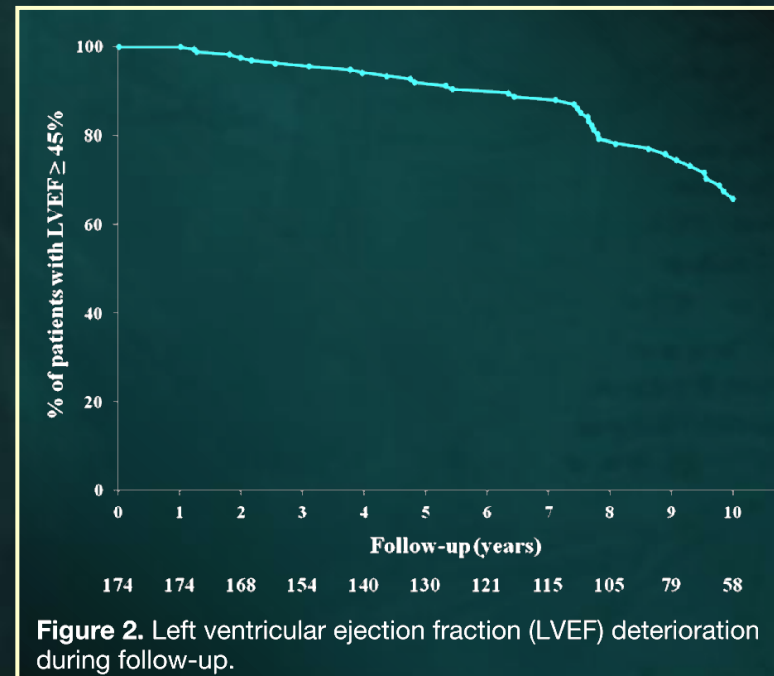
# Effect of LVRR on Long-term Px



# Effect of LVRR on Long-term Px

**Table 3. Clinical and Echocardiographic Characteristics of Patients With and Without Subsequent LVEF Deterioration**

	LVEF $\geq$ 45% at Last Follow-Up	LVEF<45% at Last Follow-Up	P Value
N	128	46	
Age, y	51 $\pm$ 13	56 $\pm$ 12	0.04
Women, %	31 (24%)	12 (26%)	0.80
NYHA I+II, %	121 (95%)	42 (91%)	0.48
NYHA III, %	7 (5%)	4 (9%)	0.48
Ischemic cardiopathy, %	31 (24%)	16 (35%)	0.29
Diabetes mellitus, %	31 (24%)	13 (28%)	0.59
Atrial fibrillation, %	10 (8%)	2 (4%)	0.74
LBBB, %	16 (13%)	14 (30%)	0.006
Heart rate before BB, bpm	90 $\pm$ 16	81 $\pm$ 14	<0.0001
Heart rate after BB, bpm	65 $\pm$ 10	59 $\pm$ 9	0.001
SBP before BB, mm Hg	122 $\pm$ 21	118 $\pm$ 20	0.22
Time to last echocardiogram, y	7.57 [3.58–9.9]	7.36 [3.13–7.71]	0.61
SBP after BB, mm Hg	119 $\pm$ 17	115 $\pm$ 17	0.16
LVEDD before BB, mm	61 $\pm$ 9	61 $\pm$ 8	0.95
LVEDD after BB, mm	56 $\pm$ 7	60 $\pm$ 7	0.001
LVEF before BB, %	33 $\pm$ 8	33 $\pm$ 7	0.95
LVEF after BB, %	54 $\pm$ 6	51 $\pm$ 6	0.002

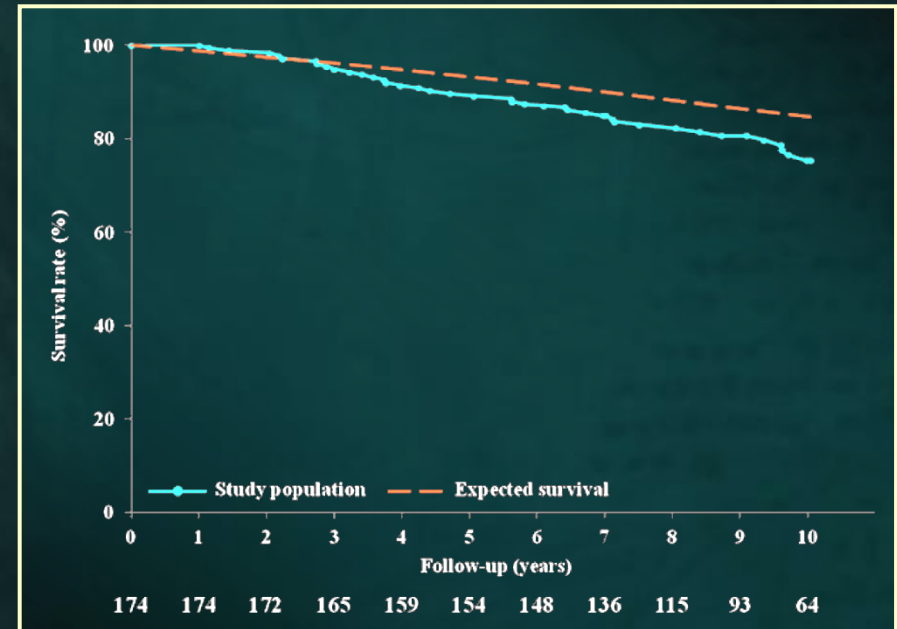




# Effect of LVRR on Long-term Px

**Table 4. Causes of Deaths in Patients With and Without Subsequent LVEF Deterioration**

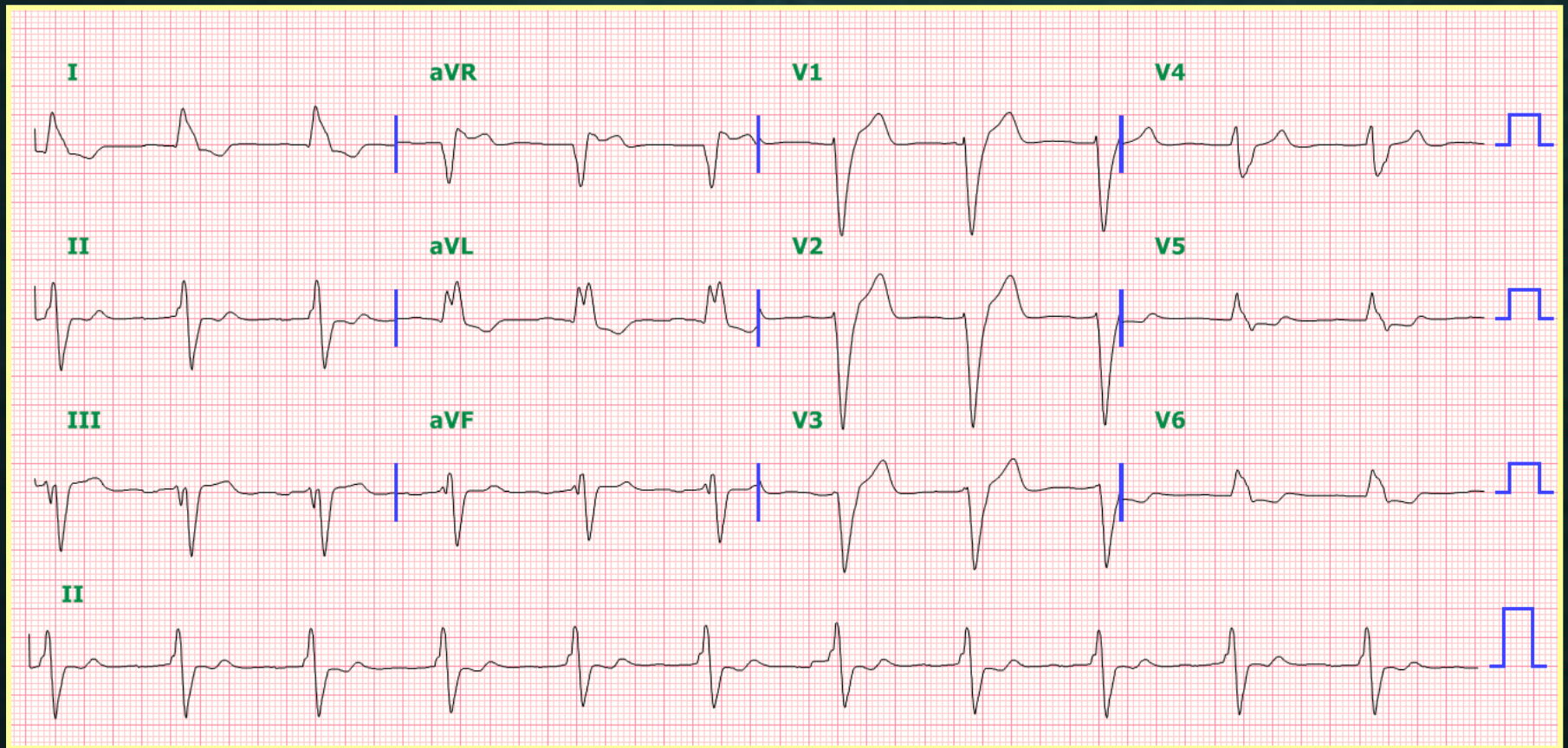
	LVEF $\geq$ 45% at Last Follow-Up	LVEF<45% at Last Follow-Up
N	128	46
Total mortality, %	25 (20%)	15 (33%)
Cardiovascular, %	5 (4%)	10 (22%)
Heart failure, %	0	5 (11%)
Sudden, %	3 (2%)	4 (9%)
Myocardial infarction, %	1 (1%)	1 (2%)
Other cardiovascular, %	1 (1%)	0
Noncardiovascular, %	16 (13%)	4 (9%)
Cancer, %	11 (9%)	4 (9%)
Other noncardiovascular, %	5 (4%)	0
Unknown, %	4 (3%)	1 (2%)



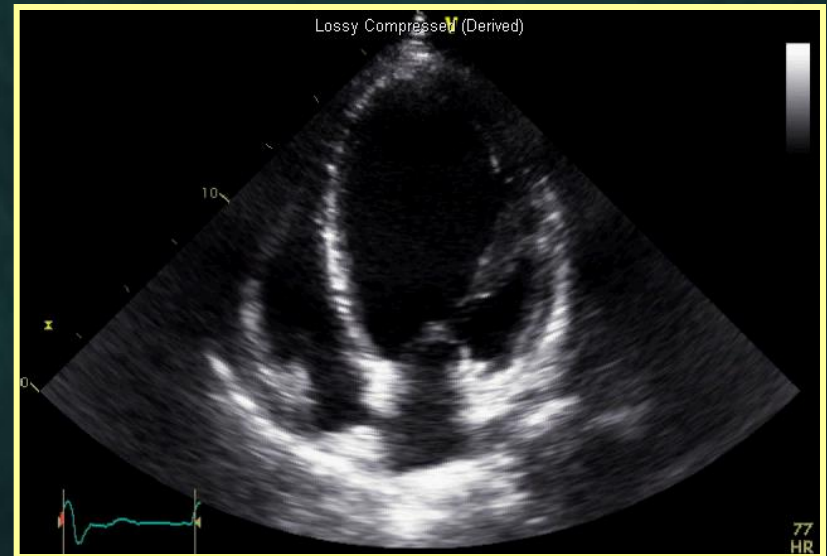
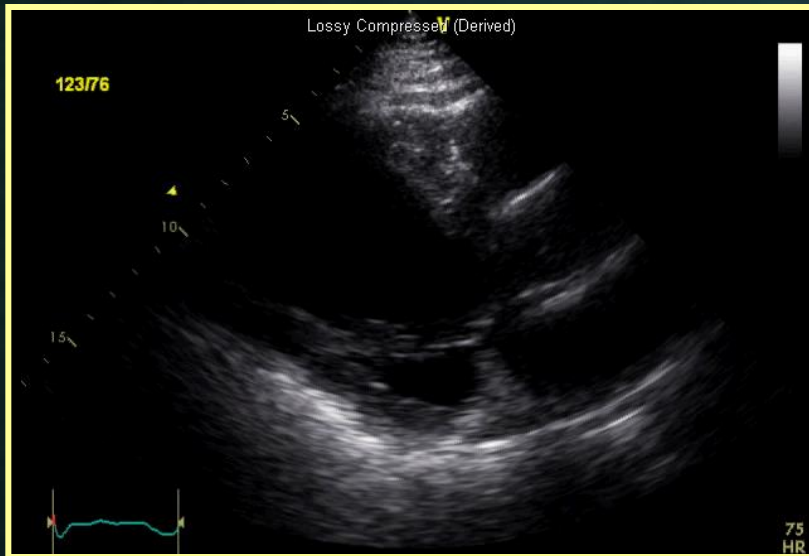
# Case IV

- **M/50**
- **DOE 10YA**
- **Sx increased**

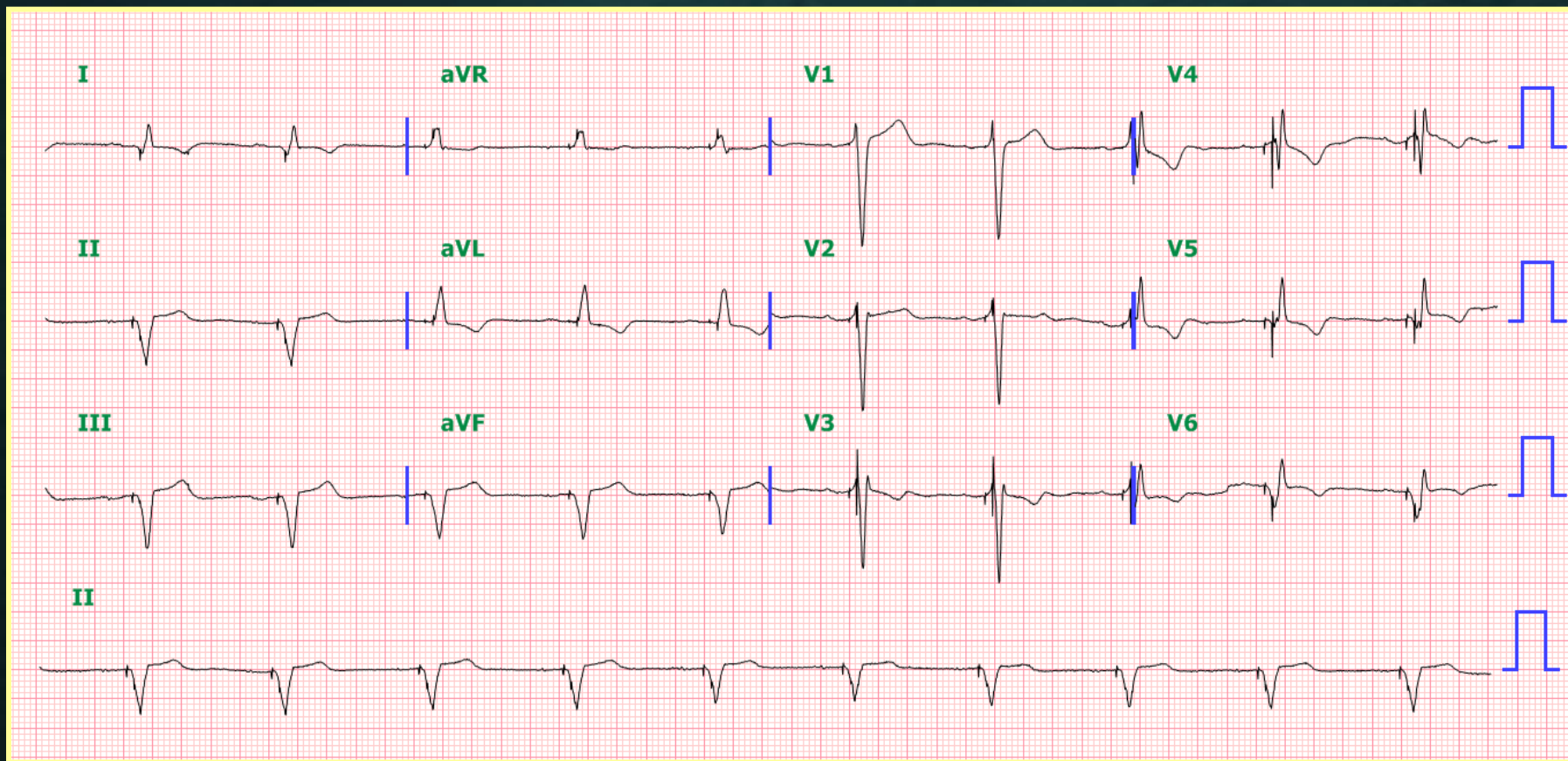




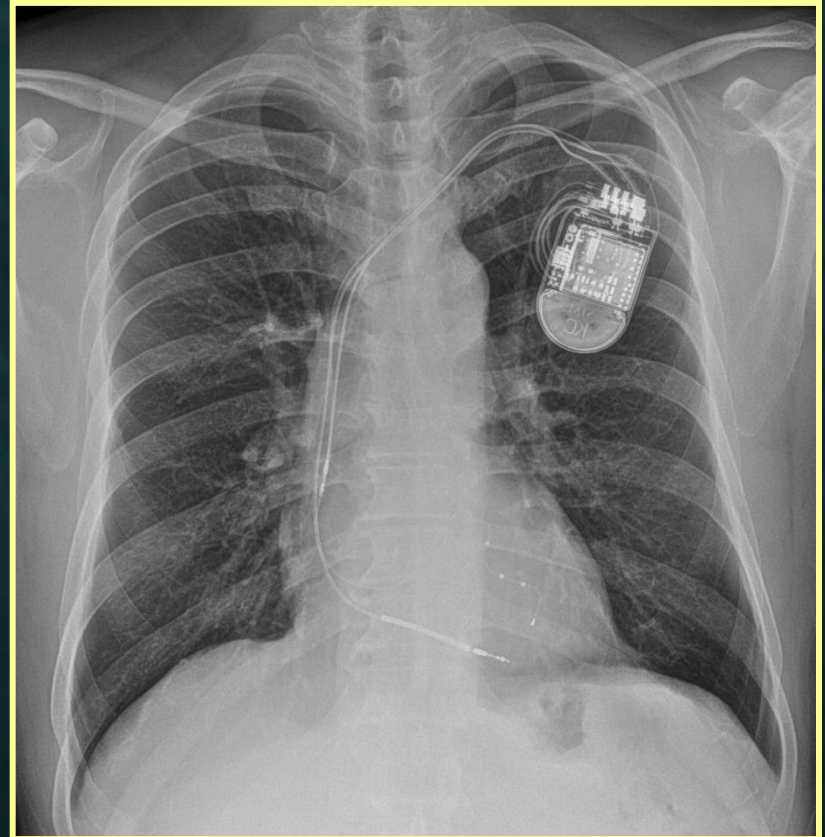
# Echo



- **Mx including**  
**ARB, BB, Lsx, Spiro, Dgx**
- **But Sx persisted as Fc III**

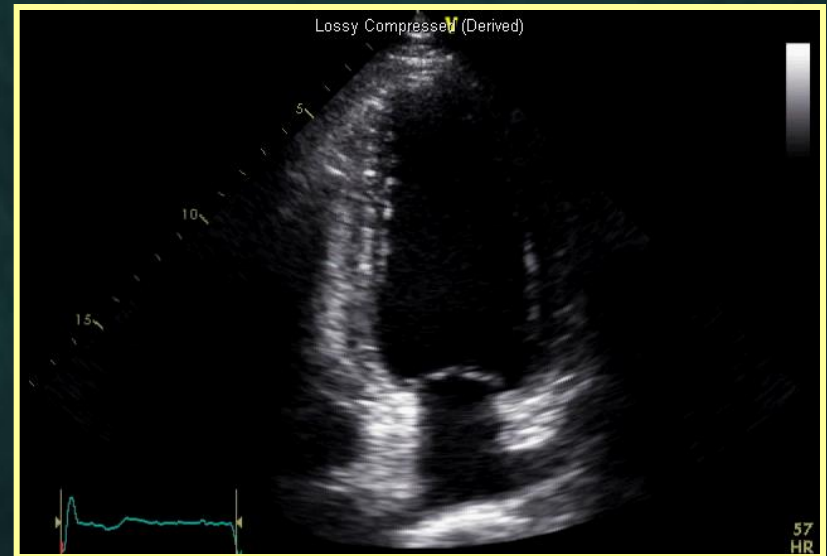
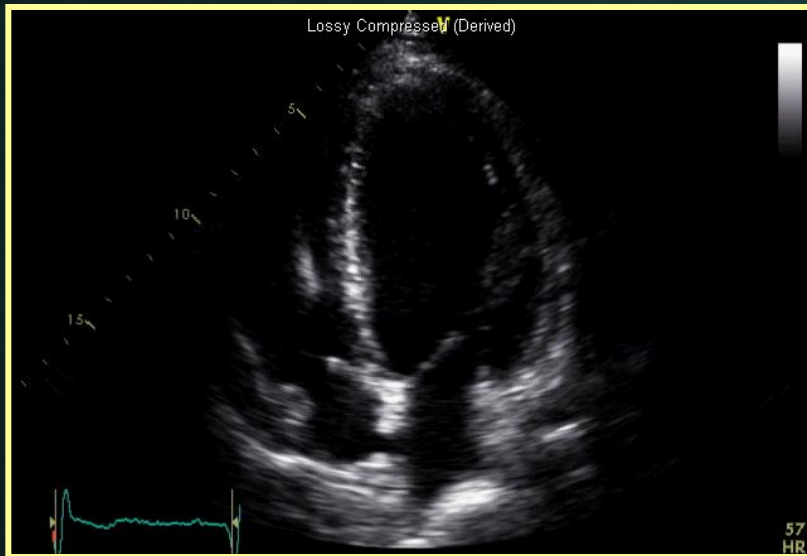


# CPA after CRT

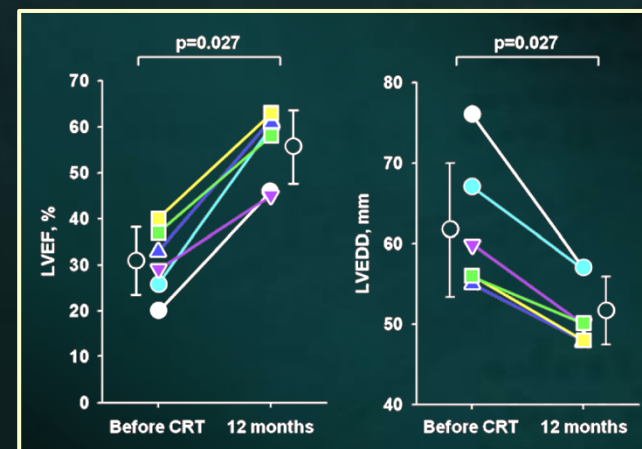
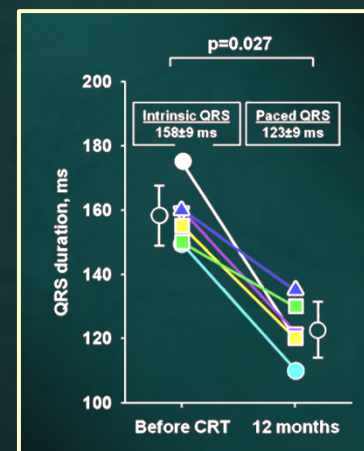
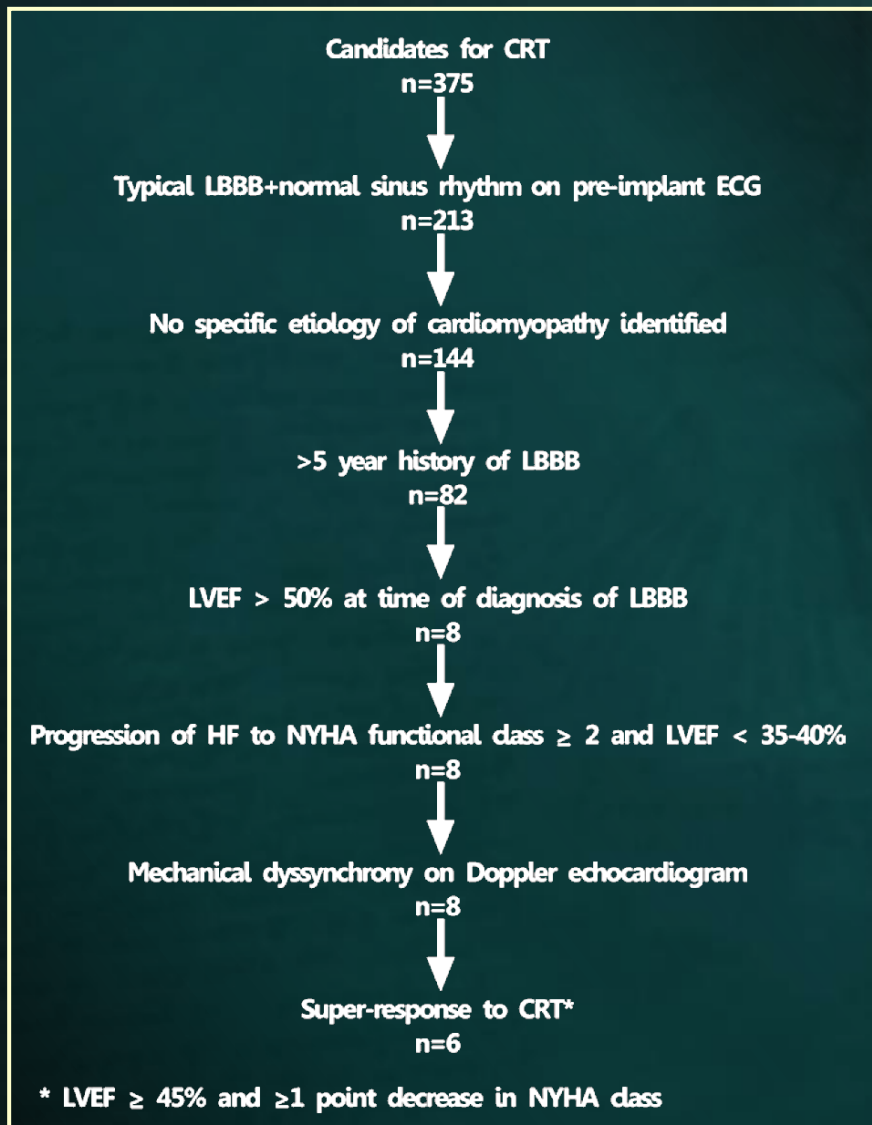




# Echo FU

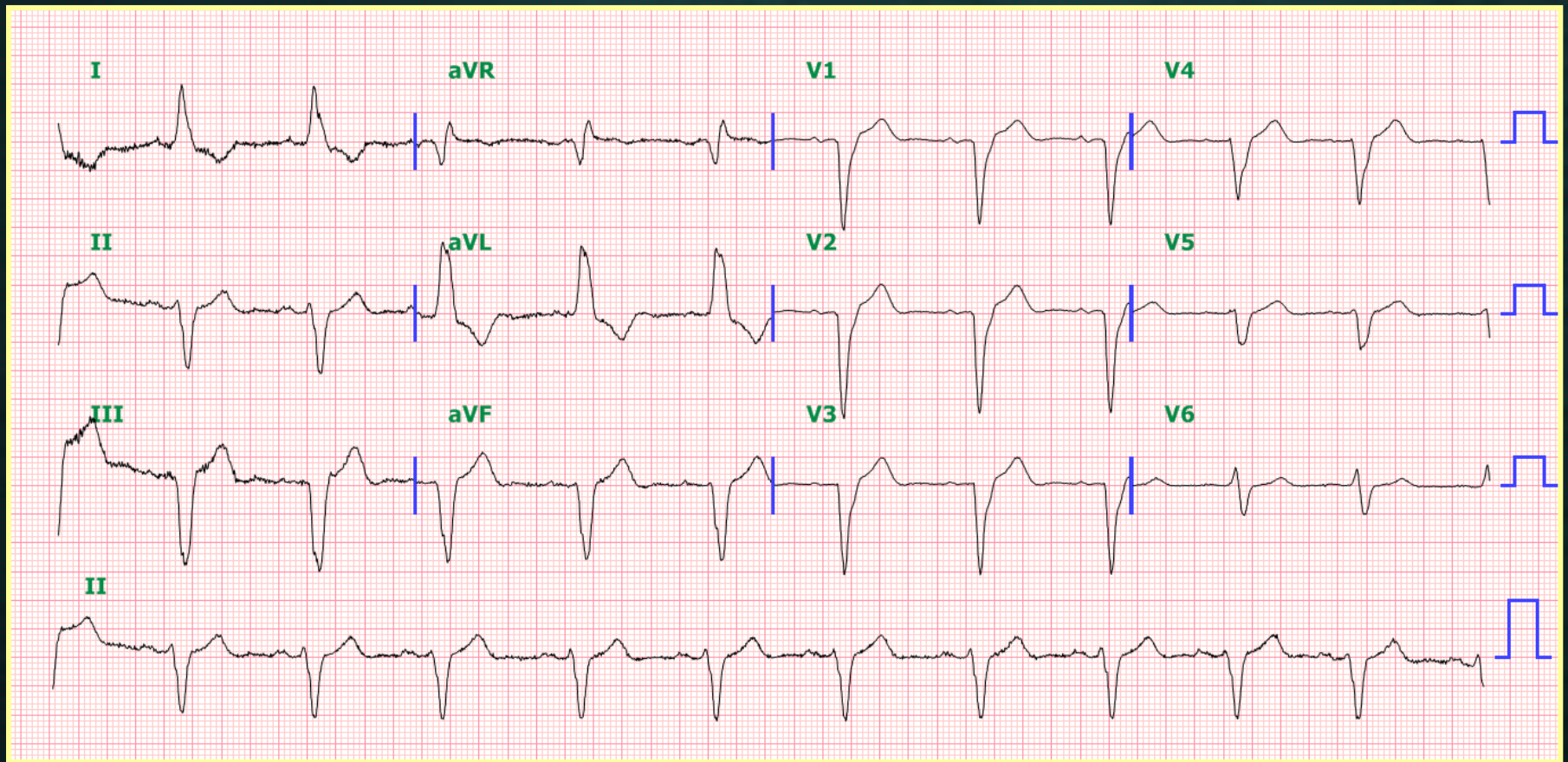


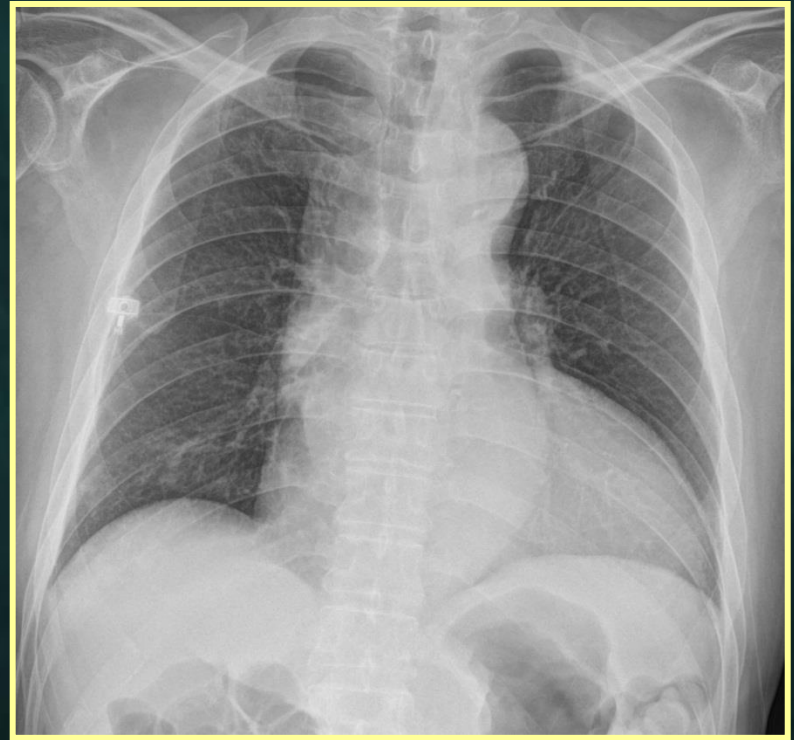
# LBBB-induced LV dysfunction reversed by CRT



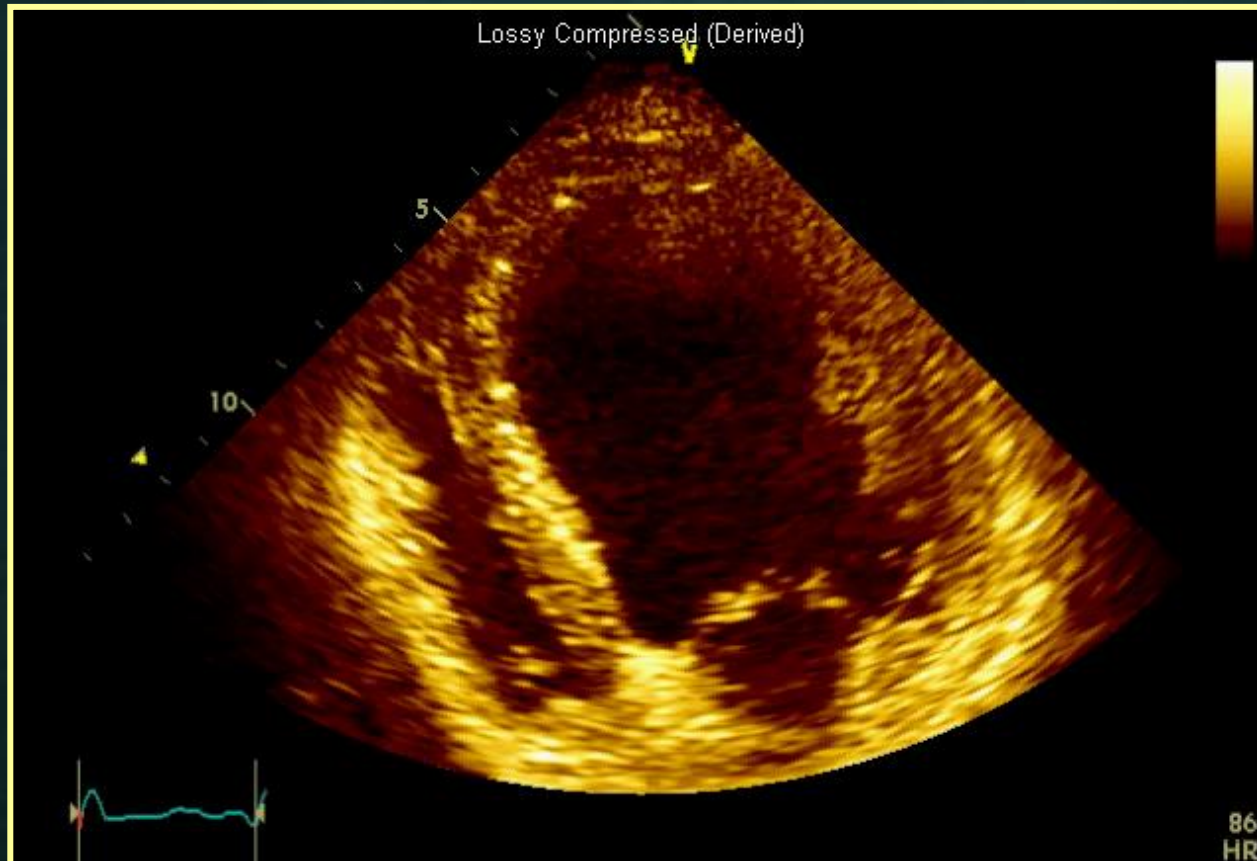
# Case V

- **M/70**
- **Prior HF with CKD (sCr 2.0-3.0 mg/dl)**
- **DM, HTN**
- **Progressive LV dysfunction and HF Sx  
in spite of Mx**
- **BP 130/70**



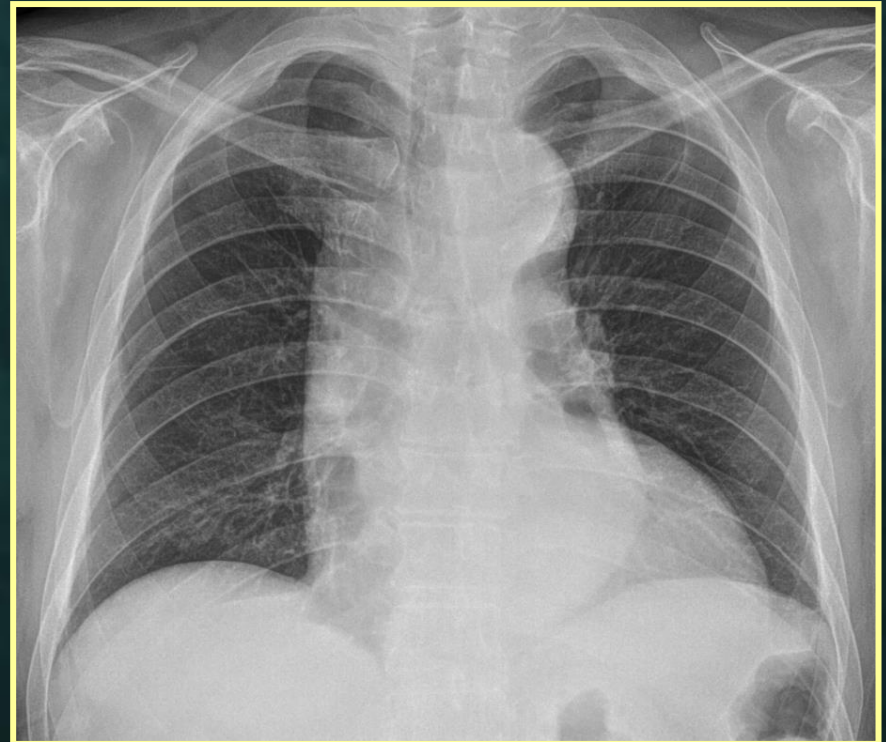
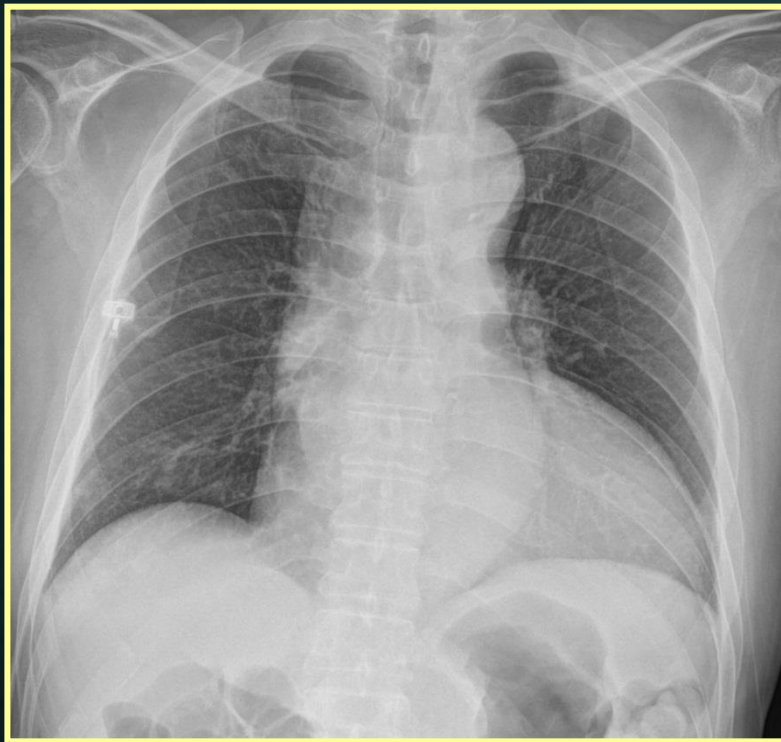


# Echo

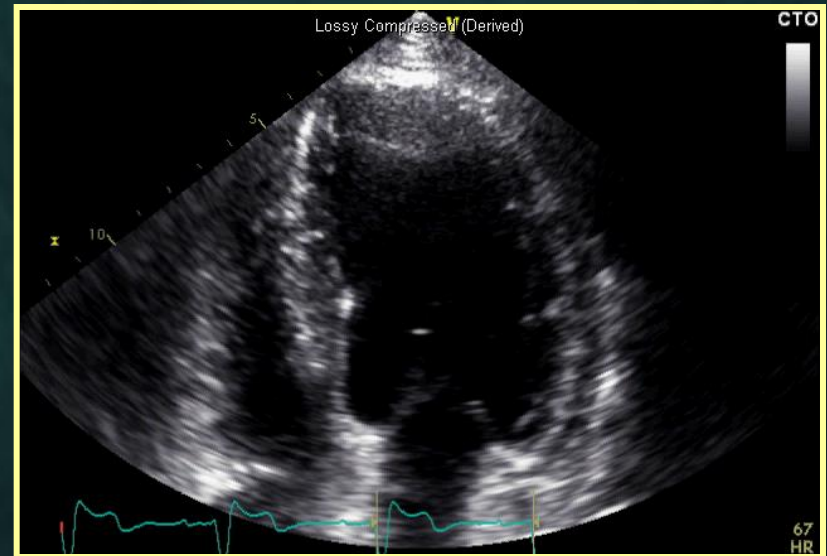
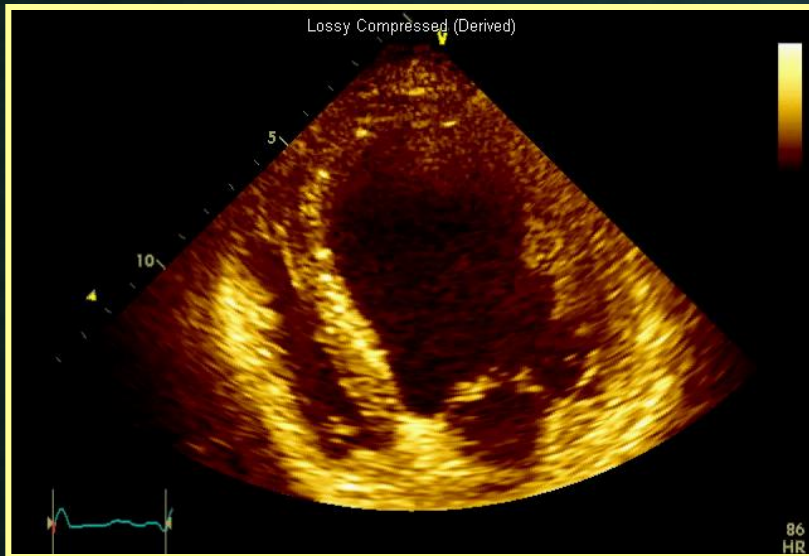


**LV 71/58 mm EF 26%**

# CPA FU with Medication



# Echo FU at 6 month



**LV 71/58 mm EF 26% → 64/46 EF 45%**



## Predictors of Spontaneous Reverse Remodeling in Mild Heart Failure Patients With Left Ventricular Dysfunction

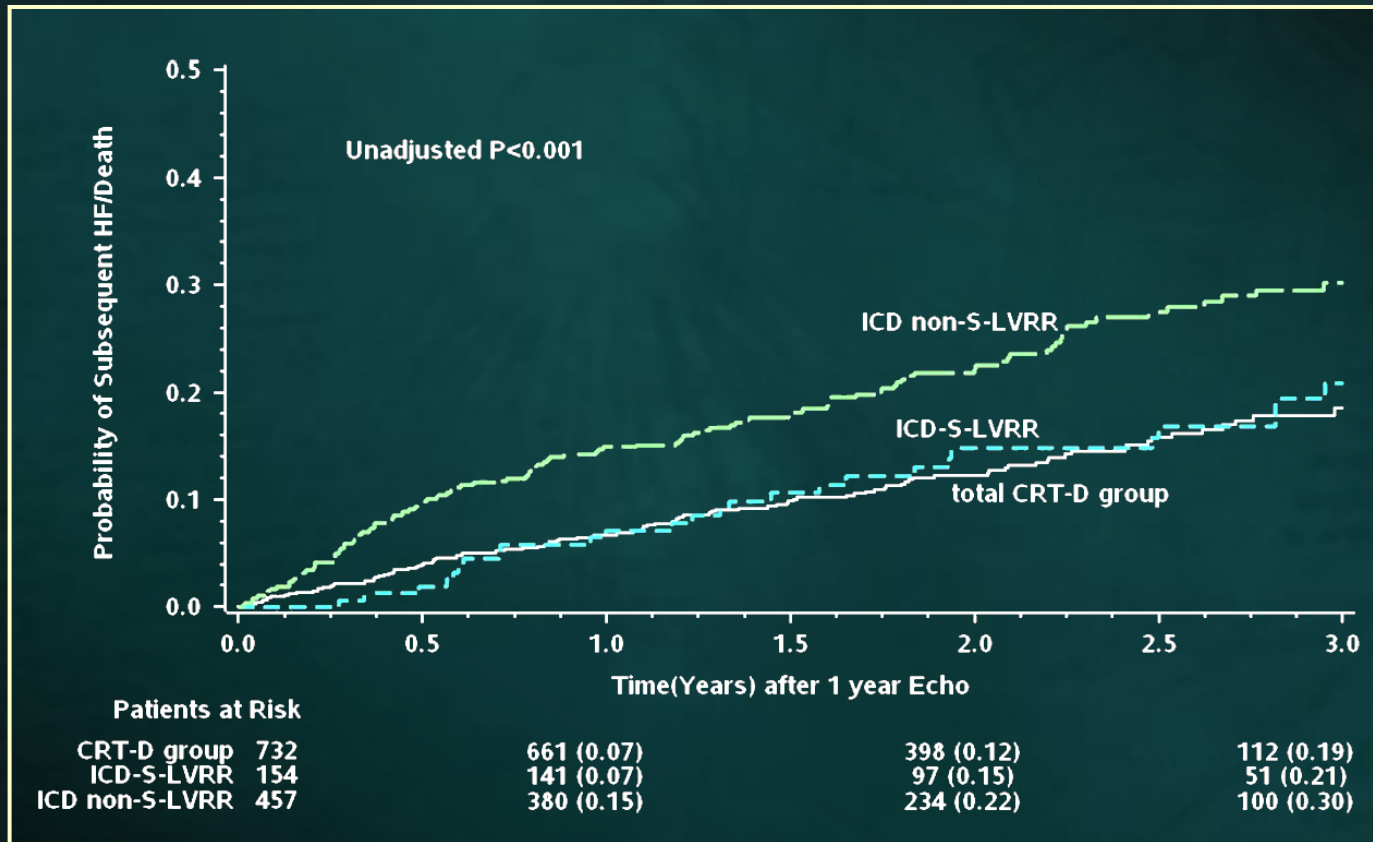
Andrew Brenyo, MD; Alon Barsheshet, MD; Valentina Kutyifa, MD;  
Anne-Christine Ruwald, MD; Mohan Rao, MD; Wojciech Zareba, MD, PhD;  
Anne-Catherine Pouleur, MD; Dorit Knappe, MD; Scott D. Solomon, MD; Scott McNitt, MS;  
David T. Huang, MD; Arthur J. Moss, MD; Ilan Goldenberg, MD

**Table 2. Predictors of Spontaneous Left Ventricular Remodeling at 1-Year Echocardiogram**

Remodeling Predictors	OR	95% CI	P Value
Baseline SBP $\geq$ 140 mm Hg	1.65	1.02–2.69	0.042
Creatinine $<$ 1.0 mg/dL	1.56	1.03–2.38	0.035
QRS duration $<$ 170 ms	1.47	1.14–1.67	0.011
Non-Ischemic Cardiomyopathy	1.29	0.94–1.52	0.09

## Predictors of Spontaneous Reverse Remodeling in Mild Heart Failure Patients With Left Ventricular Dysfunction

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# Reversible Myocardial Disease

- Stress-induced cardiomyopathy
- Alcoholic cardiomyopathy
- Peripartum cardiomyopathy
- Fulminant myocarditis
- Stunned / Hibernated myocardium
- Valvular heart diseases
- Etc

# Reverse remodeling of LV

- On Betablocker
- High BP
- Normal QRS duration or absence of LBBB
- No Delayed hyperenhancement in CMR
- AF and LV dysfunction
  - LVRR after Rate control vs ablation
- ESRD and on poor maintenance on RRT
- LBBB with CRT
  
- Very good outcome but rarely deteriorate

## Indication of CRT

- EF < 35% on Optimal Medical Tx
  - Minimum of 3-6 months
- LBBB or QRS duration > 120 msec
- Persistent Sx

## Indication of ICD

- EF < 35% on Medical Tx
  - Nonischemic DCM 3-6 month
  - Post MI after 40 days

***Thanks for your  
attentions***