Ürək çatışmazlığının idarə edilməsində son nailiyyətlər. Ürək çatışmazlığı xəstələrinin müalicəsi fərdiləşdirilə bilərmi?

Recent advances in heart failure management. Could the treatment of heart failure patients be individualised?

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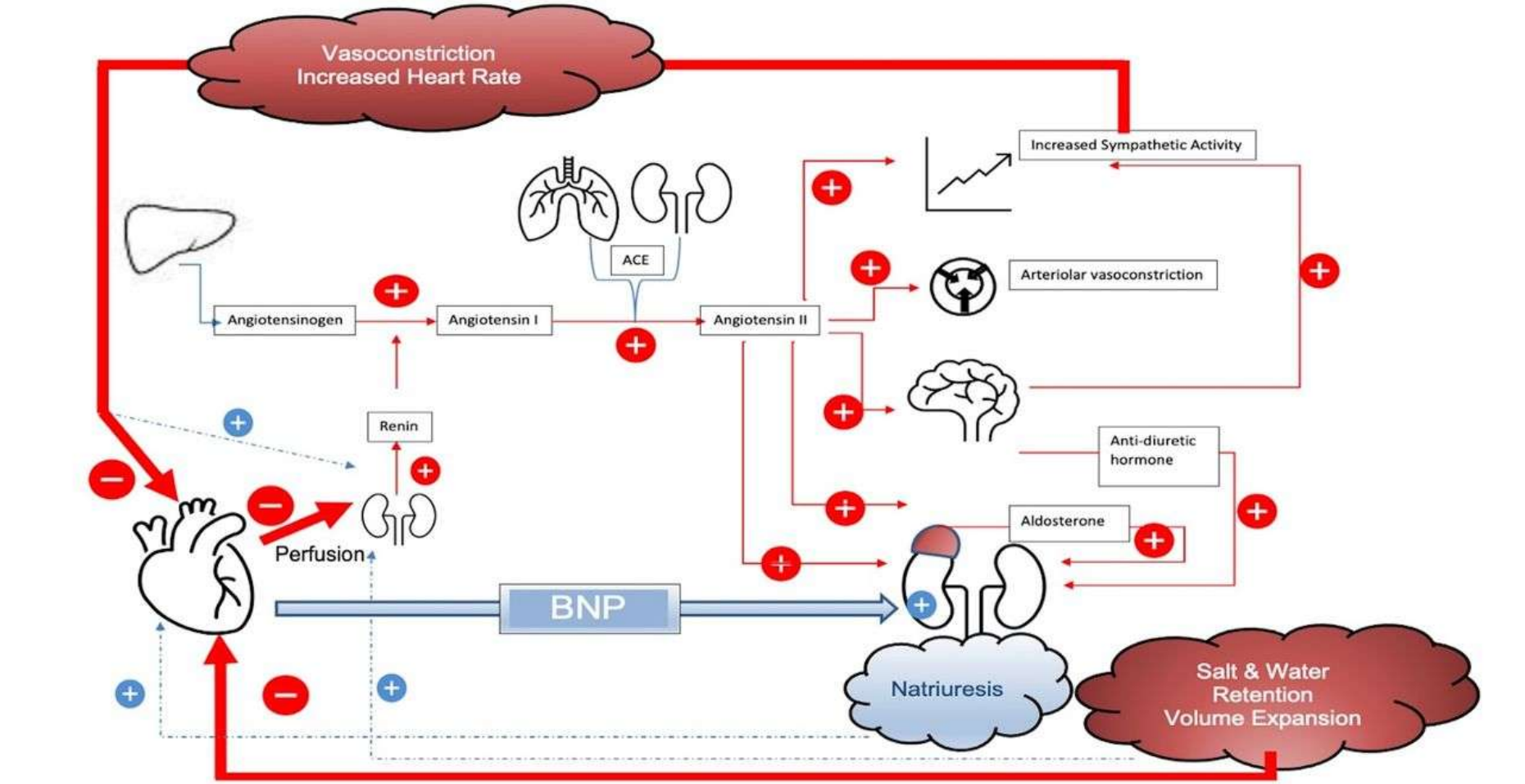
Siena University, Italy

Homeostatic mechanisms in HFrEF



Pharmacological treatments in patients with HFrEF (NYHA II-IV)

Pharmacological treatments indicated in patients with (NYHA class II--IV) heart failure with reduced ejection fraction (LVEF ≤40%)

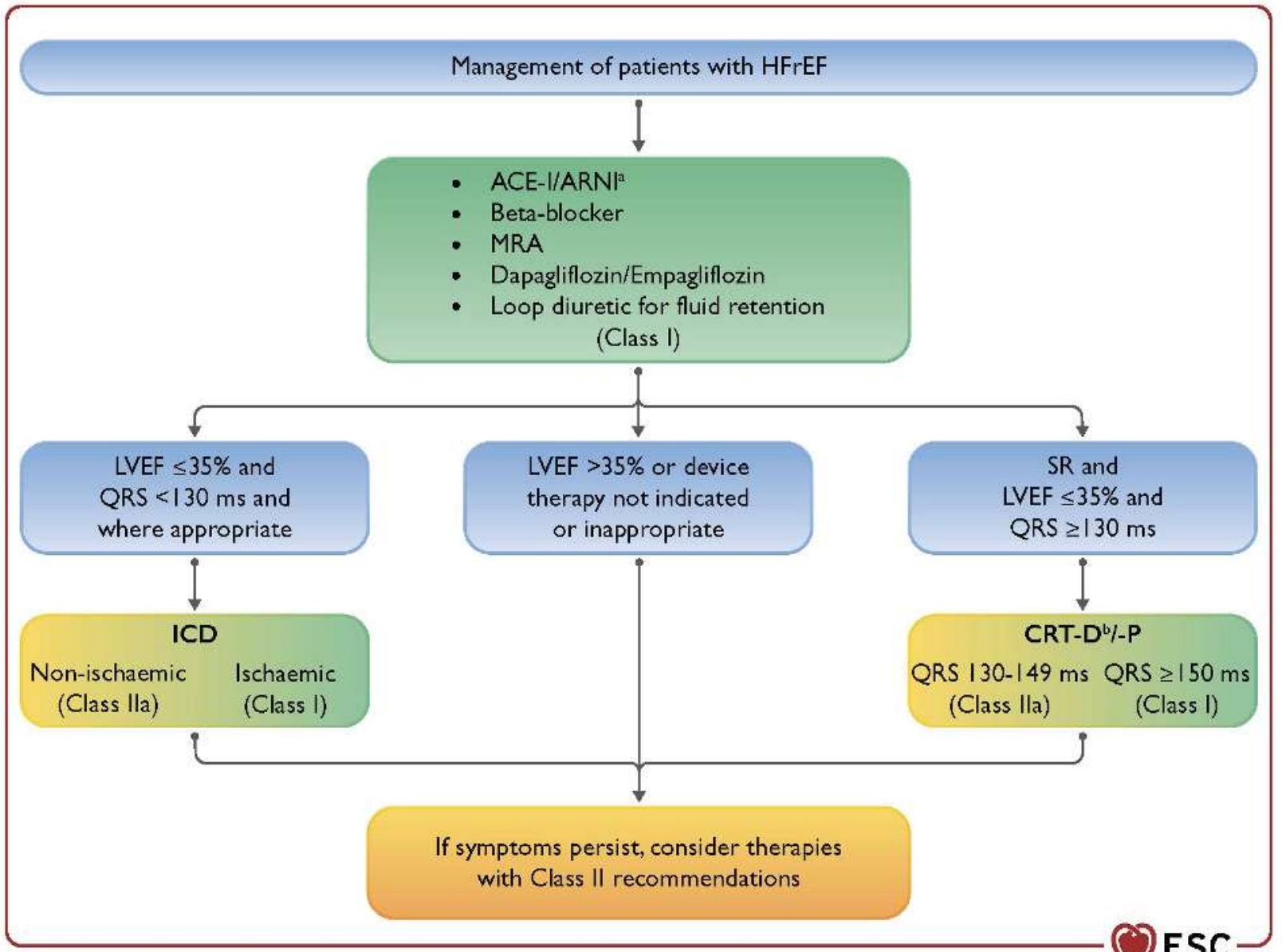
Recommendations	Class[a]	Level[b]
An ACE-I is recommended for patients with HFrEF to reduce the risk of HF hospitalization and death.[110–113]	I	A
A beta-blocker is recommended for patients with stable HFrEF to reduce the risk of HF hospitalization and death.[114–120]	I	A
An MRA is recommended for patients with HFrEF to reduce the risk of HF hospitalization and death.[121,122]	I	A
Dapagliflozin or empagliflozin are recommended for patients with HFrEF to reduce the risk of HF hospitalization and death.[108,109]	I	A
Sacubitril/valsartan is recommended as a replacement for an ACE-I in patients with HFrEF to reduce the risk of HF hospitalization and death.[105]	I	B

ACE-I = angiotensin-converting enzyme inhibitor; HF = heart failure; HFrEF = heart failure with reduced ejection fraction; LVEF = left ventricular ejection fraction; MRA = mineralocorticoid receptor antagonist; NYHA = New York Heart Association.

a Class of recommendation.

b Level of evidence.

Management of HFrEF



Definition of HF

Table 3 **Definition of heart failure with reduced ejection fraction, mildly reduced ejection fraction, and preserved ejection fraction**

Type of HF		HFrEF	HFmrEF	HFpEF
Criteria	1	Symptoms ± signs[a]	Symptoms ± signs[a]	Symptoms ± signs[a]
	2	LVEF ≤40%	LVEF 41–49%[b]	LVEF ≥50%
	3	–	–	Objective evidence of cardiac structural and/or functional abnormalities consistent with the presence of LV diastolic dysfunction/raised LV filling pressures, including raised natriuretic peptides[c]

"Types" of Heart Failure by LVEF

Classification	EF (%)	Description
HF with reduced EF (HF*r*EF)	≤ 40	Also referred to as systolic HF Majority of RCT enrolled HF*r*EF Efficacy of current HF medications only demonstrated in this group
HF with preserved EF (*HFpEF*)	≥ 50	Also referred to as diastolic HF Prevalence ~ 50% of HF patients Diagnosis of HF*p*EF is challenging because need to exclude non-cardiac causes of dyspnea Efficacious Rx have not been identified
a. HF*p*EF, borderline	41 – 49	Borderline or intermediate group Outcomes and Rx similar to HF*p*EF
b. HF*p*EF, improved	> 40	Patient with previous HF*r*EF Further research is needed to better characterize these patients

Treatment of HFpEF

ACE-I reduce all cause mortrality but not CV

A

Study or Subgroup	ACEI group Events	Total	Control group Events	Total	Weight	Odds Ratio M-H, Fixed, 95% CI	Year
Philbin,1997	23	190	30	160	13.3%	0.60 [0.33, 1.08]	1997
Philbin,2000	32	284	47	245	20.8%	0.53 [0.33, 0.87]	2000
Min Zi,2003	1	36	1	38	0.4%	1.06 [0.06, 17.56]	2003
Grigorian,2006	80	210	130	206	37.8%	0.36 [0.24, 0.54]	2006
Cleland,2006	17	424	19	426	8.5%	0.89 [0.46, 1.75]	2006
Tribouilloy,2008	58	120	73	120	17.6%	0.60 [0.36, 1.01]	2008
Yip,2008	0	45	3	50	1.5%	0.15 [0.01, 2.97]	2008
Total (95% CI)		**1309**		**1245**	**100.0%**	**0.52 [0.41, 0.64]**	
Total events	211		303				

Heterogeneity: Chi² = 7.29, df = 6 (P = 0.29); I² = 18%
Test for overall effect: Z = 5.80 (P < 0.00001)

Odds Ratio M-H, Fixed, 95% CI

0.1 0.2 0.5 1 2 5 10
Favours ACEIs Favours control

B

Study or Subgroup	ACEIs Events	Total	Control Events	Total	Weight	Odds Ratio M-H, Fixed, 95% CI	Year
Philbin,1997	11	190	11	160	11.5%	0.83 [0.35, 1.97]	1997
Zi,2003	4	36	6	38	5.3%	0.67 [0.17, 2.59]	2003
Cleland,2006	97	424	106	426	83.2%	0.90 [0.65, 1.23]	2006
Total (95% CI)		**650**		**624**	**100.0%**	**0.88 [0.66, 1.17]**	
Total events	112		123				

Heterogeneity: Chi² = 0.19, df = 2 (P = 0.91); I² = 0%
Test for overall effect: Z = 0.90 (P = 0.37)

Odds Ratio M-H, Fixed, 95% CI

0.02 0.1 1 10 50
Favours ACEIs Favours control

A

Study or Subgroup	ACEI group Events	Total	Control group Events	Total	Weight	Odds Ratio M-H, Fixed, 95% CI	Year
Philbin,1997	44	190	35	160	22.2%	1.08 [0.65, 1.78]	1997
Philbin,2000	63	284	59	245	37.4%	0.90 [0.60, 1.35]	2000
Min Zi,2003	2	36	5	38	3.5%	0.39 [0.07, 2.14]	2003
Cleland,2006	34	424	53	426	36.9%	0.61 [0.39, 0.97]	2006
Total (95% CI)		**934**		**869**	**100.0%**	**0.81 [0.63, 1.05]**	
Total events	143		152				

Heterogeneity: Chi² = 3.62, df = 3 (P = 0.31); I² = 17%
Test for overall effect: Z = 1.58 (P = 0.11)

Odds Ratio M-H, Fixed, 95% CI

0.1 0.2 0.5 1 2 5 10
Favours ACEIs Favours control

B

Study or Subgroup	ACEI group Events	Total	Control group Events	Total	Weight	Odds Ratio M-H, Fixed, 95% CI	Year
Philbin,1997	87	190	78	160	37.1%	0.89 [0.58, 1.35]	1997
Philbin,2000	130	284	116	245	54.6%	0.94 [0.67, 1.32]	2000
Min Zi,2003	7	36	13	38	8.2%	0.46 [0.16, 1.34]	2003
Total (95% CI)		**510**		**443**	**100.0%**	**0.88 [0.68, 1.14]**	
Total events	224		207				

Heterogeneity: Chi² = 1.53, df = 2 (P = 0.47); I² = 0%
Test for overall effect: Z = 0.97 (P = 0.33)

Odds Ratio M-H, Fixed, 95% CI

0.1 0.2 0.5 1 2 5 10
Favours ACEIs Favours control

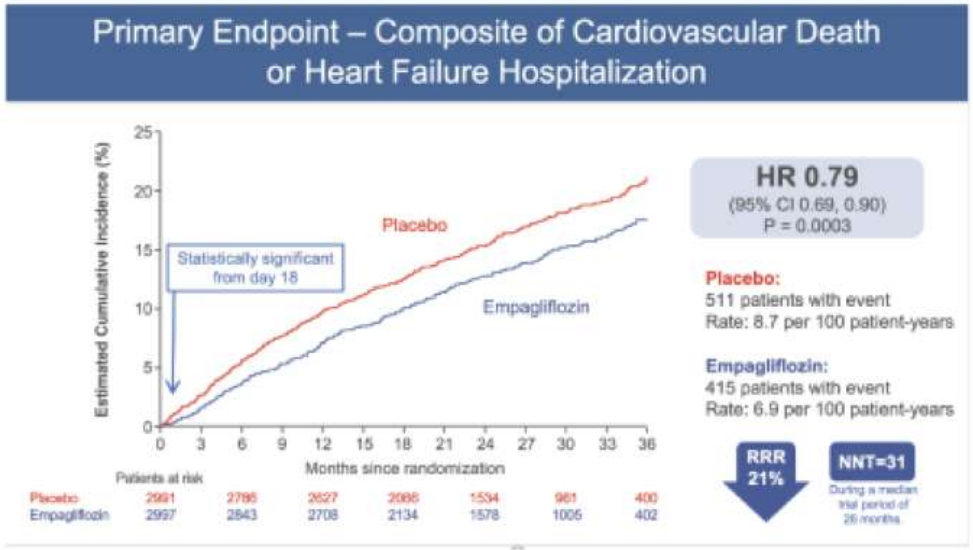
Fu M et al. Int J Cardiol 2012;155:33

CHF: EMPEROR – Preserved and DELIVER

EMPEROR-Preserved

5988 patients with HF and LVEF>40% ± T2DM at baseline

LVEF>40%, NT-proBNP>300pg/ml or 900pm/ml in AF

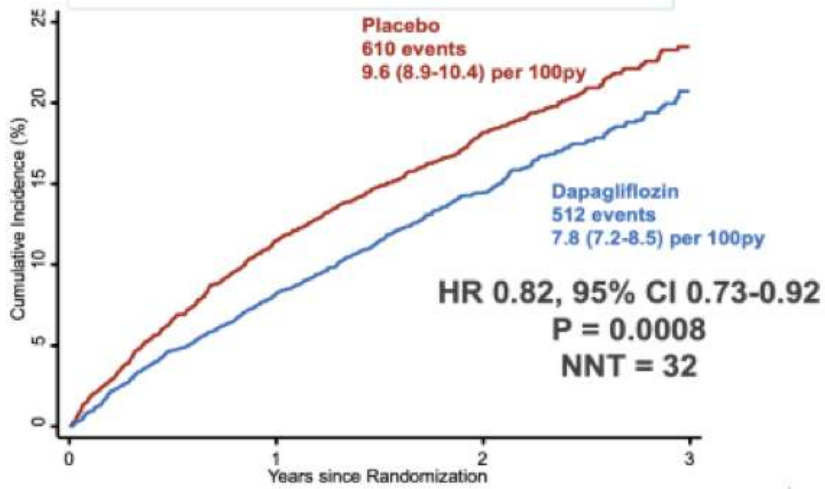


Anker SD et al. NEJM 2021;385(16):1451-1461

DELIVER

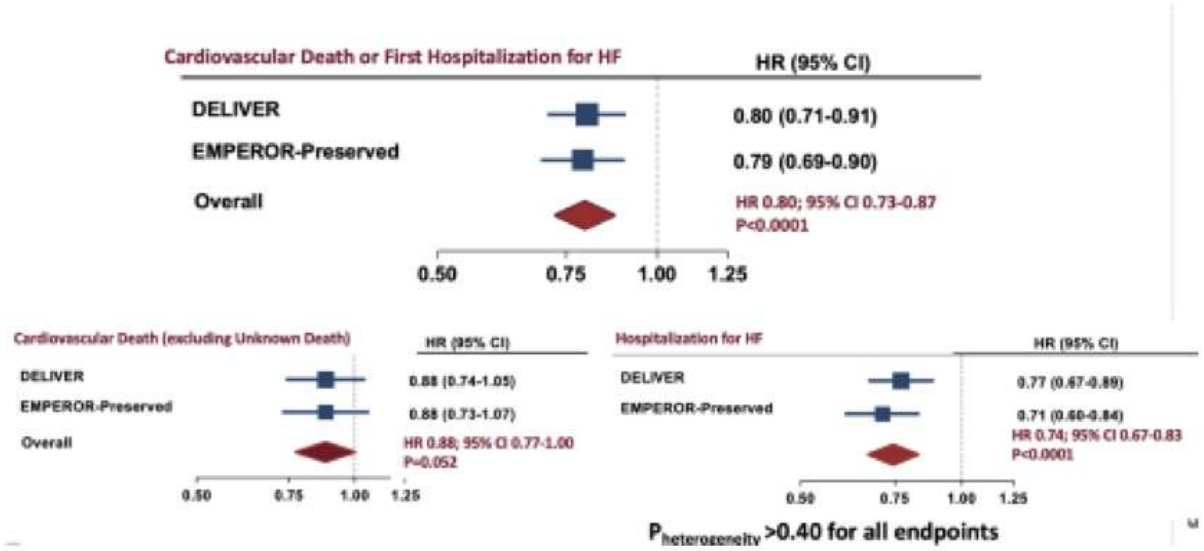
Primary composite endpoint of CV death or worsening HF

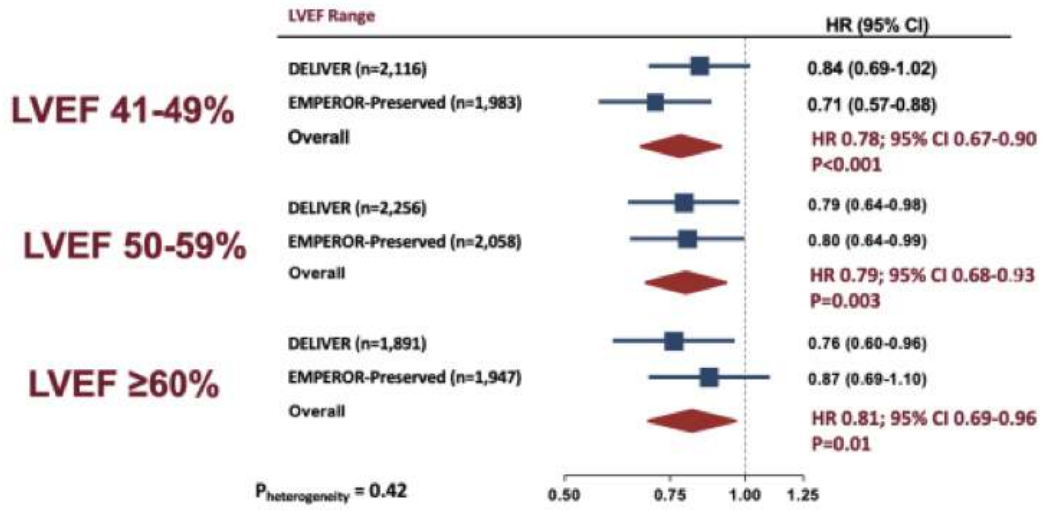
- Age ≥ 40 years
- NYHA class II-IV
- LVEF > 40% (including prior LVEF ≤ 40%)
- Structural Heart Disease (LVH or LA Enlargement)
- Elevated Natriuretic Peptides (> 300 pg/ml or 600 pg/ml in AFF)
- Either Ambulatory or Hospitalized for Heart Failure



Solomon SD et al NEJM 2022;387:1089-1098

EMPEROR – Preserved and DELIVER





Lancet 2022; 400 (10354): 757-767

Recommendation for the treatment of patients with symptomatic HFmrEF

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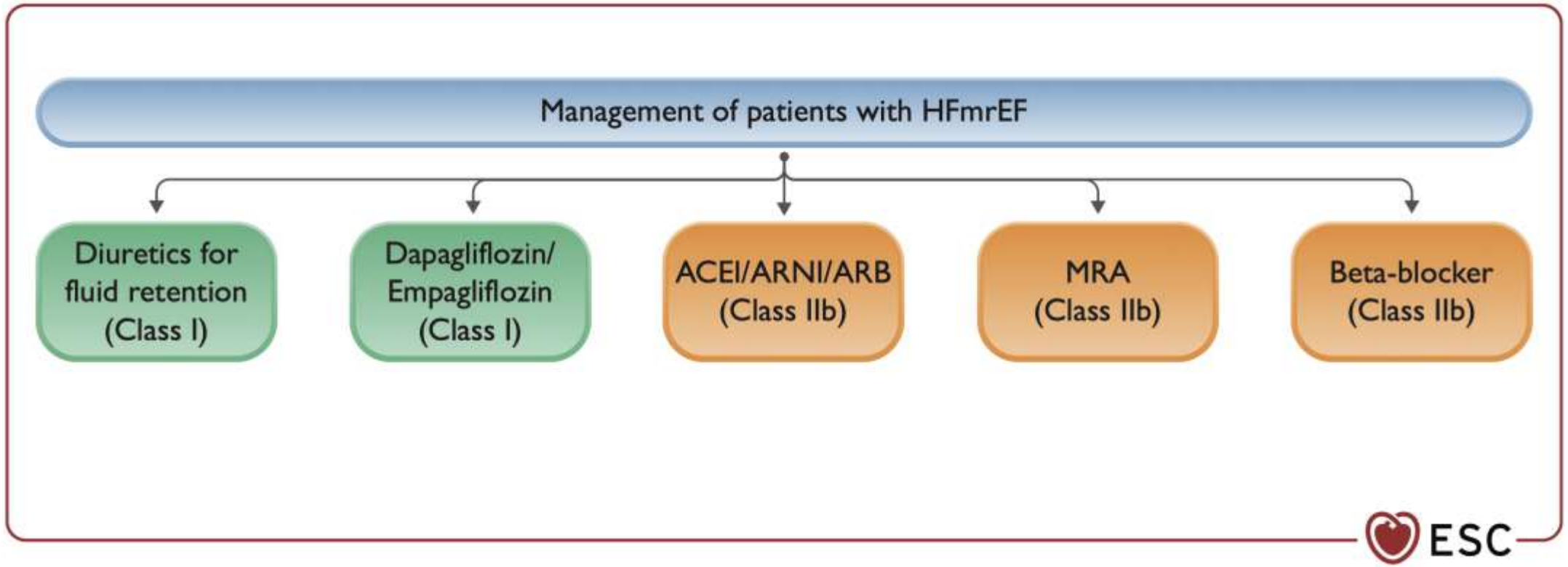
Recommendation Table 1 — Recommendation for the treatment of patients with symptomatic heart failure with mildly reduced ejection fraction

Recommendation	Class[a]	Level[b]
An SGLT2 inhibitor (dapagliflozin or empagliflozin) is recommended in patients with HFmrEF to reduce the risk of HF hospitalization or CV death.[c] [6,8]	I	A

Recommendation for the treatment of patients with symptomatic HFmrEF

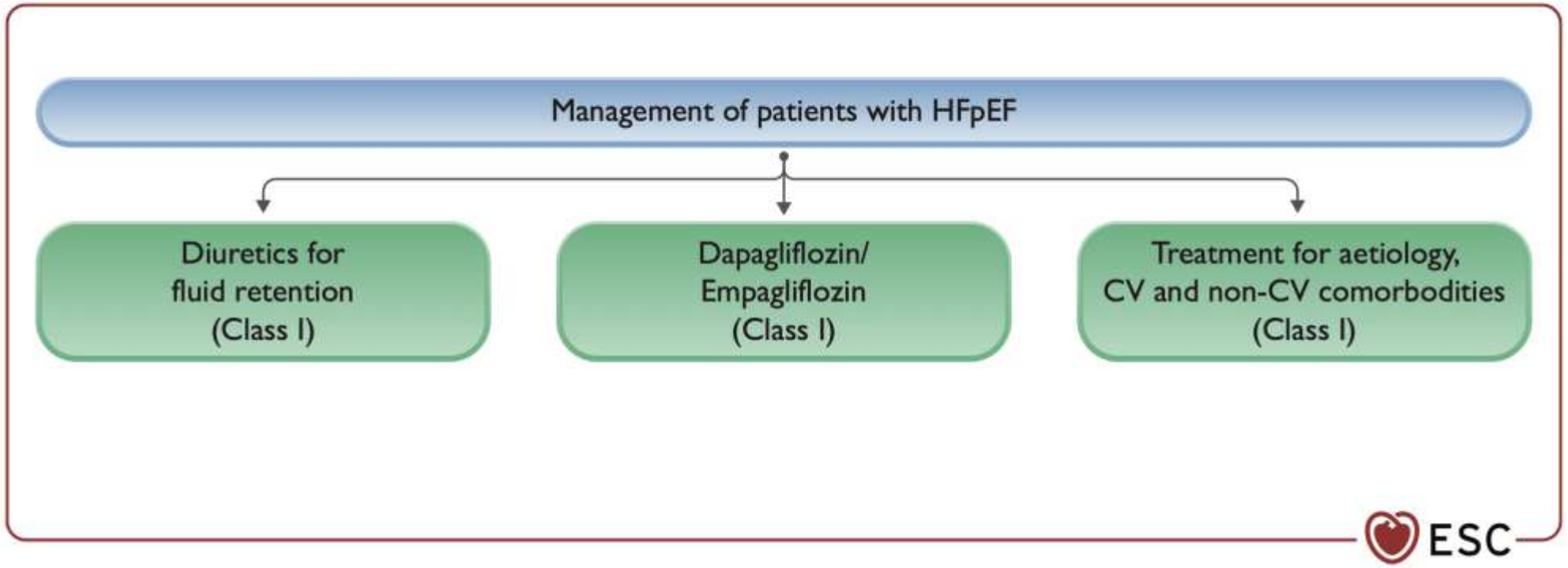


Recommendation for the treatment of patients with symptomatic HFpEF

Recommendation Table 2 — Recommendation for the treatment of patients with symptomatic heart failure with preserved ejection fraction

Recommendation	Class[a]	Level[b]
An SGLT2 inhibitor (dapagliflozin or empagliflozin) is recommended in patients with HFpEF to reduce the risk of HF hospitalization or CV death.[c] [6,8]	I	A

Recommendation for the treatment of patients with symptomatic HFpEF

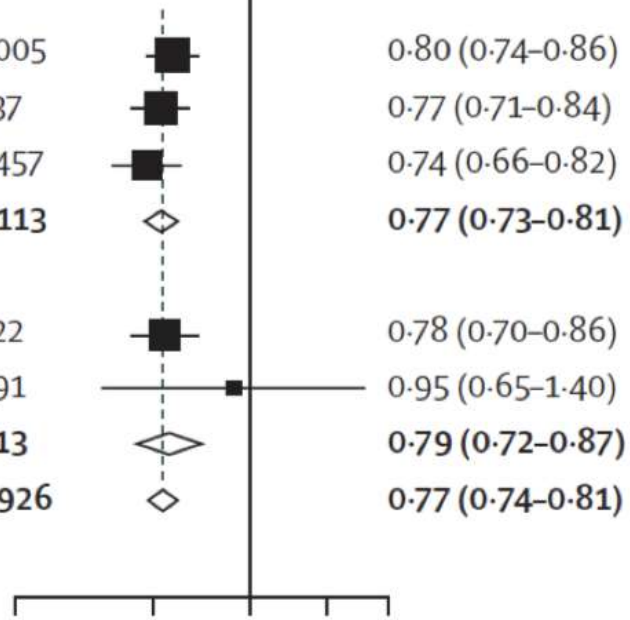


DMT_2 and CKD

Cardiovascular death or hospitalisation for heart failure*

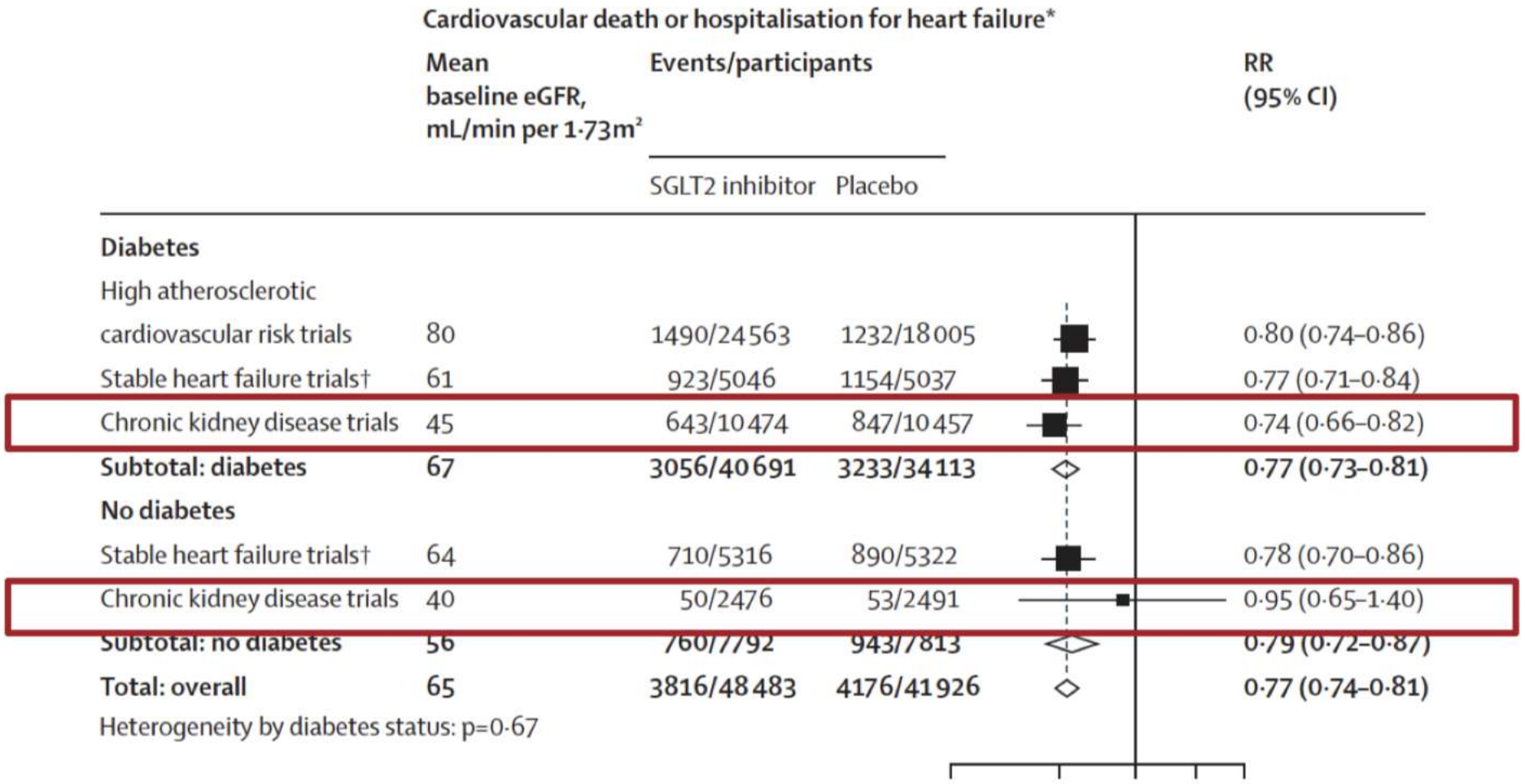
	Mean baseline eGFR, mL/min per 1·73m²	Events/participants		RR (95% CI)
		SGLT2 inhibitor	Placebo	
Diabetes				
High atherosclerotic cardiovascular risk trials	80	1490/24563	1232/18005	0·80 (0·74–0·86)
Stable heart failure trials†	61	923/5046	1154/5037	0·77 (0·71–0·84)
Chronic kidney disease trials	45	643/10474	847/10457	0·74 (0·66–0·82)
Subtotal: diabetes	**67**	**3056/40691**	**3233/34113**	**0·77 (0·73–0·81)**
No diabetes				
Stable heart failure trials†	64	710/5316	890/5322	0·78 (0·70–0·86)
Chronic kidney disease trials	40	50/2476	53/2491	0·95 (0·65–1·40)
Subtotal: no diabetes	**56**	**760/7792**	**943/7813**	**0·79 (0·72–0·87)**
Total: overall	**65**	**3816/48483**	**4176/41926**	**0·77 (0·74–0·81)**

Heterogeneity by diabetes status: p=0·67



Lancet 2022; 400 (10365): 1788-1801

DMT_2 and CKD



Cardiovascular death or hospitalisation for heart failure*

	Mean baseline eGFR, mL/min per 1·73m²	Events/participants: SGLT2 inhibitor	Events/participants: Placebo	RR (95% CI)
Diabetes				
High atherosclerotic cardiovascular risk trials	80	1490/24563	1232/18005	0·80 (0·74–0·86)
Stable heart failure trials†	61	923/5046	1154/5037	0·77 (0·71–0·84)
Chronic kidney disease trials	45	643/10474	847/10457	0·74 (0·66–0·82)
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Total: overall	65	3816/48483	4176/41926	0·77 (0·74–0·81)

Heterogeneity by diabetes status: p=0·67

Lancet 2022; 400 (10365): 1788-1801

Recommendation for the prevention of HF in patients with DMT_2 and CKD

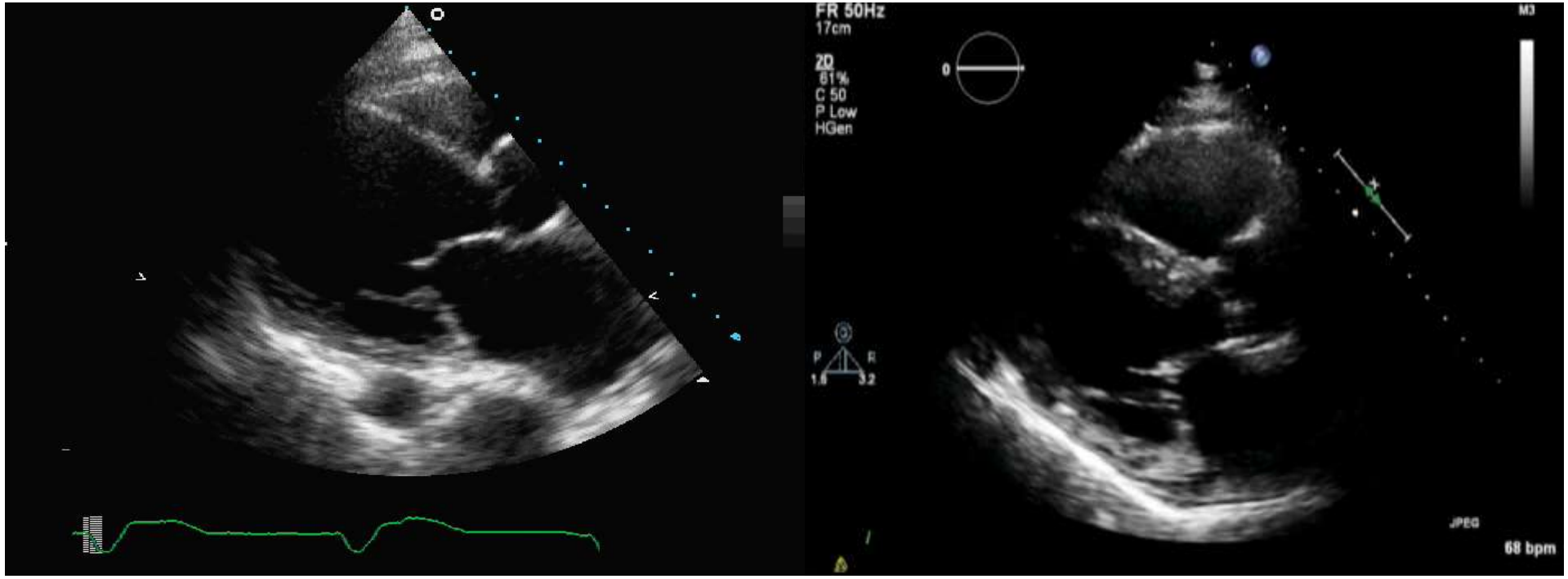
Recommendations	Class[a]	Level[b]
In patients with T2DM and CKD,[c] SGLT2 inhibitors are recommended to reduce the risk of HF hospitalization or CV death.[35]	I	A
In patients with T2DM and CKD,[c] finerenone is recommended to reduce the risk of HF hospitalization.[10,11,34,40]	I	A

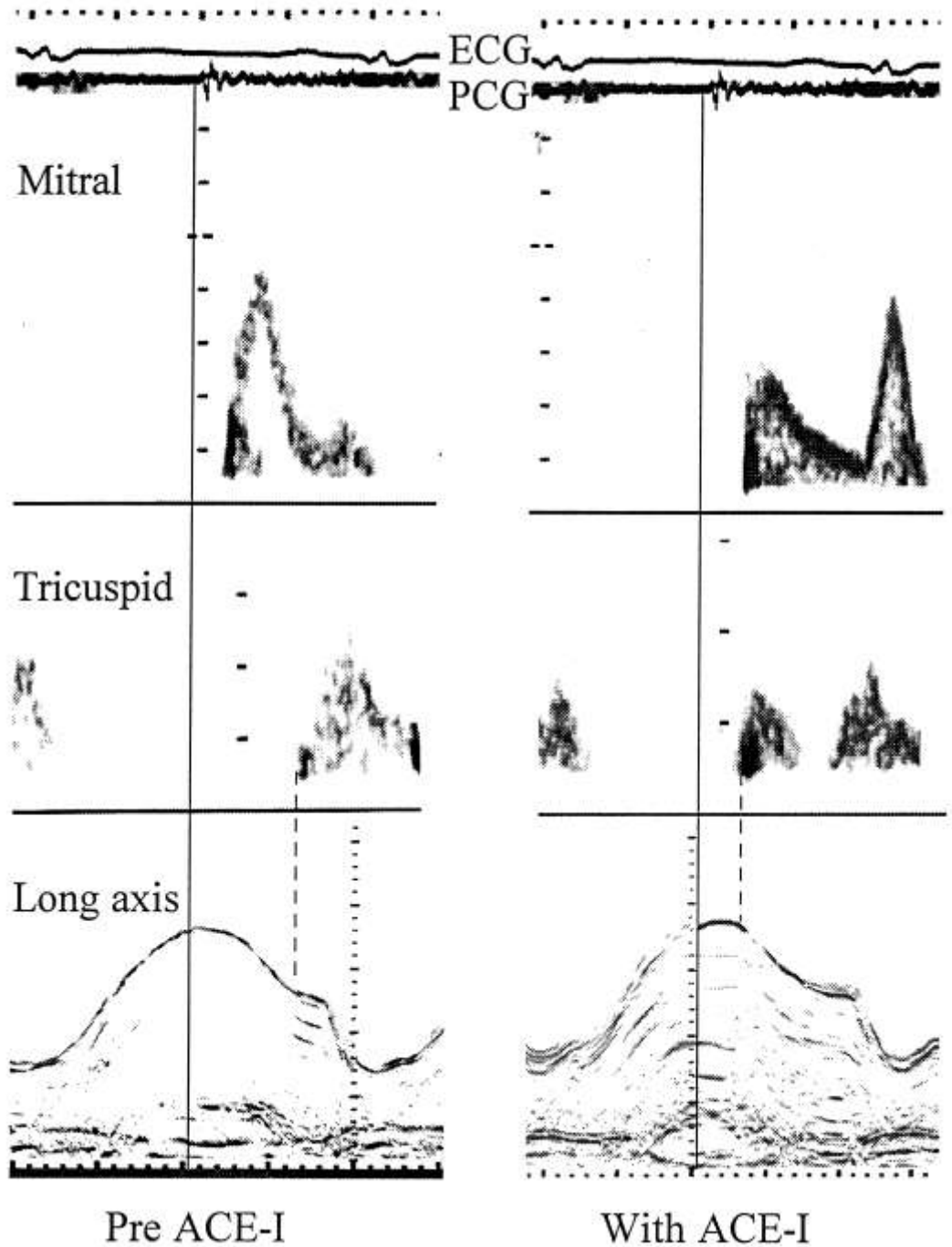
Effective treatment of Heart Failure is based on global cardiac function

- Diuretics
- ACE-Inhibitors/ARBs
- $\mathscr{B}$ Blockers
- Spironolactone
- SGLT2 inhibitors

- QRS duration
- PR interval

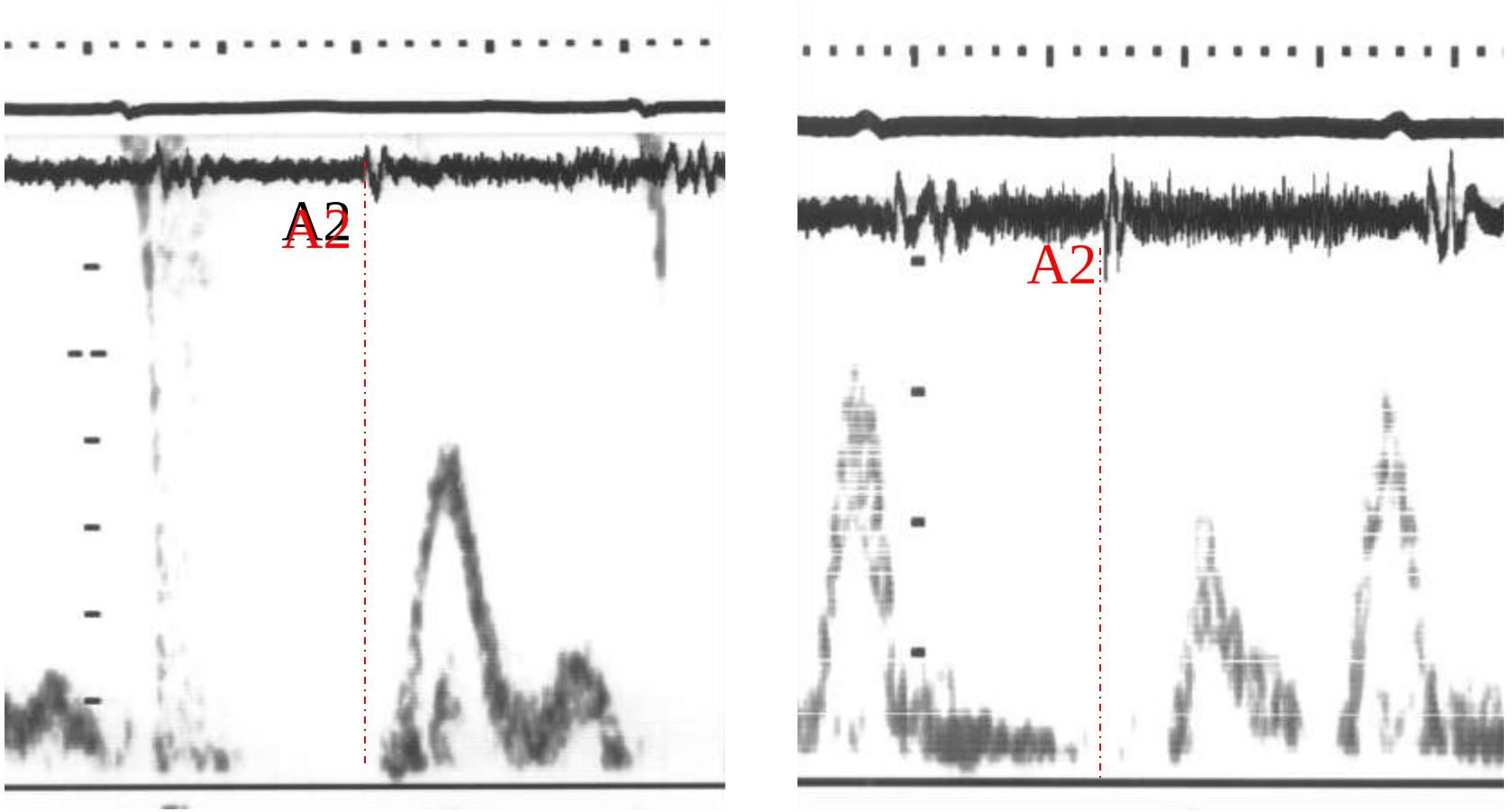
HF with wide EF range



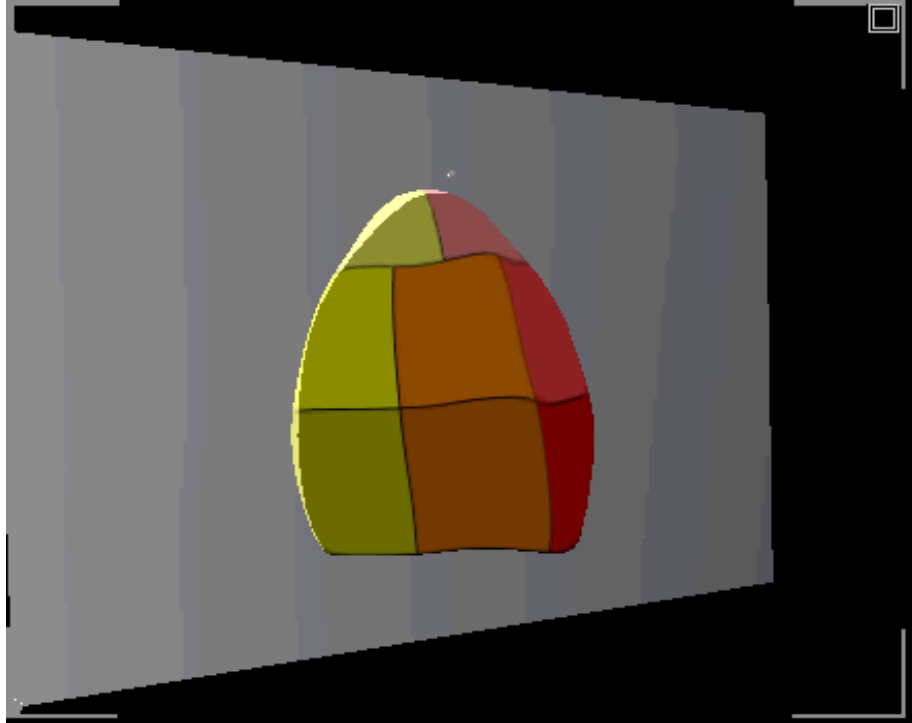


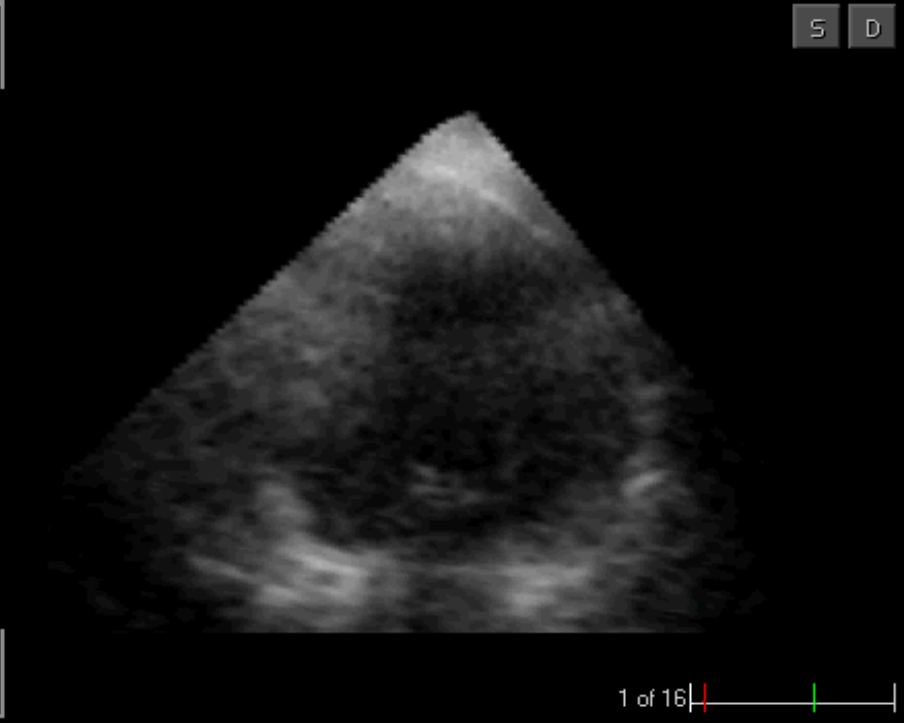
Henein M et al. JACC 1998; 32: 1187

ACE-I for restrictive LV filling



Henein M et al; HEART 1995

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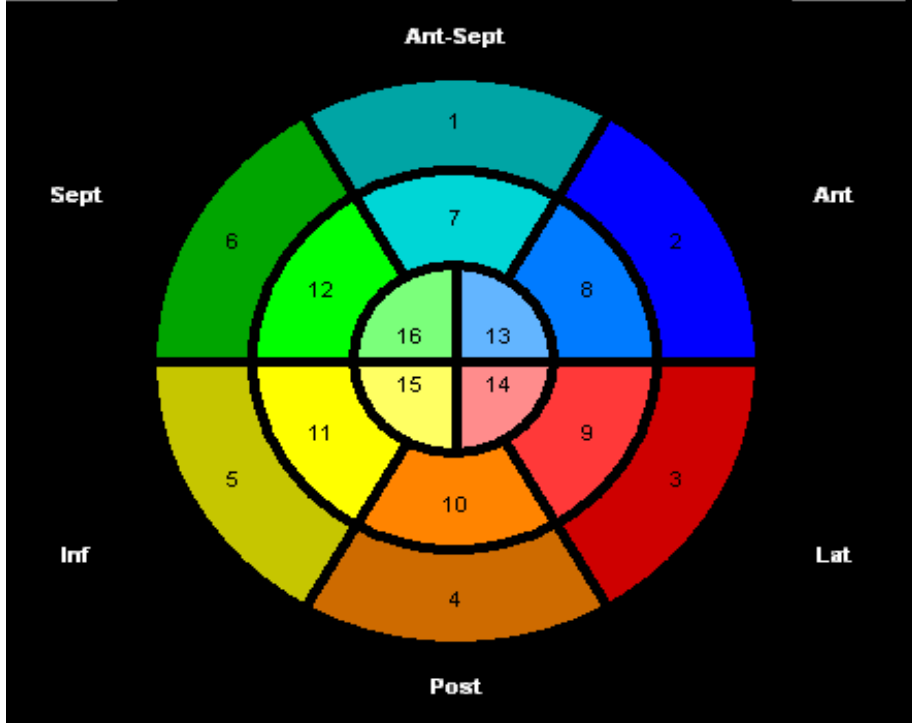
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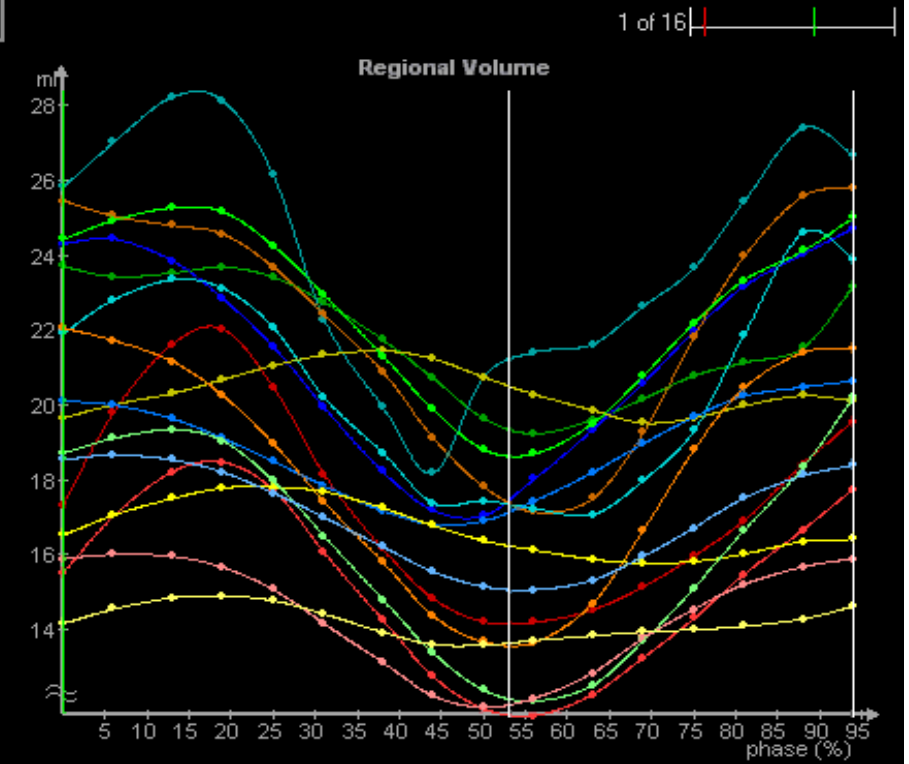

1 of 16
Regional Volume
ml
28
26
24
22
20
18
16
14
5 10 15 20 25 30 35 40 45 50 55 60 65 70 75 80 85 90 95
phase (%)

Objective of Pacing in Heart Failure

↓ symptoms

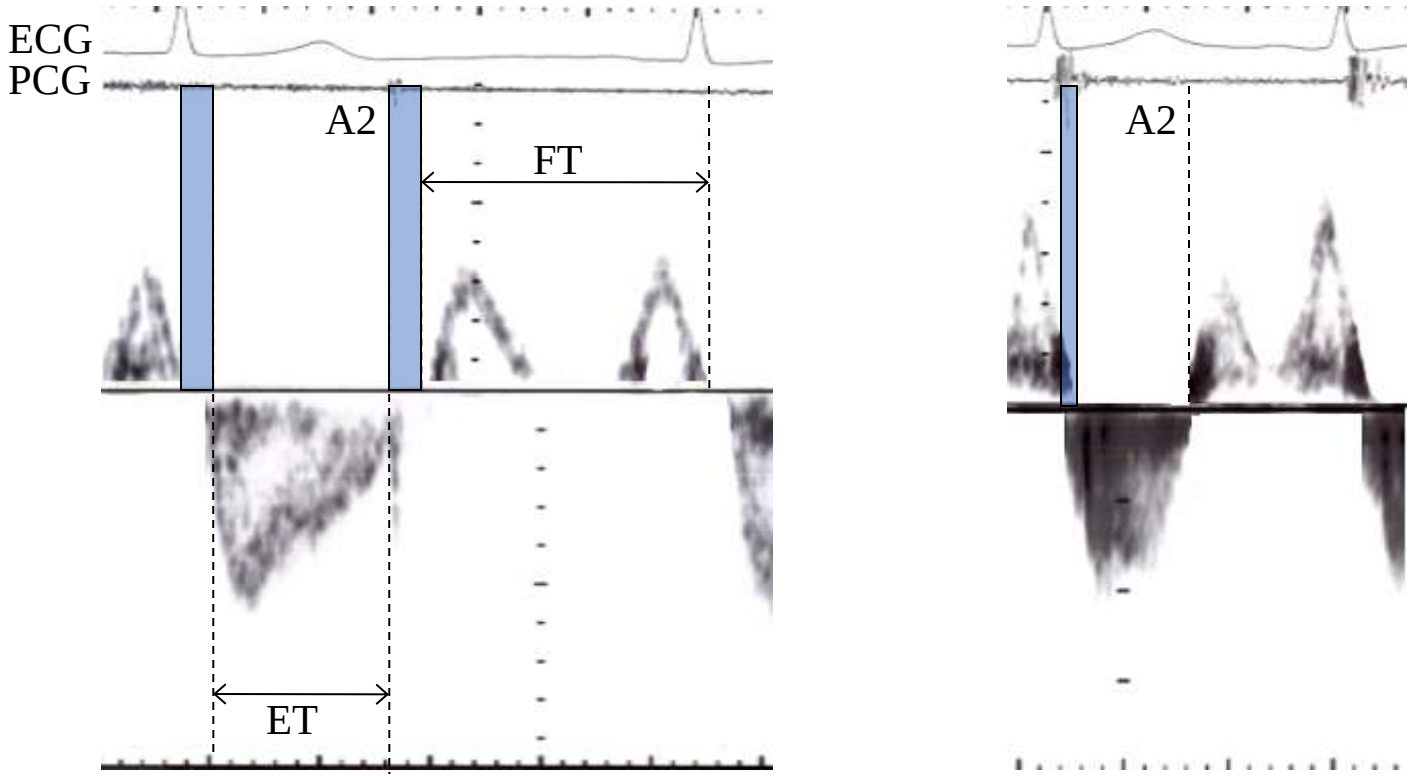
↑ stroke volume

↓ LA pressure

↑ survival

But 30 % do not respond

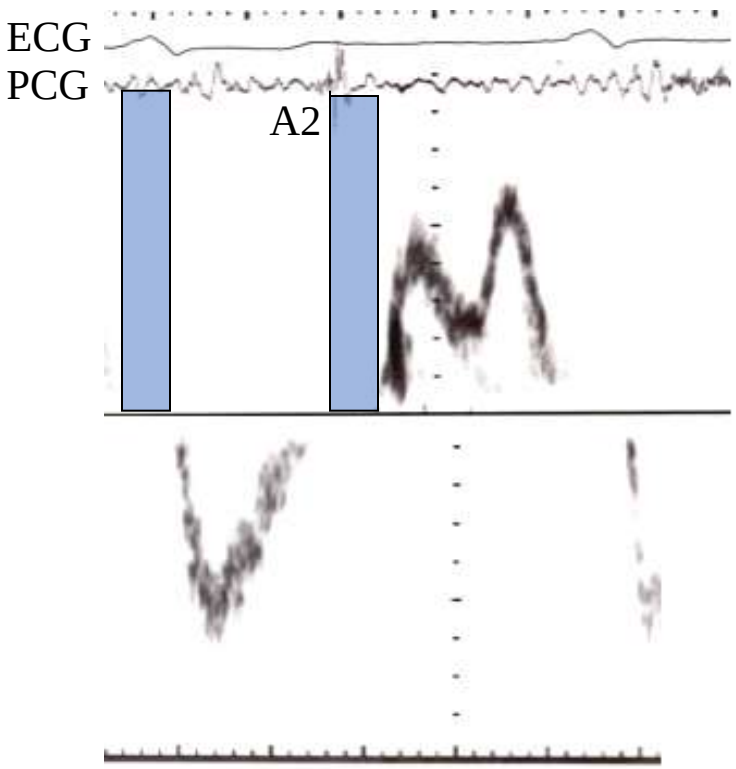
Normal Doppler response to dobutamine stress



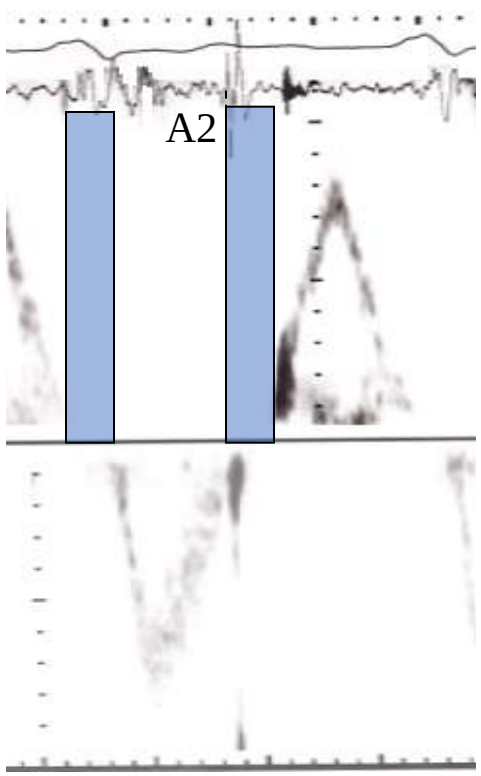
Rest Stress

ET: 20s/min vs 22s/min
FT: 31s/min vs 34 s/min
IVT: 9s/min vs 5s/min
} p<0.001

Dilated Cardiomyopathy: CAD + LBBB



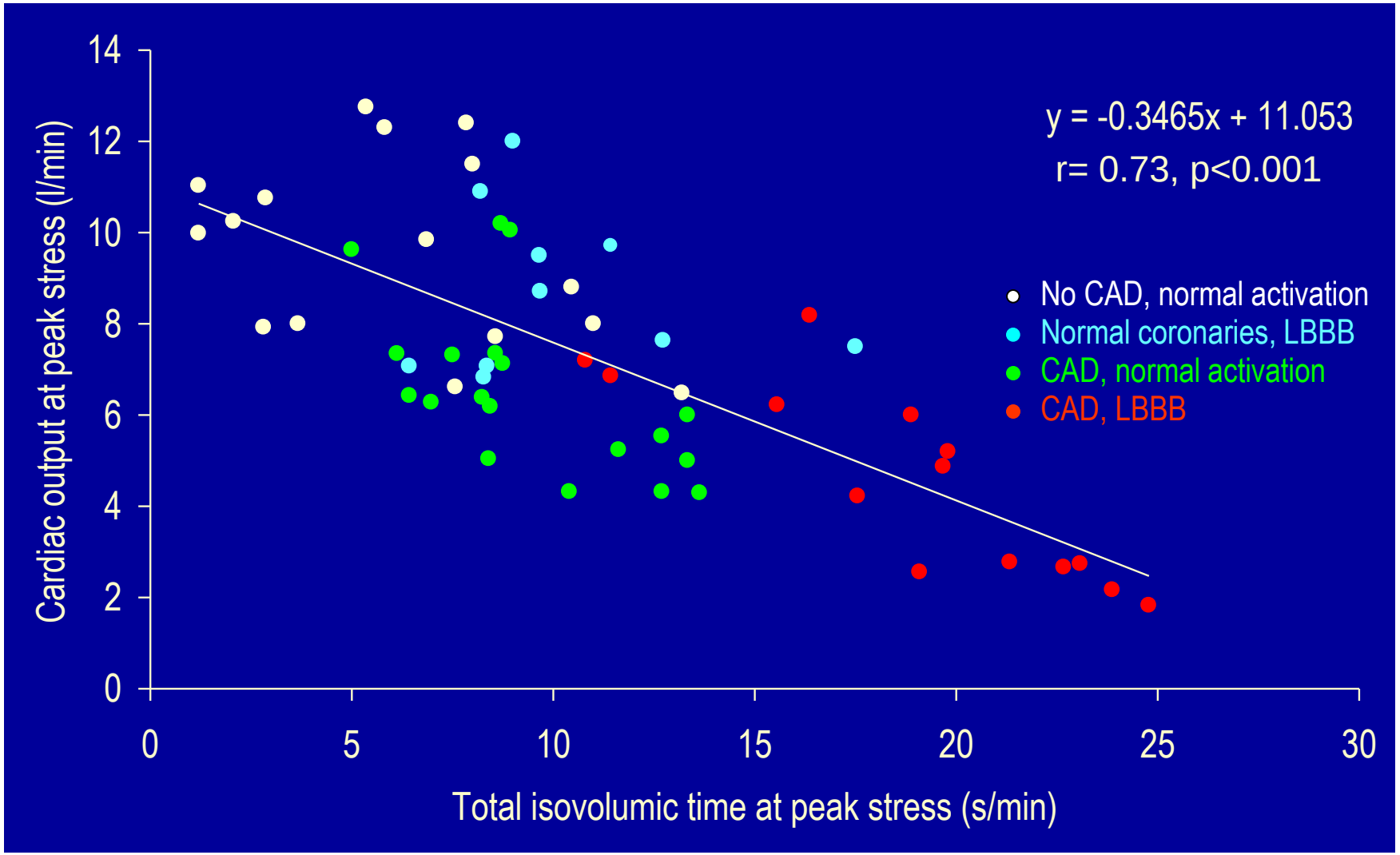
Rest



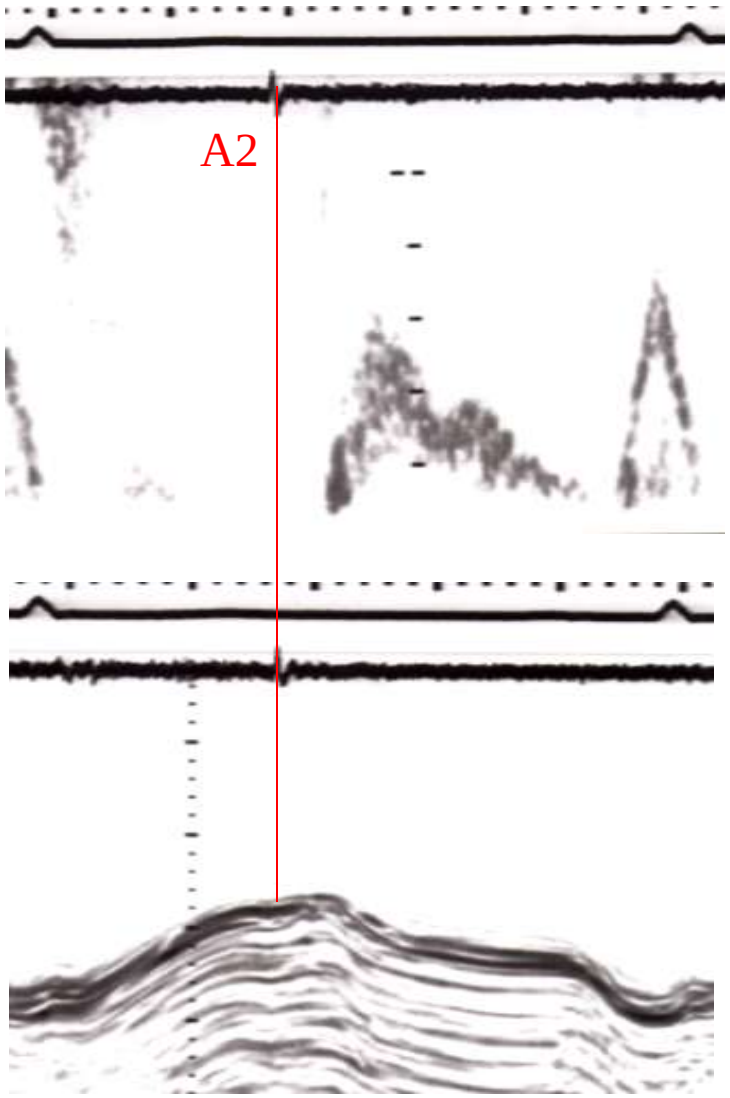
Stress

ET:	19s/min	vs 20s/min	p=ns
FT:	23s/min	vs 22s/min	
IVT:	18s/min	vs 18s/min	

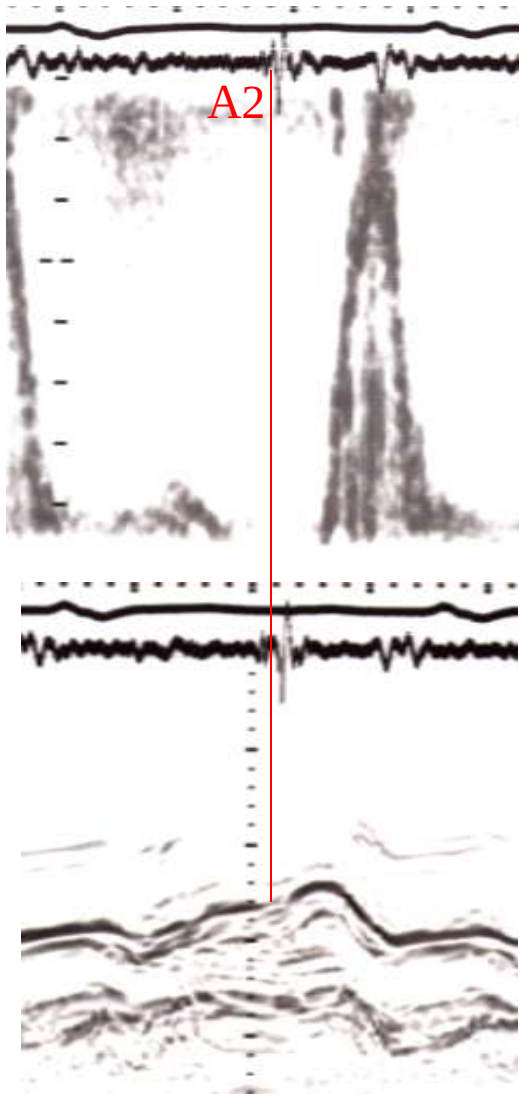
Effect of isovolumic time on CO at stress



Duncan A,… Henein M JACC 2003



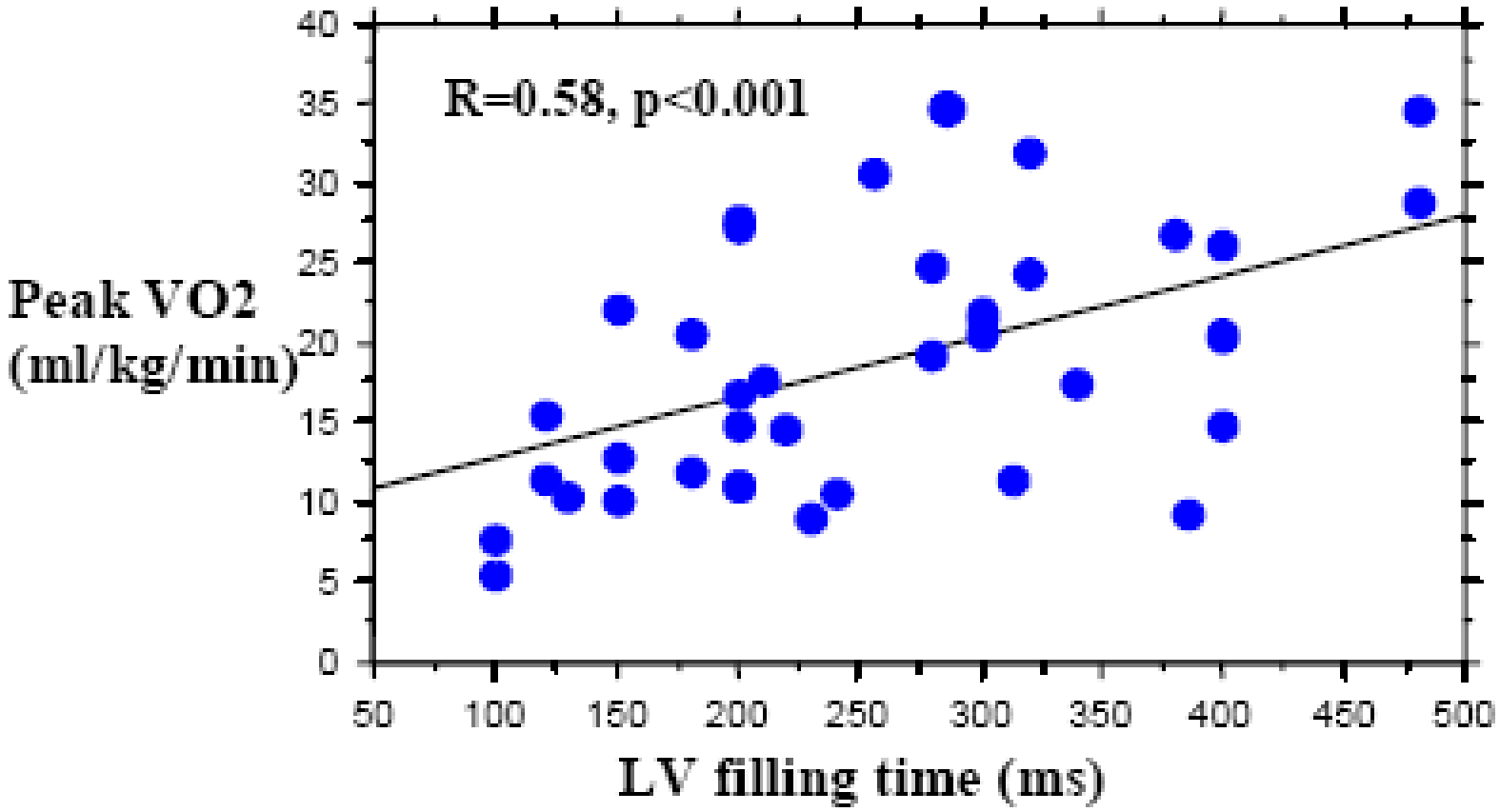
LV filling 50 %



LV filling 30%

Filling time *vs* Exercise tolerance

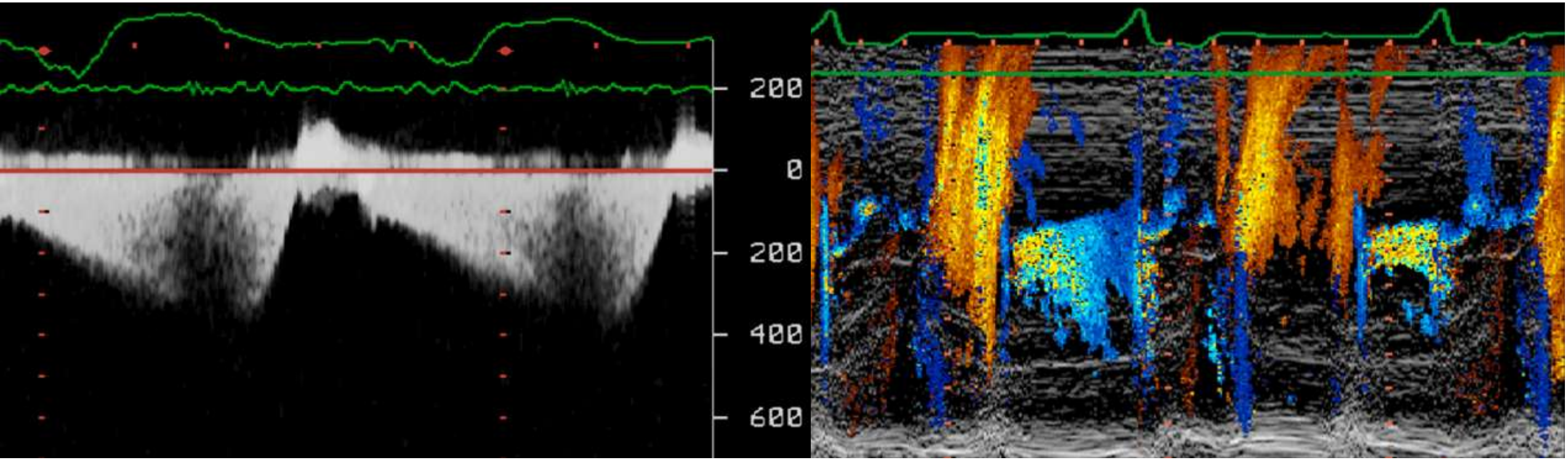
DCM



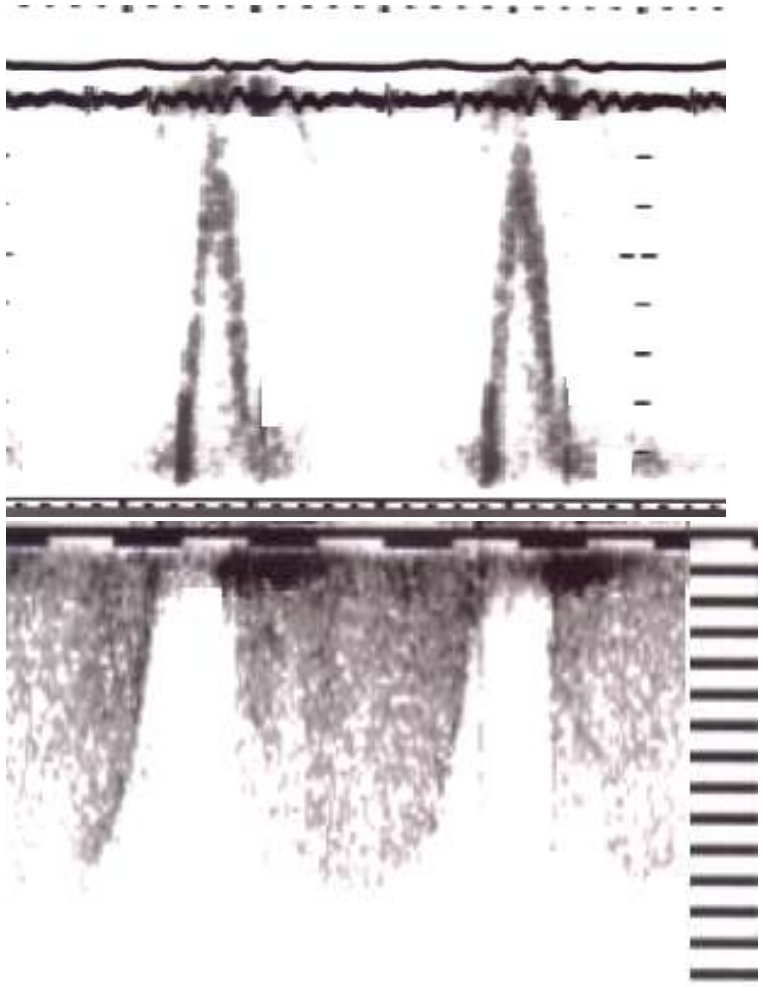
Exercise capacity in dilated cardiomyopathy: The effect of LBBB

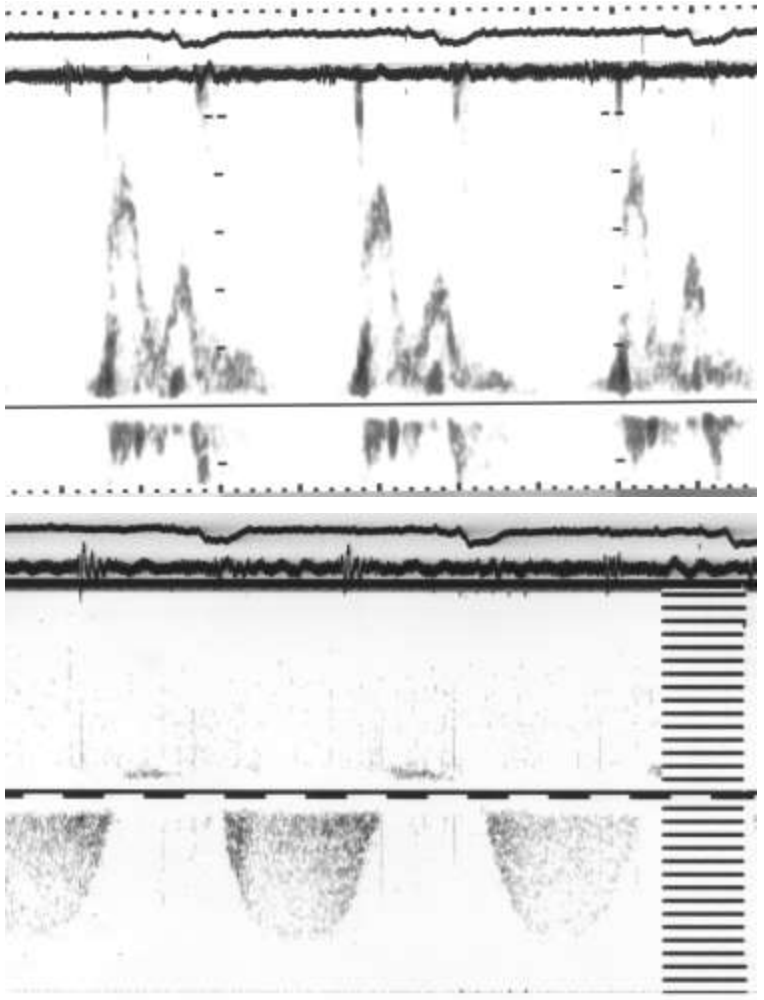
Qinghua Zhou[1,2], Tushar V. Salukhe[1], Michael Y. Henein[1]

Pre-systolic MR limiting filling
DCM

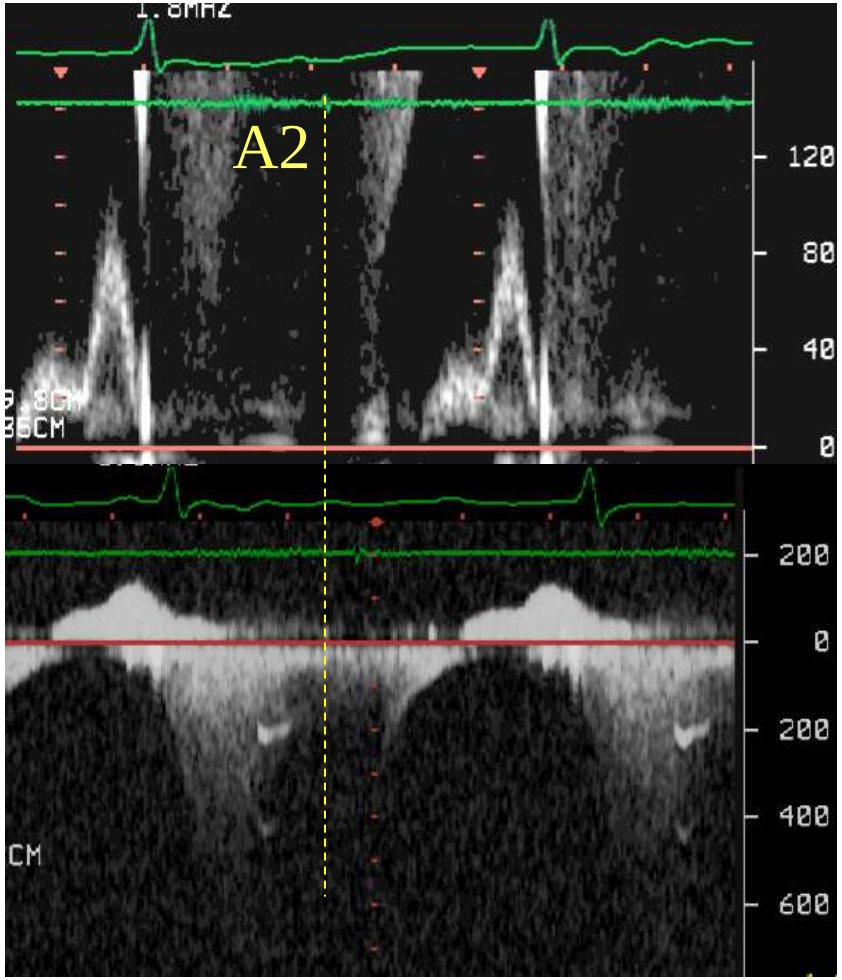


DDD prolongs filling time





Early diastolic MR limiting filling

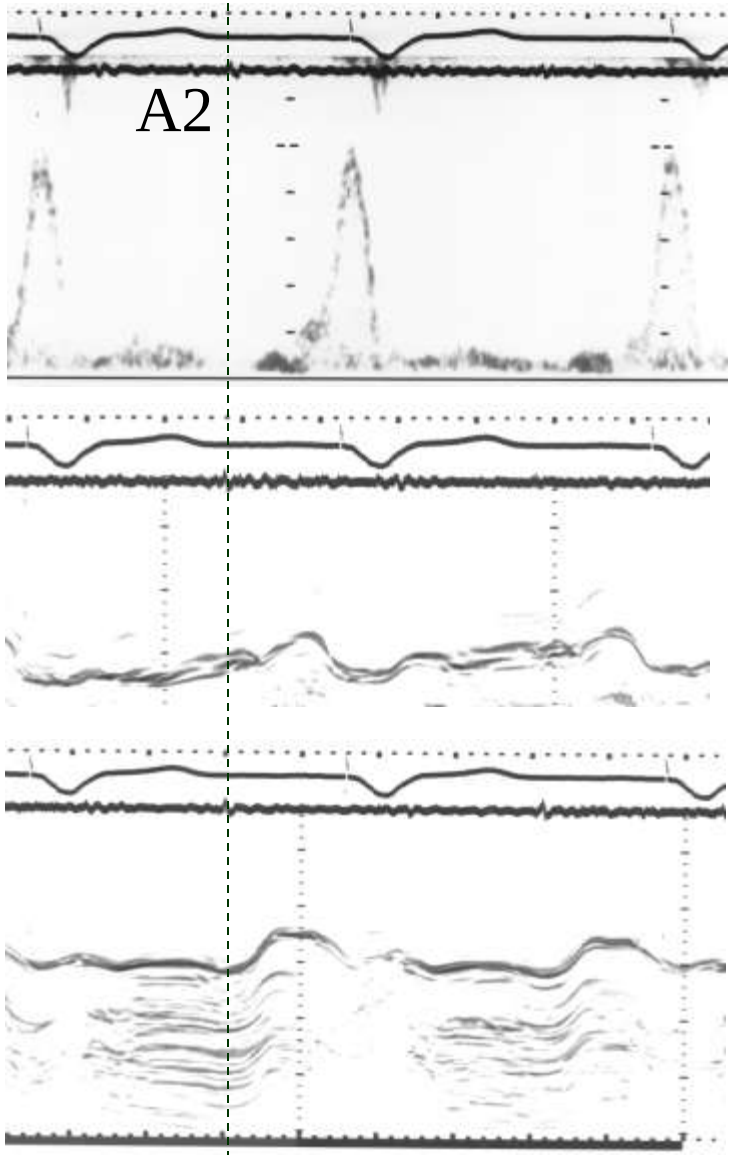


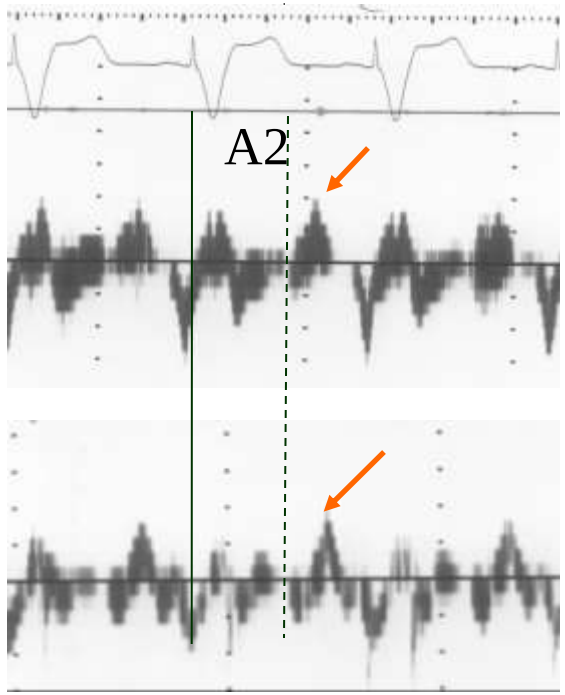
Failure to respond to DDD

LV filling

Free wall

Septum

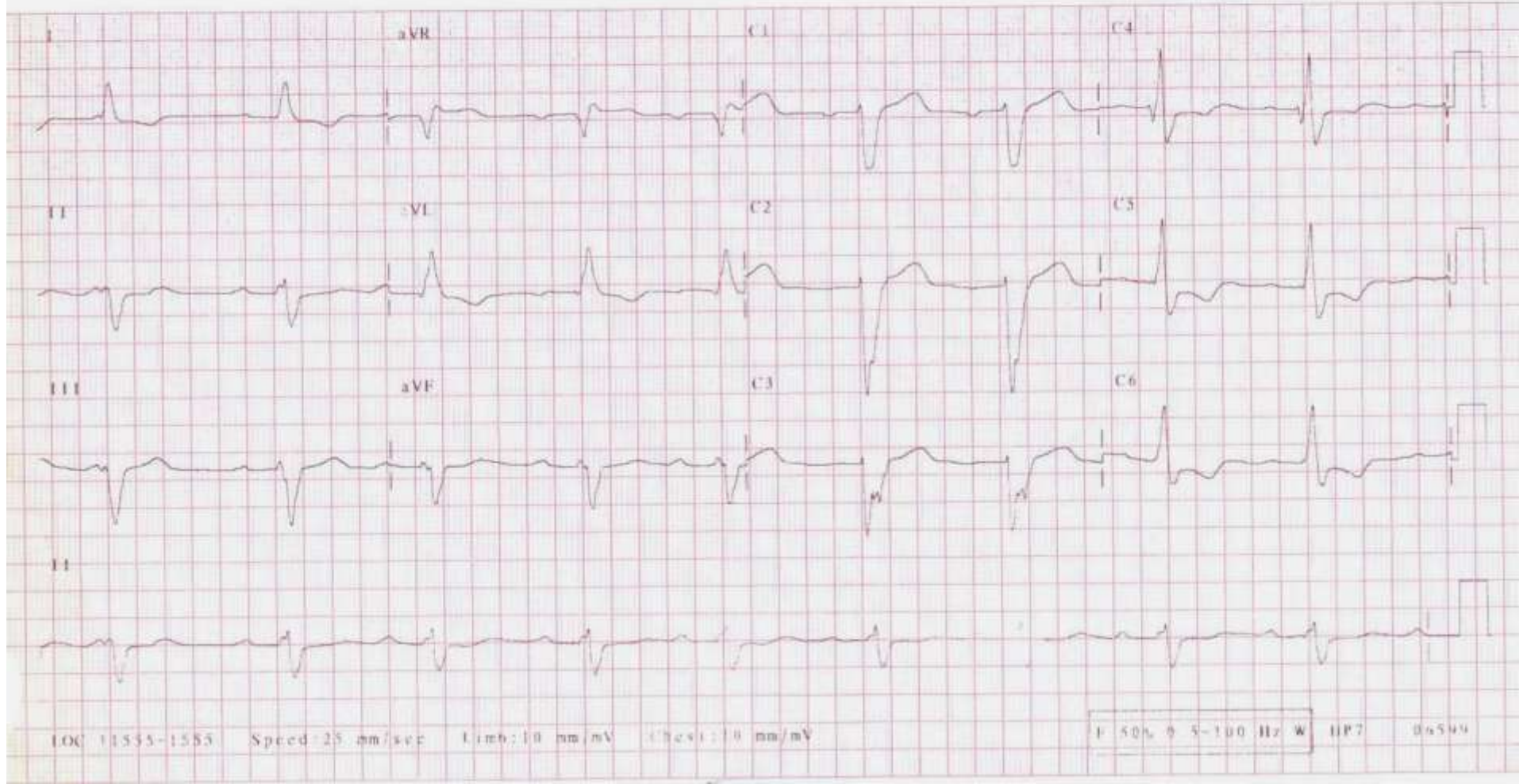




Rate 56
PR 303
QRSD 188
QT 499
QTc 482

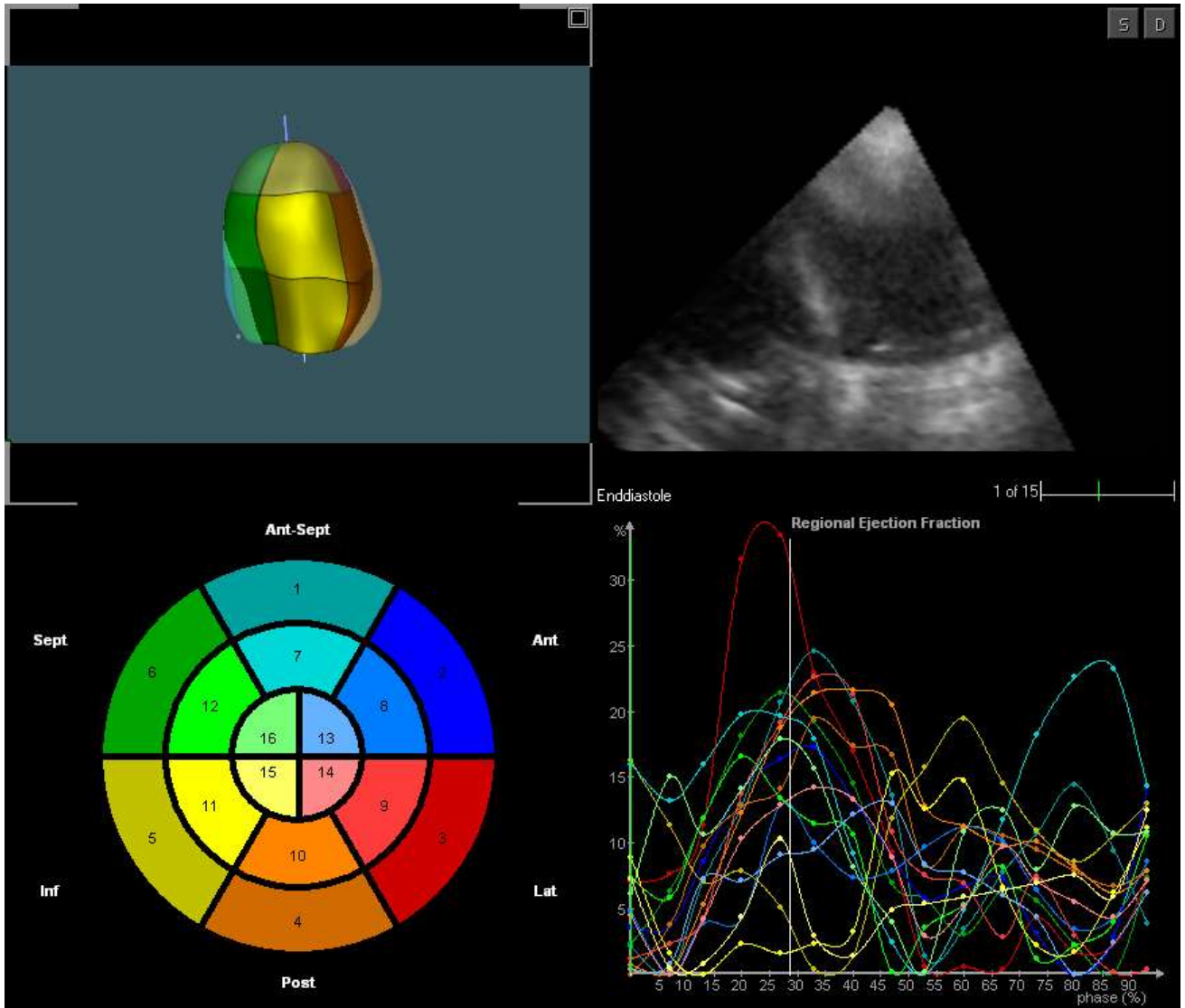
--AXIS--
P 73
QRS -55
T 149

Requested by:



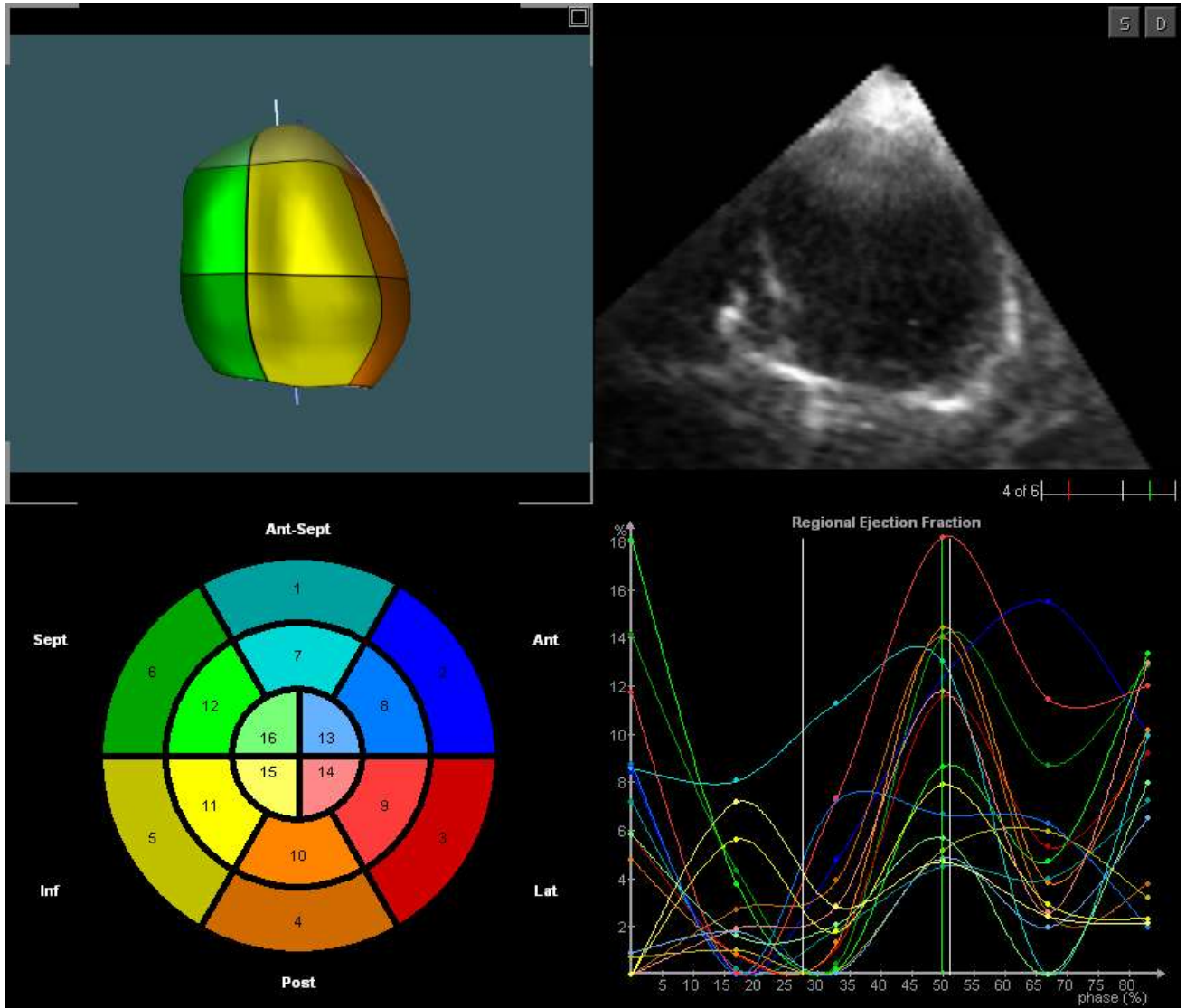
LV function in CAD

CRT – OFF

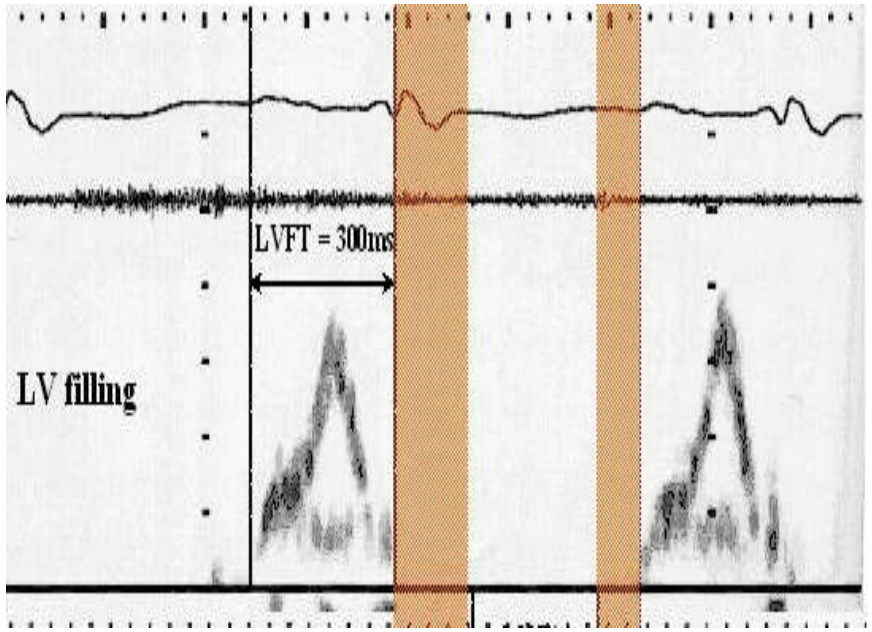


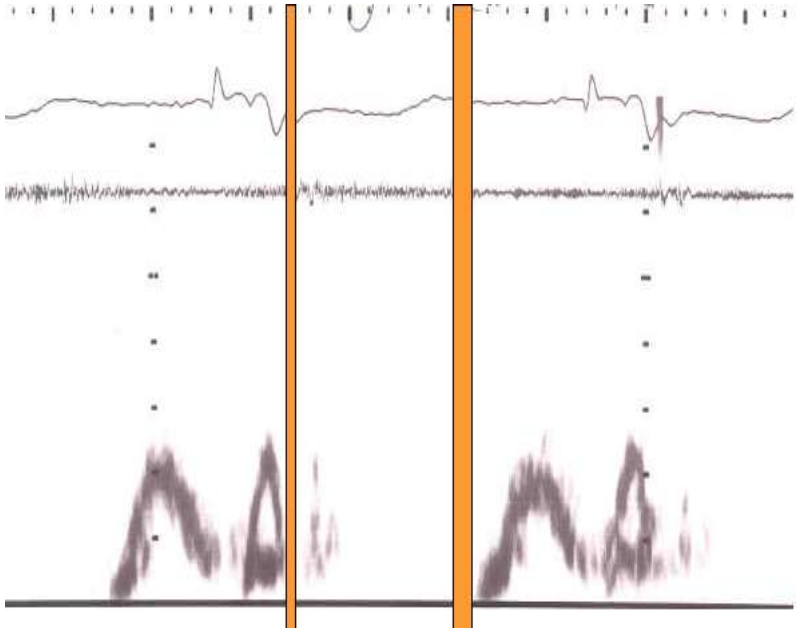
LV function in CAD

CRT – ON

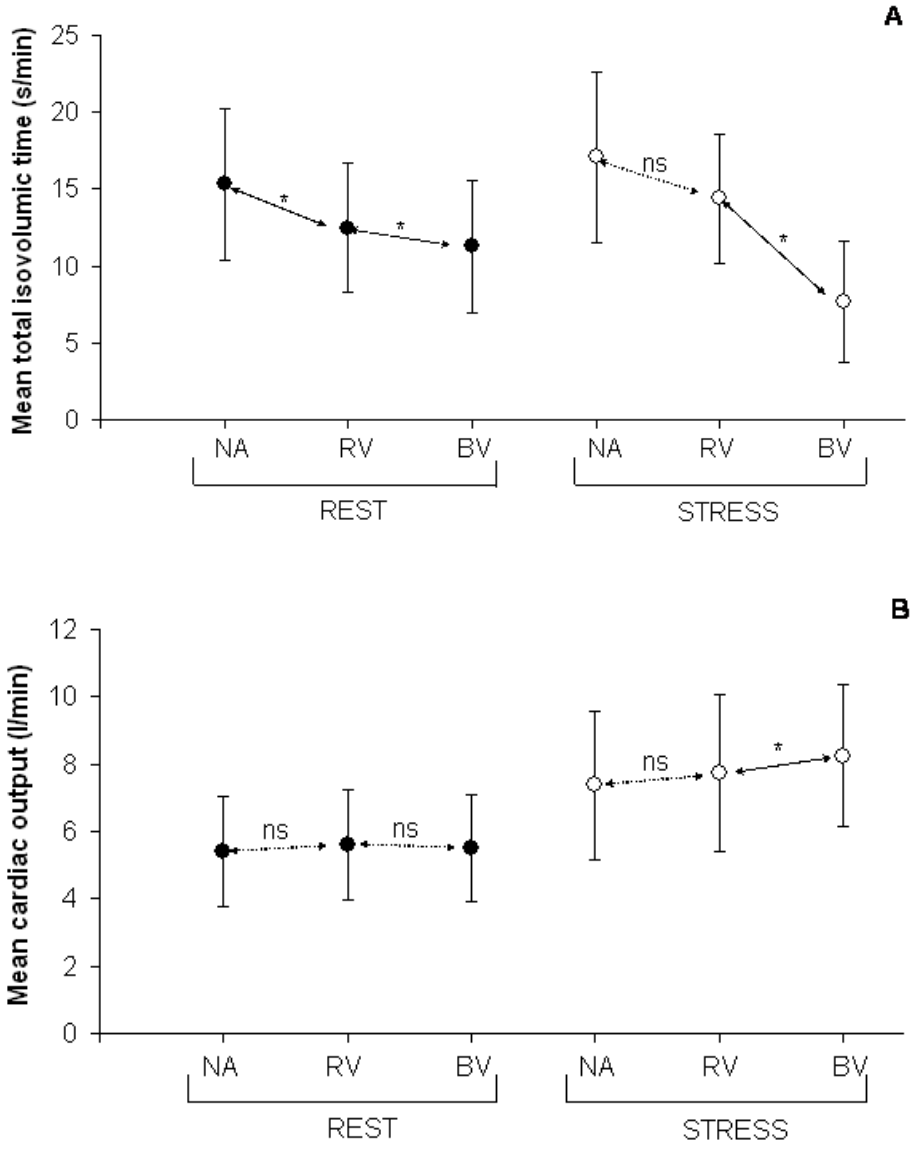


Biventricular pacing & LV filling



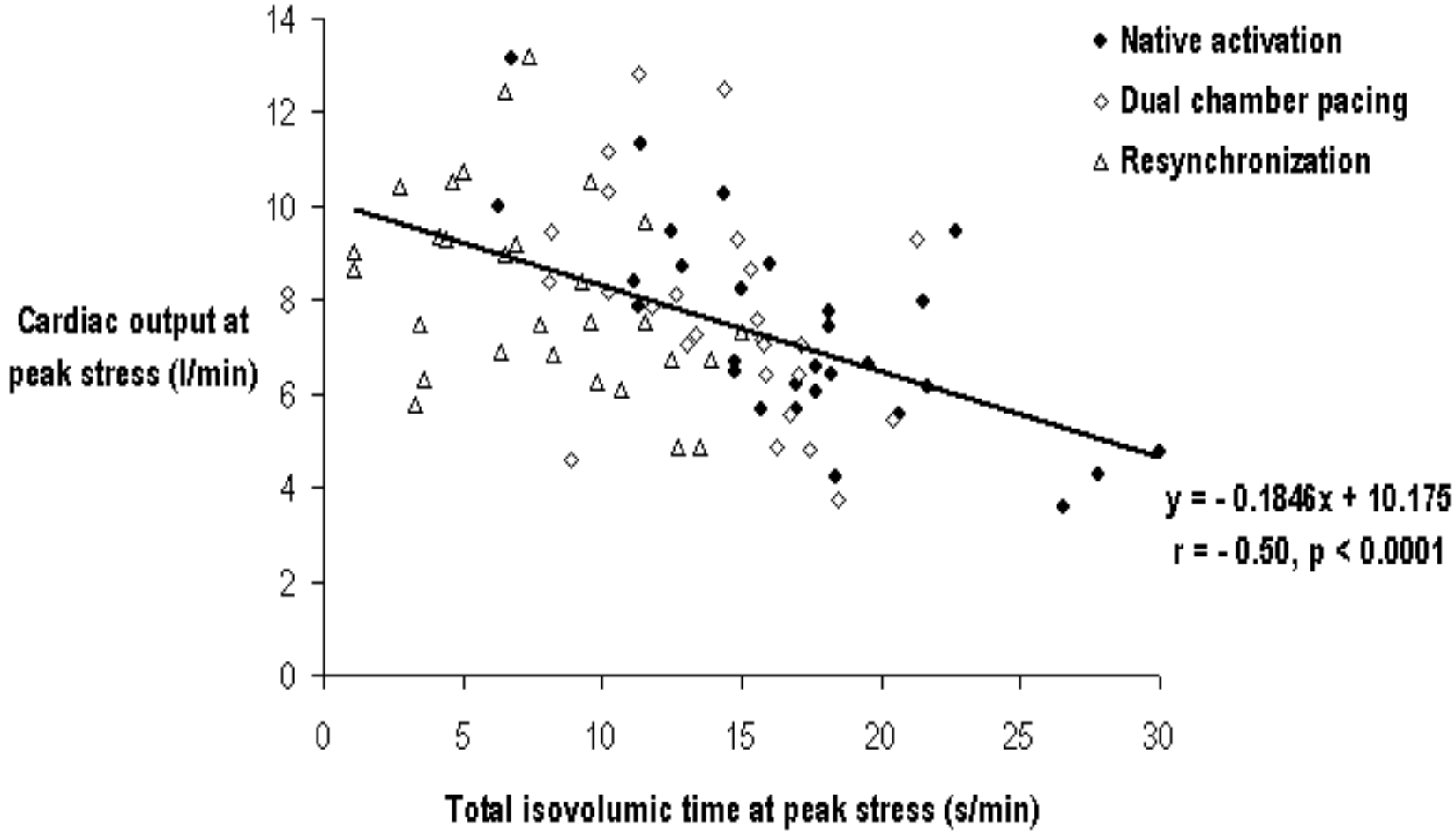


Effect of pacing mode on LV function

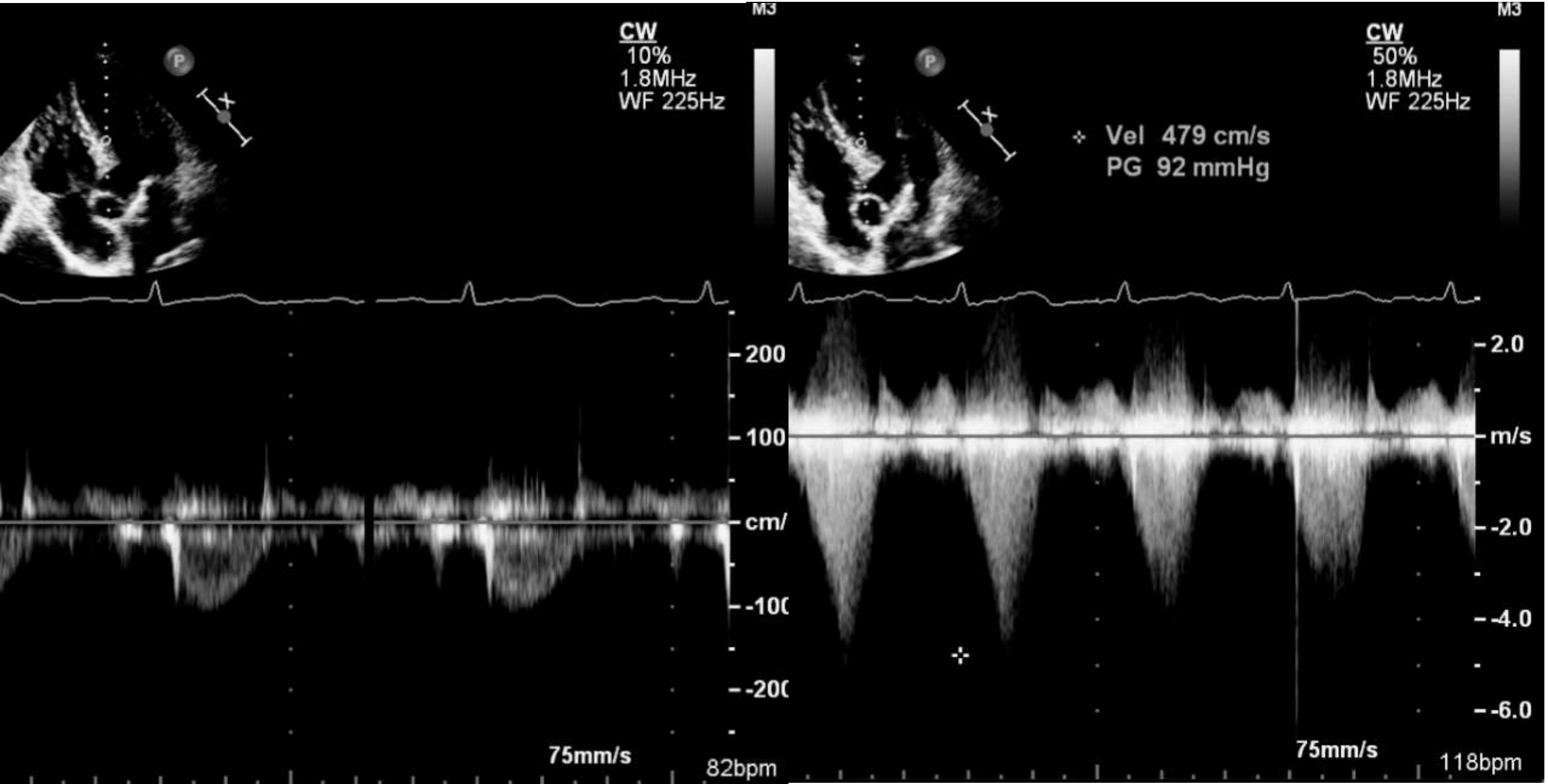


Saluke T et al, Am J Card 2006

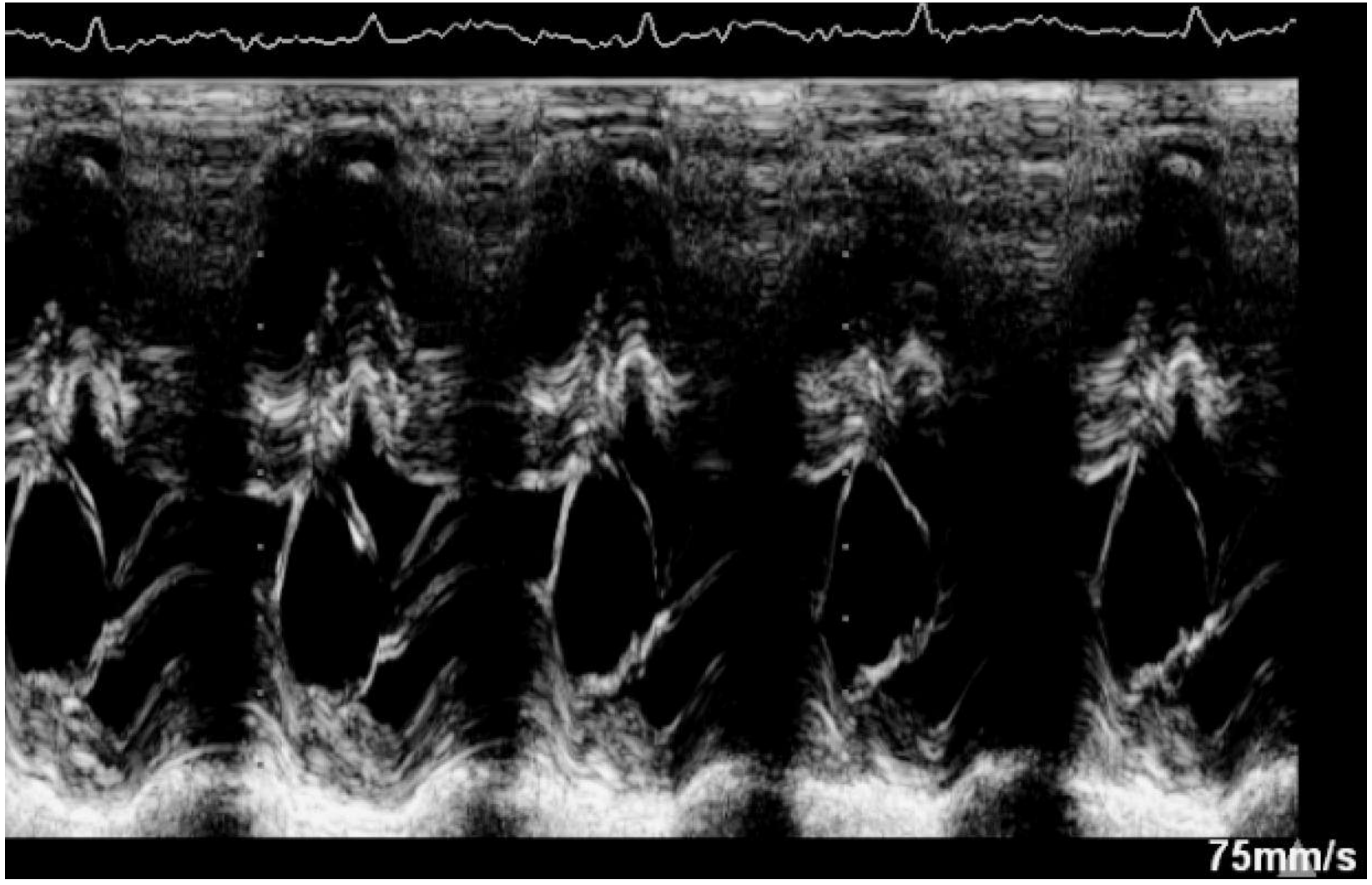
Effect of pacing mode on LV function



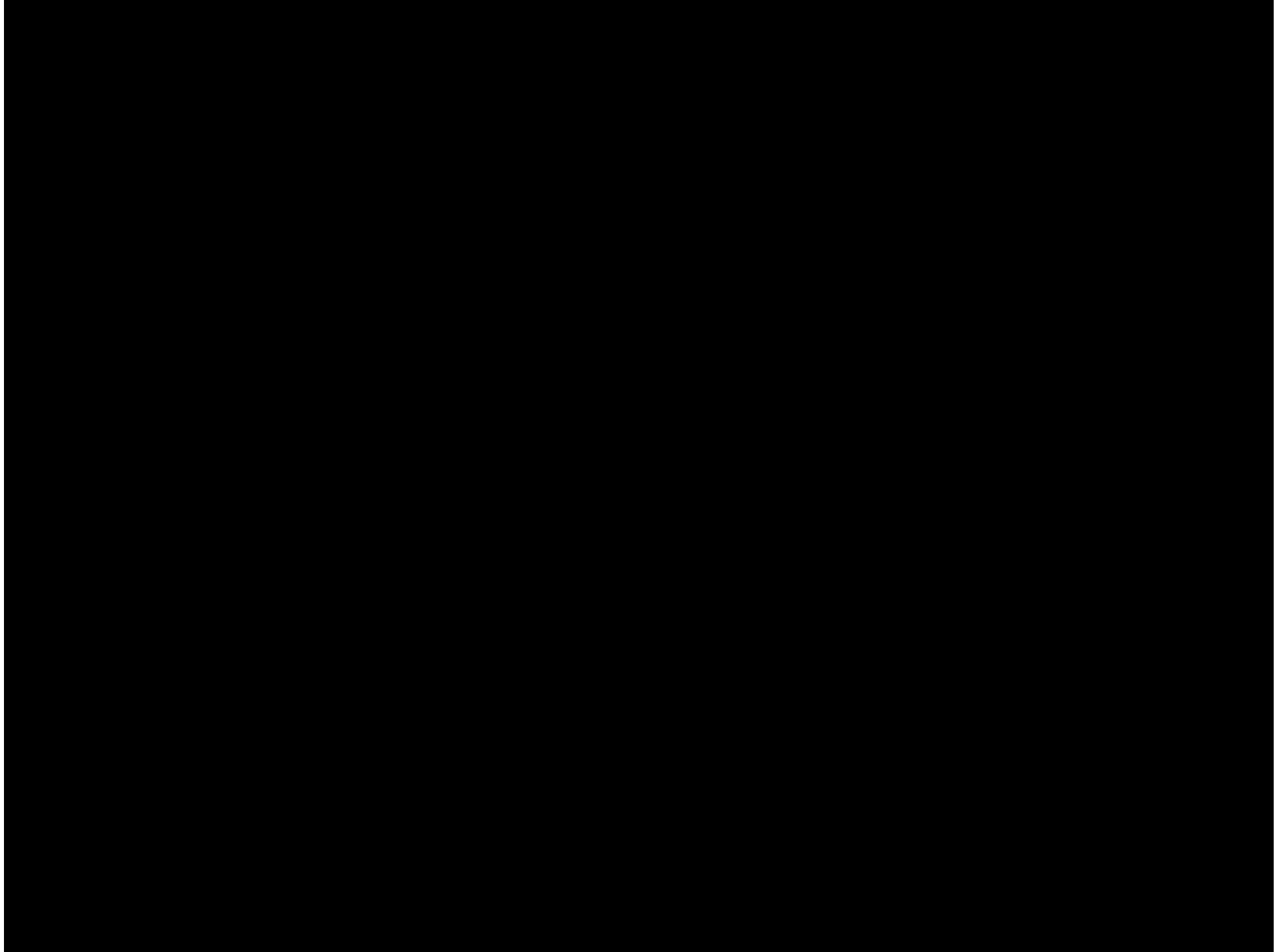
Saluke T et al, Am J Card 2006

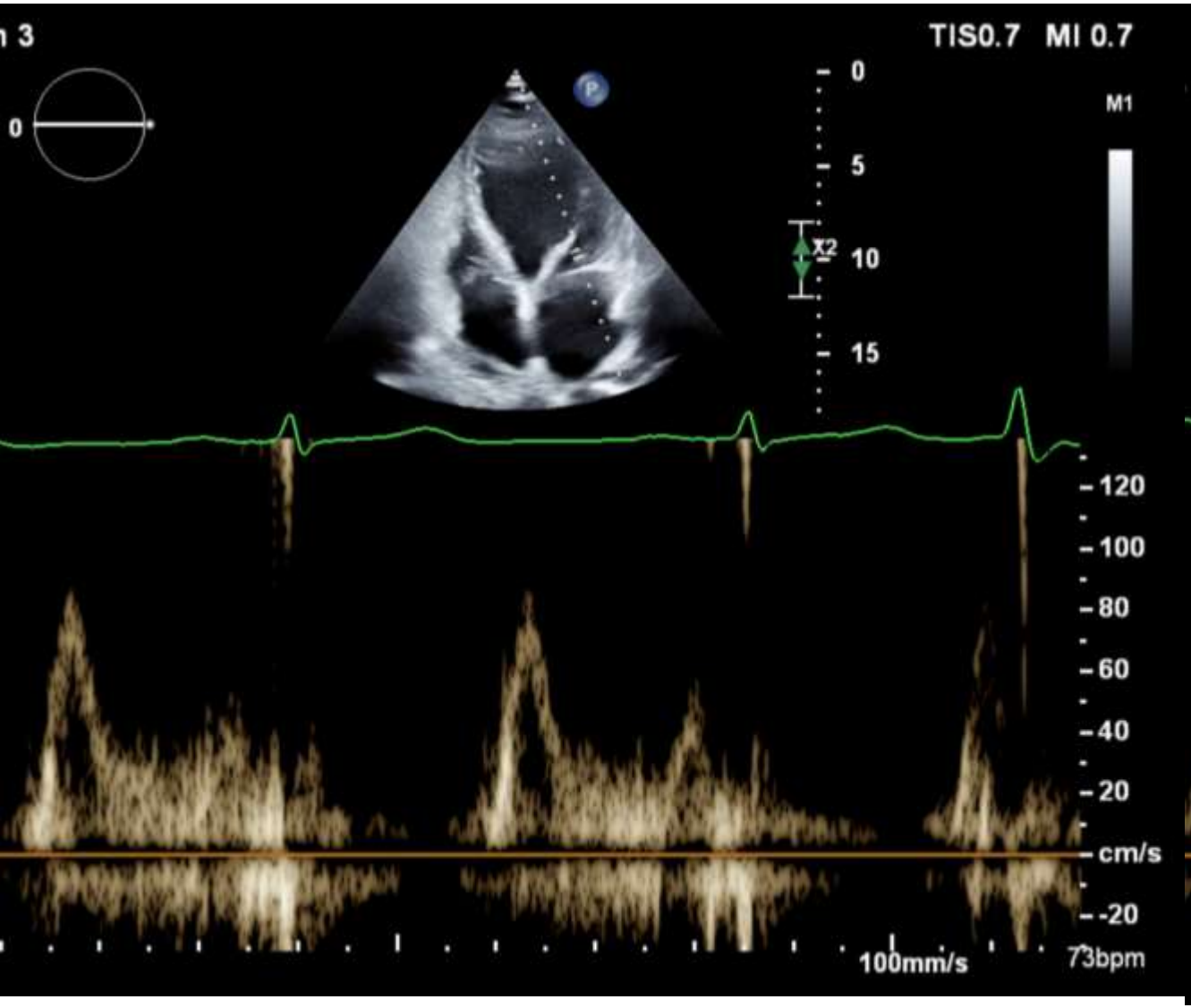

M3
CW
10%
1.8MHz
WF 225Hz
200
100
cm/
-100
-200
75mm/s
82bpm
M3
CW
50%
1.8MHz
WF 225Hz
Vel 479 cm/s
PG 92 mmHg
2.0
m/s
-2.0
-4.0
-6.0
75mm/s
118bpm

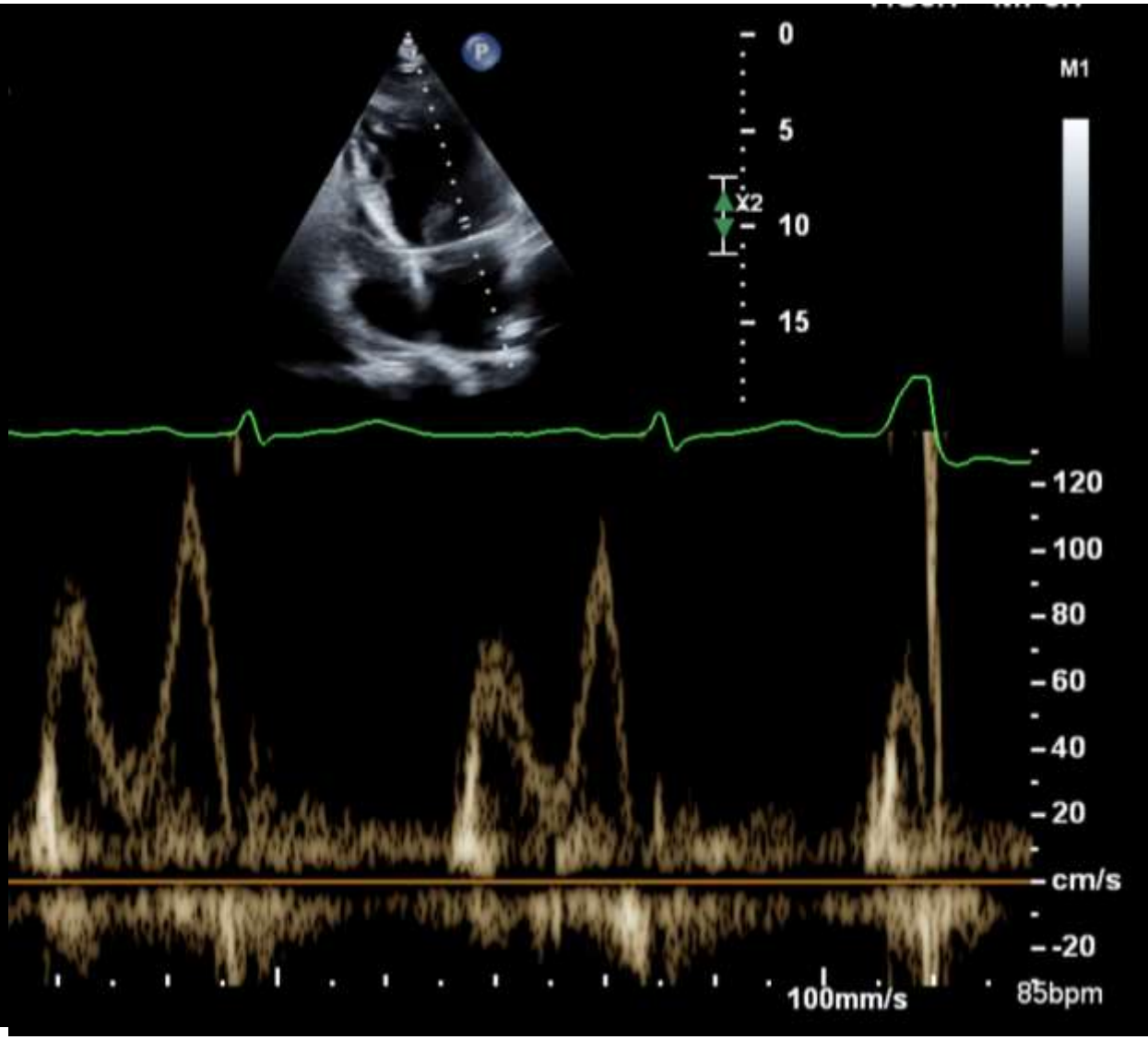
BSH causing SAM




06/11/2014 12:56:45
A1: -60
A2: -120




TIS0.7 MI 0.7
M1
0
5
10
15
X2
120
100
80
60
40
20
cm/s
-20
100mm/s
73bpm


M1
0
5
10
15
X2
120
100
80
60
40
20
cm/s
-20
100mm/s
85bpm

Summary

- Classifying heart failure patients according to a single measure of LV function i.e. EF does not help, at least, 50% of symptomatic patients.

- In contrast, aggregating patients based on raised LA pressures, irrespective of EF, might show evidence for a more consistent response to vasodilators and conventional HF therapy.

- Identifying patterns of cardiac physiology that explain patient's symptoms and clinical signs should guide towards optimum treatment.


Thank you
20 11:10 PM