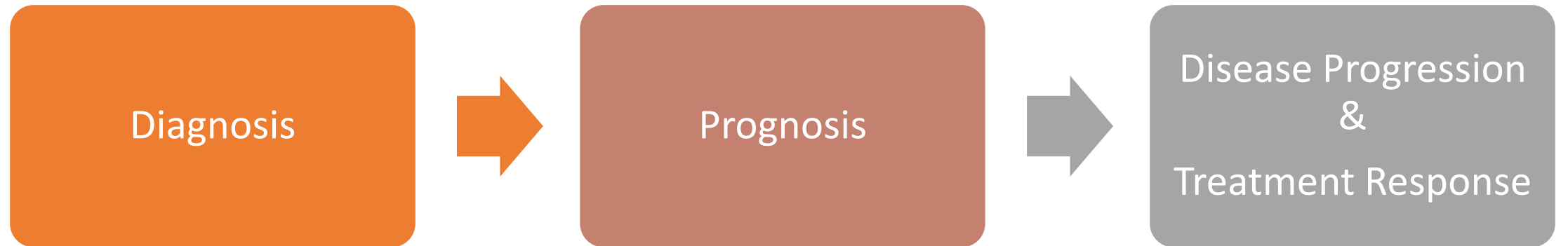


Role of Echocardiography in RCM(Special Focus on Cardiac Amyloidosis)

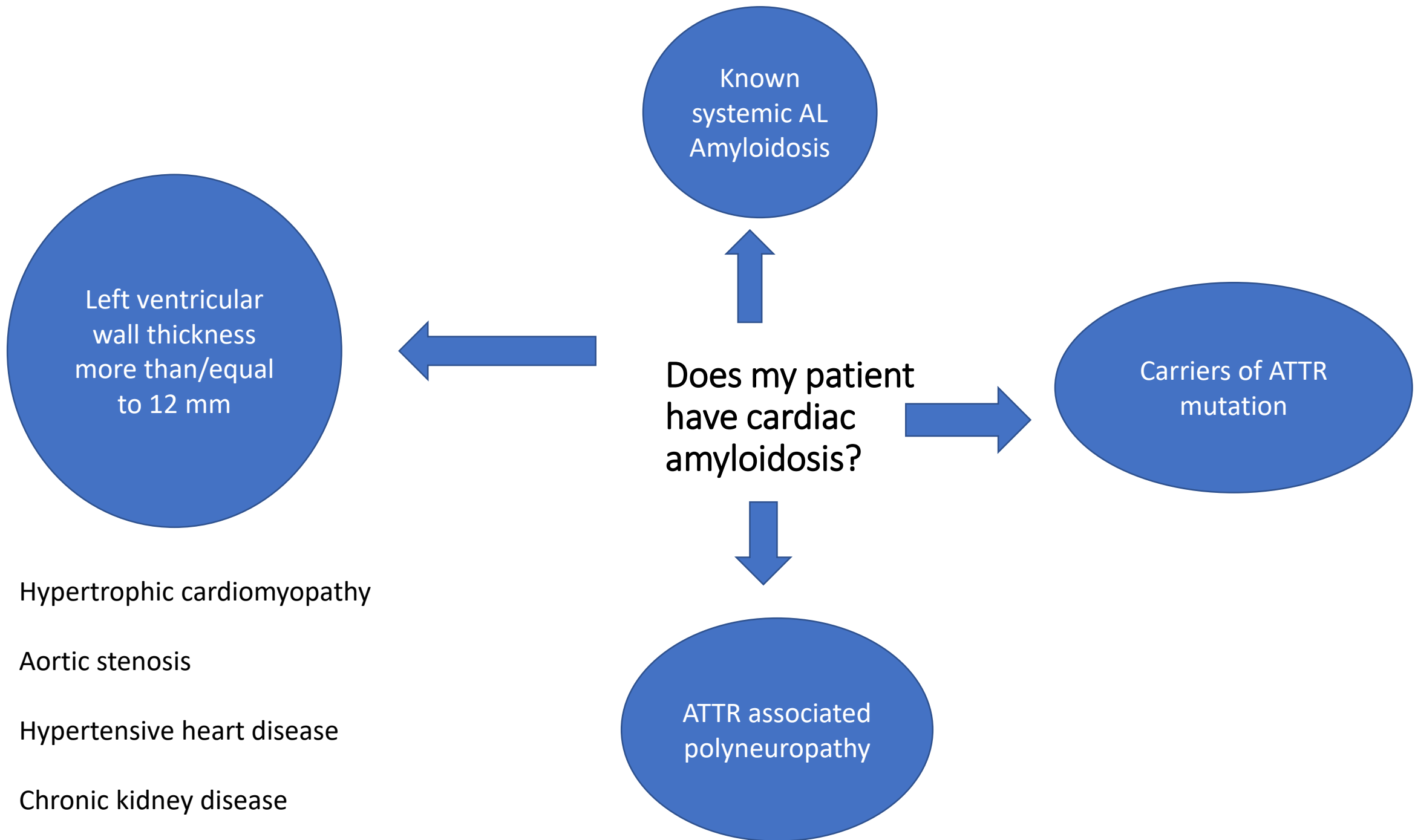
Dr M Sudhakar Rao

MD DM FACC FESC FSCAI

Overview



Role of Echocardiography in Diagnosis of Cardiac Amyloidosis



CENTRAL ILLUSTRATION: Diagnostic Confirmations and Therapeutic Managements in Severe Aortic Stenosis Patients With Cardiac Amyloidosis

Cardiac Amyloidosis

CA Red Flags

- Clinical: ≥ 65 years, Male, carpal tunnel syndrome
- ECG: Low-voltage despite LVH, Pseudo-infarction pattern
- Biomarkers: Disproportionate elevation of troponin and BNP
- TTE: Severe biventricular hypertrophy, Myocardial granular sparkling, Severe LV longitudinal systolic dysfunction with apical sparing
- CMR: Extensive LV LGE and elevated ECV values

Confirm Diagnosis of CA

- Confirm TTR-CA: Grade 2 or 3 cardiac uptake on bone scintigraphy with negative blood or urine monoclonal light chain
- Exclude CA Diagnosis: Grade 0 cardiac uptake on bone scintigraphy with negative blood or urine monoclonal light chain
- Prevalence of TTR-CA in AS: up to 15%

Therapeutic Management of CA

- AL-CA: Chemotherapy
- TTR-CA: TTR stabilizer in patients with HF
- Heart Management: CHAD-STOP

Aortic Stenosis

AS Features in Patients with CA

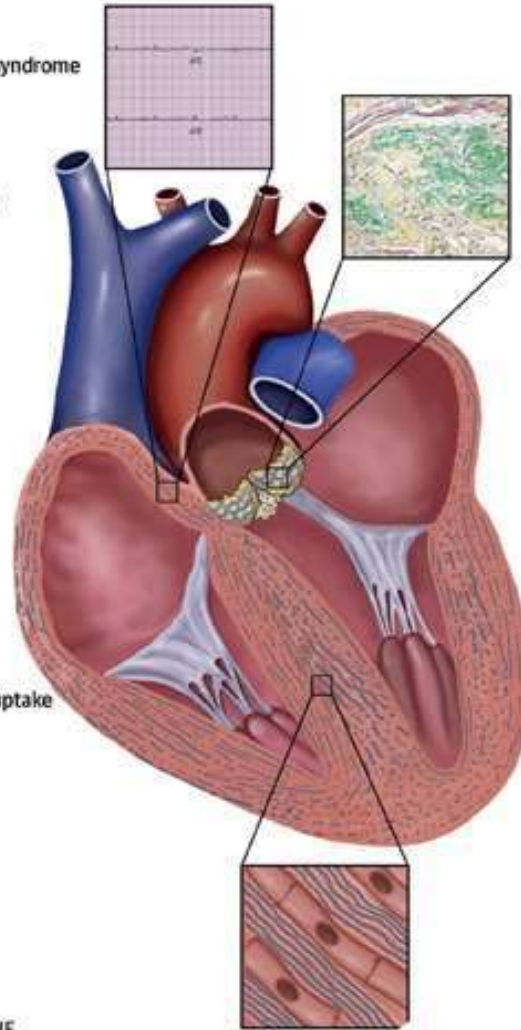
- High prevalence of paradoxical low-flow, low-gradient AS
- Aortic valve amyloid infiltration
- Faster AS progression?

Confirm AS Severity

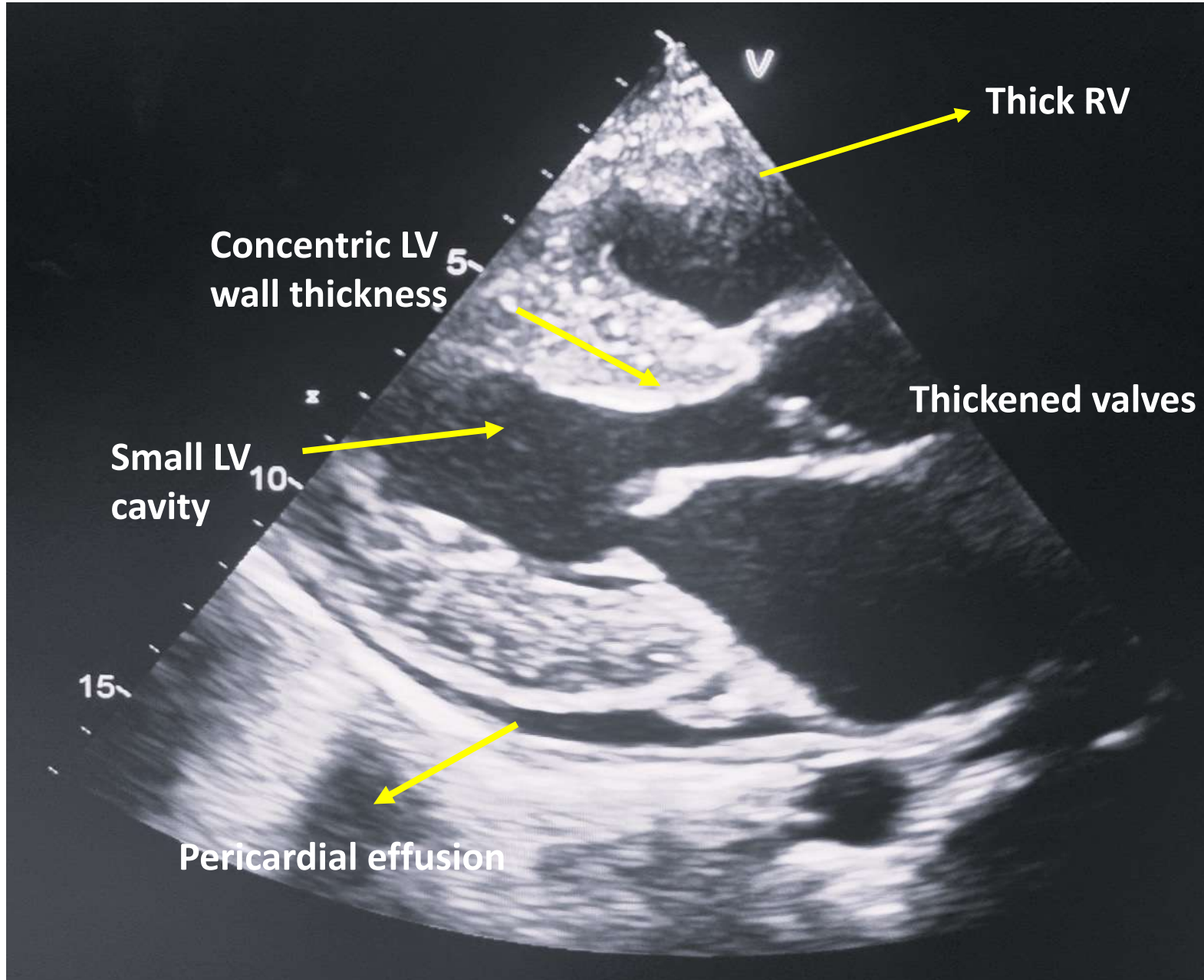
- AV Calcium Score by Non-Contrast CT
 - $\geq 1,200$ AU in women
 - $\geq 2,000$ AU in men

Therapeutic Management of AS

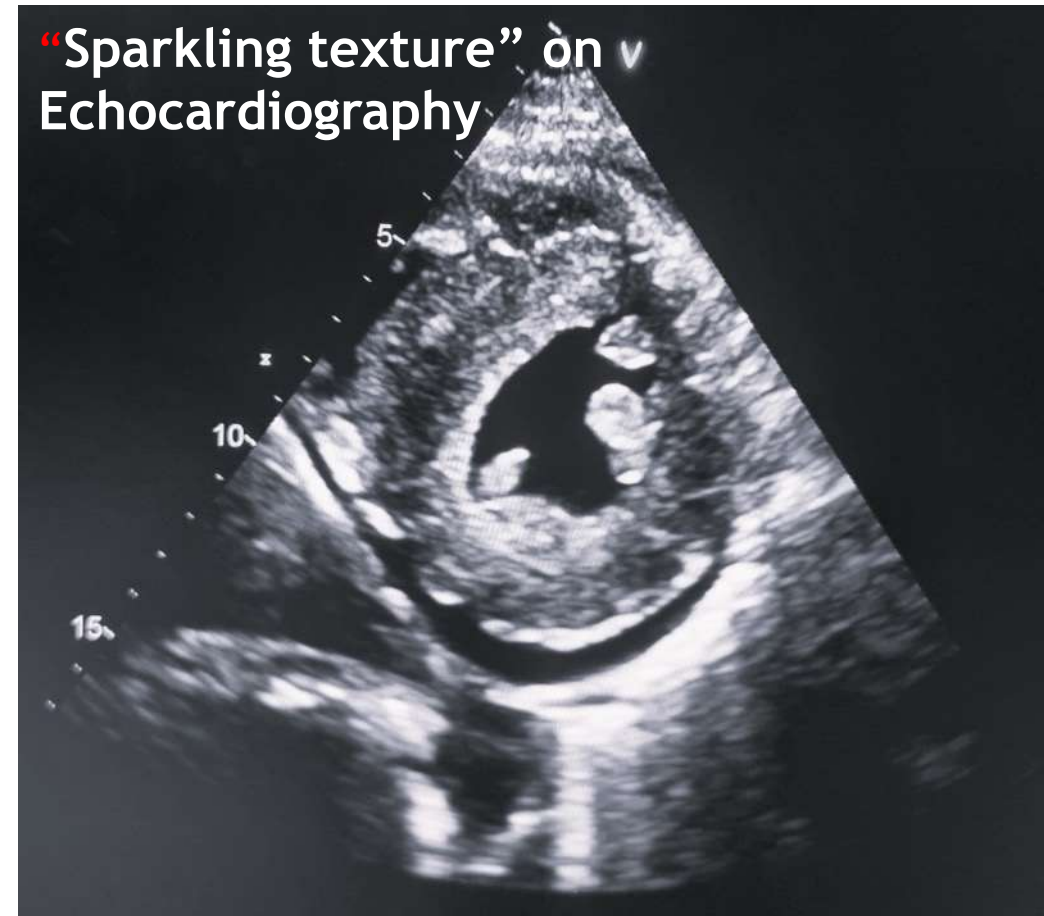
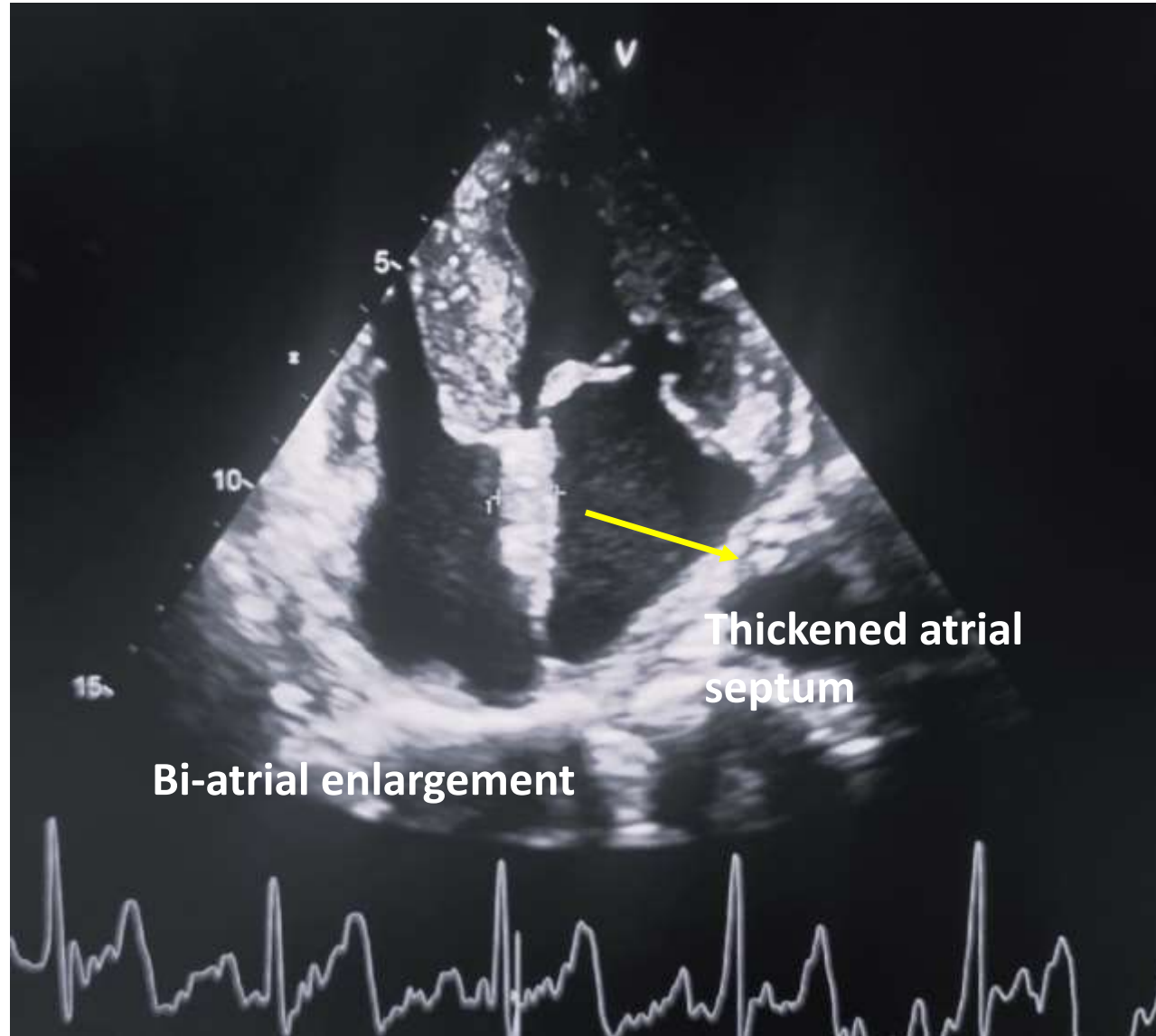
- Evaluation by Heart Team
- TAVR in low-flow, low-gradient severe AS
- TAVR in high-gradient AS with depressed LV systolic function
- SAVR or TAVR according to surgical risk in high-gradient AS with preserved LV systolic function
- Medical treatment alone in patients with high risk of AVR futility



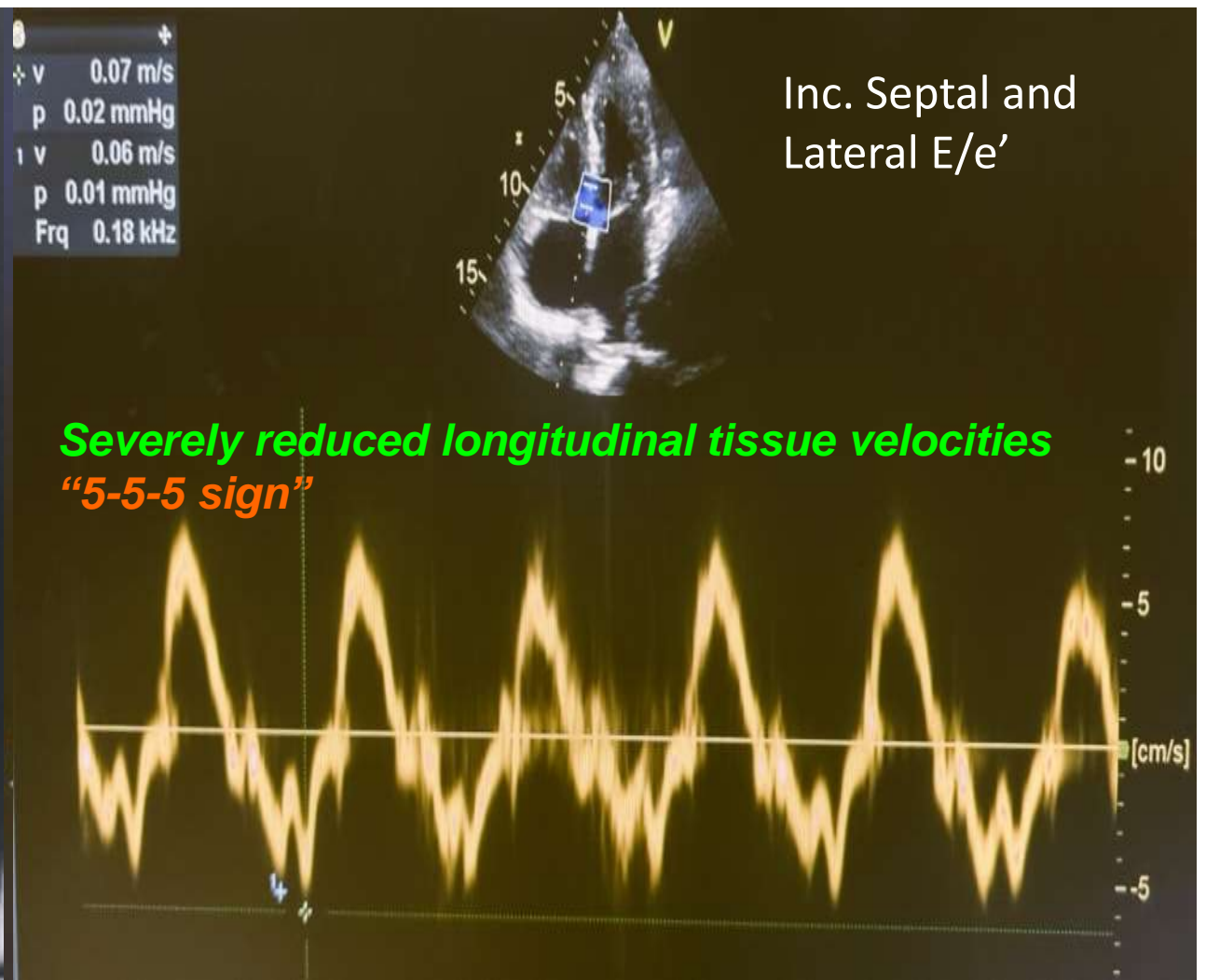
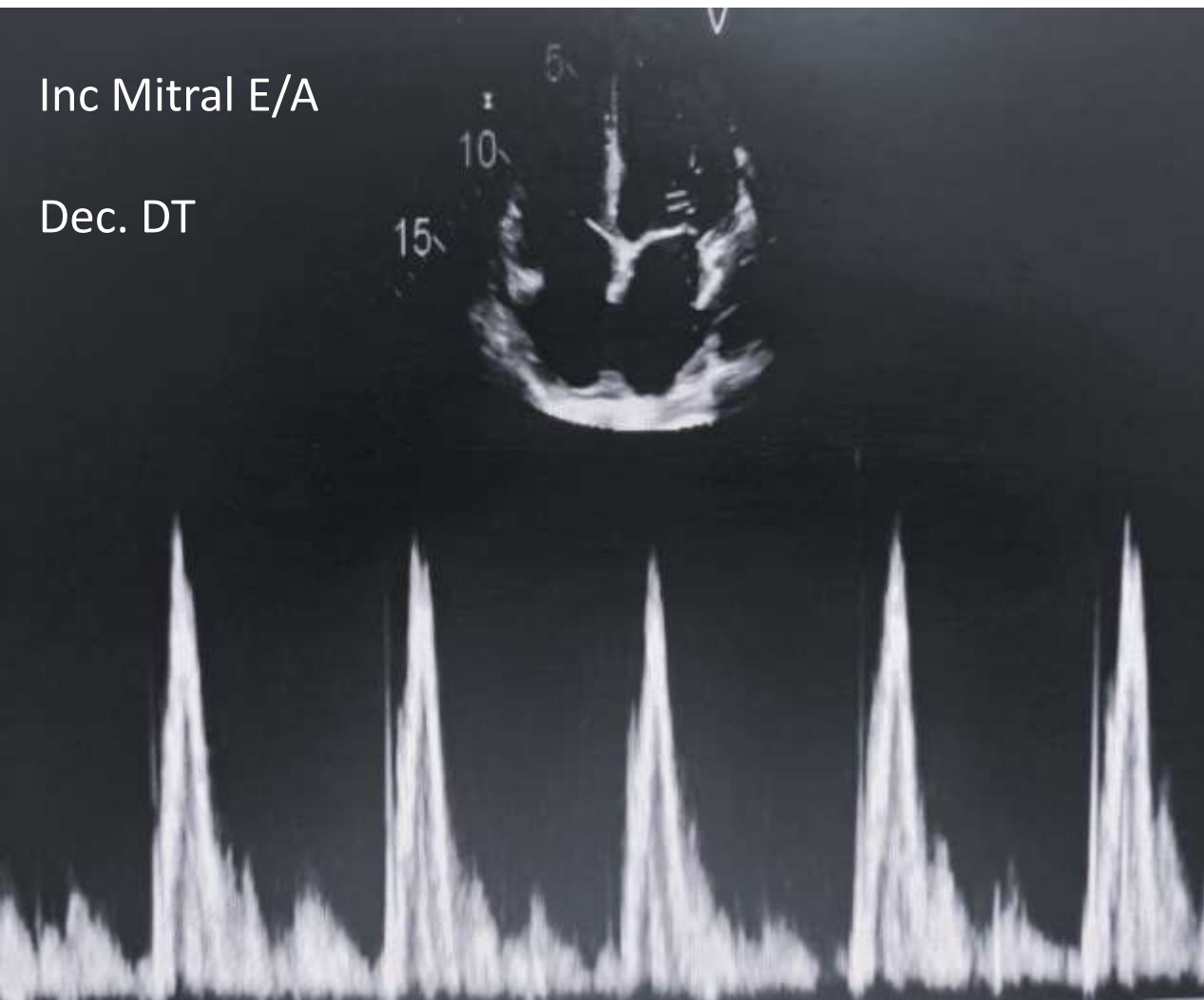
Diagnosis of Advanced Cardiac amyloidosis



Diagnosis of Advanced Cardiac amyloidosis



Diagnosis of Advanced Cardiac amyloidosis



Diagnosing early Cardiac amyloidosis

Easy to diagnose advanced disease(esp. when symptomatic)

Can miss early-stage disease

- Asymptomatic or vague symptoms
- Nonspecific echo findings

Important to recognize and diagnose the disease early so as to improve patient outcomes

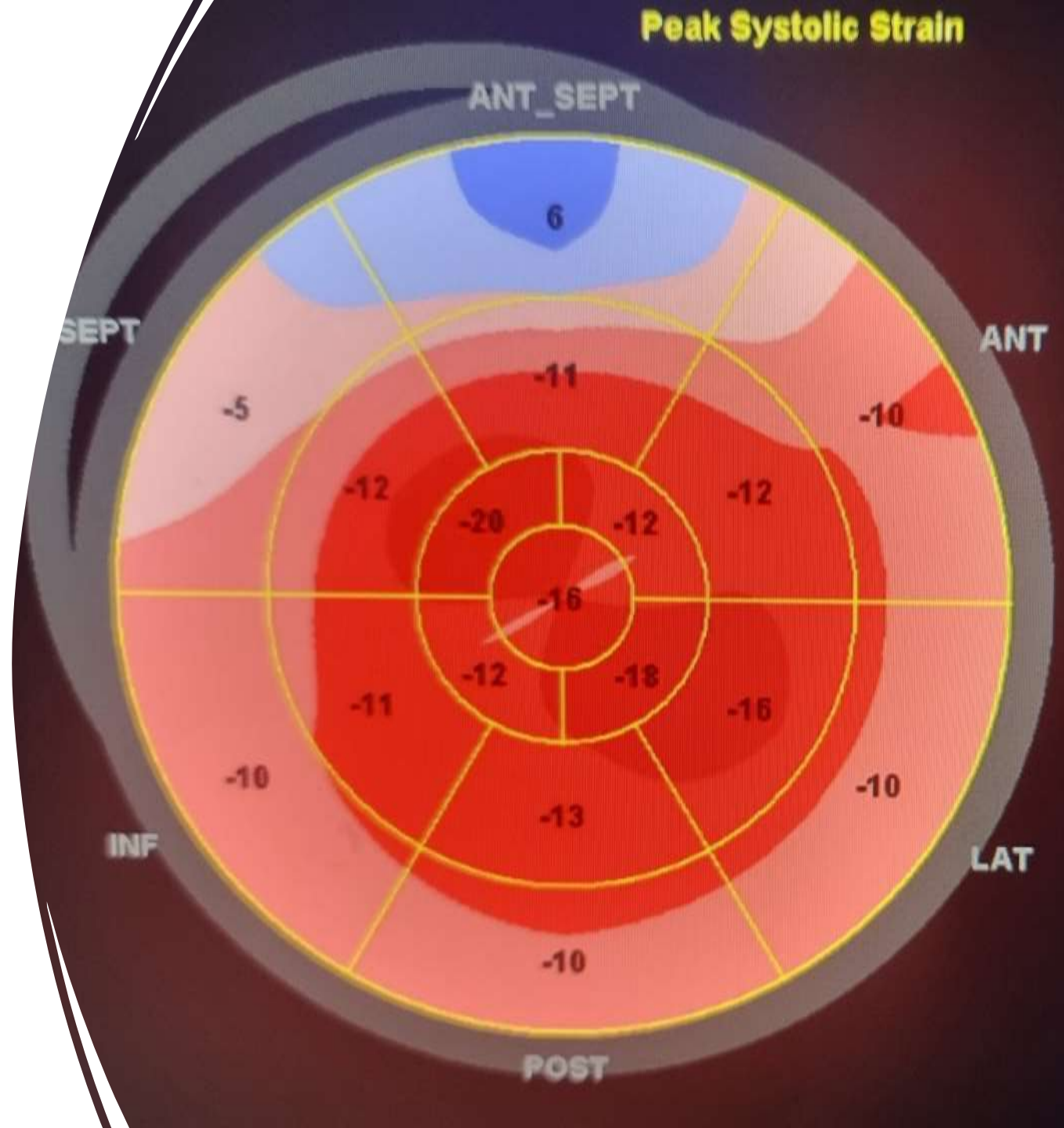
Global Longitudinal Strain(GLS)

GLS in Cardiac Amyloidosis

1. **Left ventricular GLS is reduced**
(even when EF is normal)

2. **Relative apical sparing** seen on
bulls eye strain plot (**cherry on top**)

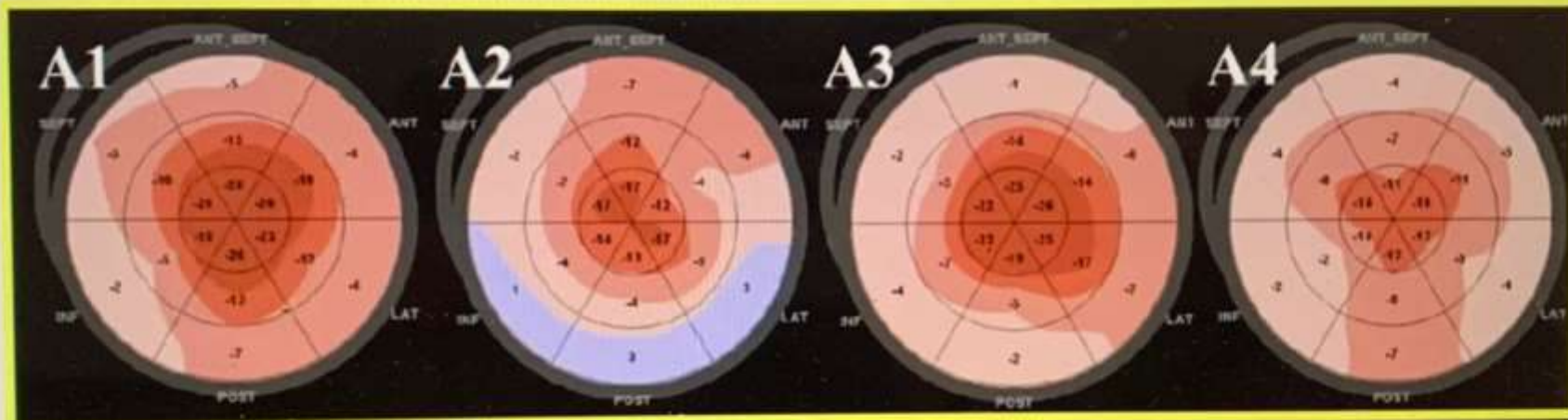
- Reduction in longitudinal strain in basal and mid LV segments
- With relative sparing in apical segments



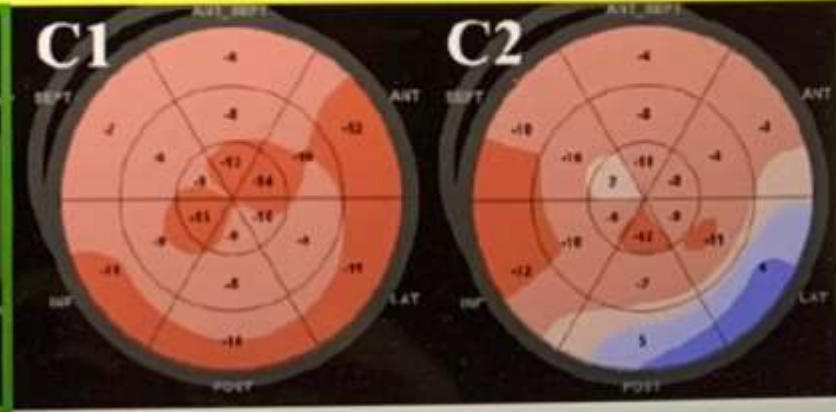
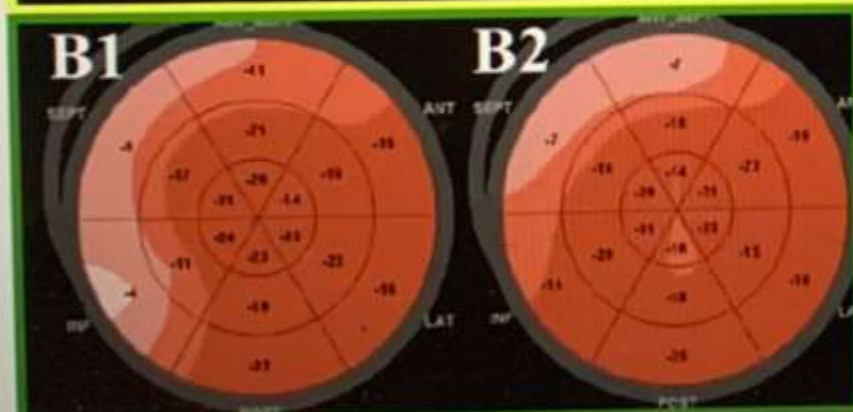
Relative apical sparing of longitudinal strain using two-dimensional speckle-tracking echocardiography is both sensitive and specific for the diagnosis of cardiac amyloidosis

Dermot Phelan, Patrick Collier, Paaladinesh Thavendiranathan, Zoran B Popović, Mazen Hanna, Juan Carlos Plana, Thomas H Marwick, James D Thomas

Cardiac amyloidosis
"Cherry on top"



Septal hypertrophic cardiomyopathy
Marked focal reduction in septal LS



Aortic stenosis
Patchy reduction

Type of left ventricular hypertrophy	Strain pattern	Typical impairment on STE
Athlete's heart	Normal GLS	None
Hypertrophic cardiomyopathy	Reduced GLS	IVS
Arterial hypertension	Normal/Reduced GLS	IVS
Cardiac amyloidosis	Reduced GLS	Apical sparing
Fabry disease	Reduced GLS	Basal posterior-lateral
Aortic stenosis	Reduced GLS and GRS	Basal LV segments/patchy
Aortic regurgitation	Reduced GLS	Diffused
Mitral regurgitation		
Initial disease	Normal/supranormal GLS	None
Advanced disease	Reduced GLS	Basal segments, lateral wall

GLS, global longitudinal strain; *GRS*, global radial strain; *IVS*, interventricular septum; *LV*, left ventricular, *STE*, speckle tracking echocardiography [25–30]

GLS in Cardiac Amyloidosis

3. Relative Regional strain ratio(RRSR)

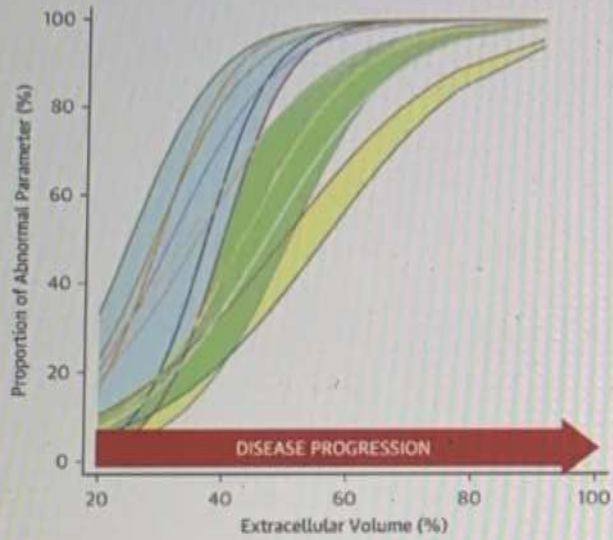
$RRSR = (\text{apical average LS}) / (\text{average basal LS} + \text{average mid LS})$

$RRSR > 1$

Highly sensitive(93 %) and specific(82 %) for diagnosis of cardiac amyloidosis

High RRSR is associated with adverse prognosis(all cause mortality, heart transplantation)

Which parameters are abnormal in early stage disease?



ECV
≥40% to <51%

Low burden:

- E/e' ←
- MCF
- IVSd
- PWTd
- RWT
- LS ←

ECV
>51% to <70%

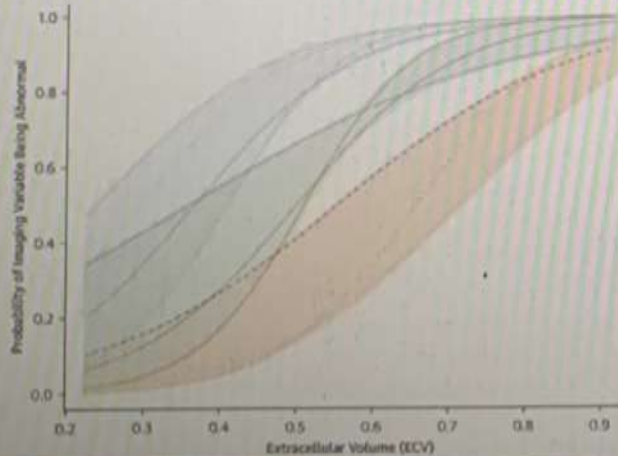
Intermediate burden:

- LAA
- E/A
- SAB
- RALS
- EFSR
- MAPSE

ECV
≥70%

High burden:

- LVEF ←
- TAPSE



Low Burden Variables

- Strain ←
- Average E/e' ←
- MAPSE
- Indexed LV Mass

Intermediate Variables

- Indexed SV
- TAPSE
- MCF

High Burden Variables

- Indexed LA Area
- LVEF ←
- RVEF
- Indexed RA Area

LV wall thickness $\geq 12\text{mm}$

Cardiac amyloidosis unlikely

Perform additional tests

Cardiac amyloidosis

Sensitivity 98% (97%-99%)
Specificity 19% (15%-24%)

Sensitivity 61% (57%-66%)
Specificity 27% (22%-32%)

Sensitivity 46% (42%-50%)
Specificity 98% (95%-99%)

135 patients (15%)
<2 points

498 patients (54%)
2 - 7 points

290 patients (31%)
 ≥ 8 points

n = 923

IWT Score

AUC = 0.87
(95% CI: 0.85-0.90)

PARAMETERS

- RWT > 0.6 3 points
- E/e' > 11 1 point
- TAPSE ≤ 19 mm 2 points
- LS $\geq -13\%$ 1 point
- SAB > 2.9 3 points

IWT = increased wall thickness
LS = longitudinal strain
RWT = relative wall thickness
SAB = systolic apex to base ratio

Known systemic
AL amyloidosis

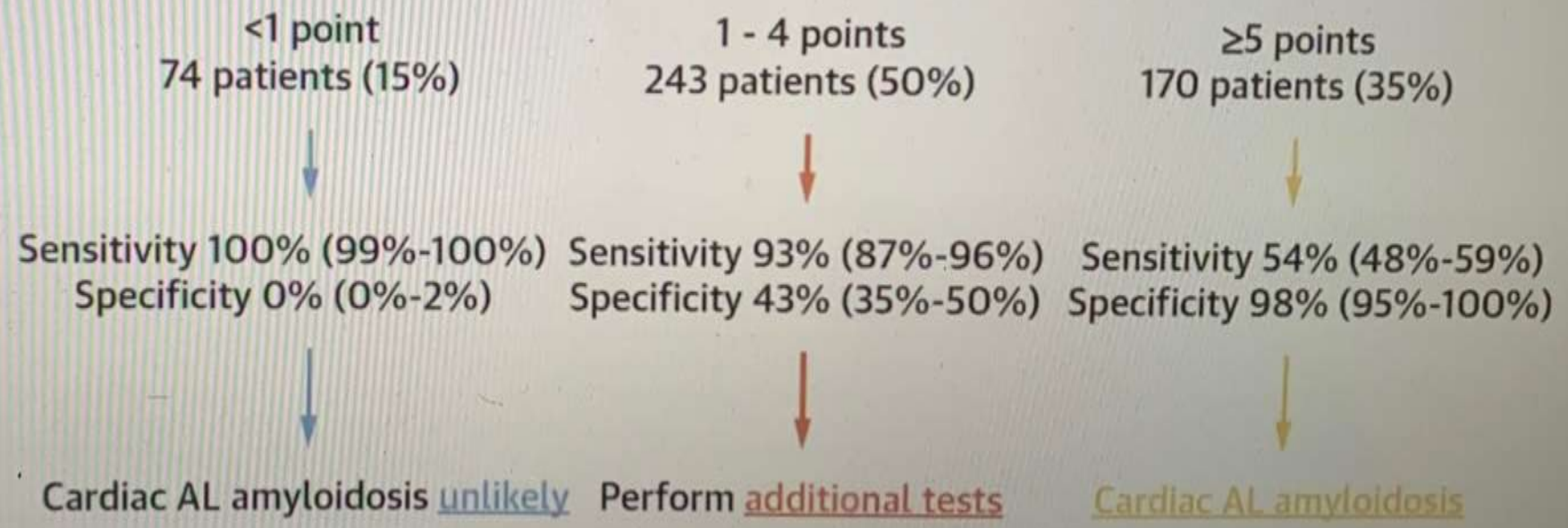
PARAMETERS

RWT >0.52	2 points
E/e' >10	2 points
TAPSE ≤19 mm	1 point
LS ≥ -14%	1 point

AUC = 0.9
(95% CI: 0.87-0.92)

Systemic AL Score

n = 487



IWT = increased wall thickness
LS = longitudinal strain
RWT = relative wall thickness
SAB = systolic apex to base ratio

Wall thickness \leq 16 mm and normal EF $>55\%$

Parameter	Cut off	Sensitivity %	Specificity %	AUC
EFSR	>4.1	89.7	91.7	0.95
RELAPS	>0.87 >1	62.5 73	85 99	0.78
SAB	>2.1 >3.1	74.2 47.5	63.7 86.7	0.67
MCF	<0.24	56.4	96.7	0.8
IVS/PW	<1.38	93	57	0.77
E/E'	>9.6	50	100	0.69

Cuddy SAM, *Circ Cardiovasc Imaging*. 2022;15(11):E014645

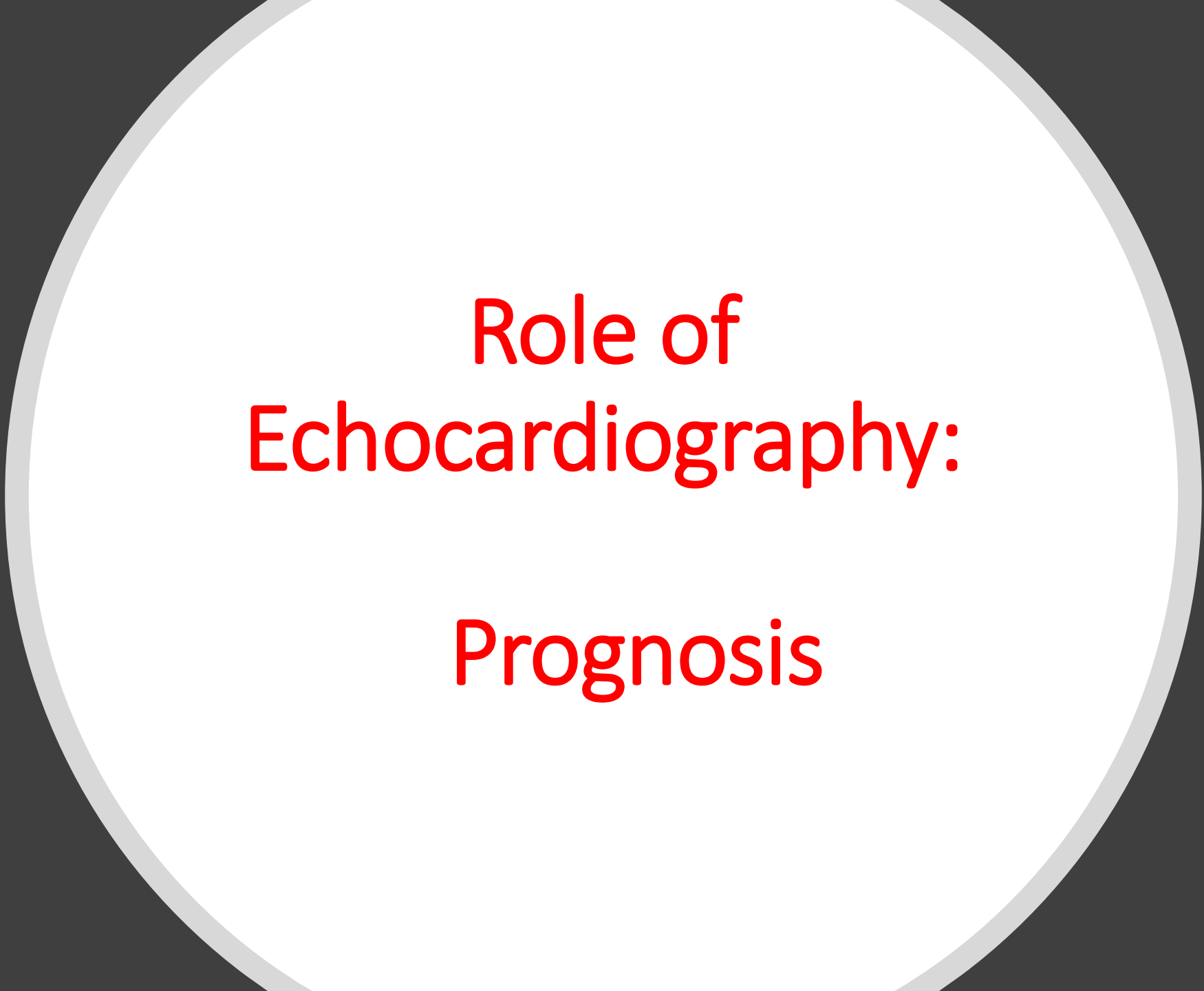
Pagourelas ED, *Circ Cardiovasc Imaging*. 2017;10(3):1-11

- Age
- Male
- Asymmetric Septal hypertrophy
- LV Mass index
- E/E'
- EF/GLS
- SAB
- RELAPS
- IWT score
- MSR

ATTR >> AL

- HF Symptoms compared to LVH
- EF
- GLS
- RVFWS
- E'
- MCF

ATTR << AL



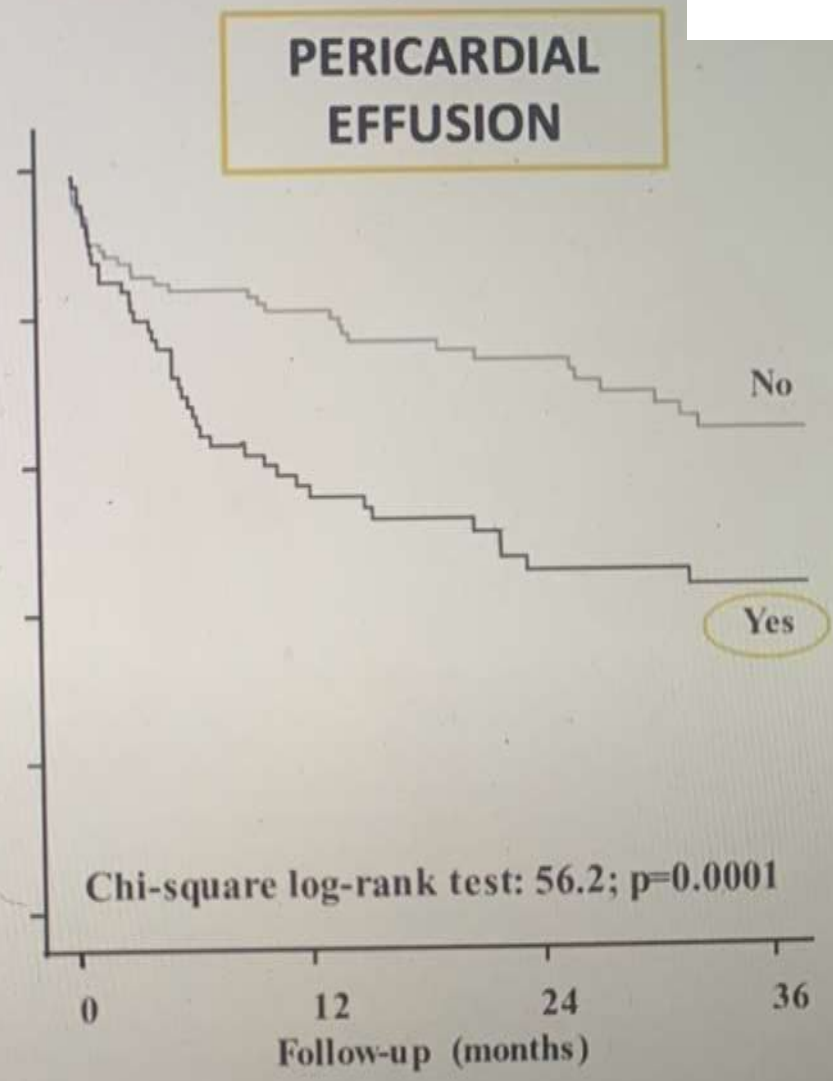
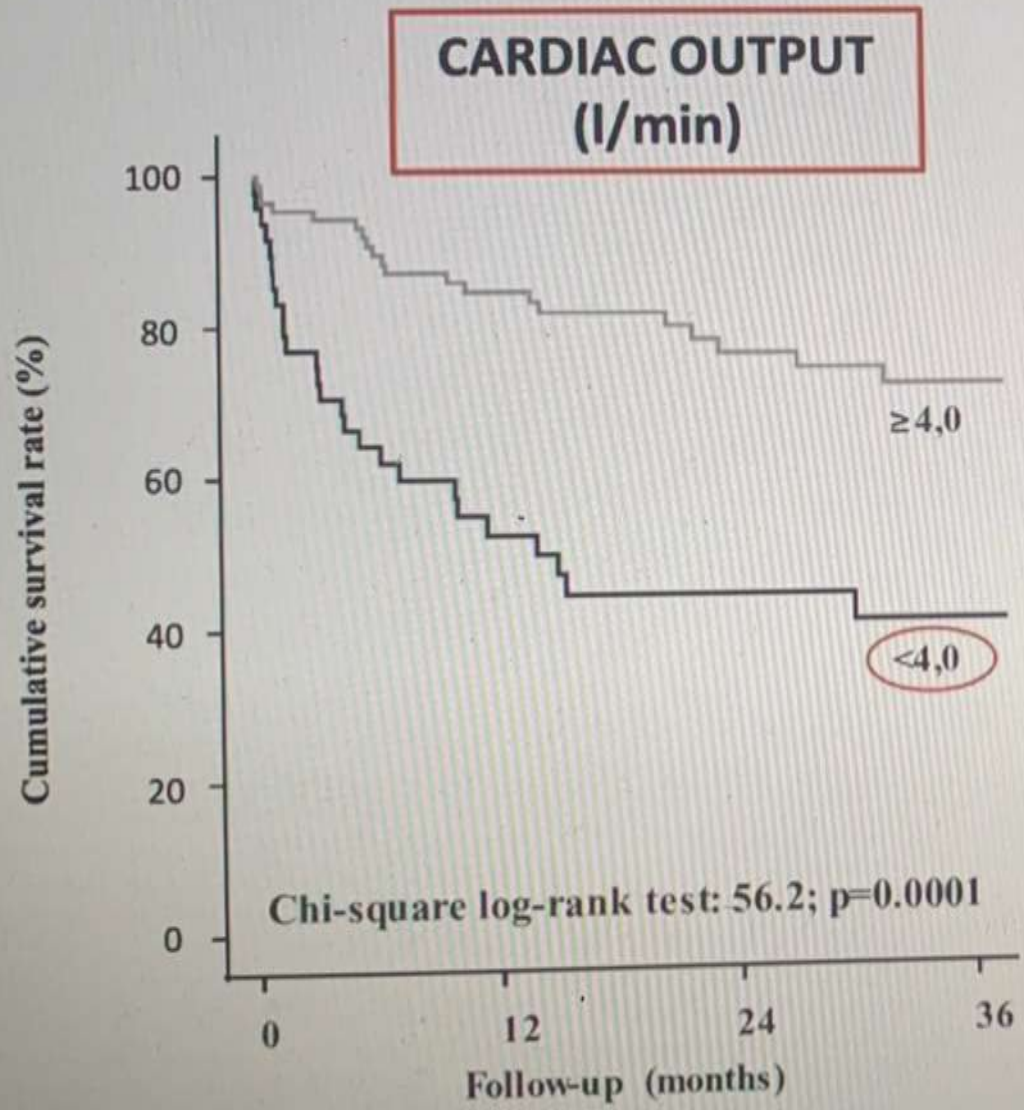
**Role of
Echocardiography:
Prognosis**

Prognosis staging

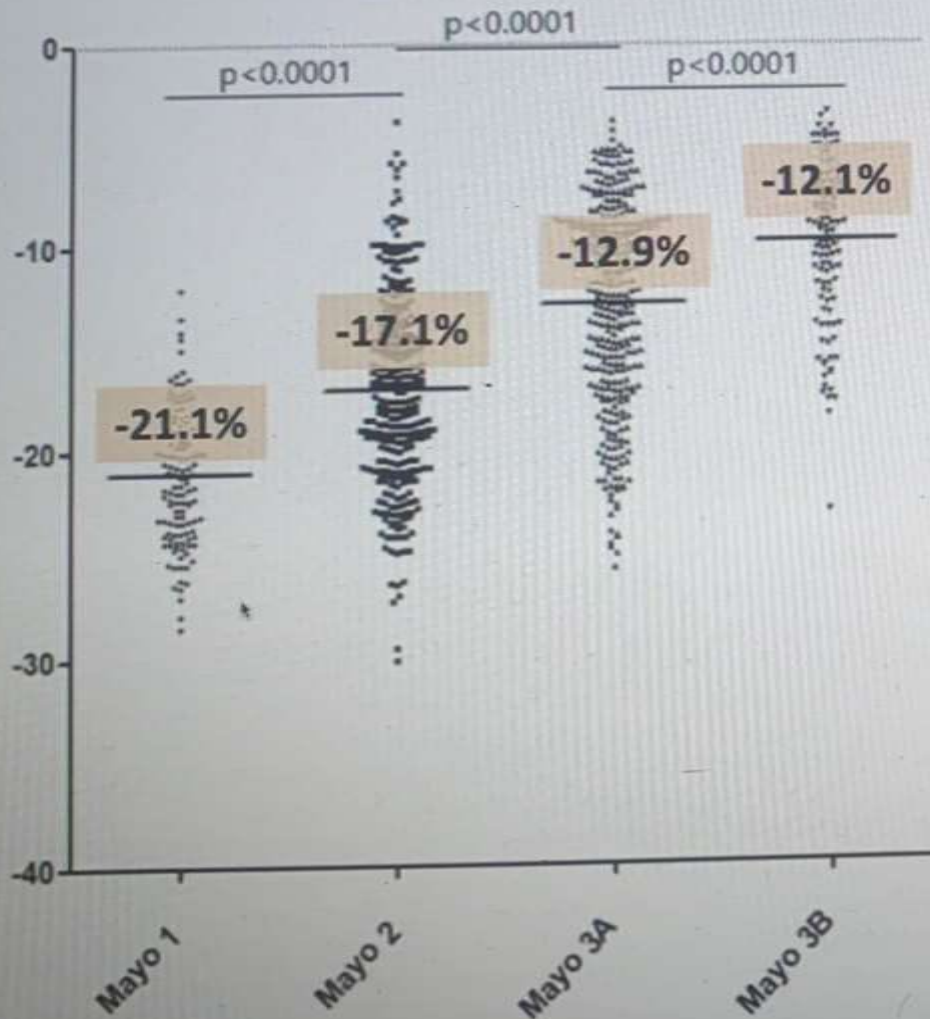
Current staging scores to assess mortality are biomarker-based¹

Kumar et al. ¹⁵ (Mayo)	Lilliness et al. ¹⁶ (BU)	Grogan et al. ¹⁷ (Mayo)	Gillmore et al. ¹⁸ (NAC)	Cheng et al. ¹⁹ (Columbia)
AL	AL	ATTRwt	ATTRv and ATTRwt	ATTRv and ATTRwt
Staging parameters: FLC-diff \geq 18 mg/dL Troponin T \geq 0.025 ng/mL NT-proBNP \geq 1800 pg/mL	Staging parameters: Troponin I $>$ 0.1 ng/mL BNP $>$ 81 pg/mL	Staging parameters: Troponin T $>$ 0.05 ng/mL NT-proBNP $>$ 3000 pg/mL	Staging parameters: eGFR $<$ 45 mL/min/1.73 m ² NT-proBNP $>$ 3000 pg/mL	Scoring parameters: Mayo or NAC score (0–2 points) Daily dose of furosemide or equivalent: 0 mg/kg (0 points), $>$ 0–0.5 mg/kg (1 point), $>$ 0.5–1 mg/kg (2 points), and $>$ 1 mg/kg (3 points) NYHA class I-IV (1 to 4 points)

No staging system that incorporates echocardiographic parameters at present

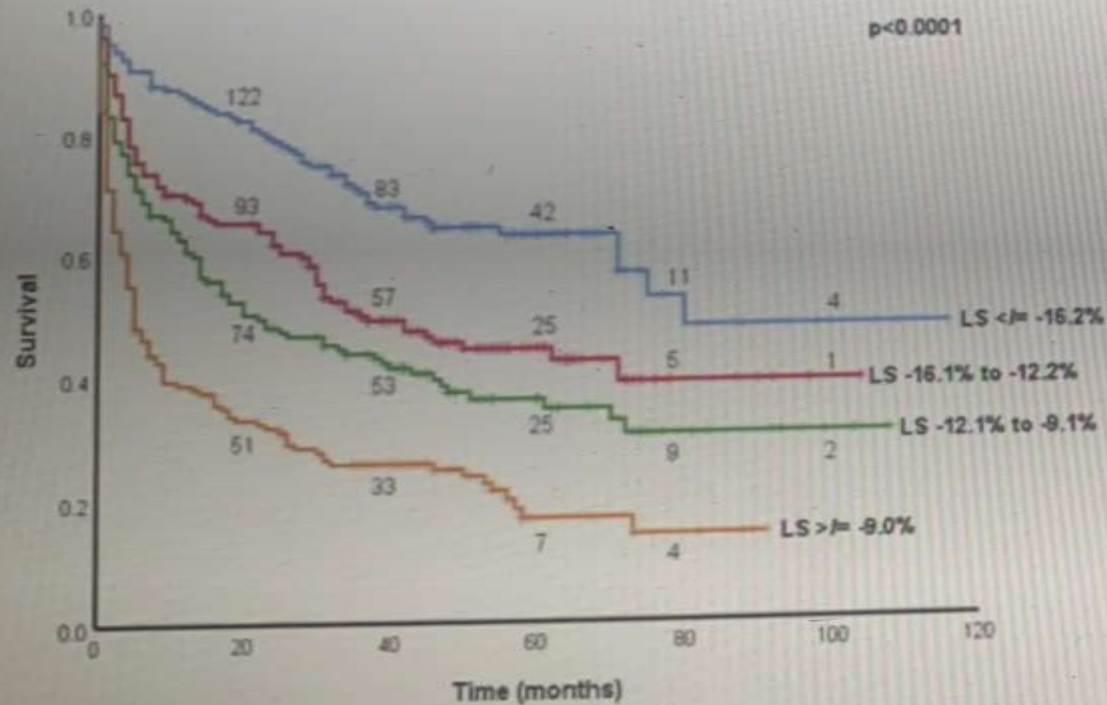


Left ventricular GLS



Left ventricular GLS worsened with advancing stages of cardiac amyloidosis assessed by Mayo staging system

Left ventricular GLS



Baseline GLS	Overall survival (95% CI)
$\leq -16.2\%$	80 months
-16.1% to -12.2%	36 months (20.9 - 51.1)
-12.1% to -9.1%	22 months (9.1 - 34.9)
$\geq -9.0\%$	5 months (3.2 - 6.8)

Right ventricle

TAPSE < 14mm

- Predicts higher events of death, heart transplantation and acute heart failure¹

RV longitudinal strain > -17%

- Predictor of mortality in AL amyloidosis (area under curve 0.79, p=0.00133)²

¹ Bodez et al. Amyloid, 2016; 23(3): 158-167

² Cappelli et al. Eur Heart J Cardiovasc Imaging, 2012; 13: 416-422

Role of Echocardiography:

Disease Progression

&

Treatment Response

Left ventricular GLS

COMPLETE HAEMATOLOGICAL RESPONSE

	CR (<i>n</i> = 82), <i>n</i> (SD)		P-value
	BL	12 m	
LV wall thickness (mm)	14.5 (2.68)	14.5 (2.66)	0.90
LV EF (%)	55.4 (9.12)	55.2 (10.02)	0.82
LV LS%	-13.7 (4.87)	-14.6 (5.21)	0.04

NO RESPONSE

	NR (<i>n</i> = 29), <i>n</i> (SD)		P-value
	BL	12 m	
LV wall thickness (mm)	14.5 (1.85)	15.3 (2.04)	0.0003
LV EF (%)	55.3 (10.63)	50.0 (11.89)	0.007
LV LS%	-14.6 (4.87)	-12.5 (4.62)	0.006

	ECHO	MRI	RADIONUCLIDE IMAGING	BNP
Suspicious	+++	++	?	++
Early diagnosis	?	++	++ (ATTR)	?
Definitive diagnosis	?	?	+++	?
Aetiologic diagnosis	?	?	+++ (ATTR)	X
Functional evaluation	+++	++	+	?
Prognosis	++	+	+	+++
Amyloid burden	X	++	?	X
Treatment response	?	?	?	+++ (AL)

+++ Very useful, recommended
 ++ Useful, to be considered
 + Possibly useful
 ? Role uncertain
 X Not useful



CardioBlogger

THANK YOU

