

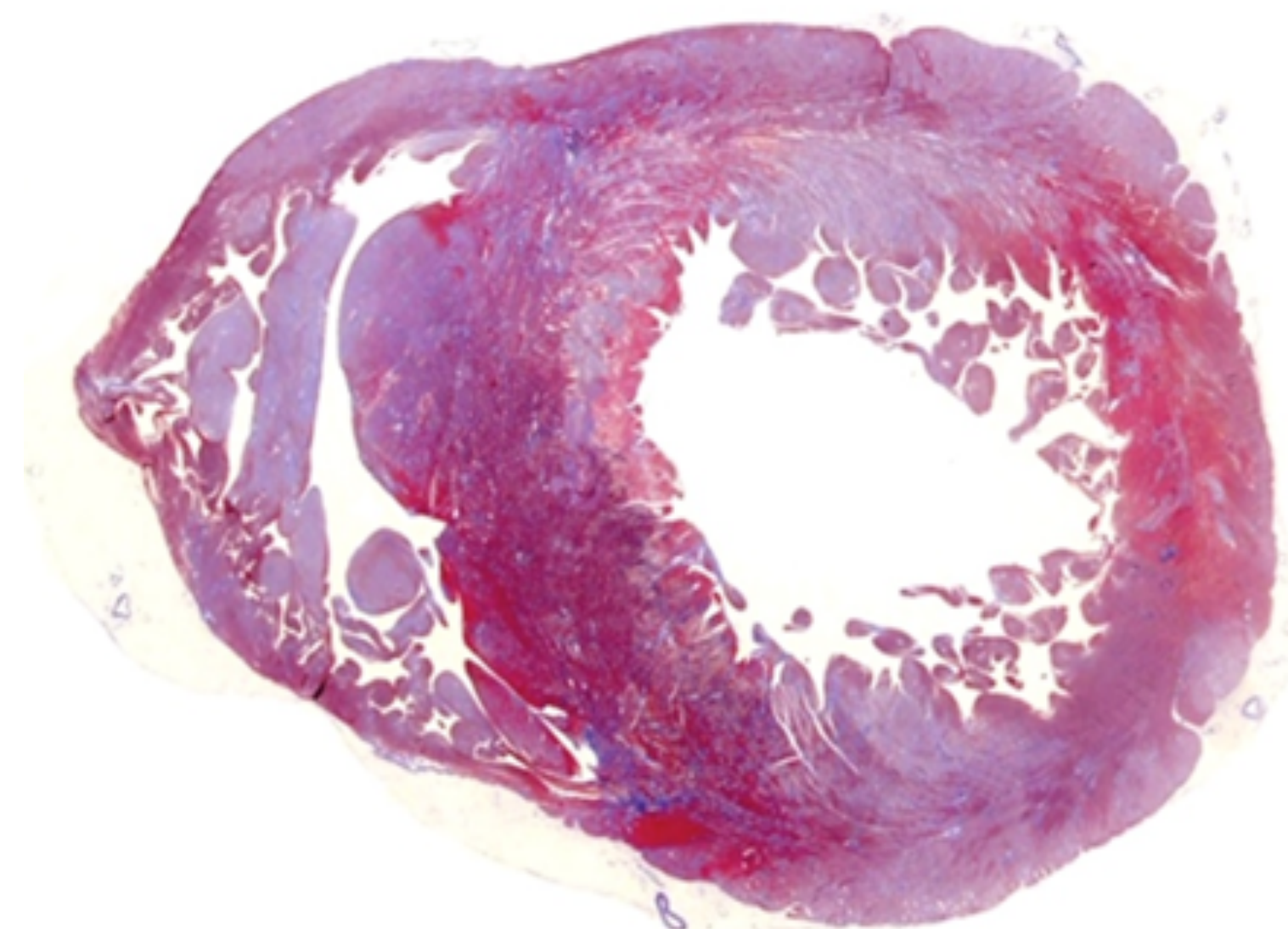


GIUSEPPE
PALMIERO



FACULTY

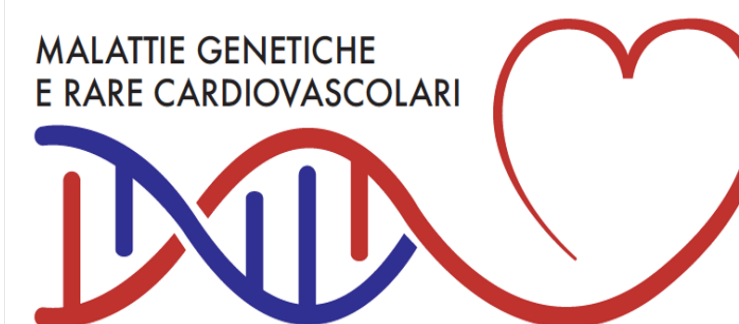
L'imaging ecocardiografico nell'Amiloidosi ATTR



V: Università
degli Studi
della Campania
Luigi Vanvitelli

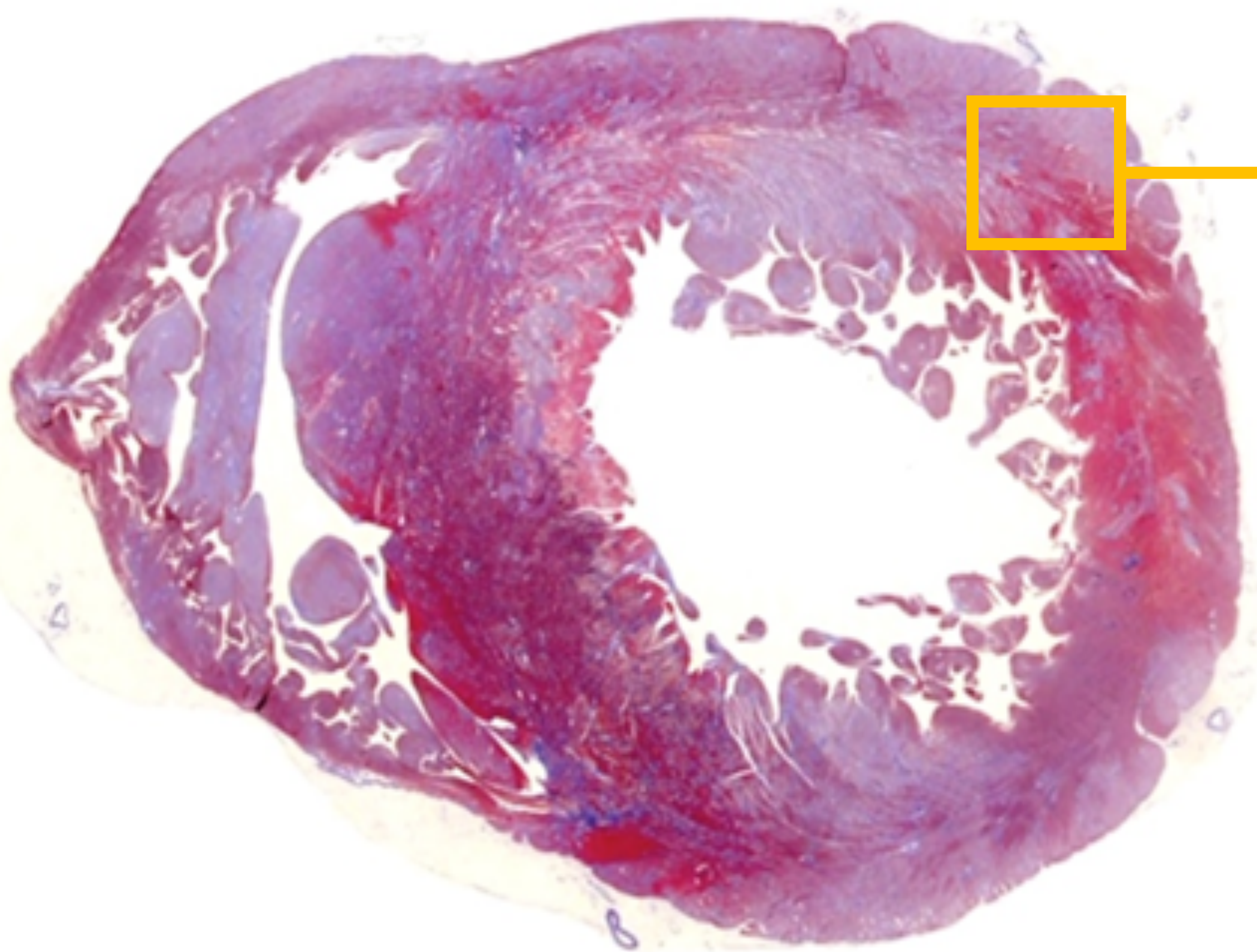
 **European
Reference
Network**
for rare or low prevalence
complex diseases
• Network
Heart Diseases
(ERN GUARD-HEART)
• Member
AORN Colli — Italia

MALATTIE GENETICHE
E RARE CARDIOVASCOLARI

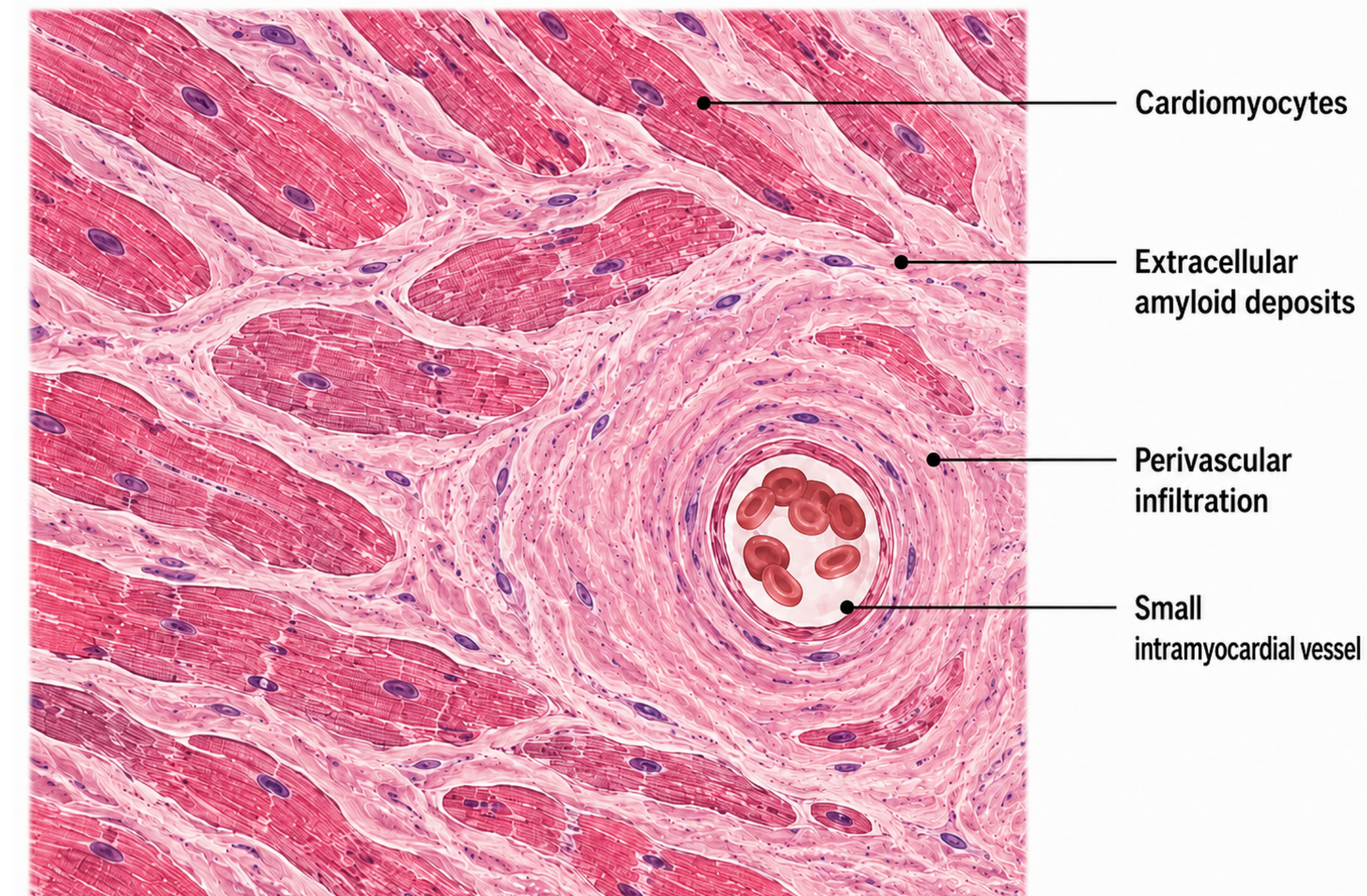


OSPEDALI DEI COLLI
MONALDI - COTUGNO - C.T.O.
"AZIENDA OSPEDALIERA
SPECIALISTICA DEI COLLI"
Monaldi - Cotugno - C.T.O.





CARDIAC AMYLOIDOSIS – HISTOLOGICAL APPEARANCE
Interstitial and perivascular amyloid infiltration



widespread but heterogeneous

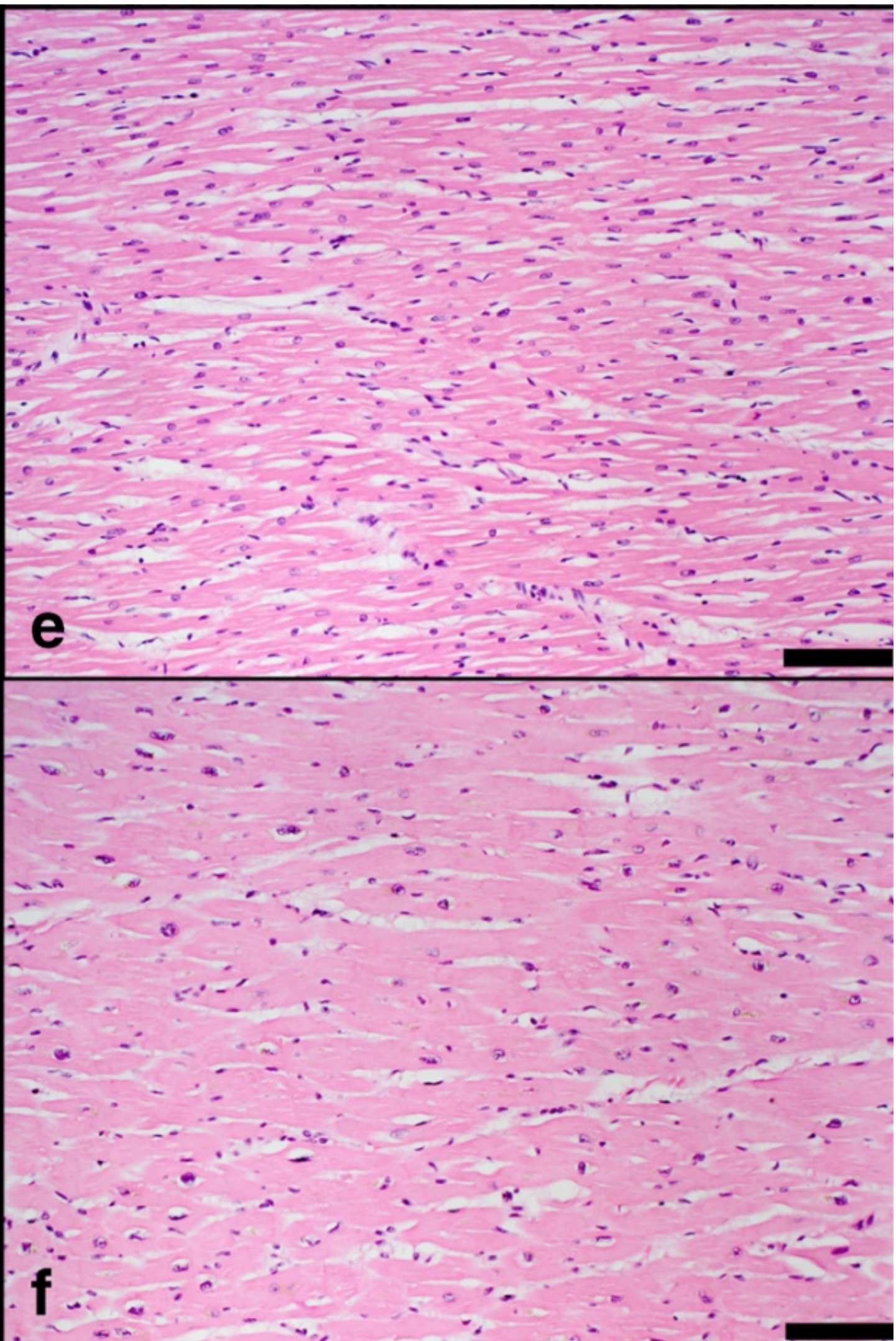
Cardiac hypertrophy at autopsy

Cristina Basso¹ • Katarzyna Michaud² • Giulia d'Amati³ • Jytte Banner⁴ • Joaquin Lucena⁵ • Kristopher Cunningham⁶ • Ornella Leone⁷ • Aryan Vink⁸ • Allard C. van der Wal⁹ • Mary N. Sheppard¹⁰ • on behalf of the Association for European Cardiovascular Pathology

Normal heart



Hypertrophied heart



INCREASED VENTRICULAR WALL THICKNESS

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graph TD; A[INCREASED VENTRICULAR WALL THICKNESS] --> B[MYOCARDIAL HYPERTROPHY]; A --> C[MYOCARDIAL PSEUDO-HYPERTROPHY]; B --> D[Physiological stimuli]; B --> E[Pathological stimuli]; D --> F["Sport<br/>Pregnancy"]; E --> G["Pressure and/or<br/>Volume overload"]; C --> H[Extracellular infiltration]; C --> I[Intracellular accumulation]; H --> J["Infiltrative<br/>cardiomyopathies"]; I --> K["Storage<br/>diseases"];
```

*MYOCARDIAL
HYPERTROPHY*

*MYOCARDIAL
PSEUDO-HYPERTROPHY*

Physiological
stimuli

Pathological
stimuli

Extracellular
infiltration

Intracellular
accumulation

Sport
Pregnancy

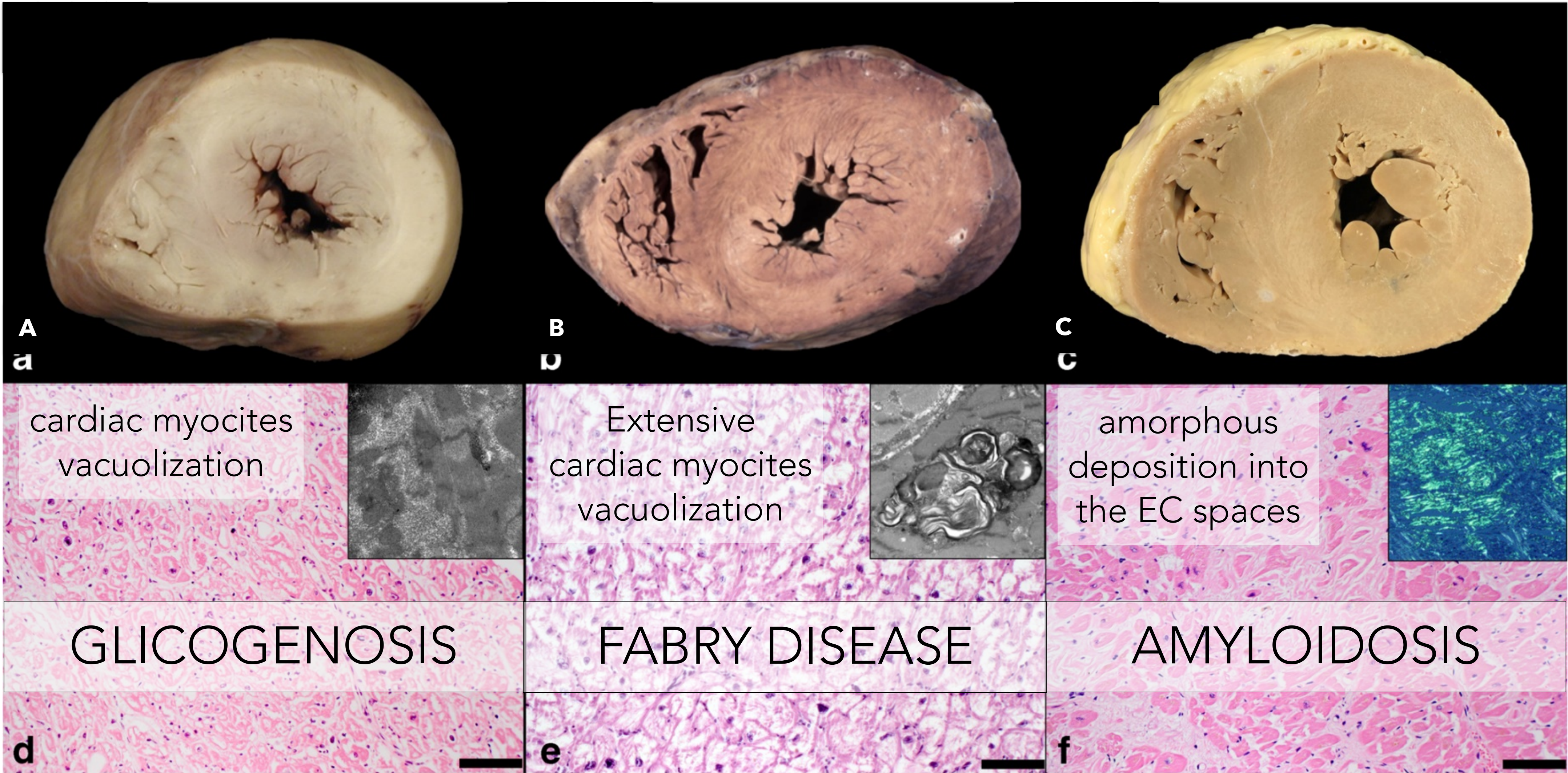
Pressure and/or
Volume overload

Infiltrative
cardiomyopathies

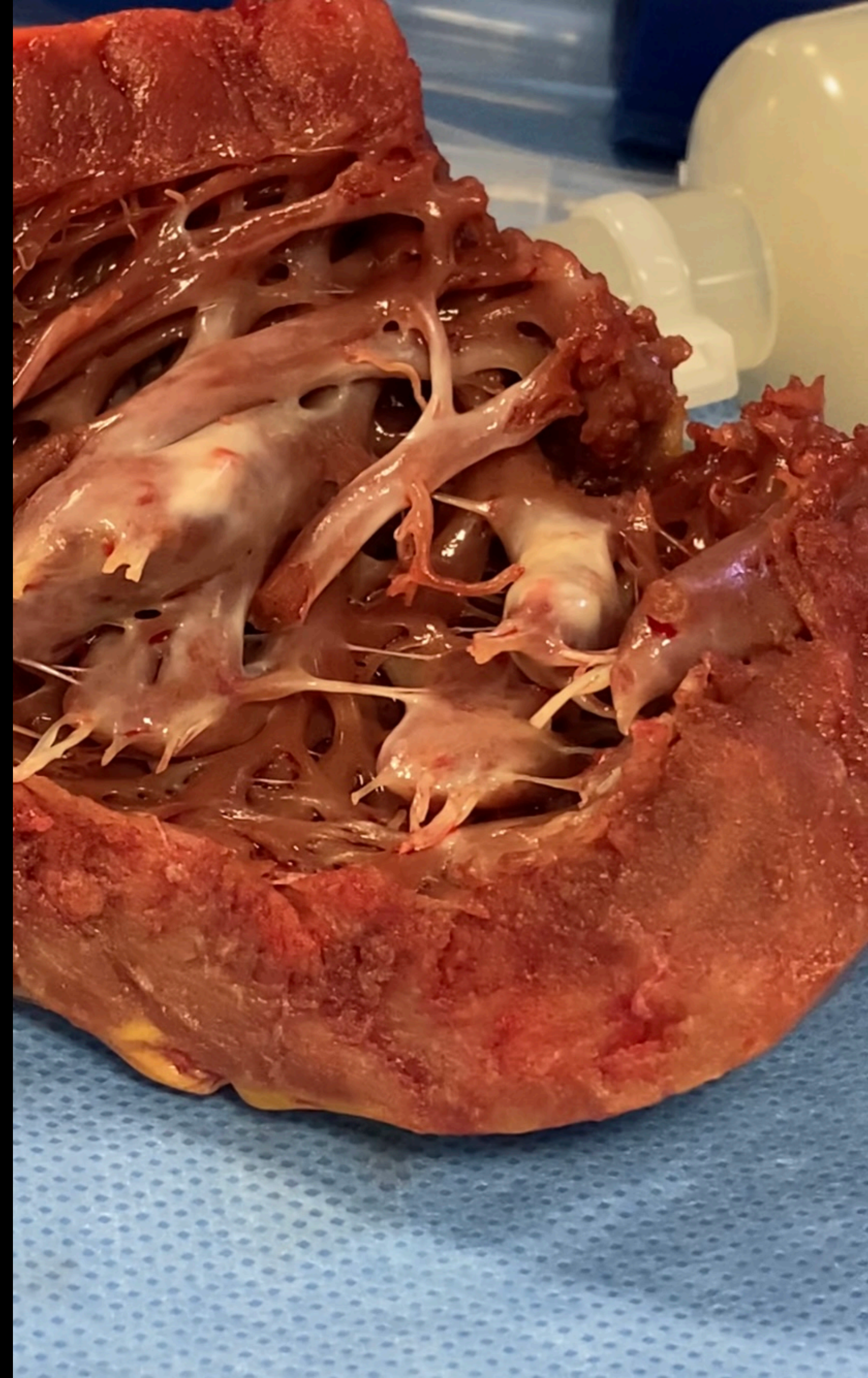
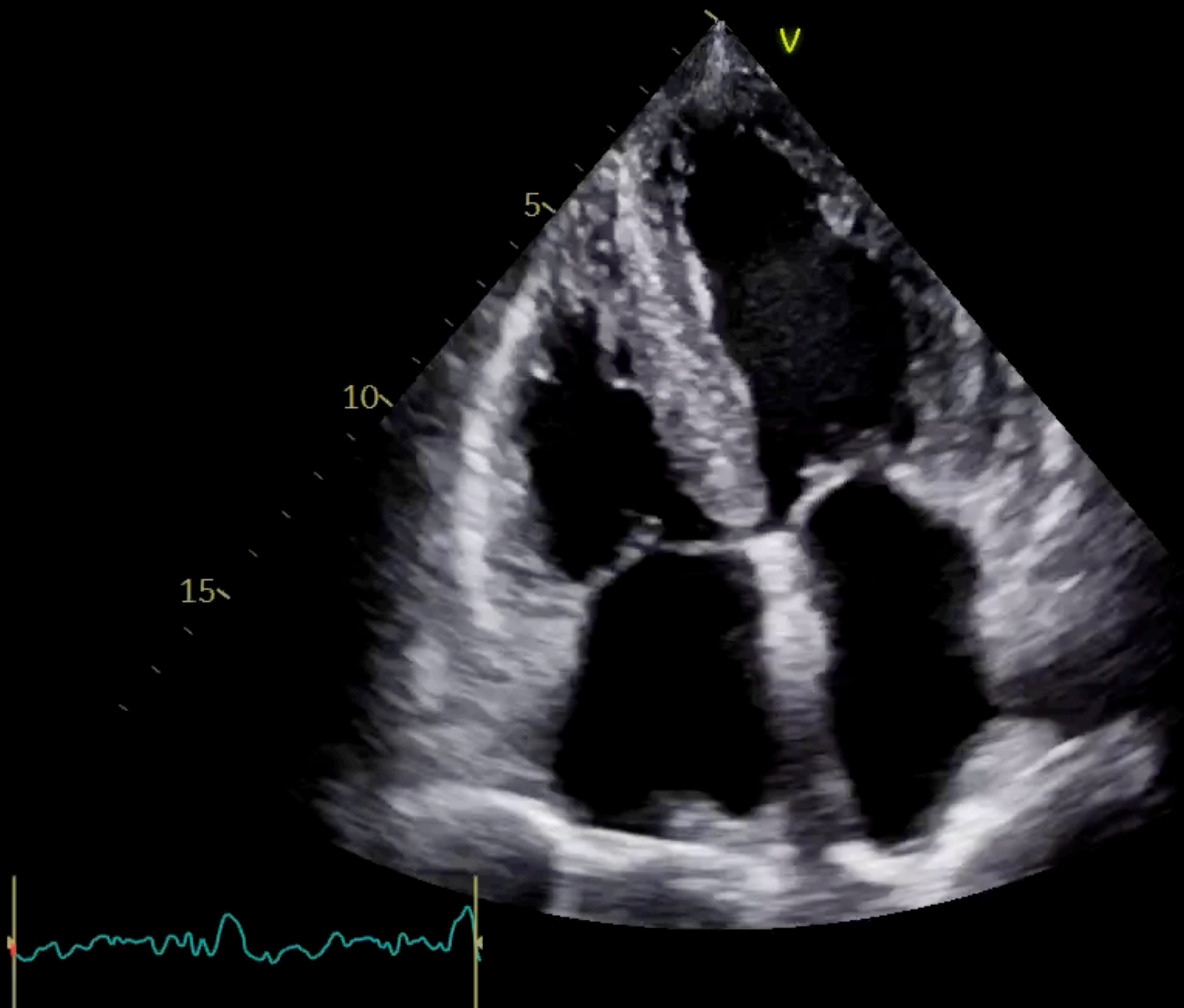
Storage
diseases

Cardiac hypertrophy at autopsy

Cristina Basso¹ • Katarzyna Michaud² • Giulia d'Amati³ • Jytte Banner⁴ • Joaquin Lucena⁵ • Kristopher Cunningham⁶ • Ornella Leone⁷ • Aryan Vink⁸ • Allard C. van der Wal⁹ • Mary N. Sheppard¹⁰ • on behalf of the Association for European Cardiovascular Pathology



03/05/2022 14:21:18
ACE

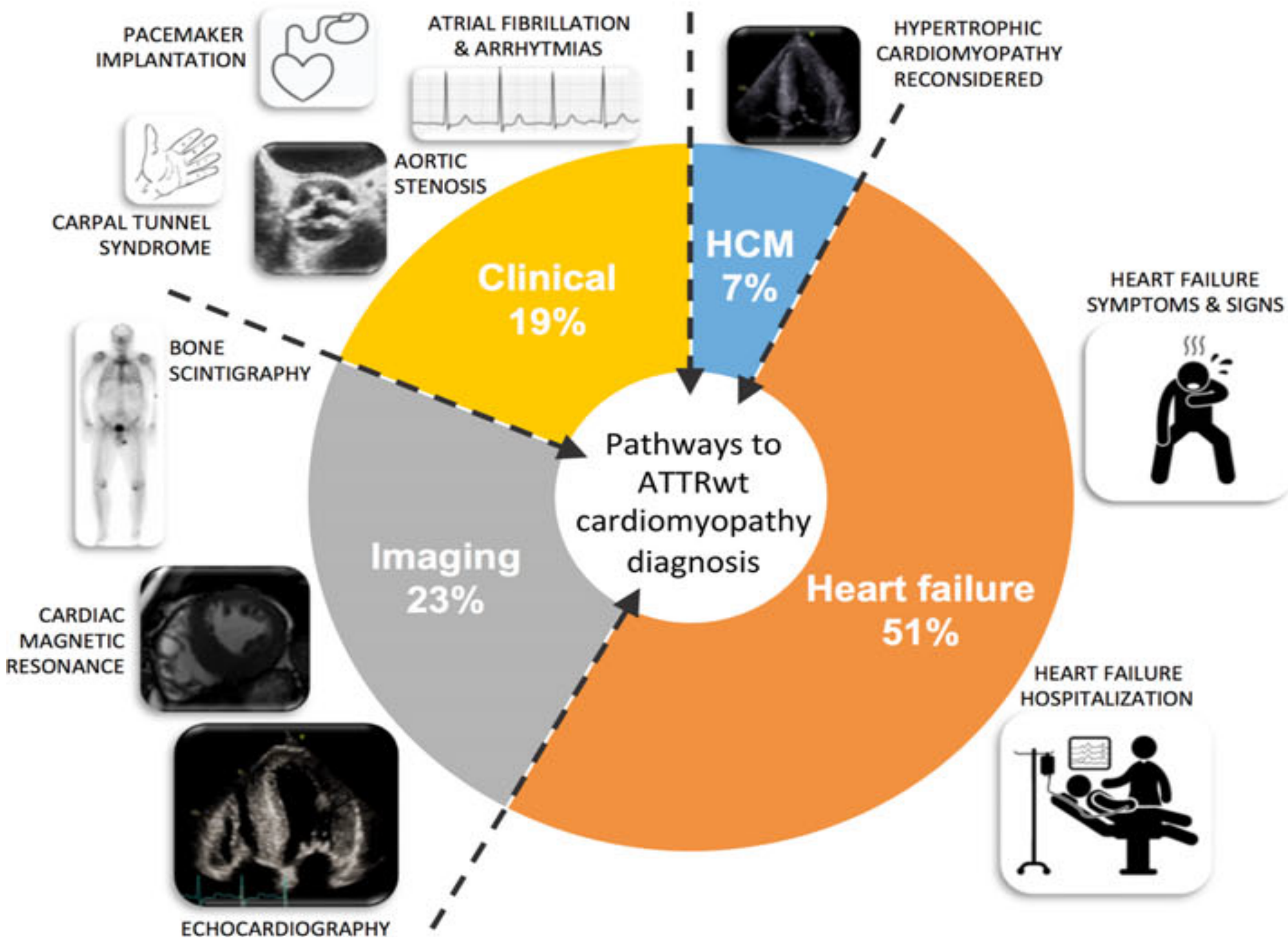


Diagnostic pathways to wild-type transthyretin amyloid cardiomyopathy: a multicentre network study

Giacomo Tini^{1,2}, Paolo Milani^{3,4}, Mattia Zampieri⁵, Angelo G. Caponetti^{6,7}, Francesca Fabris^{3,4}, Andrea Foli⁴, Alessia Argirò⁵, Carlotta Mazzoni⁵, Christian Gagliardi^{6,8}, Simone Longhi^{6,8}, Giulia Satrio^{6,7}, Giuseppe Vergaro^{9,10}, Alberto Aimo^{9,10}, Domitilla Russo², Guerino G. Varrà¹¹, Matteo Serenelli¹², Gioele Fabbri¹², Laura De Micheli¹³, Giuseppe Palmiero¹⁴, Giuseppe Ciliberti^{15,16}

1,281 patients (mean age 78 years, 89% males) from 17 Italian centers between Jan 2017 and Dec 2021

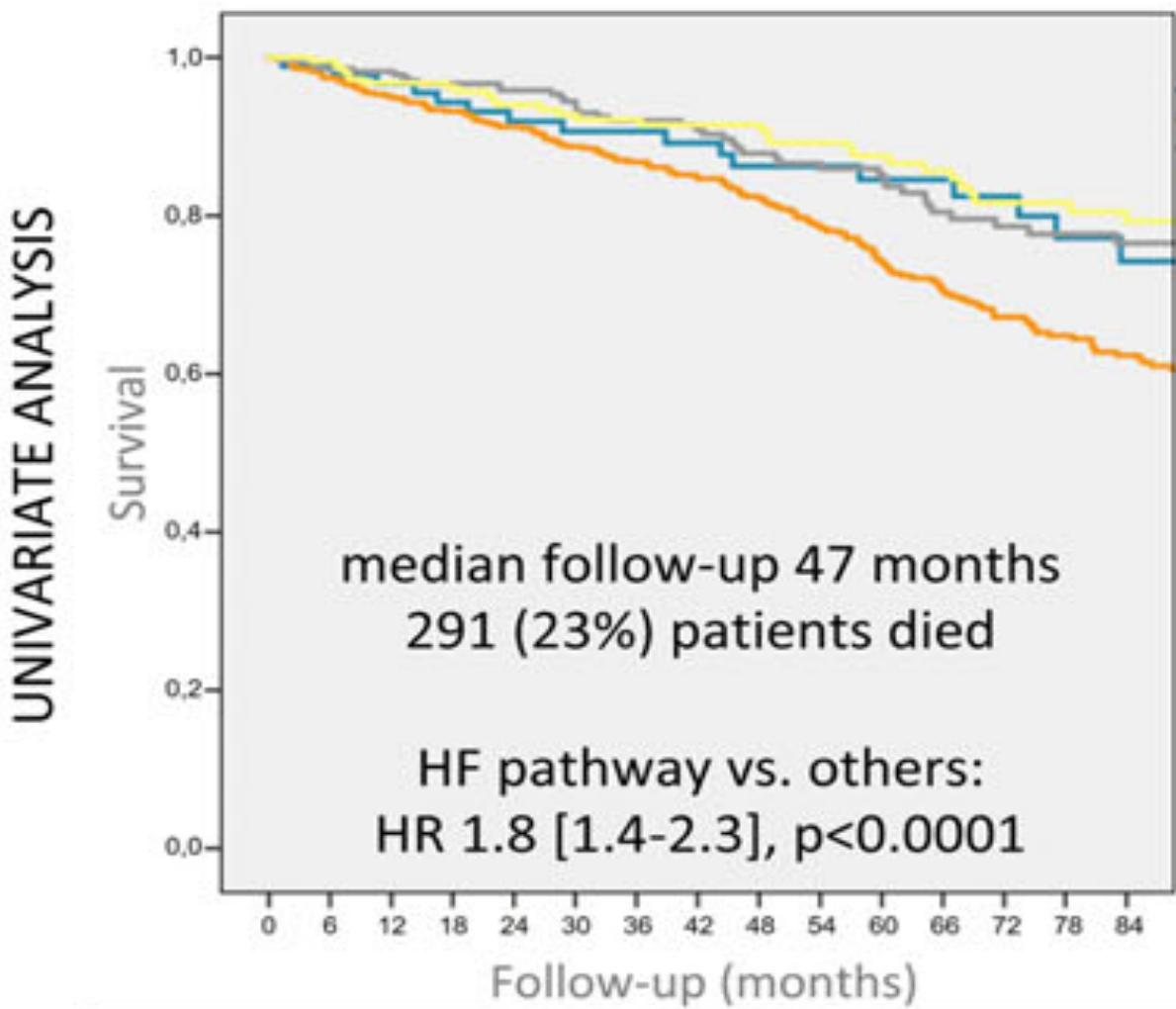
1. Prevalence



2. Characteristics

- HCM pathway (n=94):**
 - 75±7 years, 93% males
 - Red flags lead to case re-evaluation
 - 37% previous HF hospitalization
 - 16% NYHA III-IV, 33% CKD, 64% AFib
- Heart failure pathway (n=651):**
 - 79±7 years, 87% males
 - 61% during HF hospitalization
 - 52% had LVEF≥50%
 - 44% NYHA III-IV, 50 % CKD, 65% AFib
- Incidental imaging pathway (n=300):**
 - 77±7 years, 92% males
 - 74% during echocardiography for routine evaluation
 - 13% NYHA III-IV, 38% CKD, 51% AFib
- Incidental clinical pathway (n=236):**
 - 78±7 years, 90% males
 - 94% cardiovascular evaluation including AFib, PM, arrhythmias
 - 15% NYHA III-IV, 38% CKD, 70% AFib

3. Prognosis



MULTIVARIATE ANALYSIS

	HR	p value
HF vs. other pathways	-	-
Age at diagnosis	1.1 [1.0-1.1]	<0.0001
NYHA III-IV	2.2 [1.7-2.7]	<0.0001
Hypertension	1.4 [1.1-1.9]	0.01
Diabetes mellitus	1.5 [1.1-2.0]	0.01
CKD	1.4 [1.1-1.8]	0.01
Cancer (active)	1.9 [1.2-2.9]	0.01

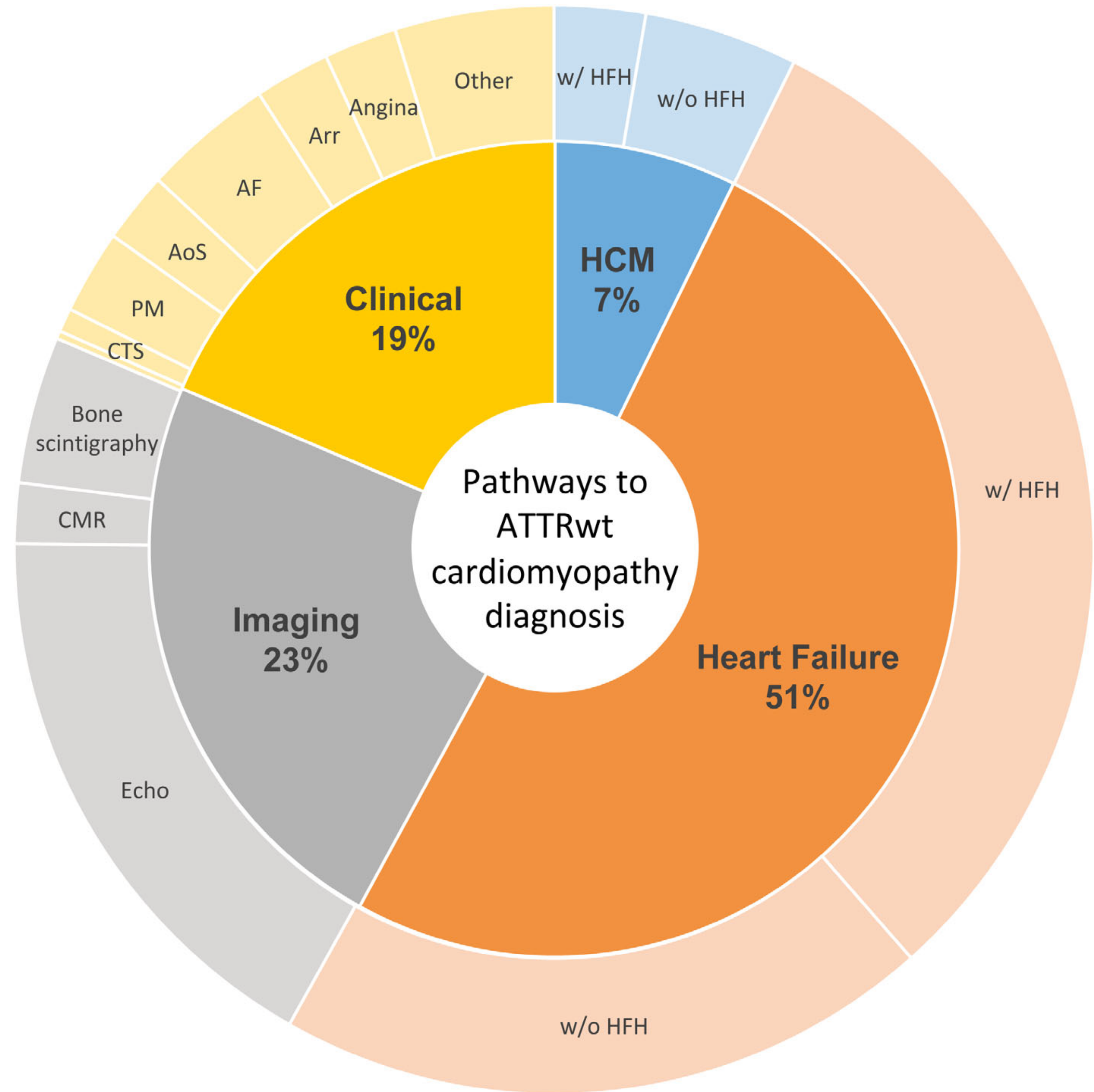
Diagnostic pathways to wild-type transthyretin amyloid cardiomyopathy: a multicentre network study

Giacomo Tini^{1,2}, Paolo Milani^{3,4}, Mattia Zampieri⁵, Angelo G. Caponetti^{6,7}, Francesca Fabris^{3,4}, Andrea Foli⁴, Alessia Argirò⁵, Carlotta Mazzoni⁵, Christian Gagliardi^{6,8}, Simone Longhi^{6,8}, Giulia Saturi^{6,7}, Giuseppe Vergaro^{9,10}, Alberto Aimo^{9,10}, Domitilla Russo², Guerino G. Varrà¹¹, Matteo Serenelli¹², Gioele Fabbri¹², Laura De Michieli¹³, Giuseppe Palmiero¹⁴, Giuseppe Ciliberti^{15,16}, Samuela Carigi¹⁷, Eugenio Sessarego¹, Giulia E. Mandoli¹⁸, Giulia Ricci Lucchi¹⁹, Valeria Rella²⁰, Enrico Monti²¹, Elisa Gardini²¹, Michela Bartolotti²², Lia Crotti^{20,23}, Elisa Merli¹⁹, Roberta Mussinelli⁴, Pier Filippo Vianello¹, Matteo Cameli¹⁸, Francesca Marzo¹⁷, Federico Guerra^{15,16}, Giuseppe Limongelli^{8,14}, Alberto Cipriani^{13,24}, Stefano Perlini^{3,4}, Laura Obici⁴, Federico Perfetto⁵, Camillo Autore^{2,25}, Italo Porto^{1,26}, Claudio Rapezzi^{12,27†}, Gianfranco Sinagra^{8,11}, Marco Merlo^{8,11}, Beatrice Musumeci², Michele Emdin^{9,10}, Elena Biagini^{6,8}, Francesco Cappelli⁵, Giovanni Palladini^{3,4}, and Marco Canepa^{1,26*}

51% Heart Failure

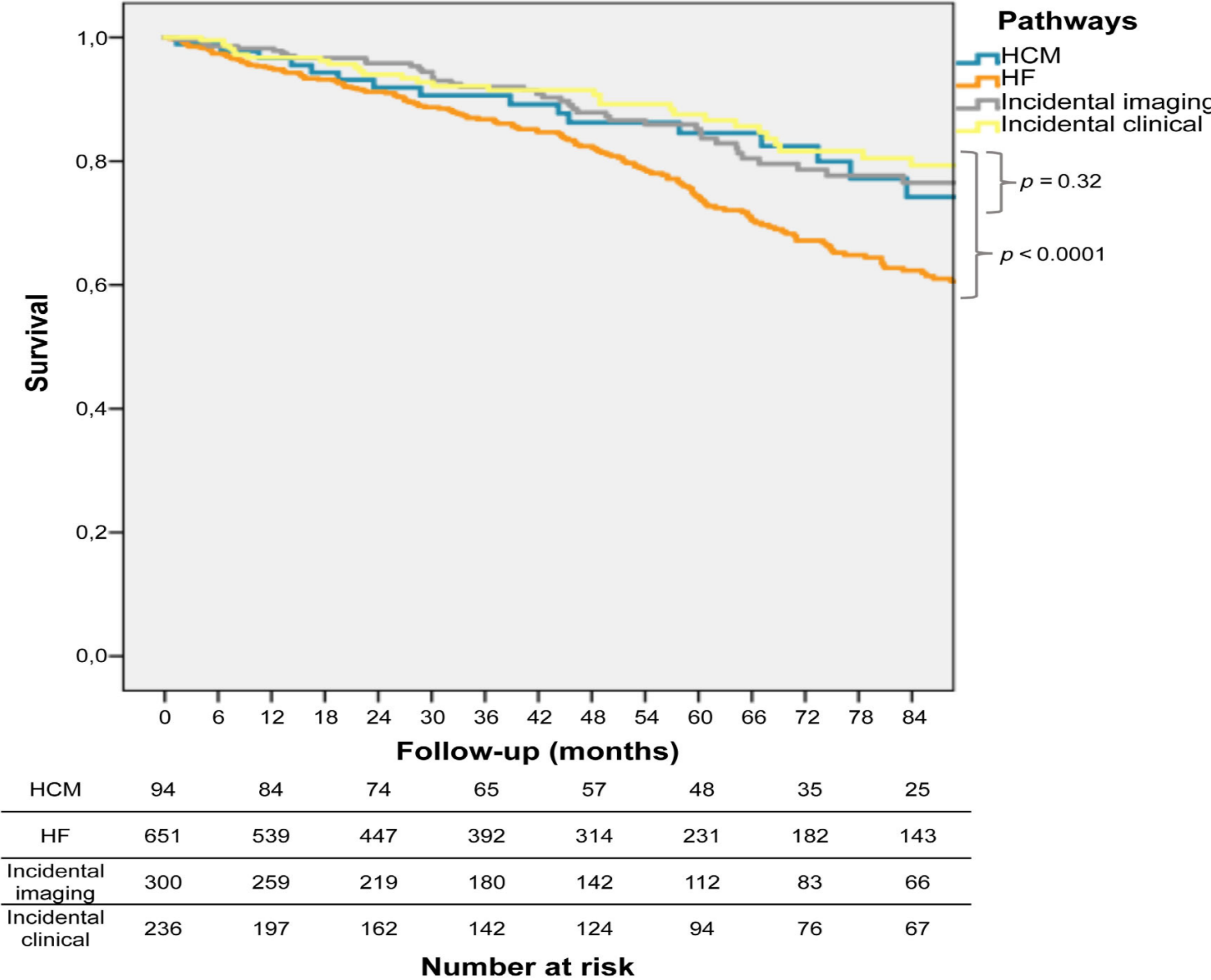
23% Imaging (LVH)

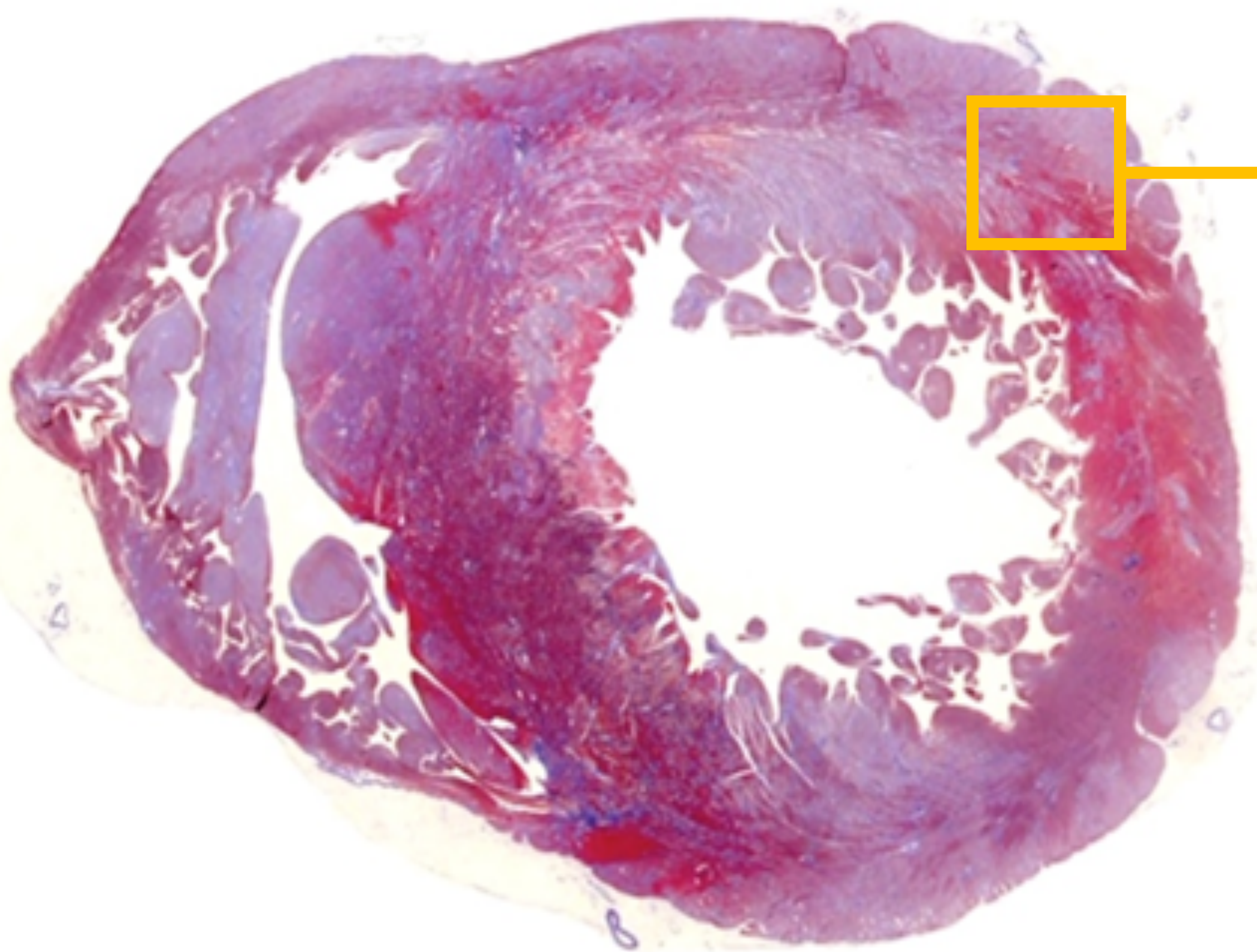
19% Clinical (AS, CTS, AF)



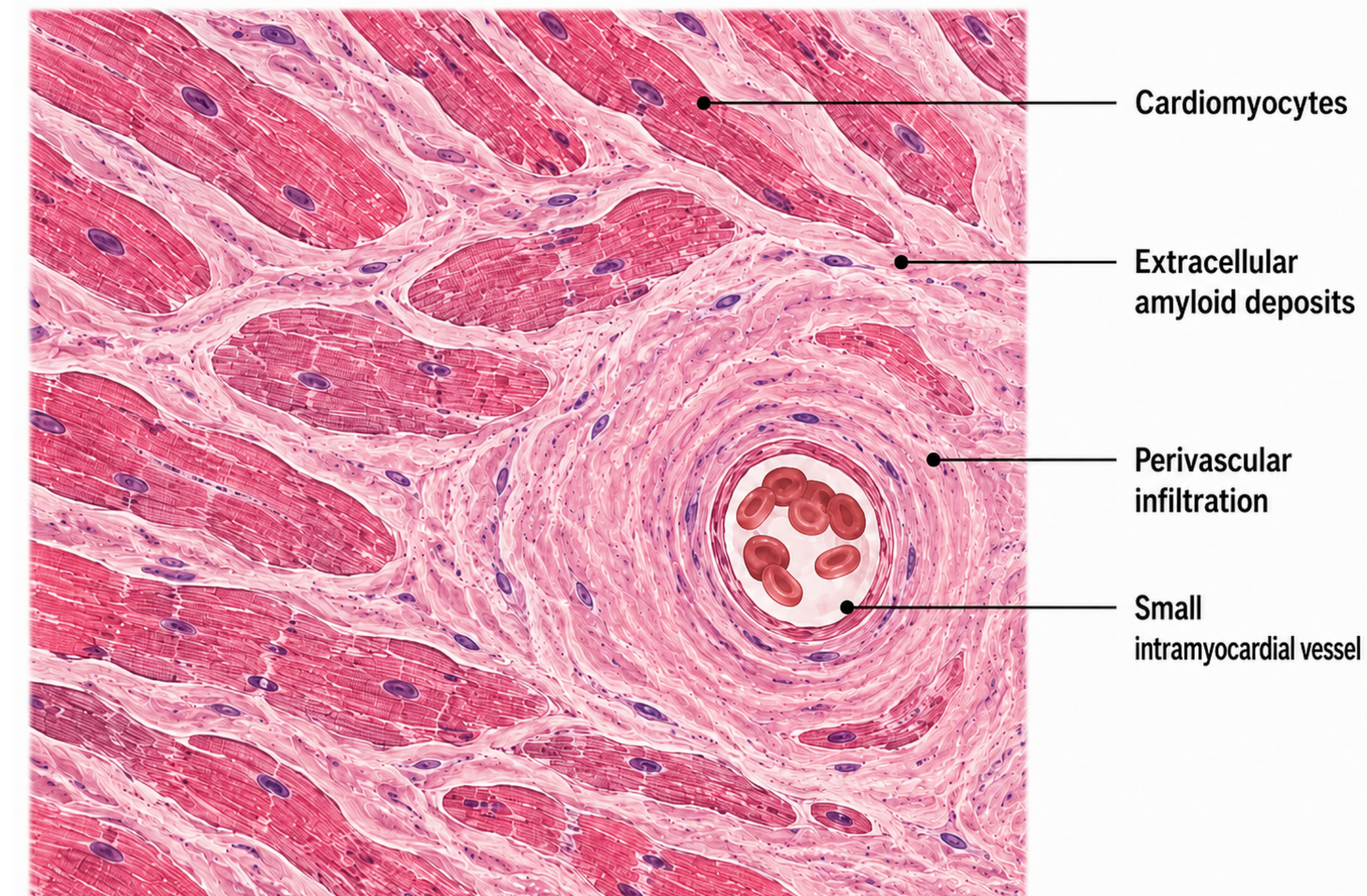
Diagnostic pathways to wild-type transthyretin amyloid cardiomyopathy: a multicentre network study

Giacomo Tini^{1,2}, Paolo Milani^{3,4}, Mattia Zampieri⁵, Angelo G. Caponetti^{6,7}, Francesca Fabris^{3,4}, Andrea Foli⁴, Alessia Argirò⁵, Carlotta Mazzoni⁵, Christian Gagliardi^{6,8}, Simone Longhi^{6,8}, Giulia Saturi^{6,7}, Giuseppe Vergaro^{9,10}, Alberto Aimo^{9,10}, Domitilla Russo², Guerino G. Varrà¹¹, Matteo Serenelli¹², Gioele Fabbri¹², Laura De Michieli¹³, Giuseppe Palmiero¹⁴, Giuseppe Ciliberti^{15,16},



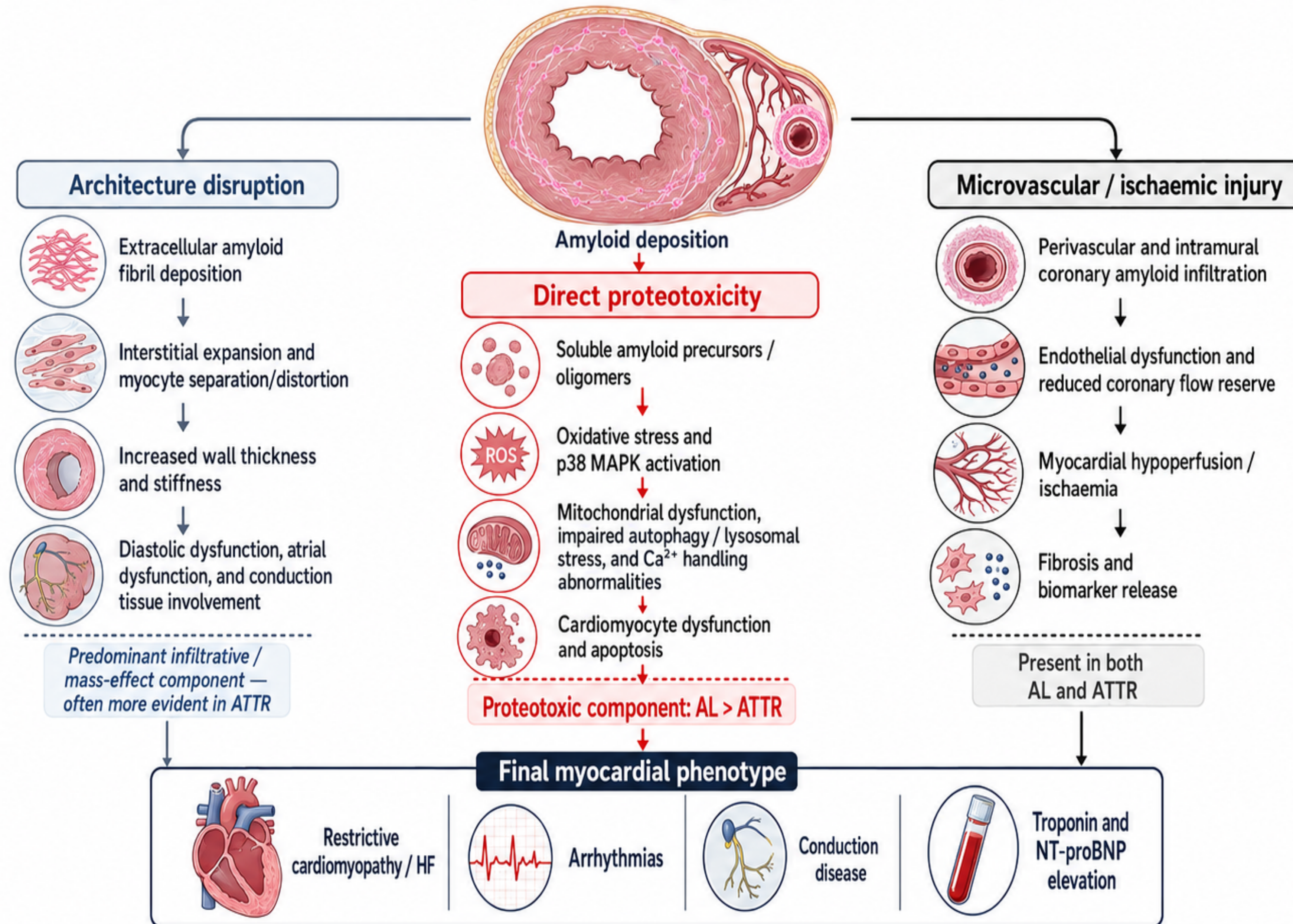


CARDIAC AMYLOIDOSIS – HISTOLOGICAL APPEARANCE
Interstitial and perivascular amyloid infiltration



widespread but heterogeneous

Mechanisms of Myocardial Injury in Cardiac Amyloidosis



03/05/2022 14:21:18

ACE

Soft



Reduced
LV cavity

LV pseudo-
hypertroph
y

RV
involvement

Valves
thickening

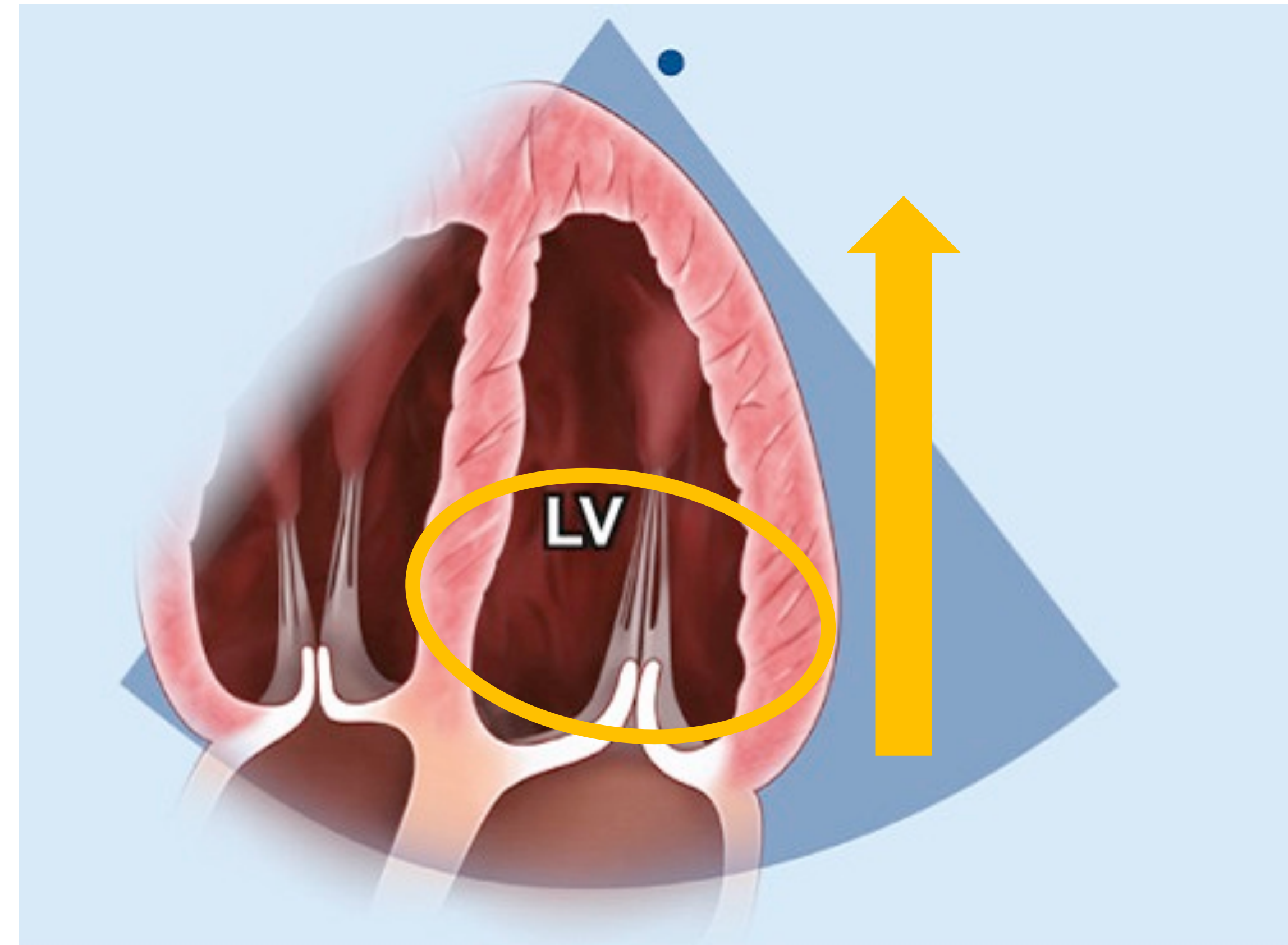
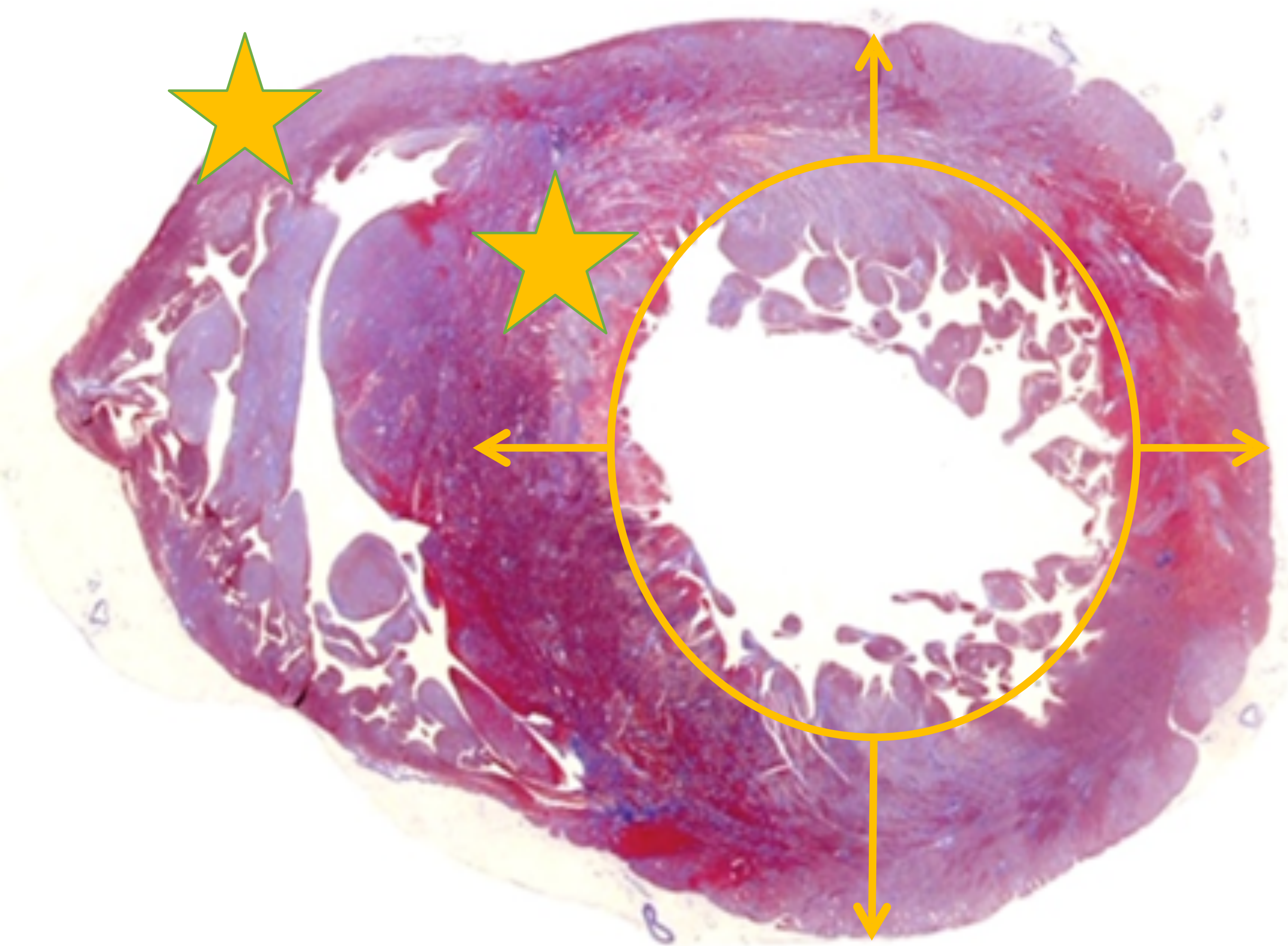
Interatrial
thickening

Atrial
involvement

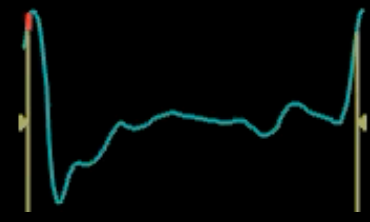
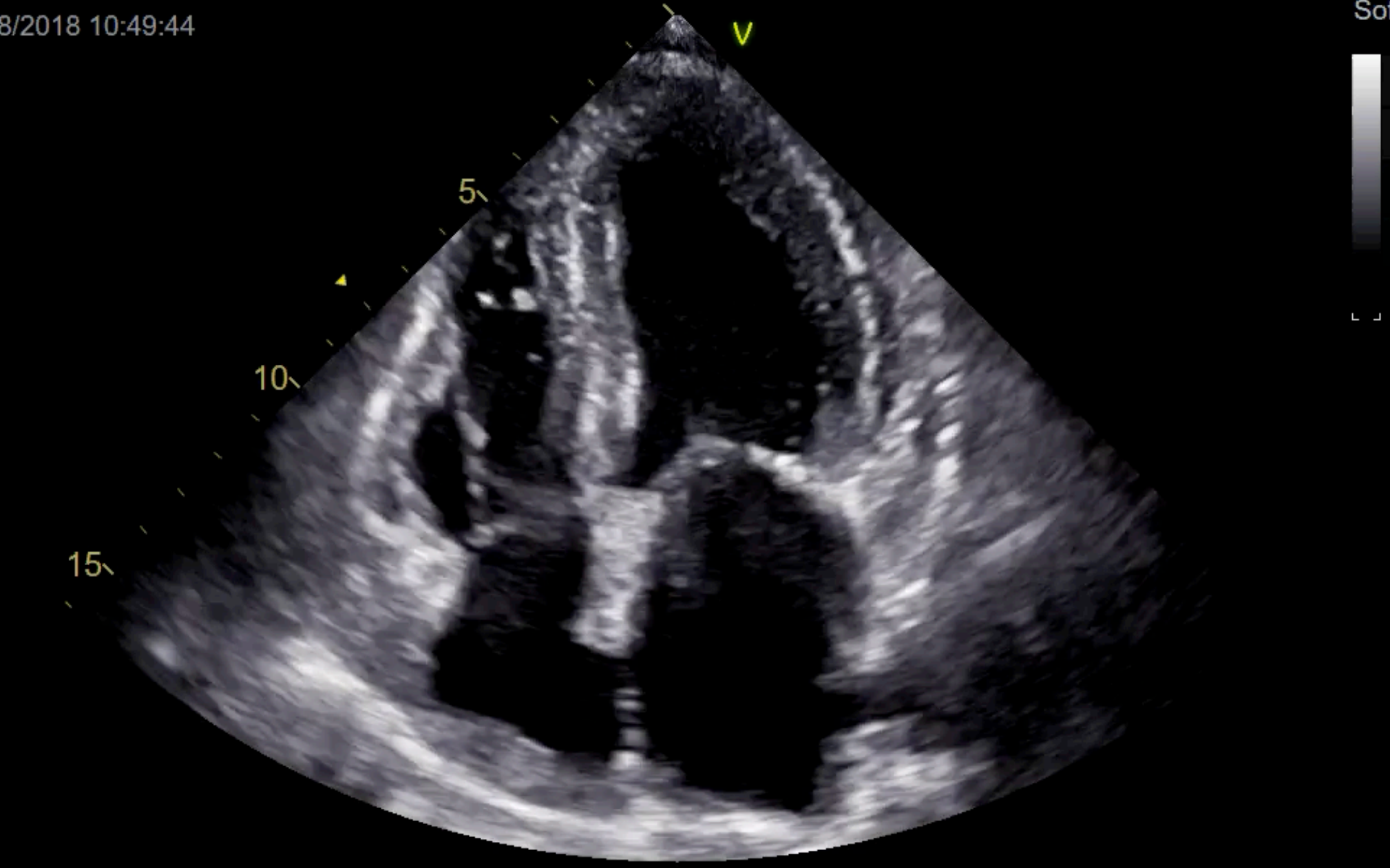
Pericardi
aleffusio
n



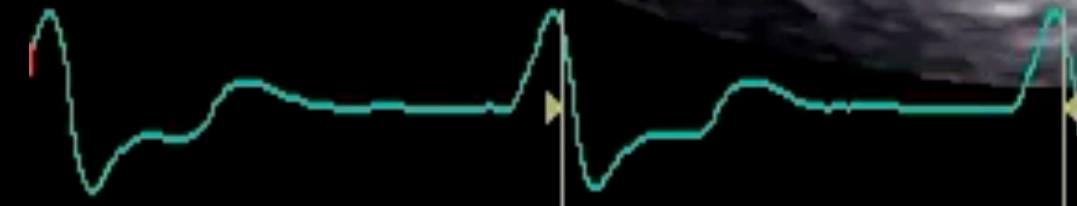
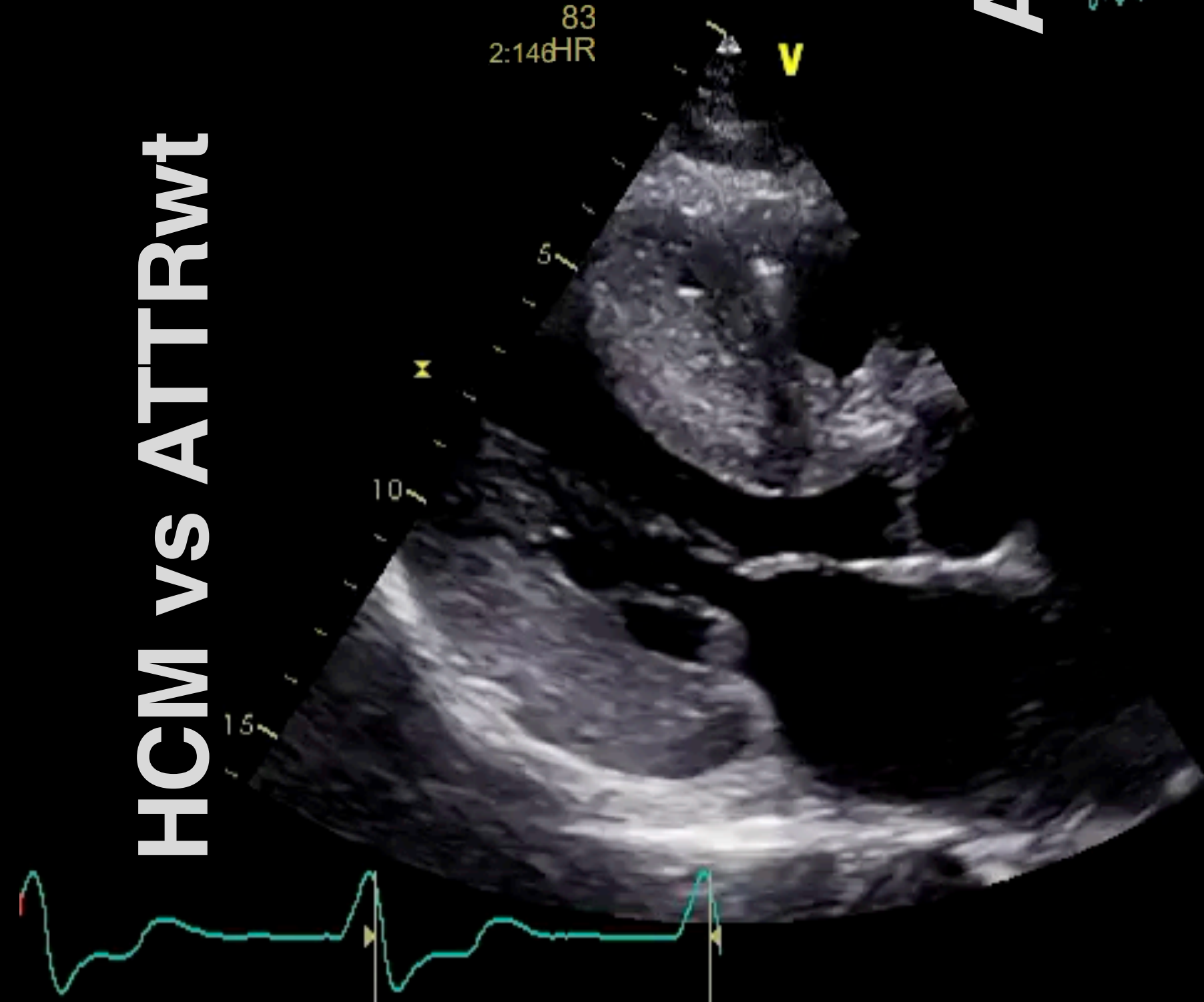
73
7:91HR



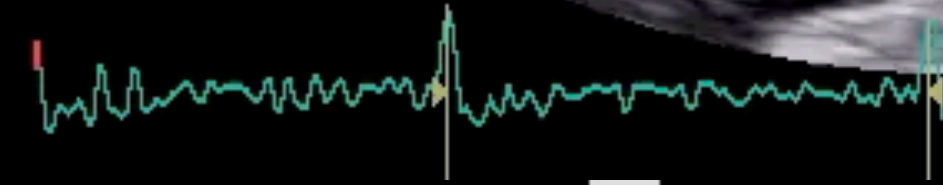
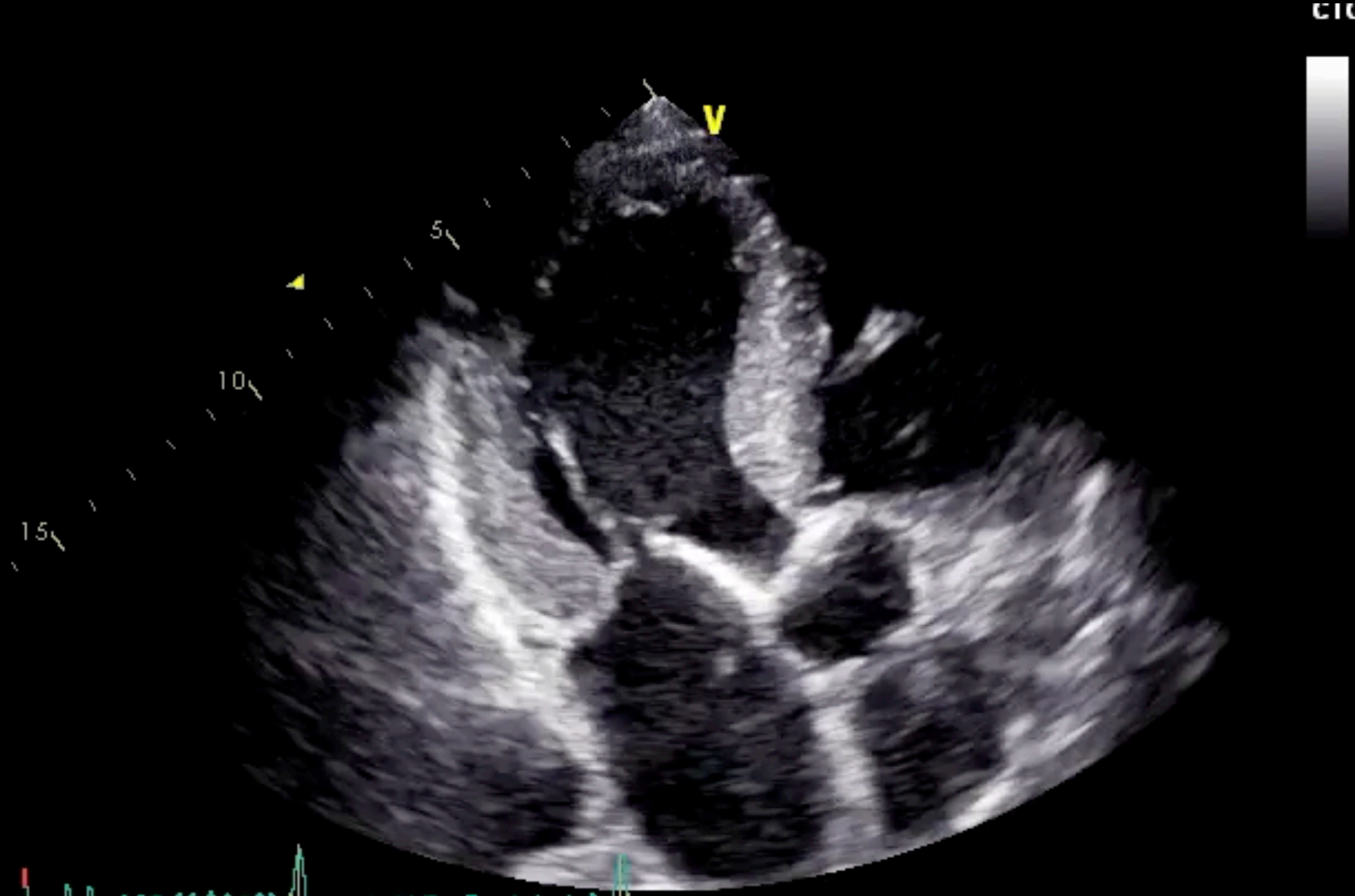
HypCM vs ATTRm



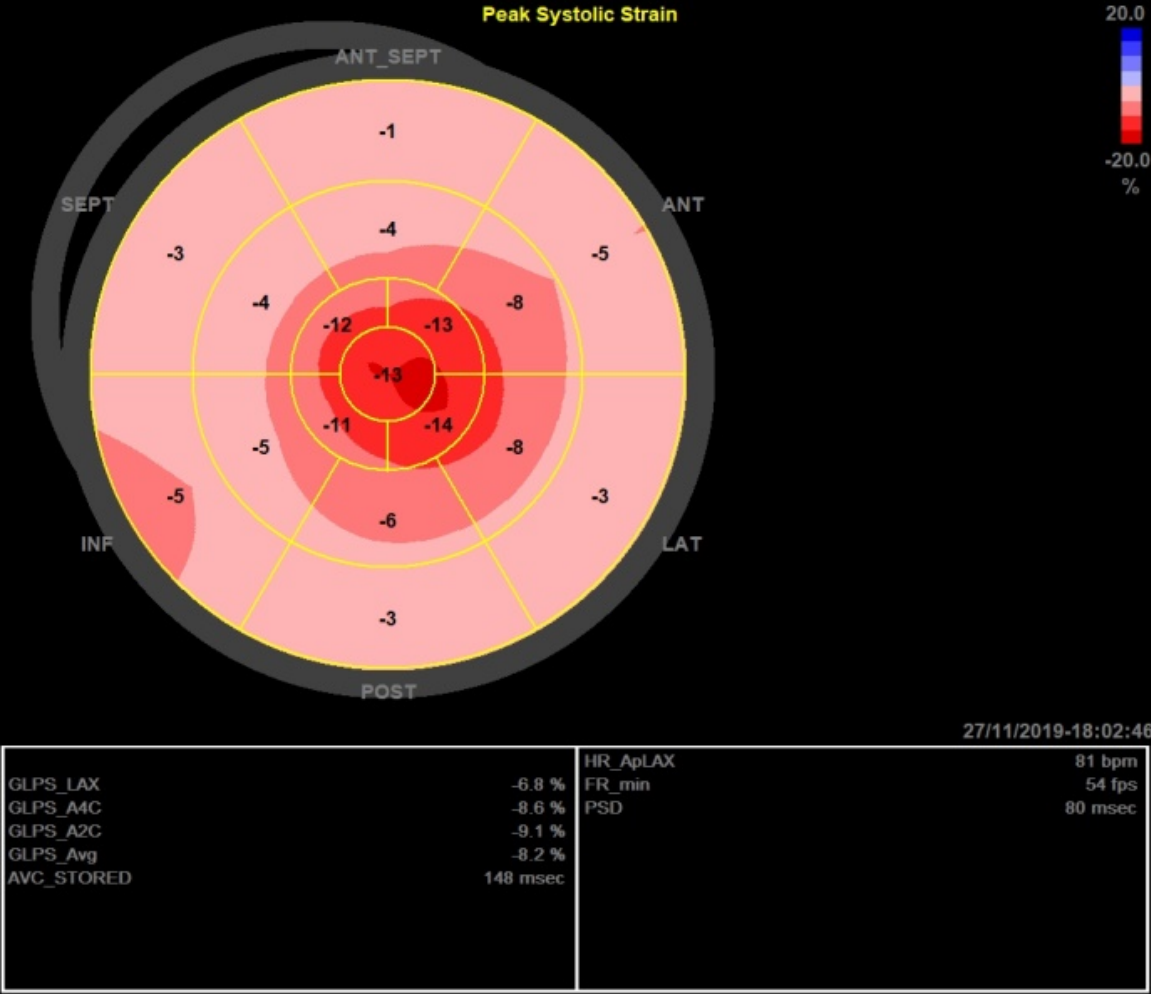
HCM vs ATTRwt



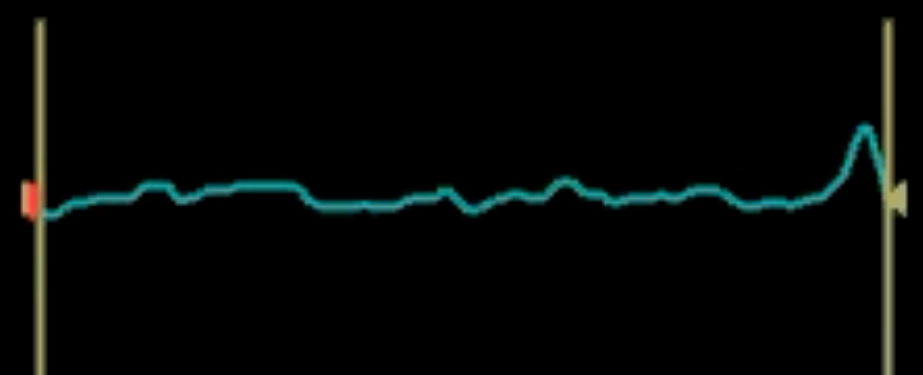
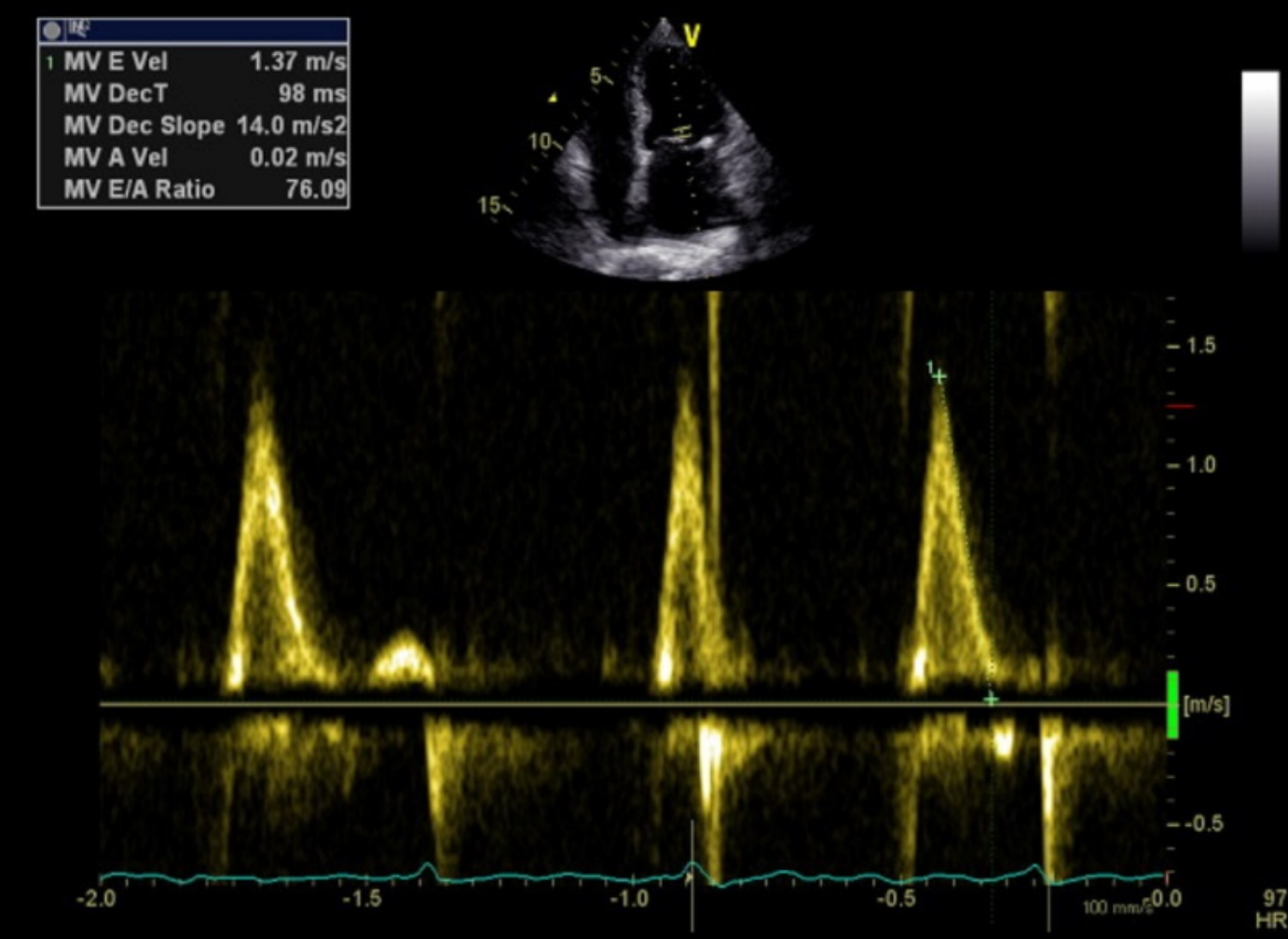
Aortic stenosis vs



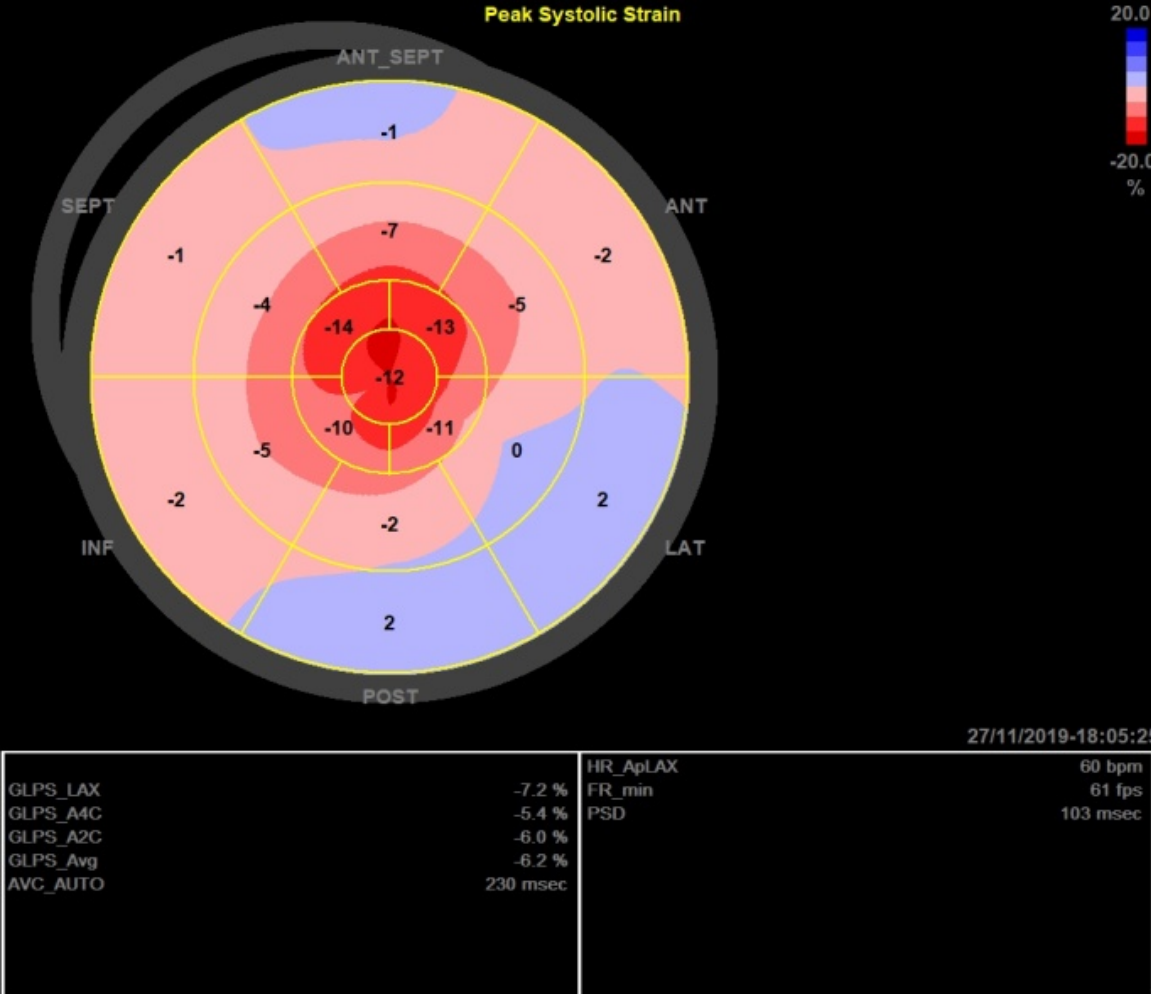
76
HR



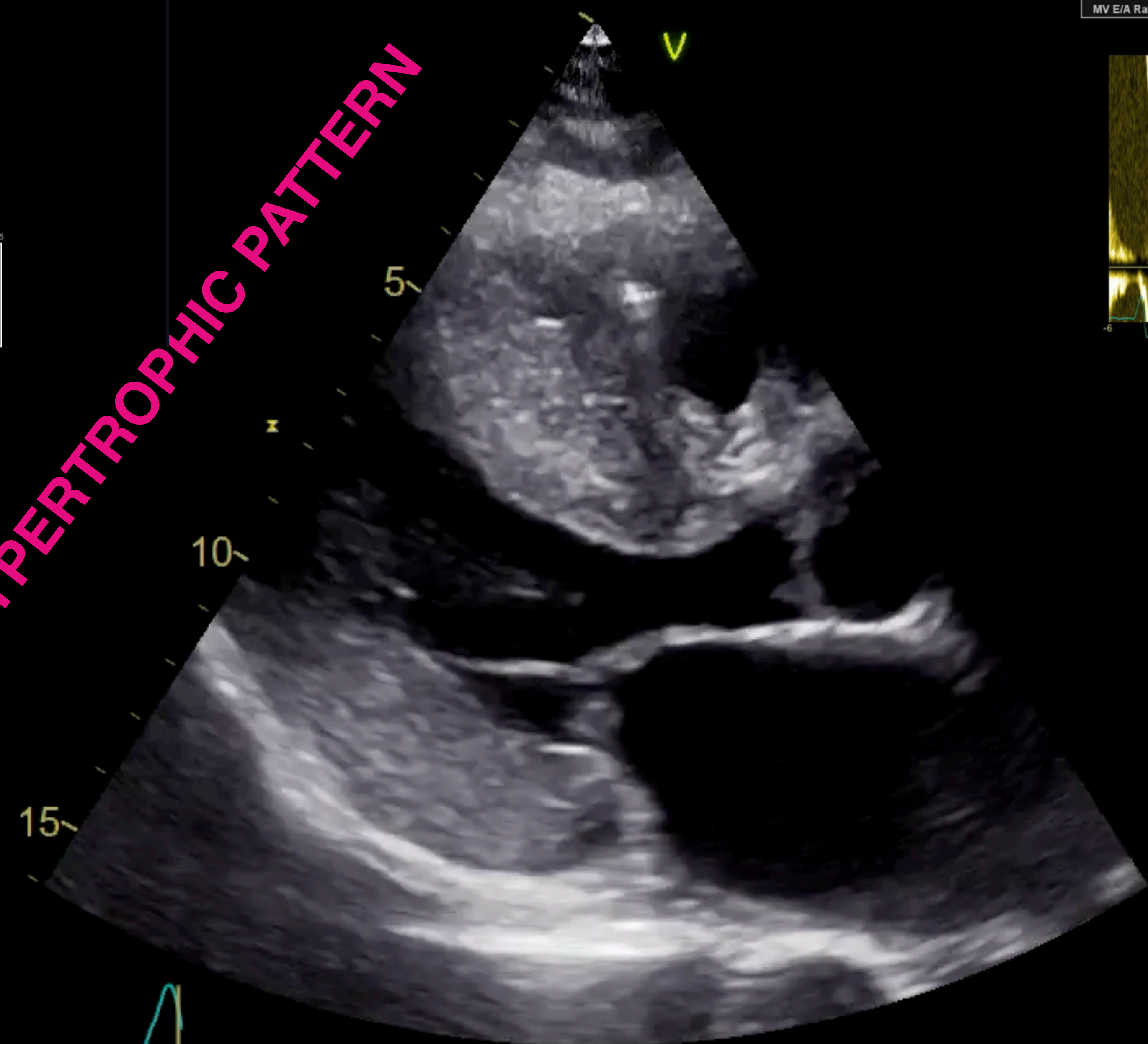
RESTRICTIVE PATTERN



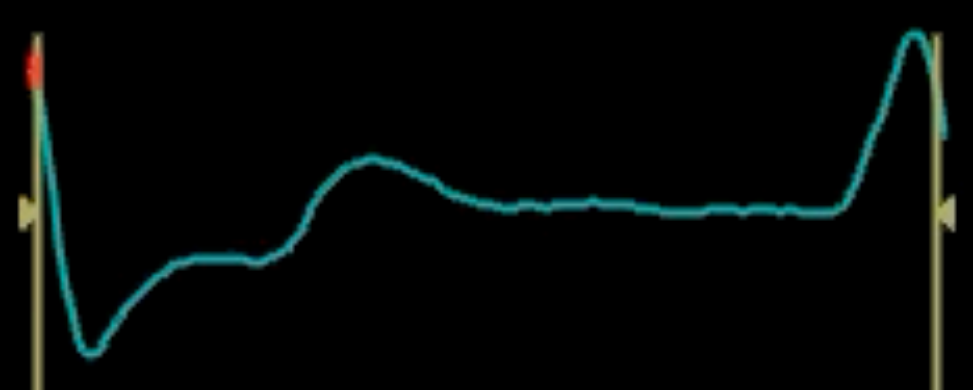
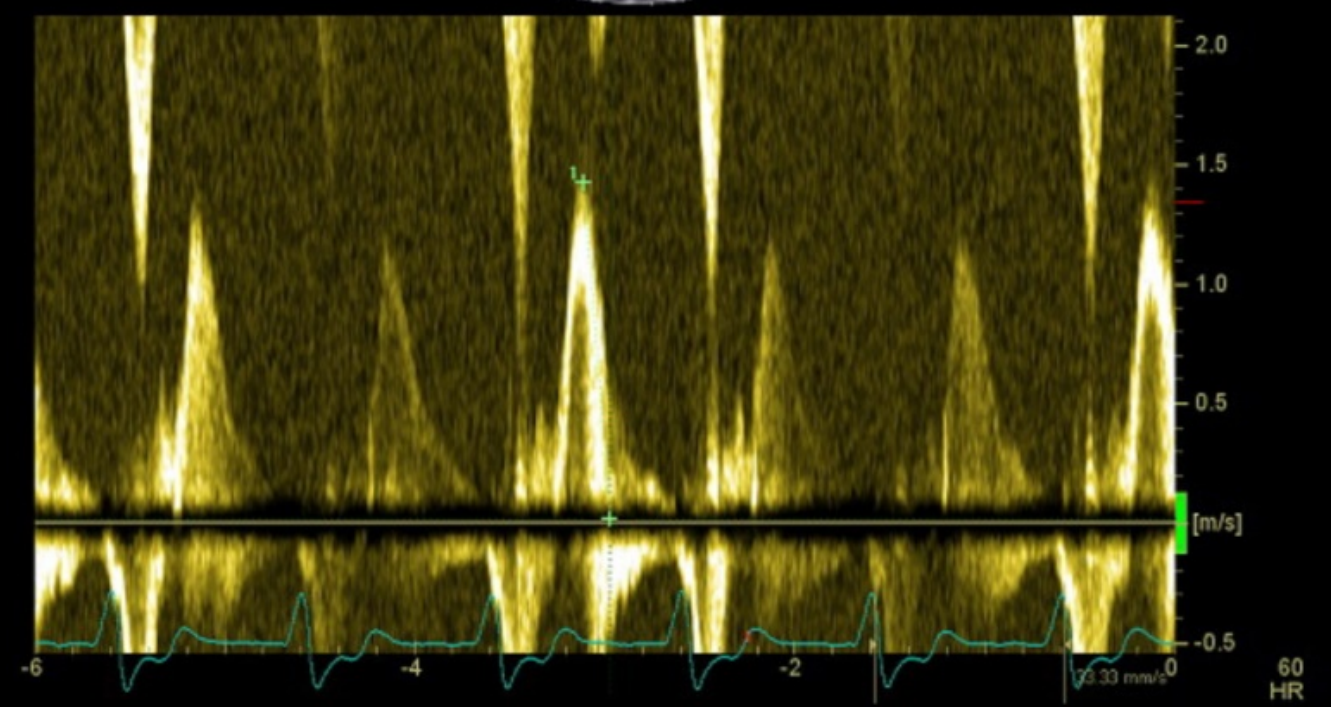
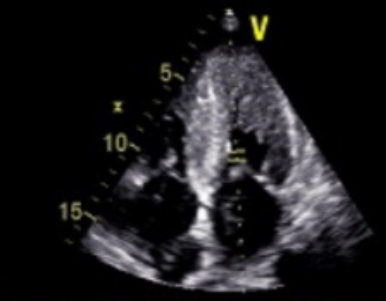
66
166:220HR



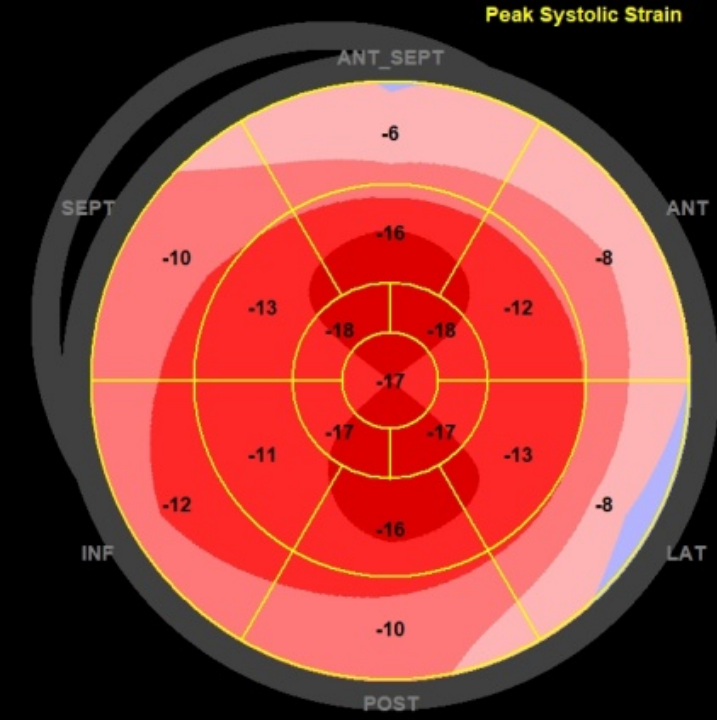
HYPERTROPHIC PATTERN



1 MV E Vel	1.43 m/s
MV DecT	140 ms
MV Dec Slope	10.2 m/s ²
MV A Vel	0.01 m/s
MV E/A Ratio	95.36

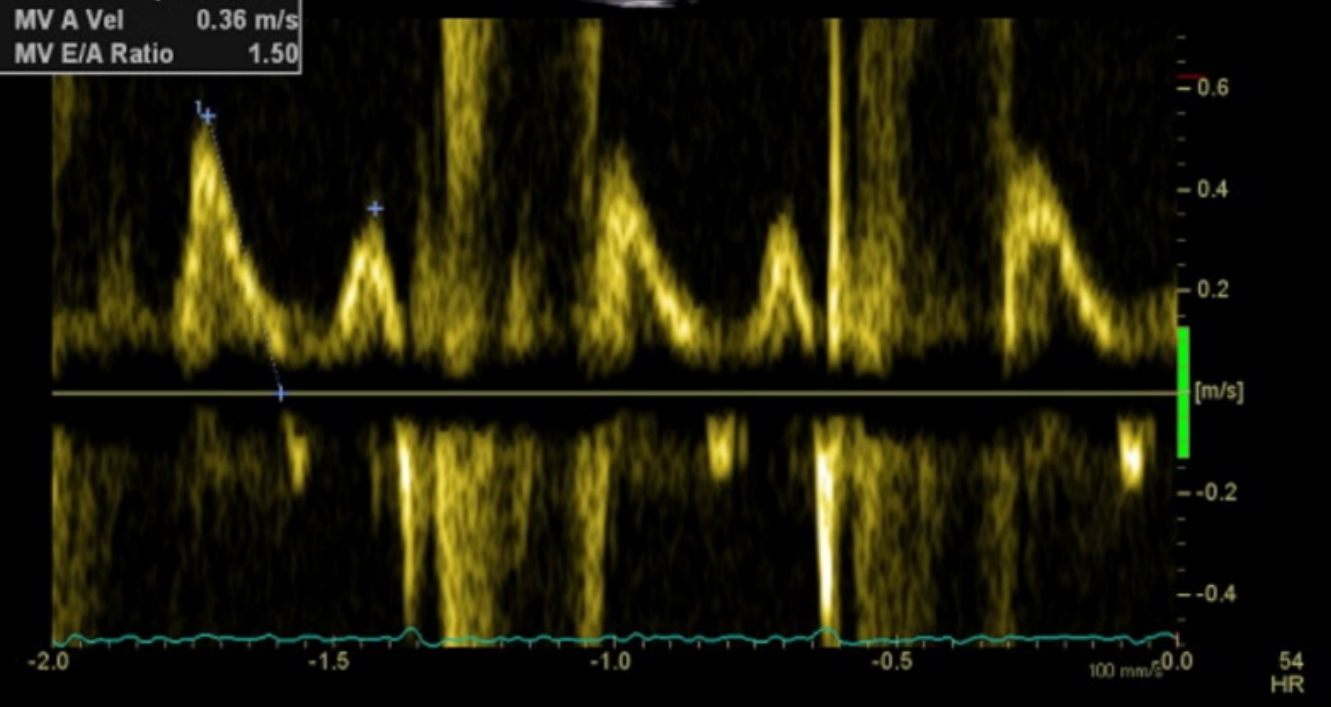


60
65:126HR



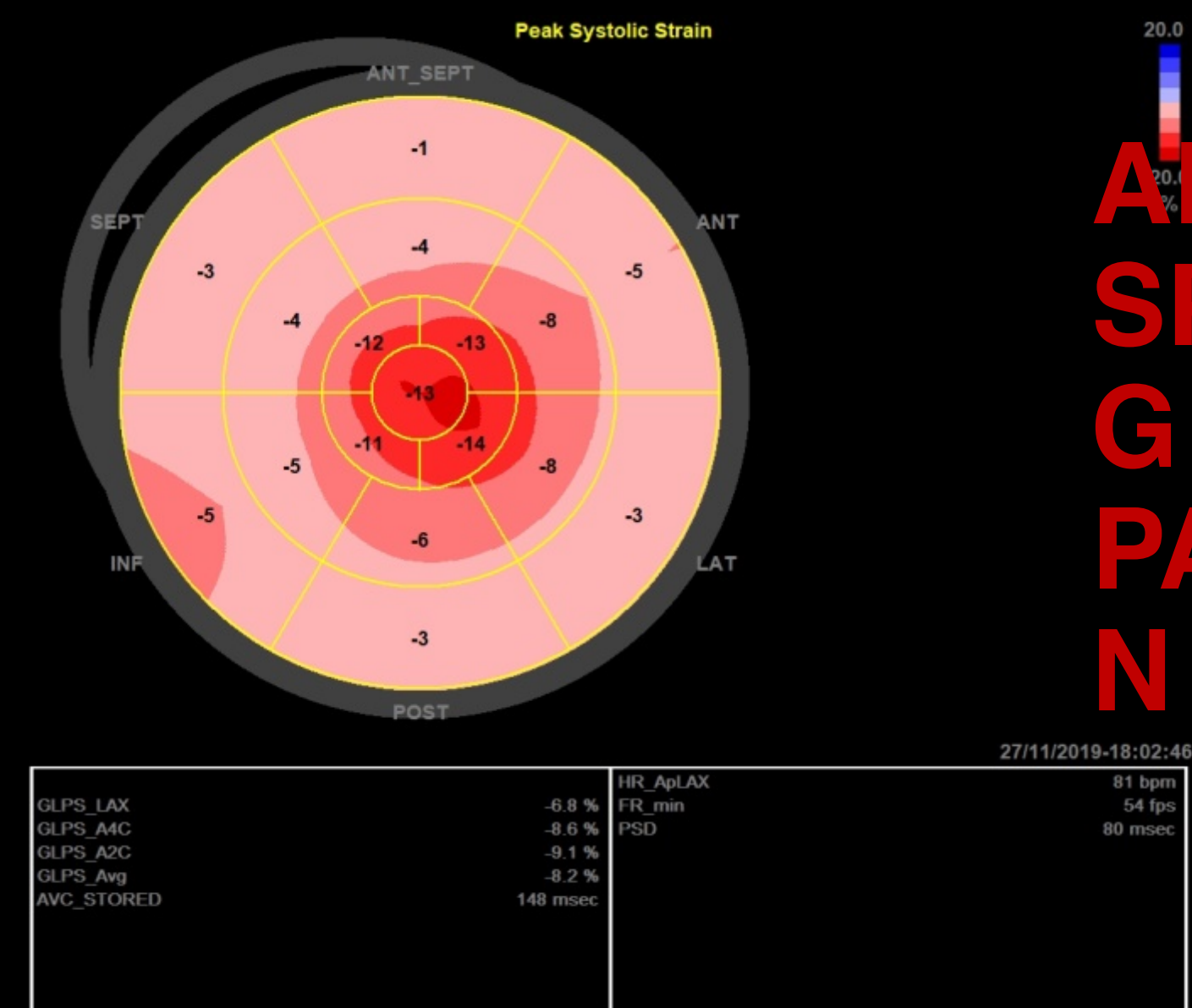
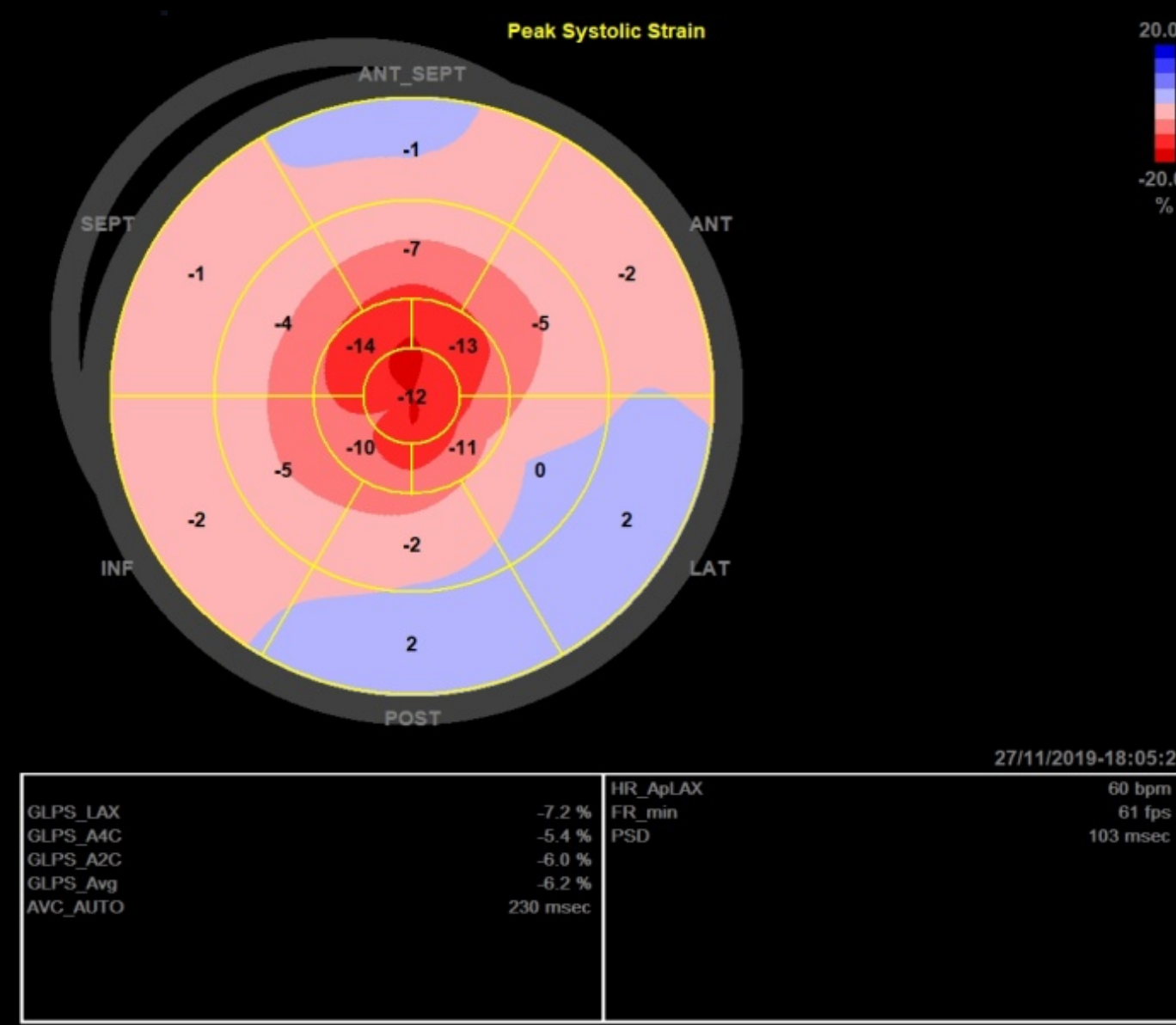
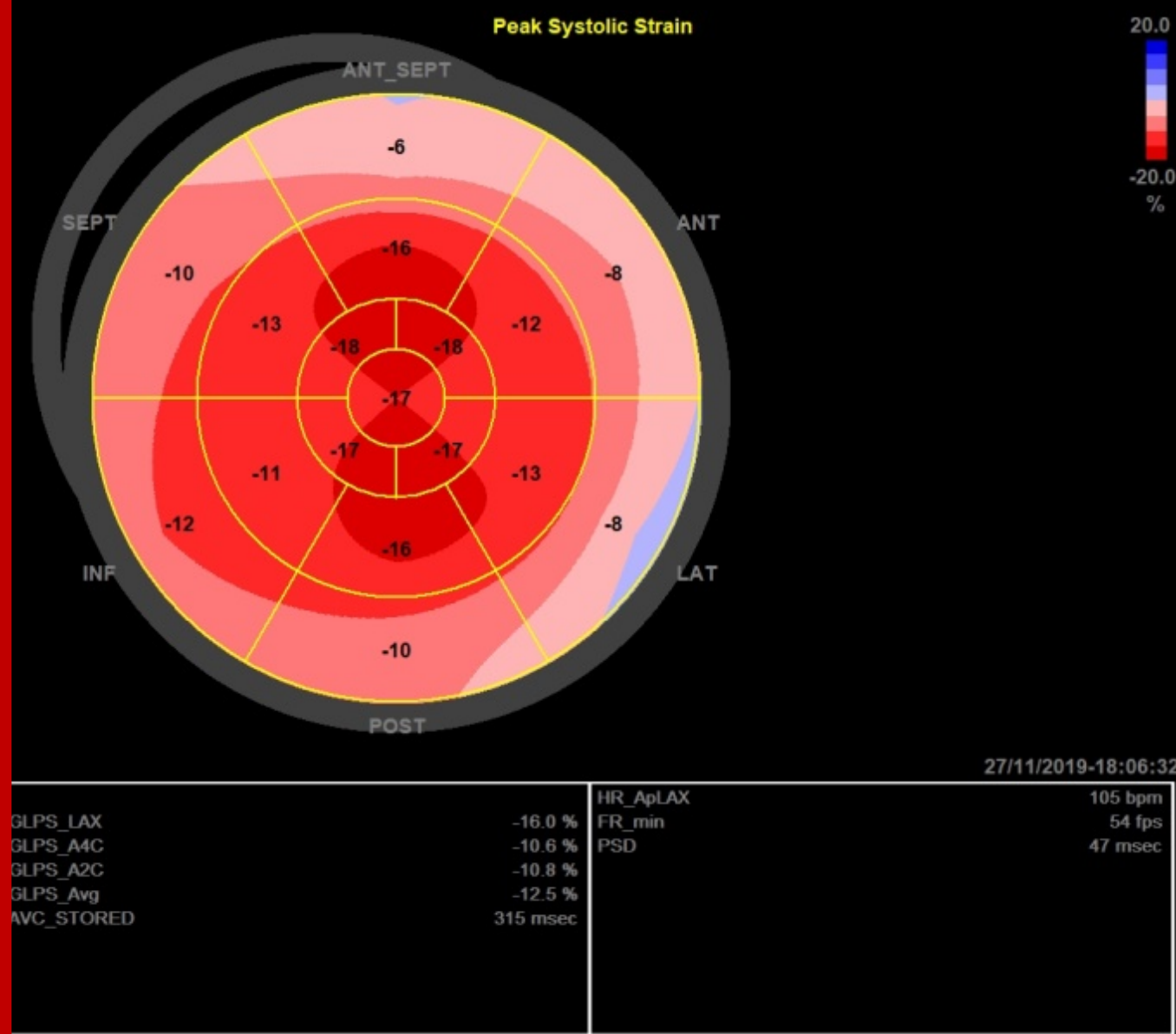
27/11/2019-18:06:32		
GLPS_LAX	-16.0 %	HR_ApLAX 105 bpm
GLPS_A4C	-10.6 %	FR_min 54 fps
GLPS_A2C	-10.8 %	PSD 47 msec
GLPS_Avg	-12.5 %	
AVC_STORED	315 msec	

E' Avg	0.05 m/s
E/E' Avg	10.48
E/E' Lat	8.44
E/E' Sept	13.80
MV E Vel	0.55 m/s
MV DecT	129 ms
MV Dec Slope	4.2 m/s ²
MV A Vel	0.36 m/s
MV E/A Ratio	1.50



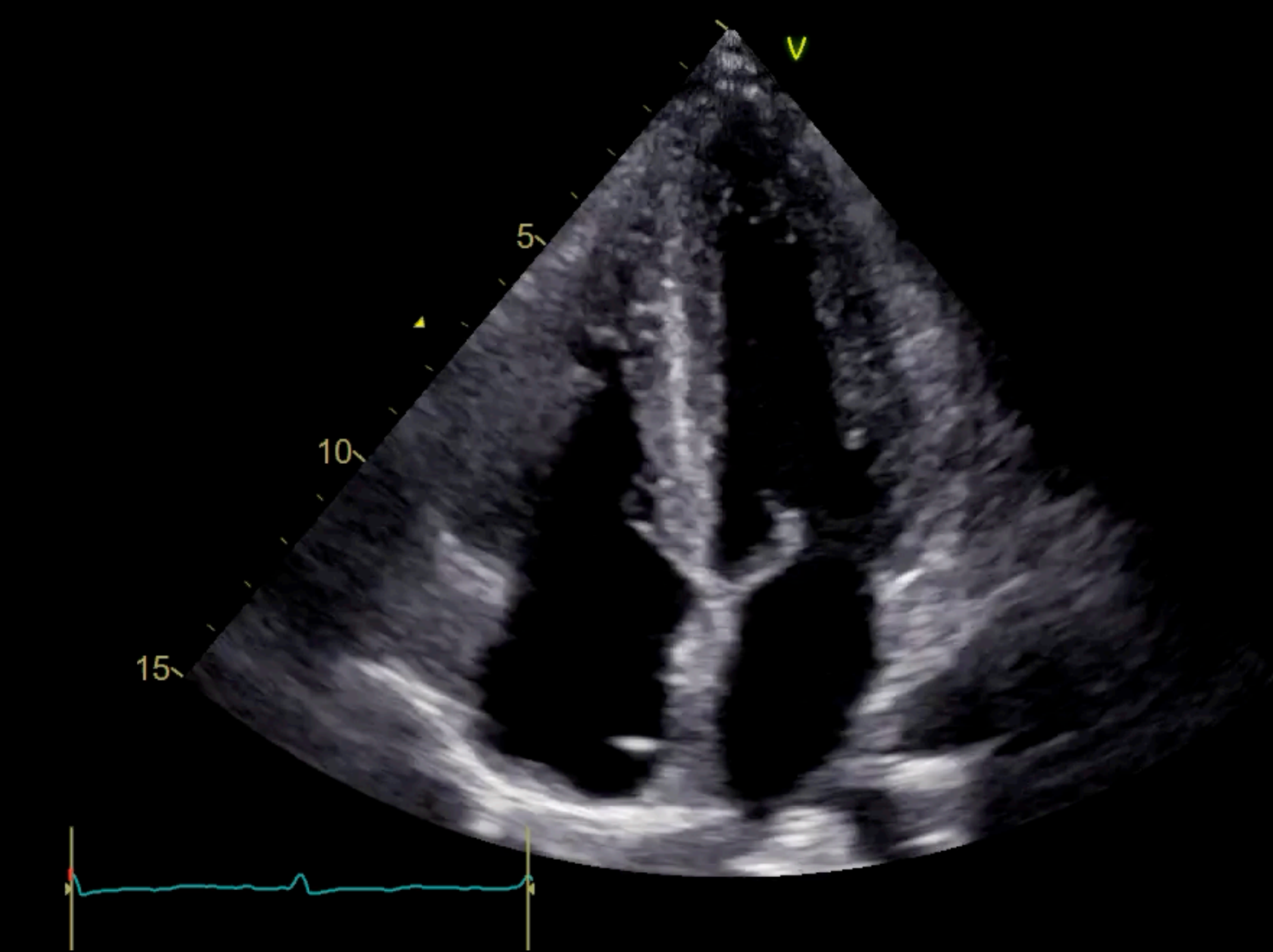
EARLY PATTERN



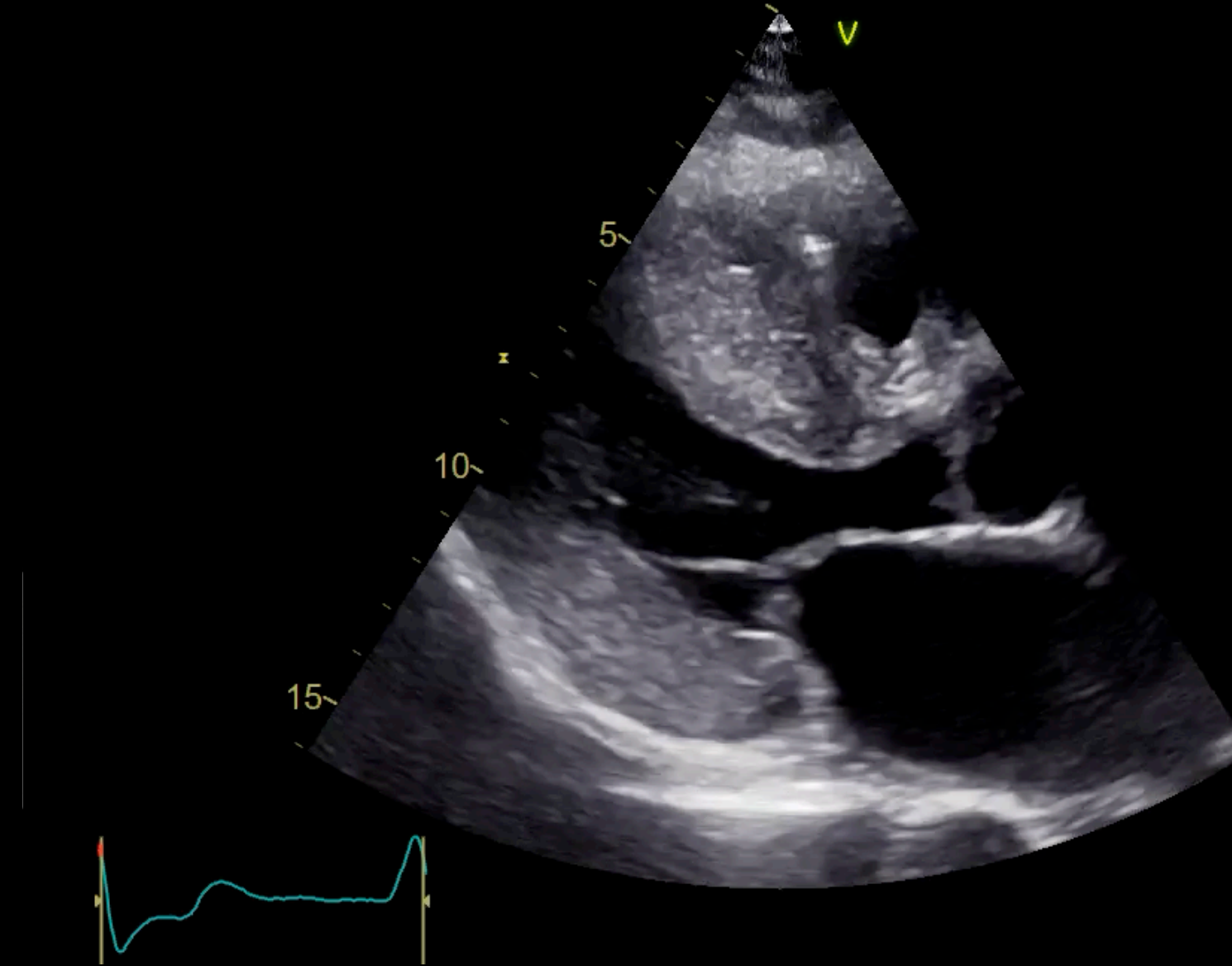


APICAL
SPARIN
G
PATTER
N

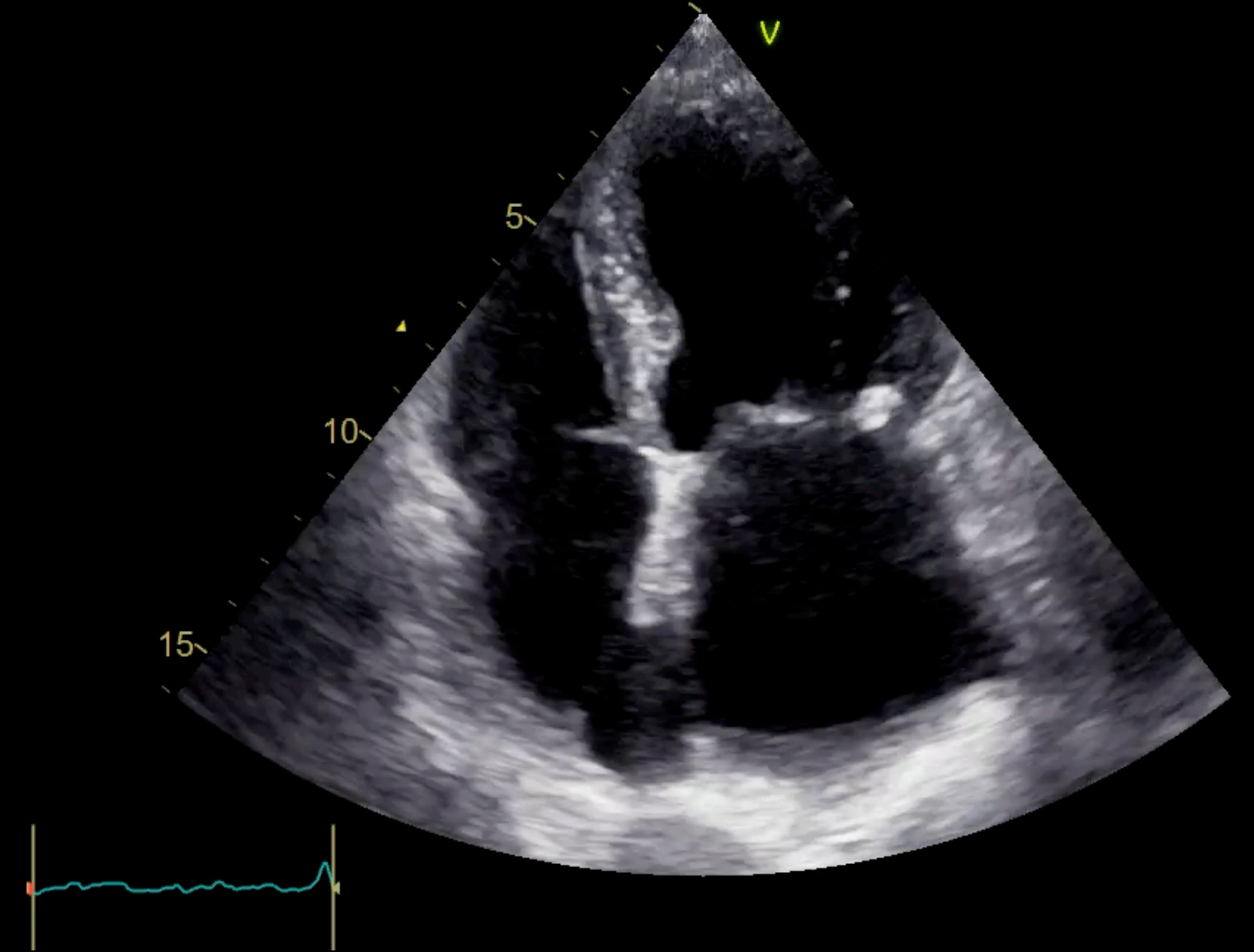
18/11/2019 18:08:12



06/11/2018 15:12:04



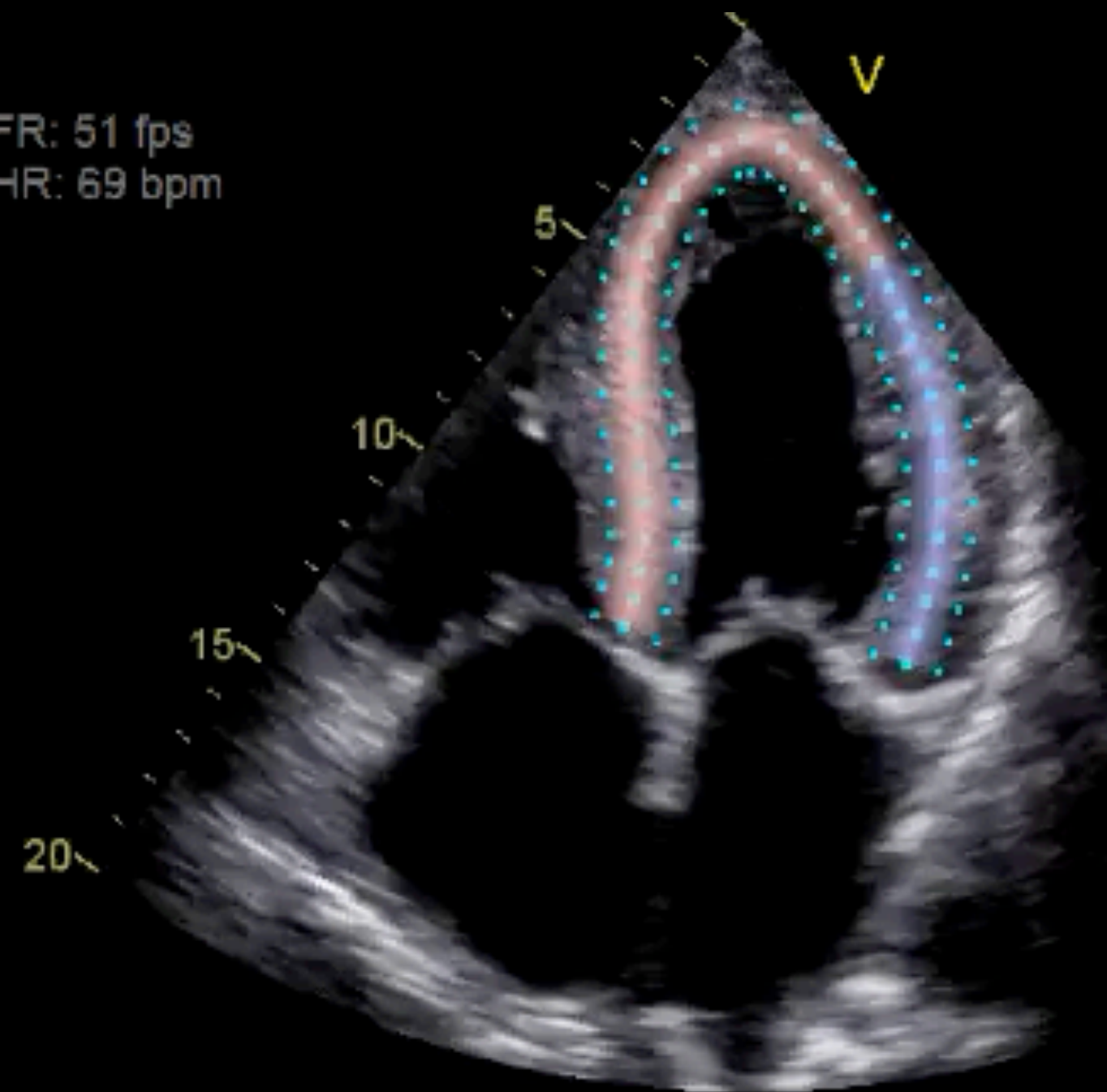
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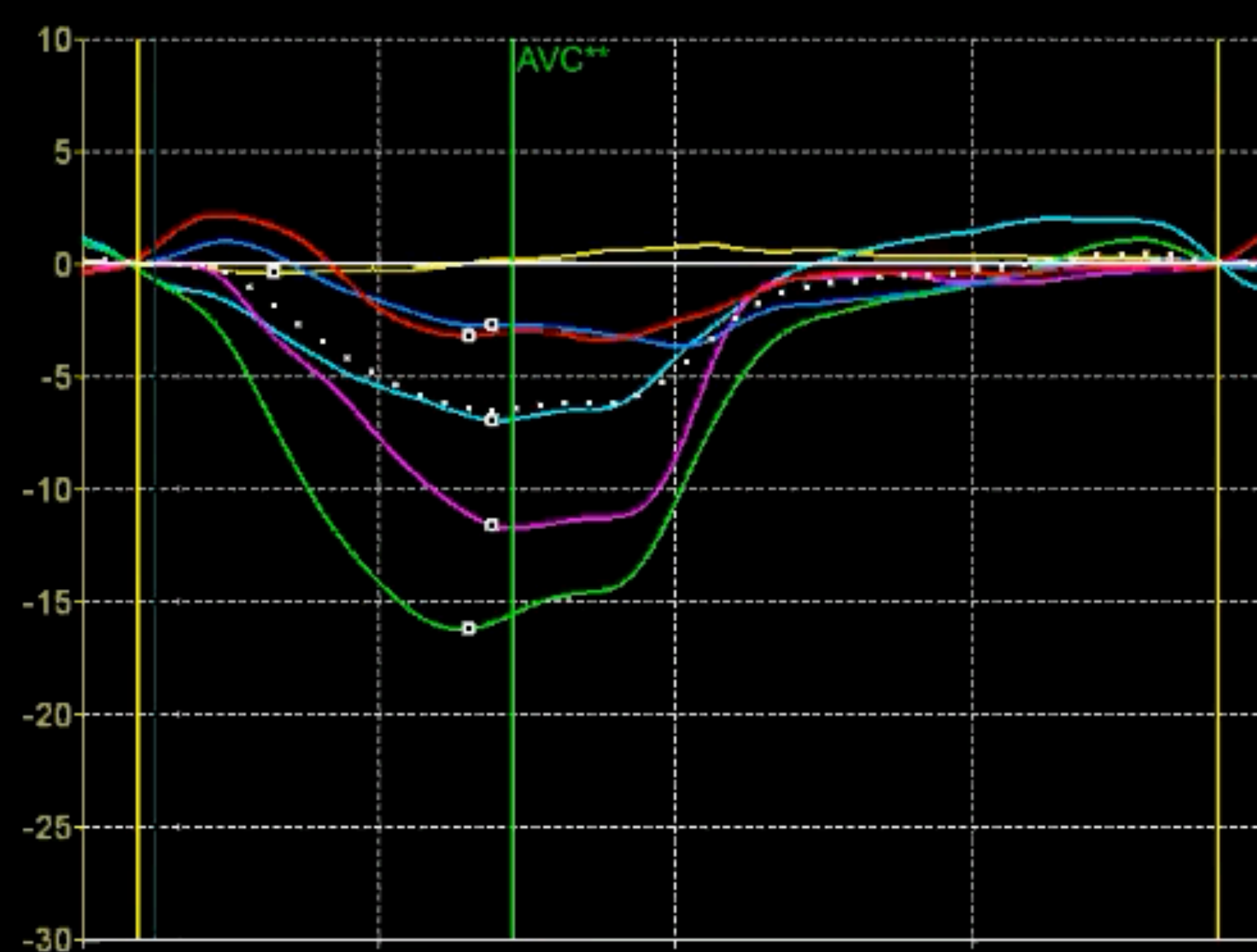
66
166:220HR

4CH

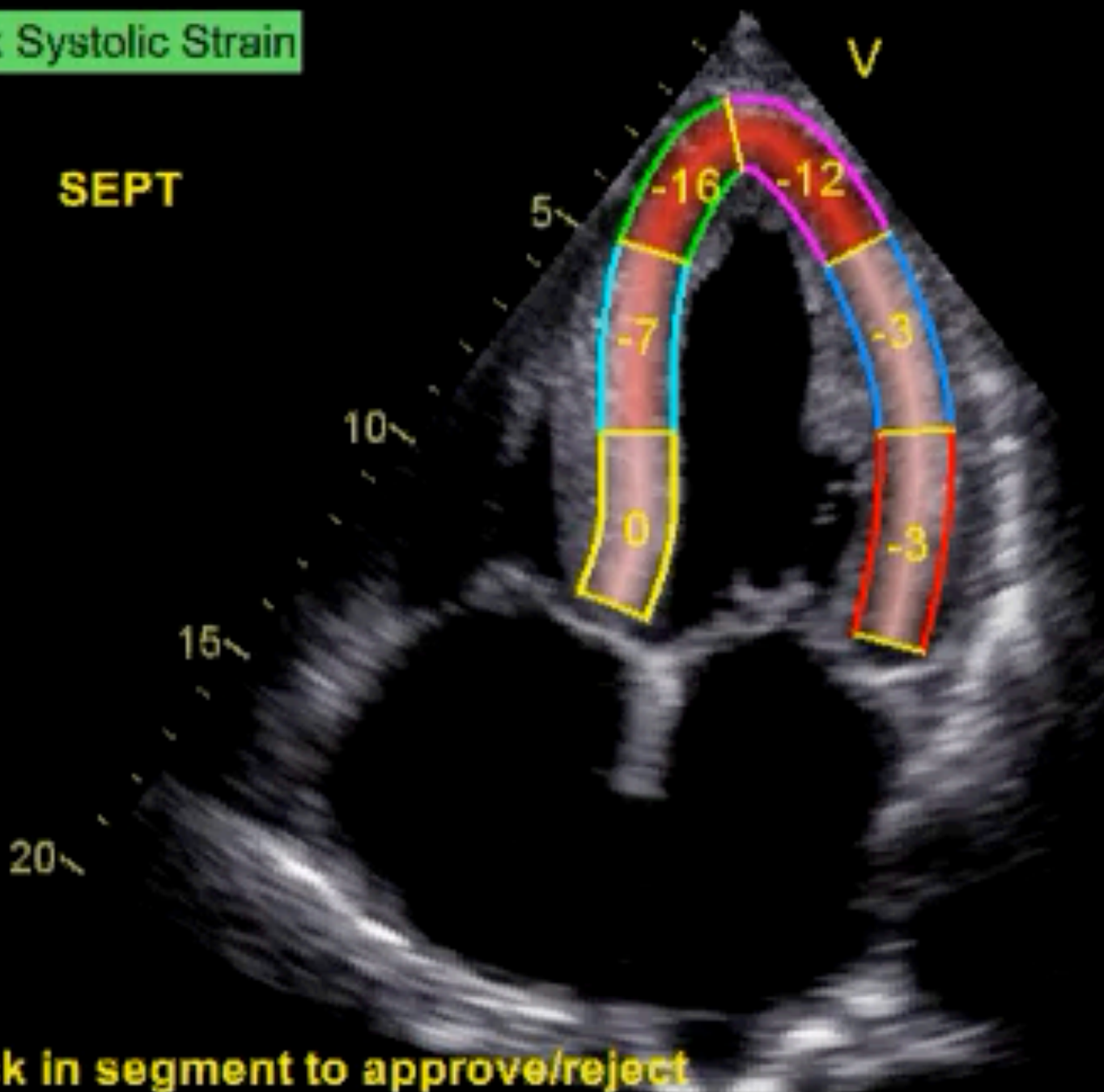
FR: 51 fps
HR: 69 bpm



GS=-6.5%



Peak Systolic Strain

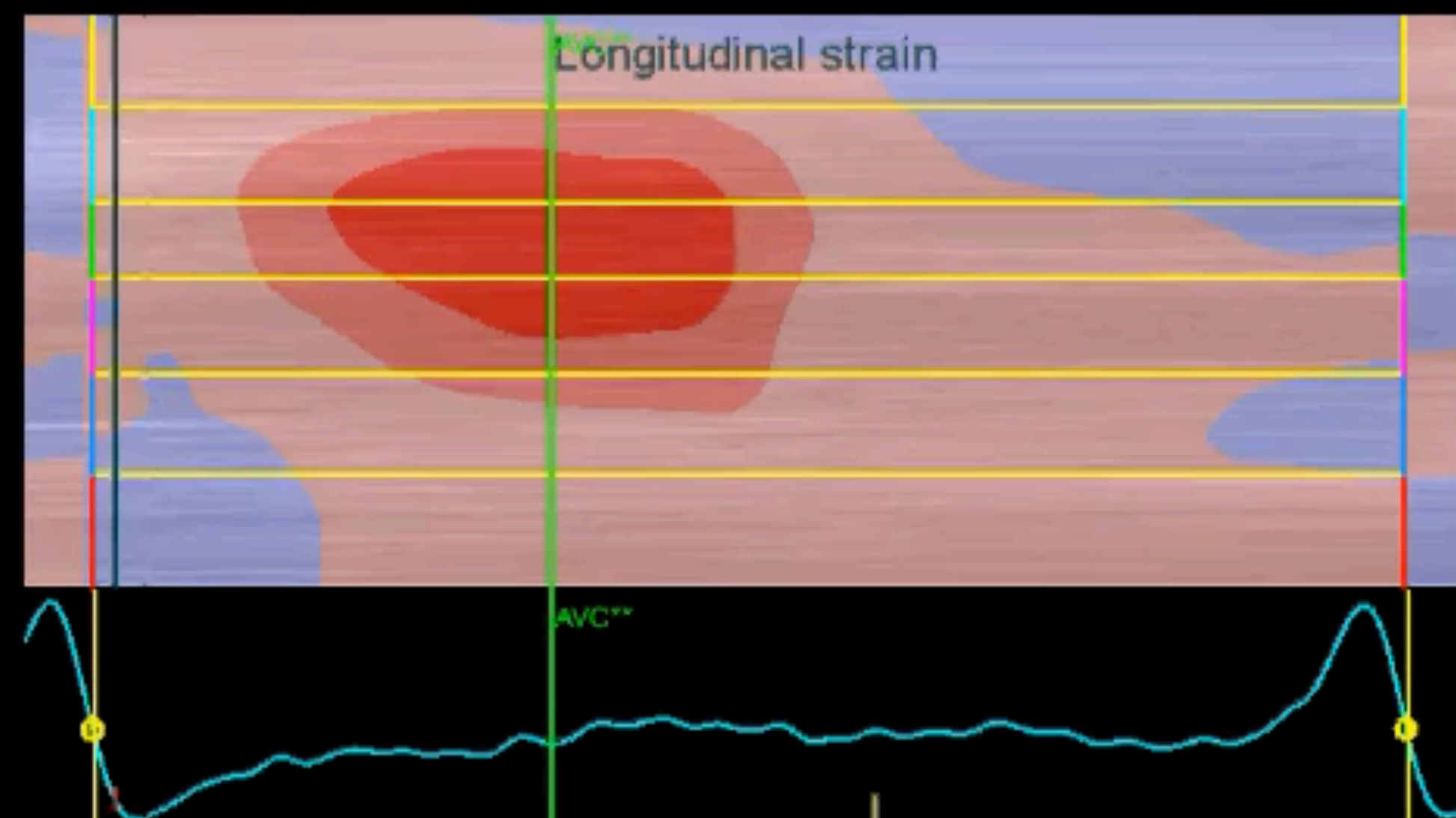


LAT

20
-20
%

Click in segment to approve/reject

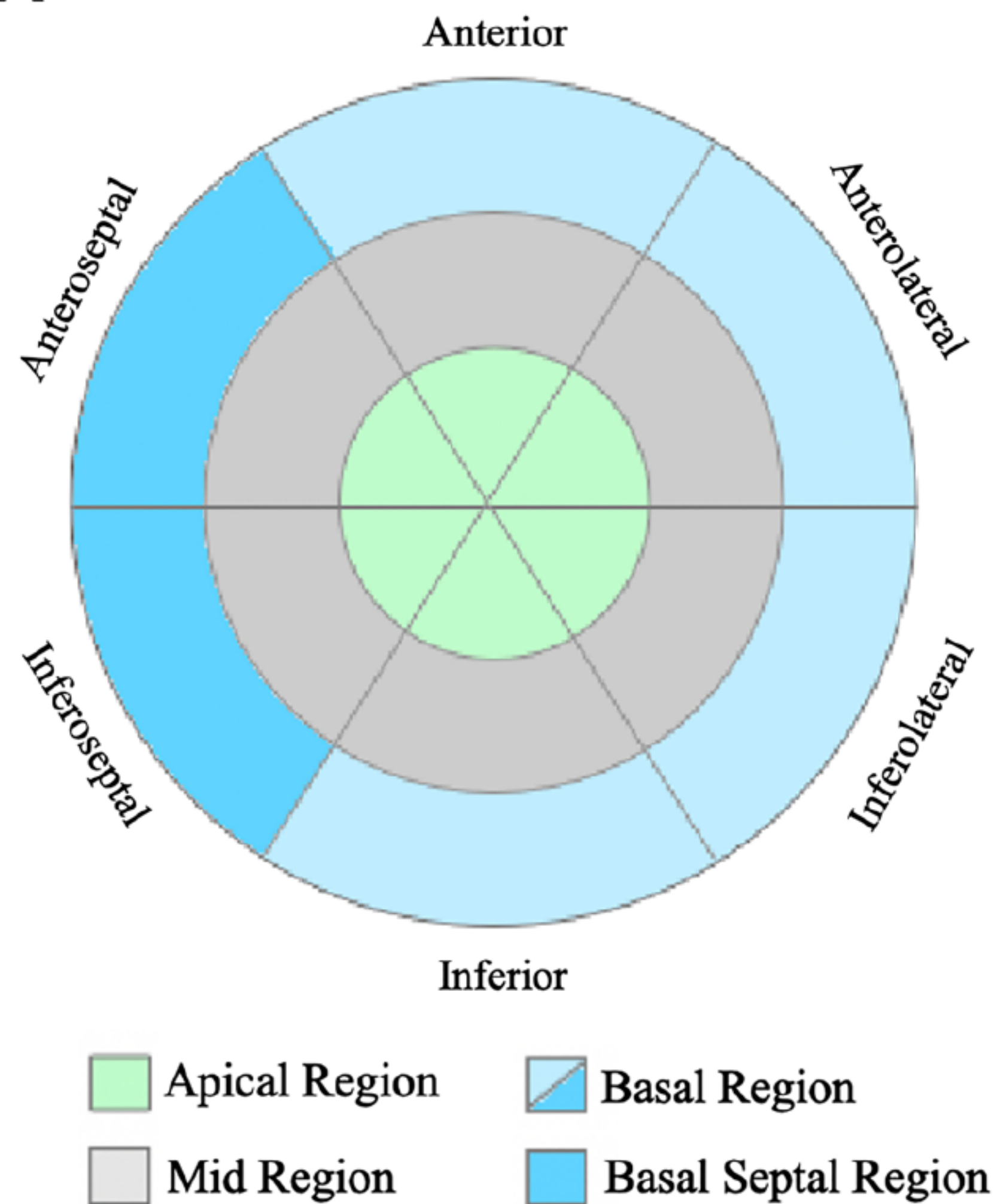
Values are temporary



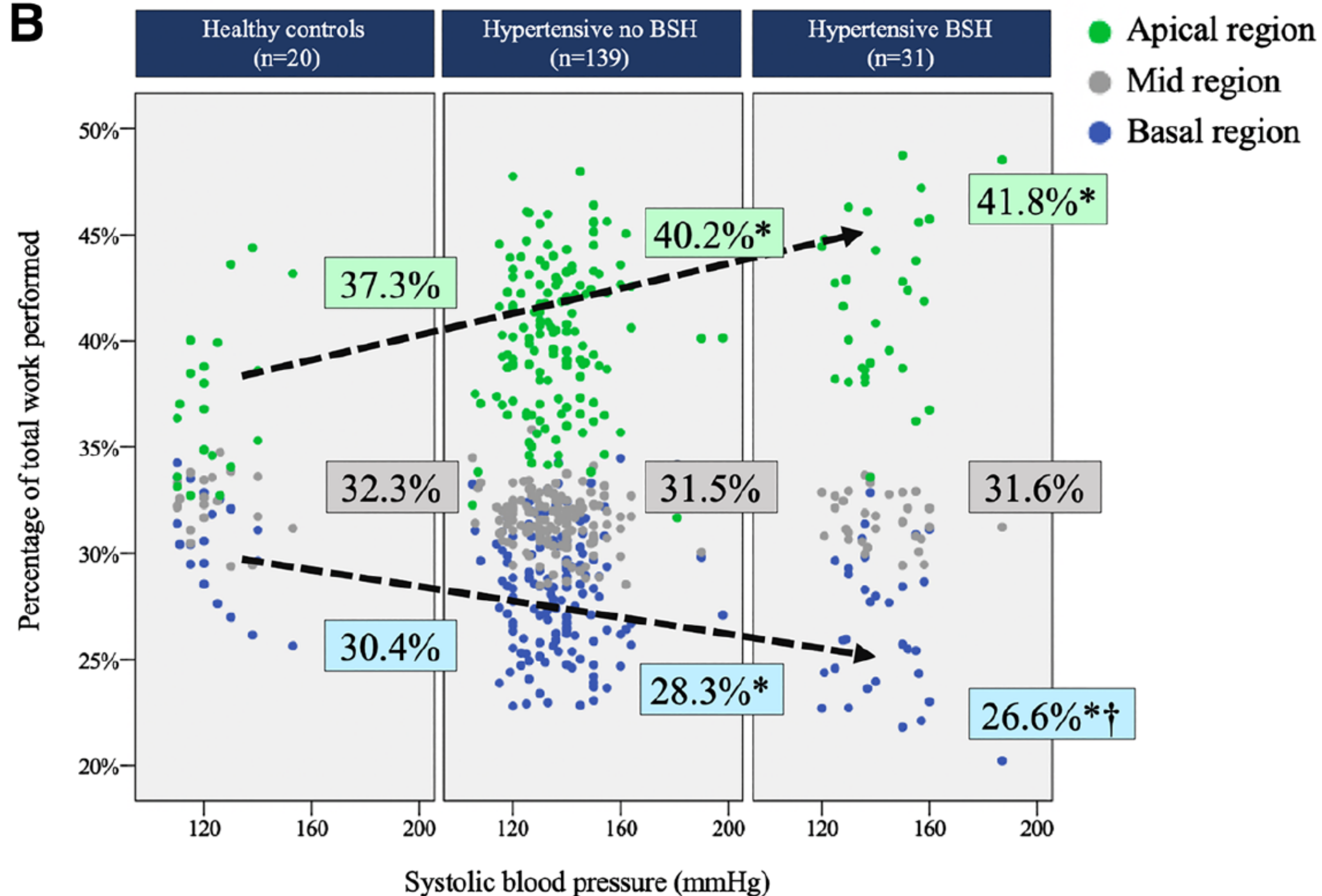
Distribution of myocardial work in arterial hypertension: insights from non-invasive left ventricular pressure-strain relations

Filip Loncaric¹ · Maciej Marciniak² · Loredana Nunno^{1,3} · Maria Mimbreno^{1,3} · Joao F. Fernandes² · Dora Fabijanovic⁴ · Laura Sanchis^{1,3} · Adelina Doltra^{1,3} · Silvia Montserrat^{1,3,5} · Maja Cikes⁴ · Pablo Lamata² · Bart Bljens^{1,6} · Marta Sitges^{1,3,5}

A



B

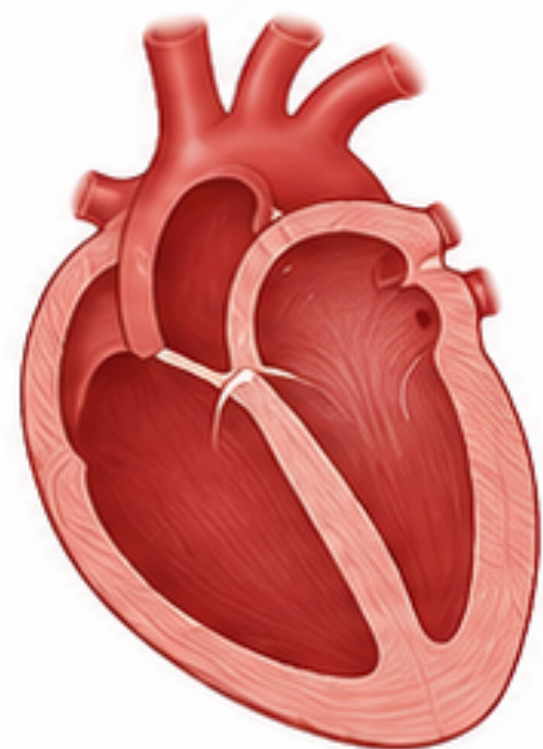


* - $P < 0.005$ versus healthy controls

† - $P < 0.005$ versus HTN patients without BSH

Reduced GLS with a base-to-apex gradient due to pressure and/or volume overload

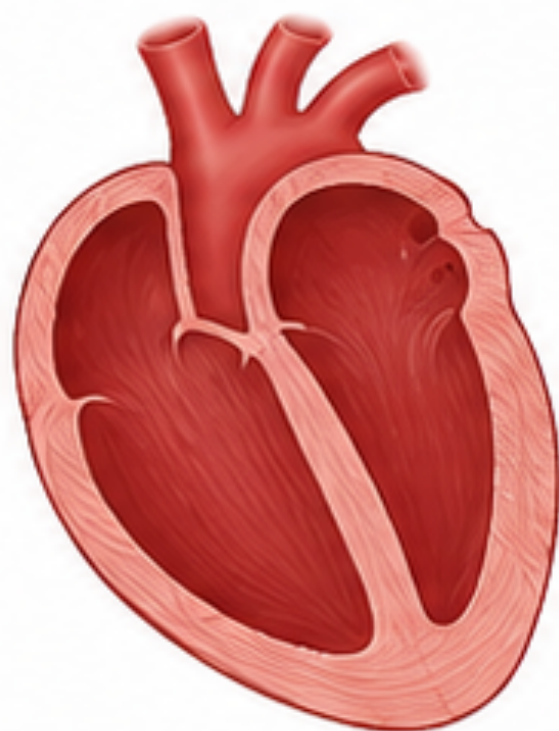
Pressure overload



Example:
aortic stenosis

Increased
pressure load

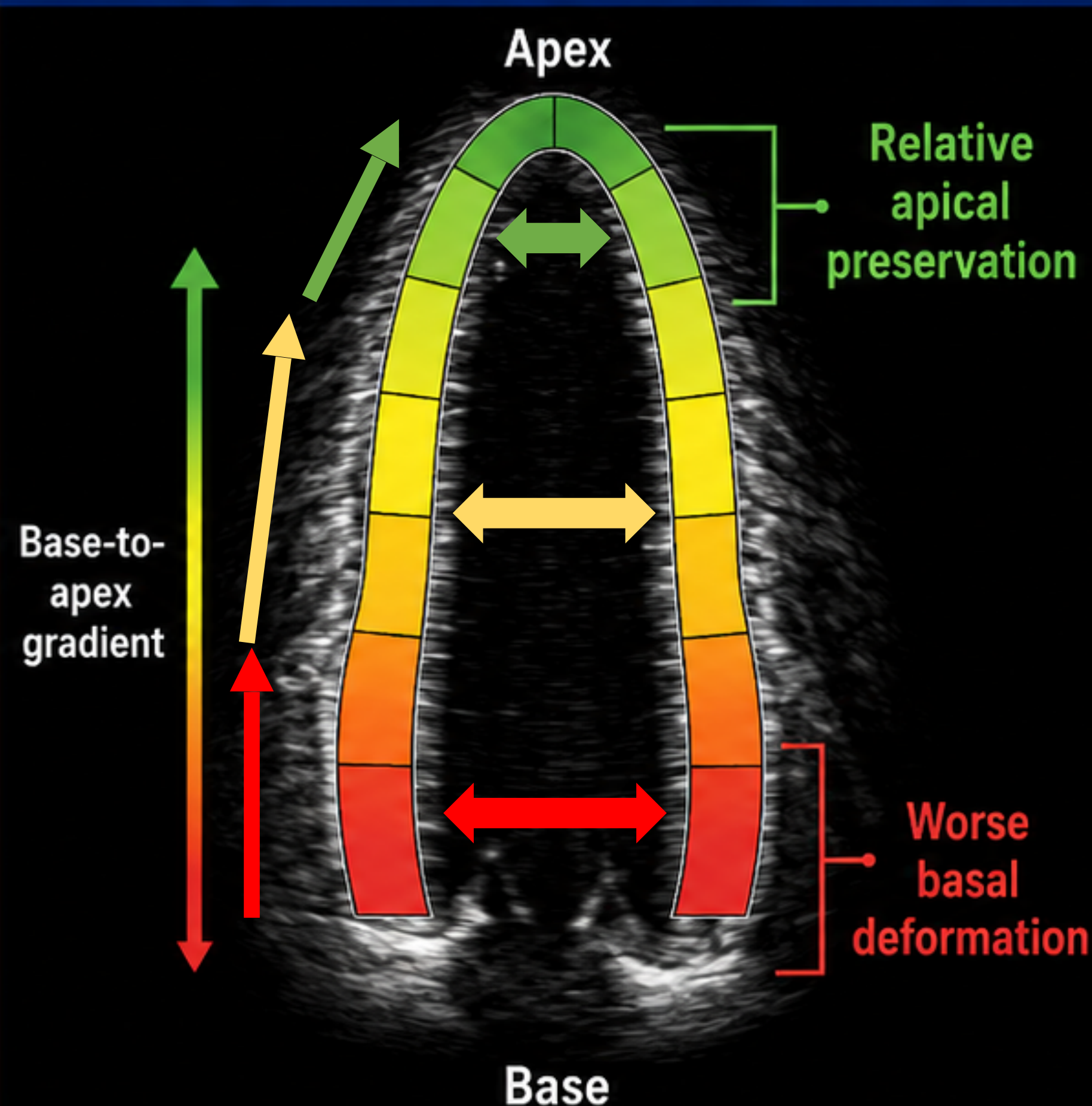
Volume overload



Example:
mitral regurgitation

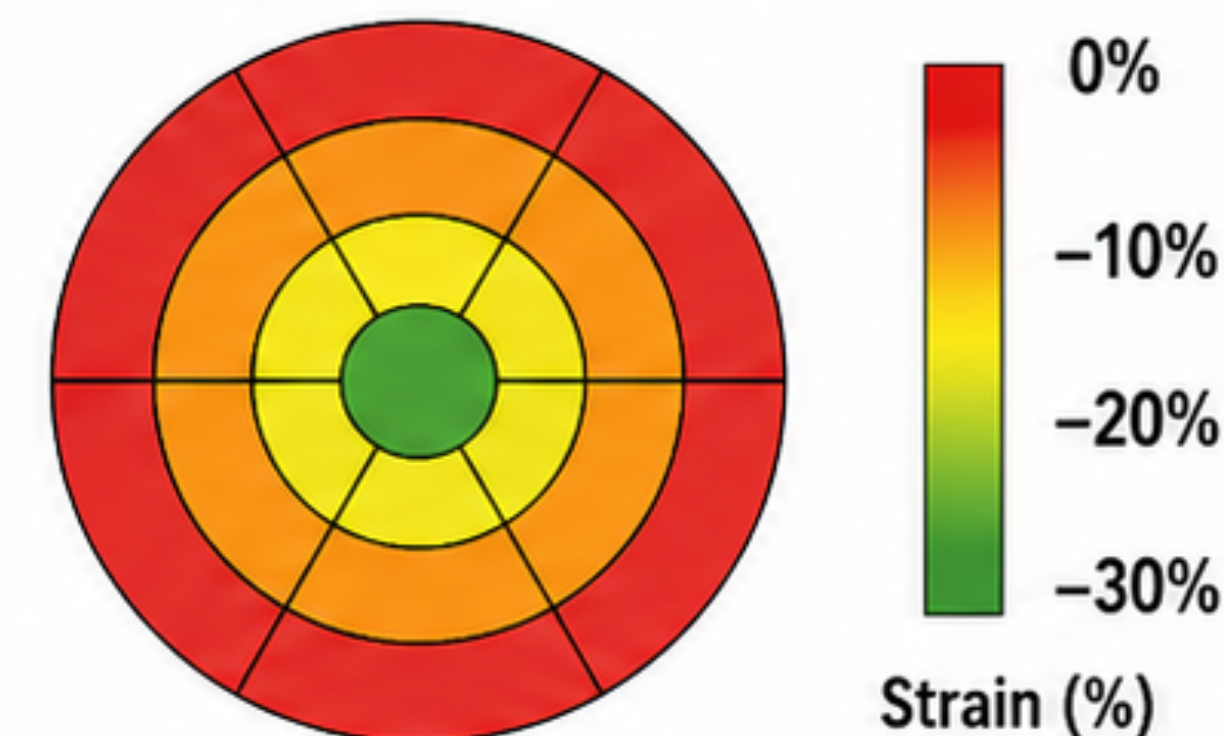
Increased
volume load

Longitudinal strain in the apical view



Summary

1) Longitudinal strain bull's-eye



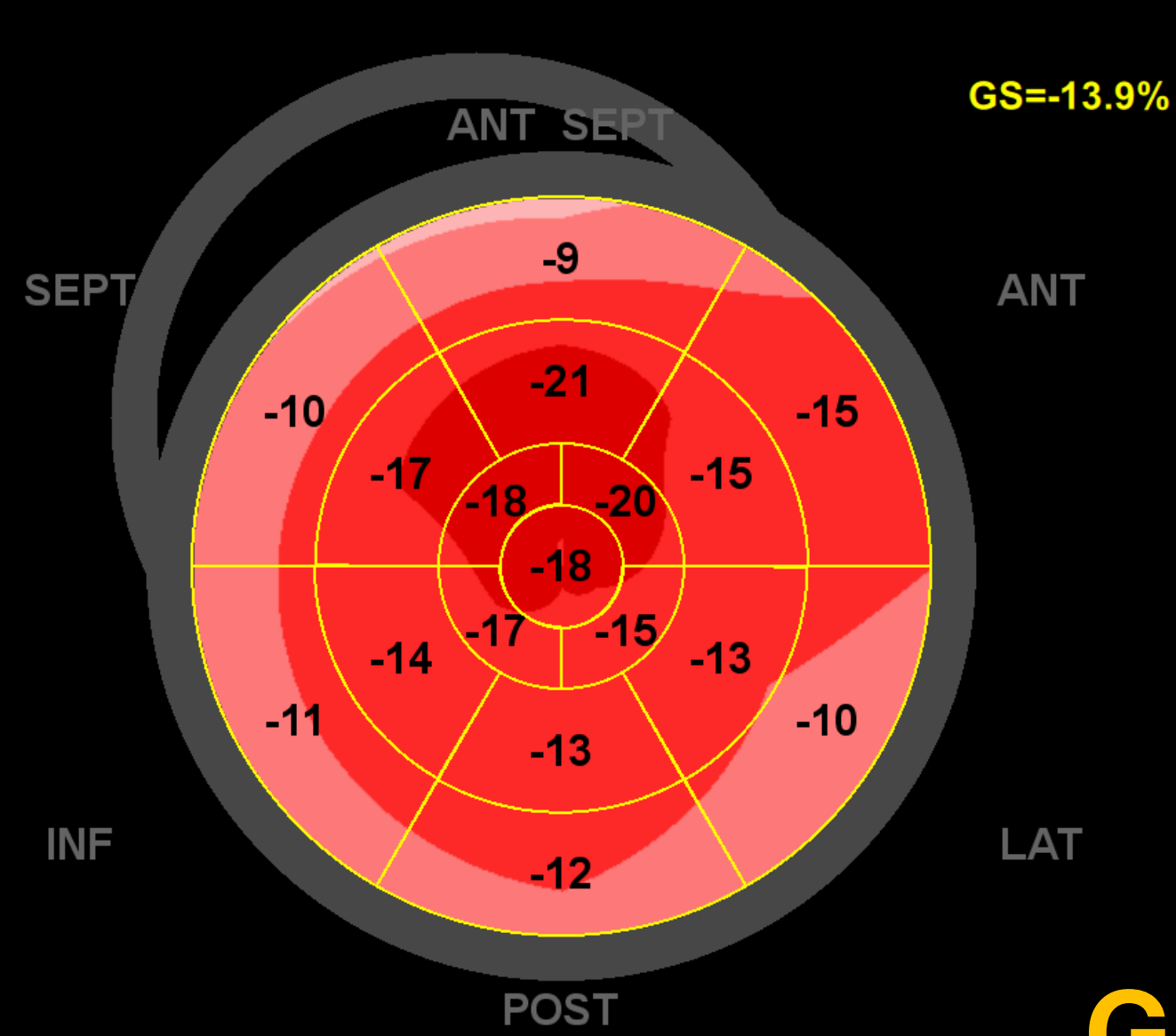
2) Example strain values by level

Basal	-10%
Mid	-15%
Apical	-20%

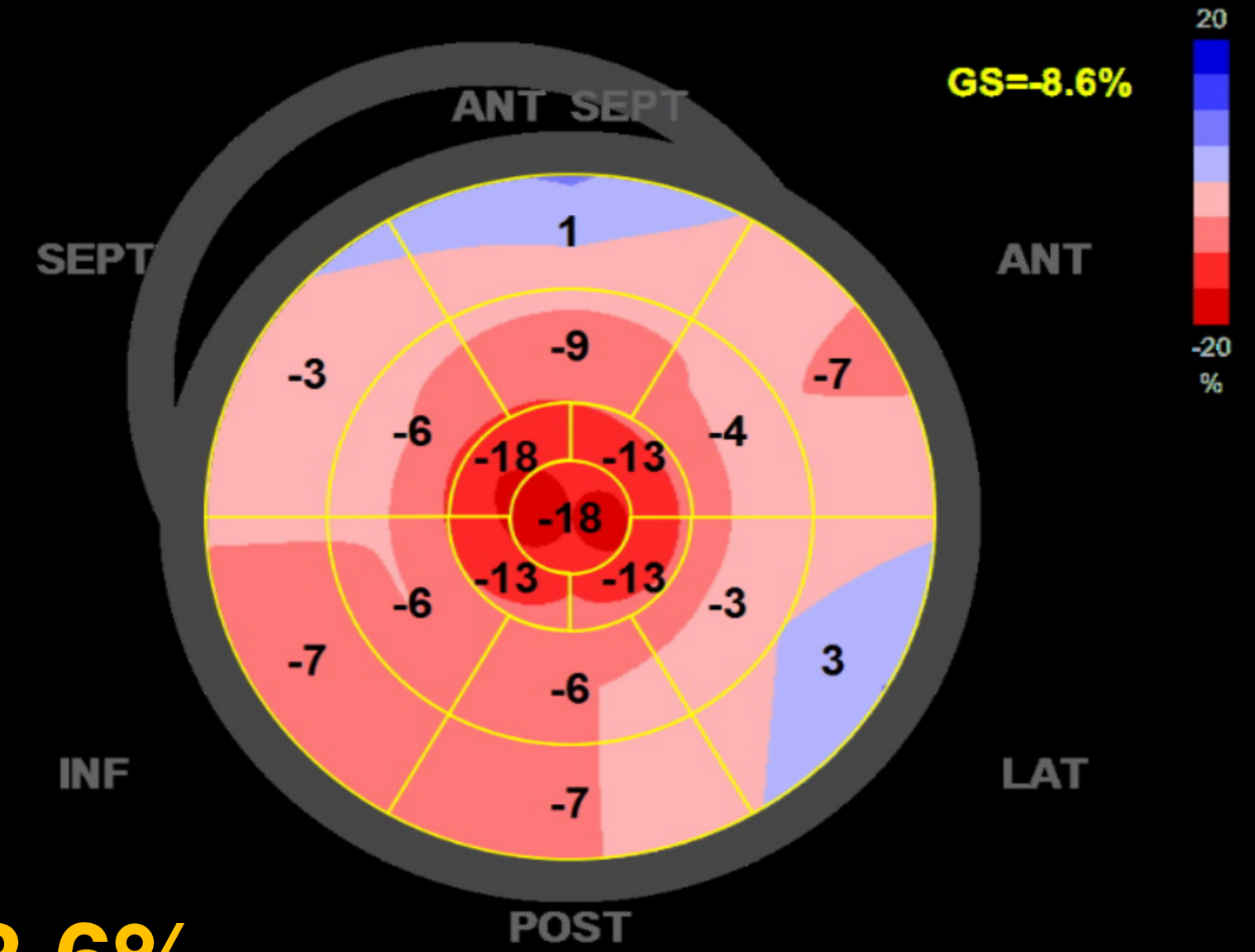
Global GLS = -15%



Pressure and/or volume overload may reduce GLS, with greater impairment of basal segments and relative preservation of apical strain.

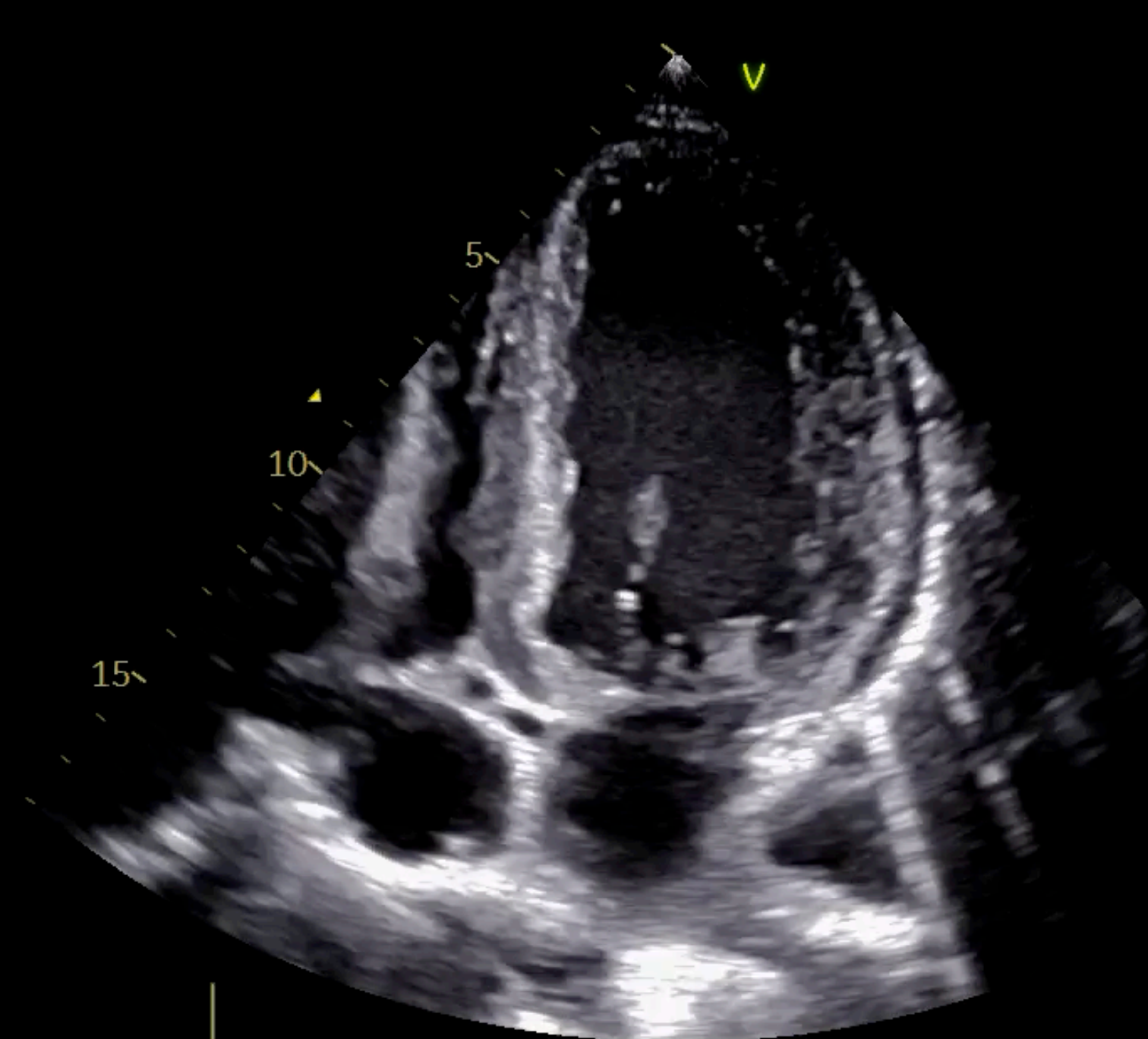


GLS -13.9%



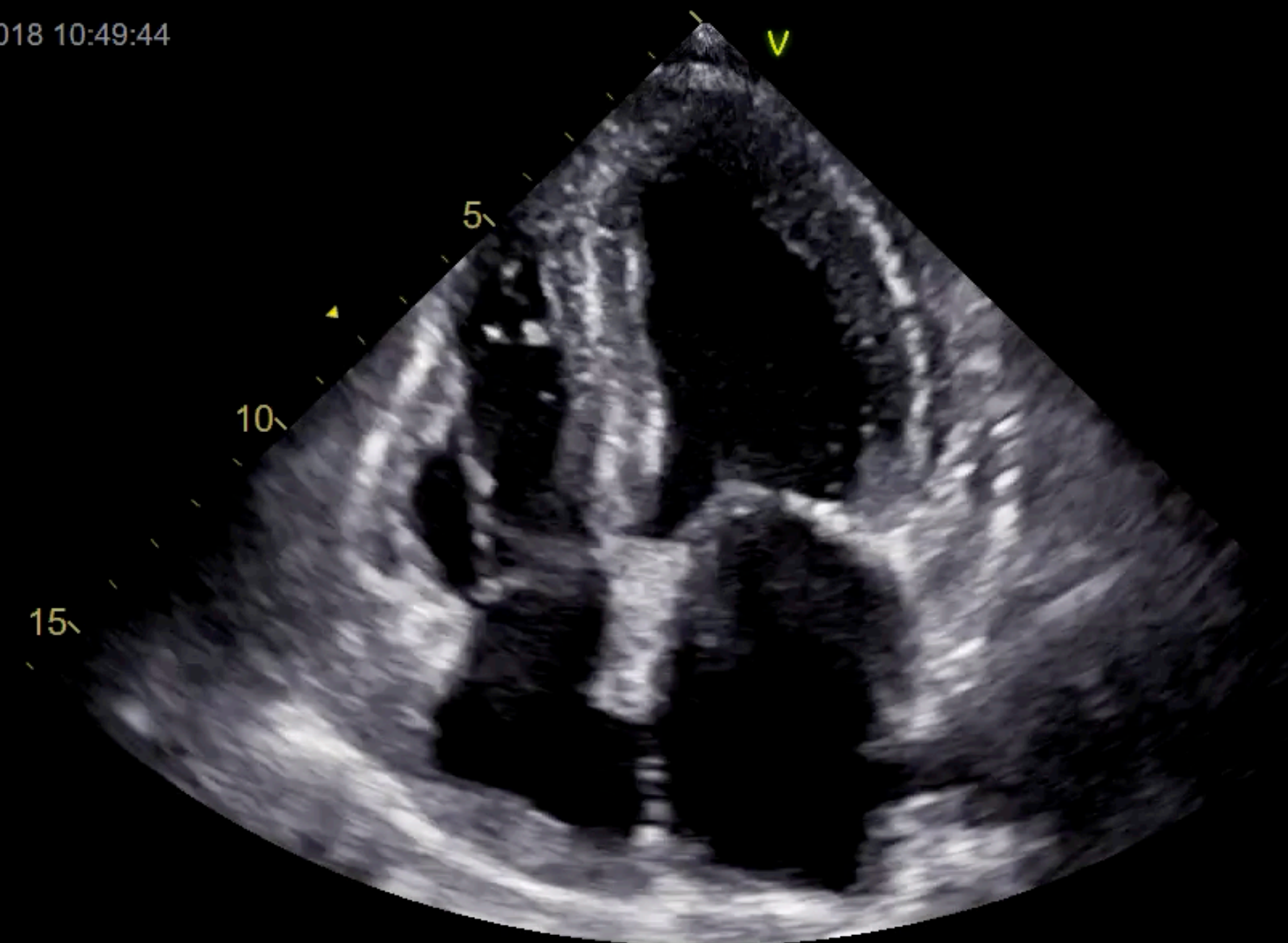
GLS -8.6%

28/02/2019 16:04:55

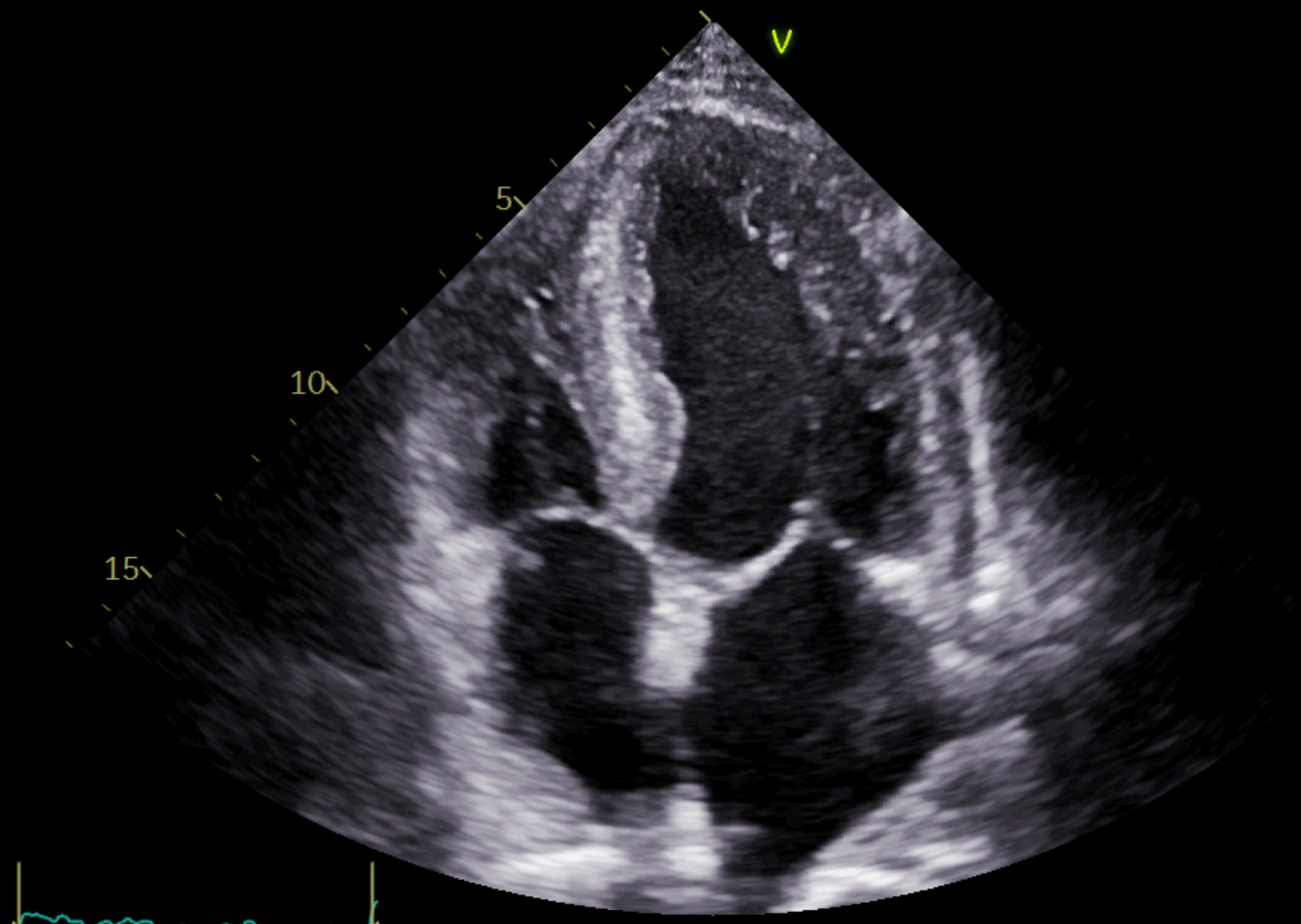


71
2:47HR

31/08/2018 10:49:44



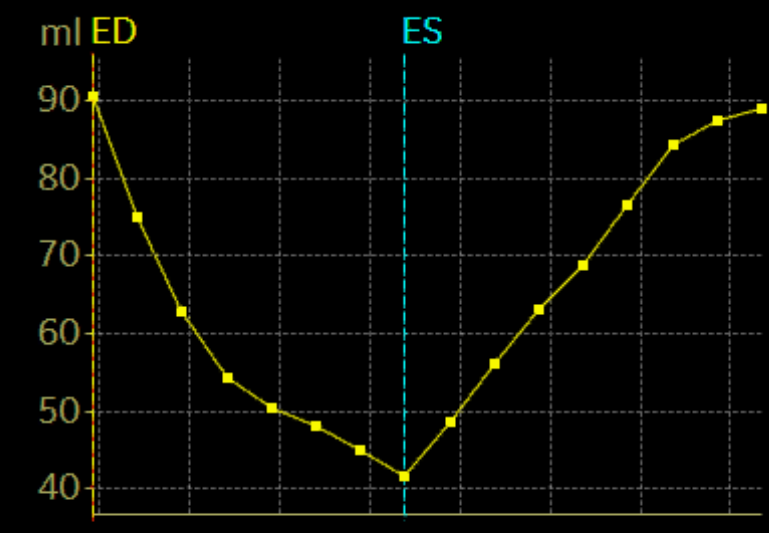
83
2:14HR

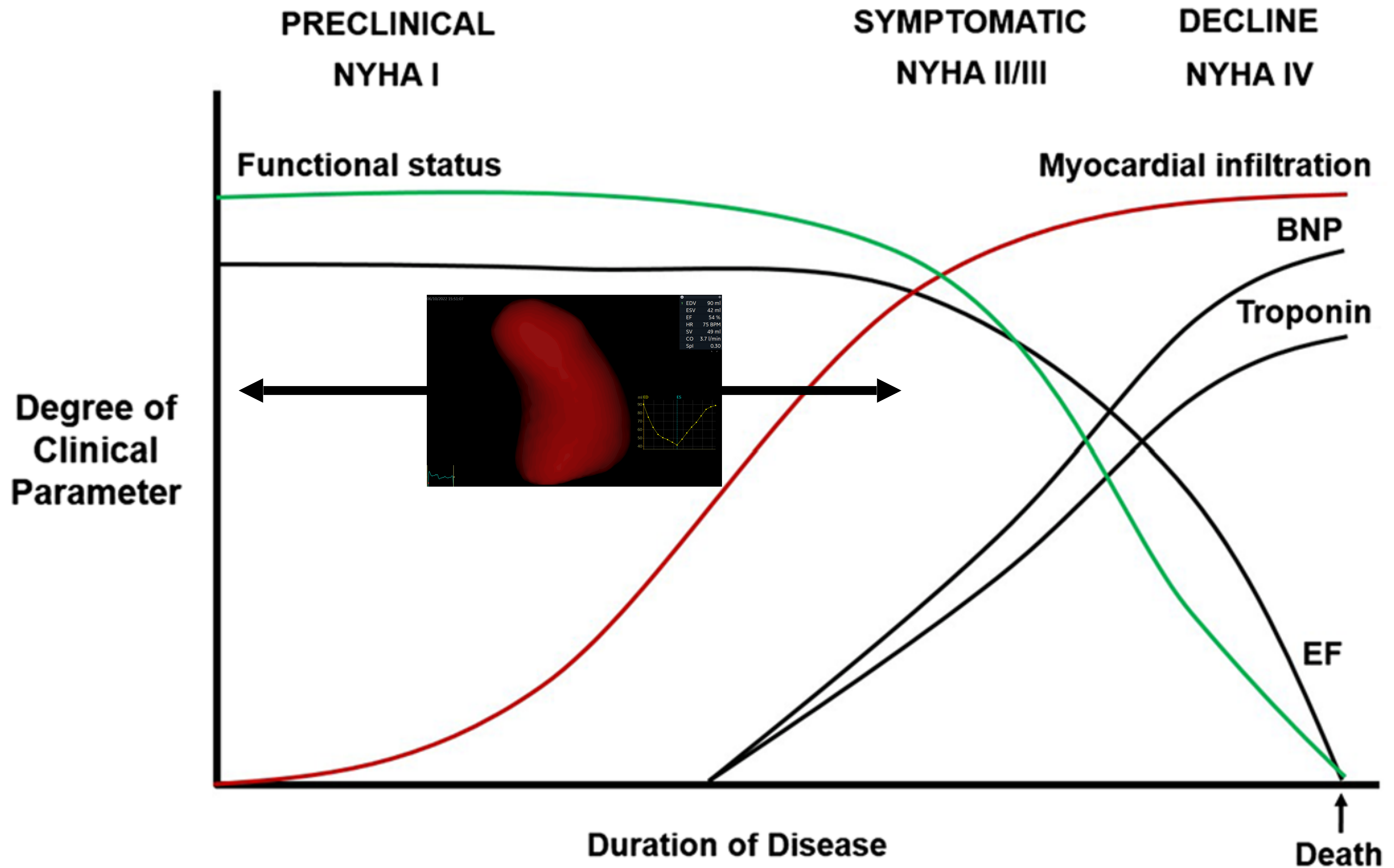


74
6:52HR



EDV	90 ml
ESV	42 ml
EF	54 %
HR	75 BPM
SV	49 ml
CO	3.7 l/min
Spl	0.30

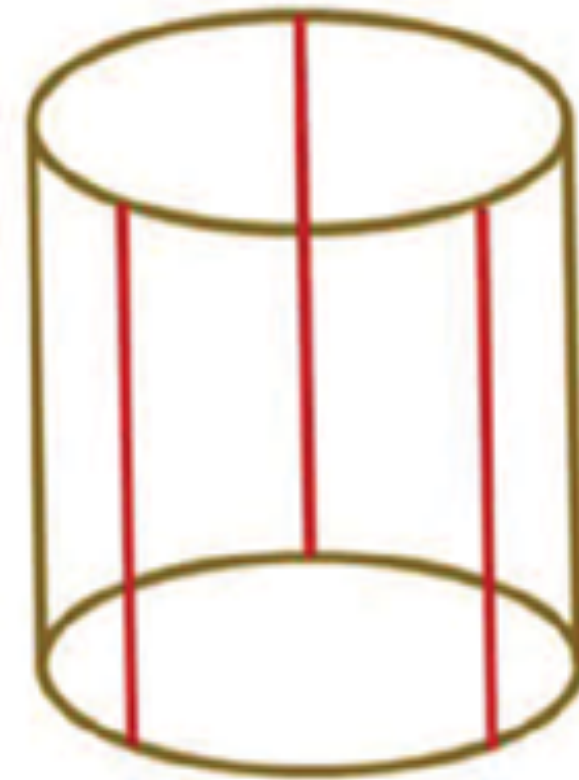




SYSTOLIC DYSFUNCTION – PRESERVED LVEF

A

Longitudinal
fibres



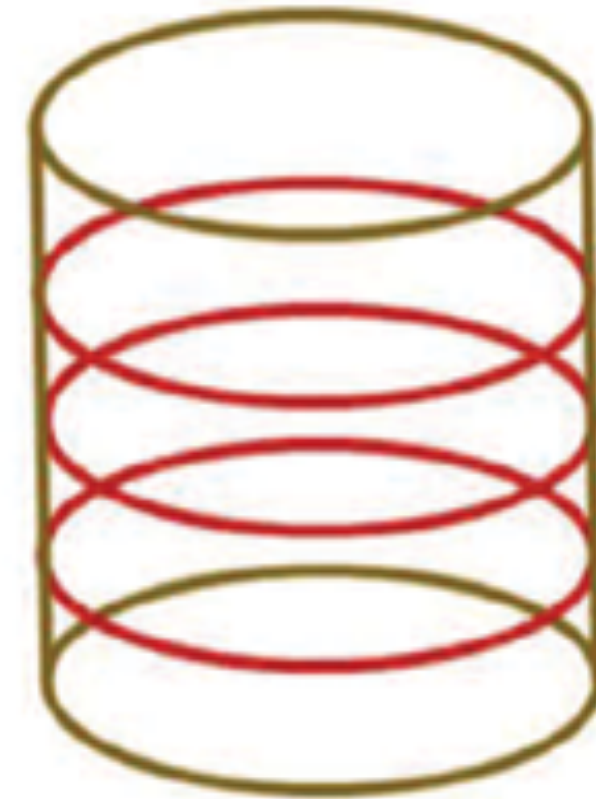
15% fibre
shortening



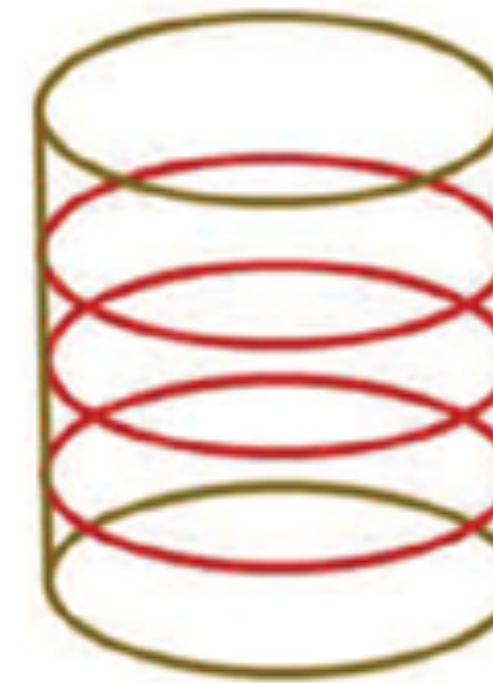
EF=15%

B

Circumferential
fibres



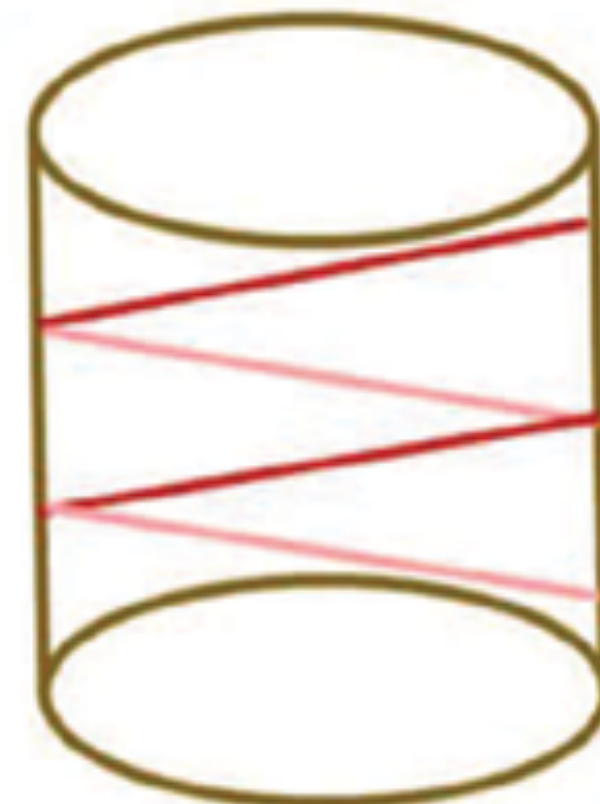
15% fibre
shortening



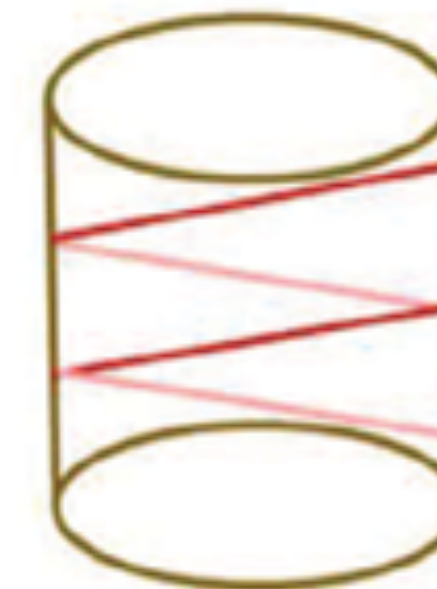
EF=30%

C

Spiral
fibres



15% fibre
shortening



EF≥60%

Echo Parameters for Differential Diagnosis in Cardiac Amyloidosis

A Head-to-Head Comparison of Deformation and Nondeformation Parameters

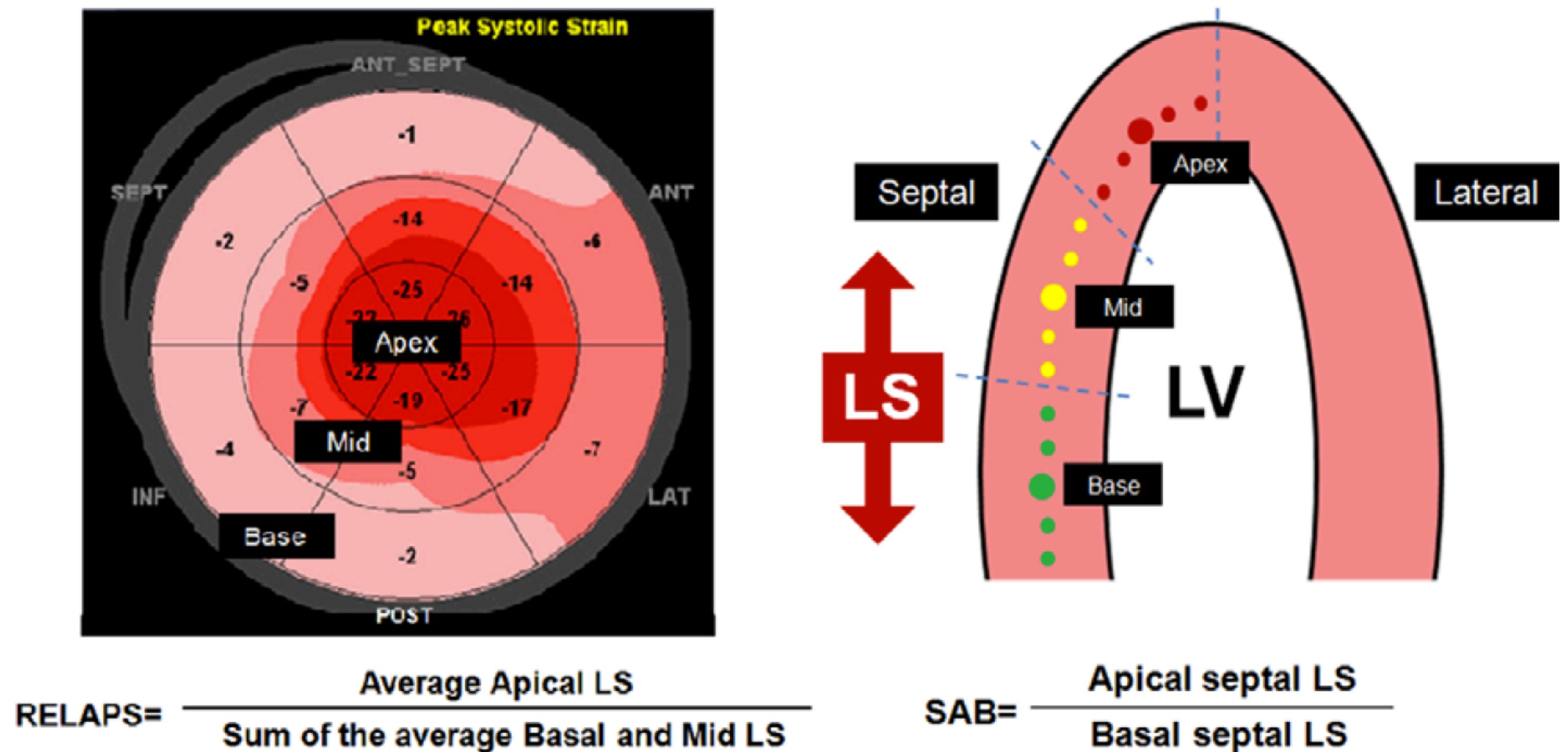
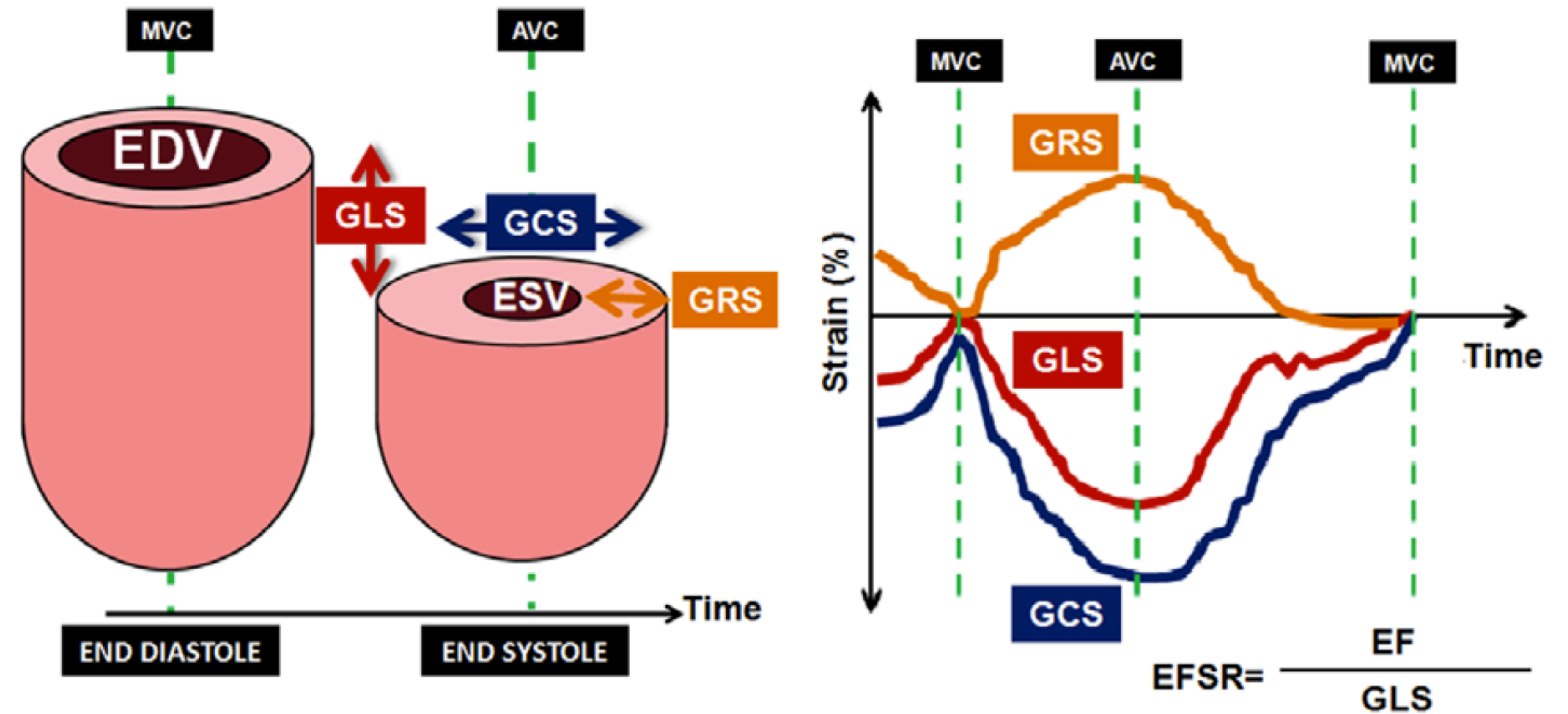
Efstathios D. Pagourelas, MD, PhD; Oana Mirea, MD, PhD; Jürgen Duchenne, MSc;
Johan Van Cleemput, MD, PhD; Michel Delforge, MD, PhD; Jan Bogaert, MD, PhD;
Tatyana Kuznetsova, MD, PhD; Jens-Uwe Voigt, MD, PhD

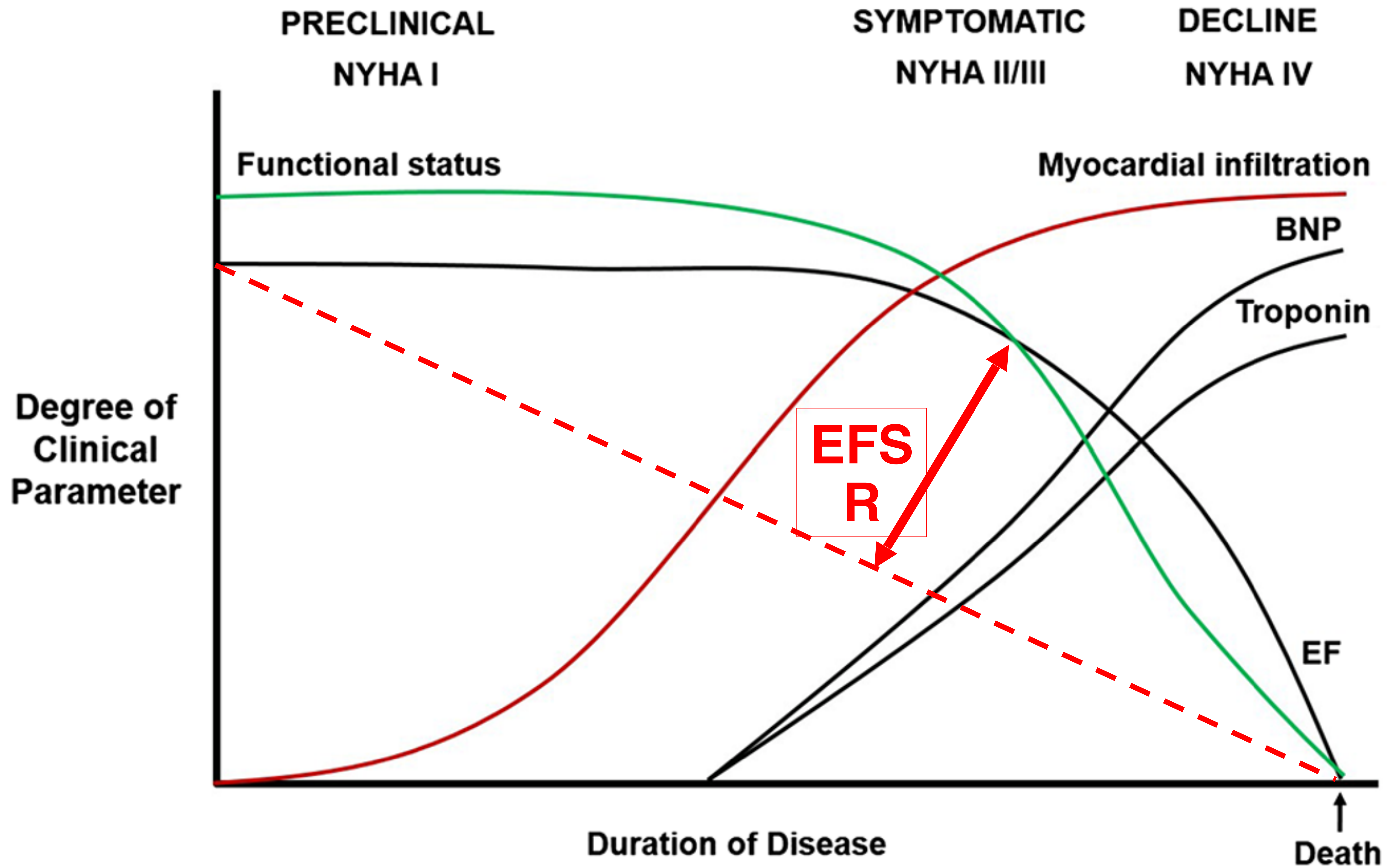
Novel deformation parameters

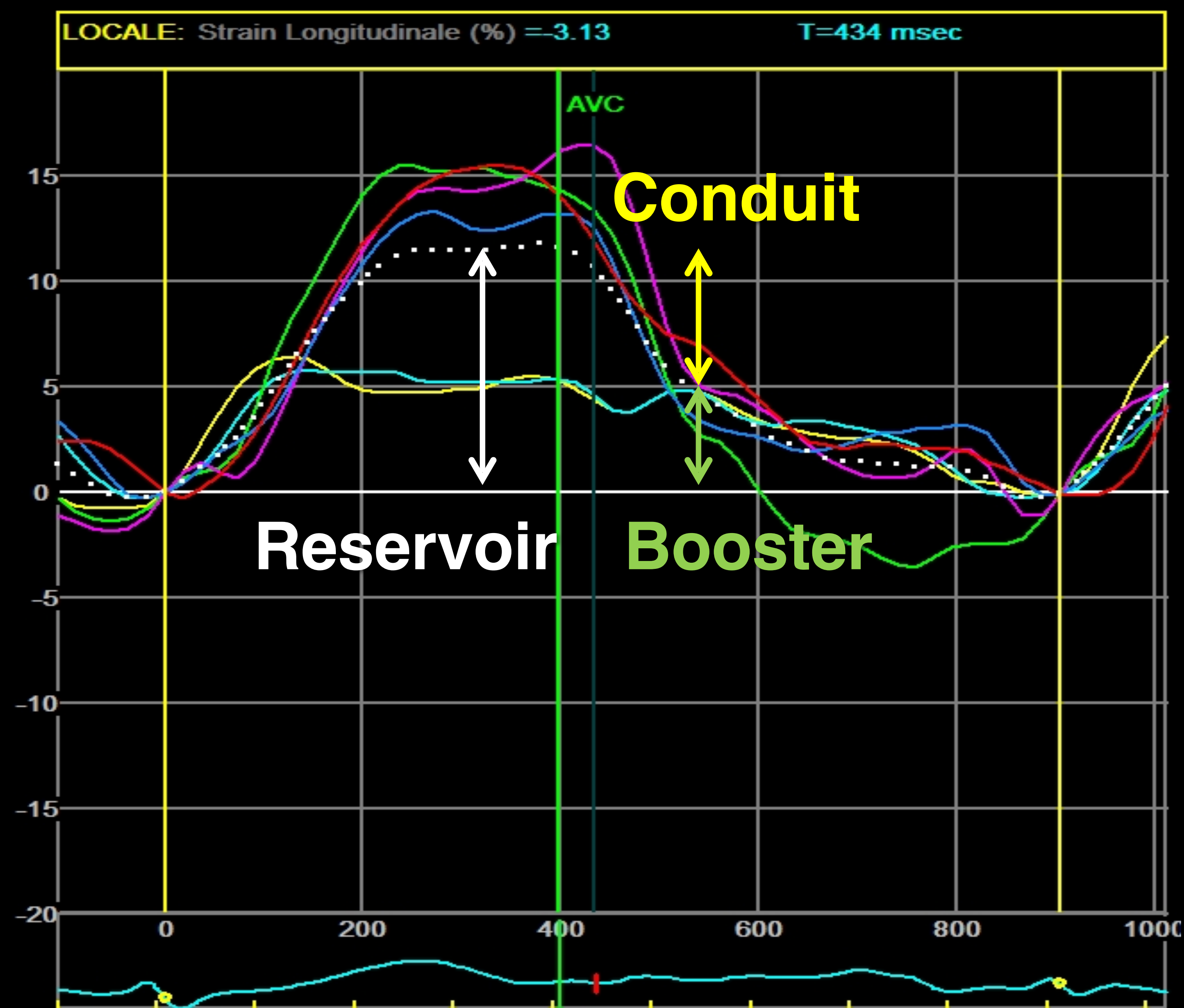
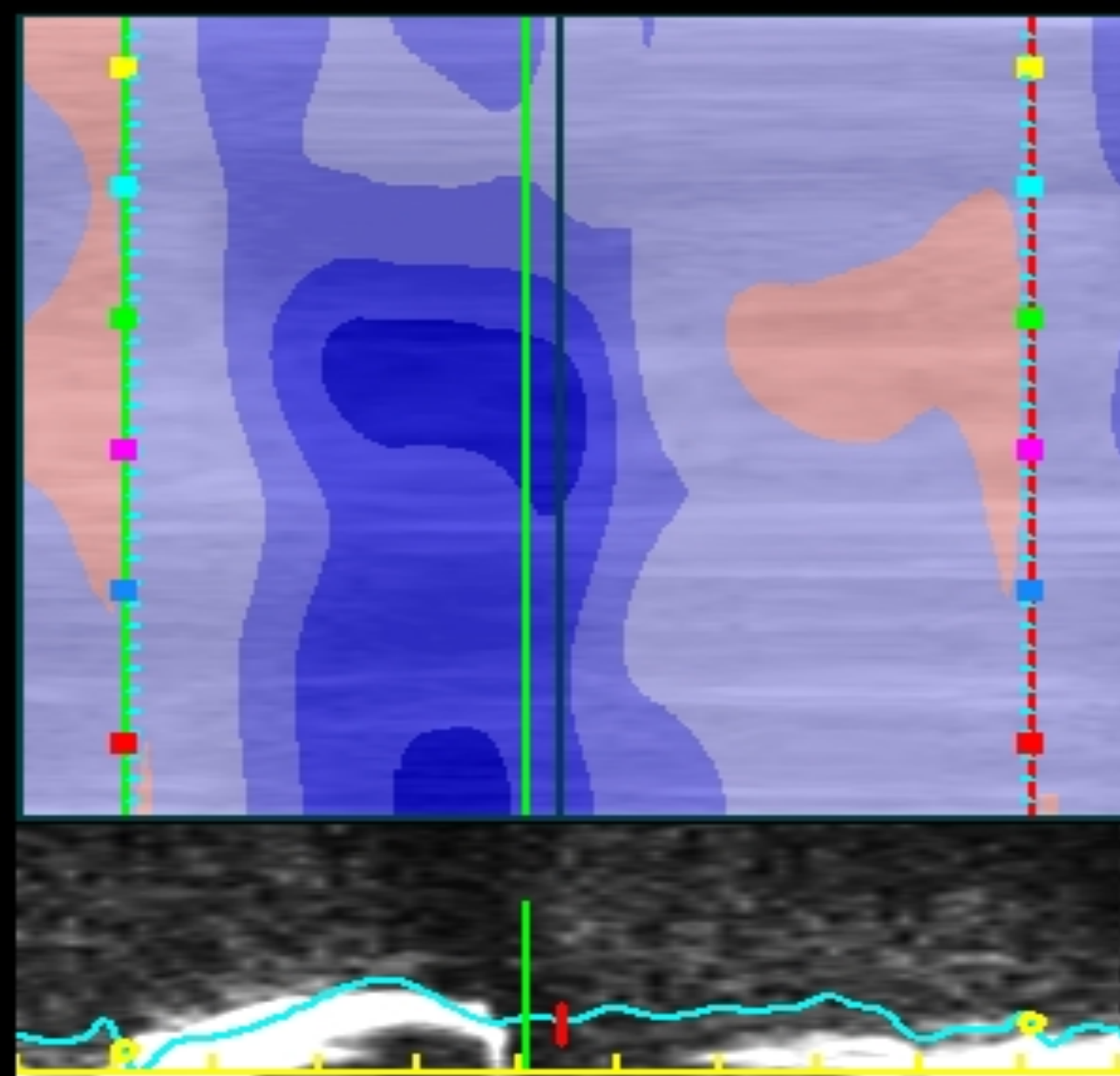
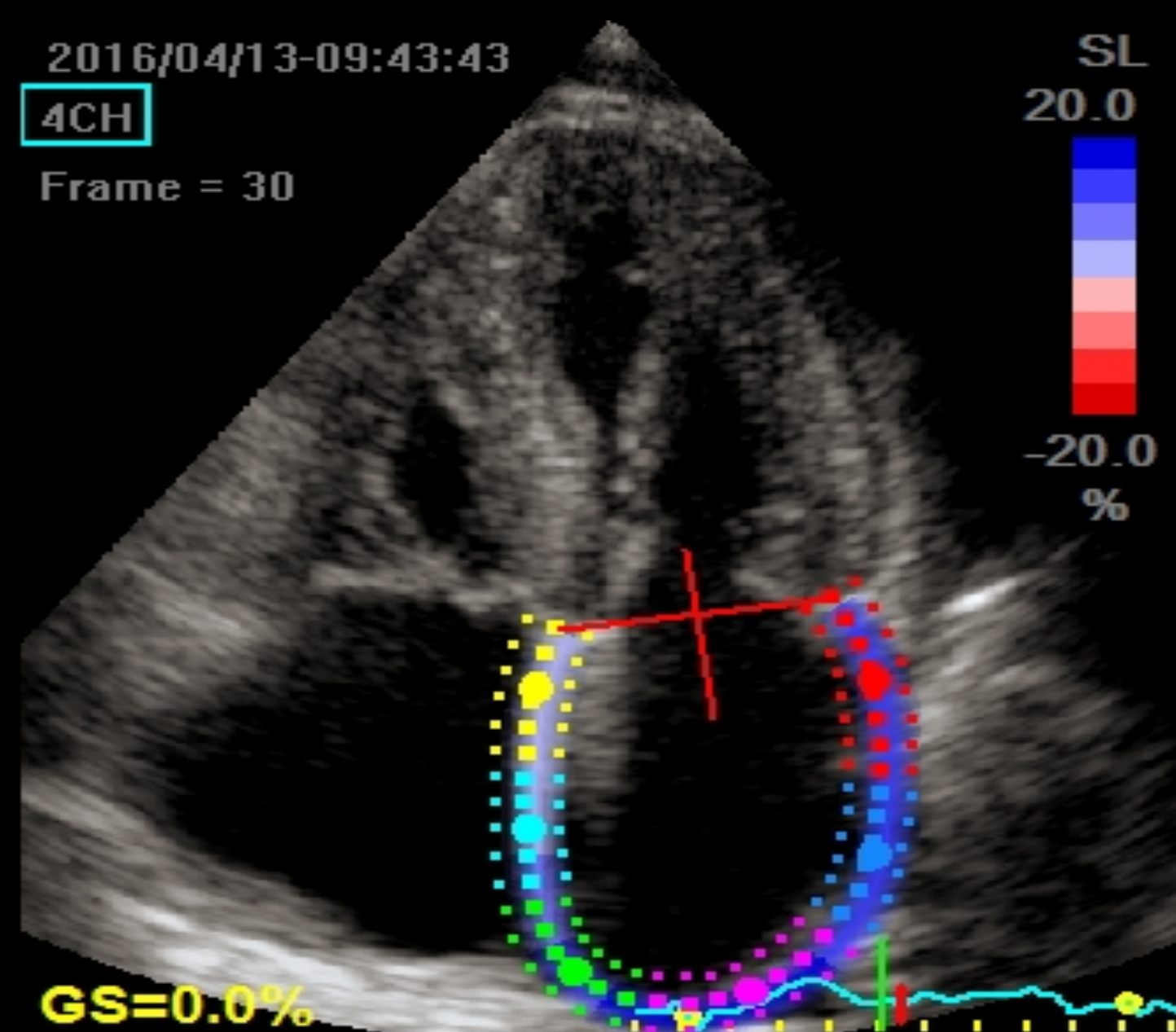
EFSR, EF/Strain ratio

RELAPS, Relative Apical Sparing

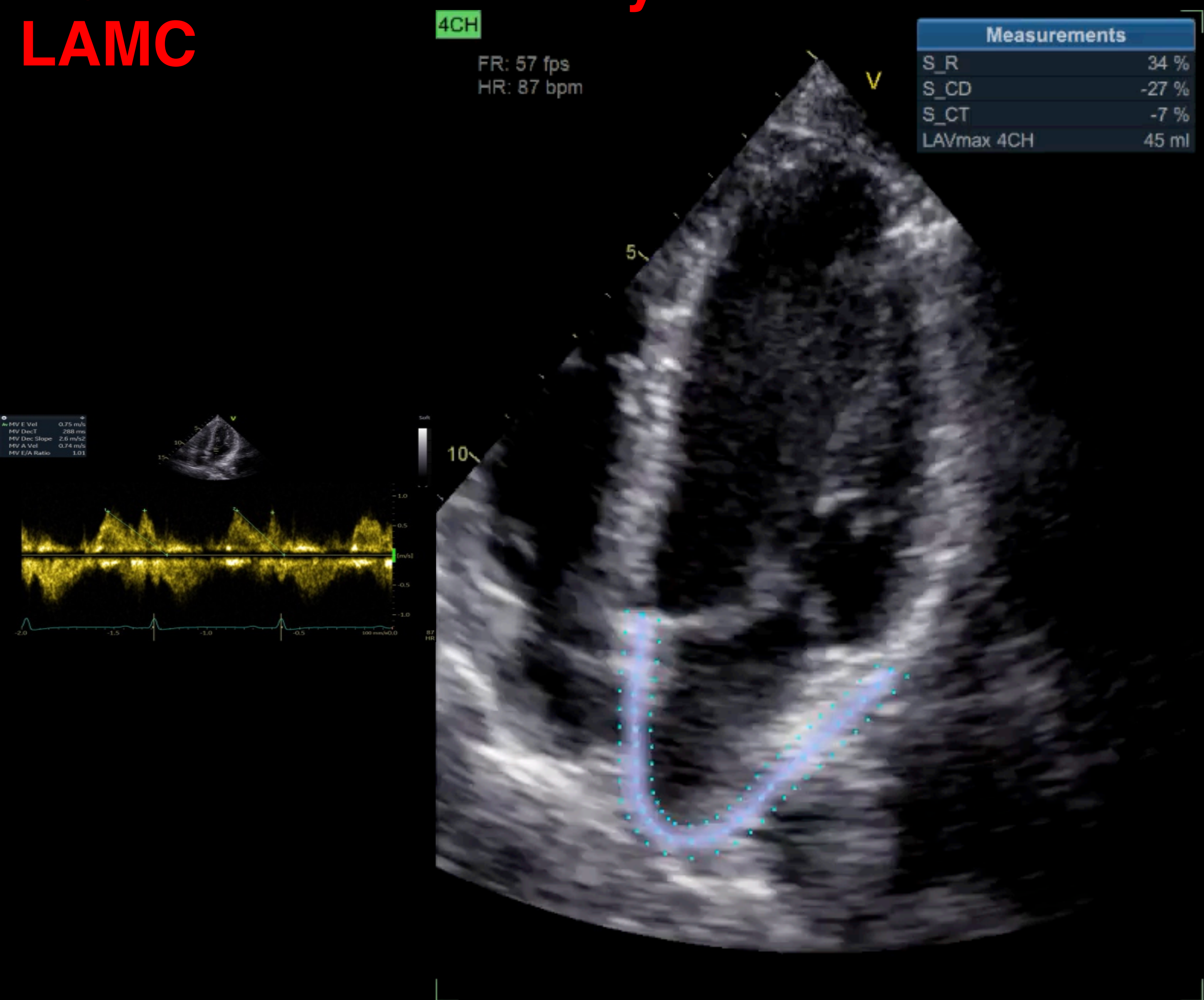
SAB, Septal Apical-to-Basal ratio



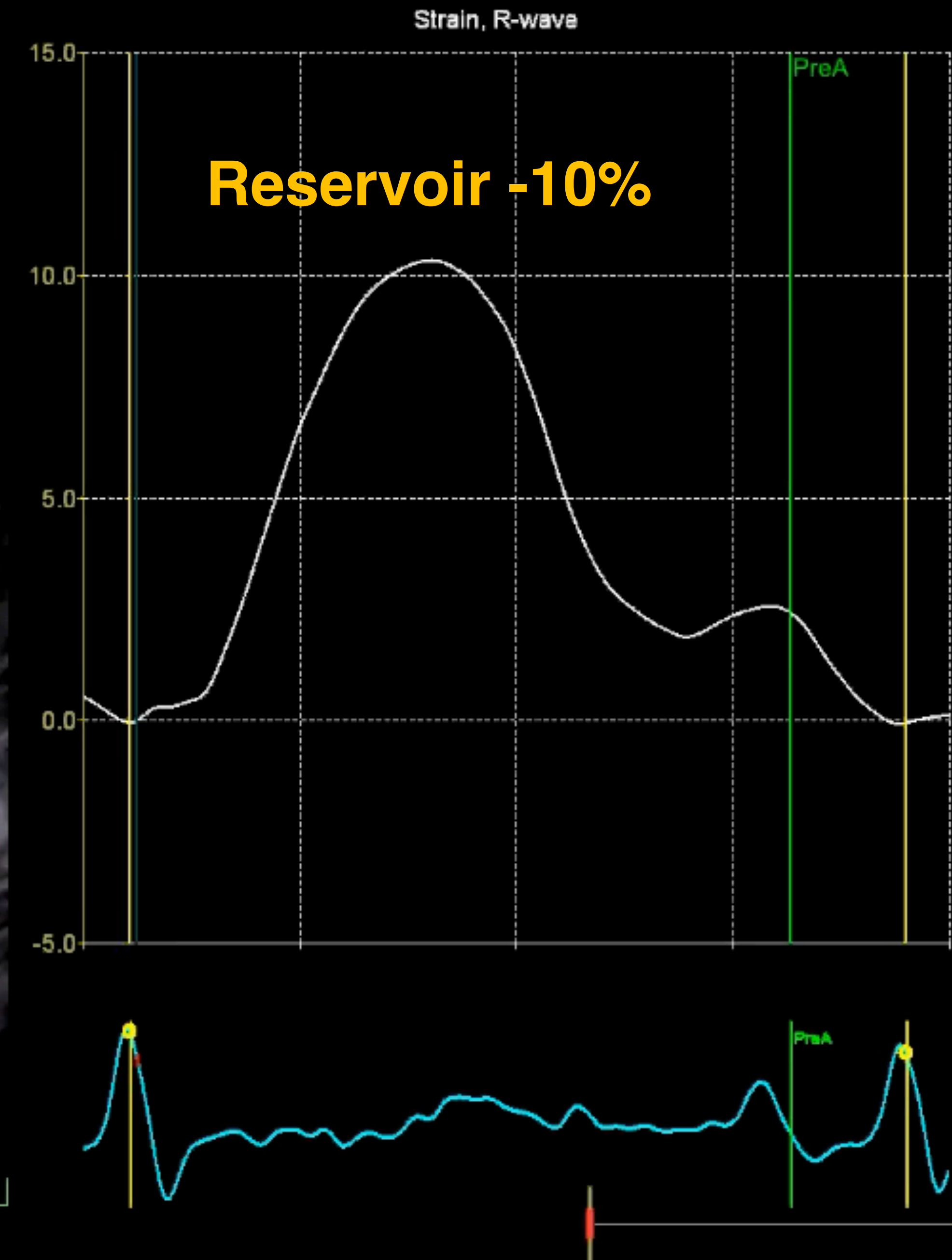
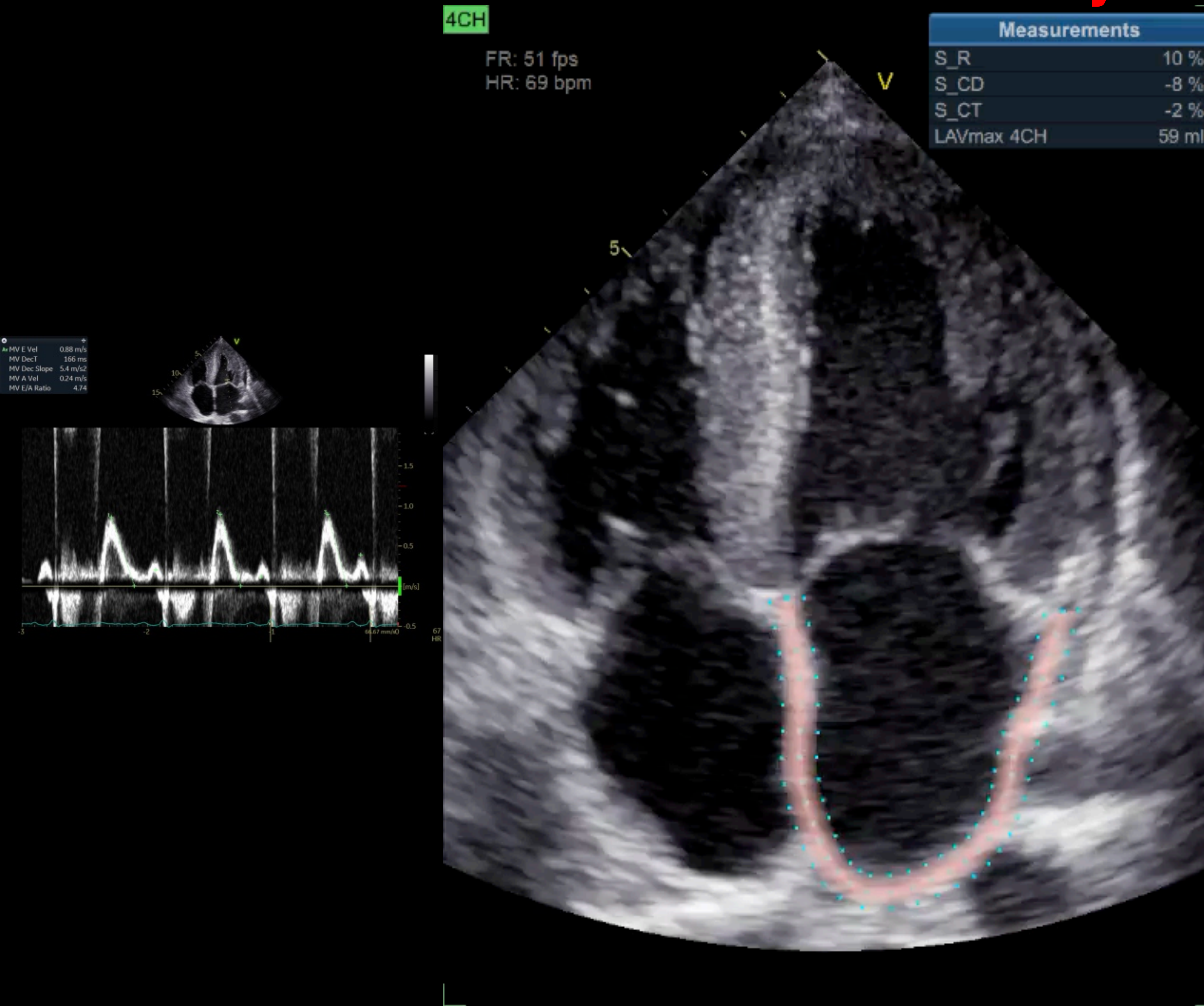




NORMAL – Sinus Rhythm with LAMC



CARDIAC AMYLOIDOSIS – Sinus Rhythm with LAMC



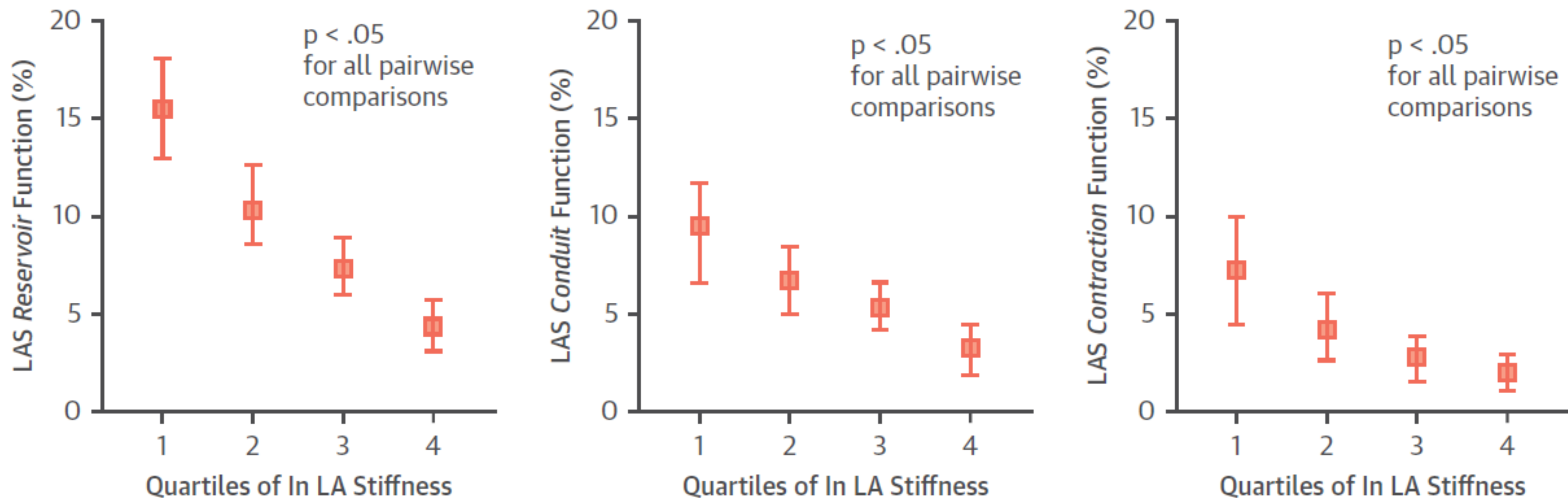
Clinical Importance of Left Atrial Infiltration in Cardiac Transthyretin Amyloidosis



Francesco Bandera, MD, PhD,^{a,b,*} Raffaele Martone, MD,^{c,*} Liza Chacko, MD,^d Sharmananthan Ganesanathan, MS,^d Janet A. Gilbertson, CSci,^d Markella Ponticos, PhD,^d Thirusha Lane, RN, PhD,^d Ana Martinez-Naharro, MD, PhD,^d Carol Whelan, MD,^d Cristina Quarta, MD, PhD,^d Dorota Rowczenio, PhD,^d Rishi Patel, MD,^d Yousuf Razvi, MD,^d Helen Lachmann, MD,^d Ashutosh Wechelakar, MD,^d James Brown, MD,^d Daniel Knight, MD,^d James Moon, MD,^e Aviva Petrie, PhD,^f Francesco Cappelli, MD,^c Marco Guazzi, MD, PhD,^{a,b} Luciano Potena, MD,^g Claudio Rapezzi, MD,^{h,i} Ornella Leone, MD,^g Philip N. Hawkins, MD, PhD,^d Julian D. Gillmore, MD, PhD,^{d,*} Marianna Fontana, MD, PhD^{d,*}

LA stiffness vs LA function

FIGURE 2 Left Atrial Reservoir, Conduit, and Contraction Function in Patients With ATTR-CM According to Increasing Left Atrial Stiffness

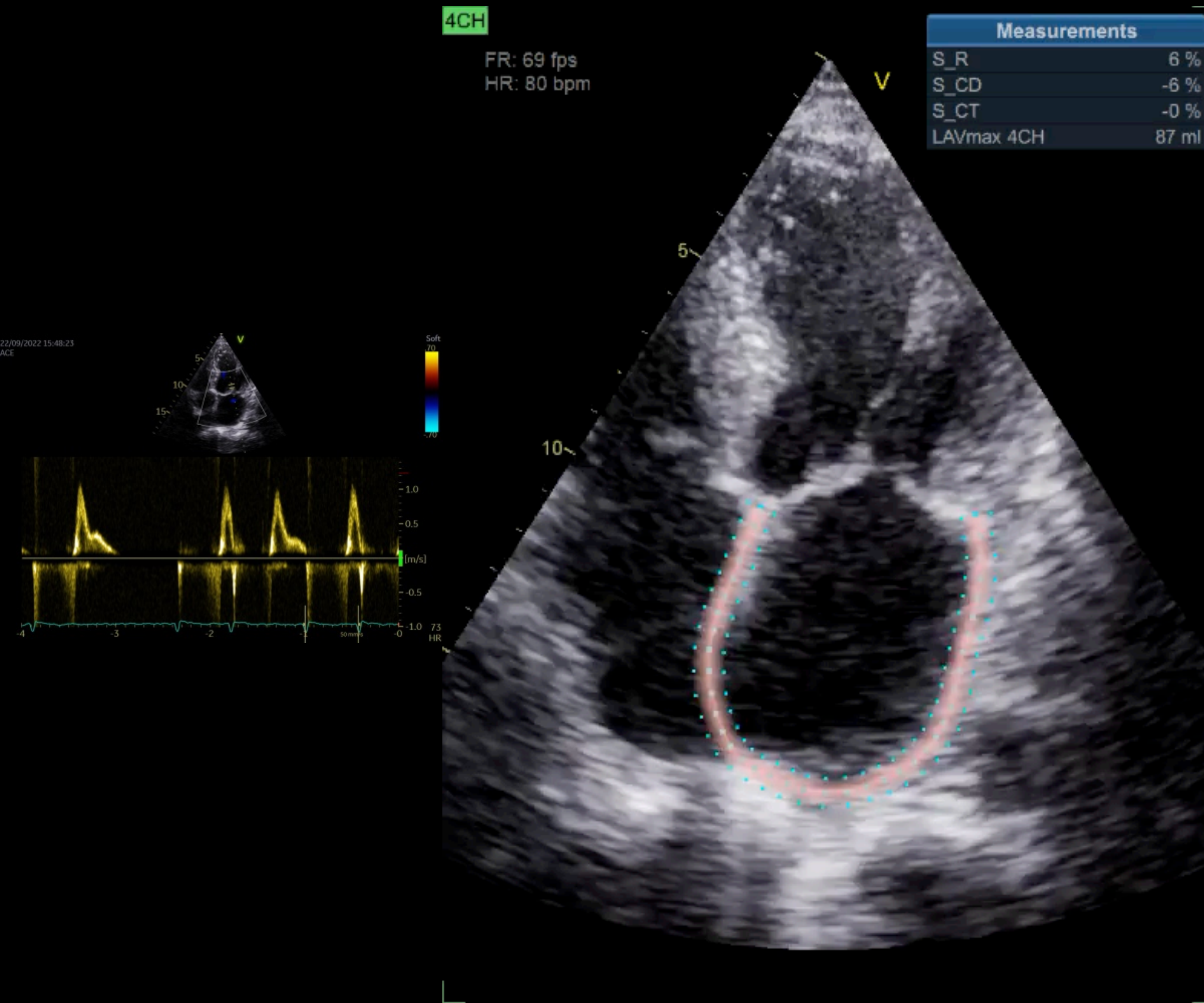


LA reservoir

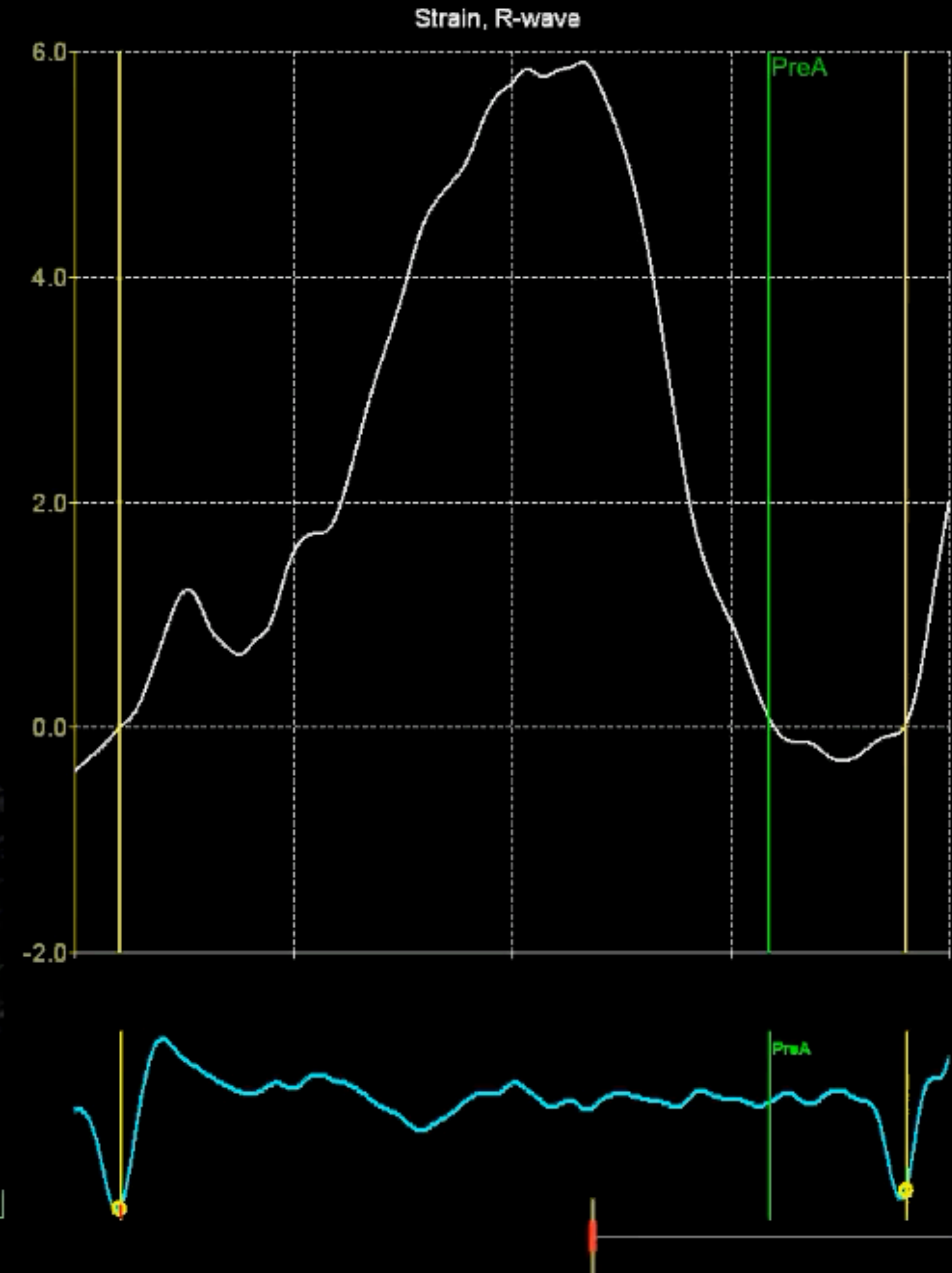
LA conduit

LA contraction

CARDIAC AMYLOIDOSIS – Atrial Fibrillation

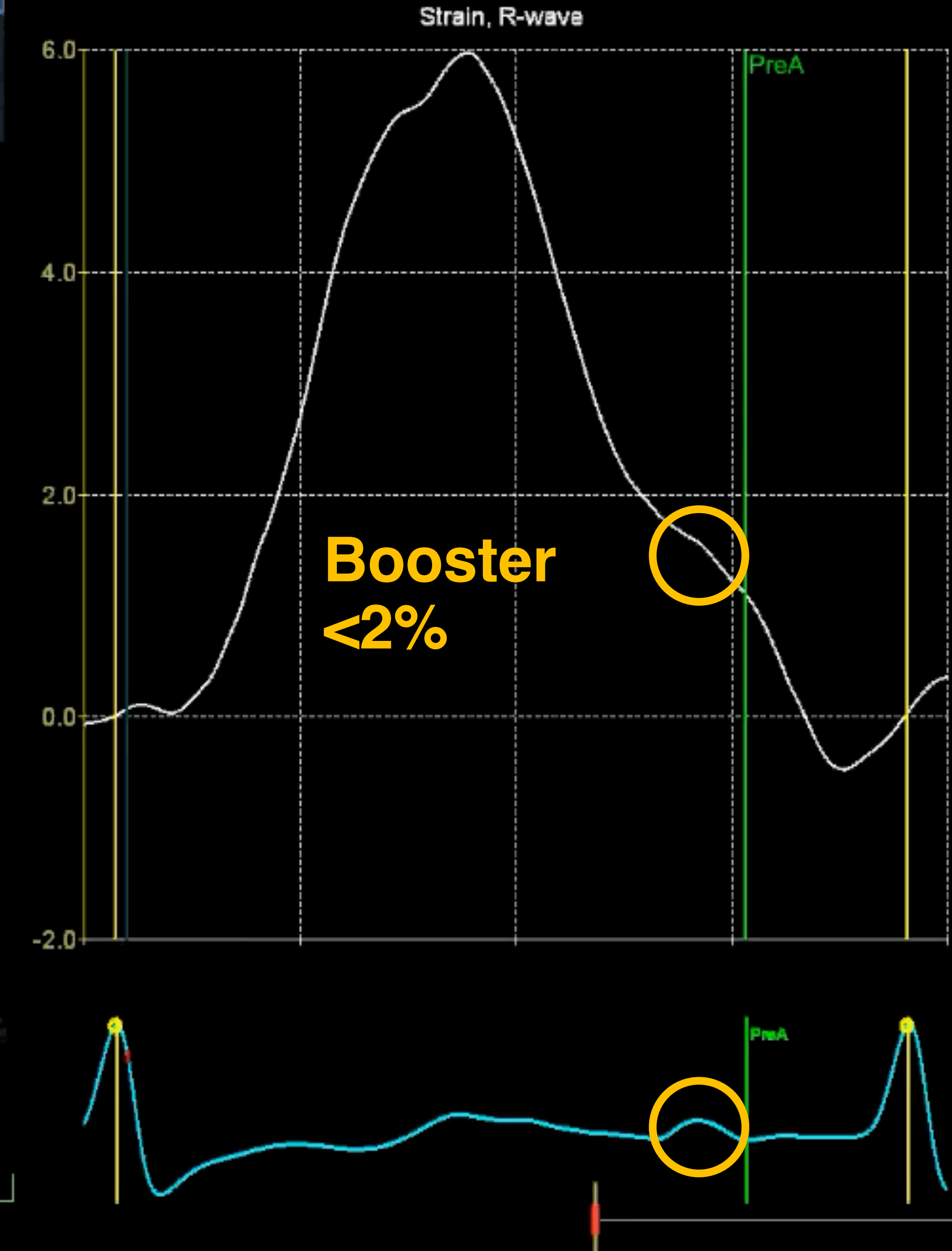


Reservoir -6%



CARDIAC AMYLOIDOSIS – Sinus Rhythm without LAMC

Reservoir -6%

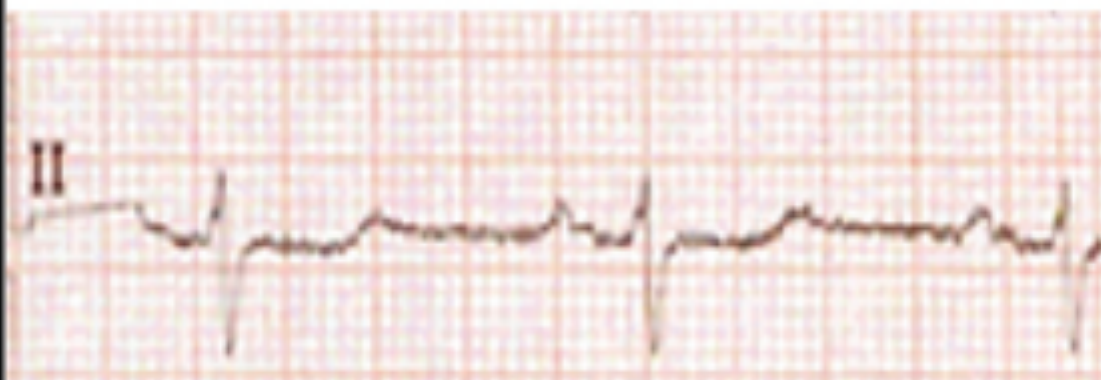
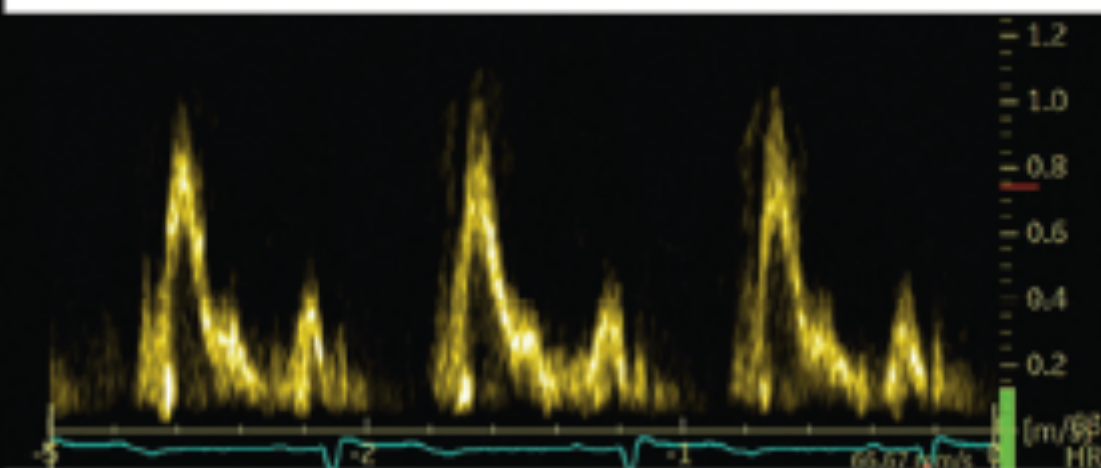
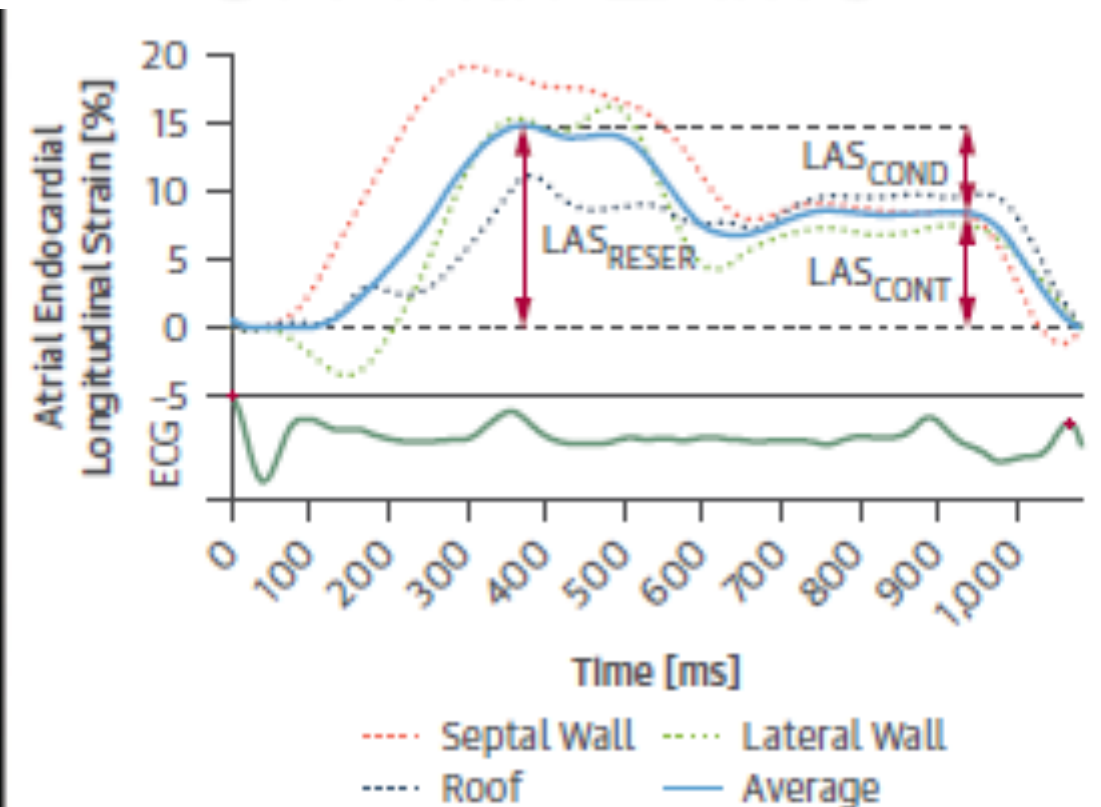


Clinical Importance of Left Atrial Infiltration in Cardiac Transthyretin Amyloidosis

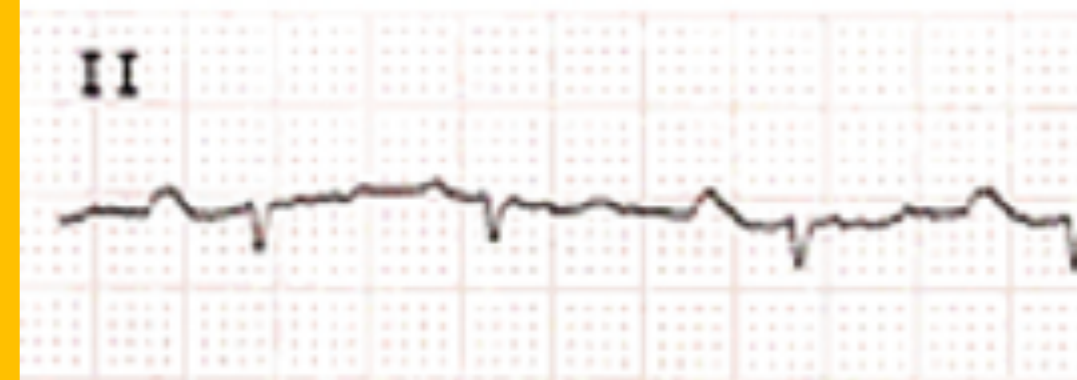
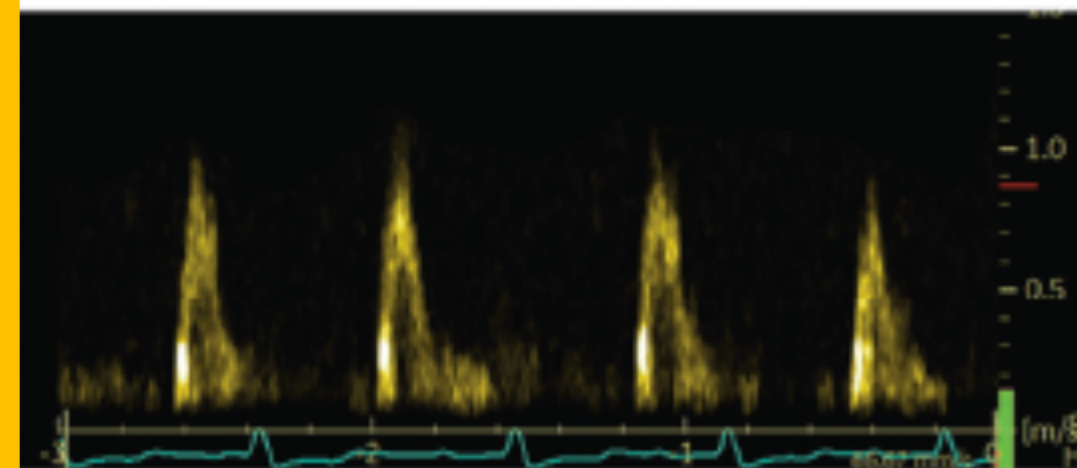
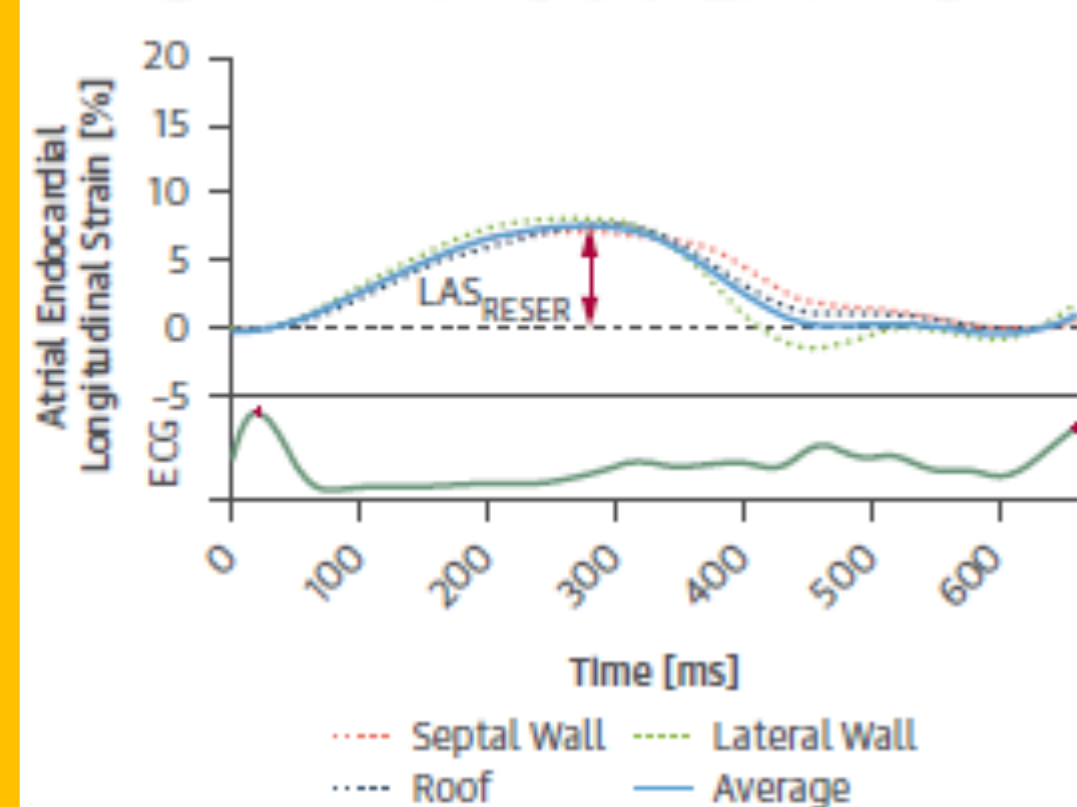


Francesco Bandera, MD, PhD,^{a,b,*} Raffaele Martone, MD,^{c,*} Liza Chacko, MD,^d Sharmananthan Ganesanathan, MS,^d Janet A. Gilbertson, CSci,^d Markella Ponticos, PhD,^d Thirusha Lane, RN, PhD,^d Ana Martinez-Naharro, MD, PhD,^d Carol Whelan, MD,^d Cristina Quarta, MD, PhD,^d Dorota Rowczenio, PhD,^d Rishi Patel, MD,^d Yousuf Razvi, MD,^d Helen Lachmann, MD,^d Ashutosh Wechelakar, MD,^d James Brown, MD,^d Daniel Knight, MD,^d James Moon, MD,^e Aviva Petrie, PhD,^f Francesco Cappelli, MD,^c Marco Guazzi, MD, PhD,^{a,b} Luciano Potena, MD,^g Claudio Rapezzi, MD,^{h,i} Ornella Leone, MD,^g Philip N. Hawkins, MD, PhD,^d Julian D. Gillmore, MD, PhD,^{d,*} Marianna Fontana, MD, PhD^{d,*}

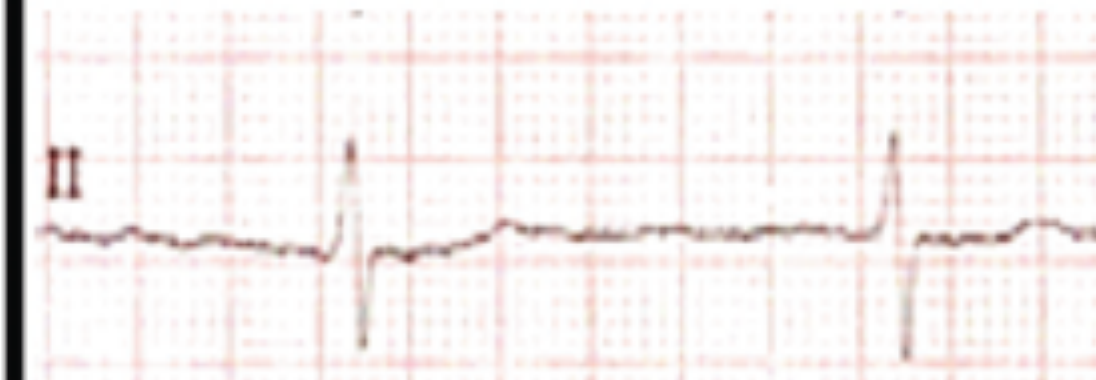
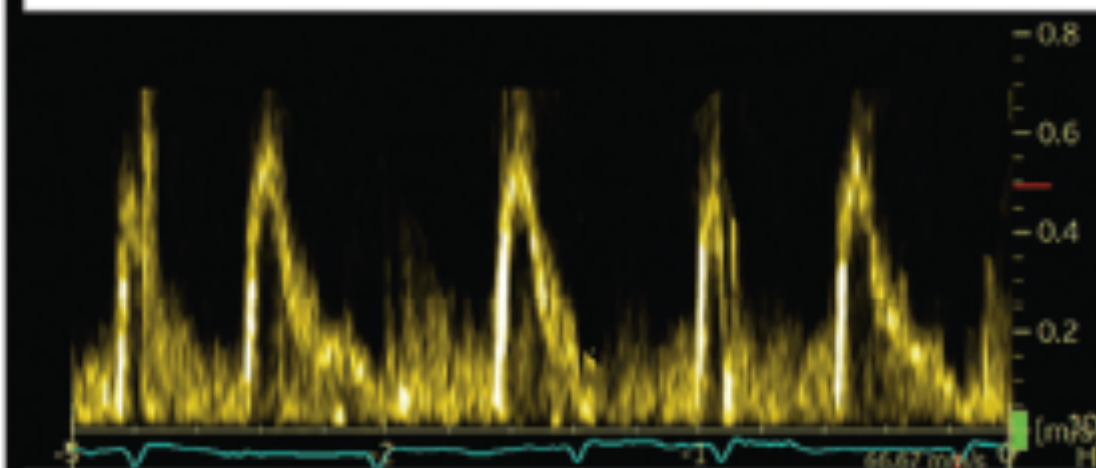
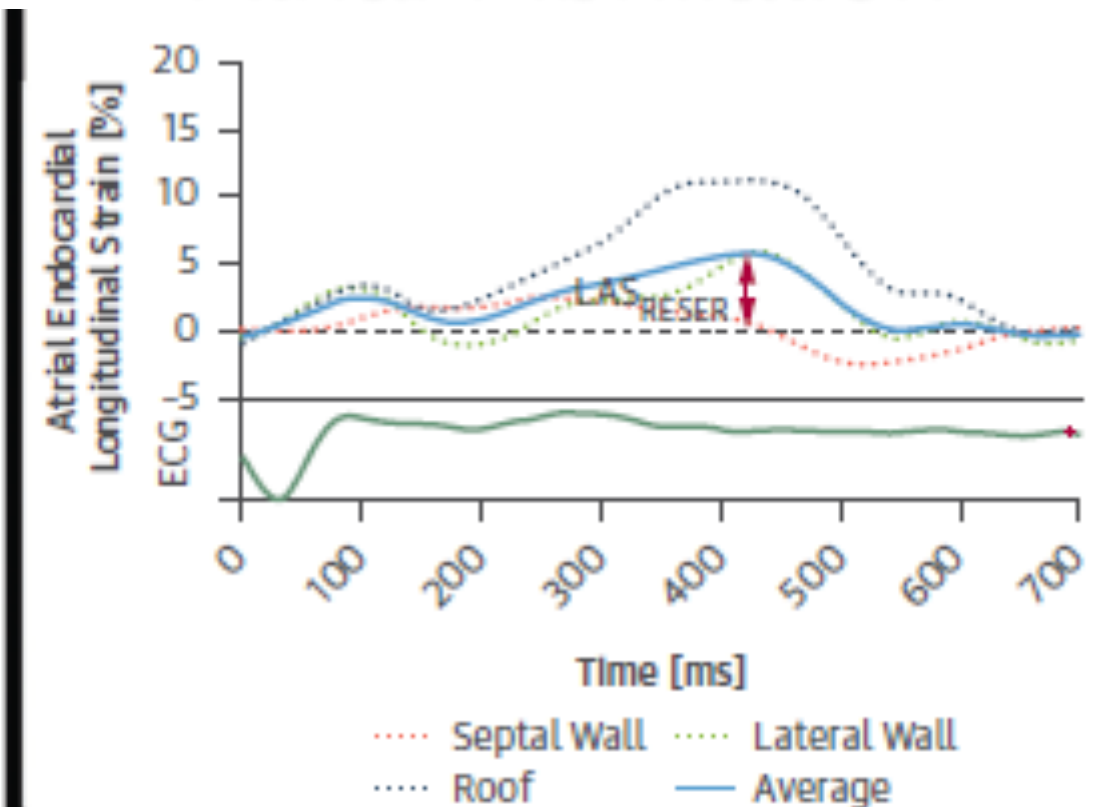
SR with LAMC



SR without LAMC



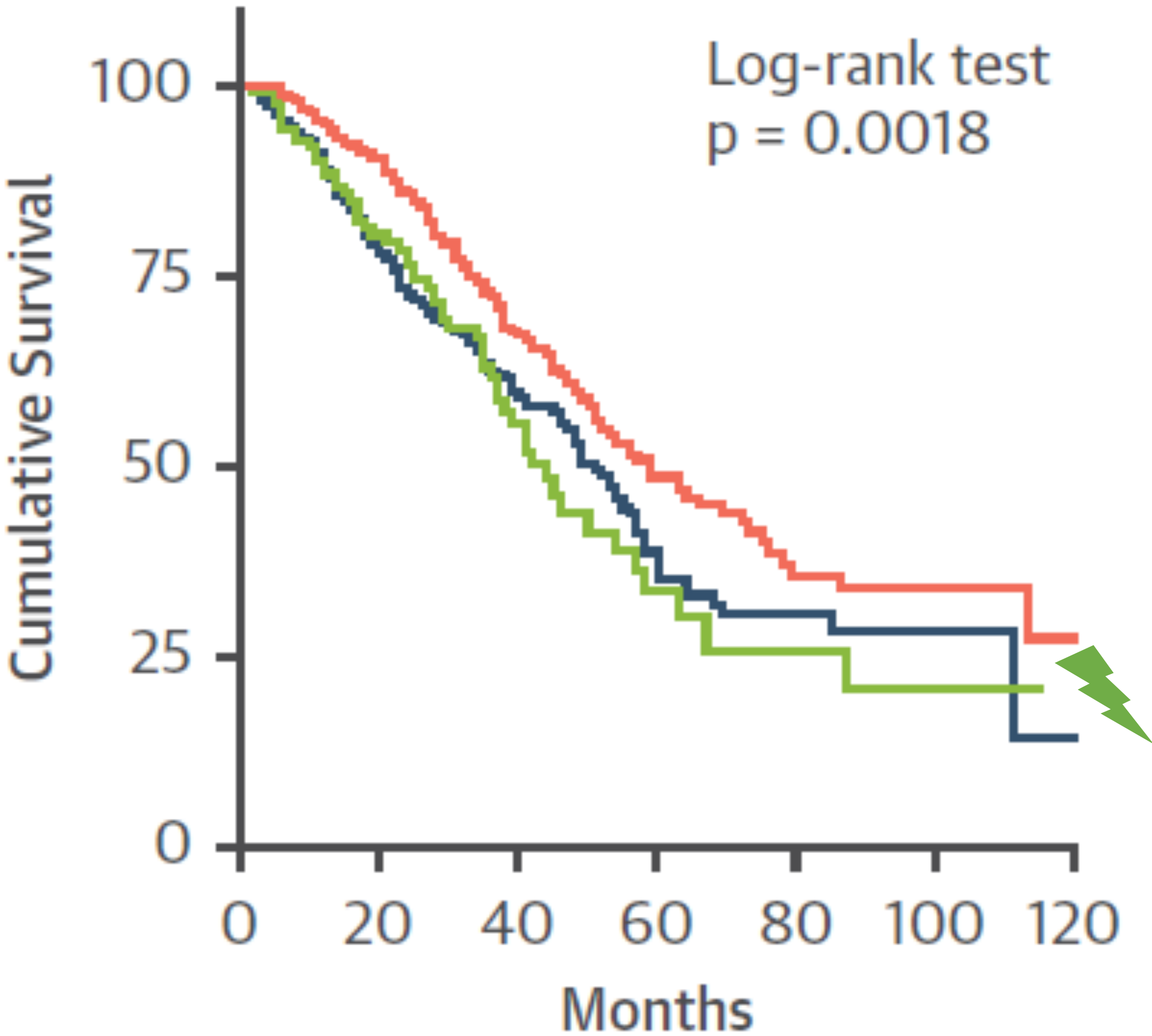
Atrial Fibrillation



Clinical Importance of Left Atrial Infiltration in Cardiac Transthyretin Amyloidosis



Francesco Bandera, MD, PhD,^{a,b,*} Raffaele Martone, MD,^{c,*} Liza Chacko, MD,^d Sharmananthan Ganesanathan, MS,^d Janet A. Gilbertson, CSci,^d Markella Ponticos, PhD,^d Thirusha Lane, RN, PhD,^d Ana Martinez-Naharro, MD, PhD,^d Carol Whelan, MD,^d Cristina Quarta, MD, PhD,^d Dorota Rowczenio, PhD,^d Rishi Patel, MD,^d Yousuf Razvi, MD,^d Helen Lachmann, MD,^d Ashutosh Wechelakar, MD,^d James Brown, MD,^d Daniel Knight, MD,^d James Moon, MD,^e Aviva Petrie, PhD,^f Francesco Cappelli, MD,^c Marco Guazzi, MD, PhD,^{a,b} Luciano Potena, MD,^g Claudio Rapezzi, MD,^{h,i} Ornella Leone, MD,^g Philip N. Hawkins, MD, PhD,^d Julian D. Gillmore, MD, PhD,^{d,*} Marianna Fontana, MD, PhD^{d,*}

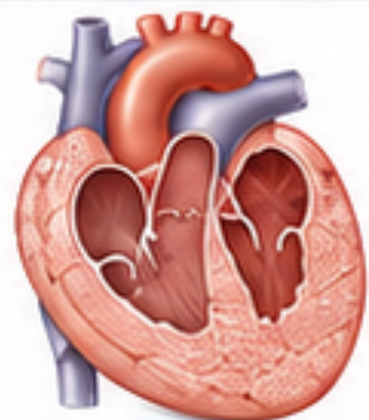


Number at risk						
— SR with LAMC	439	348	161	59	26	11
— SR without LAMC	125	87	35	12	7	2
— Non-SR	342	241	115	43	20	8

Right ventricular involvement in hypertrophic cardiomyopathy phenotypes

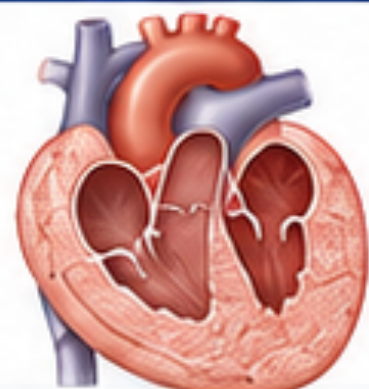
Right ventricular hypertrophy as a diagnostic clue in infiltrative and storage diseases

Infiltrative and storage diseases



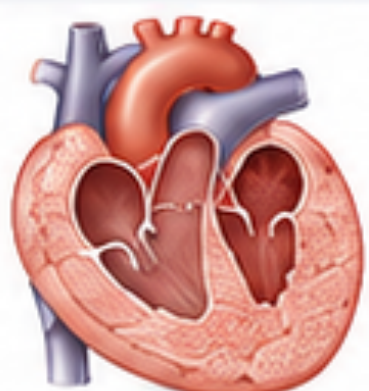
1) Cardiac amyloidosis

Biventricular thickening with thickened valvular walls



2) Fabry disease

Hypertrophic heart with lysosomal storage



3) Glycogen storage diseases / other storage disorders

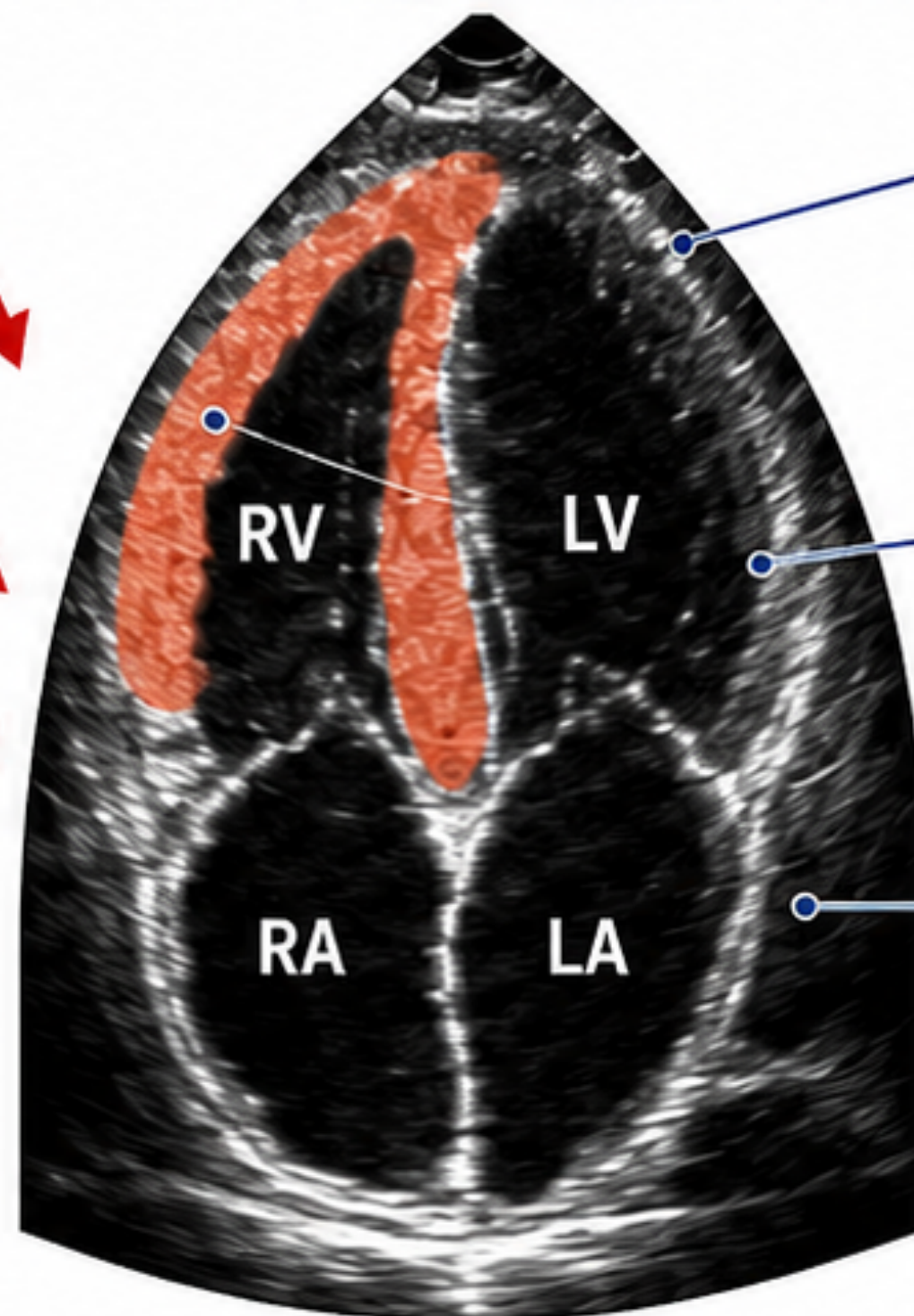
Hypertrophic heart with metabolic storage



- Right ventricular wall thickening often associated with left ventricular hypertrophy
- Diffuse biventricular involvement
- Red flag for infiltrative or storage disease when not explained by loading conditions

Hypertrophic phenotype with RV involvement

Red flag



Apical 4-chamber view

Right ventricular free-wall hypertrophy

Biventricular involvement

Supports the diagnosis of an infiltrative or storage cardiomyopathy

Forms secondary to loading conditions

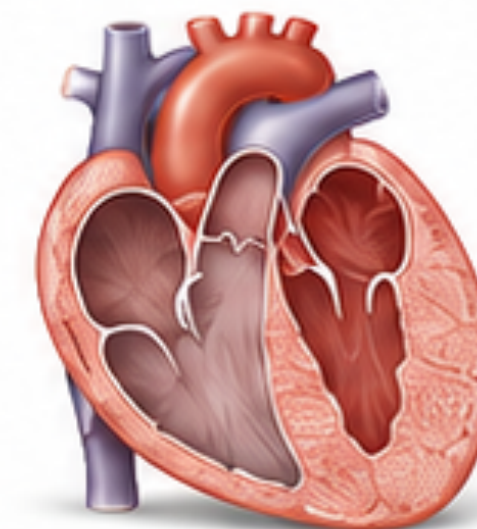
A Left ventricular pressure overload



Systemic hypertension



Aortic stenosis



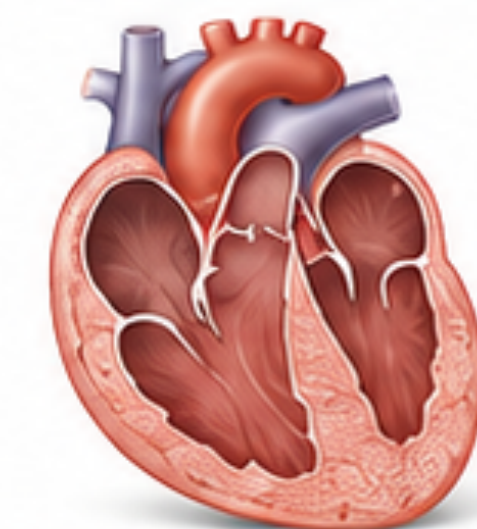
B Right ventricular pressure/volume overload



Pulmonary hypertension



Valvular or congenital heart disease



- RV hypertrophy must be interpreted in the context of hemodynamic load
- If fully explained by afterload or preload abnormalities, suspicion of infiltrative disease is reduced

Suggestive of infiltrative / storage disease

- Biventricular hypertrophy
- RV thickening not explained by loading conditions
- Diffuse phenotype, often with additional red flags

Utility in the differential diagnosis

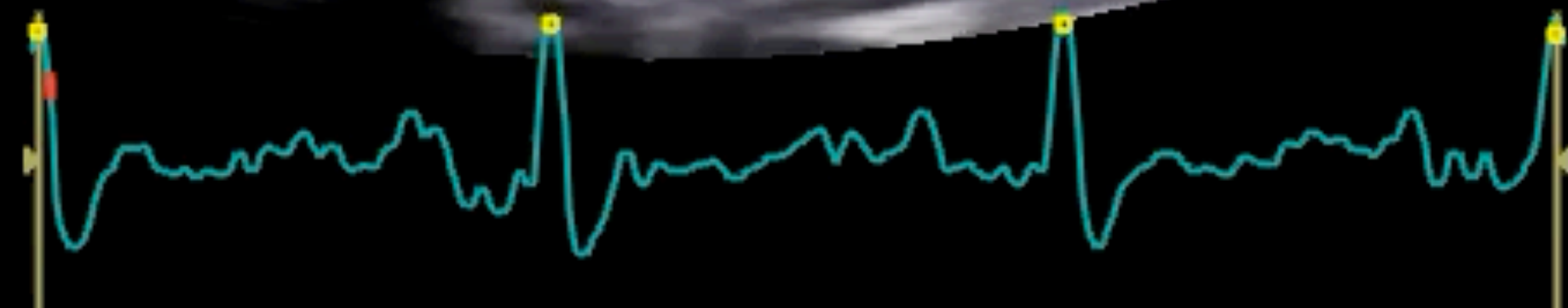
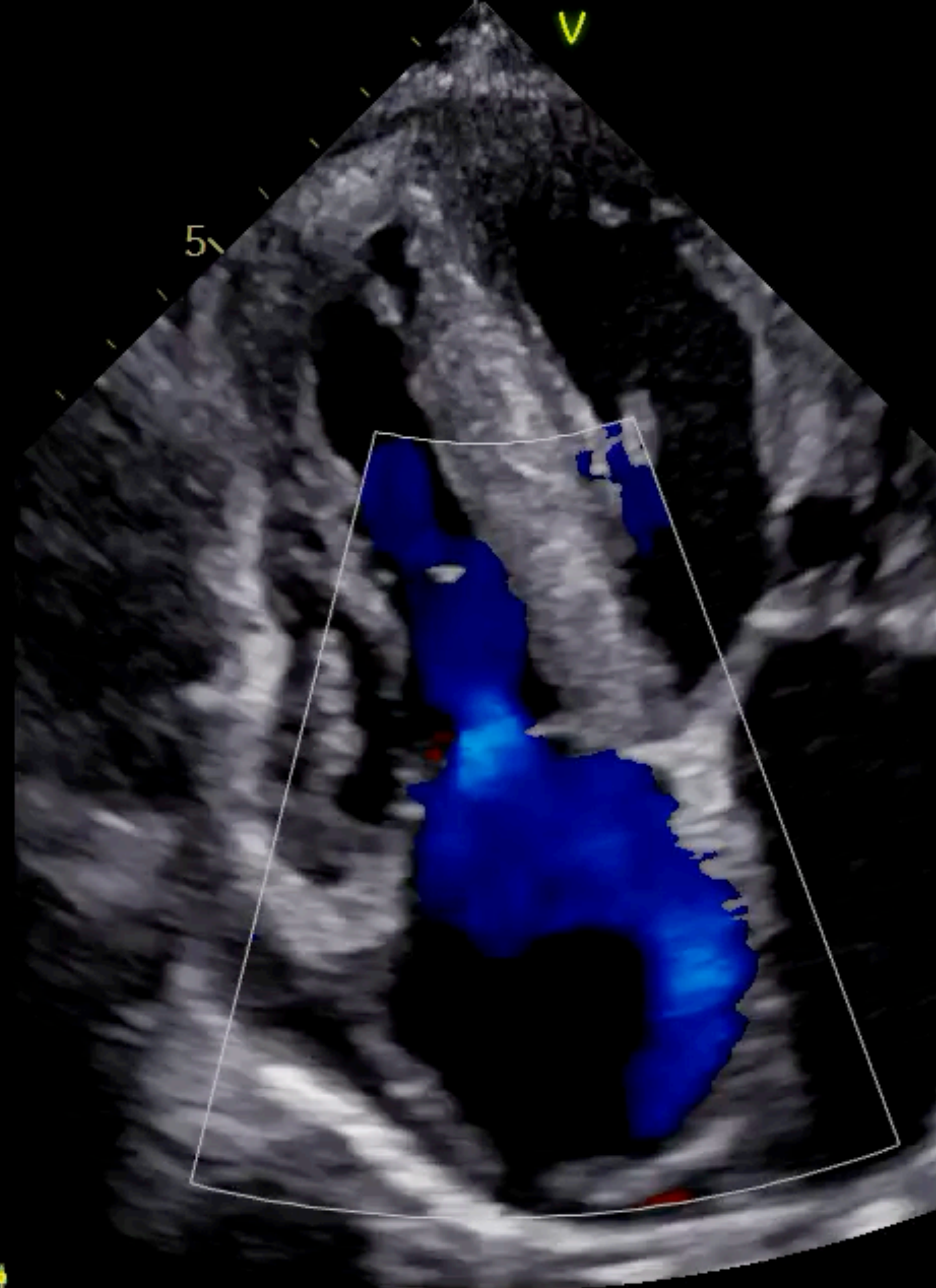


Right ventricular thickening not explained by loading conditions = important clue to infiltrative or storage disease

Suggestive of load-related forms

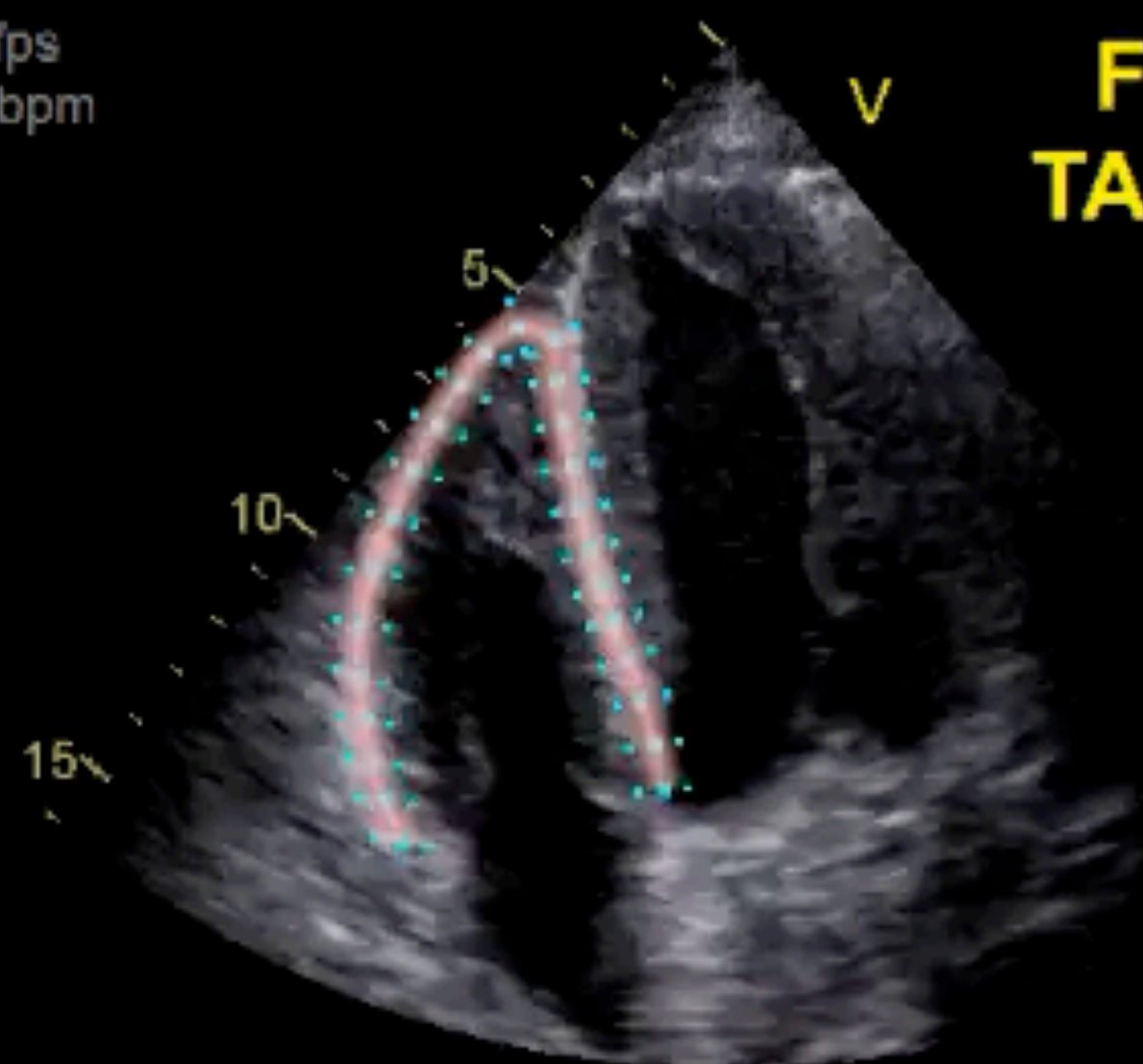
- Hypertrophy consistent with the hemodynamic overload
- Thickened RV only when right-sided overload is present
- Pattern better explained by the valvular or pressure-overload context

14/01/2021 14:52:53
ACE



87
3:46HR

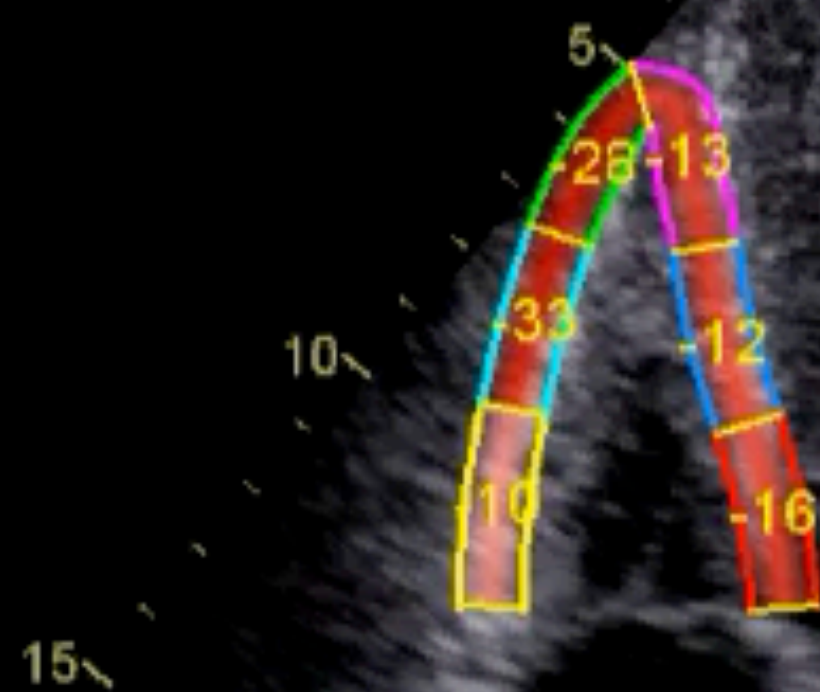
FR: 57 fps
HR: 82 bpm



GS = -18.9 %
FWS = -24.0 %
TAPSE = 1.8 cm

Peak Systolic Strain

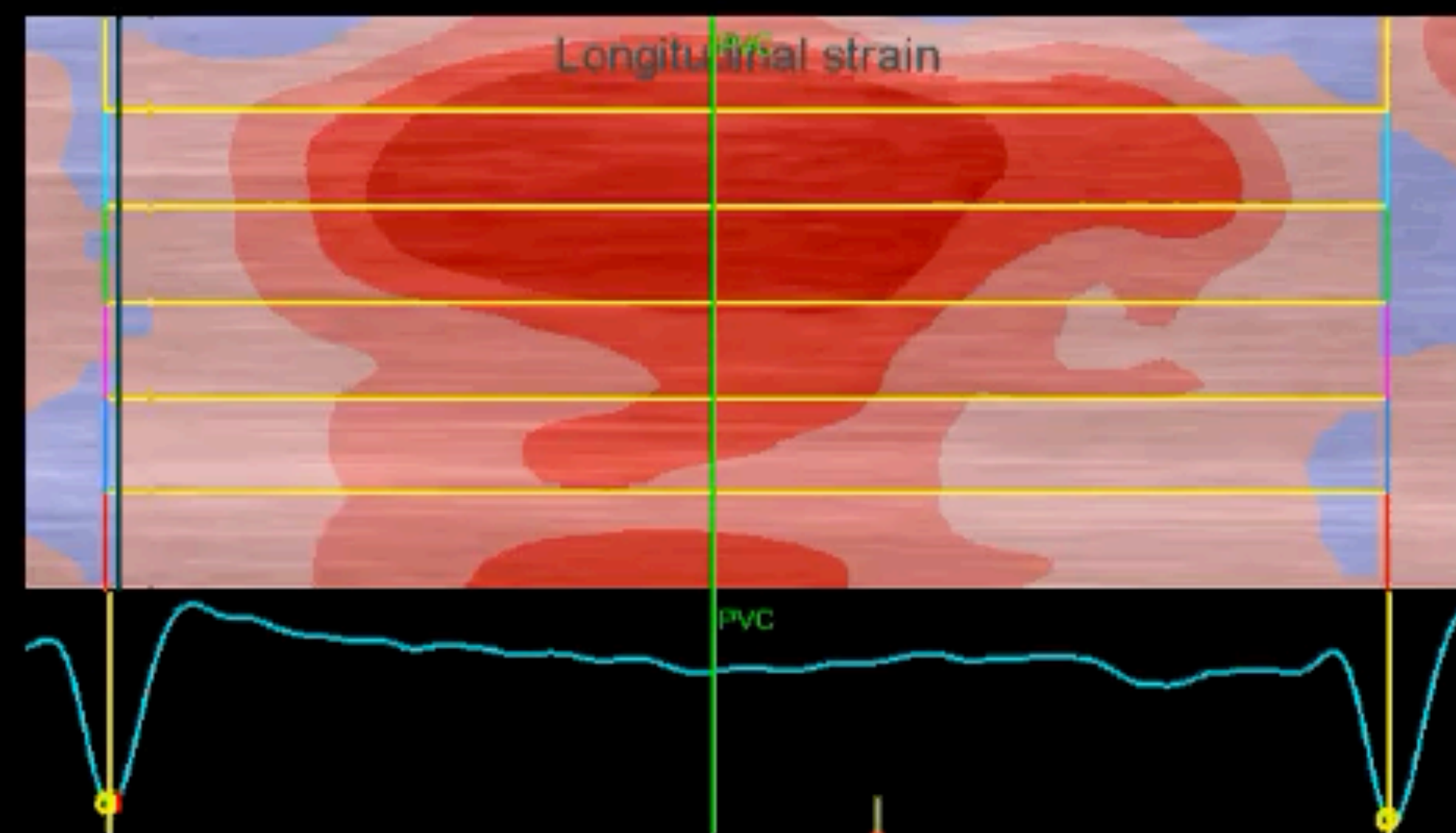
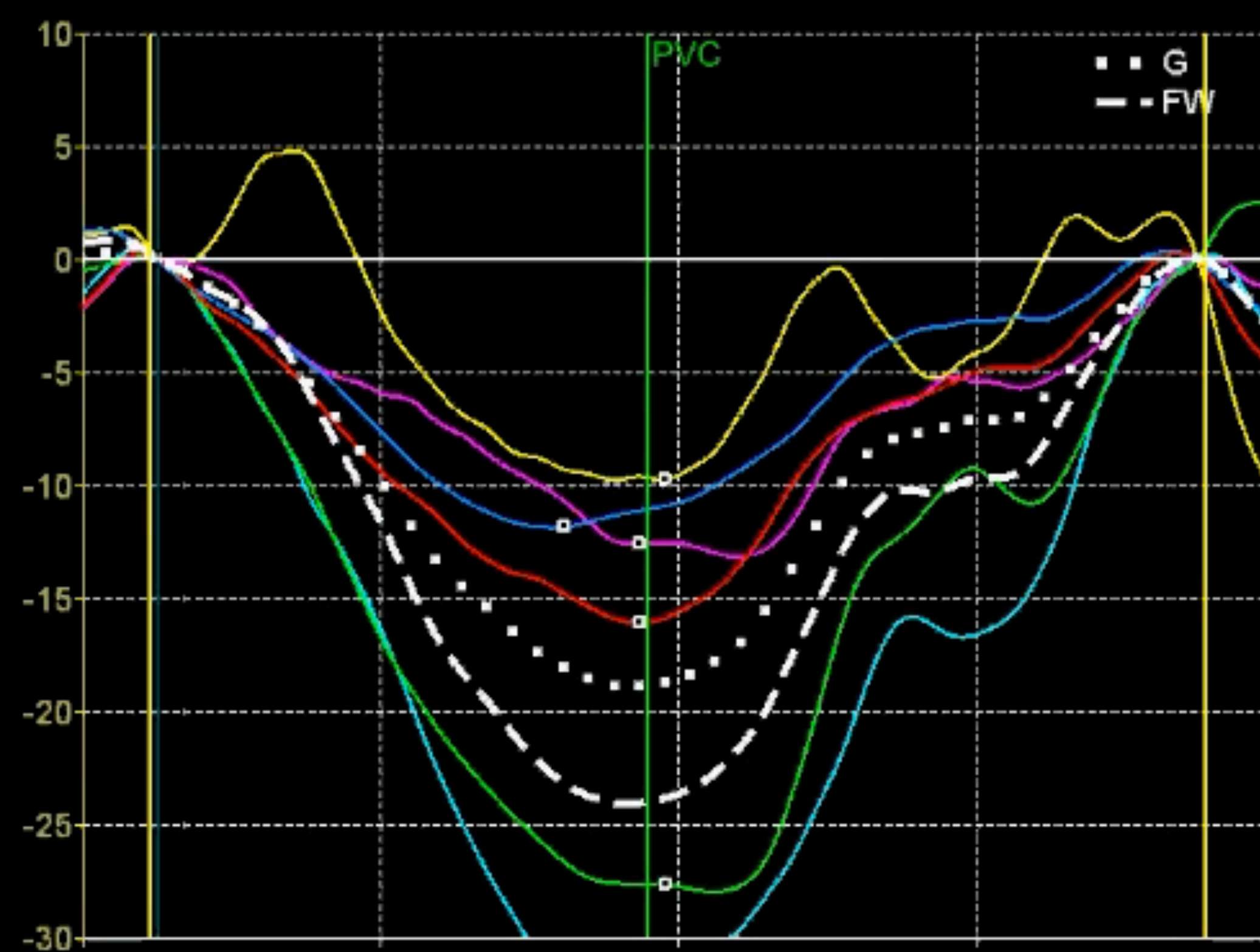
RV Free Wall



RV Sept



Click in segment to approve/reject

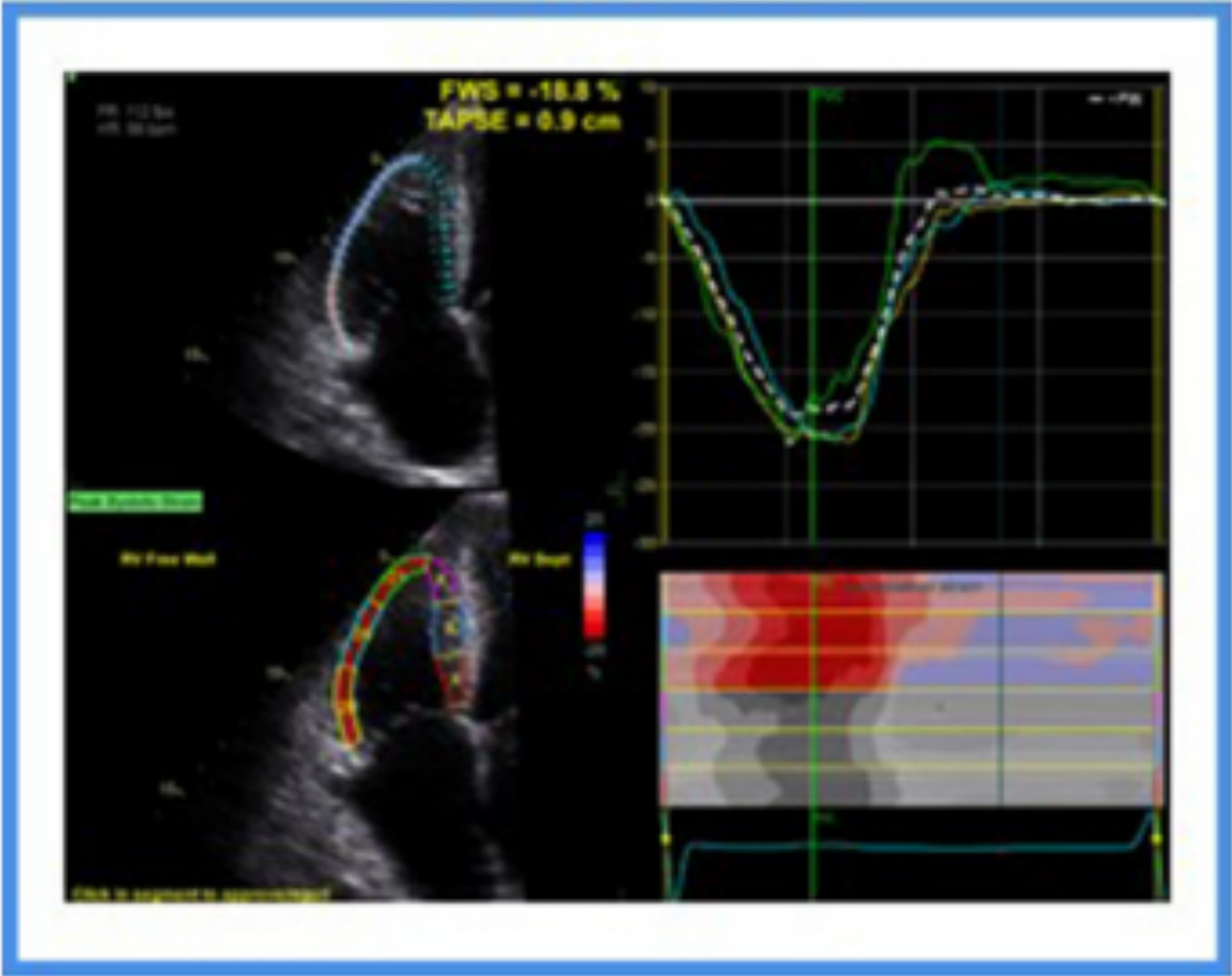


Prognostic Implications of Right Ventricular Systolic Dysfunction in Cardiac Amyloidosis

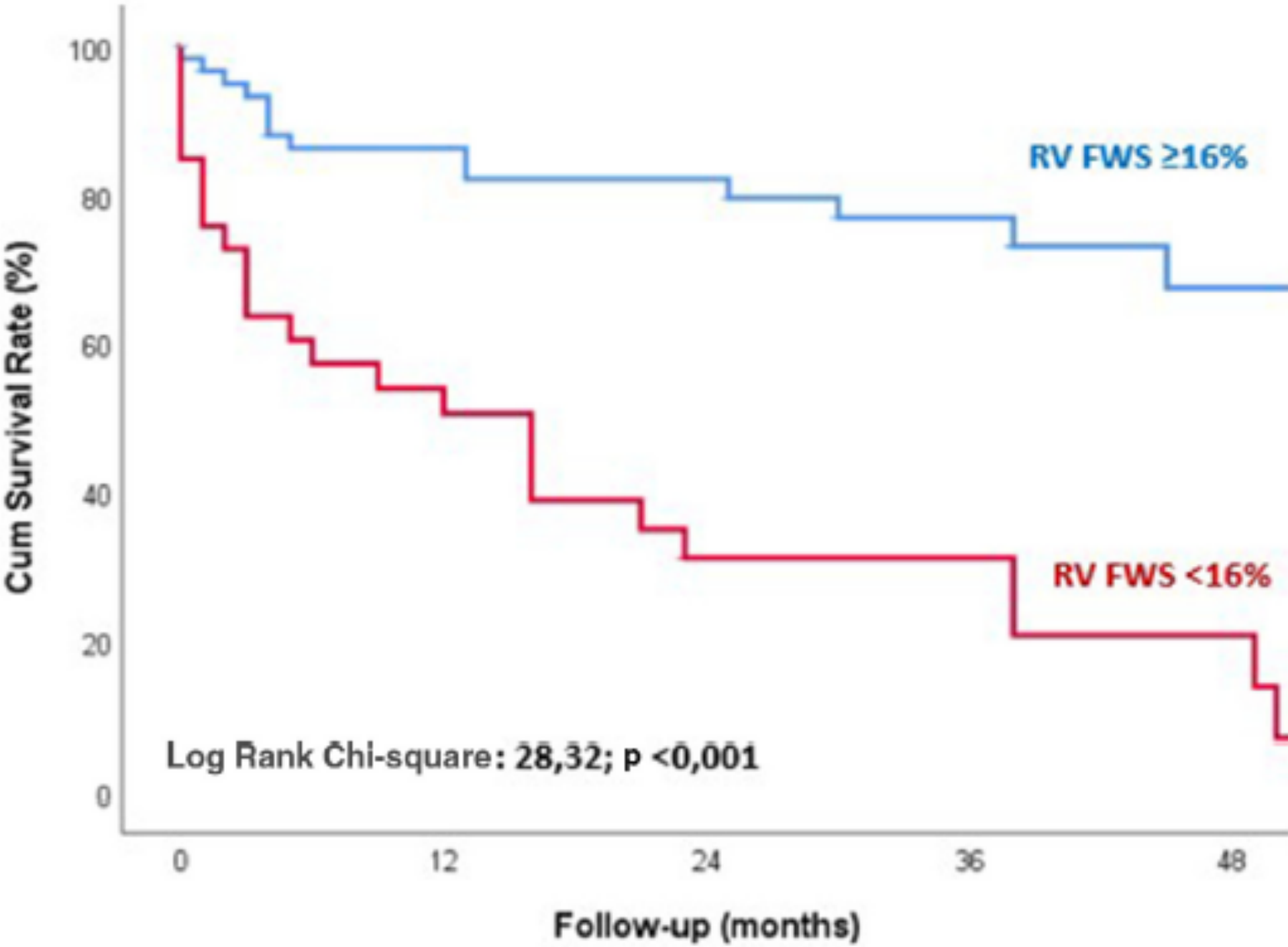
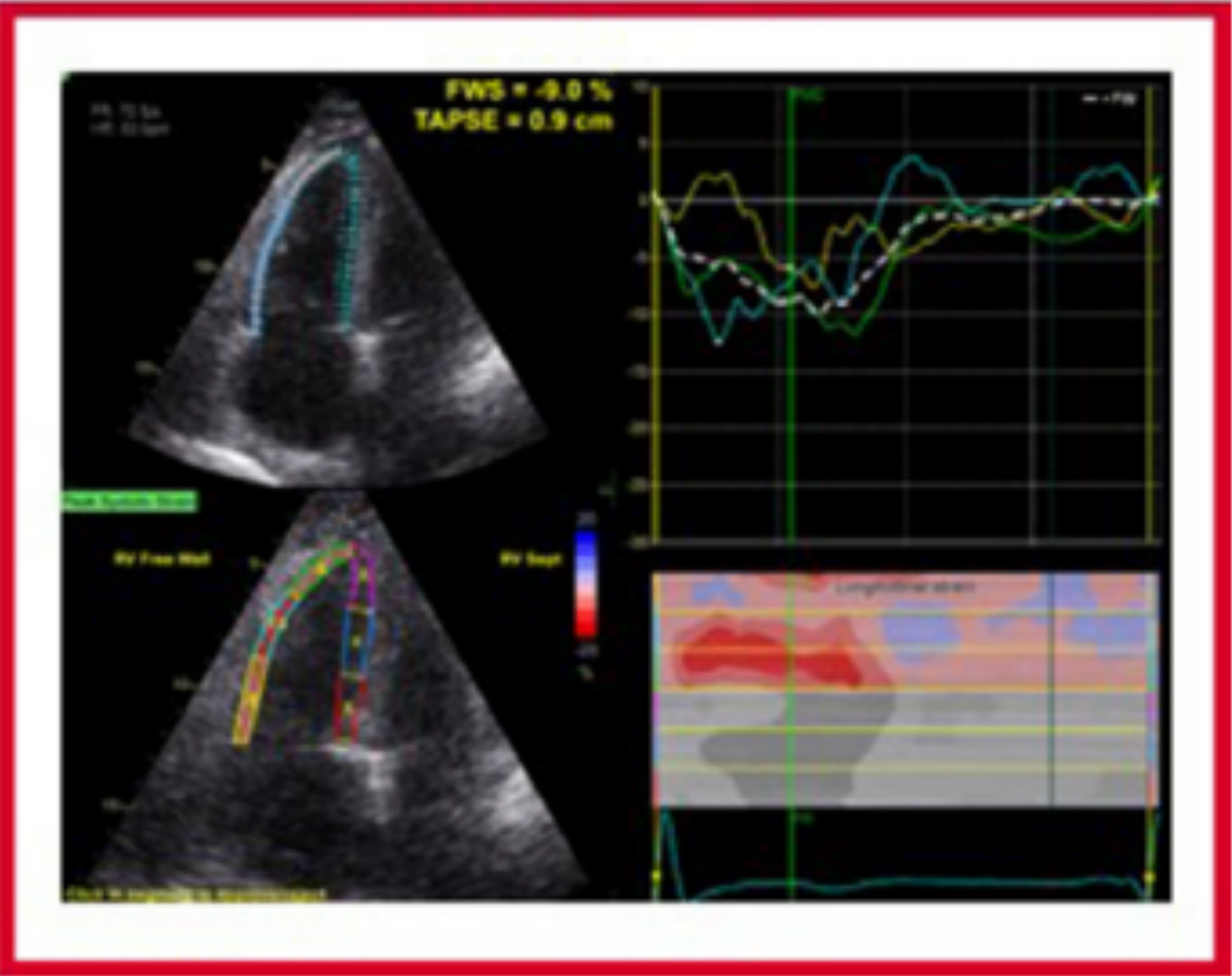


Catherina Tjahjadi, MD^a, Federico Fortuni, MD^{a,b}, Jan Stassen, MD^{a,c},
Philippe Debonnaire, MD, PhD^{a,d}, Rodolfo P. Lustosa, MD^a, Nina Ajmone Marsan, MD, PhD^a,
Victoria Delgado, MD, PhD^a, and Jeroen J. Bax, MD, PhD^{a,*}

RV FWS $\geq 16\%$



RV FWS $< 16\%$



No. at risk

RV FWS ≥ 16

RV FWS < 16

60

33

44

16

33

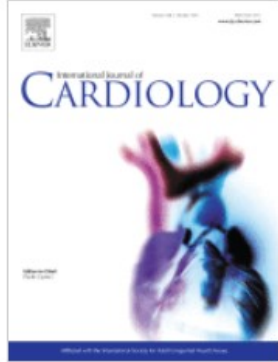
7

23

6

10

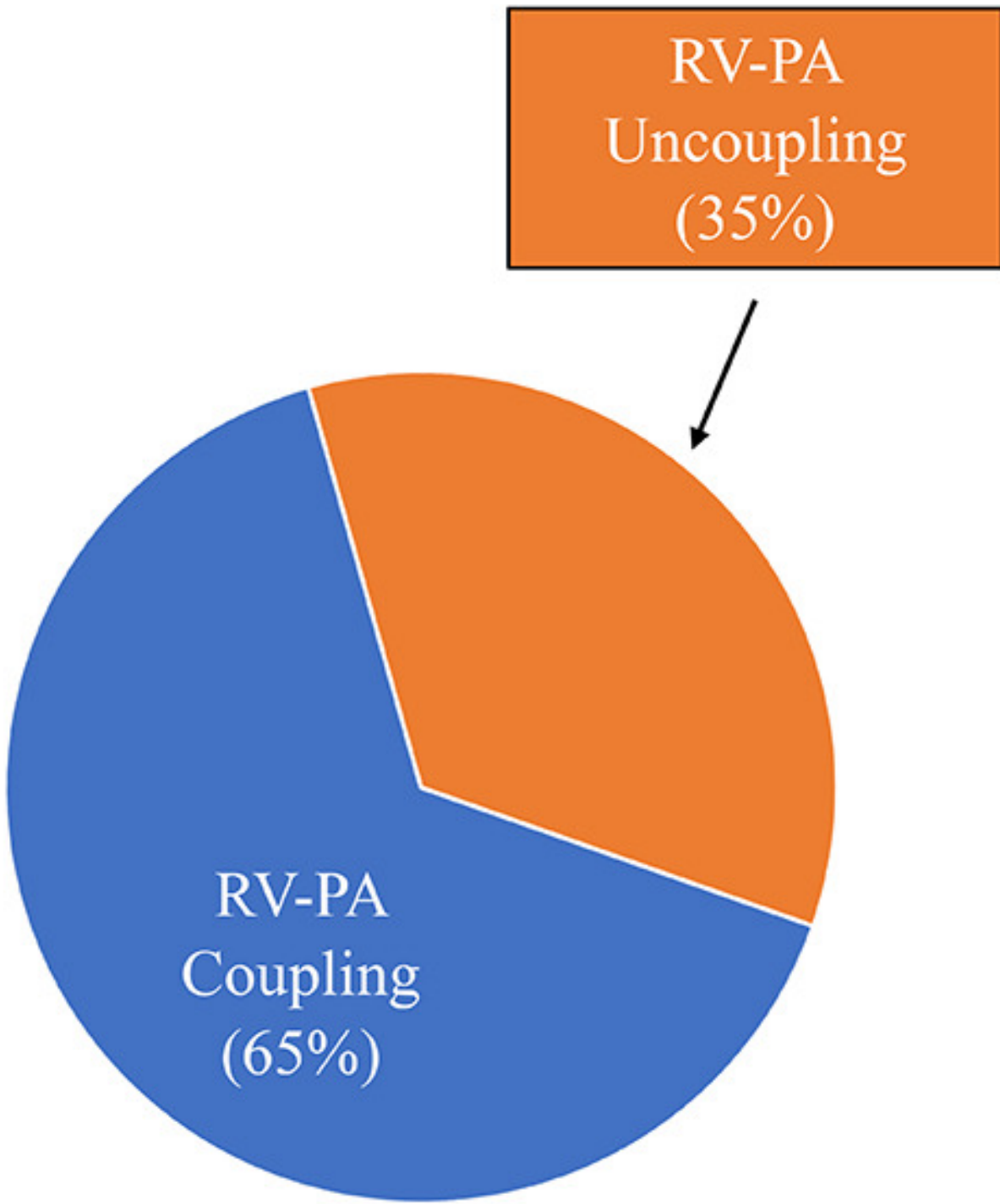
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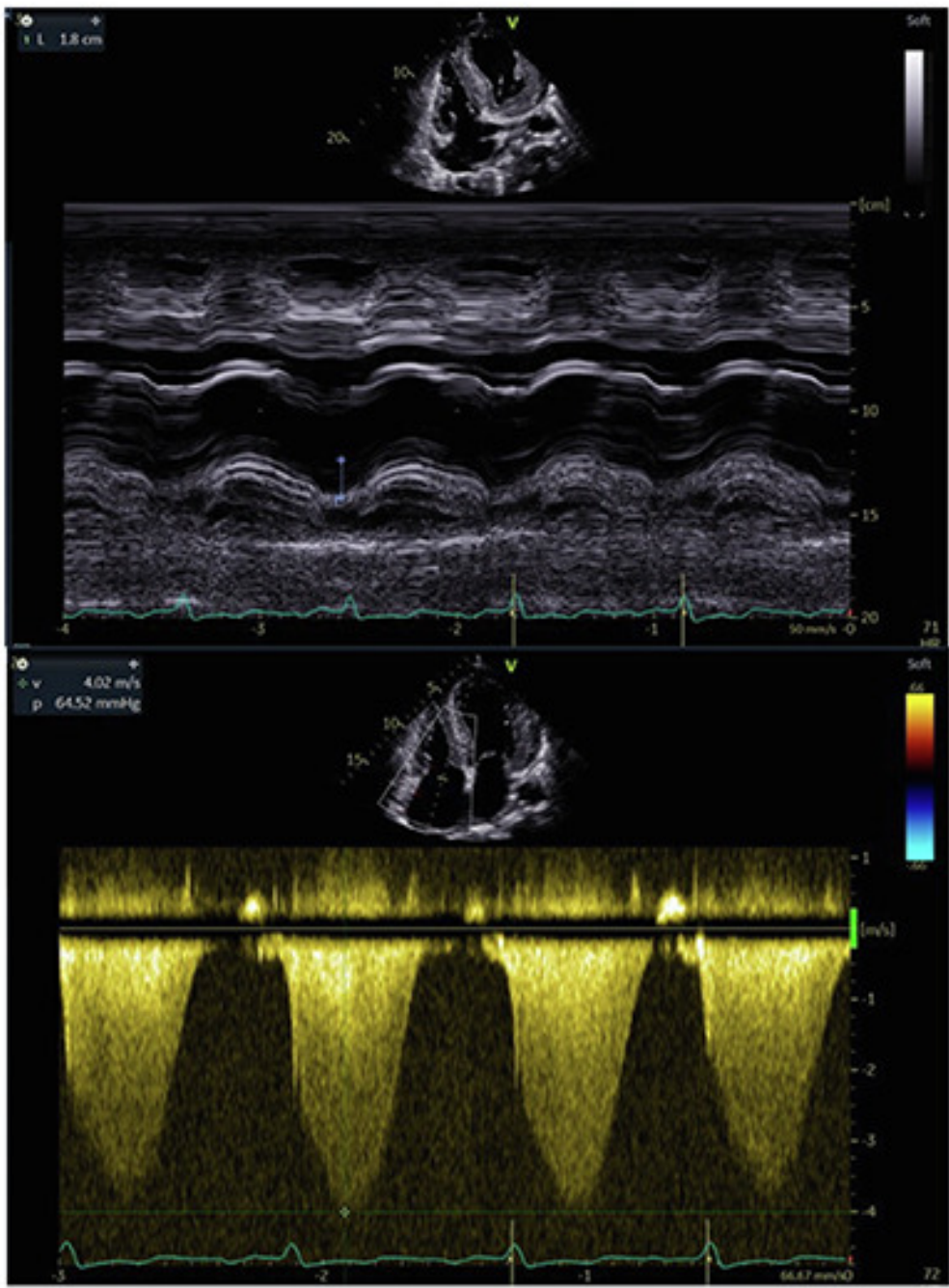
Prevalence and clinical significance of right ventricular pulmonary arterial uncoupling in cardiac amyloidosis

Giuseppe Palmiero ^{a,1} · Emanuele Monda ^{a,b,1} · Federica Verrillo ^a · Francesca Dongiglio ^a · Martina Caiazza ^a · Marta Rubino ^a · Michele Lioncino ^a · Gaetano Diana ^a · Erica Vetrano ^a · Adelaide Fusco ^a · Annapaola Cirillo ^a · Alfredo Mauriello ^a · Giovanni Ciccarelli ^{c,d} · Luigi Ascione ^e · Maria Luisa De Rimini ^f · Michele D'Alto ^c · Giuseppe Cerciello ^g · Antonello D'Andrea ^h · Paolo Golino ⁱ · Paolo Calabrò ^a · Eduardo Bossone ^j · Giuseppe Limongelli ^{a,b} Show less

Prevalence of RV-PA Uncoupling



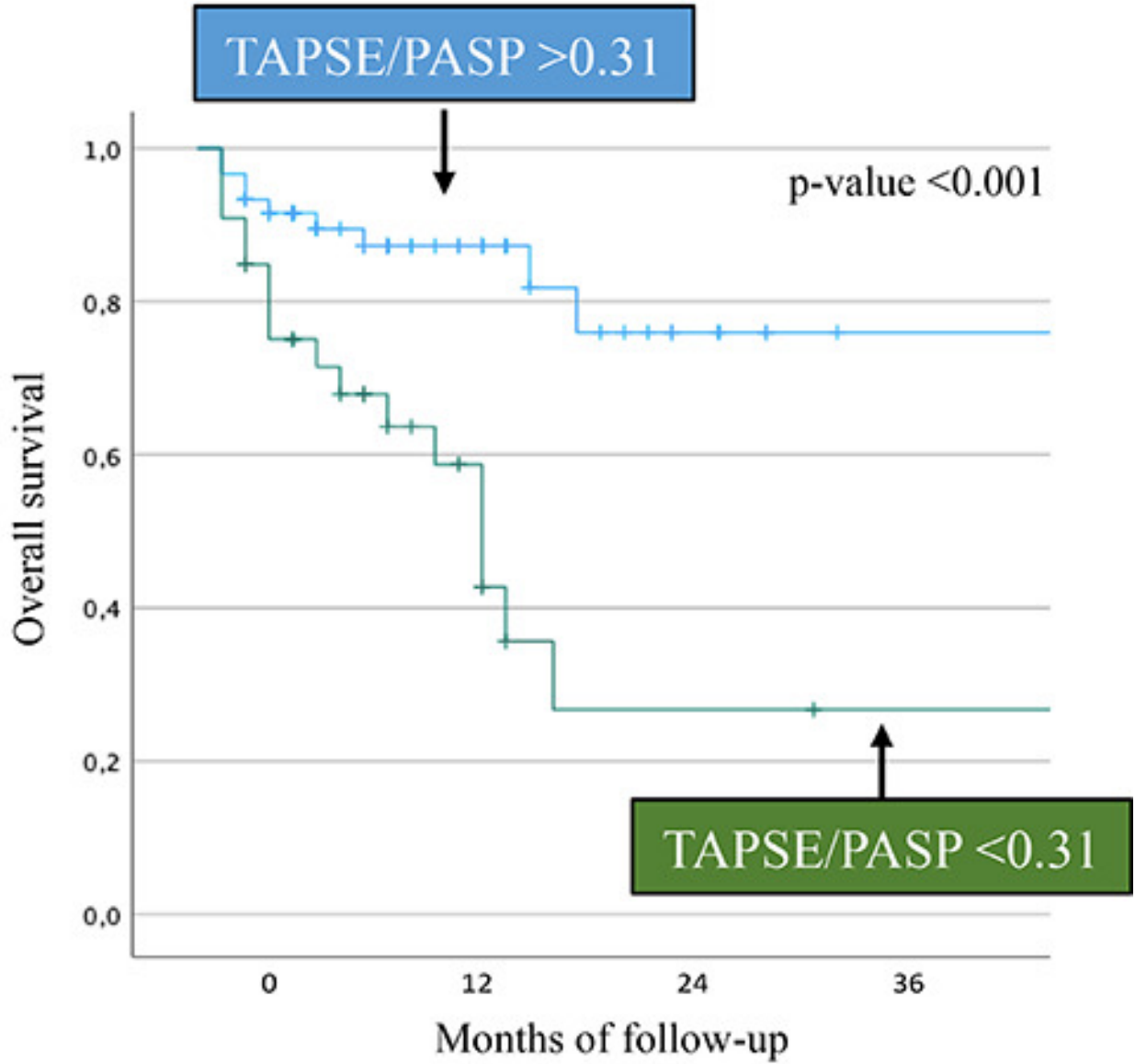
Patients with RV-PA uncoupling showed worse NYHA class and more severe LV and RV dysfunction



TAPSE/PASP <0.31

↑ NYHA Class
↓ Systemic BP
↑ Pro-BNP
↓ LVEF
↓ GLS

TAPSE-PASP is an independent predictors of CV mortality



HR 1.07 [95%CI 1.03-1.11]
per 0.01 mm/mmHg decrease
p-value 0.002