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Introduction to Strain Imaging: How Does Global Longitudinal Strain (GLS) Add to Ejection Fraction (EF)?

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Echo Hawaii, January 17, 2022

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Relevant Disclosures

none

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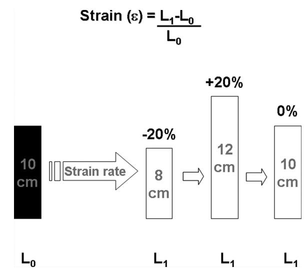
Strain in Echocardiography

Strain = myocardial deformation; the fractional change in the length of a myocardial segment.

- Strain is unitless and is usually expressed as a percentage.

-Strain can have positive or negative values, which reflect lengthening or shortening

-Myocardial regional motion by echocardiography divides strain into four types namely longitudinal, radial, circumferential, and rotational



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EXPERT CONSENSUS STATEMENT

Current and Evolving Echocardiographic Techniques for the Quantitative Evaluation of Cardiac Mechanics: ASE/EAE Consensus Statement on Methodology and Indications

Endorsed by the Japanese Society of Echocardiography

Victor Mor-Avi, PhD, FASE,* Roberto M. Lang, MD, FASE,† Luigi P. Badano, MD, FESC, Marek Belohlavek, MD, PhD, FESC, Nuno Miguel Cardim, MD, PhD, FESC, Geneviève Derumeaux, MD, PhD, FESC, Maurizio Galderisi, MD, FESC, Thomas Marwick, MBBS, PhD, Sherif F. Nagueh, MD, FASE, Partho P Sengupta, MBBS, FASE, Rosa Sicari, MD, PhD, FESC, Otto A. Smiseth, MD, PhD, FESC, Beverly Smulevitz, BS, RDCS, Masaaki Takeuchi, MD, PhD, FASE, James D. Thomas, MD, FASE, Mani Vannan, MBBS, Jens-Uwe Voigt, MD, FESC, and José Luis Zamorano, MD, FESC†, *Chicago, Illinois; Padua, Naples, and Pisa, Italy; Scottsdale, Arizona; Lisbon, Portugal; Lyon, France; Cleveland and Columbus, Ohio; Houston, Texas; Irvine, California; Oslo, Norway; Kitakyushu, Japan; Leuven, Belgium; Madrid, Spain*

(J Am Soc Echocardiogr 2011;24:277-313.)

Keywords: Ventricular function, Myocardial strain, Tissue Doppler, Myocardial Doppler, Tissue tracking, Speckle tracking, Integrated backscatter

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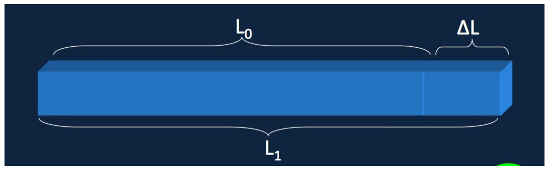
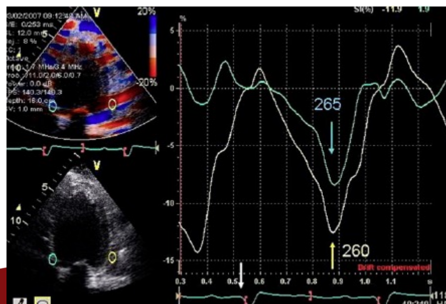
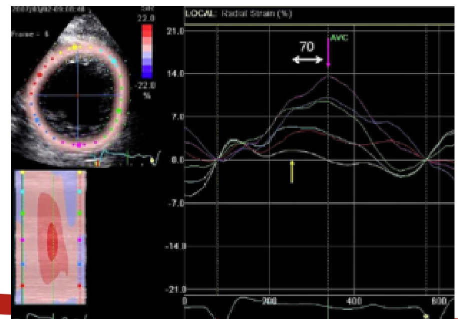
Strain Based Techniques



Strain (ε)= $(L_1 – L_0)/L_0 = ΔL/L_0$





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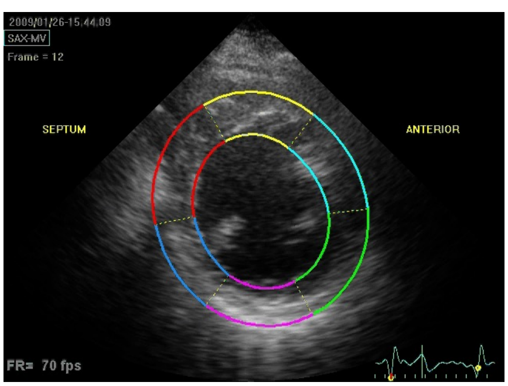
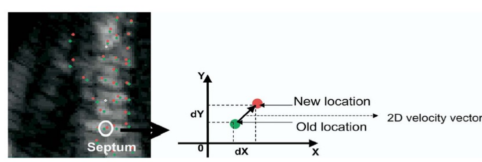
Speckle Tracking





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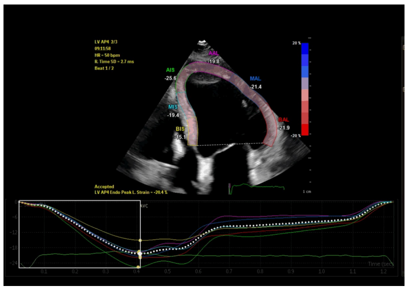
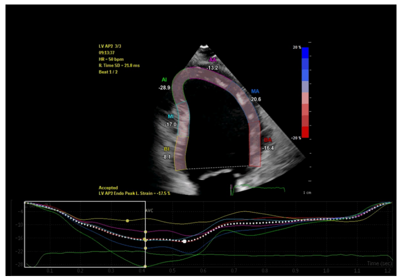
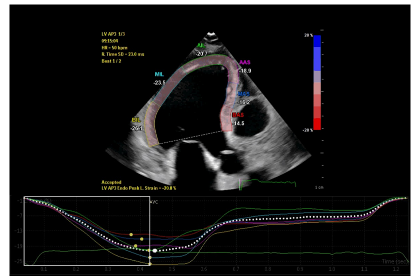
Longitudinal Strain







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Speckle Tracking Strain

- Tracking of the irregular speckled pattern generated by interference of the reflected ultrasound
- Comparability between vendors is variable: appears more robust for 2D GLS
- What is "normal" : meta- analysis of existing strain reference limit studies:

	Mean (95% CI)
Longitudinal Strain	-19.7 (-20.4 to -18.9%)
Circumferential Strain	-23.3 (-24.6 to 22.1%)
Radial Strain	47.3 (46.3 to 51.0%)

Manovi et al. *Eur J Echocardiogr* 2010;11:417-21
Nelson et al. *J Am Soc Echocardiogr* 2012;25:1189-94
Gayat et al. *J Am Soc Echocardiogr* 2011;24:878-85
Negishi et al. *Ultrasound in Med & Biol* 2013;39:714-720
Yingchoncharoen et al. *J Am Soc Echocardiogr* 2013;26:185-91
Mor-Avi et al. *J Am Soc Echocardiogr* 2011;24:277-313

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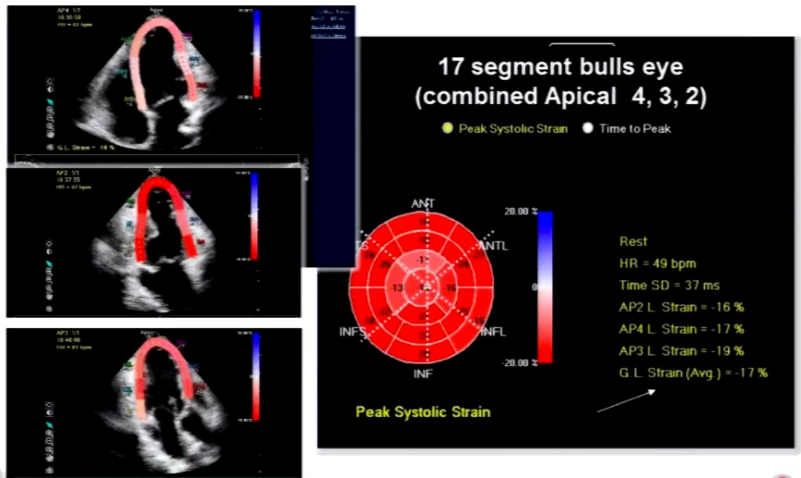
Global Longitudinal Strain (GLS)



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Clinical Utility of Strain

Clinical Applications of STE	Sources of Variability	
	Technical sources:	Clinical sources:
Undifferentiated left ventricular hypertrophy	Image quality / clip selection	Race / ethnic factors
Assessment of cardiotoxicity	Contouring / region of interest	Age and gender differences
Aortic stenosis	Tracking / timing	Hemodynamic factors
Ischemic heart disease	Choice of segmentation model	Medications
Regional strain	Choice of vendor	Volume status
Other chambers (left atrial strain, right ventricular strain)		

Collier, P. et al. J Am Coll Cardiol. 2017;69(8):1043–56.

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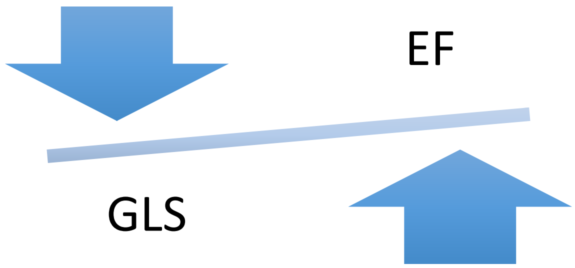

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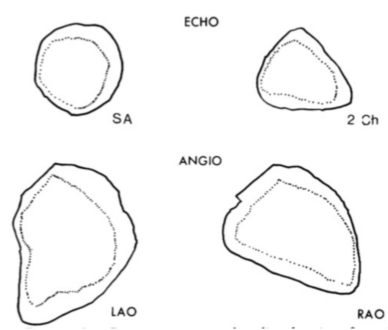
Left Ventricular Volume from Paired Biplane Two-dimensional Echocardiography

NELSON B. SCHILLER, M.D., HARRY ACQUATELLA, M.D., THOMAS A. PORTS, M.D., DENIS DREW, M.D., JON GOERKE, M.D., HANS RINGERTZ, M.D., NORMAN H. SILVERMAN, M.D., BRUCE BRUNDAGE, M.D., ELIAS H. BOTVINICK, M.D., ROBERT BOSWELL, M.D., ERIK CARLSSON, M.D., AND WILLIAM W. PARMLEY, M.D.

SUMMARY To evaluate the applicability of two-dimensional echocardiography to left ventricular volume determination, 30 consecutive patients undergoing biplane left ventricular cineangiography were studied with a wide-angle (84°), phased-array, two-dimensional echocardiographic system. Two echographic projections were used to obtain paired, biplane, tomographic images of the left ventricle. We used the short-axis view (from the precordial window) as an anolog of the left anterior oblique angiogram, and the long-axis, two-chamber view (from the apex impulse window) as a right anterior oblique angiographic equivalent.

A modified Simpson's rule formula was used to calculate systolic and diastolic left ventricular volumes from the biplane echogram and the biplane angiogram. These methods correlated well for ejection fraction ($r = 0.87$) and systolic volume ($r = 0.90$), but only modestly for diastolic volume ($r = 0.80$). These correlations are noteworthy because 65% of the patients had significant segmental wall motion abnormalities. The volumes determined from the minor-axis dimensions of M-mode echograms in 23 of the same patients correlated poorly with angiography.



Schiller et al. Circulation 1979

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Problems with Ejection Fraction

1. Imprecise physiological implications – can be normal despite LV dysfunction
2. Substantial variability across imaging modalities
3. EF cutoffs are arbitrary
4. Calculation is based on geometric assumptions and cavity border tracing methods

Triposkiadis et al. European Heart Journal. 2019

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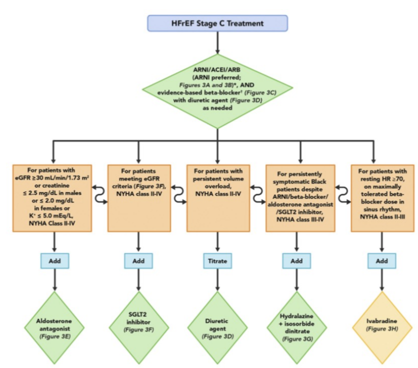
HFpEF, HFmrEF, and HFrEF

EF Guides Medical Therapy & Determines Risk for Sudden Cardiac Death

Heart Failure	Characteristics: Older Age	Characteristics: Male Sex	Characteristics: CAD	Outcomes: Morbidity	Outcomes: Mortality	Guideline-Directed Medical Therapies: ACEI	ARB	ARNI	BB	MRA
HFpEF (LVEF>50%)	+++	+	++	++	++	X	√ (IIB)	?	X	√ (IIB)
HFmrEF (LVEF40-50%)	++	++	+++	++/+++	++	?	√ (IIB)	?	?	√ (IIB)
HFrEF (LVEF<40%)	+	+++	+++	+++	+++	√ (I)	√ (I)	√ (I)	√ (I)	√ (I)

Hsu, J.J. et al. J Am Coll Cardiol HF. 2017;5(11):763-71.

EF<40%



Maddox et al.

2021 Update to 2017 ECDP for Optimization of Heart Failure Treatment

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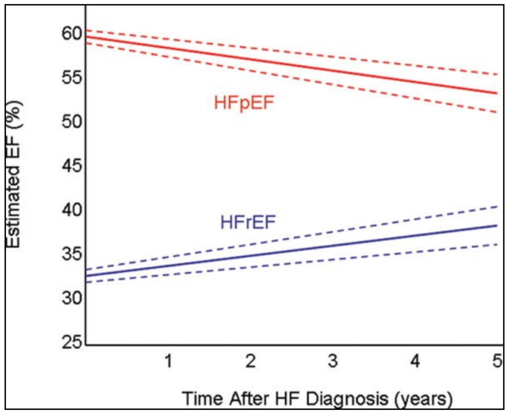
Change In Ejection Fraction (EF) For Patients With Preserved And Reduced EF



Dunlay SM. *et al.* Circ Heart Fail. 2012;5(6):720-726

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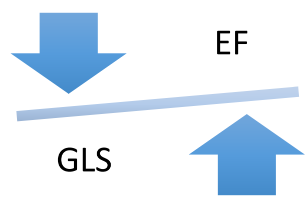
What is wrong with serial echo EF assessment? A brief review of the literature.....

- **Measurement of EF is fraught with errors, and can vary up to 20% on any given study. (1,2)**
- **Standard echo (2D noncontrast) has poor temporal variability in EF exceeding 10%. One study has suggested that an 11% is the smallest change in EF that can be recognized with 95% confidence (3)**
- **GLS has been shown to have excellent reproducibility across different vendors, and better than standard echo measurements including EF(4)**



1. Gopal et al. Circulation 1995;92:842-53.
2. Otterstad et al. Eur Heart J 1997; 18:507-13.
3. Thavendiranathan et al. J Am Coll Cardiol 2013;61:77–84)
4. Konstantinos et al. J Am Soc Echocardiogr 2015;28:1171-81.

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What does Strain Add Beyond EF?

- **Prognostic Information**
- **Regional Variation detection in function**
- **Assessment of thickening**
- **Detects subclinical changes in myocardial function before development of cardiomyopathy allowing window for therapy**

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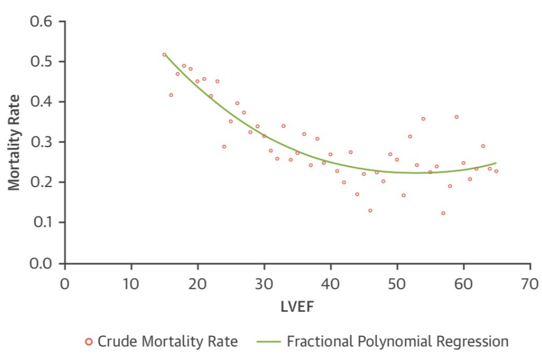
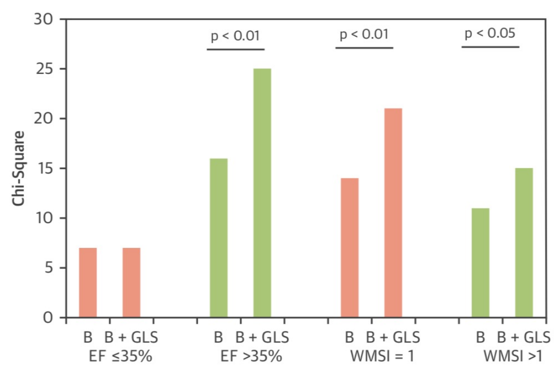
GLS adds important prognostic info beyond EF

EF and All-Cause Mortality



[1]Curtis et al. JACC 2003

GLS and Prediction of Mortality is Additive To Baseline Factors including DM2, Age, HTN



[2]Stanton et al. Circ Cardiovasc Imaging 2009

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ORIGINAL ARTICLE

Prognostic implications of global LV dysfunction: a systematic review and meta-analysis of global longitudinal strain and ejection fraction

Kashif Kalam, Petr Otahal, Thomas H Marwick

- **Meta-analysis of 16 studies with 5721 patients looking at GLS and EF**
- Mortality was independently associated with each SD change in the absolute value of baseline GLS (HR 0.50, 95% CI 0.36 to 0.69; p<0.002) and less strongly with LVEF (HR 0.81, 95% CI 0.72 to 0.92; p=0.572).
- Mortality was closely associated with GLS by a factor of 1.62 compared to LVEF

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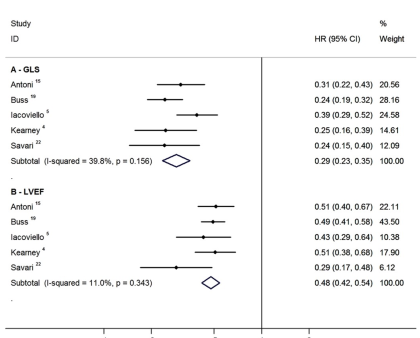
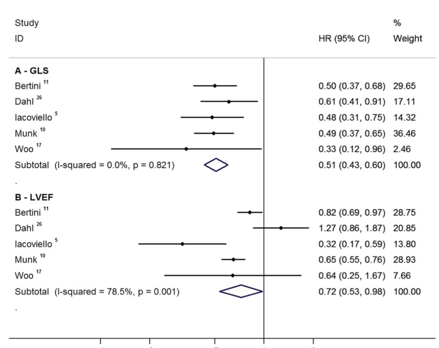
GLS and EF on Mortality



GLS and EF on Composite Endpoint



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Longitudinal 2D strain at rest predicts the presence of left main and three vessel coronary artery disease in patients without regional wall motion abnormality

Jin-Oh Choi, Sung Won Cho, Young Bin Song, Soo Jin Cho, Bong Gun Song, Sang-Chol Lee, and Seung Woo Park*

Division of Cardiology, Cardiac and Vascular Centre, Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, no. 50, Irwon-dong, Gangnam-gu, Seoul 135-710, Korea

Received 15 December 2008; accepted after revision 2 April 2009; online publish-ahead-of-print 28 April 2009

- **Study of 108 patients with left main or 3 vessel CAD without regional wall motion abnormality (RWMA) looking at GLS**
- **GLS cutoff of -17.9% has sensitivity and specificity of 79% for predicting severe CAD**

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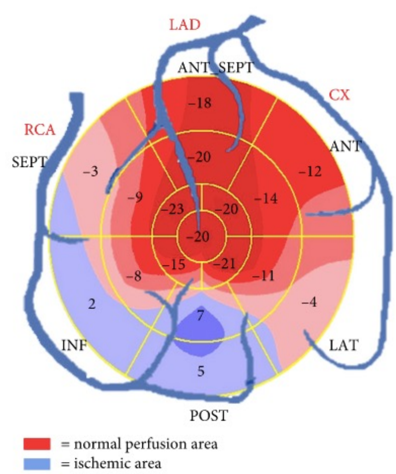

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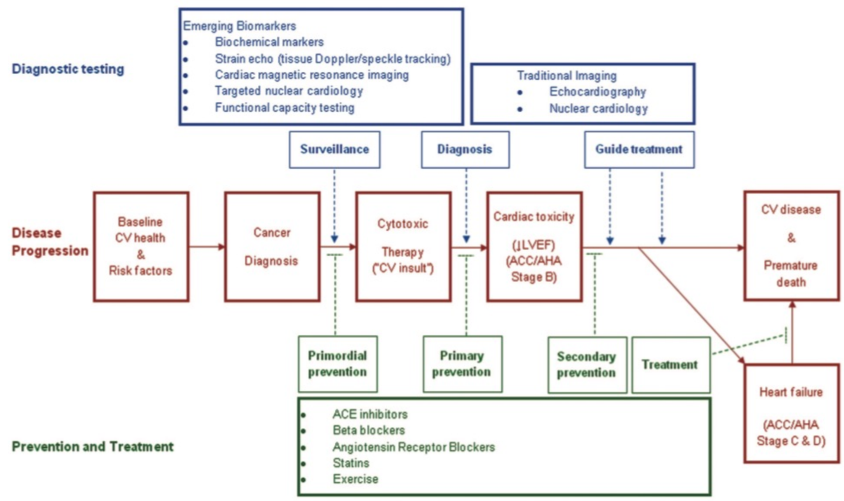
A Schematic Approach to Cardiotoxicity



Khouri et al. Circulation 2012

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Independent and Incremental Value of Deformation Indices for Prediction of Trastuzumab-Induced Cardiotoxicity

Kazuaki Negishi, MD, PhD, Tomoko Negishi, MD, James L. Hare, MBBS, PhD, Brian A. Haluska, PhD, Juan Carlos Plana, MD, and Thomas H. Marwick, MBBS, PhD, MPH, *Cleveland, Ohio; Brisbane and Hobart, Australia*

Table 3 Percent changes in echocardiographic parameters in 6 months within the groups

	No cardiotoxicity	Cardiotoxicity	*P*
GLS	0.2 ± 8.6	11.4 ± 9.8	<.001
GLSR-S	[illegible]	[illegible]	[illegible]
GLSR-E	5.1 ± 21.2	−11.9 ± 14.5	.002
s′	−5.0 ± 18.9	−17.0 ± 23.9	.04
e′	3.5 ± 37.1	−10.0 ± 28.7	.09
GCS	−1.0 ± 29.7	9.3 ± 27.4	.18
GRS	8.3 ± 48.5	−10.0 ± 39.3	.11

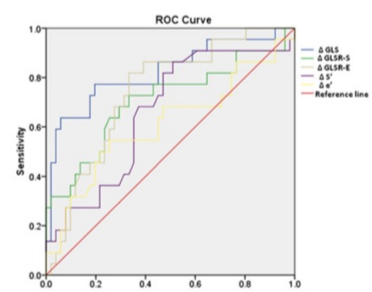

Figure 1 Receiver operating characteristic curves to predict subsequent decrease in EF. Discriminative abilities of the deformation parameters were evaluated to predict a >10% decrease in EF at 12 months.

GLS is an independent early predictor of later reductions in EF, incremental to usual predictors in patients at risk for trastuzumab-induced cardiotoxicity.

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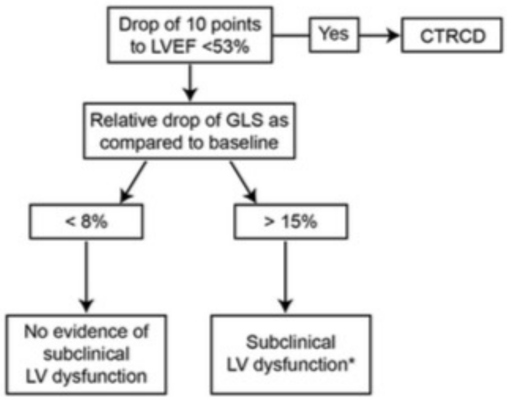
EXPERT CONSENSUS STATEMENT

Expert Consensus for Multimodality Imaging Evaluation of Adult Patients during and after Cancer Therapy: A Report from the American Society of Echocardiography and the European Association of Cardiovascular Imaging



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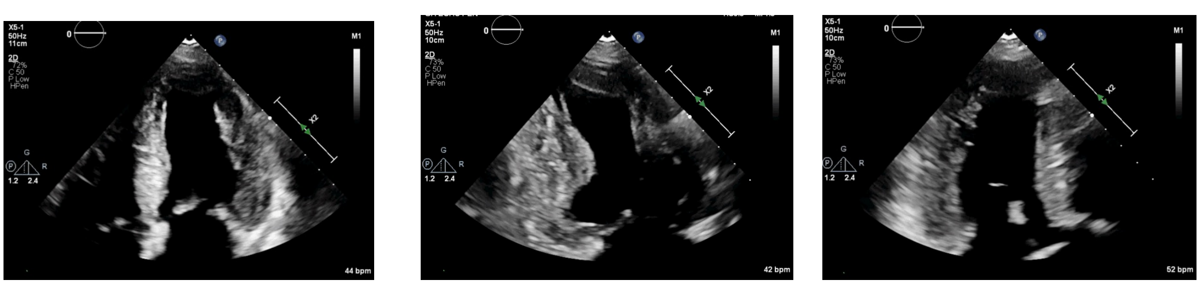
Case Example – 79 yo with HFpEF



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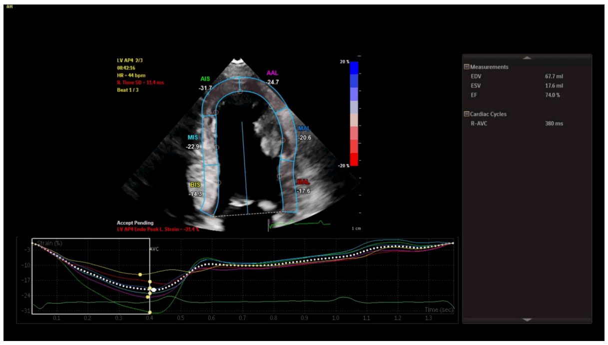

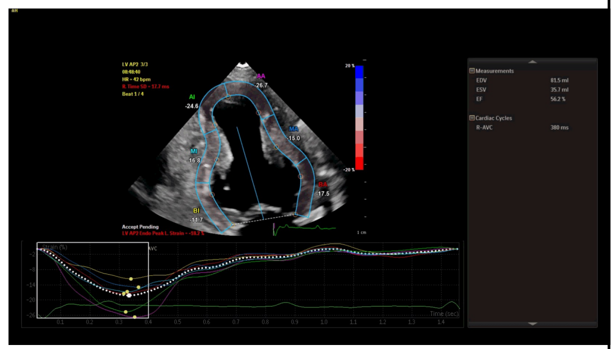

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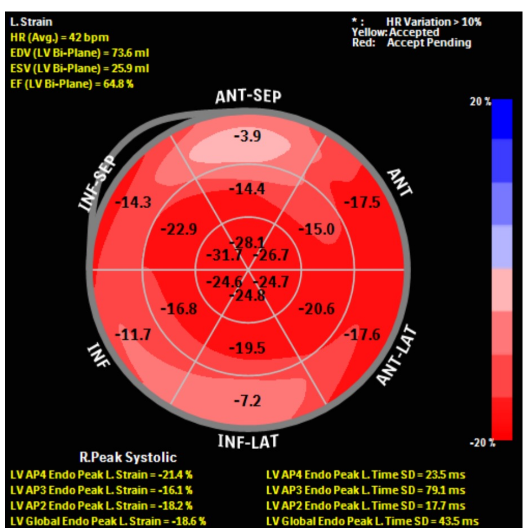
Bullseye Plot - GLS



GLS = -18.6%

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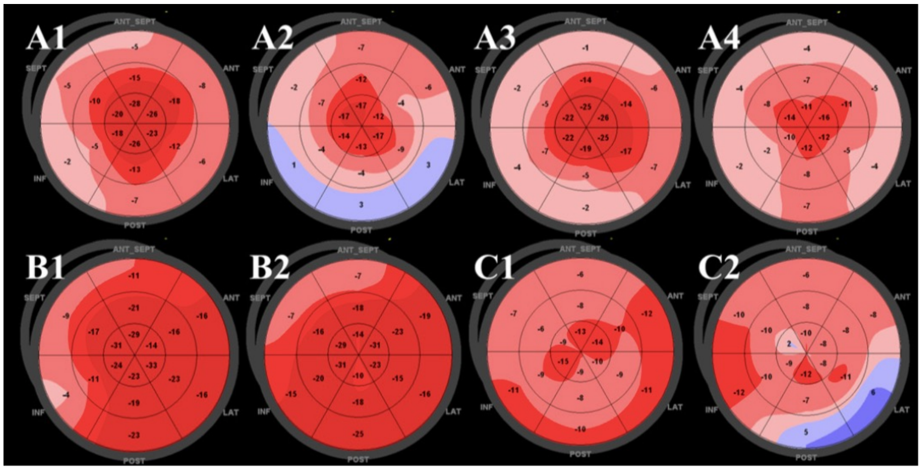
Apical Sparing seen in Cardiac Amyloidosis



A1-A4 : Cardiac Amyloidosis
B1-B2: HCM, C1-C2: Aortic Stenosis

Phelan et al. Heart 2012;98:1442e1448.

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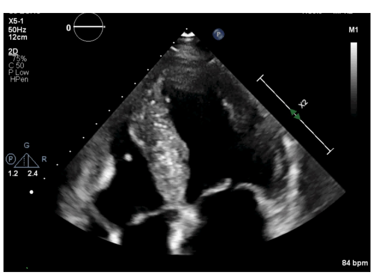
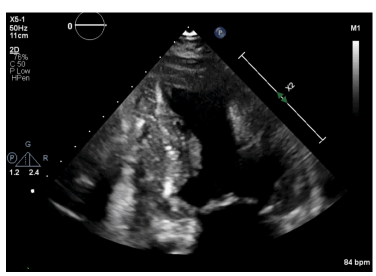
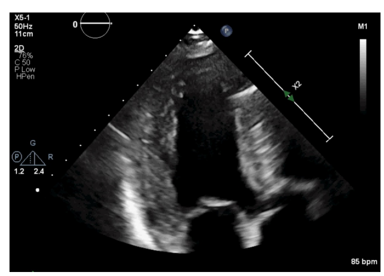
1 year later







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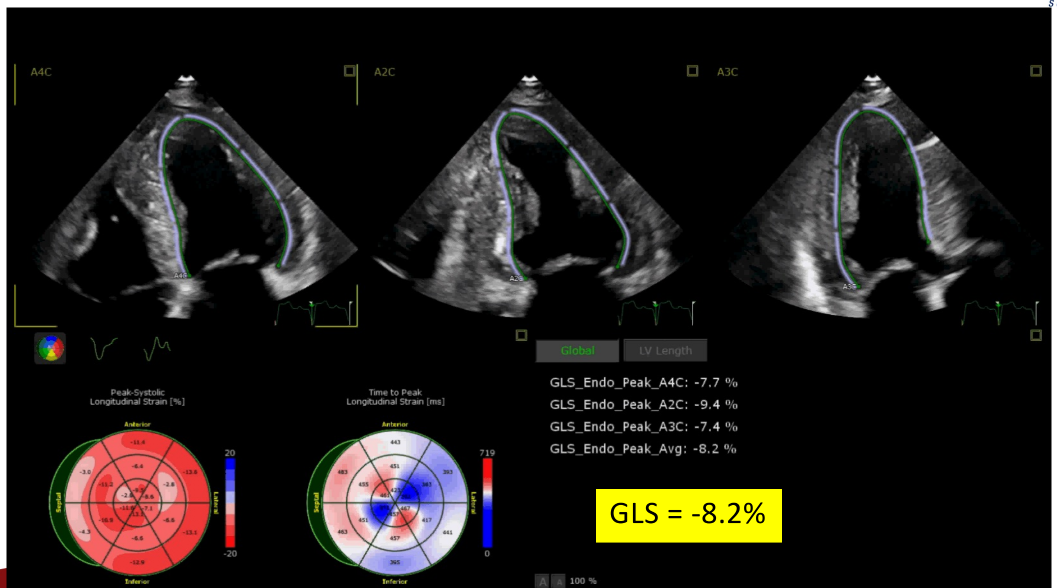

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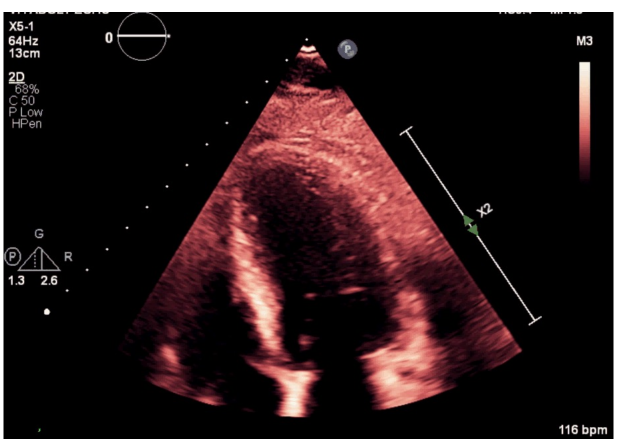
65 yo with normal thickness, normal EF



Patient recently diagnosed with Myeloma and AL amyloid

Question: Is there cardiac involvement?

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Strain to the Rescue

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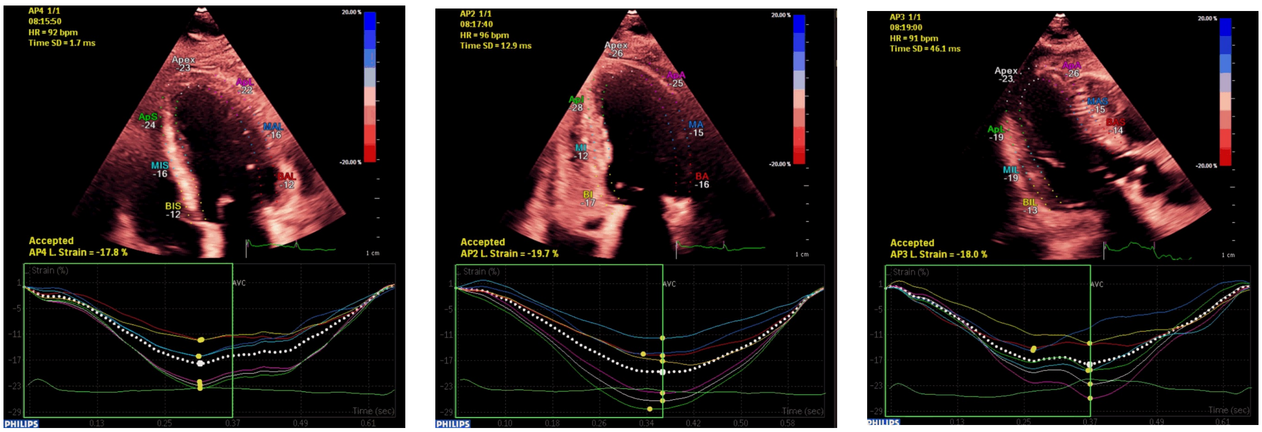

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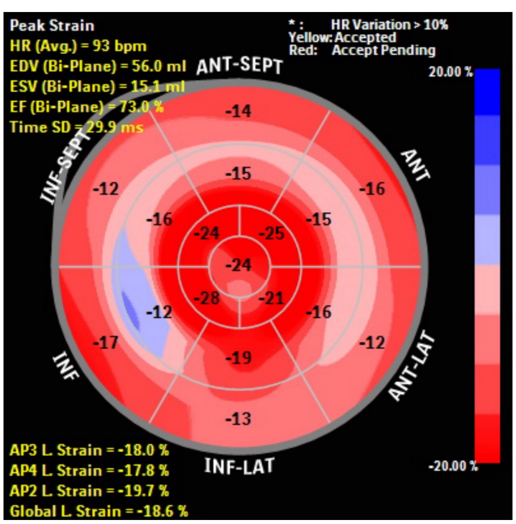

$$\text{RELAPS} = \frac{\text{Average Apical LS}}{\text{Sum of the average Basal and Mid LS}}$$

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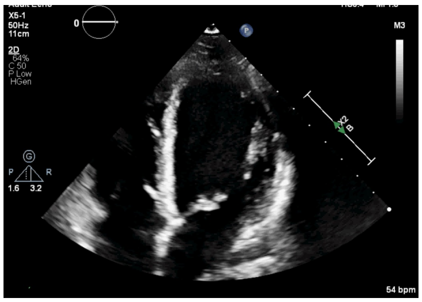
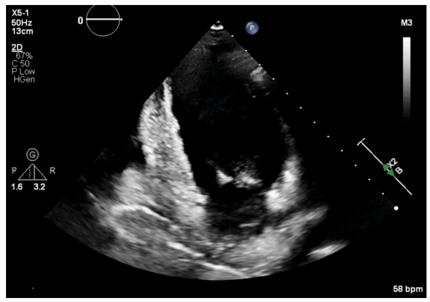
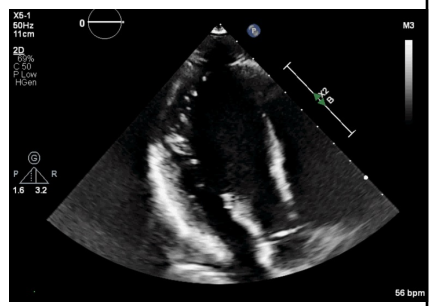
19 yo male with normal EF







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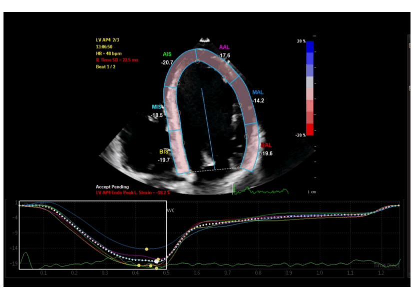

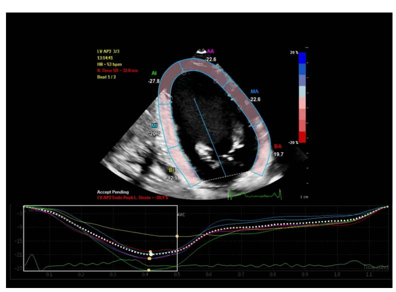

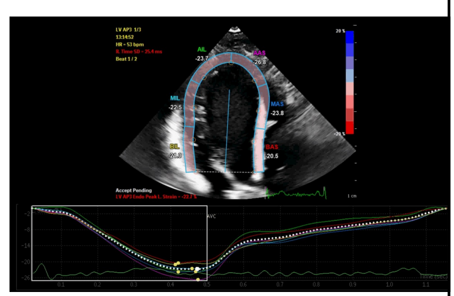

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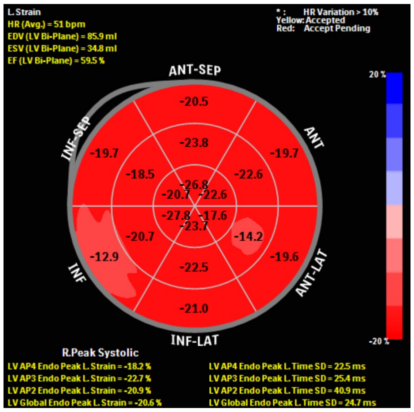
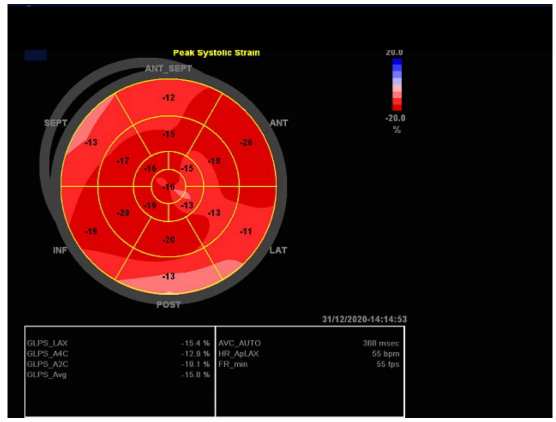
GLS = -20.6%



4 months prior:
GLS = -15.8%



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Further History and Observations

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- **Presented with myocarditis Dec 2020, 6 weeks following diagnosis of COVID-19 infection. Initial echo showed normal LV function but reduced strain in basal inferior wall and basal septum corresponding with nonischemic LGE in both areas. Initial Echo EF 50-55%**
- **Subsequent Echo 8 months later showed EF 55% with GLS still reduced at -16%**
- **Full normalization of LV function, EF 65% associated with normal GLS**

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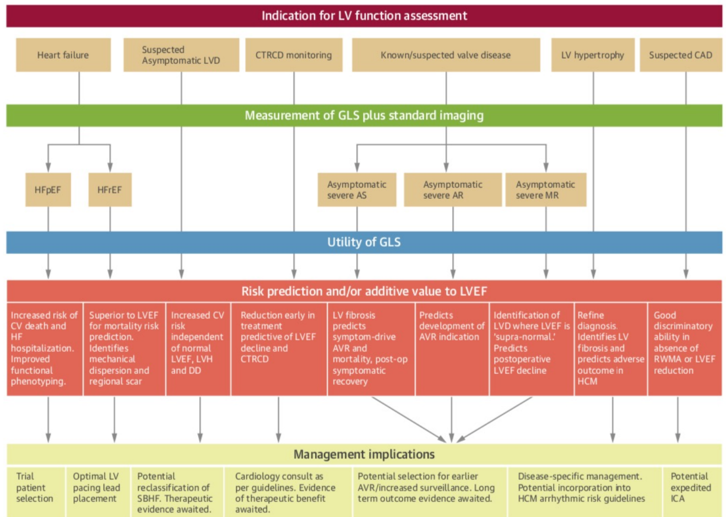
Utilities of Strain Beyond EF



Potter, E. et al. J Am Coll Cardiol Img. 2018;11(2):260-74.

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Summary and Conclusions

- Strain and GLS provide important prognostic information independent of Ejection, and insight into subclinical disease
- Consider its use in patients with both normal and reduced ejection fractions
- Both regional strain and GLS provide important information for clinical decision making

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Thank-you!

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