



## CardioTox 2019

Presente y futuro de la  
Cardio-Oncología

20-21 de marzo de 2019



Sede: Aula Ortiz Vázquez  
Hospital Universitario La Paz



ciberccv  
Centro de Investigación Biomédica en Red  
Enfermedades Cardiovasculares



aecc  
Contra el Cáncer

gepac  
PACIENTES/  
CÁNCER

Imagen en la prevención y  
diagnóstico de la cardiotoxicidad  
¿Qué necesitamos?

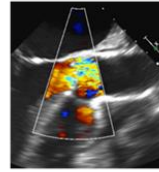
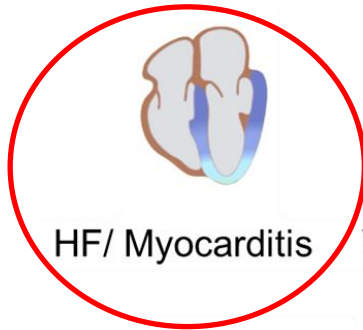
# FEVI o Strain: ¿tenemos dudas?

Teresa López-Fernández  
Hospital Universitario La Paz

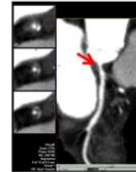
@TeresaLpezFdez

# What we need?

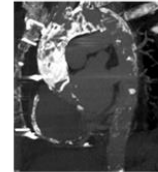
# Cardio-Oncology: How big is the problem?



Valvular HD



Ischemic HD



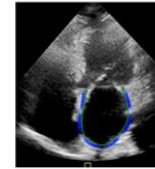
Vascular Diseases



Pulmonary Hypertension



Pericardial HD



Cardiac Arrhythmias

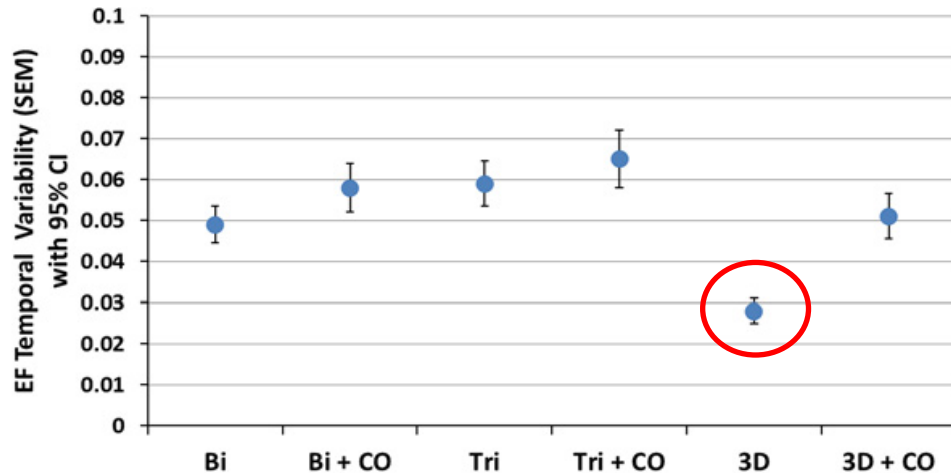
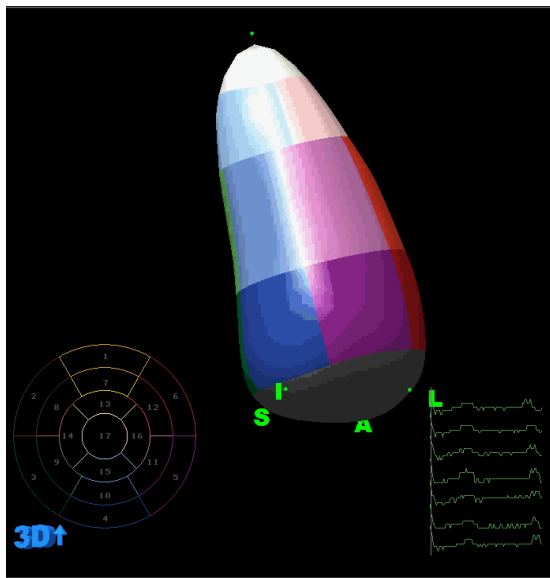
## Diagnosis & Prognosis

# Where EF is not enough

Functional Marker	Echo Modality	Other Modality
Left ventricular		
Systolic mechanics	Tissue velocity and 2D strain	CMR
Diastolic dysfunction	Tissue velocity, LA size	CMR
Hemodynamics	Doppler	RHC
Viability & ischemia	2D strain, MCE, stress	CMR, PET
LV synchrony	Tissue velocity and 2D strain	—
LV mass	3D	CMR
Myocardial characterization	2D strain	CMR
Non-LV		
RV size and function	Tissue velocity and 2D strain	CMR
Left atrial size	2D and 3D echo	CMR
Mitral regurgitation	Doppler, 3D	CMR

Marwick, T.H. J Am Coll Cardiol. 2018;72(19):2360–79.

# We need more reproducible parameters



EF SEM	0.049	0.058	0.059	0.065	0.028	0.051
95% CI	(0.045–0.054)	(0.053–0.065)*	(0.054–0.065)	(0.058–0.072)	(0.025–0.031)	(0.046–0.057)*

**3DE variability (5.8%) vs 2DE (9.8%)**

Thavendiranathan P et al. J Am Coll Cardiol 2013;61:77–84

# EF vs strain

## What's new?

# The added value of the 3D

**Technical  
issues**



- Precise LVEF measurements

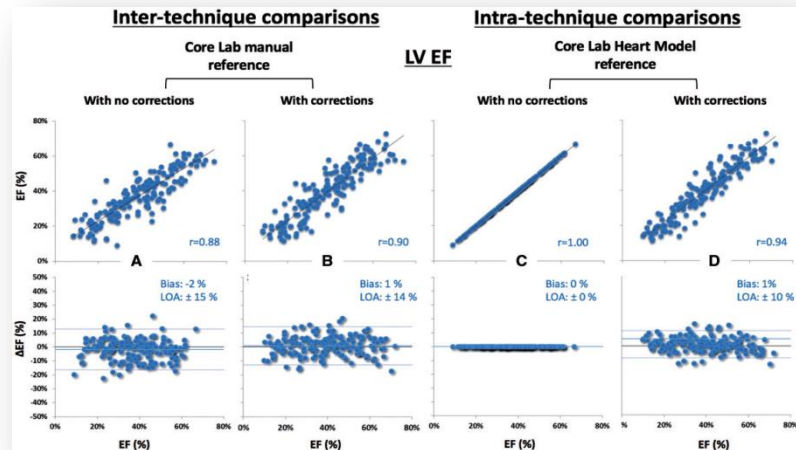


- Experience
- Time consuming

# 3DEF Automated Quantification

## Reproducibility

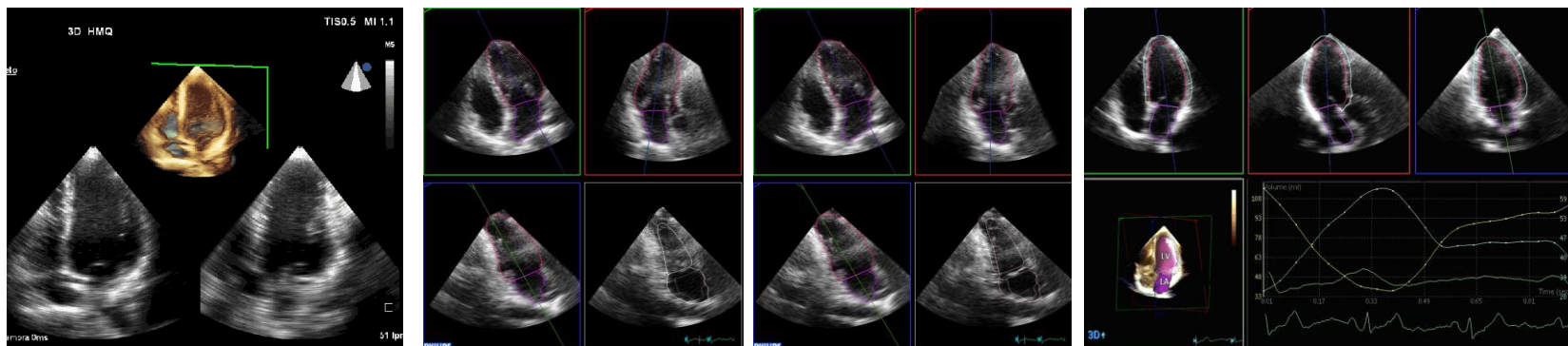
### Manual 3DE vs Automatic 3DE



Eur Heart J Cardiovasc Imaging. 2018 Jan 1;19(1):47-58 J Am Soc Echocardiogr 2017 Nov;30(11):1049-1058



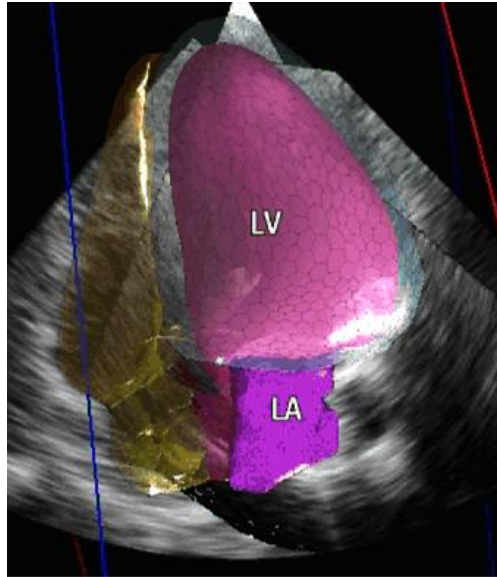
# 3D Dynamic Automatic Quantification



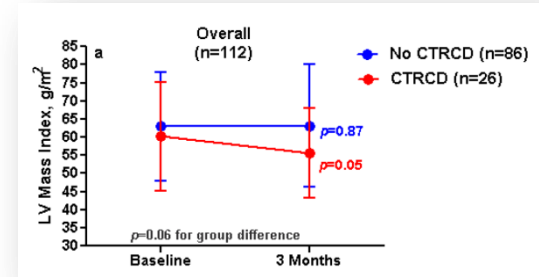
↓ Analysis time (<30 sec); Feasibility >90%; ↑ Reproducibility

Multi-beat analysis (5 beats)

# 3D Dynamic Automatic Quantification



Average (1, 2, 3)	
Left Ventricle	
EDV	154 ml
ESV	54 ml
EF	65 %
EDL	9.0 cm
ESL	6.8 cm
SV	99 ml
CI	3.61 l/min/m <sup>2</sup>
ED Mass	166 g
Left Atrium	
LAVmax	68 ml
LAVmin	19 ml
LAEF	72 %
LAVI	31 ml/m <sup>2</sup>
HR	
HR	80 bpm



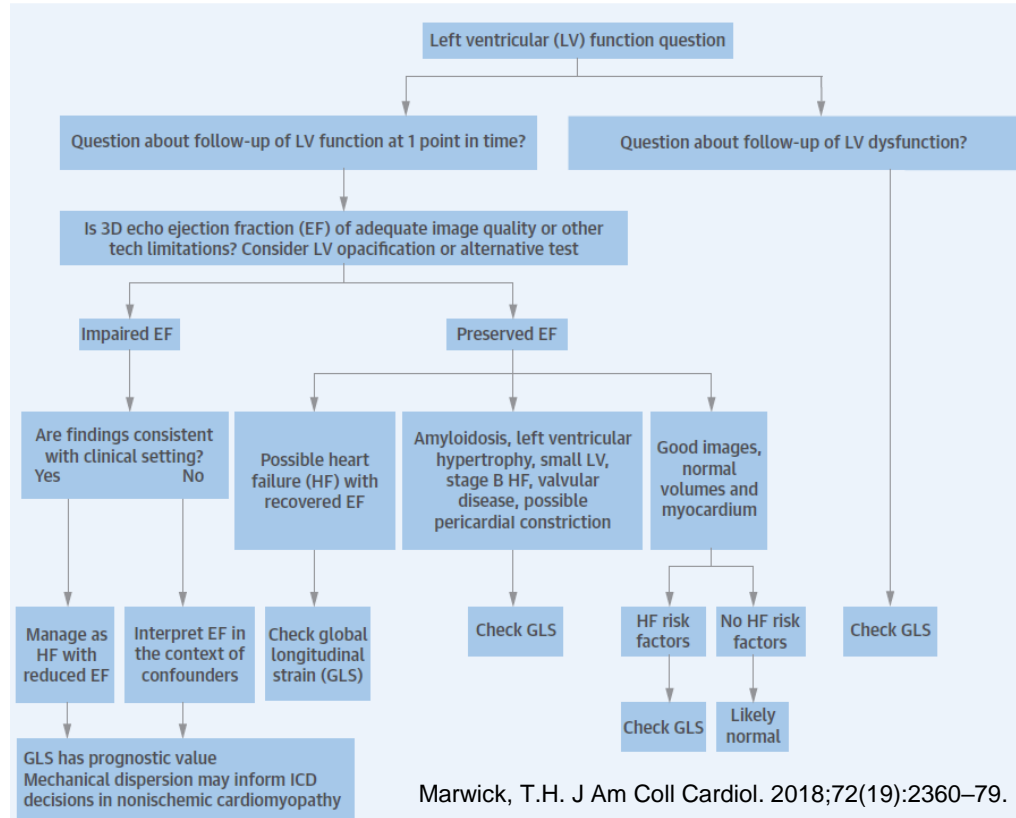
Plana JC Euroecho 2016

## Predictors of atrial fibrillation in ibrutinib-treated CLL patients: a prospective study

Gianluigi Reda<sup>1\*</sup>, Bruno Fattizzo<sup>2</sup>, Ramona Cassin<sup>1</sup>, Veronica Mattiello<sup>2</sup>, Tatiana Tonella<sup>3</sup>, Diana Giannarelli<sup>4</sup>, Ferdinando Massari<sup>3</sup> and Agostino Cortelezzi<sup>2</sup>

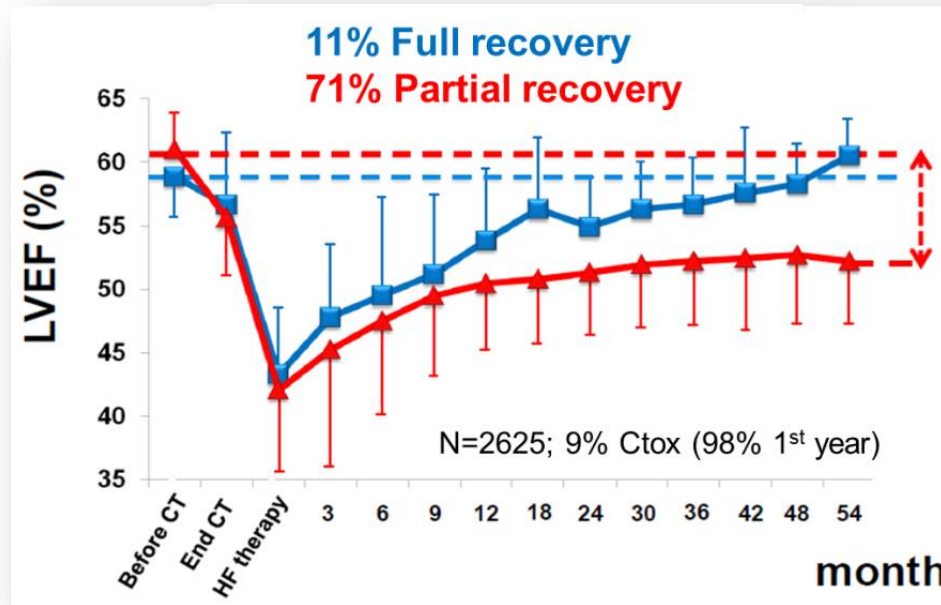
Reda et al. Journal of Hematology & Oncology (2018) 11:79

# LV function question



# We need more sensitive parameters

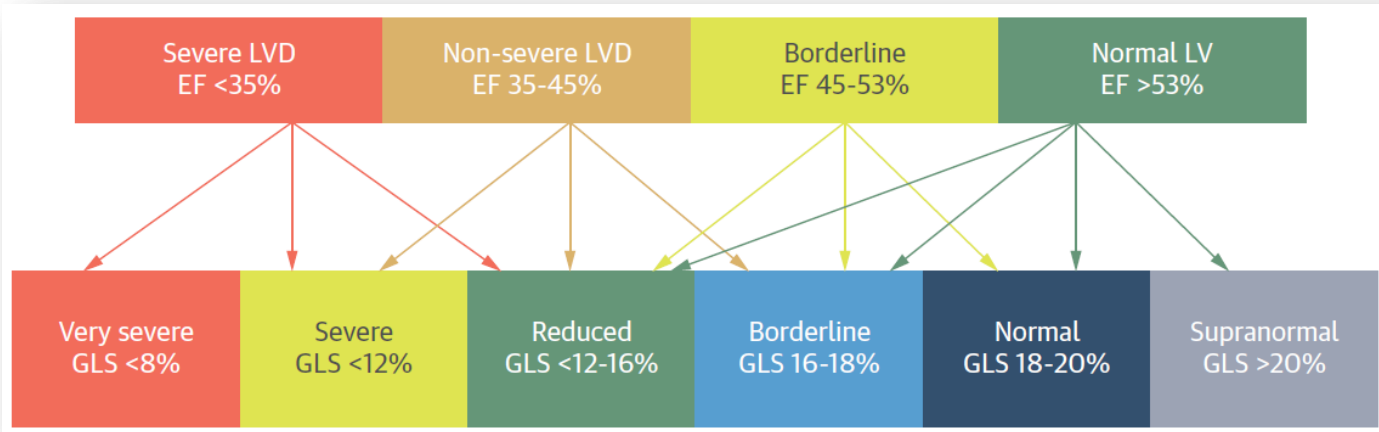
## Early HF treatment (EF-based)



Cardinale D et al. Circulation 2015;131:1981-88

# Deformation imaging: what we know?

## HF re-classification with GLS



- Patients at risk of HF

- Patients with HFpEF

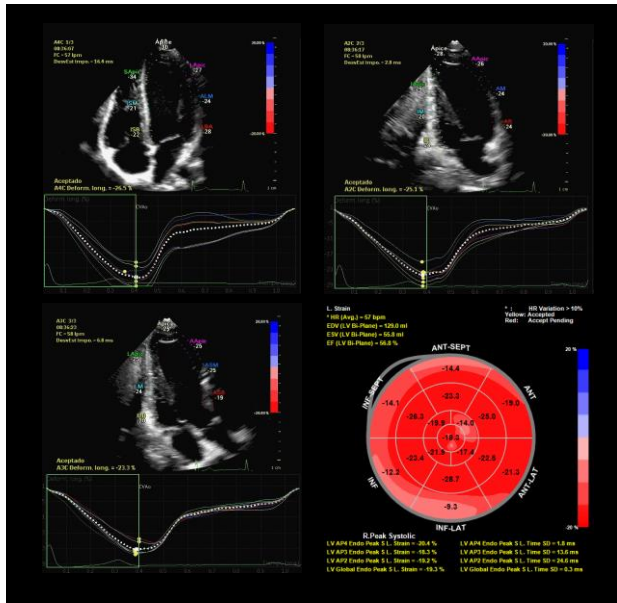
Eur J H F 2016; 18: 1331–1339

J Am Soc Echocardiogr 2015;28:652-66

J Am Coll Cardiol Img 2018;11:260–74

# Deformation imaging: what we know?

## 2D Speckle tracking: pros and cons

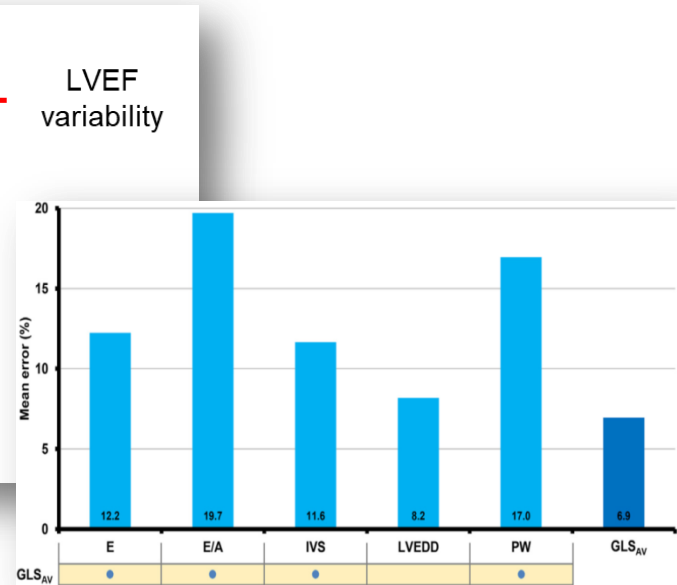
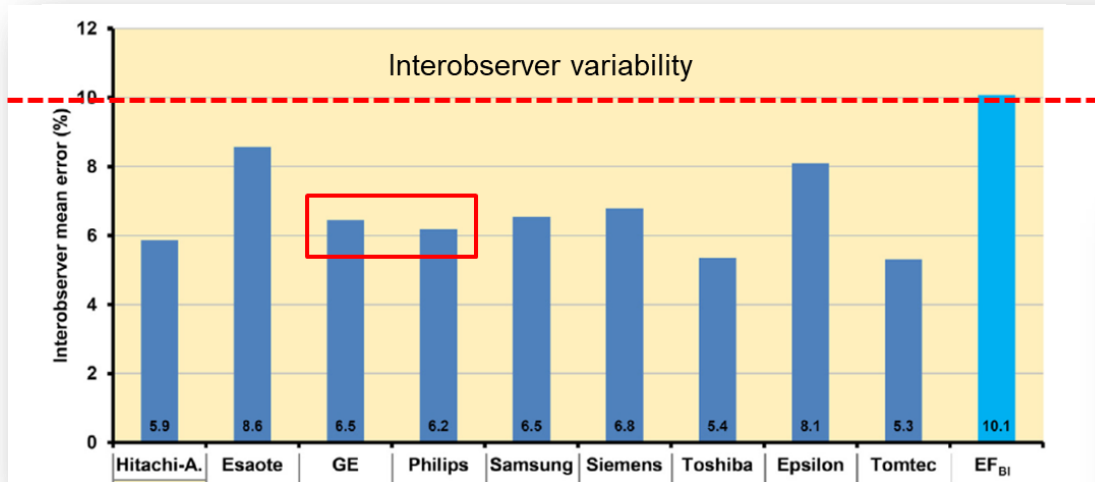


1. Feasibility >90%
2. Analysis time <2min
3. GLS Standardization
4. Reproducibility
5. Learning curve

- No universal normal values
- Load dependence

# Deformation imaging: what we know?

## 2D Speckle tracking **standardization**



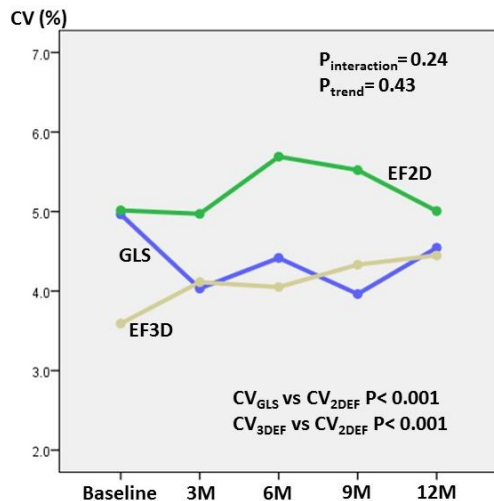
J Am Soc Echocardiogr 2015;28:1171-81

# Deformation imaging: what we know?

## 2D Speckle tracking reproducibility

Precision and stability of parameters for assessment of LV systolic function in clinical trials: lessons from the SUCCOUR Trial

### Coefficient of Variance between Core lab and Sites



GLS (%)	Baseline	3M	6M	9M	12M
Core lab	21.2±2.2	19.6±2.2	19.5±2.6	19.1±2.2	19.4±2.4
Site	20.3±2.2	19.4±2.4	19.3±2.8	19.3±2.5	19.5±2.4

2DEF (%)					
Core lab	61±3	58±4	58±4	57±4	57±6
Site	62±6	61±6	60±7	60±6	60±7

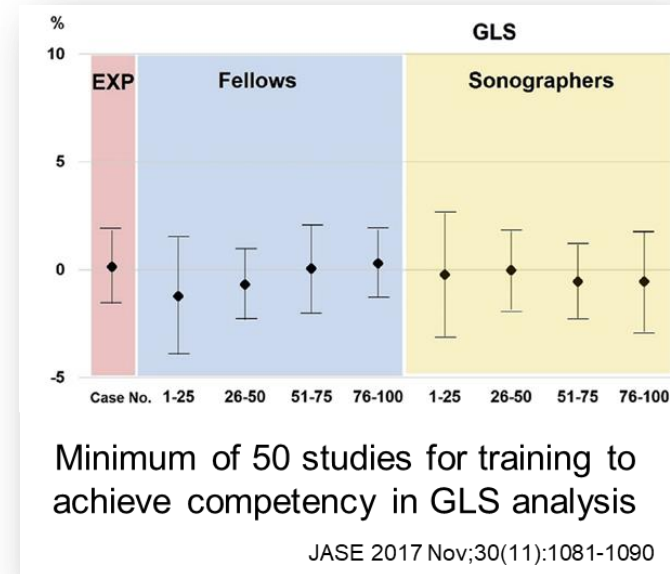
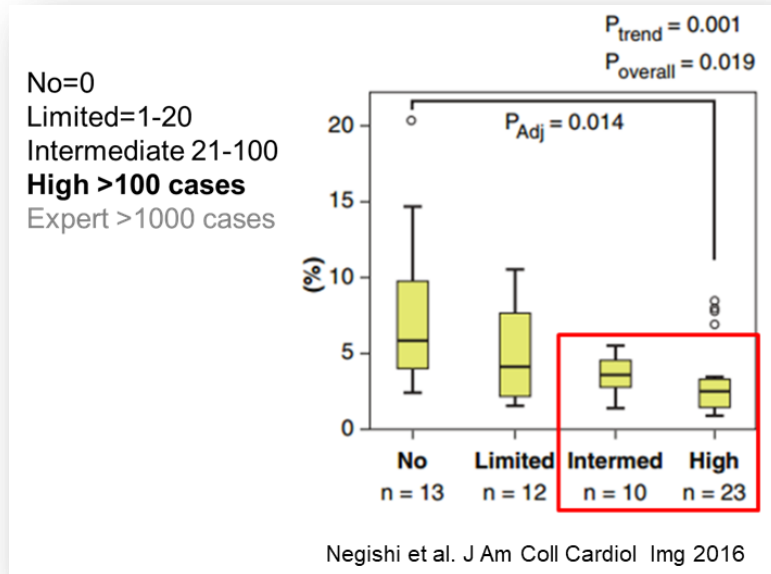
3DEF (%)					
Core lab	60±4	58±4	58±4	57±4	57±5
Site	61±4	59±5	59±5	59±5	58±5

Negishi et al. ACC 19 presented (1174-321)



# Deformation imaging: what we know?

## Implementing quality control of GLS: the learning curve

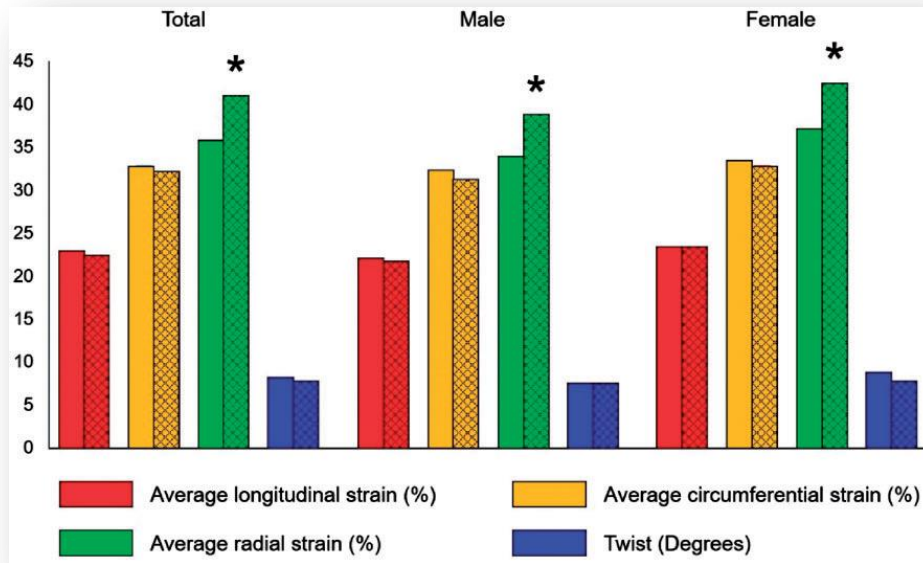


Echocardiographic reference ranges for normal left ventricular 2D strain: results from the EACVI NORRE study

N=549  
45.6 ± 13.3 yo



\* P <0.05 vs GE

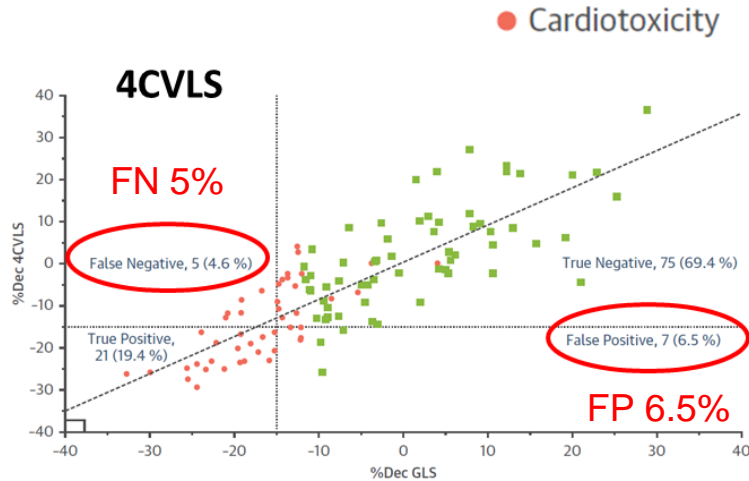


GLS low normal values  
-16,7% men  
-17,8% women

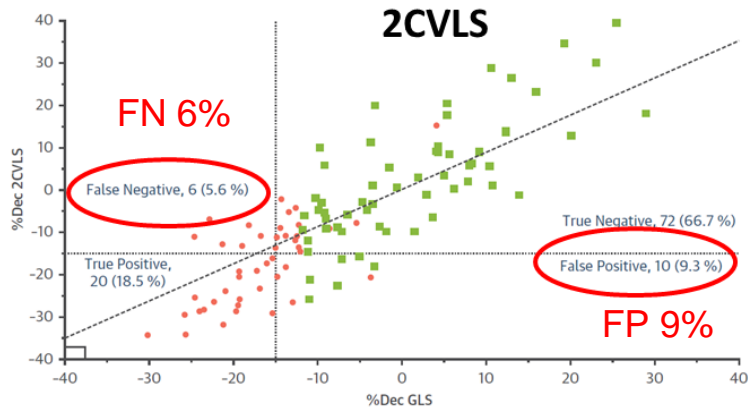
GCS low normal values  
-22,3% men  
-23,6% women

# Deformation imaging: what we know?

## 2D Speckle tracking: not a single plane!!



Discordance rate of 11%  
Diagnostic accuracy of 89%

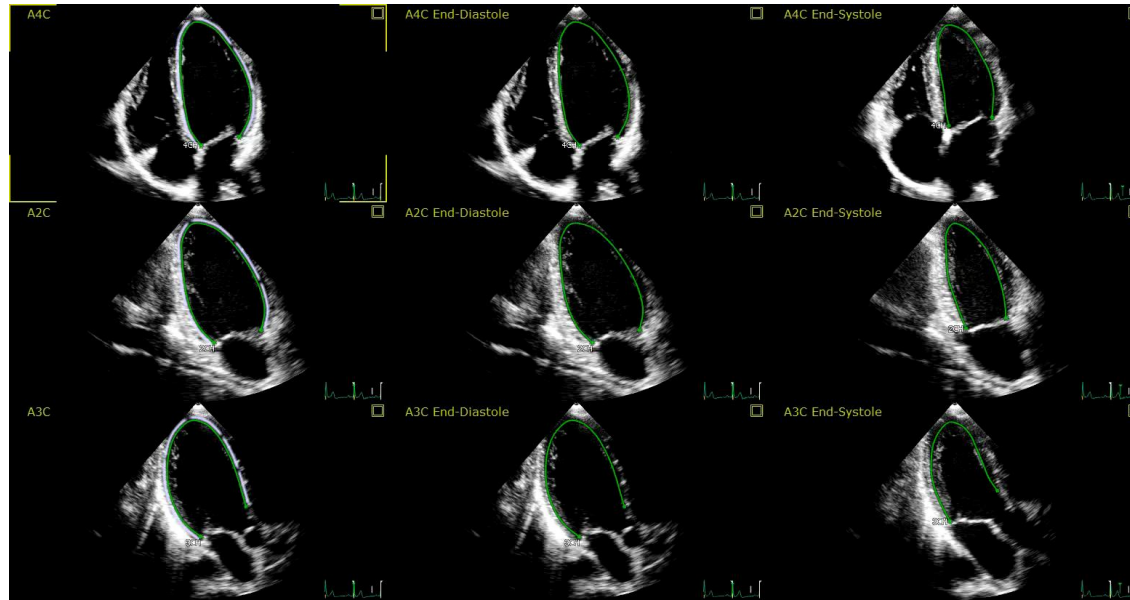


Discordance rate of 15%  
Diagnostic accuracy of 85%

JACC Cardiovasc Imaging 2018, 11(8):1109-1118.

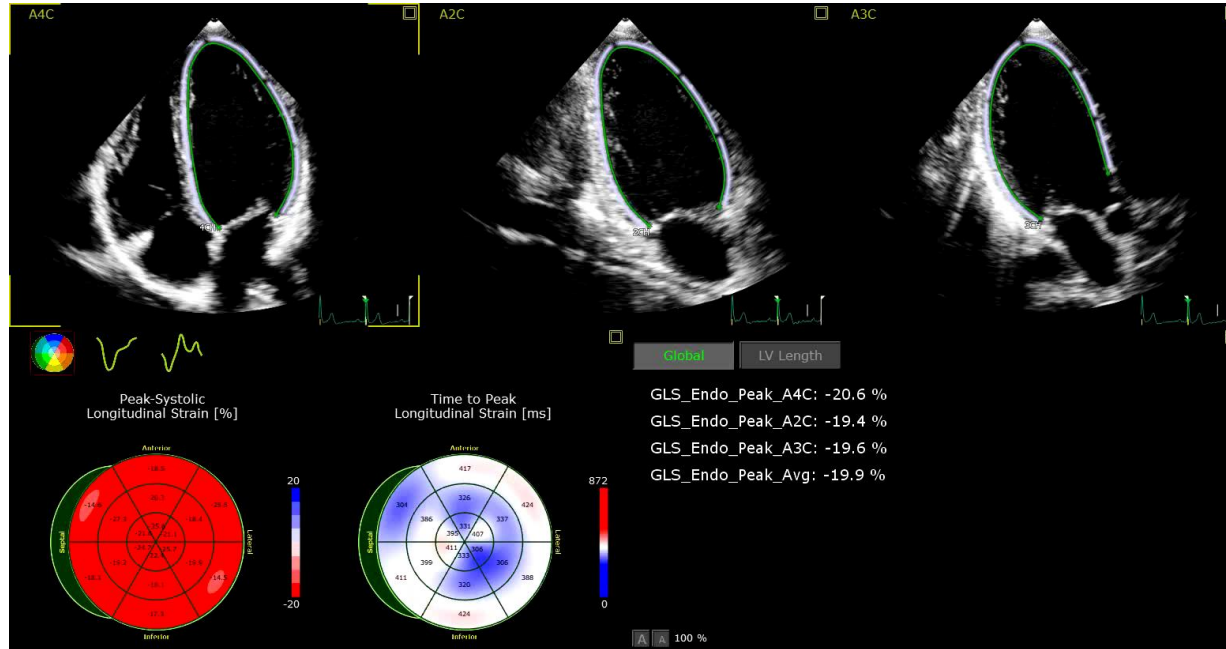
# Deformation imaging: what we need?

## Auto-strain



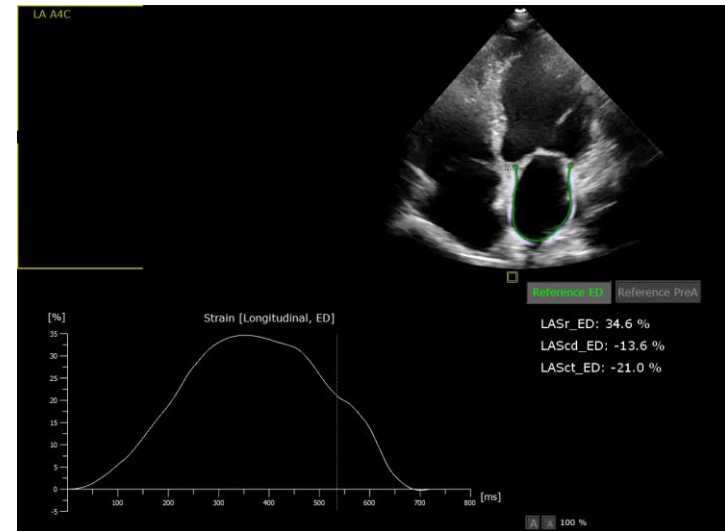
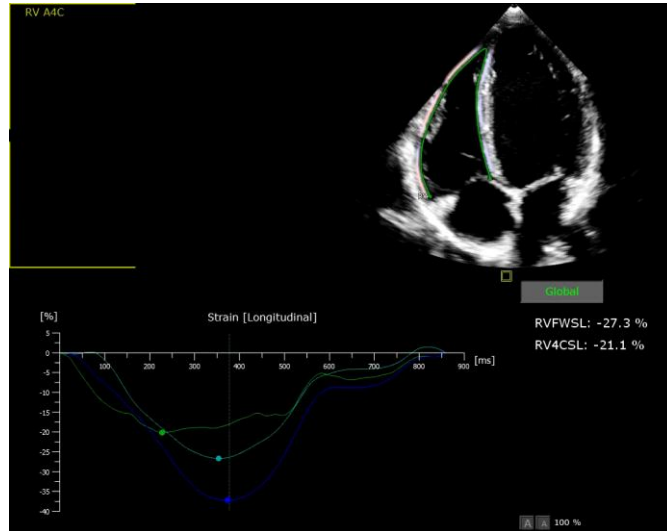
# Deformation imaging: what we need?

## Auto-strain



# Deformation imaging: what we need?

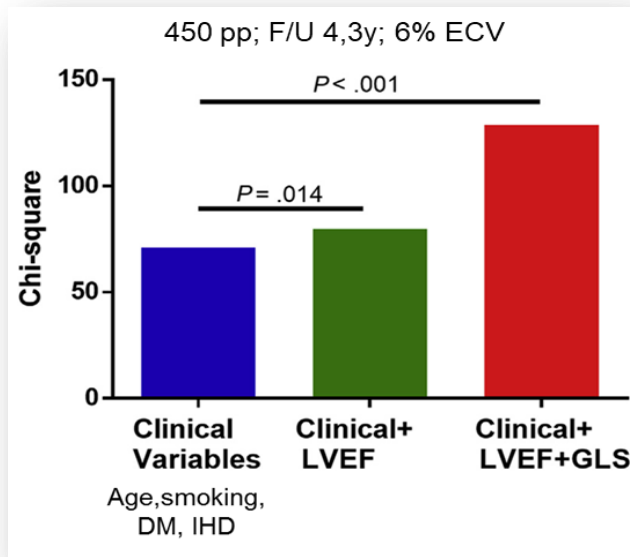
## Auto-strain



# Baseline risk

## GLS risk stratification

- EF 50-55%
- Smoking
- HTN
- DM
- CAD



**GLS > -17.5 %**



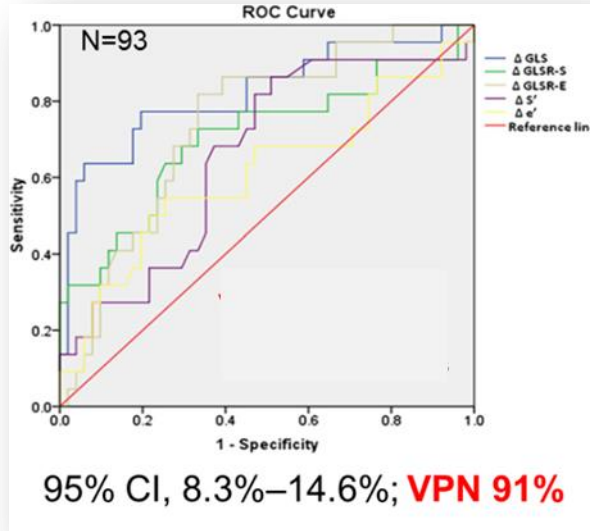
**↑x6 RR**

**Death/HF**

Eur H J Cardiovasc Imaging 2015; 16: 977–984

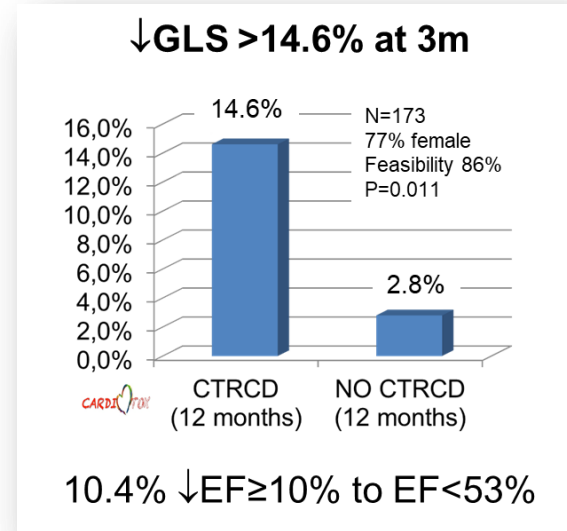
J Am Soc Echocardiogr 2016;29:522-27

# Early identification of injury during therapy



**↓GLS >11%**

JASE 2013; 26:493-8

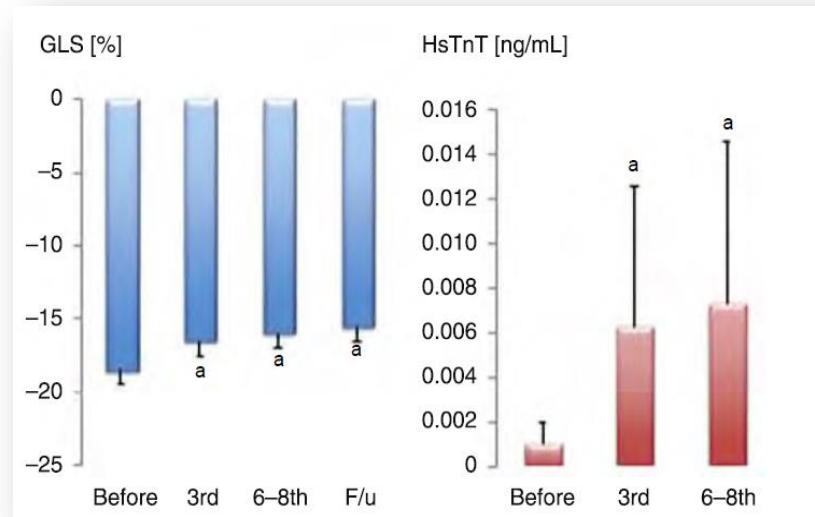


**↓GLS >14.6%**

Eur H J Cardiovasc Imaging 2014;15(Suppl. 2): ii109–36



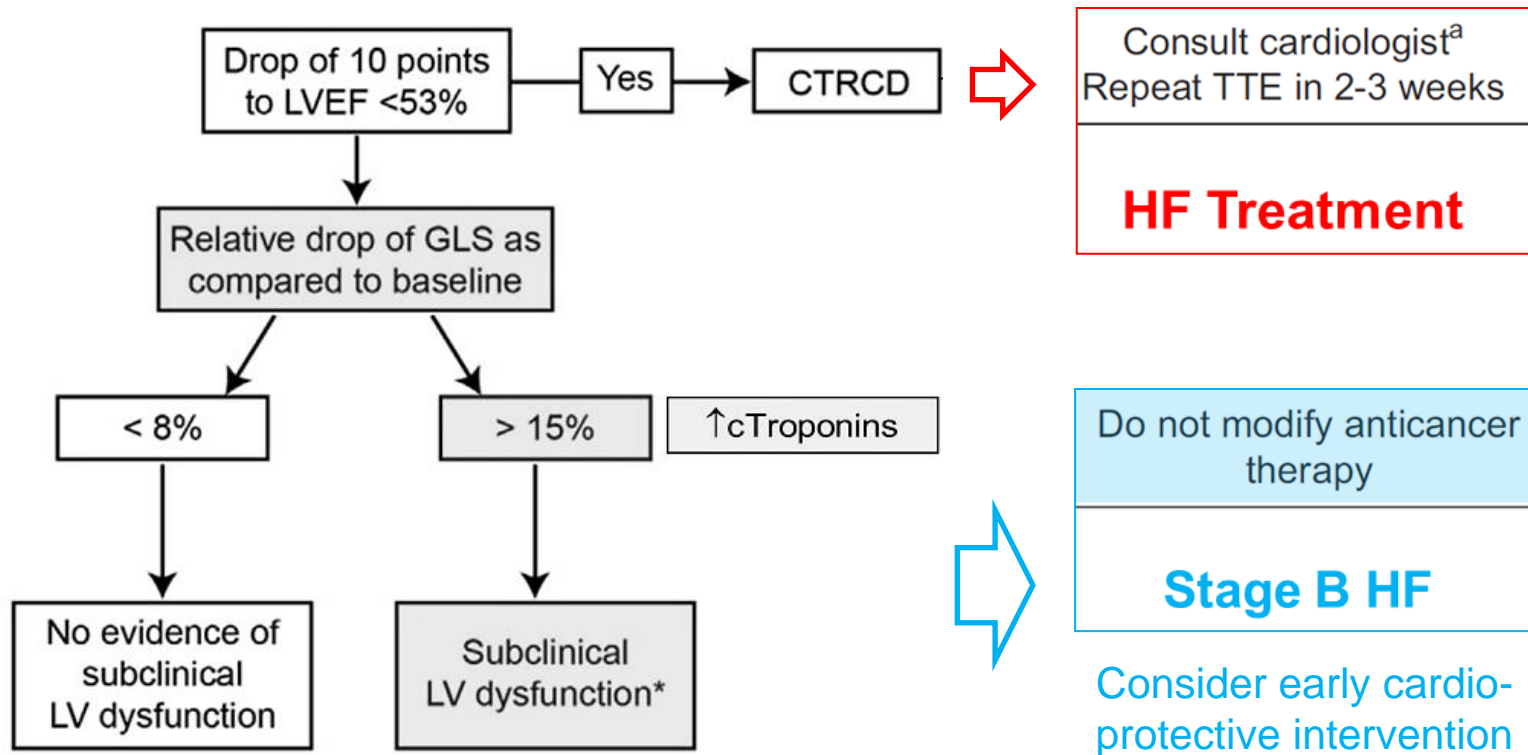
# Early identification of injury during therapy



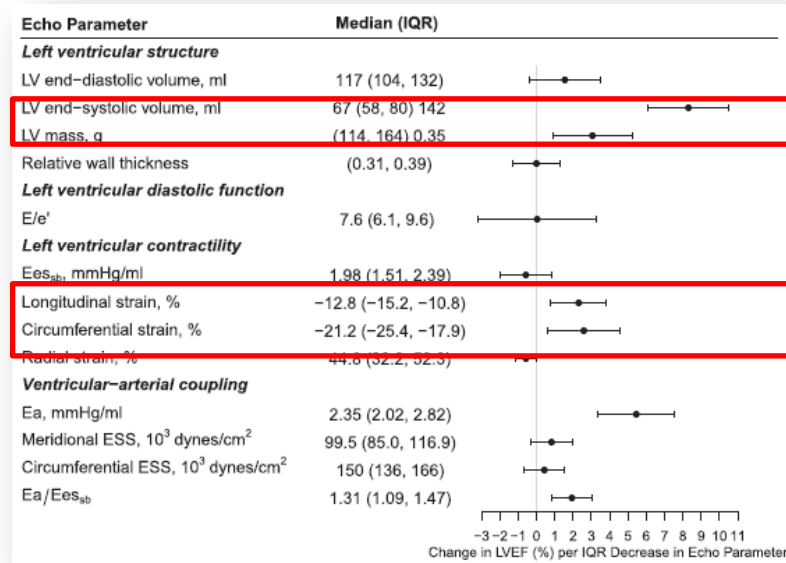
↓GLS+/-↑troponins predicts LVD with a high NPV

Eur JHF 2014;16(3):300-8

# Cardio-protection treatment guidance



# Prediction of LVD recovery

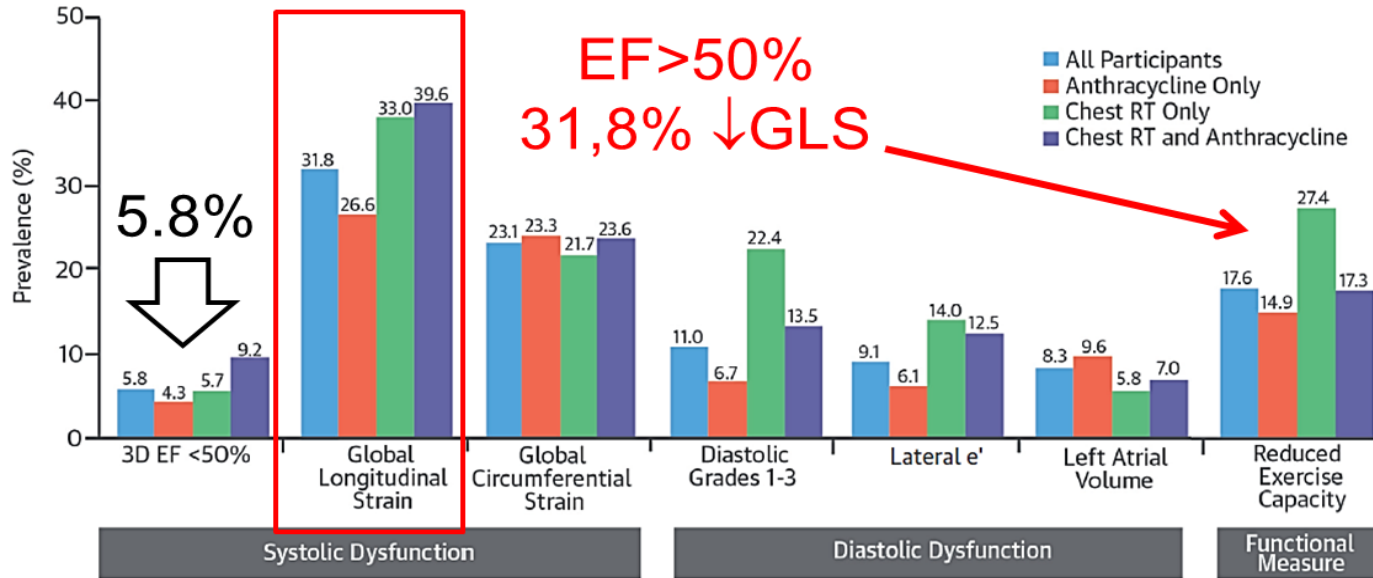


**CONCLUSIONS:** Doxorubicin and trastuzumab resulted in modest, persistent declines in LVEF at 3 years. Changes in volumes, strain, and ventricular-arterial coupling were consistently associated with concurrent and subsequent LVEF declines and recovery across therapies.

Ky B et al *Circulation*. 2017;135:1397–1412.

# End-treatment and long term cancer survivors

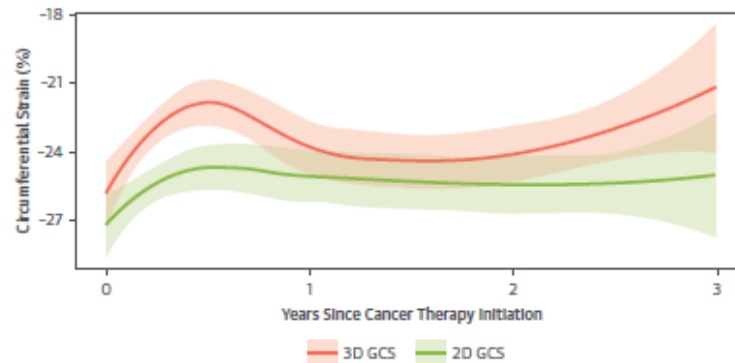
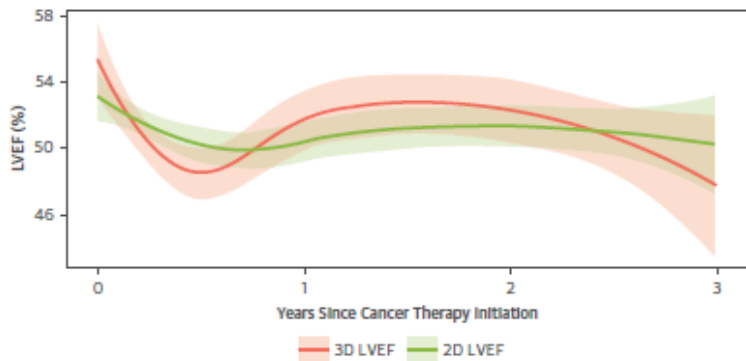
St Jude Lifetime Cohort Study: 1820 patients (mean age 31; F/U 23 years)



J Am Coll Cardiol 2015;65:2511–22

## Abnormalities in 3-Dimensional Left Ventricular Mechanics With Anthracycline Chemotherapy Are Associated With Systolic and Diastolic Dysfunction

Kathleen W. Zhang, MD,<sup>1</sup> Brian S. Finkelstein, MD, PhD,<sup>2</sup> Gaurav Gulati, MD,<sup>3</sup> Hari K. Narayan, MD,<sup>4</sup> Jenica Upshaw, MD,<sup>5</sup> Vivek Narayan, MD,<sup>6</sup> Ted Plappert, CVT,<sup>7</sup> Virginia Englefield, CVT,<sup>7</sup> Amanda M. Smith, BA, MS,<sup>7</sup> Carina Zhang, BA,<sup>1</sup> W. Gregory Hundley, MD,<sup>8</sup> Bonnie Ky, MD, MScE,<sup>2b</sup>



Both 3D LVEF and GCS had independent value in predicting subsequent reduction in 2D LVEF (over 2D LVEF and 2D GCS)

# Future Needs

# Cardio-protection treatment guidance

## SUCCOUR Trial

International multicenter prospective  
randomized trial  
N=320 (88% BC) F/U 3y

### Inclusion criteria

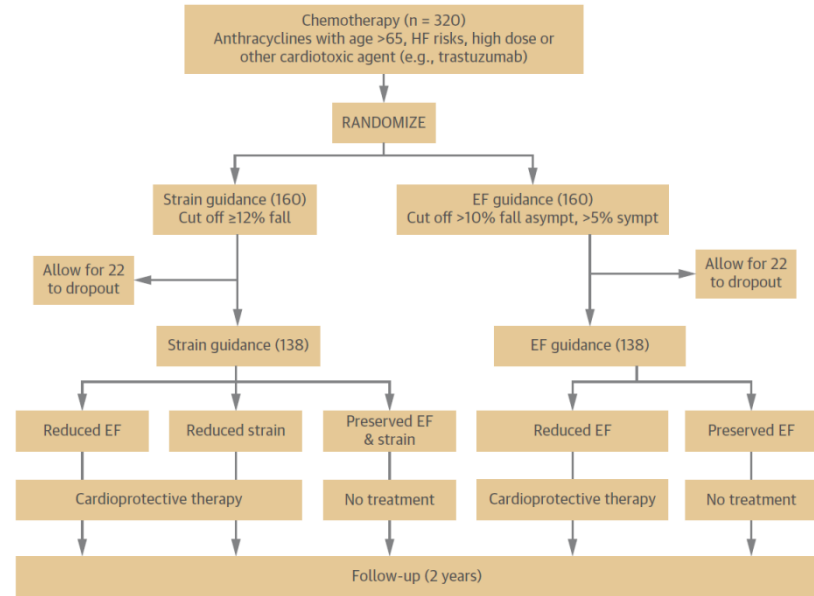
Cardiotoxic chemo +  $\geq 1$  HF-risk factor

### HF-risk factors

34% Hypertension  
10% DM

### Baseline

3DEF 61 $\pm$ 4%  
GLS 20.3 $\pm$ 2.5%



J Am Coll Cardiol Img 2018;11:1098–105

# Need to agree on monitoring protocols

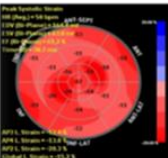
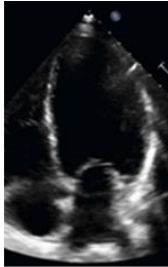
Cancer Therapeutics	Stage A Risk Stratification and Modification	Stage B Screening for LV Dysfunction	Stage C Symptomatic HF	Stage D Advanced HF
Anthracyclines	✓	✓	✓	✓
HER-2 Therapy	✓	✓	✓	✓
VEGF Inhibitors	✓*	✓*	✓	○
Proteasome Inhibitors	○	○	✓	○
Immune Checkpoint Inhibitors	○	○	✓	○

Kenigsberg B et al. JACC Heart Fail. 2018 Feb;6(2):87-95.



# Take home messages: Cardiac imaging in CO

Cardio-Oncology Team



**LVEF** is the currently recommended method to guide therapy

**3D echo** is the method of choice for sequential calculation of LVEF

**GLS** is more sensitive than 2DEF for the detection of minor changes in LV function (Better intra and inter-observer variability than LVEF)

Abril — Junio  
2019

Programa de formación en  
Cardio-Onco-Hematología



Un proyecto de:

SOLEDAD  
ESPAÑOLA DE  
CARDIOLOGÍA

SEH  
Sociedad Española de  
Hematología y Hemoterapia

SEOM  
Sociedad Española  
de Oncología Médica

SEOR  
SOCIEDAD ESPAÑOLA DE  
ONCOLOGÍA RADIOTERÁPICA

SEMG  
Sociedad Española de  
Medicina General y de Familia

MARTES  
**02**  
abril  
2019

**MÓDULO I**  
**ACTUALIZACIÓN EN INSUFICIENCIA CARDIACA  
EN PACIENTES ONCO-HEMATOLÓGICOS**

MARTES  
**07**  
mayo  
2019

**MÓDULO II**  
**CÁNCER Y RIESGO CARDIOVASCULAR:  
NECESIDAD DE EQUIPOS MULTIDISCIPLINARES**

MARTES  
**04**  
junio  
2019

**MÓDULO III**  
**ANTICOAGULACIÓN Y CÁNCER ACTIVO.  
¿QUÉ SABEMOS Y QUÉ NOS FALTA?**

**[coh19.secardiologia.es](http://coh19.secardiologia.es)**

# Cardio-Onco-Hemato (COH) en la práctica clínica

## Formación de equipos en Atención Primaria



Sección de  
Cardiología  
Clínica | Grupo de  
Cardio-oncología

## ACTIVIDAD ACREDITADA CON 23,11 CRÉDITOS CASEC



SOLICITADA ACREDITACIÓN OFICIAL ante el Sistema Acreditador de Formación Continuada de las Profesiones Sanitarias de Galicia. Esta acreditación tiene validez en todo el territorio nacional.

Con la colaboración de las siguientes sociedades:



Sociedad Española de  
Hematología y Hemoterapia



Asociación Española de  
Enfermería en Cardiología



# [www.doctopedia.es](http://www.doctopedia.es)



**Hospital Universitario  
La Paz**  
Hospital Carlos III  
Hospital Cantoblanco



**Gracias**

tfernandez8@gmail.com



**CardioTox 2019**

