Guideline-Driven Care in Cardio-Oncology: Utilizing Recommendations Across Disciplines

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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

- Summarize the key points
- Science behind the recommendations
- Apply the document to clinical practice
- Take home messages

(J Am Soc Echocardiogr 2014;27:911-39.)

Keywords: Chemotherapy, Doxorubicin, Trastuzumab, Left ventricular dysfunction, Three-dimensional echocardiography, Early detection, Strain, Biomarkers

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

I. CTRCD – definition, classification and mechanisms of toxicity
II. Echocardiographic evaluation of the patient undergoing cancer therapy
III. Early detection of toxicity
IV. Other imaging modalities
V. Integrated approach

I. CTRCD – definition, classification and mechanisms of toxicity

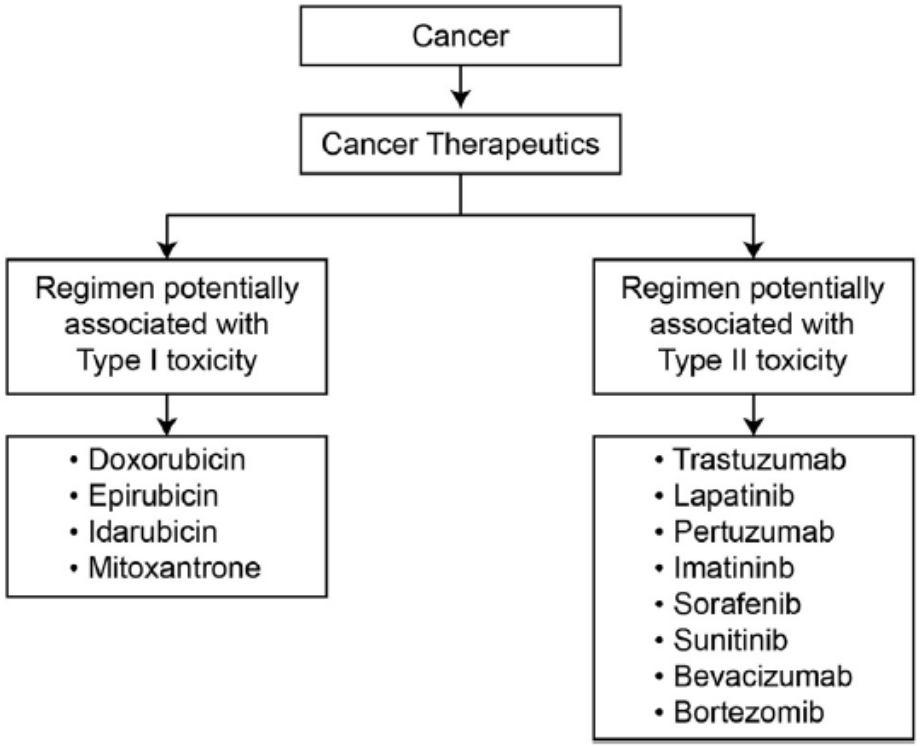
Forms of Cardiotoxicity

- LV dysfunction
  - *Cancer therapeutics-related cardiac dysfunction or CTRCD*
- Ischemia
- HTN
- Arrhythmia
- Thromboembolism
- QT prolongation

I. Cancer Therapeutics-Related Cardiac Dysfunction (CTRCD)

- Definition
  - A decline in EF from baseline of >10% to a value <53%
- Symptomatic or asymptomatic
- Reversible or irreversible
- Type 1 or Type 2

Classification of CTRCD
Type 1 vs. Type 2



Consensus Statement: Differentiation of CTRCD into Type 1 and Type 2

Type I CTRCD

- Prototype: doxorubicin
  - Cumulative dose-dependent
  - Irreversible damage
  - Cellular apoptosis/necrosis
  - Ultrastructural changes on biopsy

Type II CTRCD

- Prototype: trastuzumab
  - Not cumulative dose dependent
  - mostly reversible LV dysfunction
  - Cellular dysfunction
  - No biopsy changes

II. Echocardiographic Evaluation of Cardiac Structure and Function in Cancer Patients

LVEF Measurement

Consensus Statement: EF determination
3D LVEF preferred; 2D EF biplane MOD (consider contrast)

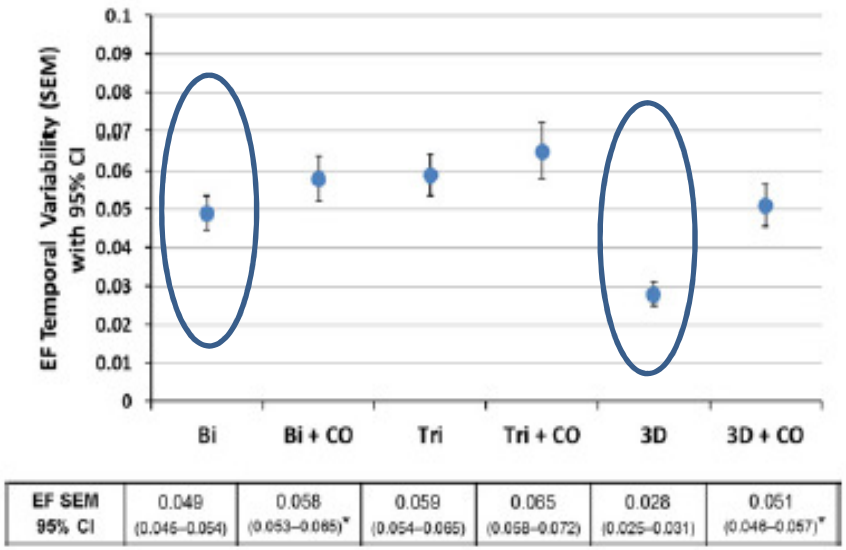
Reproducibility of Echocardiographic Techniques for Sequential Assessment of Left Ventricular Ejection Fraction and Volumes

Application to Patients Undergoing Cancer Chemotherapy

Paaladinesh Thavendiranathan, MD, MSc, Andrew D. Grant, MD, Tomoko Negishi, MD, Juan Carlos Plana, MD, Zoran B. Popović, MD, PhD, Thomas H. Marwick, MD, PhD, MPH

Cleveland, Ohio

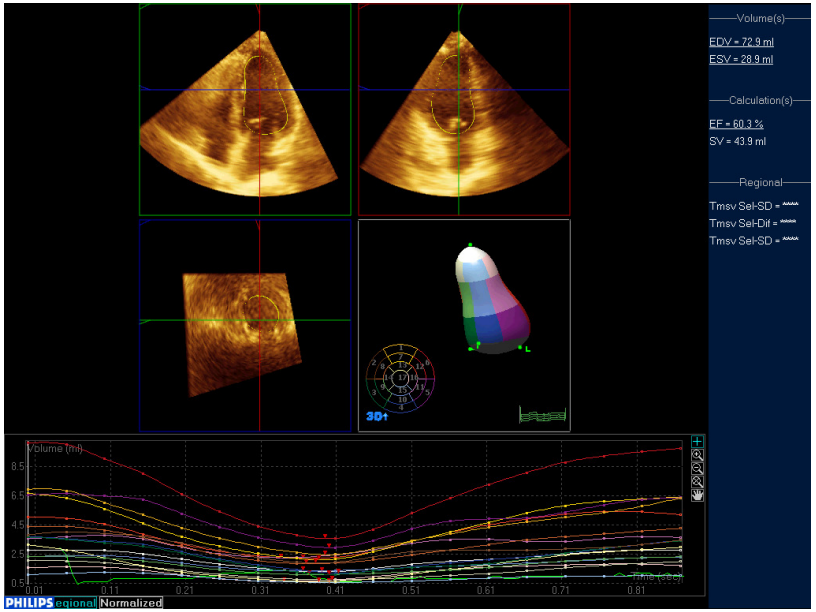
JACC 2013

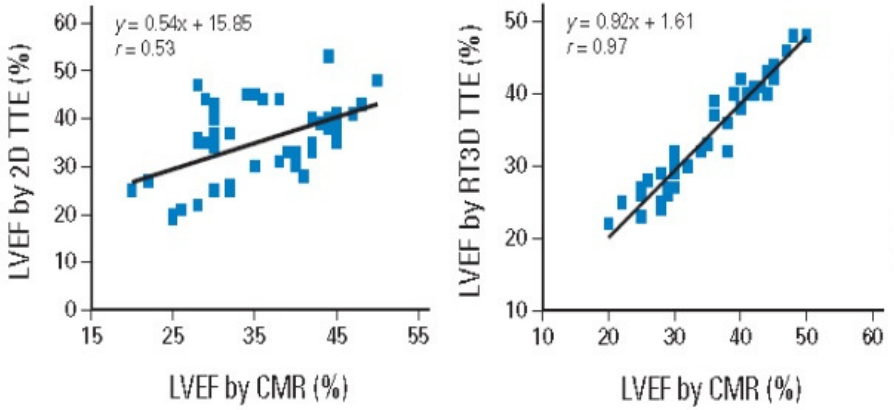


EF SEM 95% CI	0.049 (0.046–0.054)	0.058 (0.053–0.065)*	0.059 (0.054–0.065)	0.065 (0.058–0.072)	0.028 (0.025–0.031)	0.051 (0.046–0.057)*

- Min change in EF not attributable to measurement variability
  - 2D EF: 10%
  - 3D EF: 6%
- Definition of CTRCD
  - EF reduction from baseline >10% to a value <53%

EF Determination: 3D Echo





Walker et al, JCO 2010

- Advantages:
  - More accurate and reproducible than 2D
  - No geometric assumptions
  - Minimize foreshortening
  - Semi-automated border detection
- Disadvantages:
  - Dependent on image quality
  - Learning curve; experience with image acquisition and analysis
  - Availability with equipment and expertise*

Consensus Statement
EF at baseline and during therapy

Prognostic value of LVEF

LVEF Monitoring: Is it useful?

Table 2. Risk Factors for Trastuzumab-/Chemotherapy-Induced Cardiac Events in NSABP B-31

Risk Factor	No. of Patients	CHF		*P*	Hazard Ratio	95% CI
		No.	%			
Baseline LVEF						
≥ 65%	423	9	2.1	Reference		
55%-64%	451	19	4.2	.092	1.98	0.89 to 4.37
50%-54%	70	9	12.9	< .001	6.72	2.67 to 16.92
Post-AC LVEF						
≥ 65%	351	4	1.1	Reference		
55%-64%	473	19	4.0	.020	3.58	1.22 to 10.52
50%-54%	111	14	12.6	< .001	11.84	3.90 to 35.99

Romond JCO 2012

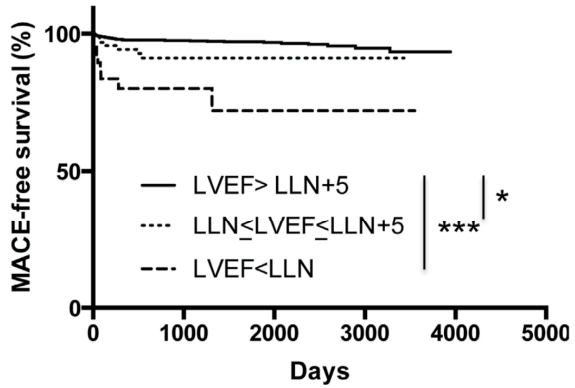


Figure 1. Survival estimates of cardiac event-free survival function according to the baseline LVEF. *p <0.01, ***p <0.0001.

Scherrer-Crobsie AJC 2015

III. Detection of Subclinical LV Dysfunction

- Imaging
  - Global longitudinal strain (GLS) with 2D echo
- Serum cardiac biomarkers
  - Troponin

STATE-OF-THE-ART PAPERS

Use of Myocardial Strain Imaging by Echocardiography for the Early Detection of Cardiotoxicity in Patients During and After Cancer Chemotherapy

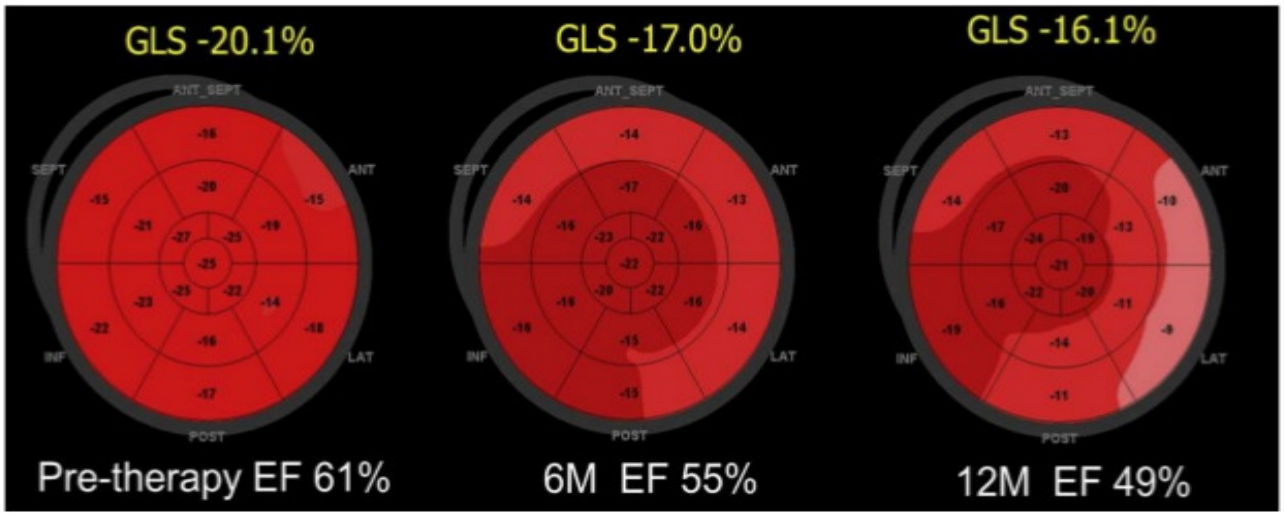
A Systematic Review

Paaladinesh Thavendiranathan, MD,*† Frédéric Poulin, MD,* Ki-Dong Lim, MD,*
Juan Carlos Plana, MD,‡ Anna Woo, MD,* Thomas H. Marwick, MD§

Toronto, Ontario, Canada; Cleveland, Ohio; and Hobart, Australia

JACC 2013

Early reduction in GLS predicts subsequent cardiotoxicity

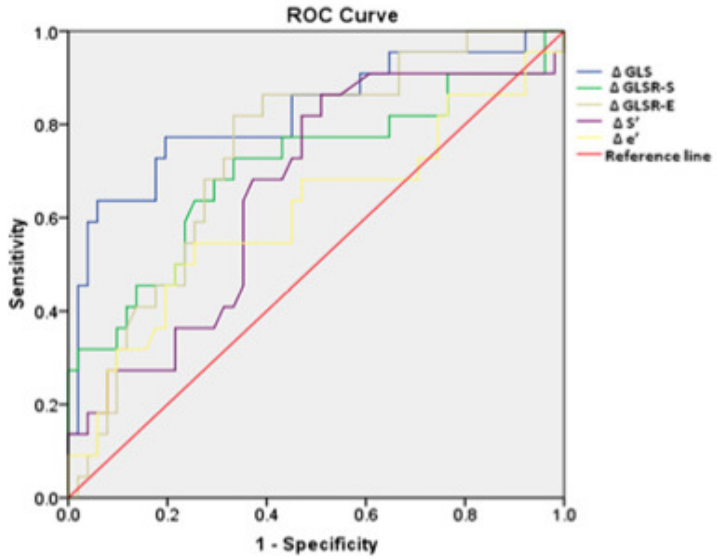


Consensus Statement:

- Decrease GLS >15%, subclinical LV dysfunction likely
- Decrease <8%, no evidence of subclinical LV dysfunction

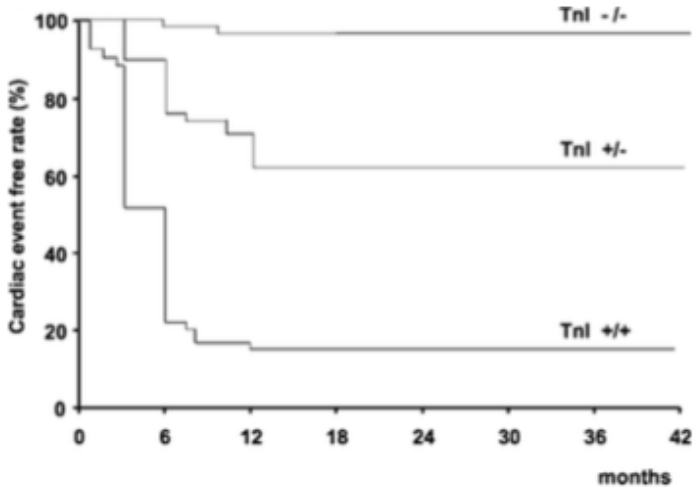
81 BC patients w/ trastuzumab +/- AC

Negichi K, Marwick T JASE 2013



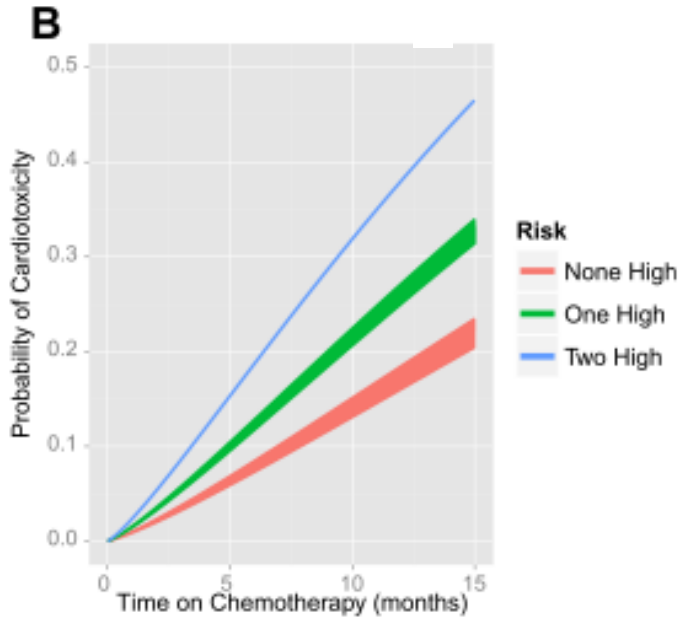
- Decrease of 11% predictive
  95% CI (8.3% - 14.6%)

Prognostic value of biomarkers: troponin



703 pts receiving high dose chemotherapy

Cardinale D, Circ 2002



78 BC pts receiving AC + Trastuzuamb

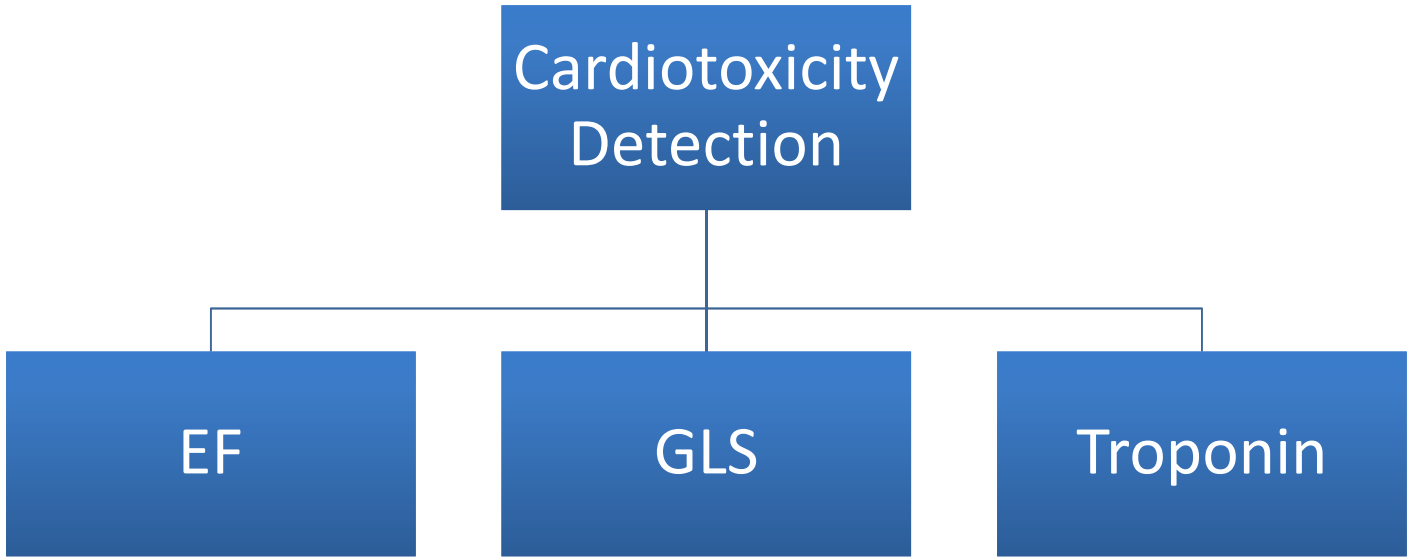
Ky B, J Am Coll Cardiol 2014

IV Other Imaging Modalities

- MUGA
- Cardiac MRI

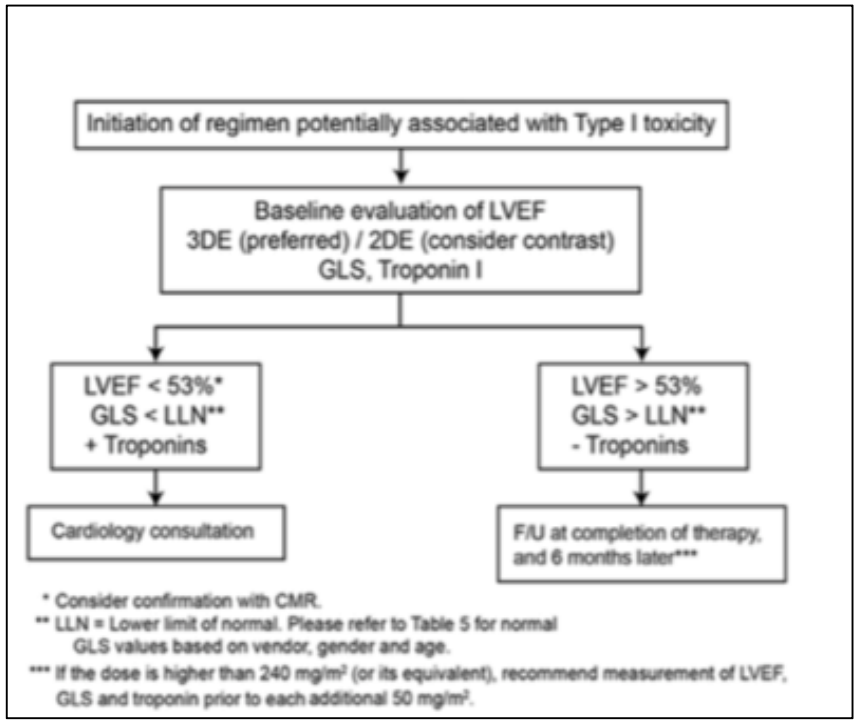
Consensus Statement:
Important to keep imaging modality consistent for baseline and follow-up studies.

V. Integrated Approach

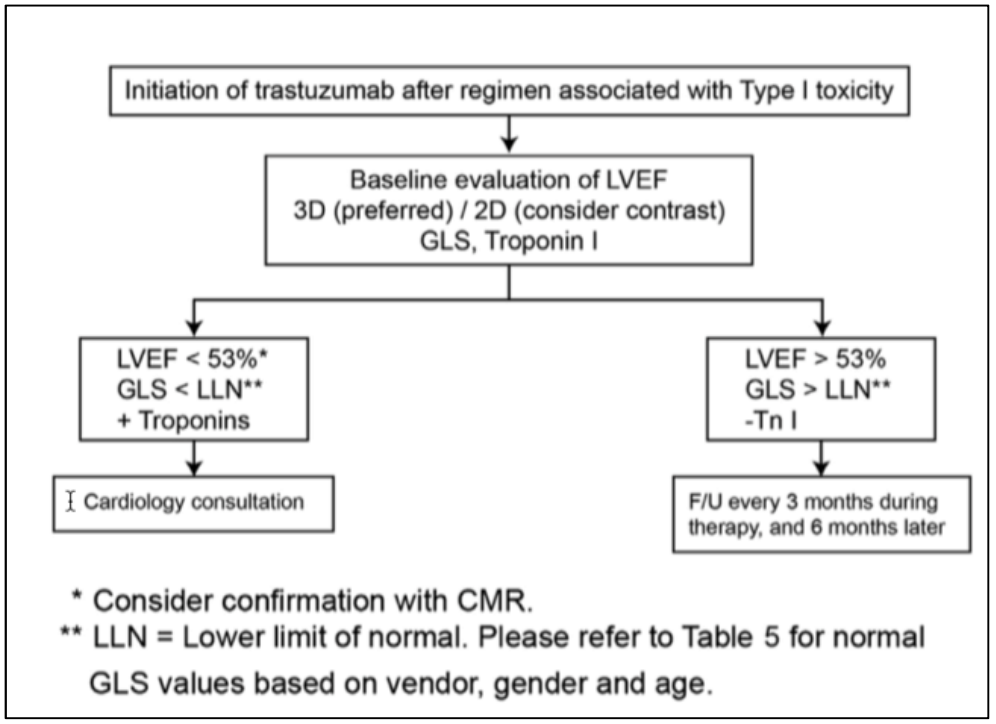


Baseline Assessment and Monitoring

Type I Agents



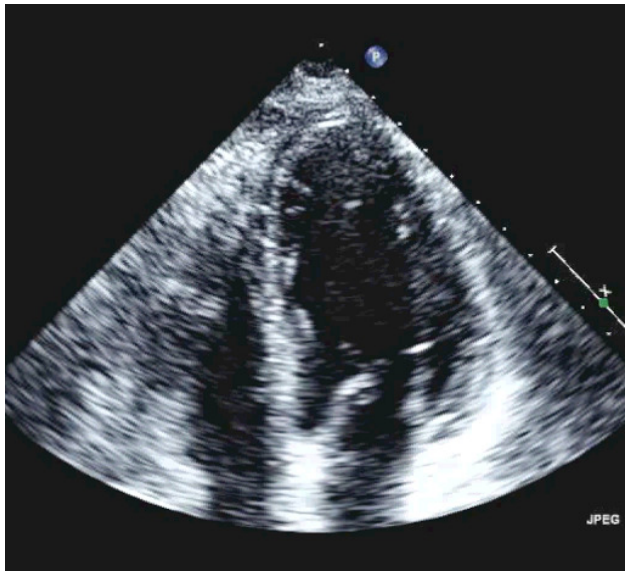
Type II agents



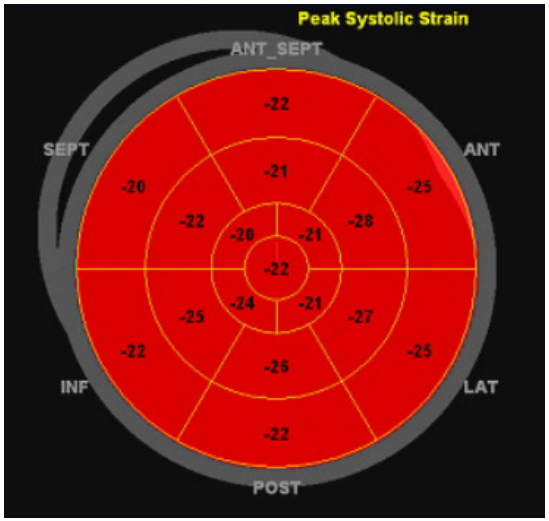
Case

- 57 year old woman with HTN, DM and hyperlipidemia
- Breast cancer with high grade invasive ductal CA, ER/PR (-) HER2 (+)
- Recommended treatment:
  - Mastectomy
  - Adriamycin, Cytoxan, Taxol
  - Trastuzumab (1 year treatment)
  - Radiotherapy

Case Study

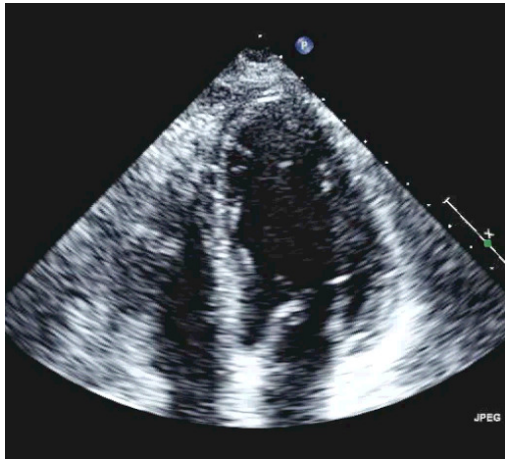


Baseline EF 63%



Baseline GLS -22.6%

Case Study



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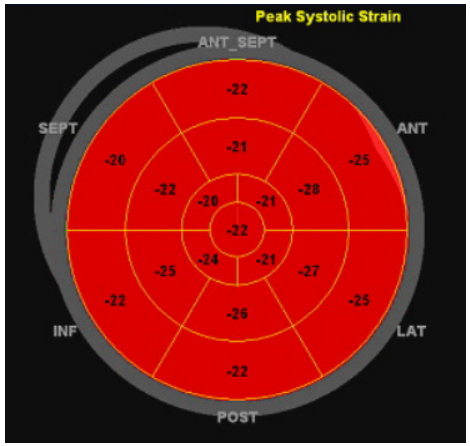

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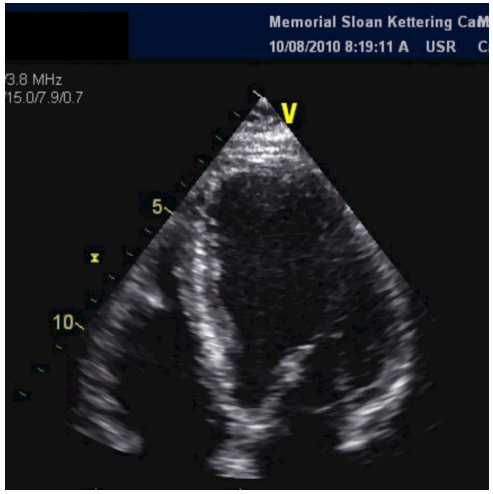
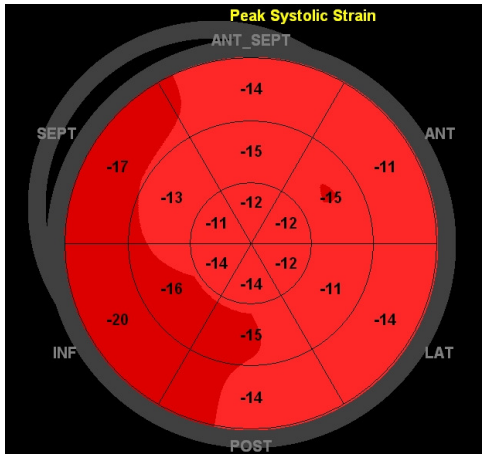
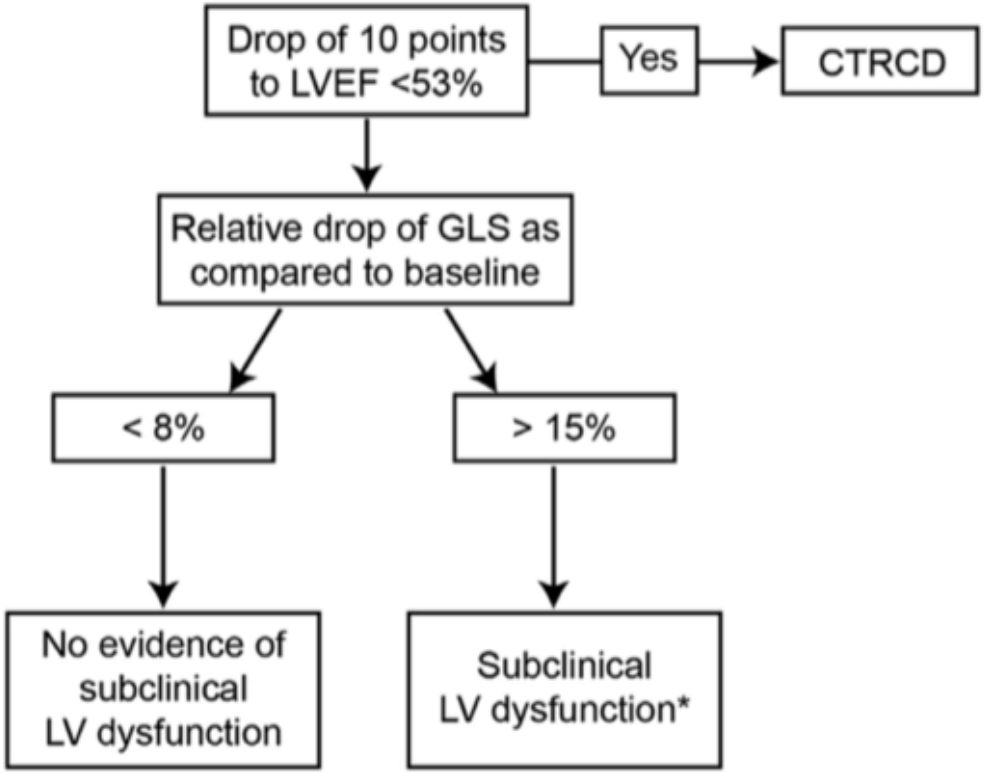


Post AC, pre-trastuzumab
EF 54%



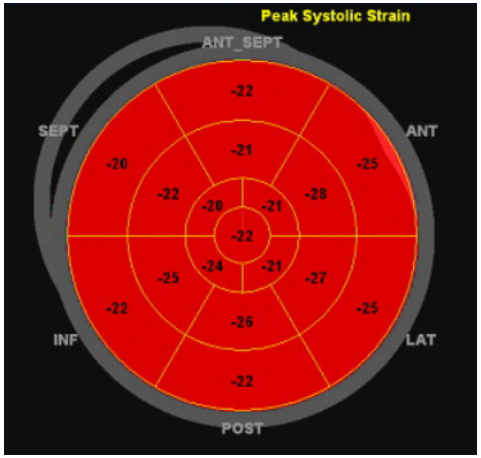
Post AC, pre-trastuzumab
GLS -17%

What to do?
Algorithm for Adjudicating CTRCD

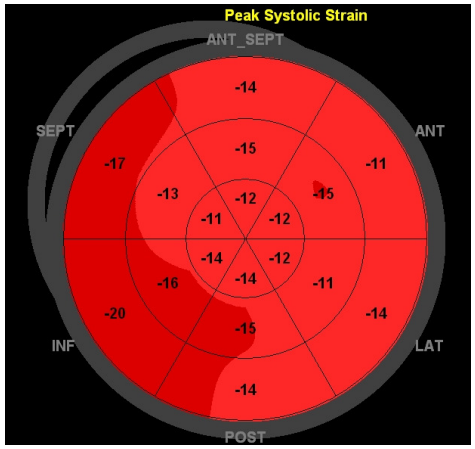


Baseline 64%
3 mos EF 54%
= EF drop 9%

3 Month f/u



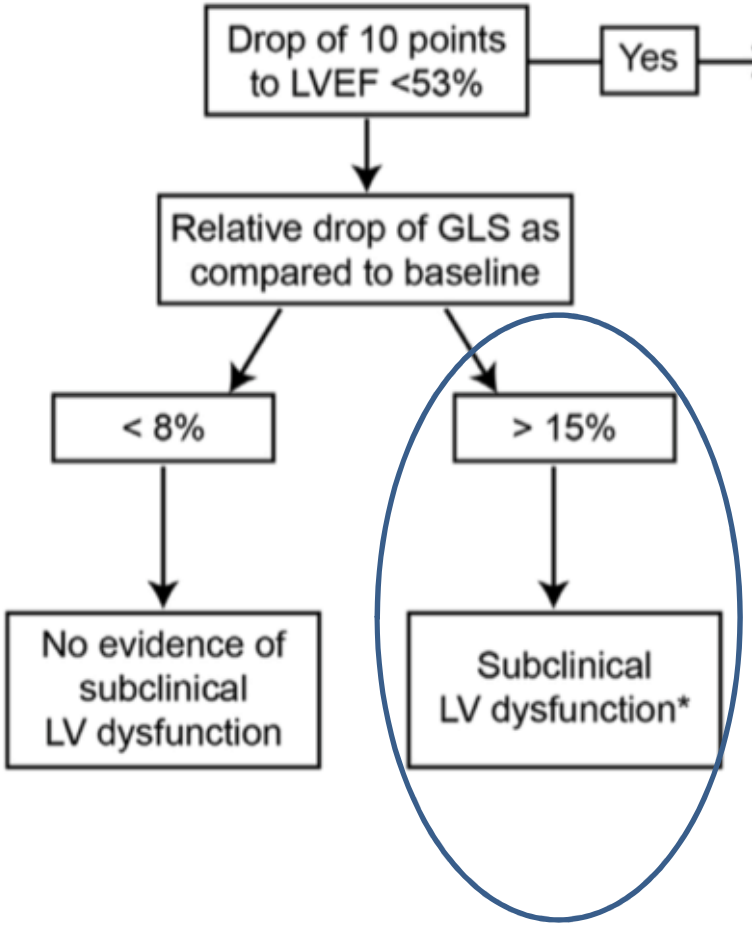
GLS -22.6%
Baseline



GLS = -17.0%
3 months

Δ GLS = 22.6-17.0/22.6 =25%

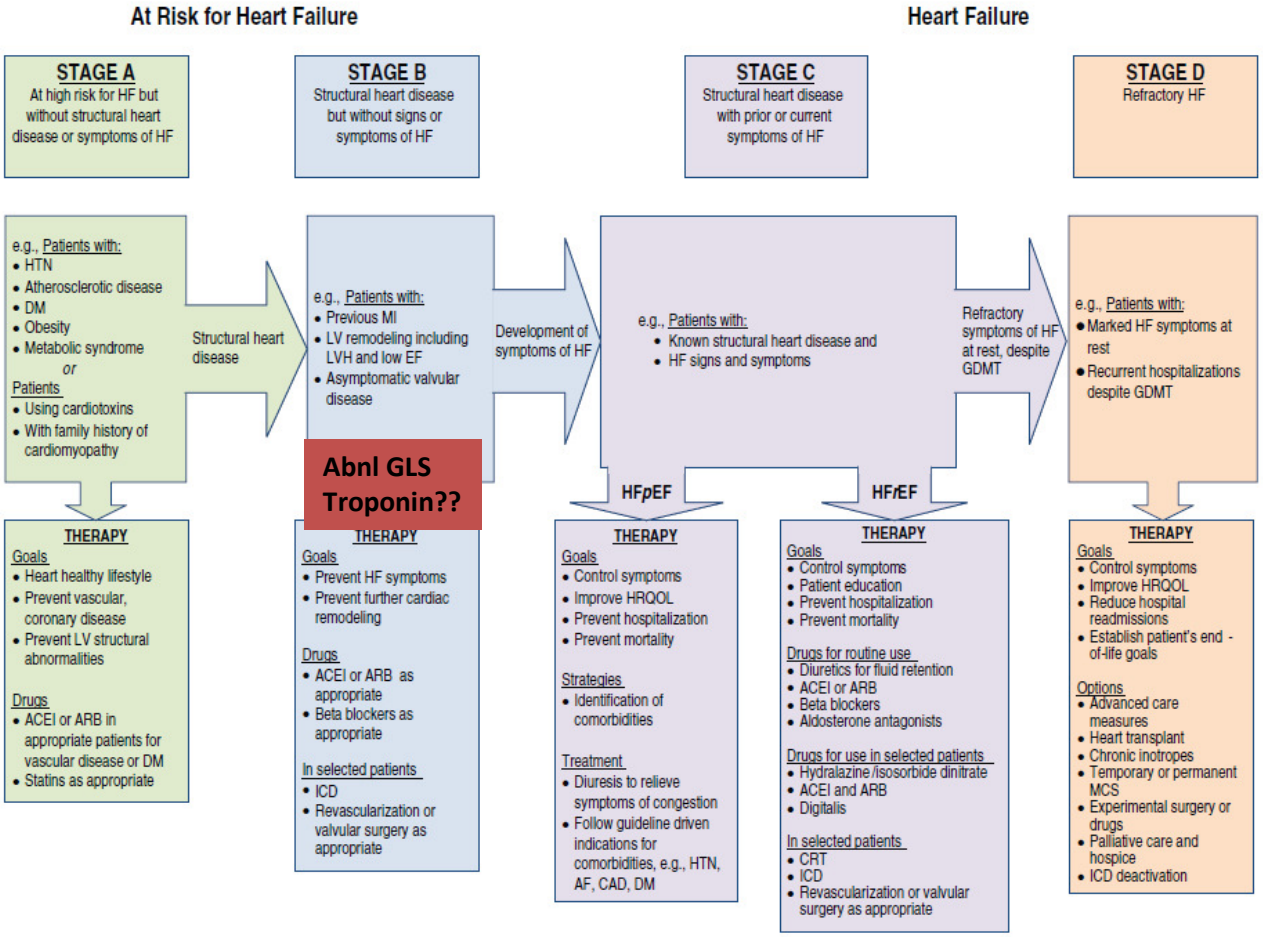
What to do?
Algorithm for Adjudicating CTRCD



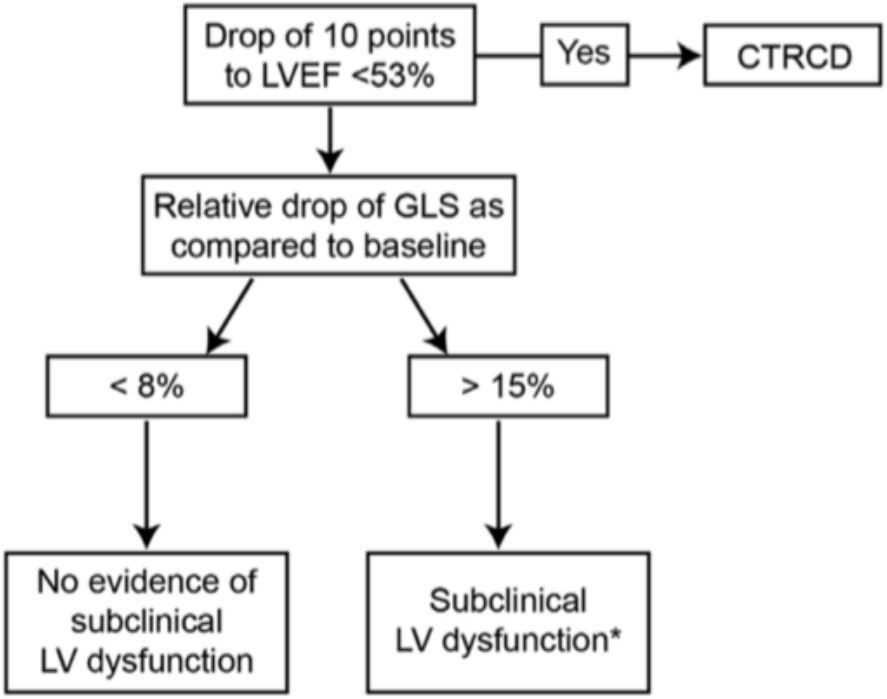
Baseline 64%
3 mos EF 54%
= EF drop 9%

Δ GLS = 22.6-17.0/22.6
= 25%

Management of Heart Failure
ACCF/AHA Guideline



What to do?
Adjudication of CTRCD



Consensus Statement:

* The data supporting the initiation of cardioprotection for the treatment of subclinical LV dysfunction is limited.

Take Home Messages

- Two categories of CTRCD: Type 1 exemplified by doxorubicin and Type 2 exemplified by trastuzumab.
- Cardiotoxicity or CTRCD is defined as a drop in EF >10% from baseline to a value <53%.
- LVEF measurement at baseline, during and after therapy:
  - 3D echo preferred or 2D Biplane MOD +/- contrast
  - Keep imaging modality consistent in follow-up
- Strategy of early detection of cardiotoxicity with GLS and/or and troponin
- Cardiology consultation recommended for abnormal echo or troponin
- Cooperation between cardiologists and oncologists is absolutely essential.

Thank You

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