Echocardiography in Cardio-Oncology: Strain, 3D Imaging & Disatolgy

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No Disclosures
Session Objectives

• Demonstrate the role of echocardiography in the diagnosis and management of cancer patients with cardiovascular disease
• Demonstrate advanced imaging techniques in identifying cancer patients at risk for developing cardiovascular disease
  – 2DE Left Ventricular (LV) function
  – 3DE LV function
  – Diastolic Function
  – Myocardial Strain
• Learn and practice strain acquisition
Acquisition of the left ventricular function across echocardiographic modalities
GUIDELINES AND STANDARDS

Recommendations for Cardiac Chamber Quantification by Echocardiography in Adults: An Update of Echocardiography of CHF

Robert M. Lang, MD, FASE, F
Jonathan Afifalo, MD, M
Frank A. Flachskauf, M
Tatiana Kuznetsova, MD, PH
Michael H. Picard, MD, FASE, Ernst
FSE, Wendy Tsang, MD, and Jens-U
and Toronto, Ontario, Canada; Balti
Washington, District of C

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

Juan Carlos Plana, MD,
Michael S. Ewer, MD,
Javier Ganame, MD, F,
Luigi P. Badano, MD,
Joseph Carver, MD, Manuel
Scott D. Flamm, MD
Jennifer E. Lu, M
Liza Y. Sanchez, R
and Patrizio Lancellotti, MD

2016 ESC Position Paper on cancer treatments and cardiovascular toxicity developed under the auspices of the ESC Committee for Practice Guidelines

The Task Force for cancer treatments and cardiovascular toxicity of the European Society of Cardiology (ESC)

Authors/Task Force Members: Jose Luis Zamorano* (Chairperson) (Spain), Patrizio Lancellotti* (Co-Chairperson) (Belgium), Daniel Rodriguez Muñoz (Spain), Victor Aboyans (France), Riccardo Astegiano (Italy), Maurizio Galderisi (Italy), Gilbert Habib (France), Daniel J. Lenihan1 (USA), Gregory Y. H. Lip (UK), Alexander R. Lyon (UK), Teresa Lopez Fernandez (Spain), Dania Mohty (France), Massimo F. Piepoli (Italy), Juan Tamargo (Spain), Adam Torbicki (Poland), and Thomas M. Suter (Switzerland)
2D Echocardiography

2D LVEF

Is the most studied and verified echo parameter for detection of LV dysfunction

LVEF measurement techniques

- Linear 2D
- M-mode
- Fractional Shortening
- Modified biplane Simpson’s
How do we define LV dysfunction in the cancer population?

| CREC (1988) | • Global decrease in LVEF or more severe in the septum  
|             | • Symptoms of HF  
|             | • Signs of HF (S3 gallop, tachycardia, or both)  
|             | • **Decline in LVEF of at least 5% to less than 55% with** signs or symptoms of HF  
|             | • **Decline in LVEF of at least 10% to less than 55% without** signs or symptoms of HF |

| HERA (2009) | • **Decline in baseline LVEF ≥10% and to less than 50%**  
|             | • Symptomatic CHF: LVEF decline, with symptoms defined by cardiologist and/or NYHA III-IV functional class  
|             | • Confirmed asymptomatic: no change in decline in LVEF at 3 weeks with NYHA I-II functional class |

| BCIRG (2013) | • **Decline in baseline LVEF >10%** |

| ASE/ECAI (2014) | • **Decrease in LVEF >10% to a value of <53%**  
|                | • GLS >15% change from baseline suggests subclinical disease |

| ESC (2016) | • **Decrease LVEF: >10 percentage points decrease to a value below the lower limit of normal**  
|           | • GLS: >15% relative percentage reduction from baseline may suggest risk of cardiotoxicity |

Table adapted from Patel, et al. 2016

**CREC** Cardiac Review and Evaluation Committee  
**ASE** American Society of Echocardiography  
**EACI** European Association of Cardiovascular Imaging  
**HERA** HERceptin Adjuvant study  

Plana JC. J Am Soc Echocardiogr. 2014;  
Zamorano et al, EHJ 2016
Stage B is the key...?
Points to consider:
• Accurate assessment is of the utmost important
• Variability of echo is approximately 9-10%
  – Image quality, loading conditions, geometric assumptions and wall motion abnormalities
  – Limits evaluation of subclinical disease

Questions:
• How does 2D compare to other modalities of measuring LVEF?
• Can we predict LV dysfunction if we identify subclinical disease?
3DE is comparable to Contrast 2D LV volume and function

3DE is superior to 2D methods for LV function in patients with prior infarct
3D Echocardiography

3D Echo has less intra and inter-observer variability

Dorosz, J Am Coll Cardiol. 2012
3D Echocardiography

3D Echo shows less variability over time when compared to 2D methods.
Points to consider:

• Availability

• More studies are needed
Diastolic Dysfunction

85 patients with breast cancer undergoing Anthracycline +/- trastuzumab therapy

Diastolic Dysfunction developed in >50% of study patients

Significant decrease in tissue Doppler (S’ at the septal and lateral mitral annuli)
Diastolic Dysfunction

- 170 with breast cancer who underwent radiation therapy +/- chemotherapy
- RR of HFpEF increased with radiation exposure
- DD often precedes systolic dysfunction in patients receiving cancer therapy

22% of survivors in this cohort had diastolic dysfunction at 10 year follow up.
Points to consider:

• Angle dependence
• Affected by LV loading conditions
• Decreased reproducibility
Pre-therapy hematologic malignancy:

- GLS <-17.5% at baseline associated with cardiovascular events (HF or death)
- Abnormal GLS at baseline was also associated with later development of cardiotoxicity

### Table

<table>
<thead>
<tr>
<th>Variable</th>
<th>HR</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>1.03</td>
<td>1.006-1.056</td>
<td>.013</td>
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<tr>
<td>Gender (female)</td>
<td>1.47</td>
<td>0.70-3.10</td>
<td>.300</td>
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<tr>
<td>Cancer type (leukemia)</td>
<td>1.87</td>
<td>1.26-2.75</td>
<td>.002</td>
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<tr>
<td>Hypertension</td>
<td>2.22</td>
<td>1.02-4.80</td>
<td>.040</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>1.80</td>
<td>0.60-5.20</td>
<td>.279</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>7.06</td>
<td>3.36-14.85</td>
<td>.000</td>
</tr>
<tr>
<td>Smoking</td>
<td>0.87</td>
<td>0.12-6.44</td>
<td>.890</td>
</tr>
<tr>
<td>Prior coronary artery disease</td>
<td>3.61</td>
<td>1.37-9.51</td>
<td>.009</td>
</tr>
<tr>
<td>Prior cardiomyopathy</td>
<td>5.21</td>
<td>1.8-15.06</td>
<td>.002</td>
</tr>
<tr>
<td>Dose of anthracyclines</td>
<td>0.99</td>
<td>0.99-1.002</td>
<td>.230</td>
</tr>
<tr>
<td>ACE inhibitors/ARBs</td>
<td>5.42</td>
<td>1.88-15.66</td>
<td>.002</td>
</tr>
<tr>
<td>Statins</td>
<td>5.45</td>
<td>2.39-12.46</td>
<td>.000</td>
</tr>
<tr>
<td>β-blockers</td>
<td>2.80</td>
<td>1.19-6.63</td>
<td>.018</td>
</tr>
<tr>
<td>Baseline LVEF (%)</td>
<td>0.93</td>
<td>0.89-0.98</td>
<td>.005</td>
</tr>
<tr>
<td>LV EDV</td>
<td>0.99</td>
<td>0.98-1.01</td>
<td>.580</td>
</tr>
<tr>
<td>LV EDVI</td>
<td>1.00</td>
<td>0.97-1.03</td>
<td>.910</td>
</tr>
<tr>
<td>LV ESV</td>
<td>1.01</td>
<td>0.98-1.04</td>
<td>.370</td>
</tr>
<tr>
<td>LV ESVI</td>
<td>1.05</td>
<td>0.99-1.11</td>
<td>.058</td>
</tr>
<tr>
<td>Average segmental longitudinal strain</td>
<td>1.85</td>
<td>1.65-2.08</td>
<td>.000</td>
</tr>
</tbody>
</table>

Pre-therapy breast cancer:

- Lower Baseline Circumferential strain associated with development of cardiotoxicity
- 1% baseline difference associated with 31% increased odds

Narayan HK, JACC Cardiovascular Imaging 2016
Pre-therapy AL Amyloidosis:

- GLS and mitral E/A ratio ratio were strong predictors of survival post Autologous HCT

- >-17% GLS associated with increased survival at 5 years (95% vs 47%)
81 patients with trastuzumab +/- Anthracyclines for breast cancer

Results: GLS can be an earlier predictor of subsequent reductions of EF, preceding the change in LVEF by 3-6 months.

43 patients with Anthracyclines & Trastuzumab for breast cancer

Results: GLS predicts the development of cardiotoxicity

42 patients with Anthracyclines + Trastuzumab for breast cancer

Results: TVI and strain imaging were able to detect pre-clinical changes in LV systolic function, before conventional changes in LVEF.
<table>
<thead>
<tr>
<th>Studies/First Author (Ref. #)</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fallah-Rad et al. (44)*</td>
<td>79%</td>
<td>82%</td>
<td>60%</td>
<td>92%</td>
</tr>
<tr>
<td>2% absolute (10.1% relative) decrease in LS</td>
<td>86%</td>
<td>81%</td>
<td>60%</td>
<td>95%</td>
</tr>
<tr>
<td>0.8% decrease in RS</td>
<td>86%</td>
<td>81%</td>
<td>60%</td>
<td>95%</td>
</tr>
<tr>
<td>Sawaya et al. (41)</td>
<td>10% decrease in GLS</td>
<td>78%</td>
<td>79%</td>
<td>50%</td>
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<tr>
<td>Elevated hsTnl</td>
<td>55%</td>
<td>97%</td>
<td>83%</td>
<td>89%</td>
</tr>
<tr>
<td>10% decrease in GLS and elevated hsTnl</td>
<td>89%</td>
<td>65%</td>
<td>40%</td>
<td>97%</td>
</tr>
<tr>
<td>10% decrease in GLS or elevated hsTnl</td>
<td>89%</td>
<td>65%</td>
<td>40%</td>
<td>97%</td>
</tr>
<tr>
<td>Sawaya et al. (40)</td>
<td>GLS &lt;19%</td>
<td>74%</td>
<td>73%</td>
<td>53%</td>
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<tr>
<td>hsTnl &gt;30 pg/ml</td>
<td>48%</td>
<td>73%</td>
<td>44%</td>
<td>77%</td>
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<tr>
<td>LS &lt;19% and usTnl &gt;30 pg/ml</td>
<td>35%</td>
<td>93%</td>
<td>67%</td>
<td>77%</td>
</tr>
<tr>
<td>LS &lt;19% or usTnl &gt;30 pg/ml</td>
<td>87%</td>
<td>53%</td>
<td>43%</td>
<td>91%</td>
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<tr>
<td>Negishi et al. (42)†</td>
<td>11% reduction in global GLS</td>
<td>65%</td>
<td>95%</td>
<td></td>
</tr>
<tr>
<td>3.6% reduction in global GLSR early diastole</td>
<td>82%</td>
<td>67%</td>
<td></td>
<td></td>
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<tr>
<td>6.4% reduction in global GLSR</td>
<td>73%</td>
<td>67%</td>
<td></td>
<td></td>
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<tr>
<td>Absolute GLS at 6 months &lt;–20.5%</td>
<td>96%</td>
<td>66%</td>
<td></td>
<td></td>
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<tr>
<td>Mornos et al. (39)ji</td>
<td>71% × 6 reduction in GLS × LV twist</td>
<td>90%</td>
<td>82%</td>
<td></td>
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<tr>
<td>2.77% absolute (~13% relative) reduction in GLS</td>
<td>79%</td>
<td>73%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.75° absolute reduction in apical rotation</td>
<td>70%</td>
<td>78%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baratta et al. (37)ji</td>
<td>≥15% decrease in GLS</td>
<td>86%</td>
<td>86%</td>
<td></td>
</tr>
<tr>
<td>≥10% decrease in GRS</td>
<td>86%</td>
<td>69%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥15% decrease in GLS AND ≥10% decrease in GRS</td>
<td>71%</td>
<td>97%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

GLS range that predicted cardiotoxicity: Decrease of 10% to 19% from baseline
High NPV
A CHANGE of >15% from baseline represents dysfunction.
Abnormal Strain in Cancer Survivors

Central Illustration: Prevalence of Cardiac Dysfunction and Reduced Exercise Capacity in Adult, 10-Year Survivors of Childhood Cancer.
Points to consider:

- Vendor variability
- GLS can predict subclinical dysfunction, but can we prevent overt LV dysfunction?

Stay tuned for emerging studies that will clarify this question...
Role of Echo in Cancer Therapy

Proposed algorithm using ejection fraction (EF) and global longitudinal strain (GLS) for the evaluation and management of cancer therapy-related cardiac dysfunction. *Frequency of echocardiographic evaluation during cancer treatment based primarily on oncology clinical trials. **Marker of increased risk. Consider contributing pathology (hypertension, coronary artery disease, infiltrative disease). Optimize existing cardiovascular risk factors with closer surveillance and consider cardioprotective medications. ***As per 2013 American College of Cardiology/American Heart Association guideline for the management of stage B heart failure. 2DE = 2-dimensional echocardiography; 3DE = 3-dimensional echocardiography; CV = cardiovascular; LLN = lower limit of normal; LV = left ventricular; LVEF = left ventricular ejection fraction.

Summary

2D Echo:
• most verified parameter in detection of LV dysfunction in cancer patients

3D Echo:
• Accurate & reproducible over time
• Should be performed if available!

Diastolic Dysfunction:
• May detect subclinical disease
• Is susceptible to loading conditions

Myocardial Strain:
• GLS and CS predict cardiac events/cardiototoxicity prior to therapy
• GLS detects subclinical disease during therapy
• GLS may identify subclinical disease post therapy
Techniques in Imaging Workshop

Drs. Aarti Patel, Eric Harrison, Jennifer Liu, Juan Carlos Plana & Dinesh Thavendiranathan
Select images

Select the LV AP3, LV AP2, and LV AP4 chamber views and launch the aCMQ app.

Note: It is recommended to have less than a 10% difference in heart rate between the 2D loops when calculating Peak Systolic and End Systolic GLS.
Select loop & confirm view

Select the loop associated with the LV AP3 and confirm by selecting LV AP3. (If utilizing a SmartExam, this step is automated.)

If Auto ROI is enabled (checked), then points will be placed automatically.

Selecting draw (recommended method) allows users to place the basal and apical points resulting in a Manual ROI.

Note: Always analyze the LV AP3 view first.
Reference point placement

Accurate placement of the reference points is important to obtain accurate quantification.

Place the reference points on the blood pool / tissue border at the mitral valve leaflet insertion, the LVOT and the apex.

Place the reference points on the blood pool / tissue border at the left and right mitral valve leaflet insertion, and the apex.

Place the reference points on the blood pool / tissue border at the left and right mitral valve leaflet insertion, and the apex.
Edit ED and Edit ES

Edit ED (End Diastole) and Edit ES (End Systole) allow the user to confirm placement of the ROI over the underlying tissue matching the inside edge of the ROI to the blood tissue interface.

Click Edit ED and confirm the placement of the annular and apical points. Edit if needed. Click Edit ES and confirm the placement of the annular and apical points. Edit if needed.

Click Accept to confirm results.

Complete aCMQ by performing the steps above on the LV AP4 and LV AP2.
Review results and display

Review the results and display for all the apical views in the 4-up display as seen using the AP3.
Optimizing the Image Position

1. Center the intersection of the red and green plane indicators on the blue plane MPR view.
2. Rotate the green plane indicator in the blue plane MPR view until the full apex is visible.
3. For correct segment orientation, orient the yellow arrow in the blue plane so it points to the middle of the LV septum (between the RV and LV septum).
4. In the green plane MPR view, center the red plane indicator through the true apex.
5. In the red plane MPR view, center the green plane indicator through the true apex.
Adding a 2Ch/4Ch Template Trace

1. Click on the left of the mitral valve.
2. Click on the right of the mitral valve.
3. Click the apex.
4. If measuring LV mass, click straight up from the apex on the epicardial wall.
Measuring Distance

1. Click Distance.
2. Click the initial anchor position.
3. Right-click the terminal anchor position.

The distance measurement value appears in the results.
Performing a Sequence Analysis

1. Calculate the ejection fraction.
2. Click **Sequence Analysis**.
   The quality index for the global sequence analysis appears, and the bull’s eye is colored to reflect the quality indexes for each segment.
3. Click the 3D view and drag to rotate it.
4. Select **Segments**.
5. Select one or more segments from the bull’s eye or the 3D view and note the correspondence between the two.
   If the waveforms display is enabled, the regional or normalized %EDV curves corresponding to the selected segments in the 3D view are highlighted.