Ο ρόλος των κλασικών και νεότερων ηχωκαρδιογραφικών τεχνικών

How and when new echo techniques help in cardio-oncology patients?

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New echo techniques in cardio-oncology

1. What are we missing with current strategies?
2. What’s new in echo?
3. Tips and tricks for daily practice
Cardiovascular complications in cancer

Role of echo in cardio-oncology

<table>
<thead>
<tr>
<th>Baseline evaluation</th>
<th>During treatment</th>
<th>End-treatment LT survivors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk stratification</td>
<td>Early detection of injury</td>
<td>Prediction of recovery</td>
</tr>
</tbody>
</table>

Role of echo in cardio-oncology

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

EurHJ- Cardiovasc Imaging (2017) 0, 1–14

EACVI appropriateness criteria for the use of transthoracic echocardiography in adults: a report of literature and current practice review

EurHJ- Cardiovasc Imaging (2017) 0, 1–14
No standardized monitoring protocols

<table>
<thead>
<tr>
<th>Cancer Therapeutics</th>
<th>Stage A</th>
<th>Stage B</th>
<th>Stage C</th>
<th>Stage D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anthracyclines</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>HER-2 Therapy</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>VEGF Inhibitors</td>
<td>✓*</td>
<td>✓*</td>
<td>✓</td>
<td>0</td>
</tr>
<tr>
<td>Proteasome Inhibitors</td>
<td>0</td>
<td>0</td>
<td>✓</td>
<td>0</td>
</tr>
<tr>
<td>Immune Checkpoint Inhibitors</td>
<td>0</td>
<td>0</td>
<td>✓</td>
<td>0</td>
</tr>
</tbody>
</table>

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

How and when new echo techniques help in cardio-oncology patients?

tlfernandez8@gmail.com
### CTRCD definitions

<table>
<thead>
<tr>
<th>Condition</th>
<th>Definition</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>↓EF &gt;0.10</td>
<td>From baseline to &lt;0.50</td>
<td>ESC 2016</td>
</tr>
<tr>
<td>↓EF &gt;0.10</td>
<td>From baseline to &lt;0.53</td>
<td>ASE-EACVI 2014</td>
</tr>
</tbody>
</table>

2D-LVEF needs help!  
(variability 8-11%)
What’s new in echo?

We need more reproducible and sensitive parameters
We need precise LVEF measurements

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

3D Dynamic Automatic Quantification

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

Multi-beat analysis (5 beats)
3DEF Automated Quantification

Reproducibility

Manual 3DE vs Automatic 3DE

cMRI vs Automatic 3DE


We need more sensitive parameters

Early HF treatment (EF-based)

We need more sensitive parameters

Eur J Heart Failure 2017; 19: 307–313
2D Speckle tracking: GLS quantification

1. Feasibility >90%
2. Reproducibility: GLS >2DEF (inter-obs variability <4%)
3. Differences between vendors lower than 2D-EF variability
4. No universal normal values: relative changes during F/U

Tips and tricks for daily practice
Local clinical protocols adapted to local resources
Assessment of baseline risk of CV complications

- No CVRF/CVD
  - 1st onco event
- No CVRF/CVD
  - Previous cancer
- CVRF +/- CVD
  - 1st onco event
- CVRF +/- CVD
  - Previous cancer

- Age
- Genetics
- Comorb.
- Treatment
- Prognosis
Assessment of baseline risk of CV complications

Echo: >65yo; >2CVFR; previous CVD/cancer; abnormal ECG/biomarkers
Assessment of baseline risk of CV complications

No CVRF/CVD 1st onco event <65yo

Baseline echo & abnormal findings

Routine echo rarely identified significant cardiac damage to change treatment decisions

Cancer 2012;118:1919-24

EuroEcho 2015
Assessment of baseline risk of CV complications

EF risk stratification

- LLN 55%
- Reference ≥ 65%
- LVEF 55-64% HR 4.0
- LVEF 50-54% HR 12.6

How and when new echo techniques help in cardio-oncology patients?

J Clin Oncol 2012; 30:3792-3799
Assessment of baseline risk of CV complications

GLS risk stratification

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

GLS ≥-17.5 %

\[ \uparrow \times 6 \text{ RR} \]
Death/ HF

Early identification of injury during therapy

1. Accurate adjudication of SE
2. Best method for EF: 3DEF
3. Identify potential sources of error related with load conditions

- Optimize CVRF and CVDs
- Follow-up
  - Sign and symptoms
  - Biomarkers (early LVD)
  - ECG
  - Echo: CTRCD Diagnosis
    Identify early LVD
- Reduce Rx interruptions

Early identification of injury during therapy

No CVRF/CVD
1st onco event <65yo

TnI evaluation at each cycle

TnI POS
Cardiology consultation

TnI NEG
ECHO 6 months after completion of therapy

Early identification of injury during therapy

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

<table>
<thead>
<tr>
<th>GLS of 11%</th>
<th>n</th>
<th>Sn</th>
<th>Sp</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>93</td>
<td>65%</td>
<td>94%</td>
<td>91%</td>
</tr>
</tbody>
</table>

J Am Soc Echocardiogr 2013;26:493-8

<table>
<thead>
<tr>
<th>GLS &gt;15.9% or cTnT &gt;0.004ng/ml</th>
<th>n</th>
<th>Sn</th>
<th>Sp</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>75</td>
<td>93%</td>
<td>66%</td>
<td>98%</td>
</tr>
</tbody>
</table>

Eur J Heart Failure 2014; 16: 300–308

<table>
<thead>
<tr>
<th>GLS &gt;10% or ▲hs-TNI</th>
<th>n</th>
<th>Sn</th>
<th>Sp</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>43</td>
<td>65%</td>
<td>97%</td>
<td>97%</td>
</tr>
</tbody>
</table>

Am J Cardiol 2011, 107(9): 1375-80

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Prediction of LVD recovery

<table>
<thead>
<tr>
<th>Echo Parameter</th>
<th>Median (IQR)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Left ventricular structure</strong></td>
<td></td>
</tr>
<tr>
<td>LV end-diastolic volume, ml</td>
<td>117 (104, 132)</td>
</tr>
<tr>
<td>LV end-systolic volume, ml</td>
<td>67 (58, 80)</td>
</tr>
<tr>
<td>LV mass, g</td>
<td>(114, 164)</td>
</tr>
<tr>
<td>Relative wall thickness</td>
<td>(0.31, 0.39)</td>
</tr>
<tr>
<td><strong>Left ventricular diastolic function</strong></td>
<td></td>
</tr>
<tr>
<td>E/e</td>
<td>7.6 (6.1, 6.6)</td>
</tr>
<tr>
<td>Ees, mmHg/mil</td>
<td>1.98 (1.61, 2.39)</td>
</tr>
<tr>
<td><strong>Left ventricular contractility</strong></td>
<td></td>
</tr>
<tr>
<td>Longitudinal strain, %</td>
<td>-12.8 (-15.2, -10.6)</td>
</tr>
<tr>
<td>Circumferential strain, %</td>
<td>-21.2 (-25.4, -17.9)</td>
</tr>
<tr>
<td>Radial strain, %</td>
<td>44.5 (32.2, 52.3)</td>
</tr>
<tr>
<td><strong>Ventricular-arterial coupling</strong></td>
<td></td>
</tr>
<tr>
<td>Ea, mmHg/ml</td>
<td>2.35 (2.02, 2.82)</td>
</tr>
<tr>
<td>Meridional ESS, 10^3 dynes/cm^2</td>
<td>99.5 (85.0, 116.9)</td>
</tr>
<tr>
<td>Circumferential ESS, 10^3 dynes/cm^2</td>
<td>150 (136, 166)</td>
</tr>
<tr>
<td>Ea/Ees_{33}</td>
<td>1.31 (1.09, 1.47)</td>
</tr>
</tbody>
</table>

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.  

Cardio-protection treatment guidance

Drop of 10 points to LVEF <53%

Relative drop of GLS as compared to baseline

< 8%

No evidence of subclinical LV dysfunction

> 15%

Subclinical LV dysfunction

↑cTroponins

Yes

CTRCD

Consult cardiologist
Repeat TTE in 2-3 weeks

HF Treatment

Do not modify anticancer therapy

Stage B HF

Consider early cardio-protective intervention

Cardio-protection treatment guidance

SUCCOUR Trial

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

Inclusion criteria
Cardiotoxic chemo + ≥1 HF-risk factor

HF-risk factors
34% Hypertension
10% DM

Baseline
3DEF 61±4%
GLS 20.3±2.5%

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J Am Coll Cardiol Img 2018;11:1098–105
Early identification of CV injury during therapy

Not only HF!!

Vascular toxicities, valvular HD, pericardium, RT…

High clinical suspicion & CVRF control

How and when new echo techniques help in cardio-oncology patients?
Take home messages: Cardiac imaging in CO

- Stratify CTox risk
- Optimize CV conditions
- Preventive strategies
- Early identification and treatment of CTox
- ↓ treatment interruptions
- ↓CV events
Take home messages: Cardiac imaging in CO

**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)
**Take home messages:** unresolved issues

**CTox definitions:** Risk prediction models & clinical strategies

<table>
<thead>
<tr>
<th>Type</th>
<th>Classification</th>
<th>Definition</th>
<th>Onco management</th>
<th>Cardio management</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Early biochemical</td>
<td>↑ Biomarkers (≥20% if baseline abnormal)</td>
<td>No change</td>
<td>Consider close monitoring or cardioprotective therapy</td>
</tr>
<tr>
<td>2</td>
<td>Early functional</td>
<td>↓ GLS +/- diastolic dysfunction</td>
<td>No change</td>
<td>Start cardioprotection</td>
</tr>
<tr>
<td>3</td>
<td>Early mixed</td>
<td>↑ Biomarkers + ↓GLS/DD</td>
<td>No change</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Symptomatic HFpEF</td>
<td>HFpEF</td>
<td>Review risk/benefit</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Asymptomatic LVD</td>
<td>New EF &lt;50% or ↓ &gt;10% to EF &lt;55%</td>
<td>Review risk/benefit</td>
<td>HF treatment</td>
</tr>
<tr>
<td>6</td>
<td>Symptomatic LVD</td>
<td>New EF &lt;50% or ↓ &gt;10% to EF &lt;55%</td>
<td>Interrupt and review risk/benefit</td>
<td></td>
</tr>
</tbody>
</table>

PareekN….Lyon AR. European Journal of Heart Failure (2018)
Ευχαριστώ